

**A Petition to the
Board of Pharmacy Specialties
Requesting Recognition of
Solid Organ Transplantation Practice
as a Specialty**

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Definition of Solid Organ Transplantation Pharmacist Specialists

Solid organ transplantation (SOT) pharmacist specialists have the specialized training and knowledge needed to manage complex medication regimens unique to the solid organ transplantation population. Additionally, they are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. They care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings.

SOT pharmacist specialists provide evidence-based, patient-centered medication management. They design, implement, monitor, and modify pharmacotherapeutic plans to improve safety and efficacy, which leads to optimal short-term and long-term patient and allograft outcomes. Core responsibilities of SOT pharmacist specialists are to analyze and reevaluate multifaceted clinical and outcomes data to improve care and demonstrate ongoing quality assessment and process improvement as required by regulatory agencies. Finally, SOT pharmacist specialists are integral members of the interprofessional transplant team that facilitate medication adherence and pharmacotherapy education.

**American College of Clinical Pharmacy (ACCP)
American Society of Health-System Pharmacists (ASHP)**

**A Petition to the Board of Pharmacy Specialties (BPS) Requesting Recognition of
Solid Organ Transplantation Pharmacist Specialists**

Executive Summary

Definition of Solid Organ Transplantation Pharmacist Specialists

Solid organ transplantation (SOT) pharmacist specialists have the specialized training and knowledge needed to manage complex medication regimens unique to the solid organ transplantation population. Additionally, they are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. They care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. SOT pharmacist specialists provide evidence-based, patient-centered medication management. They design, implement, monitor, and modify pharmacotherapeutic plans to improve safety and efficacy, which leads to optimal short-term and long-term patient and allograft outcomes. Core responsibilities of SOT pharmacist specialists are to analyze and reevaluate multifaceted clinical and outcomes data to improve care and demonstrate ongoing quality assessment and process improvement as required by regulatory agencies. Finally, SOT pharmacist specialists are integral members of the interprofessional transplant team that facilitate medication adherence and pharmacotherapy education.

—ACCP/ASHP Task Group

Background

By acquiring specialized knowledge and skills and creating a unique practice beyond the scope of pharmacy practice defined by licensure examination, an increasing number of pharmacists have distinguished themselves through the care of patients with solid organ transplants according to the above Definition of Solid Organ Transplantation Pharmacist Specialists. In recognition of these efforts, the American College of Clinical Pharmacy (ACCP) and the American Society of Health-System Pharmacists (ASHP) have partnered to develop a petition to the Board of Pharmacy Specialties (BPS) to recognize solid organ transplantation pharmacy practice as a specialty.

Petition Overview

In 2017, 34,769 SOT procedures were conducted, and there are 114,939 people on the waiting list for an organ in the United States. A new patient is added to the national transplant waiting list every 10 minutes.¹ Commonly, new transplant recipients will be prescribed a median of

eight medications, with some requiring as many as 10-15 chronically. Many of these medications have a narrow therapeutic index, significant drug interactions, a high potential for adverse effects, and are very expensive, resulting in the need for intense monitoring.²

SOT pharmacy practice focuses on the care of SOT patients. SOT pharmacist specialists practice in a variety of settings, including adult and pediatric medical intensive care units (ICU), surgical ICU, inpatient acute care, outpatient ambulatory care clinics, academic settings, pharmaceutical industry, and research institutions. SOT pharmacist specialists possess specialized knowledge and experience in the care of SOT patients. Many have completed formal, post-graduate residency training in SOT practice environments. They possess unique knowledge of the epidemiology and pathophysiology of SOT; the pharmacotherapy of transplant patients; the application of pharmacokinetics, pharmacodynamics, and pharmacogenomics to transplantation; operational and clinical systems designed to assure medication safety; patient/parent/caregiver counseling to optimize medication adherence; and long-term disease prevention and health maintenance in patients receiving life-long immunosuppressants. They also contribute to, and evaluate, biomedical literature pertinent to immunology and transplant pharmacotherapy.

BPS Petition Process

The *BPS Petitioner's Guide for Recognition of a Pharmacy Practice Specialty* outlines seven criteria, each with a list of supporting guidelines, to be addressed in a petition for specialty recognition. The petitioning organizations conducted a comprehensive literature review and examined, in detail, the *BPS Role Delineation Study for Solid Organ Transplantation Pharmacists* to support the development of this petition. We also conducted a web-based survey of solid organ transplantation pharmacists and their employers, the *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification*, to provide additional, timelier data for the petition. The evidence presented in the petition for each of the BPS criteria is briefly summarized below.

Criterion A: Need

This criterion identifies the public health and patient care needs that are currently unmet by pharmacists in generalized practice, pharmacists practicing in other specialty areas, or other health professionals. The petition establishes how solid organ transplantation pharmacist specialists can effectively meet these needs.

SOT pharmacist specialists produce a substantial effect on outcomes for transplant patients in a wide variety of roles, largely through the optimization of medication use, avoidance of adverse drug reactions, and transition of care activities focused on medication reconciliation and

patient education. According to the published literature, transplant patients have substantial unmet needs in the areas of medication adherence, managing and preventing adverse drug events, patient education and support, and clinical and economic outcomes.

According to the *BPS Role Delineation Study for Solid Organ Transplantation*, solid organ transplantation pharmacists have the specialized knowledge and expertise needed to manage complex medication regimens unique to the solid organ transplantation population in addition to clinical and regulatory needs not encountered in any other pharmacy specialty. Solid organ transplantation pharmacists are specially trained to design, recommend, implement, monitor, and modify pharmacotherapeutic plans to optimize outcomes. They review, analyze, and reevaluate multifaceted clinical and outcomes data in order to provide quality care and assess program effectiveness. Finally, they provide education and counseling throughout the transitions of care.³

There is a need for a mechanism to identify, recognize, and provide access to SOT pharmacist specialists who can meet patient needs for specialized medication management. Individuals who have obtained specialist recognition and have attained the additional training, experience, and expertise to lead patients, the profession, other health care providers, and society to better public health are necessary for managing diseases and reducing preventable conditions, complications, and sequelae. Specialty recognition of SOT pharmacy practice by the Board of Pharmacy Specialties (BPS) would provide a mechanism through which pharmacists could attain voluntary certification that recognizes achievement of a focused and distinct level of specialized knowledge, experience, and skills in serving the unique medication needs of patients.

There is likely some potential level of overlap between the proposed SOT pharmacist specialist and the existing BPS specialties in pharmacotherapy, critical care, pediatrics, ambulatory care, infectious disease and oncology. The petitioning organizations feel strongly that the evidence presented in this petition will justify a SOT pharmacist specialty as a stand-alone specialty.

BPS certification of solid organ transplantation pharmacist specialists will lay the groundwork for committed and interested pharmacists to focus their professional development, training, and educational efforts on preparing themselves to fully meet this public health need.

Criterion B: Demand

The criterion establishes that there exists a significant and clear health demand to provide the necessary public reason for certification. This is demonstrated through employer survey data, assessment of employment opportunities for solid organ transplantation pharmacist specialists, and letters and statements by individuals in specific areas within the health care system.

Demand is viewed as a willingness and ability to purchase the services of a board certified pharmacist.

SOT pharmacist specialists are involved with transplant patients before, during, and after transplantation. They evaluate patients prior to the transplant, evaluate all medications, develop and implement the patient's care plan, follow-up to evaluate the care plan, monitor medications, and document each step of the process. Additionally, SOT pharmacist specialists support patients post-transplant through ambulatory care practice. Care of transplant patients is complex and unique, requiring full engagement with an interprofessional care team.

Regulations for transplantation pharmacists' involvement in the care team are exhibited by federal regulatory bodies, practice standards, and guidance. The Centers for Medicare and Medicaid Services (CMS) began certifying transplant centers and outlining the expectations for those centers to receive approval and reapproval to perform organ transplants. CMS expects "the team will include an individual with expertise in transplant pharmacotherapy" (e.g., clinical pharmacist) to be a requirement for accreditation, given the highly specialized and complex drug regimens used.⁴ Additionally, the Organ Procurement and Transplantation Network (OPTN), a public-private partnership that connects organ donation and transplantation professionals, is administered by the United Network for Organ Sharing (UNOS) under contract with the Department of Health and Human Services. UNOS developed bylaws detailing the roles and responsibilities of the pharmacist on the transplantation team. The International Society for Heart and Lung Transplantation (ISHLT) created the *ISHLT Guidelines for the Care of Heart Transplant Recipients* and asserts, "Transplant centers should strive to have specialty-trained pharmacists or physicians with expertise in pharmacology as part of the multidisciplinary team." Lastly, the value of the pharmacist's role in addressing patient nonadherence is recognized by the *Kidney Disease: Improving Global Outcomes (KDIGO)* guideline. The recognition of the SOT pharmacist specialist's role and impact by federal regulatory agencies, as well as national and international transplant teams speaks to the demand of the SOT pharmacist specialist.

The demand for solid organ transplantation pharmacist specialists is demonstrated through sustained growth in employer demand and the increase in specialty training programs. Additionally, 12 individuals and organizations contributed letters of support that specifically attest to the demand for pharmacists with training and knowledge to provide specialized services in solid organ transplantation pharmacy practice.

The value of specialty recognition is becoming increasingly important to employers of solid organ transplantation pharmacist specialists. The *Survey of Solid Organ Transplantation*

Pharmacists Interested in Board Certification included a subset of questions that were completed by individuals with direct responsibility for hiring pharmacists in solid organ transplantation practice. Hiring managers from 36 organizations that responded indicated that they had recruited for 81 solid organ transplantation pharmacist specialists over the past 3 years and had filled more than 93% of these positions. These same employers estimate that they will fill an additional 47 positions over the next 3 years and currently report 15 vacant positions within their organizations. Employers also estimated the growth in the number of solid organ transplantation pharmacy positions within their organizations over the next 5 years, with 100% of respondents anticipating an increase in these positions.

Almost 90% of employers responding to the *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* indicated that it was “highly likely,” “likely,” or “somewhat likely” that they would require a new specialty credential in solid organ transplantation if approved by BPS for newly hired pharmacists. Of those responses, over 83% indicated that it was “highly likely,” “likely,” or “somewhat likely” that they would require a new specialty credential in solid organ transplantation if approved by BPS for currently employed SOT pharmacist specialists. The survey also showed that only 47% of SOT pharmacist specialist positions currently require BPS certification or another earned credential. These results imply that a credential more targeted to the specific needs of SOT pharmacist specialists would be in demand in the marketplace.

Criterion C: Number and Time

This criterion quantifies that there are a reasonable number of individuals who devote of their practice to solid organ transplantation pharmacy practice.

The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* was fielded to approximately 760 members of ACCP and ASHP who self-identified as SOT pharmacist specialists, which received a 36.4% (277) response rate. Of the responding pharmacists, 97% indicated that they are practicing at a specialty level. Based on these survey results and the available literature, we draw the conclusion that 1,000–1,200 pharmacists are currently engaged as SOT pharmacist specialists. Likely, this number is underestimated because not all SOT pharmacist specialists are members of the partnering professional organizations. However, we believe that pharmacists who are engaged as members of professional associations are more likely than others to pursue specialty recognition.

SOT pharmacy practice has significantly grown over the past decade, as evidenced by the increased number of postgraduate year two (PGY2) specialty residency programs in SOT pharmacy. In 2007, there were two ASHP-accredited specialty residency programs in SOT.

Today, these programs number 39, a 1,750% increase. Approximately 43 SOT pharmacists graduate annually from these programs.

Results from the role delineation study show that respondents are highly engaged in SOT pharmacy practice, with an average of 72% of respondents reporting 90-100% of their time spend in SOT pharmacy practice. The *Survey of Cardiology Pharmacists* also showed that over 91% of respondents, or 231 pharmacists, indicated that they would be “highly likely,” “likely,” or “somewhat likely” to pursue specialty recognition in SOT certification within 5 years if such recognition were made available.

Criterion D: Specialized Knowledge and Criterion E: Specialized Tasks/Skills

These criteria outline the specialized knowledge of one or more of the pharmaceutical sciences and the biological, physical, behavioral, and administrative sciences which underlie them that are required by solid organ transplantation pharmacist specialists and represent the specialized tasks/skills of solid organ transplantation pharmacist specialists, which are distinct from other BPS-recognized pharmacy specialties.

BPS has conducted a role delineation study for solid organ transplantation pharmacy practice and issued a call for petitions in this specialty area. Therefore, Criterion D and Criterion E are not required as part of the petition to BPS.

Criterion F: Education and/or Training

This criterion describes the education, training, and experience required to acquire specialized knowledge and skills to perform the specialized functions and distinguishes from the generalized practitioner and the requirements of initial licensure.

According to the Accreditation Council for Pharmacy Education’s *Accreditation Standards and Guidelines for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree*, the pharmacy curriculum provides a thorough foundation in the biomedical, pharmaceutical, social/behavioral/administrative, and clinical sciences. The degree program prepares graduates to:

- Enter advanced pharmacy practice experiences (APPE-ready)
- Provide direct patient care in a variety of health care settings (practice-ready)
- Contribute as a member of an interprofessional collaborative patient care team (team-ready)⁵

Following licensure, pharmacists can acquire the differentiated knowledge and skills required for specialized SOT pharmacy practice by a variety of methods. These methods may include, but are not limited to:

- Doctor of Pharmacy degree, clinical work experience, and self-study
- Doctor of Pharmacy degree, postgraduate year one (PGY1) residency training, clinical work experience, and self-study
- Doctor of Pharmacy degree, PGY1 residency training, clinical and/or research fellowship programs, clinical work experience, and self-study
- Doctor of Pharmacy degree, PGY1 residency training, postgraduate year two PGY2 specialty residency in solid organ transplantation, clinical work experience, and self-study

The most effective way to prepare for a career as a SOT pharmacist specialist is to complete a PGY1 pharmacy residency and a PGY2 residency in solid organ transplant. PGY2 SOT residency programs provide the most comprehensive experiential learning opportunities in SOT pharmacy practice. In the *Survey of Solid Organ Transplantation Pharmacist Specialists Interested in Board Certification*, fielded by the petitioning organizations, employers of SOT pharmacist specialists were asked the desired level of training for pharmacists practicing in this specialty. Ranked highest was a PGY2 residency in solid organ transplant. As of January 3, 2018, there were 39 PGY2 solid organ transplant specialty residency programs with 42-43 residency positions. There are also six solid organ transplant pharmacy fellowship programs.

Criterion G: Transmission of Knowledge

The criterion establishes that there is adequate transmission of specialized knowledge through professional, scientific, and technical literature directly related to specialized solid organ transplantation pharmacy practice.

Transmission and dissemination of specialized knowledge in SOT pharmacy practice occurs through national standards and guidance, formal networking groups within professional practice associations, peer-reviewed publications and periodicals, live educational programming, and enduring educational resources in print- and web-based vehicles. National standards and guidance transmit knowledge through rules, regulations, standards, guidelines, and position papers authored by national organizations and government entities. Professional organizations and networking groups help SOT pharmacist specialists practice at the top of their license by encouraging professional interactions and providing opportunities for practice advancement through educational programming, newsletters, research networks, and leadership. Each year, pharmacy and other health care organizations offer live and web-based continuing pharmacy education opportunities related to new developments and issues concerning SOT pharmacy practice that facilitate the dissemination of knowledge and practice excellence. Enduring resources are also available through various methods. A significant number of articles pertaining to SOT pharmacy practice are published annually and are detailed

within the petition.

Conclusion

Pharmacists have played an important role in the care of transplant patients since at least the mid-1970s. The pioneers in this specialty served on the cutting edge of practice, establishing more than just the safety and efficacy of modern immunosuppression. Over the last 30 years, pharmacists have helped move immunosuppression from its experimental stages into accepted pharmacotherapy. Pharmacists have worked closely with scientists and other clinicians to establish monitoring guidelines, to minimize adverse effects, to improve adherence, and to create and manage immunosuppressive regimens and protocols for other conditions seen in transplant recipients.⁶

The ultimate goal of recognition of SOT pharmacist specialists is to ensure quality patient care and improve therapeutic outcomes. As the transplantation field continues to expand in both scope and complexity, there will be an increasing need for highly trained pharmacotherapy specialists with expertise in transplantation. A stand-alone specialty in SOT pharmacy practice would clearly identify for employers, third-party payers, physicians, patients and the public those individuals who have specialized competencies and expertise in transplantation.

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CRITERION A: Need

The area of specialization shall be one for which specifically trained practitioners are needed to fulfill the responsibilities of the profession of pharmacy in improving the health and welfare of the public, which responsibilities may not otherwise be effectively fulfilled. ***This criterion addresses NEED.*** BPS defines NEED as a condition of requiring supply.

Solid organ transplantation (SOT) has experienced significant growth and expanded clinical sophistication over the last several decades, leading to dramatic improvements in graft and patient survival. SOT pharmacist specialists are recognized as integral and respected members of the interprofessional transplantation team for over three decades, and their expertise has become coveted in industry, government, and administrative and academic positions, aside from their established clinical roles.¹ These specialists are uniquely trained and positioned to contribute knowledge and skills to the management of highly complex transplantation patients.² Incorporation of SOT pharmacist specialists into the interdisciplinary transplantation team is now standard, and their roles within the multidisciplinary care model have expanded to include all phases of transplantation.^{3,4,5}

In 2017, 34,769 SOT procedures were conducted, and there are 114,939 people on the waiting list for an organ in the United States. A new patient is added to the national transplantation waiting list every 10 minutes.⁶ Commonly, new transplantation recipients will be prescribed a median of eight medications, with some requiring as many as 10-15 chronically. Many of these medications have a narrow therapeutic index, significant drug interactions, a high potential for adverse effects, and are very expensive, resulting in the need for intense monitoring.⁷

SOT pharmacy practice focuses on the care of SOT patients. SOT pharmacist specialists practice in a variety of settings, including adult and pediatric medical intensive care units (ICU), surgical ICU, inpatient acute care, outpatient ambulatory care clinics, academic settings, pharmaceutical industry, and research institutions. SOT pharmacist specialists possess specialized knowledge and experience in the care of SOT patients. Many have completed formal, post-graduate residency training in SOT practice environments. They possess unique knowledge of the epidemiology and pathophysiology of SOT; the pharmacotherapy of transplantation patients; the application of pharmacokinetics, pharmacodynamics, and pharmacogenomics to transplantation; operational and clinical systems designed to assure medication safety;

patient/parent/caregiver counseling to optimize medication adherence; and long-term disease prevention and health maintenance in patients receiving life-long immunosuppressants. They also contribute to, and evaluate, biomedical literature pertinent to immunology and transplantation pharmacotherapy.

GUIDELINE 1. Identify specific public health and/or patient care needs which are not being met currently and which pharmacists in the proposed specialty can meet effectively. If these needs are currently being met by another BPS Specialty, other areas of pharmacy practice, or by other health professionals, describe how these needs can be met more effectively by pharmacists in the proposed specialty.

The clinical role of the SOT pharmacist specialist is varied and requires a broad knowledge of immunosuppression, critical care, infectious diseases, and in-depth knowledge of each organ system. SOT pharmacist specialists are engaged across the spectrum of SOT.⁸ In a study conducted to determine how SOT pharmacists are being integrated into transplantation clinical practice, a majority of responding transplantation centers indicated that pharmacists had multi-organ transplantation responsibilities. Eighty-six percent of pharmacists were involved in kidney transplantation, 71% in liver transplantation, 50% in pancreas transplantation, 25% in heart transplantation, and 7% in lung transplantation.⁹

Despite advances in medicine and technology, as well as an increased awareness of organ donation and transplantation, there continues to be a gap between supply and demand. Currently, almost 115,000 people are waiting for a lifesaving organ transplantation.¹⁰ The financial costs of transplantation are also enormously high, with costs for kidney transplants averaging \$414,800, liver transplants averaging \$812,500, double lung transplants averaging \$1,190,700, and heart transplants averaging \$1,382,400.¹¹ SOT pharmacist specialists provide medication management of complex immunosuppressant therapies that help preserve valuable, transplanted organs and ensure optimal clinical outcomes for SOT patients.

Roles of Solid Organ Transplantation Pharmacist Specialists

Pharmacists have played an important role in the care of transplantation patients since at least the mid-1970s. The pioneers in this specialty served on the cutting edge of practice, establishing more than just the safety and efficacy of modern immunosuppression. Over the last 30 years, pharmacists have helped move immunosuppression from its experimental stages into accepted pharmacotherapy. Pharmacists have worked closely with scientists and other clinicians to establish monitoring guidelines, to minimize adverse effects, to improve adherence, and to create and manage immunosuppressive regimens and protocols for other conditions seen in transplantation recipients.¹²

As the number of transplantation programs have expanded across the U.S., so have the roles and responsibilities for SOT pharmacist specialists within direct patient care. These expanded roles are supported by evidence of the benefits that SOT pharmacist specialists provide as members of the interprofessional care team and the recognition of federal regulatory bodies of this critical role. The 2011 revised bylaws of the United Network for Organ Sharing (UNOS) codified the role of the pharmacist on the SOT team as a required member with responsibilities during and after transplantation. Such responsibilities include medication reconciliation, discharge planning, drug therapy protocol development, and provision of drug information, among others.¹³

Regulations of the Centers for Medicare and Medicaid Services (CMS) also require a pharmacist to be an active participant in the care of transplantation patients. Transplantation centers must be members in good standing with UNOS in order to perform organ transplants and must be certified by CMS to participate with Medicare. CMS specifically outlines the hospital conditions of participation and details the requirements for approval and re-approval of transplantation centers to perform organ transplants. This rule sets forth clear expectations for safe, high quality transplantation service delivery in Medicare-participating facilities.¹⁴

The Organ Procurement and Transplantation Network (OPTN) is a unique public-private partnership that links all professionals involved in the U.S. donation and transplantation system. OPTN has personnel requirements, with their bylaws requiring that “each transplant program identify at least one clinical transplant pharmacist on staff who will provide pharmaceutical expertise to transplant recipients. The clinical transplant pharmacist should be a member of the transplant team, providing comprehensive pharmaceutical care to transplant recipients.” The bylaws further state that “the transplant pharmacist will work with patients and their families and members of the transplant team, including physicians, surgeons, nurses, clinical coordinators, social workers, financial coordinators and administrative personnel. The transplant pharmacist should be a licensed pharmacist with experience in transplant pharmacotherapy.”¹⁵

Roles of the SOT Pharmacist Specialist During the Phases of Transplantation

As summarized in a joint position paper from the American Society of Transplantation (AST) Transplant Pharmacy Community of Practice and the American College of Clinical Pharmacy (ACCP) Immunology/Transplantation Practice and Research Network, the fundamental activities of transplantation pharmacists include:¹⁶

- Prospective pharmacokinetic, pharmacodynamic, and therapeutic drug monitoring evaluation of all drug and non-drug therapy in the transplantation recipient;

- Coordinate development, implementation, adherence and outcome measures of departmental policies and procedures and drug therapy protocols;
- Perform medication reconciliation, medication therapy management, and discharge counseling;
- Provide education and training to members of the transplantation team and practitioners in training;
- Facilitate cost containment strategies, pharmacotherapy optimization, and participation in quality assurance programs to maximize patient- and center-specific outcomes;
- Provide pre-and post-transplantation medication education;
- Lead and assist with clinical and pharmacoeconomic research;
- Identify, manage, and prevent medication-related adverse events;
- Monitor every stage of medication therapy to improve all aspects of effectiveness
- Document education provided and pharmacotherapeutic recommendations in the medical record;
- Provision of consultation to institutional committees (e.g., Pharmacy and Therapeutics Committee) regarding immunosuppressant and immunomodulating pharmacotherapeutic agents; and
- Coordinate and provide outpatient medication therapy management.

The SOT pharmacist specialist has a number of responsibilities during the pre-, peri- and posttransplant period. These include continual assessment of drug therapy prescribing, appropriateness, effectiveness and safety monitoring including drug concentrations and pharmacokinetics, pharmacodynamics, drug (drug, food, over-the-counter and dietary supplement) interactions, drug administration, delivery, and costs. Also, specialists assume the role of admission and discharge medication reconciliation/facilitation/planning in conjunction with the nurse coordinator, midlevel practitioner, social worker and other members of the patient care team. Another major emphasis of practice is patient and caregiver education, not only in the posttransplant period but also during the pretransplant work-up to identify barriers associated with access to medications posttransplant. In addition, the transplantation pharmacist is frequently asked to evaluate and participate in discussions to determine which immunosuppression regimens and other drug therapies are best for the individual and most likely to result in positive outcomes. As a result, SOT pharmacist specialists, in conjunction with the rest of the patient care team, can play a vital role in coordinating drug therapy as they follow the patient throughout their continuum of care.¹⁷

The results of a 2015 national workforce survey of transplantation pharmacists across accredited SOT programs in the U.S. provide a detailed and comprehensive assessment of the day-to-day activities of SOT pharmacist specialists. The data demonstrates that a majority of

SOT pharmacist specialists provide core activities, including direct patient care, immunosuppressant medication therapy management, and patient/caregiver education. Direct patient care provided by pharmacists during the other phases of transplantation is more varied and is not as consistently provided, as compared to the initial transplantation event phase. These activities are detailed below.¹⁸

Evaluation Phase

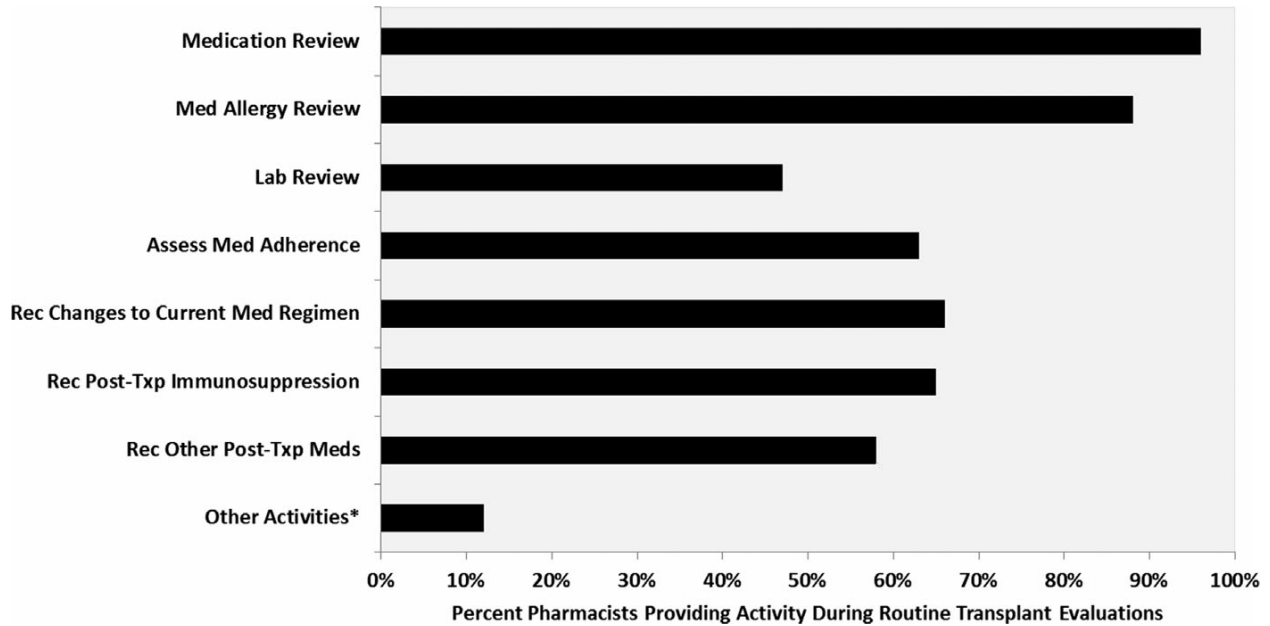
The process of selecting appropriate candidates for transplantation involves multidisciplinary assessment to evaluate a patient's mental, social, physical, financial, and medical readiness for successful surgery and good posttransplantation outcomes. SOT pharmacist specialists are mandated by CMS and UNOS to be involved in the evaluation of patients being considered for organ donation and transplantation, and they play a critical role in the recognition and stratification of both pharmacologic and nonpharmacologic risk factors during the transplantation evaluation process.¹⁹ SOT pharmacists can play important roles in the recognition and stratification of pharmacologic and nonpharmacologic risks in prospective kidney transplantation recipients and the identification of issues that require a mitigation strategy.²⁰

SOT pharmacist specialists evaluate pharmacologic and non-pharmacologic contraindications to transplantation, perform allergy and medication reconciliation, review immunization records and make recommendations, and conduct patient medication education and adherence assessments. Specialists also make drug selection, dose, and monitoring recommendations and manage drug interactions. From an administrative perspective, SOT pharmacist specialists assist with prior authorizations and medication assistance programs, develop protocols and monitor adherence to established protocols, and are involved with quality improvement, drug utilization evaluations, and research.²¹

According to a survey by Taber et al, 60% of SOT pharmacist specialists evaluate patients prior to transplantation with 86% documenting this evaluation in the medical record. The majority of pharmacists evaluate all potential transplantation recipients (67%), while others only evaluate a subset (20%), or by consult only (13%). Pharmacist evaluations were conducted during the selection meeting (32%), by review of medical records (50%), via a telephone interview (8%), and by other mechanisms (10%).²² Activities performed during the evaluation phase are displayed in Figure A-1. Medication education is provided by 55% of SOT pharmacist specialists. When pharmacists identify significant issues regarding transplantation candidacy, these are communicated to the team verbally (42%), documented in the medical record (35%), emailed (11%), or through other methods (12%, e.g. selection meeting). History of unchanged nonadherence was the most common reason for pharmacologic contraindication to

transplantation, followed by lack of financial or social support; though 88% of 140 respondents indicated that formal adherence monitoring is not conducted during the evaluation phase.²³

Figure A-1. Transplant Pharmacist Activities During the Transplant Evaluation Phase of Care in Adult Only Transplant Centers



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Transplantation Phase

In this phase, the SOT pharmacist specialist typically rounds with the inpatient transplantation team and performs medication reconciliation, education, and adherence assessments from the outpatient setting, particularly during readmission periods and daily medication review. They also provide drug selection recommendations, dosing, and monitoring recommendations to the inpatient team. Specialists are involved with approval of restricted medications, assist with prior authorizations, coordinate discharge medications, and verify medication reconciliations performed by non-transplantation trained providers. They are closely involved in anti-infective pharmacotherapy management through reviewing allergies and immunizations; providing recommendations regarding drug selection, dosing, and monitoring; assessing and managing drug-drug interactions; and evaluating the appropriateness of the medication choice and dose over the course of treatment. The SOT pharmacist specialist is also involved in transplant-related anti-infective drug selections, order set development, monitoring guidelines, medication use evaluations, and participates in pharmacy and therapeutics committee.²⁴

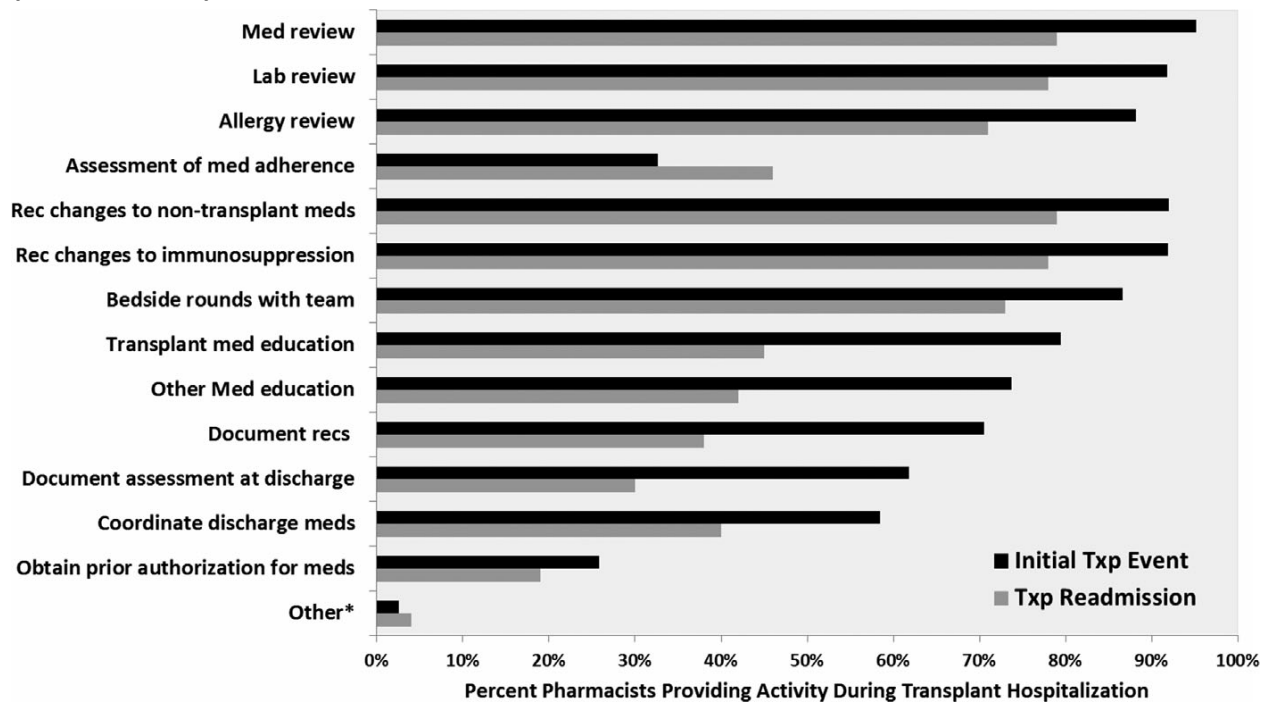
The vast majority of SOT pharmacist specialists (96%) provide direct patient care to all transplantation recipients, with 4% providing it only to a subset of patients and 1% providing

care on a consult basis only. Most SOT pharmacist specialists spend an average of 16-30 minutes on each patient per day performing these activities. Medication reconciliation was performed by 60% of pharmacists at both admission and discharge during the transplantation phase; 84% provide medication education with variable delivery methods.²⁵

Posttransplant Phase (Hospital Readmission)

Fifty-nine percent of SOT pharmacist specialists provide direct patient care to all transplantation recipients that are readmitted to the hospital, 19% see only a subset of patients, and 12% provide this care only when consulted. Twenty-five percent of SOT pharmacist specialists performed medication reconciliation on readmission and discharge; 24% performed this function only at admission; 10% performed this activity only at discharge; and 15% performed medication reconciliation during all transitions of care.²⁶ Figure A-2 displays the activities that are performed by the pharmacist during the transplantation and posttransplant (readmissions) phases of care.²⁷

Figure A-2. Transplant Pharmacist Activities During the Transplant and Posttransplant (Readmissions) Phases of Care



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Posttransplantation Phase (Ambulatory Care)

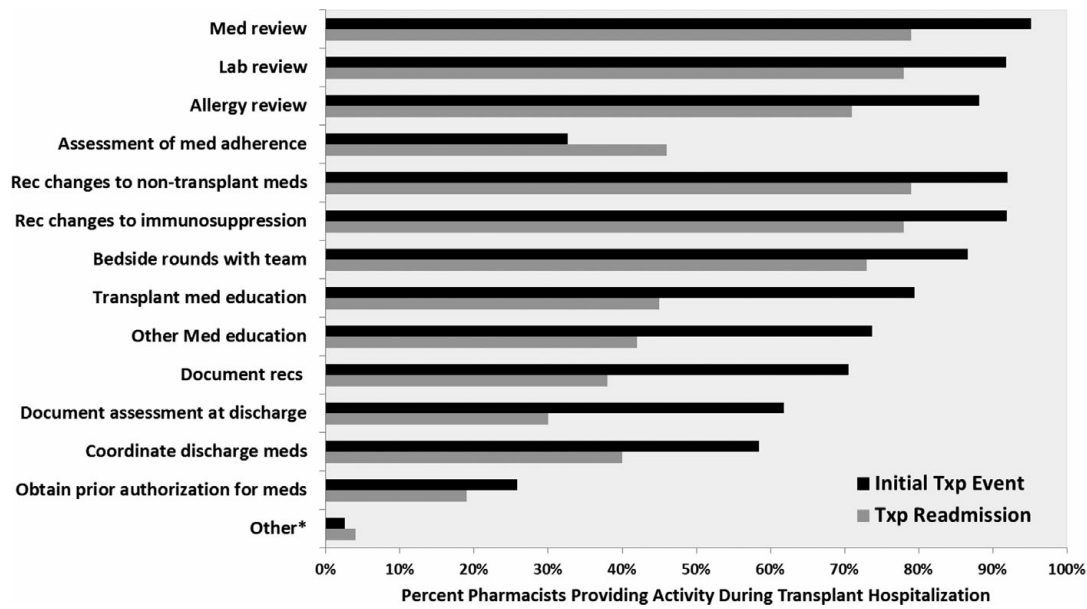
SOT pharmacist specialists are also involved in post-transplantation ambulatory care in various capacities. In the post-transplantation phase, transplantation pharmacists can provide medication reconciliation, education, adherence assessments, drug selection, dosing, and

monitoring recommendations. They assist with prior authorizations and help patients to obtain outpatient prescriptions. Specialists in this phase are closely involved in anti-infective pharmacotherapy management through reviewing allergies, immunizations, drug selection, dose, monitoring, assessing for drug-drug interactions, and evaluating the appropriateness of the choice and dose over the course of treatment. They also play an important role in implementing adherence to prophylaxis protocols and recommending dose adjustments when needed.²⁸

In the ambulatory care or clinic setting, SOT pharmacist specialists evaluate patients in a similar manner as the inpatient team but with particular focus on disease state management and minimizing long-term complications utilizing the principles of medication therapy management. Time is dedicated to discussing side effects and changes in drug therapy with the patient in attempt to proactively manage and enhance medication adherence. In this setting, SOT pharmacist specialists may also assist in billing, prescription coverage assistance and cost reduction measures to aid the patient and health care facility. With the growing number of ambulatory practitioners, there will be improved continuity of care between the inpatient and outpatient settings.²⁹

Outpatient participation in direct patient care activities are critical to transplantation success. The majority of transplantation centers have clinics at least two days a week, with 77% providing care to transplantation recipients during their initial outpatient visit. Time spent during ambulatory clinic visits varied, with 48% of respondents reporting 11-20 minutes per patient per visit. Most outpatient medication education provided by pharmacists is done verbally (69%). Nineteen percent is offered through other forms, such as written materials and medication schedules, and video is used for 5% of patient education. SOT pharmacist specialists provide multiple activities during this phase, as shown in Figure A-3.³⁰

Figure A-3. Transplant Pharmacist Activities During the Posttransplant (Ambulatory) Phase of Care



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Other Solid Organ Transplantation Pharmacist Specialist Activities

In addition to direct patient care responsibilities, SOT pharmacist specialists are involved in quality assurance and process improvement measures. These typically involve developing transplantation medication-use protocols, ensuring adherence to protocols during the transplantation process, and proactively measuring protocol-related outcomes through data collection, which results in continuous modifications to protocols over time. The data collection involved in evaluating the effectiveness of protocols is often the basis of clinical research at the transplantation center, with the SOT pharmacist specialist taking an important lead in these projects. The results often prove meaningful to peer institutions and have contributed to the growing literature describing methods for optimizing patient outcomes.³¹ Following protocol implementation, the SOT pharmacist specialist is often called upon to measure the outcomes and effectiveness of these protocols and suggest modifications based on internal findings and the published literature.³² SOT pharmacist specialists participate in administrative activities, including order set development, involvement in quality assessment performance improvement (QAPI), approval for restricted drugs, medication use evaluation (MUE), and participation in pharmacy and therapeutics committee.

With their established role, SOT pharmacist specialists are able to facilitate integration of pharmacy trainees into the multidisciplinary transplantation team. SOT specialists teach didactically to pharmacy and medical students, are engaged with residency and fellowship programs and are involved with student precepting. They also provide education to prescribers, nurses, other pharmacists, and other health care professionals through the development and delivery of disease state and patient case presentations, participation in provider in-services,

responses to drug information questions, and participation in journal clubs.³³ In addition, specialists continually evolve their practice sites and further develop precepting skills to mentor future generations of practitioners.³⁴

The majority of SOT pharmacist specialists participate in clinical research, including protocol design, budget preparation, administration of informed consent, preparation of investigational drugs, data analysis, and manuscript preparation. A substantial number of the research questions explored in transplantation surround immunosuppression and its sequelae. The transplantation pharmacist's education, training, and role uniquely position them to be an integral part of the research team. The design and execution of clinical research, specifically in transplantation, necessitates a bridge between the different levels of care and a working knowledge of the logistics of medication use system. In addition, the transplantation pharmacist is able to assist with obtaining pilot data, study design, data collection, and analysis. Many centers have adopted transplantation PharmDs as their directors of clinical research or given them leading roles within their research teams associated with the development of research protocols, navigation/implementation of industry sponsored trials, regulatory, and reporting efforts.³⁵

SOT pharmacist specialists produce a substantial effect on outcomes for transplantation patients in a wide variety of roles, largely through the optimization of medication use, avoidance of adverse drug reactions, and transition of care activities focused on medication reconciliation and patient education. According to the published literature, transplantation patients have substantial unmet needs in the areas of medication adherence, managing and preventing adverse drug events, patient education and support, and clinical and economic outcomes. It has been well established that the work of SOT pharmacist specialists increase adherence rates and improve transplantation outcomes.^{36,37,38,39,40} Documented contributions by SOT pharmacist specialists are detailed in the following sections.

Medication Adherence

The International Society for Pharmacoeconomics and Outcomes Research defines medication adherence as the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen. Depending on how it is calculated, nonadherence to medications can account for nearly 70% of medication-related hospital admissions and approximately \$100 billion to \$300 billion in health care costs annually.⁴¹ SOT pharmacist specialists have been shown to improve medication adherence for SOT patients.⁴²

The transplantation patient's therapeutic regimen consists of lifelong medication requirements, including immunosuppressive medications, monitoring for signs and symptoms related to

complications, avoidance of risk factors for cardiovascular disease and cancer, avoidance of abuse/dependence of alcohol or illegal drugs, as well as attending regular clinical checkups. Adherence to all aspects of a prescribed regimen is critical. Nonadherence has been related to negative clinical outcomes in view of acute rejections, graft vasculopathy, higher costs, and mortality.⁴³ Patient adherence to medication regimens is essential to prevent organ rejection after SOT.^{44,45, 46,47,48,49,50,51} Barriers to medication adherence among SOT recipients include lack of adequate follow-up with the transplantation team, confusion concerning proper use of medications, lack of appropriate instructions from practitioners, apathy, adverse events from medications, economic issues, and complex drug regimens.^{52,53,54}

Nonadherence to medication therapy is common and has a large impact on transplantation survival.⁵⁵ The role of drug therapy is not limited to immunosuppression; transplantation recipients may have infections, hypertension, diabetes, osteoporosis, hyperlipidemia, and many other conditions that require additional drug therapy. The complexity, duration, and adverse effects of these regimens can contribute to noncompliance.⁵⁶ Additional risks to nonadherence include dialysis, decreased productivity, reduced quality of life, and increased morbidity, mortality, and health care costs.⁵⁷ Reports of nonadherence range from rates of 2% to 68% and is seen among recipients of all types of solid organ transplants.⁵⁸ A meta-analysis of 36 studies on the frequency and impact of nonadherence in adult renal transplantation recipients showed that the odds of graft failure increased 7-fold in nonadherence subjects compared with adherent subjects.⁵⁹

Numerous studies in the literature highlight the challenges of medication adherence in SOT and demonstrate the value of SOT pharmacist specialists. Examples of these studies include:

- A retrospective, case-control study in 384 adult kidney transplantation patients assessed the effect of patient and process factors on 30-day readmission rates. Pharmacist identification of poor understanding or adherence was associated with an increased risk of readmissions. After controlling for risk factors, readmission rates were independently predicted by pharmacist identification of patient lack of understanding or adherence regarding post-transplantation medications (OR 2.3, 95% CI 1.10–4.71, $p = 0.026$), which was significantly modified by history of diabetes.⁶⁰
- An exploratory, qualitative study evaluated results of five focus groups comprised of members of kidney transplantation teams to obtain an understanding of how health professionals support the kidney transplantation patient to take their medications as prescribed long-term. Analysis revealed that adherence was a collective responsibility involving the whole of the transplantation team, including the pharmacist and the patient via education in the hospital, identifying and managing nonadherence, promotion of self-advocacy, and the partnership between the patient and health

professional. Patients were directed how to take their complex medications and be self-empowered.⁶¹

- A review of medication nonadherence and the evolution of contributing factors necessitates initial, ongoing, and consistent assessment by the health care team. Evaluation of individual risk factors for nonadherence may aid in the formulation of mitigation strategies to improve outcomes. Allotting time for pharmacists, financial coordinators, and social workers to spend with patients in conjunction with the medical team during annual evaluations may aid in identifying gaps in these areas contributing to nonadherence.⁶²
- A prospective study with 74 renal transplantation recipients using a sequential control group design was performed to investigate the impact of a pharmaceutical intensified care program led by a clinical pharmacist on daily drug adherence during the first year after renal transplantation. Clinical pharmacist intervention improved patients' medication adherence remarkably, suggesting that the applied additional care program can improve outcomes after organ transplantation.⁶³
- A clinical pharmacy services program implemented in a renal transplantation clinic improved medication access, adherence, and health and economic outcomes among renal transplantation recipients. As part of the intervention, a clinical pharmacist reviewed and optimized medication therapy, provided instructions on how to take medication, and assisted with enrollment into medication assistance programs, decreasing financial barriers to adherence. Significant differences were found between renal transplantation recipients who did and did not receive clinical pharmacy services.⁶⁴
- A prospective, randomized, controlled trial examined the influence of pharmaceutical care on liver transplantation patients' compliance with immunosuppressive therapy. Patients who received pharmaceutical care with traditional patient care showed significantly better compliance with their immunosuppressive medication than patients who received only traditional patient care. Pharmaceutical care proved to be an effective intervention that should be implemented in posttransplantation care.⁶⁵
- A study by Pinsky et al, described factors associated with immunosuppression compliance after kidney transplantation in 15,525 patients and observed significant increases in the risk of graft failure with compliance levels less than excellent, not only related to poor compliance.⁶⁶
- A randomized, controlled trial evaluated the impact of clinical pharmacy services compared to traditional patient care services. Patients receiving clinical pharmacy services had better compliance with immunosuppressants than patients who only received traditional patient care services. Results of this study suggest a multidisciplinary team that includes a clinical pharmacist as part of the care for post-transplantation patients is beneficial for enhancing medication compliance.⁶⁷

Managing Medication Therapy

Two decades ago, the primary focus of immunosuppressant regimens was prevention of acute rejection using either 2 or 3 drug combinations that, in retrospect, seem simplistic. Advances in immunosuppressant regimens have dramatically reduced acute rejection rates but concurrently increased the complexity of immunosuppressant regimens. As a result, the role of the pharmacist has expanded to include designing, implementing, and counseling patients on individualized drug regimens.⁶⁸ Patients are at increased risk for adverse drug reactions if they have one or more of the following indicators:

- More than three concurrent disease states
- Medication regimen changed four or more times during the past 12 months
- Five more medication doses in the present drug regimen
- 12 or more medication doses per day
- History of non-compliance, and
- Presence of drugs that require therapeutic monitoring

The more indicators present, the more likely a patient will have an adverse outcome.

Transplantation patients require lifetime immunosuppression. With the extended life span of transplantation recipients, they often require additional medications for concomitant chronic diseases, such as hypertension, diabetes, osteoporosis, and hyperlipidemia, increasing the number and complexity of required medications.⁶⁹

Greater than 50% of medication errors are estimated to occur during transitions of care, and SOT recipients are at an increased risk for errors due to significant changes in their medication regimen following transplantation. Though all patient populations are at-risk for medication errors during transitions of care, patients whose home medication regimen will undergo significant changes during the hospitalization may be at increased risk. During their short hospital stay, SOT recipients may be initiated on nine or more new medications for the purposes of immunosuppression, prophylaxis against bacterial, viral and fungal infections, and gastrointestinal, bowel, and pain management.⁷⁰ An estimated 20–50% of kidney transplantation recipients and 9–21% of liver transplantation recipients also develop new-onset diabetes after transplantation and will therefore be initiated on insulin therapy with frequent blood glucose monitoring.⁷¹ In addition, the patient's home medications taken prior to surgery may or may not be necessary after transplantation. The process of discharge medication reconciliation is of the utmost importance in this patient population due to the risk for rejection and other complications in the post-transplantation period.⁷²

SOT pharmacist specialists have demonstrated their expertise in preventing medication errors and performing medication reconciliation for SOT patients. Evidence that supports this role is as follows:

- A prospective, observational study was conducted to evaluate the discharge process for transplantation recipients and determine if transplantation pharmacist involvement would improve safety. The results of this study demonstrate that transplantation patients are at very high risk for medication errors at the time of discharge, and the formalized involvement of transplantation pharmacists in the medication reconciliation process, particularly at the time of discharge, leads to improved medication safety through the significant reduction of medication errors.⁷³
- A multidisciplinary quality improvement initiative, including pharmacists, improved medication safety in kidney transplantation patients through a quality improvement initiative was developed that targeted eliminating medication use and safety issues in kidney transplantation patients. The team developed key initiatives, including improved medication reconciliation, development of a diabetes management service, and improved discharge medication dispensing, delivery, education, and scrutiny. Follow-up analysis demonstrated reduced medication discrepancies by >2 per patient with patients obtaining 100% adherence with reconciliation. Pharmacists reviewed discharge medications, reaching 100% by study end, leading to a 40% reduction in medication safety issues. Length of stay remained short, and delayed discharges were reduced by 14%; 7-day readmission rates decreased by 50%. Acute rejection and infection rates also significantly decreased.⁷⁴
- A retrospective, observational analysis evaluated the pharmacists' contributions to improved inpatient medication practices and educational services for kidney transplantation recipients at a community hospital. The participation of pharmacists on the kidney transplantation team enhanced a hospital's medication management, discharge planning, and patient education services for transplantation recipients, helping to reduce their average length-of-stay (LOS) (from 7.8 days in 2007 to 3.4 days in 2011, $p < 0.001$), with no adverse effect on all-cause 30-, 90-, and >90-day readmission rates (all $p > 0.09$). The pharmacists also yielded substantial cost savings, with annual cost savings attributable to the reduction in LOS estimated at \$279,180.⁷⁵
- A retrospective observational study of 476 adults who received kidney transplants showed that patient-induced medication errors and associated adverse drug events were common in kidney transplantation patients, with 8% of the population developing a clinically significant medication-related problem (MRP). Patients with MRPs had significantly higher rates of acute rejection (11% vs 30%, $p=0.004$), cytomegalovirus infection (15% vs 30%, $p=0.033$), and 30-day readmissions (5% vs 16%, $p=0.018$). Graft survival was also significantly lower in patients who had MRPs ($p<0.001$).⁷⁶

- A 4-year prospective study of drug-related problems (DRP) detected by pharmacists concluded that pharmacists detected many prescription errors with potential clinical implications, and that could be the basis for education measures. The most frequent DRP concerned improper administration mode (26%), drug interactions (21%), and overdose (20%). Pharmacist interventions resulted in a change in the method of administration (25%), dose adjustment (24%) and drug discontinuation (23%).⁷⁷
- This study assessed drug therapy problems (DTPs), pharmacist recommendations, and patient satisfaction with pharmacist services for 43 lung transplantation patients. The most common DTPs identified by the pharmacist were adverse drug effects (27%) and untreated indication (25%). Overall, 62% of pharmacist recommendations were rated very significant or significant. The study concluded that pharmacists can make valuable contributions in a lung transplantation clinic setting by identifying DTPs and making recommendations with a positive impact on patient outcomes and satisfaction.⁷⁸

Patient Education and Support

Recipients of solid organ transplants face many challenges, including daily self-care needs and complex medication regimens that must be continued for life. Medication counseling by SOT pharmacist specialists is a recognized component of effective transplantation care. Along with building patient knowledge and confidence, counseling may improve patient compliance and outcomes.⁷⁹ When SOT pharmacist specialists proactively work with patients to identify and resolve barriers to medication adherence and address drug therapy problems, their activities prevent disruptions in patient care. The engagement of the pharmacist with the patient at hospital discharge decreases the differences between pre- and post-admission therapeutic regimens, improves compliance with treatment, reduces drug-related adverse events, and decreases rehospitalizations.⁸⁰ Additional evidence of the value of patient education and supports is as follows:

- A French study demonstrated that patients' knowledge about antirejection medications increased from 53% to 75% after counseling by pharmacists. The knowledge level about other drugs, such as antimicrobial and antihypertensive agents, was 15% before pharmacist counseling and increased to 50-60% following counseling.⁸¹
- In a prospective, randomized controlled study, compliance with transplantation medications was improved when pharmacists counseled patients during routine clinic visits compared with clinic visits that did not include counseling by a pharmacist.⁸²

Clinical and Economic Outcomes

The clinical and economic benefits of providing high-quality, transplantation-related pharmacy services include reduction in medication errors and adverse drug events, reduction in acute rejection and infection rates, and decreases in delayed discharges and readmissions.^{83,84,85,86}

A review of clinical pharmacy services in SOT summarized the available evidence regarding the role and impact of clinical pharmacy services in the care of SOT patients. Interventions performed in these studies consisted of routine clinical pharmacy services with a focus on identifying, resolving, and preventing drug related problems (DRPs); clinical pharmacy services with a focus on therapeutic drug monitoring; and those with a focus on compliance enhancement and educational interventions. Acceptance rates were generally above 95%, and most studies reported that clinical pharmacy services had a positive impact on the care of SOT patients. Positive perceptions of patients and health care professionals were also reported.⁸⁷ Examples of the published literature that demonstrate positive clinical outcomes with the engagement of SOT pharmacist specialists include:

- A prospective, observational study of 237 adults developed a model to predict which patients are at highest risk of DRPs to streamline pharmacists' workflow in a chronic kidney transplantation clinic. This study demonstrated that a straightforward, 5-minute survey completed by renal transplantation recipients prior to their clinic visit may be capable of effectively determining those at-risk of having six or more DRPs, potentially allowing use as a screening tool for transplantation pharmacists' workflow prioritization.⁸⁸
- A retrospective cost-benefit analysis described and evaluated the clinical and economic implications of pharmacists' interventions as members of the liver transplantation team for hospitalized liver recipients. The study documented 1,880 interventions for 420 liver transplantation recipients. The most common drug therapy problem was "need additional drug therapy" (42.6%), followed by "dosage problems" (23.5%). The study showed a clear cost-benefit of the pharmacists' activities with a cost-benefit ratio of 3.8.⁸⁹
- This retrospective analysis of patients at risk of cytomegalovirus (CMV) reactivation who received kidney and/or pancreas transplants, determined whether early identification and enrollment in patient assistance programs (PAP) can prevent CMV-related events. The incidence of CMV viremia was lower in the PAP group (12.8% vs 36.2%, respectively). Pharmacists play a crucial role in this process and cost benefit analysis found that hiring a full-time pharmacy employee for enrolling patients in PAPs was cost beneficial for the institution/health care system.⁹⁰
- A retrospective review evaluates the impact of a SOT pharmacist specialist on nephrotoxicity, therapeutic drug monitoring, and revenue generation in adult kidney patients on tacrolimus. There was no significant difference in the incidence of acute nephrotoxicity in adult kidney patients on tacrolimus after the inclusion of a full-time SOT pharmacist specialist on the abdominal transplantation team. However, there was a significant increase in the rate of appropriately drawn tacrolimus troughs and prescription capture rates.⁹¹

- A retrospective longitudinal, cross-sectional study of 219 individual kidney transplantation patients determined if a pharmacist-executed comprehensive chart review could serve as sufficient substitution for direct participation during outpatient clinic visits in the post-discharge, follow-up treatment of kidney transplantation recipients. The results of this study suggest that comprehensive chart review by pharmacists prior to patient clinic visits may not be as effective as in-person consultation in communicating recommendations to providers. Providers accepted a greater percentage of recommendations that were delivered directly compared with recommendations presented via a note in the patient folder following chart review (92% vs. 28%, respectively). Directly provided recommendations were also associated with higher severity scores.⁹²
- A case study describes the implementation and outcomes of a program combining electronic home blood pressure monitoring (HBPM) and pharmacist-provided medication therapy management (MTM) services in a renal transplantation clinic. Implementation of electronic HBPM and pharmacist-provided MTM services implemented in a renal transplantation clinic was associated with sustained improvements in blood pressure control. Incorporation of a pharmacist in the renal transplantation clinic resulted in the detection and resolution of medication-related problems.⁹³
- This feasibility study describes clinical outcomes for patients receiving the care transition intervention delivered through a pharmacist-managed diabetes and cardiovascular risk reduction clinic (PMDC) during the first year of service implementation. This feasibility study showed evidence that embedding an endocrinology-trained provider improves the care transition of kidney transplantation recipients with diabetes from the inpatient to ambulatory care setting. Readmission rates were reduced at 30- and 90-days but not following completion of the intervention period.⁹⁴
- A retrospective observational analysis evaluates the pharmacists' contributions to improved inpatient medication practices and educational services for kidney transplantation recipients at a community hospital. The participation of pharmacists on the kidney transplantation team enhanced a hospital's medication management, discharge planning, and patient education services for transplantation recipients, helping to reduce their average LOS (from 7.8 days in 2007 to 3.4 days in 2011, $p < 0.001$), with no adverse effect on all-cause 30-, 90-, and >90-day readmission rates (all $p > 0.09$). The pharmacists also yielded substantial cost savings, with annual cost savings attributable to the reduction in LOS estimated at \$279,180.⁹⁵
- A prospective trial investigated the effects on treatment outcomes by clinical pharmacist engagement in renal transplantation clinics. Pharmacists interviewed

patients, reviewed medication regimens, and made therapeutic recommendations. Fifty-five pharmacotherapy recommendations were made for 37 renal transplantation patients during the trial period, of which 81.8% were classified as clinically significant. The drug classes most commonly involved were cardiovascular medications, immunosuppressants, and antimetabolites (32.6%, 23.9%, and 26.1 %, respectively). Physician acceptance rates of recommendation types and drug classes were 96.0% and 97.1 %, respectively. Among the cases in which the recommendations were accepted, 94.2% of patients showed improved conditions.⁹⁶

- A randomized study evaluated direct patient care services provided by a clinical pharmacist, in addition to routine clinical services, have a positive impact on the blood pressure of African-American renal transplantation patients. Patients in the intervention group received services including medication reviews, with an emphasis on preventing or resolving medication-related problems and providing medication recommendations.⁹⁷

Clinical Care for Renal Transplantation Patients

Kidney transplantation has been established as a life extending intervention that can have profound effects on end-stage renal disease patients' quality and length of life. In 2017, there were 16,804 kidney transplants in the U.S.⁹⁸ Type 2 diabetes and hypertension are two of the leading causes of renal failure resulting in the need for transplantation. Renal transplantation patients require long-term therapy with multiple medications for immunosuppression as well as to treat concomitant chronic diseases such as diabetes, hypertension, and hyperlipidemia. Since some medications prescribed for these patients have narrow therapeutic ranges, optimal pharmacotherapy is vital. Direct patient care services by pharmacists can improve the health of renal transplantation patients.⁹⁹

Considering the prior or underlying disease and comorbidities of the patient, the complexity and hazards of ongoing immunosuppression, the risk of acute rejection, and the need for optimized general health care, adequate follow-up for kidney transplantation recipients is essential.¹⁰⁰ Numerous studies have correlated non-adherence to prescribed treatment plans with allograft rejection and graft loss.^{101,102,103,104,105,106} The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline on the monitoring, management, and treatment of kidney transplantation recipients is intended to assist practitioners, including pharmacists, caring for adults and children after kidney transplantation. The guideline specifically addresses the value of the pharmacist's role in addressing patient nonadherence and the value of pharmacists' contributions within the health care team to ensure positive patient outcomes.¹⁰⁷

The role of the pharmacist in kidney transplantation spans the inpatient management of acute complications to medication selection, management of maintenance immunosuppression, as well as monitoring for adverse drug reactions and drug-drug interactions. A multidisciplinary collaborative approach must be taken to ensure the best outcomes for this patient population.¹⁰⁸ The vast majority of drug-related problems encountered by post-renal transplantation patients are in relation to antihypertensive, antimicrobial, or immunosuppressant medications.^{109,110} Drug-related admissions and noncompliance with medications are common in renal transplantation patients.^{111,112,113} These renal transplantation challenges reflect the need for a constant review of medication regimens in this patient population, a need that is being addressed by SOT pharmacist specialists.

SOT pharmacist specialists often play a very important role in the financial aspects of improving access to medications for renal transplantation patients and financially supporting the services of SOT pharmacist specialists. Reports in the peer-reviewed literature demonstrate that a pharmacist-led medication assistance program that included MTM services improved medication access, clinical outcomes, and quality of life in renal transplantation recipients.¹¹⁴ A clinical pharmacist-managed medication assistance program in a renal transplantation clinic produced substantial cost savings over this 1-year study period. For each dollar spent in pharmacist's time, a minimum of \$4 was returned to the institution.¹¹⁵

There are several randomized controlled trials that support the use of SOT pharmacist specialists in the care of kidney transplantation patients to minimize side effects, decrease costs, and improve adherence to immunosuppressant medications.^{116,117,118} In addition, a prospective, observational study demonstrated significant decreases in errors upon discharge following kidney transplantation when the medication regimen was reviewed by an SOT pharmacist specialist.¹¹⁹

Clinical Care for Heart and Lung Transplantation Patients

Heart transplantation is an established treatment for patients with end-stage heart failure, and more than 4,000 heart transplants are performed annually.¹²⁰ Although advanced surgical techniques, better immunosuppressive therapies, and improved infection control measures have dramatically improved short-term outcomes in organ transplantation, long-term survival rates have remained stable.¹²¹ Heart transplantation recipients are regarded as chronically ill and need life-long medical supervision for their transplanted organ as well as for new or existing co-morbidities like hypertension, diabetes mellitus, obesity, chronic kidney disease, or cancer.^{122,123,124} Moreover, heart transplantation patients have to engage in a healthy lifestyle and adherence to their treatment plan to prevent complications like acute rejection and reduce onset and progression of co-morbidities.^{125,126,127}

The International Society of Heart and Lung Transplantation (ISHLT) guidelines for the care of heart transplantation recipients provide guidance to the health care team responsible for the care of heart transplantation patients and recommends that transplantation centers should have specialty-trained pharmacists or physicians with expertise in pharmacology as part of the multidisciplinary team.¹²⁸ A data analysis of the multi-center, cross-sectional Building Research Initiative Group: Chronic Illness Management and Adherence in Transplantation (BRIGHT) study showed that while the composition of follow-up teams in heart transplantation centers varied, the majority of centers met the ISHLT recommendations for a multidisciplinary team, and this was associated with higher levels of chronic illness management.¹²⁹

Lung transplantation has become a viable treatment therapy for end-stage lung disease patients. The most common etiologies of end-stage lung disease, which can require a transplant, are chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, pulmonary arterial hypertension, and pulmonary fibrosis. Approximately 2,070 lung transplants were performed in 2017, and the 5-year post-transplantation survival rate is 50%.¹³⁰ The medical care of the lung transplantation recipient is complex and dynamic, particularly in the early post-transplant period. The role of the pharmacist spans the inpatient management of acute complications to medication selection, management of maintenance immunosuppression, as well as monitoring for adverse drug reactions and drug-drug interactions. A multidisciplinary collaborative approach must be taken to ensure the best outcomes for this patient population.¹³¹

In a descriptive pilot study, pharmacists provided direct patient care in the lung transplantation clinic. The impact of the pharmacist was assessed by examining the rate of drug therapy problem identification at pharmacist consult visits compared to the current standard of care. Notably, the number of drug therapy problems identified per pharmacist consult visit was twice that of the standard visit ($p = 0.018$). This is particularly significant because the majority of pharmacist visits were routine postdischarge referrals rather than consults for specific medication-related concerns. When compared to historical control visits, the rate of DTP identification in pharmacist consult visits was also numerically higher. In addition, there was a 98% acceptance rate of pharmacist recommendations. The quality and clinical importance of pharmacist recommendations are reflected in the fact that 62% were judged as significant or very significant by the expert clinician panel.¹³²

Other Clinical Services Provided by SOT Pharmacist Specialists

The incidence of diabetes is increased in adult organ transplantation recipients. As many as 30-45% of solid organ adult transplantation patients have diabetes before transplantation or

develop post-transplantation diabetes. Multifactorial causes include a lower threshold for the diagnosis of diabetes, an increase in awareness by transplantation providers, and an increase in the ethnic diversity, age, and weight of the transplantation patient population. Increased use of immunosuppressive regimens also had an impact on the development of diabetes. The complexity of medical management, pharmacologic therapy, and diet and lifestyle changes are often overwhelming for the transplantation patient who also has diabetes. Patient-centered education and intervention that is integrated within the transplantation team and includes the pharmacist providing the support needed to allow the patient with post-transplantation diabetes to have optimal organ function with minimal complications associated with diabetes and is crucial to long-term management of post-transplantation diabetes.¹³³

SOT pharmacist specialists have also demonstrated clinical value in supportive care services for transplantation patients.

- A single center, retrospective study evaluated the impact of SOT pharmacist specialist interventions on the completion of vaccination schedules at the time of kidney transplantation. Patients who received pharmacist-led vaccination recommendations prior to transplantation were compared to patients without pharmacist recommendations. The pharmacist intervention resulted in significantly more patients being up-to-date with vaccination schedules at the time of transplantation and suggest that an SOT pharmacist specialist can increase vaccination schedule compliance between time of evaluation and transplantation.¹³⁴
- The management of non-melanoma skin cancers in SOT transplantation recipients presents unique clinical challenges. SOT recipients are at a 65-fold increased risk for developing cutaneous squamous cell carcinomas, the most common non-melanoma skin cancer that develops after transplantation. Management requires patient education, frequent motivation for vigilance, regular follow-up, and interdisciplinary collaboration between members of the transplantation team, including pharmacists.¹³⁵

Recognition of SOT Pharmacist Specialists

Transplantation patients have uniquely complex pharmacological needs. Pharmacists require extensive post-doctoral training to develop the expertise necessary to serve this patient population. While many physicians, advanced nurse practitioners, and physician assistants certainly understand basic principles of pharmacology, transplantation patients have greater pharmacotherapy needs which demand the skills of a transplantation pharmacist who has undergone specialized training. Pharmacists provide knowledge of pharmacology, optimal dosing, appropriate monitoring, management of drug interactions, and management of medication side effects while contributing to program-wide initiatives and clinical program developments. Transplantation pharmacists are best positioned to "translate" an ideal

theoretical medication regimen into one that is practical (e.g., scheduling medications for optimal outcomes considering drug interactions and pharmacology, medication adjustments per insurance/hospital formulary or affordability) and provide the corresponding medication education and training for the patient to prevent rejection and readmission.¹³⁶

The transplantation pharmacist's highly specialized training, designed to maximize patient outcomes in this unique patient population, cannot be replicated by other professions on the interdisciplinary team. A transplantation team without the contributions of a pharmacist's specialized training and expertise would result in suboptimal outcomes. From a pharmacotherapy perspective, transplantation recipients are among the most complex of all inpatient populations to manage.

There is a need for a mechanism to identify, recognize, and provide access to SOT pharmacist specialists who can meet patient needs for specialized medication management. Individuals who have obtained specialist recognition and have attained the additional training, experience, and expertise to lead patients, the profession, other health care providers, and society to better public health are necessary for managing diseases and reducing preventable conditions, complications, and sequelae. Specialty recognition of SOT pharmacy practice by the Board of Pharmacy Specialties (BPS) would provide a mechanism through which pharmacists could attain voluntary certification that recognizes achievement of a focused and distinct level of specialized knowledge, experience, and skills in serving the unique medication needs of patients.

A significant number of pharmacists have prepared themselves to meet public health needs by providing specialized care for SOT patients that includes comprehensive medication management, collaborating with other health care providers, and addressing a broad range of other health-related needs. In addition, SOT pharmacist specialists have provided leadership in the profession in establishing patient care services, precepting student pharmacists in required advanced pharmacy practice experiences (APPEs) and introductory pharmacy practice experiences (IPPEs), and training other pharmacists through residencies, fellowships, and live and enduring educational programs. These pharmacists have also engaged in leadership positions within multidisciplinary transplantation organizations such as the American Society of Transplantation, the American Society of Transplant Surgeons (ASTS), the ISHLT, and the National Kidney Foundation (NKF).

By any measure, the complex issues facing transplant patients cannot be adequately addressed by pharmacists with entry-level knowledge and skills in general practice or other types of pharmacy specialties. BPS certification of SOT pharmacist specialists will lay the groundwork for

other committed and interested pharmacists to focus their professional development, training, and educational efforts on preparing themselves to fully meet this public health need.

Overlap with Other BPS Specialties

There is likely some potential level of overlap between the proposed SOT pharmacist specialist and the existing BPS specialties in pharmacotherapy, critical care, pediatrics, ambulatory care, infectious disease, and oncology. The petitioning organizations feel strongly that the evidence presented in this petition will justify a SOT pharmacist specialty as a stand-alone specialty.

SOT pharmacist specialists combine the principles of several subspecialties to be effective members of the transplantation patient care team. This includes optimization of pharmacotherapy across the continuum of care from the pre-surgical evaluation through the perioperative period and advancing through long-term care in the outpatient setting for adult and pediatric transplantation recipients and living donors. Knowledge of drug delivery systems, pharmacoeconomics, drug information and drug literature evaluation, statistics, immunology, pharmacokinetics, pharmacology, pharmacogenomics, pathophysiology, pharmacotherapy, pharmacovigilance, regulatory standards, and medication safety is a necessity. SOT pharmacist specialists have substantial expertise in the management of novel and traditional immunosuppression and incorporate this with other subspecialties, such as infectious diseases, cardiology, hepatology, nephrology, pulmonology, endocrinology, hematology, pediatrics, internal medicine, and critical care, in order to manage patients with multiple comorbidities.¹³⁷

There are significant differences between the specialized practices of SOT pharmacy practice and pharmacotherapy that make it important to recognize SOT pharmacist specialists independently. The knowledge, skills, training, and functions of pharmacotherapy, critical care, pediatrics, ambulatory care, infectious disease, and oncology specialists lack the depth of specificity required to provide care to SOT patients, without additional training and experience.

It has long been recognized that the base of knowledge and skills in medicine far exceeds an individual's ability to master every facet of medicine. Currently, physicians may become certified in any of 150 medical specialties or subspecialties.¹³⁸ Among the specialties in medicine, overlap is apparent in many areas. This overlap is unavoidable given the complexities and commonalities within patient care. In comparison with the potential SOT and pharmacotherapy specialties, separate and distinct medical specialties dealing with transplantation are present in internal medicine and pediatrics and represent three subspecialties. Likewise, in pharmacy, the breadth and depth of knowledge exceed an individual's ability to master content and skills at an advanced level in all areas of practice and pharmacotherapy. A specialty SOT pharmacy practice is distinct from other BPS specialties in its

emphasis on a complex and unique patient population that requires substantially distinct specialized knowledge, skills, and abilities working. It is in the best interest of both the profession and patients to recognize pharmacists with specialized training and expertise in SOT.

GUIDELINE 2. Specify how the functions performed by pharmacists in the proposed specialty address these specific needs of the public's health and well-being such as improved safety, cost, quality of life and outcomes. Included in this discussion should be a description of how the public's health and well-being may be at risk if the services of practitioners in the proposed specialty are not provided.

According to the *BPS Role Delineation Study for Solid Organ Transplantation*, SOT pharmacists have the specialized knowledge and expertise needed to manage complex medication regimens unique to the SOT population in addition to clinical and regulatory needs not encountered in any other pharmacy specialty. SOT pharmacists are specially trained to design, recommend, implement, monitor, and modify pharmacotherapeutic plans to optimize outcomes. They review, analyze, and reevaluate multifaceted clinical and outcomes data in order to provide quality care and assess program effectiveness. Finally, they provide education and counseling throughout the transitions of care.¹³⁹

Functions of SOT Pharmacist Specialists

SOT pharmacist specialists have extensive clinical skills and expertise in therapeutic management. These specialists evaluate patients for living donation or transplantation using appropriate assessment methods and resources in order to identify pharmacologic risks, contraindications, and other considerations. Specialists interpret pertinent health-related information in accordance with evidence, standards, and guidelines throughout all phases of transplant-related care in order to determine if and when modifications to therapy are warranted. Individualized treatment plans are developed in accordance with evidence, standards, and guidelines. SOT pharmacist specialists facilitate continuity of care by communicating pertinent patient information during transitions of care in order to avoid medication-related errors and complications. These pharmacists advocate for access to medications using prescription drug plans and other resources and implement a plan to overcome patient-specific barriers to care using continuous assessment.¹⁴⁰

Administration and practice development are core functions of SOT pharmacist specialists. These professionals establish sustained, collaborative, professional relationships with members of the interdisciplinary transplantation team and consultant services in order to promote patient care across the continuum. SOT pharmacist specialists contribute to the transplantation team and enable team members to have a more in-depth and comprehensive perspective when

designing and implementing drug regimens for each transplantation recipient.¹⁴¹ The utilization of a team approach to SOT patient care and a growing body of evidence supports the expanded role of clinical pharmacists as members of the health care team with beneficial contributions directly related to safe, effective, and appropriate medication in SOT patients. A study of 290 kidney transplantation patients evaluated the impact of a transplantation specialty pharmacy (TSP) program on health care provider satisfaction. Ninety-six percent of providers (nurses, nurse practitioners, and physician assistants) believed the pharmacy improved continuity of care, and 91% reported spending less time on pharmacy-related problems after the program's initiation.¹⁴²

SOT pharmacist specialists establish institutional guidelines, policies, procedures, and formularies that are consistent with evidence, regulation, and/or current practice guidelines and standards in collaboration with other stakeholders in order to facilitate patient care. They perform quality improvement activities in order to enhance the safety and effectiveness of medication-use processes in SOT. Specialists monitor compliance with guidelines, policies, procedures, and formularies in partnership with institutional leadership in order to identify shortcomings and implement performance improvement initiatives. SOT pharmacist specialists implement processes for cost effective care focusing on continuous quality improvement, patient safety, and outcomes in order to justify modifications in transplantation pharmacy services.¹⁴³

Core functions for SOT pharmacist specialists include information management and education. Specialists evaluate biomedical literature with regard to study design, statistical analysis, and applicability of results to the SOT population. They contribute to the body of transplantation knowledge for the purpose of improving patient outcomes and medication use. SOT pharmacist specialists educate SOT candidates, recipients, donors, and caregivers on issues related to medications and medication adherence. They also disseminate information regarding public health initiatives in order to promote health, safety, and wellness in transplantation patients. Specialists have a specific focus on educating health care professionals, trainees, and other stakeholders concerning medication-related issues associated with the care of transplantation patients.¹⁴⁴

Preserving and ensuring public health is also a function of SOT pharmacist specialists. These pharmacists use population-level data to develop, implement, and assess practices or strategies for addressing health promotion and disease prevention. They also provide information and guidance to the public regarding organ donation and allocation.¹⁴⁵

GUIDELINE 3. Describe how functions provided by the practitioners in the proposed specialty will fulfill the responsibility of the profession of pharmacy in improving the public's health. Petitioners may use the following Vision for Pharmacists' Practice adopted by the Joint Commission of Pharmacy Practitioners in January 2014 when defining responsibilities of the profession:

Patients achieve optimal health and medication outcomes with pharmacists as essential and accountable providers within patient-centered, team-based health care

Pharmacists have a responsibility to the American public to ensure that medications are used appropriately and desired medication outcomes are achieved. Most national pharmacy organizations, including the American Pharmacists Association, the American Society of Health-System Pharmacists, the American College of Clinical Pharmacy, the American Association of Colleges of Pharmacy, and BPS, support expanded credentialing of pharmacist specialists, similar to credentialing in other health professions, to meet the vision for the future of pharmacy practice and to improve patient care.

Achieving the vision of the Joint Commission of Pharmacy Practitioners will require recognized and credentialed SOT pharmacist specialists with the knowledge, skills, and abilities to manage complex medication needs specifically for transplantation patients. SOT pharmacist specialists manage sophisticated medication regimens, develop and refine individualized patient care plans, work collaboratively as members of the interdisciplinary health care team, conduct and publish research, and maintain long-term relationships with patients, families, and caregivers.

SOT pharmacist specialists serve as practice leaders within their institutions, organizations, the profession of pharmacy, and the more expansive area of transplantation. They often serve as preceptors for advanced pharmacy practice experiences (APPEs), introductory pharmacy practice experiences (IPPEs), and postgraduate year one and postgraduate year two residency experiences. A new specialty in SOT pharmacy practice would be consistent with the BPS mission: "to improve patient care by promoting the recognition and value of specialized training, knowledge, and skills in pharmacy and specialty board certification of pharmacists."¹⁴⁶ BPS specialty certification is not only the pharmacist's path to advancement in contemporary medicine but also a roadmap for pharmacists who desire to gain additional training and knowledge to differentiate themselves from pharmacists in general practice or other specialty practices. By achieving certification, pharmacists acquire a tool that provides assurance of their specialized knowledge and skills to other health professionals, stakeholders, and society. Additionally, the complexities of care for transplantation patients continue to multiply. Advances in medications and technology are driving the need for specialized training to expand

pharmacists' pharmacotherapy knowledge and patient care skills to manage highly complex medication regimens for SOT patients.

All pharmacists perform important patient care functions in serving the public health needs of society. By definition, pharmacists who voluntarily choose to earn BPS certification are prepared to meet the needs of patients within their respective specialty areas more effectively than entry-level pharmacists because they have acquired specialized knowledge and training beyond the Doctor of Pharmacy degree and minimum standards for licensure. In all areas of SOT pharmacy practice, collaboration with other members of the health care team is critical to prevent medication errors, ensure appropriate medication use, ensure that desired therapeutic outcomes are achieved, and decrease graft failures. The needs of SOT patients are sufficiently distinct to support recognition of SOT pharmacist specialists as a separate and distinct specialty. Effective, successful, high-quality care for these patients will require the full application of specialized knowledge and skills of SOT pharmacist specialists and those who would seek to achieve specialty recognition in SOT pharmacy practice.

The ultimate goal of pharmacotherapy specialization is to ensure quality patient care and improve therapeutic outcomes. As the transplantation field continues to expand in both scope and complexity, there will be an increasing need for highly trained pharmacotherapy specialists with expertise in transplantation. A stand-alone specialty in SOT pharmacy practice would clearly identify for employers, third-party payers, physicians, patients and the public those individuals who have specialized competencies and expertise in transplantation.

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CRITERION B: Demand

The area of specialization shall be one in which there exists a significant and clear health demand to provide the necessary public reason for certification. ***This criterion emphasizes DEMAND.*** BPS defines DEMAND as a willingness and ability to purchase the services of a Board Certified Pharmacist.

The demand for solid organ transplantation (SOT) pharmacist specialists can be expressed in terms of the value of interprofessional collaboration and is expressed by other health professionals and patients through letters of support. Employment trends and surveys that document increased demand for SOT pharmacist specialists also reflect a significant and clear health demand.

Demand for Solid Organ Transplantation Pharmacist Specialists' Services

SOT pharmacist specialists engage in patient evaluation prior to transplant, ensuring a systematic assessment of a patient's clinical status, evaluation of all medications (including prescription and nonprescription agents and herbal/nutritional supplements), development and implementation of a care plan, follow-up evaluation and medication monitoring, and accurate documentation for the entire process of care. Increasingly, SOT pharmacist specialists are engaged in ambulatory care practice supporting patients post-transplant. The continuum of care for transplant patients is complex and unique and requires full engagement with an interprofessional care team.

The importance of demonstrating compliance with regulatory and practice requirements is expected within the health care landscape. Requirements for transplantation pharmacists' involvement in the care team are well codified by federal regulatory bodies as well as practice standards and guidance. As the role of the SOT pharmacist specialists has grown, so has the number of transplant pharmacists across the U.S. This is particularly the case since the Centers for Medicare and Medicaid Services (CMS) began certifying transplant centers. CMS has outlined the specific expectations for transplant centers within the Medicare program, hospital conditions of participation, and requirements for approval and reapproval of transplant centers to perform organ transplants. "Section 482.98(e) of this final rule states that the multidisciplinary transplant team must be composed of individuals with the appropriate qualifications, training, and experience in the relevant areas of medicine, nursing, nutrition, social services, transplant coordination, and pharmacology;" CMS expects that "the team will

include an individual with expertise in transplant pharmacotherapy” (e.g., clinical pharmacist) to be a requirement for accreditation, given the highly specialized and complex drug regimens used.¹

The Organ Procurement and Transplantation Network (OPTN) is a unique public–private partnership that links all of the professionals involved in organ donation and transplantation. The OPTN is administered by the United Network for Organ Sharing (UNOS) under contract with the Department of Health and Human Services. Bylaws developed by UNOS specify the exact criteria that each transplantation program must follow to be compliant with the standards and specifically recognize and identify the roles and responsibilities of the pharmacist as an essential member of the transplantation team. Specifically, these bylaws mandate that “all transplantation programs should identify one or more pharmacists who will be responsible for providing pharmaceutical care to solid organ transplant recipients.” Further, the bylaws state that the transplantation pharmacist should be the designated member of the team to serve as the drug information expert and should be responsible for ensuring the adherence to institutional protocols, screening requirements, preventing drug interactions, and providing patient and caregiver education, along with additional responsibilities as outlined by the transplantation center.²

The International Society for Heart and Lung Transplantation (ISHLT) also strongly supports and recognizes the value of SOT pharmacist specialists. The *ISHLT Guidelines for the Care of Heart Transplant Recipients* state, “Transplant centers should strive to have specialty-trained pharmacists or physicians with expertise in pharmacology as part of the multidisciplinary team.” The guideline further asserts, “Integration of input from pharmacists and infectious disease specialists is important during the development of treatment protocols for heart transplant recipients.”³

The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline on the monitoring, management, and treatment of kidney transplant recipients assists practitioners, including pharmacists, in caring for adults and children after kidney transplantation. The guideline specifically recognizes the value of the pharmacist’s role in addressing patient nonadherence and highlighting the value of pharmacist contributions within the health care team.⁴

Given these mandates for the specific composition of the interprofessional transplant team, the demand for SOT pharmacist specialists has increased rapidly and dramatically. So much so that, in order to meet the needs of these accreditation standards, some transplant centers may have

hired and/or identified pharmacists without specific organ transplantation training due to lack of available fully trained personnel, which speaks directly to the demand for trained and credentialed pharmacists in SOT.⁵

The inclusion of pharmacists as part of the clinical practice team for transplantation is also strongly reinforced in the literature. Pharmacists play a critical role in medication management, resolution of drug therapy problems, adherence, and the management of other chronic diseases for transplantation patients. A review of available evidence regarding the role and impact of pharmacy services in the care of SOT patients concluded that clinical pharmacists address unmet needs, resolve common drug-therapy problems, ensure disease- and treatment-related outcomes, manage medication compliance, and counsel transplantation patients on medication-related issues.⁶ The breadth and depth of literature supporting the role of the SOT pharmacist specialist can be found in Appendix G-1 and Appendix G-2.

GUIDELINE 1. Include statements of support by stakeholder organizations and other entities, other than petitioners, that attest to the demand for pharmacists with training and knowledge to provide services in the proposed specialty. Stakeholder organizations can include non-pharmacist health professional organizations, public and private health care entities, and consumer organizations.

Appendix B-1 provides statements from the following individuals and organizations that specifically attest to the demand for pharmacists with training and knowledge to provide services in SOT practice:

- **American Society of Transplantation**
 - Ronald G. Gill, PhD
President
 - Dianne McKay, MD
President-Elect

- **Baylor Scott & White Health**
 - Bruce Kaplan, MD
 - Raleigh R. White Professor and Vice President
 - Department of Surgery

- **E. M.**
 - Patient

- **Medical University of South Carolina (MUSC)**
 Prabhakar K. Baliga, MD
 Fitts-Raja Professor of Surgery
 Chairman, Department of Surgery
 Chief, Division of Transplant Surgery

- **Ochsner Medical Center**
 George E. Loss, Jr., MD, PhD
 Chief of Surgical Services
 Chairman, Department of Surgery
 Chief, Multi-Organ Transplant Institute

- **Lana Schmidt, MBA**
 Patient

- **Tampa General Hospital**
 Melissa N. Roberts, MSN, RN, CPTC
 Divisional Director, Transplant Center and MCS Program

- **University of Illinois**
 - Andrew J. Donnelly, PharmD, MBA, FASHP
 Director of Pharmacy
 University of Illinois Hospital & Health Sciences System
 Clinical Professor and Associate Dean for Clinical Affairs
 University of Illinois at Chicago College of Pharmacy

- **University of New Mexico**
 - Joanna Saczek, BSN, RN
 Transplant Services Director
 - Pooja Singh, MD, FASN
 Associate Professor of Medicine
 Division of Nephrology
 Medical Director, Renal Transplant Services
 - Louis E. Achusim, PharmD, MS
 Executive Director, Pharmaceutical Services
 Clinical Associate Professor, College of Pharmacy

- **University of Virginia School of Medicine**

Josè Overholzer, MD, MHCM, FACS
Professor, Surgery and Biomedical Engineering
Director, Charles O. Strickler Transplant Center
Chief, Division of Transplantation

- **University of Wisconsin (UW) Health**
 - Arjang Djamali, MD, MS, FASN
Professor of Medicine and Surgery
Head, Nephrology Division
Department of Medicine
 - Dixon B. Kaufman, MD, PhD, FACS
Ray D. Owen Professor and Chair
Division of Transplantation
Department of Surgery
Medical Director, Transplant Service Line
Surgical Director, Kidney Transplantation
 - Didier Mandelbrot, MD
Professor of Medicine
Medical Director of Kidney and Pancreas Transplantation
Medical Director of Living Kidney Donation

- **Cassandra Votruba, PharmD**
 - Patient
 - PGY1 General Clinical Practice Resident
University of Wisconsin Hospital and Clinics

Key points within these letters of support speak to the demand for SOT pharmacist specialists. Some of the valuable points that underscore the demand for specialty recognition are outlined below, and the complete letters of support are attached as Appendix B-1:

Ronald G. Gill, PhD, President of the **American Society of Transplantation (AST)** and **Dianne McKay, MD**, President-Elect of AST detail the role and significance of the SOT pharmacist specialist to the transplant team and the patient. *Their practice is unique among other pharmacy specialties because they care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. Their role on the SOT team includes creation of a customized pharmacotherapeutic regimen, they provide knowledge of pharmacology, optimal dosing, appropriate monitoring,*

management of drug interactions, and management of medication side effects while contributing to program-wide initiatives and clinical program developments. Just as important is the SOT pharmacist specialist's understanding of the everyday challenges, both socially and financially, that may impact a patient's ability to comply with this plan. The SOT pharmacist specialist is key to this effort, understanding the patient's medical needs while recognizing potential challenges from both the patient and caregiver perspective in managing the often-challenging routine of multiple medications at multiple times to protect the lifesaving organ graft.

The SOT pharmacist specialist is a valued member of the transplant team within our Society's membership and in transplant programs across the country. They bring an expertise that is critical to the clinical planning for an individual's transplant journey, but they also serve as an educational resource and advocate for their patients beyond the transplant event and hospitalization. They meet with recipients and donors to teach them about their medication plans before hospital discharge. Additionally, they serve as a trusted advocate from a regulatory perspective when patients struggle with coverage issues for their critical medications. Their understanding of FDA regulation and payer coverage is just as valuable as their clinical knowledge to the success of our patients in many cases. '

Bruce Kaplan, MD, is a practicing transplant physician and is co-chair of the American Society of Transplantation Kidney and Pancreas Community of Practice. He serves as the Executive of *Transplantation* and served as Deputy Editor of the *American Journal of Transplantation* for 14 years. His letter outlines the demand for the unique skills and duties SOT pharmacist specialists employ at **Baylor Scott & White Health**. *Transplant recipients make a unique population of patients whose postoperative outcomes depend on lifelong adherence to a complex medication regimen. Transplant medications are often prescribed "off label," and active interpretation of available literature is essential to ensure medications are utilized to their best potential. Moreover, management of comorbidities and drug toxicities often requires specialized training. Transplant pharmacists are uniquely positioned to collaborate with physicians to meet and maintain complex needs of the transplant population. Consequently, transplant regulatory agencies recognize that transplant pharmacists are essential members of every transplant team today. Their participation is required in the evaluation and care of organ donors, transplant candidates and transplant recipients. They also participate in Transplant Suitability Committees, Adverse Event Analysis, and Quality Assurance & Performance Improvement Committees. Transplant pharmacists have made significant contributions to the field of transplant research that lead to lasting and significant*

changes in practice. They are key members of the interdisciplinary research team. In this role, they catalyze research initiatives, organize, analyze, and interpret data in a highly regulated field. As investigators, their contribution allowed us to make considerable progress in evaluating safety and efficacy of immunosuppressant medications in transplant recipients.

Transplant patient **E. M.** shared a specific experience that illustrates the impact a SOT pharmacist specialist during a kidney transplant. *Approximately five years ago, I was told by my transplant physician that I had indications for diabetes. Apprehensive and worried for what this new development would have on my transplant and health, my transplant physician had me speak with my transplant pharmacist. My transplant pharmacist proceeded to go thru all of my [current] medications and new medications, more than 15 individual scripts. She answered questions about each medication and how it would interact with other medications and my transplant. She also gave me tips on ideal methods and best practices for taking my medications. On a late Friday afternoon, near the end of clinic time, as the last patient in a busy clinic, my transplant pharmacist spent over an hour helping me to adjust to these circumstances. The specialized knowledge of transplant care coupled with their pharmaceutical expertise made sure that I knew what was ahead of me. From my conversations with other members of my care team, this is not a singular instance but a standard to ensure that patients are well equipped to deal with their treatment regimen. While this is an experience regarding one transplant pharmacist and one patient, I feel it is indicative of the overarching value and care that is and can be provided by having a transplant pharmacist with specialized training in transplant. Physicians, nurses, and other members of the care team are made better where a transplant pharmacist, who has the training and specialized knowledge to deal with transplant issues, is a part of the care team.*

Prabhakar K. Baliga, MD, is a Fitts-Raja Professor of Surgery, Chairman of the Department of Surgery, and Chief of the Division of Transplant Surgery at the **Medical University of South Carolina**. Dr. Baliga specifically describes the demand for the specialized role of the SOT pharmacist specialist. *Drug therapy for solid organ transplant recipients is becoming increasingly complex. Solid organ transplant pharmacotherapy must consider the complex comorbidities of donors and recipients. Protocols and guidelines must be continually updated and adapted based on novel practice and individual center outcomes. Transplant pharmacists are involved in each phase of transplant (pre, peri, and post) and optimize transitions of care. Complex combinations of drug therapy may present special issues related to drug interactions or adverse events that are unique in the solid organ transplant population. Most of these complex patients*

are treated in inpatient or outpatient centers where a number of other similarly complex solid organ transplant patients are seen. This concentration of patients in these centers creates a demand for placement of pharmacists to help manage their drug therapy, in collaboration with other caregivers.

Dr. Baliga also speaks to the value of board certifications and the value that certification of SOT pharmacist specialists would bring. *Medical staff, other hospital leaders and the public recognize “board certification” as important evidence of some degree of competency. The Transplant Pharmacy Specialist credential will provide an essential credential to ensure the transplant pharmacist pedigree is not compromised; I therefore strongly encourage pursuit of this petition*

The Chief of **Ochsner Medical Center’s** Multi-Organ Transplant Institute, **George E. Loss, Jr., MD, PhD**, explains the multidisciplinary and safety functions of a transplantation pharmacist. *Our multidisciplinary approach is mandated by UNOS and CMS, and a crucial member of our team is the transplant trained specialty pharmacist. Our PharmDs are integrated within the specific organ transplant teams. Drug interactions are common, and our PharmDs are necessary to ensure that we deliver effective, safe care. Transplant recipients are among the most complex patients in our hospital. Sepsis is the most common cause of death, and rejection is the most common cause of allograft dysfunction. The transplant pharmacist is necessary to help create and optimize our immunosuppression strategies and thus optimize outcomes. Solid organ transplant programs are almost always located in academic medical centers. Beyond direct patient care, patient education and protocol development, transplant pharmacists are often involved in discovery and research. Dr. Loss further states that certification will ensure that pharmacists who want to pursue a career in transplantation understand and are prepared for the unique and complex challenges of working in this specialty. It is truly a unique set of skills that are required and it deserves special recognition.*

Lana Schmidt, MBA, is a **patient** who received a kidney transplant and benefitted from the expertise of a SOT pharmacist specialist. *I had a very unusual situation with extremely high antibodies...and the chances of getting a transplant were slim to none. The transplant pharmacist thoroughly did all of the research on the novel drug and put together a comprehensive manual that we could use to try to attempt to secure funding for the drug. The information my transplant pharmacist put together was extremely useful and so specific to my situation. She would go out of her way and speak to the organization we were trying to secure funding with and explain specifics even further. Because of her outstanding work and remarkable transplant knowledge, we were able to*

secure the funding so I could receive a kidney transplant! She helped pave the way for this drug to be used more widely and gave hope to highly sensitized patients to be able to receive a transplant. Ms. Schmidt also described the value and importance of specialists in her care, differentiating her experience with generalist practitioners, offering her observations that “I trust the care, information and expertise I receive from the transplant pharmacists. The regular pharmacists lack the specialized knowledge and training to understand transplant and the unique needs of transplant patients. It is critical to have pharmacists that understand the nuances of drugs used for transplantation.”

Melissa N. Roberts, MSN, RN, CPTC, Divisional Director of **Tampa General Hospital’s** Transplant Center and MCS Program illustrates the demand of transplant pharmacists. *At my previous organization, with the onset of the new CMS regulations in 2007, we tripled the Transplant Pharmacy support we had for all of our organ programs to remain in compliance with the regulations. At Tampa General, we are currently drafting a proposal to double the size of our Transplant Pharmacy team due to the need expressed by both patients and our teams. The presence of our pharmacists on rounds, in our clinics, and in our multidisciplinary meetings makes for much safer care for our patients. I have observed Transplant Pharmacists catch errors in the ordering of immunosuppression time and time again. [O]ur transplant pharmacists are oftentimes the first to detect a financial barrier with a patient after transplant, and they work to ensure that patient received needed medications. The Transplant Pharmacist has a vast fund of knowledge that includes not only specialty medications, but health literacy, patient adherence, assessment, and an understanding of the pharma industry. The training and expertise of our Transplant Pharmacists is absolutely irreplaceable.*

Andrew J. Donnelly, PharmD, MBA, FASHP, the Director of Pharmacy at the **University of Illinois Hospital & Health Sciences System**, explored the history, expansion, and value of the pharmacy transplant program within his organization. *One of the first areas that we identified the need for patient-focused clinical pharmacy services was transplant, and we have had dedicated clinical pharmacists practicing in this specialty since 1977. It was also one of the first areas in which we developed a collaborative drug therapy management (CDTM) agreement. More recently, the CDTM agreement has been modified to a clinical care protocol, which allows our transplant clinical pharmacists the ability to order/adjust medications, labs, etc. per the protocol pathway in the electronic health record. This was one of the first protocols developed in the hospital and approved by the Medical Staff Executive Committee, which is an indication of the value senior level leadership and the medical staff places on the services provided by our transplant clinical*

pharmacists. Our transplant clinical pharmacists are key members of and contributors to transplant's research and quality teams, as well as its operations committee. Over the last decade, we have increased the size of our transplant clinical pharmacist team from 2 to 5. We have been working for several years to navigate the credentialing and privileging process for our clinical pharmacists. As a testament to our transplant clinical pharmacist group's scope of practice and integration with the transplant group, we selected this group to be the first to undergo this process. We have identified board certification, which would be transplant board certification, if it was available, as one item needed for credentialing. All our transplant clinical pharmacists are board certified (BCPS), an indication of this group's understanding of the importance of board certification. Dr. Donnelly also shares the value that his health system places on board certification sharing that pharmacists who obtain board certification receive a \$2,000 salary increase as recognition for their certification.

Transplant leaders from the **University of New Mexico** explained the importance of hiring a qualified pharmacist trained in transplantation, as well as the significance a SOT pharmacist specialist has on the transplant team. *Our institution waited almost a year to hire a transplant pharmacist. We were committed to finding the right person with the experience and knowledge needed to help us grow our program. Our (transplant) pharmacist sees virtually every transplant recipient pre- and post-transplant and makes interventions to optimize treatment in the hospital and clinical settings. It is evident that a transplant pharmacist's knowledge of clinically relevant drug interactions is much deeper than pharmacists who are unfamiliar with transplant medications, and this makes a huge difference in complex treatment regimens. Additionally, the sharing of this knowledge has improved the understanding of transplant medications not only for patients but for our transplant staff. Our pharmacist is also actively involved with protocol development and quality improvement projects and elevates these initiatives with her expertise in transplant medication management. The state of New Mexico has created a specific license for pharmacist clinicians. These pharmacists operate independently under the supervision of a physician and are able to expand patient access to health care. For us, board certification in transplant pharmacy would help us identify pharmacists who have the expertise needed to be a successful and credible transplant pharmacist clinician. As we expand our program, it is our goal to have our pharmacist obtain a pharmacist clinician license. Board certification in transplant pharmacy will give us leverage to discuss reimbursement strategies with local insurance companies so that we can continue to provide high quality care.*

Josè Overholzer, MD, MHCM, FACS, of the University of Virginia School of Medicine

explains the growth occurring in the transplant field and the significant role SOT pharmacist specialists have on the transplant team. *Within the Charles O. Strickler Transplant Center, we are able to offer our patients access to six specialized SOT pharmacists. With continued additions to the transplant waitlist, we as an institution are strategizing to double our transplant volumes. Our philosophy within the Division of Transplantation is that of teamwork and multidisciplinary care. Ensuring quality outcomes for our many patients cannot be achieved without the implementation, design, and monitoring of pharmacotherapeutic plans. Incorporating PharmDs into daily transplant care has become a crucial part of all multidisciplinary transplant programs.*

Members of the transplant team at **University of Wisconsin (UW) Health**, delve into the significance of solid organ transplantation pharmacist specialists on the transplant team. *At UW Health, transplant pharmacists are involved in all phases of care, including both inpatient and outpatient settings. These pharmacists are expertly trained to provide high quality, direct patient care to a very unique and challenging patient population. They are essential members of our multidisciplinary health care team and provide critical input by optimizing pharmacotherapeutic regimens to improve outcomes, safety, and adherence, all of which are necessary for a successful transplant. Their expertise in transplant-specific drug interactions, medication adverse effects, and alternative modes of therapy is crucial and a clear indicator that specialization should be required for advanced practice. Furthermore, our pharmacists independently practice under several delegation protocols to treat specific disease states. Not only does this save us a considerable amount of time but we fully trust in their specialized training to manage these complex patients. Beyond patient care, our pharmacists are heavily involved in academic research and patient safety initiatives, including protocol development, guideline authorship, and quality metrics analysis. These projects are often high quality, very detailed, and serve as evidence that specialized knowledge is needed to contribute to a robust transplantation program. On top of that, our pharmacists are committed to advancing the practice of transplantation medicine and are involved nationally within the American Society of Transplantation. As medication therapies for solid organ transplantation becomes more complex and expensive, we believe that the pharmacist has a unique role on our team to ensure effective and safe medication use. With a board certified specialty in solid organ transplantation pharmacy, we can ensure that skilled pharmacists are identified to support and help expand our transplant program. Furthermore, certification will show other providers that the individual pharmacist has specialized knowledge in solid organ transplantation pharmacotherapy and continues to maintain that knowledge.*

Cassandra Votruba, PharmD, shares a unique perspective of transplantation pharmacist specialists as both a transplant patient who is also studying to become a transplantation pharmacist specialist. *I first became interested in pharmacy over a decade ago when I was undergoing chemotherapy for acute myeloid leukemia (AML) in which a medication preparation/order error resulted in a pulmonary toxic dose requiring a double lung transplant for survival. My world was upturned in the matter of a few days; I was a healthy teenager (except for the AML) who was seeing the light at the end of the tunnel with chemotherapy to being intubated with the limited possibility of ever getting off of a ventilator with a poor prognosis. While I had fantastic physicians who provided excellent clinical care, there were a lot of holes in the information being relayed to me. It was the transplant pharmacist who spent the time to explain the process and what to expect and who reassured me that I could get through this experience. It was the interactions that I had with my transplant pharmacist that I truly believe helped save my life, kept me healthy throughout the past decade, and ignited my interest in the pharmacy profession. As a PGY1 resident currently, I have had the privilege of completing an extended rotation in transplant in which I was able to learn a significant amount about transplant at one of the largest transplant facilities in the United States. Learning the intricacies of balancing immunosuppression with prophylactic and treatment anti-infectives with patient specific factors is a complexity that requires time and passion to learn. Developing the skills to be able to educate patients on their extensive medications, which often go from a handful prior to transplant to over 20 after, requires refining in order to not overwhelm the patient while still having an impact. All of these complexities combine to make complex patients who benefit best from trained, specialized pharmacists.*

These statements are representative of the broad base of support and acceptance for recognition of SOT pharmacist specialists and reflect the widespread and growing demand for specialized pharmacy services for SOT patients. All letter writers indicated their support for the recognition of SOT pharmacy practice as a specialty.

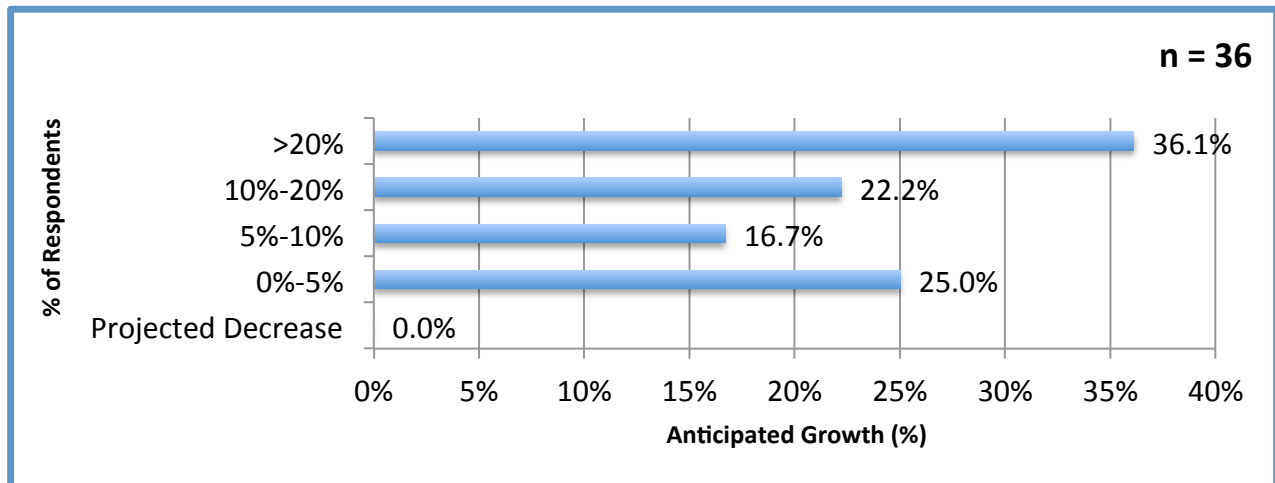
GUIDELINE 2. Include estimates of positions for pharmacists with specialized training and knowledge in the proposed specialty that are currently filled and those that are currently unfilled. Identify these positions by practice settings, if possible. Describe the sources and methods used to determine these estimates.

In an effort to estimate the number of positions for pharmacists with specialized training and knowledge in SOT practice, the petitioning organizations conducted a survey of SOT pharmacist specialists. The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* included a subset of questions that were completed by individuals with direct

responsibility for hiring pharmacists in SOT. Thirty-six individuals completed that portion of the survey.

Responding employers were asked to provide the total number of full-time equivalents (FTEs) allocated to serving SOT patients within their organization. Although the number of positions varied (range, 1 to 11 allocated FTEs), the average number of FTEs across responding organizations was 4.2. Hiring managers from 36 organizations that responded indicated that they had recruited for 81 SOT pharmacist specialists over the past 3 years and had filled more than 93% of these positions. These same employers estimate that they will fill an additional 47 positions over the next 3 years and currently report 15 vacant positions within their organizations. Employers also estimated the growth in the number of SOT pharmacy positions within their organizations over the next 5 years. These results are provided in Figure B-1.

Figure B-1. Anticipated Growth in Solid Organ Transplantation Specialist Pharmacist Positions over the Next 5 Years



This information provided by employers of SOT pharmacist specialists demonstrates a consistent and growing market for SOT pharmacist specialists.

Notably, the value of specialty recognition is becoming increasingly important to employers of SOT pharmacist specialists. Almost 90% of employers responding to the *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* indicated that it was “highly likely,” “likely,” or “somewhat likely” that they would require a new specialty credential in SOT if approved by the Board of Pharmacy Specialties (BPS) for newly hired pharmacists. Of those

responses, over 83% indicated that it was “highly likely,” “likely,” or “somewhat likely” that they would require a new specialty credential in SOT if approved by BPS for currently employed SOT pharmacist specialists. The survey also showed that only 47% of SOT pharmacist positions currently require BPS certification or another earned credential. These results imply that a credential more targeted to the specific needs of SOT pharmacist specialists would be in demand in the marketplace.

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- ⁵ Alloway RR, Dupuis R, Gabardi S, et al. Evolution of the role of the transplant pharmacist on the multidisciplinary transplant team. *Am J Transplant.* 2011 Aug;11(8):1576-83.
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CRITERION C: Number and Time

The area of specialization shall include a reasonable number of individuals who devote most of their practice to the specialty area. ***This criterion relates to the NUMBER of practitioners and the amount of TIME spent in the practice of the specialty.***

The data sources for determining the number of solid organ transplantation (SOT) pharmacist specialists in practice and the proportion of time spent in this specialized area of practice include:

- The *Role Delineation Study for Solid Organ Transplantation Pharmacists* conducted by Castle Worldwide on behalf of the Board of Pharmacy Specialties (BPS).¹
- Analysis of membership records of the American College of Clinical Pharmacy (ACCP) and the American Society of Health-System Pharmacists (ASHP).
- *A 2015 National Survey Assessing the Current Workforce of Transplant Pharmacists Across Accredited U.S. Solid Organ Transplant Programs*, published by the *American Journal of Transplantation*.²
- The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification*, administered in November 2017 by the petitioning organizations.

GUIDELINE 1. Estimate the number of pharmacists currently practicing in the proposed specialty. Identify the types of practice settings for these pharmacists (e.g., academic, hospital, managed health care, community). Describe the sources and methods used to determine these estimates.

SOT pharmacy practice has significantly grown over the past decade, as evidenced by the increased number of postgraduate year two (PGY2) specialty residency programs in SOT pharmacy. In 2007, there were two ASHP-accredited specialty residency programs. Today, these programs number 39, a 1,750% increase. Approximately 43 SOT clinical pharmacists graduate annually from these programs. The growth trend is toward expansion of specialty SOT pharmacy residency programs. Comparatively, the numbers of current PGY2 programs for other BPS recognized specialties are:

- Ambulatory care pharmacy – 151 programs
- Cardiology pharmacy – 33 programs
- Critical care pharmacy – 136 programs

- Infectious diseases pharmacy – 98 programs
- Nutrition support pharmacy - 1 program
- Oncology pharmacy – 101 programs
- Pediatric pharmacy – 54 programs
- Psychiatric pharmacy – 70 programs³

Analysis of the membership records from the petitioning organizations reveals approximately 760 pharmacists who self-identified as SOT pharmacist specialists. This number likely underestimates the actual number of practicing SOT pharmacist specialists since, presumably, not all practicing SOT pharmacist specialists in practice are members of the petitioning organizations or have self-identified as practicing SOT pharmacist specialists.

The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* was developed by the petitioning organizations to obtain additional quantitative data regarding workforce demand for SOT pharmacist specialists, proportion of time spent in SOT practice, and education and training pathways utilized. The survey was distributed to administratively identified ACCP and ASHP members in November 2017. The overall response rate was 36.4% (277 respondents), with 259 pharmacists indicating current practice in SOT. A majority of respondents (186) signed the online petition supporting specialty recognition for SOT pharmacist specialists. A copy of the survey instrument is attached as Appendix C-1.

As the number of transplant programs increase and the role of transplant pharmacists has expanded, so has the number of transplant pharmacists across the U.S. Driven by the Centers for Medicare and Medicaid Services (CMS) certification of transplant centers, SOT pharmacist engagement in multidisciplinary care has become the standard of care.^{4,5} A national survey of transplant centers identified that there was a median of 1.4 transplant pharmacist FTE positions (range 0.1-7.1) per 100 transplants. Currently, there are 254 transplant centers in the U.S. that performed 31,837 transplants from January through November 2017 alone.⁶ Transplant pharmacists are involved in the evaluation and care of all potential transplant candidates, follow patients post-transplant, and serve as a consultant for transplant patients managed on non-transplant services. Therefore, the number of patients that need transplant pharmacist involvement is exponentially higher than annual transplant volume.

As the enhanced role and scope of practice has created additional opportunities for SOT pharmacist specialists, there remains a need for additional specialists to fill these roles. Over 61% of respondents indicated that they are understaffed to perform the requirements for comprehensive coverage of transplant pharmacy services, and most felt that they needed 1-2 additional full-time employees (FTEs).⁷

Based on survey results and available literature, we estimate that a total of 1,000-1,200 pharmacists are currently engaged as SOT pharmacist specialists in the United States.

Of the pharmacists surveyed by the petitioning organizations, 97% indicated that they are practicing at a specialty level according to the following definition:

Definition of Solid Organ Transplantation Pharmacist Specialists

Solid organ transplantation (SOT) pharmacist specialists have the specialized training and knowledge needed to manage complex medication regimens unique to the solid organ transplantation population. Additionally, they are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. They care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. SOT pharmacist specialists provide evidence-based, patient-centered medication management. They design, implement, monitor, and modify pharmacotherapeutic plans to improve safety and efficacy, which leads to optimal short-term and long-term patient and allograft outcomes. Core responsibilities of SOT pharmacist specialists are to analyze and reevaluate multifaceted clinical and outcomes data to improve care and demonstrate ongoing quality assessment and process improvement as required by regulatory agencies. Finally, SOT pharmacist specialists are integral members of the interprofessional transplant team that facilitate medication adherence and pharmacotherapy education.

The *Role Delineation Study for Solid Organ Transplantation Pharmacists* describes pharmacists' responses about the practice setting and their primary role within that setting. Over 40% of the respondents reported practicing in a university-affiliated hospital setting or university hospital (21.0% university-affiliated hospital; 20.5% university hospital), while 23.5% practice in an academic institution. Another 18.5% reported practicing in an acute care/inpatient setting.⁸ Similarly, for the *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification*, most respondents were university hospital based (34.7% university-affiliated hospital; 39.2% university hospital), with approximately 13% of respondents from the community hospital, not-for-profit setting.

GUIDELINE 2. For the pharmacists identified in Guideline C1, estimate the percentage of time they devote exclusively to the practice of the proposed specialty. Describe the sources and methods used to determine these estimates.

Results from the role delineation study show that respondents are highly engaged in SOT practice, with 72% of respondents reporting 90-100% of their time spent in SOT pharmacy practice.⁹ The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* showed similar results with almost 68% of respondents spending 90-100% of their

time in SOT practice. A comprehensive national survey conducted by Taber et al. found that 64% of respondents reported that their time is dedicated entirely to transplant, while the remaining also cover nontransplant inpatient and outpatient services or have a staffing component. Most respondents (92%) stated there is a transplant pharmacist on site at least 5 days per week, and 71% of respondents indicated that on-call transplant pharmacist coverage is available 24 hours/7 days a week.¹⁰

The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* respondents indicated hours worked per week in their SOT practice as well as the proportion of time devoted to providing direct patient care according to the Definition of SOT Pharmacist Specialists. Figures C-1 and C-2 demonstrate that the majority of SOT pharmacist specialists practice full-time (81.8%) and provide direct patient care and services at the specialty level more than 50% of the time (91.3%).

Figure C-1. Hours Worked per Week in Solid Organ Transplantation Practice Site

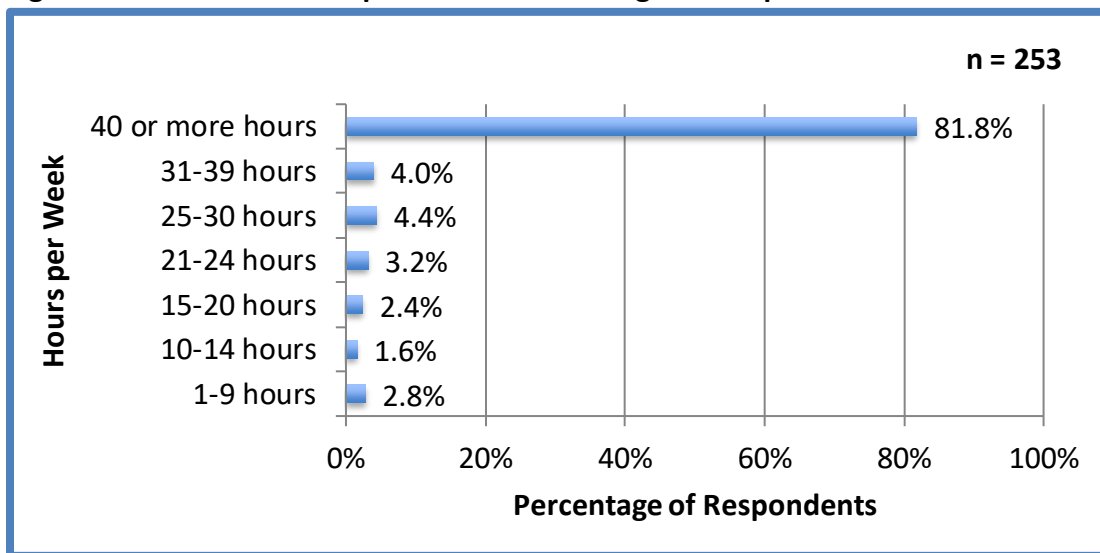
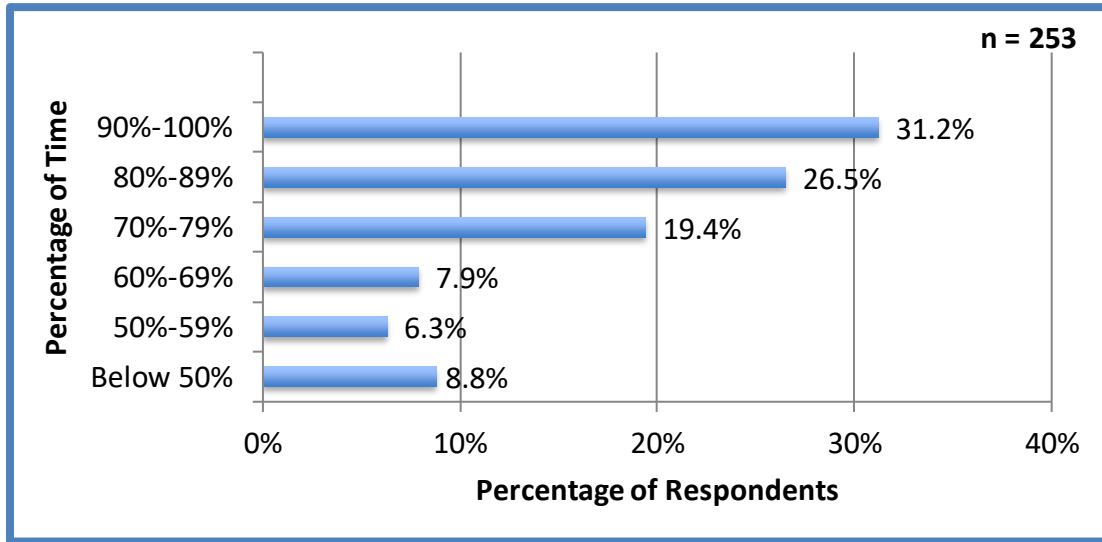


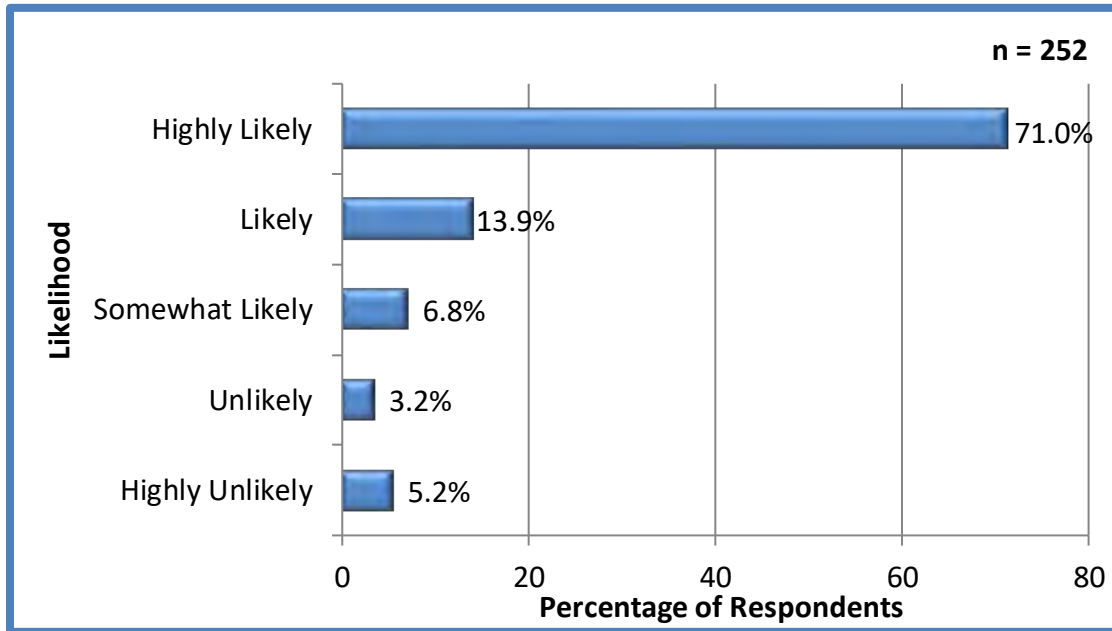
Figure C-2. Percent of Time Devoted Exclusively to Providing Direct Patient Care and Services According to the Definition of Solid Organ Transplantation Pharmacist Specialists



GUIDELINE 3. Estimate the number of pharmacists who would likely seek board certification in the proposed specialty during the first five years in which board certification would be available. Describe the sources and methods used to determine these estimates.

The *Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification* queried respondents on the likelihood they would pursue specialty certification within the next 5 years if the BPS petition to recognize SOT pharmacist specialists were approved. Over 91% of respondents, or 231 pharmacists, indicated that they would be “highly likely,” “likely,” or “somewhat likely” to pursue specialty recognition in SOT (Figure C-3).

Figure C-3. Likelihood of Pursuing Specialty Recognition as a Solid Organ Transplantation Pharmacist Specialist within the Next 5 Years



Since this survey presumably sampled a portion of the individuals who may be engaged in SOT specialty practice, the number of individuals who would seek certification is possibly underrepresented. Recognition of SOT practice as a specialty has broad acceptance within the profession as evidenced by the petitioning organizations and will increase the number of individuals who are likely to seek certification.

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CRITERION D: Specialized Knowledge

The area of specialization shall be based on specialized knowledge of one or more of the pharmaceutical sciences and the biological, physical, behavioral, and administrative sciences which underlie them. Procedural or technical services and the specific environment in which pharmacy is practiced are not applicable to this criterion.

This criterion relates to SPECIALIZED KNOWLEDGE.

CRITERION E: Specialized Tasks/Skills

The area of specialization shall represent an identifiable field of pharmacy practice which requires specialized tasks/skills by the practitioner and which is distinct from other BPS-recognized pharmacy specialties. ***This criterion refers to SPECIALIZED TASKS/SKILLS.***

The Board of Pharmacy Specialties (BPS) has conducted a role delineation study for solid organ transplantation pharmacy practice and issued a call for petitions in this specialty area.

Therefore, Criterion D and Criterion E are not required as part of the petition to BPS. The *Role Delineation Study for Solid Organ Transplantation Pharmacists* is attached as Appendix D-1.

CRITERION F: Education and/or Training

The area of specialization shall be one in which schools and colleges of pharmacy and/or other organizations offer recognized education and training programs to those seeking advanced knowledge and skills in the area of specialty practice. ***This criterion addresses EDUCATION and/or TRAINING.***

GUIDELINE 1. Describe in detail the education, post-graduate training programs and/or experience required to acquire the specialized knowledge and skills. Discuss how such education, post-graduate training programs and/or experience differ from the education, post-graduate training programs and/or experience of a recent graduate with a Doctor of Pharmacy degree.

According to the Accreditation Council for Pharmacy Education (ACPE) *Accreditation Standards and Key Elements for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree*, the pharmacy curriculum provides a thorough foundation in the biomedical, pharmaceutical, social/behavioral/administrative, and clinical sciences. The degree program prepares graduates to:

- Enter advanced pharmacy practice experiences (APPE-ready)
- Provide direct patient care in a variety of health care settings (practice-ready)
- Contribute as a member of an interprofessional collaborative patient care team (team-ready)¹

The pharmacy curriculum emphasizes optimal medication therapy outcomes and patient safety and satisfies the educational requirements for licensure. The curriculum also fosters development of knowledge, skills, attitudes, and values, as well as the ability to integrate and apply learning both to the present practice of pharmacy and to the advancement of the profession. The pharmacy curriculum provides the basic education and training that graduates need to practice at a generalist level.

The ACPE standards and guidelines require a pharmacist to be knowledgeable and competent in many areas critical to the foundation and delivery of effective patient care. The standards outline broad, general requirements for pharmacist-provided care for targeted populations,

including patients with acute and chronic disease. These requirements indicate that pharmacists must be competent in pathophysiologic and pharmacotherapeutic alterations specific to special population patients for prescription and nonprescription medications, dosage calculations and adjustments, and drug monitoring for positive/negative outcomes.¹

Experientially, ACPE standards require students to complete introductory and advanced pharmacy practice experiences (IPPEs and APPEs, respectively). Furthermore, ACPE standards require that APPEs include primary, acute, chronic, and preventive care for patients of all ages and that these experiences promote practice competencies. ACPE standards *do not require* APPEs to specifically address the area of solid organ transplantation (SOT) practice. Schools and colleges of pharmacy do not typically require completion of an APPE and/or IPPE in SOT; however, elective SOT rotations may be available. When available, these experiences can improve confidence and knowledge regarding SOT, provide direct exposure to unique patient populations and help student pharmacists obtain valuable insights regarding clinical pharmacy services provided to transplant patients.^{2,3,4} When unavailable, SOT practice experience may be limited to brief encounters during inpatient, ambulatory care, or acute care medicine required rotations.

Following completion of the Doctor of Pharmacy degree program, pharmacists must pass the North American Pharmacist Licensure Examination (NAPLEX) developed by the National Association of Boards of Pharmacy. Successful performance on the NAPLEX is an indication that the candidate demonstrates the knowledge, judgment, and skills required of an entry-level pharmacist. The NAPLEX Competency Statements provide a blueprint of the topics covered on the examination. The two areas of expected competency assessed on the NAPLEX are as follows⁵:

- *Area 1: Ensure Safe and Effective Pharmacotherapy and Health Outcomes*
- *Area 2: Safe and Accurate Preparation, Compounding, Dispensing, and Administration of Medications and Provision of Health Care Products*

Following licensure, pharmacists can acquire the differentiated knowledge and skills required for specialized SOT pharmacy practice by a variety of methods. These methods may include, but are not limited to:

- Doctor of Pharmacy degree, clinical work experience, and self-study
- Doctor of Pharmacy degree, postgraduate year one (PGY1) residency training, clinical work experience, and self-study
- Doctor of Pharmacy degree, PGY1 residency training, clinical and/or research fellowship programs, clinical work experience, and self-study

- Doctor of Pharmacy degree, PGY1 residency training, postgraduate year two (PGY2) specialty residency in solid organ transplantation, clinical work experience, and self-study

The most effective way to prepare for a career as an SOT pharmacist specialist is to complete a PGY1 pharmacy residency and a PGY2 residency in SOT. PGY2 SOT residency programs provide the most comprehensive experiential learning opportunities in SOT pharmacy practice.

The petitioning organizations conducted a *Survey of Solid Organ Transplantation Pharmacist Specialists Interested in Board Certification* that asked employers of SOT pharmacist specialists the desired level of training for pharmacists practicing in this specialty. In ranked order of preference, the responses from 36 individuals responsible for hiring within their organizations were as follows (from most desirable to least desirable):

- PGY2 residency in Solid Organ Transplant
- PGY2 residency in another specialty
- PGY1 pharmacy practice residency
- Employer-provided training
- None required or desired

The Doctor of Pharmacy degree alone does not provide knowledge of sufficient depth and breadth for SOT pharmacist specialists to provide specialized care. Additional education and training, clinical work experience, and study are necessary. Because SOT is an evolving specialty, some SOT pharmacist specialists may have obtained specialized knowledge and skills through mechanisms other than accredited residency training programs. According to a study by Taber et al., the vast majority of respondents (98%) earned a doctorate level degree (PharmD) and have been practicing ≥ 10 years (81%). Most completed at least one year of postgraduate training (PGY1), while 53% completed a PGY2 specialty residency. Of those, 86% reported that their specialty training was in the field of transplantation. More than half of those surveyed (53%) are board certified pharmacotherapy specialists (BCPS), and 6% have obtained a masters' degree.⁶

GUIDELINE 2. Describe in detail the nature of training programs in the area of specialty practice including their length, content and objectives.

As stated above, there are several ways in which pharmacists can acquire the knowledge and skills needed to provide a specialized practice in SOT. The most efficient way is through an accredited PGY2 specialty residency program in SOT pharmacy practice. A copy of the current *Required Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2)*

Pharmacy Residencies in Solid Organ Transplant is attached as Appendix F-1. Traditionally, completion of these goals and objectives would provide the education and training needed to sit for the Board of Pharmacy Specialties certification exam.

Residency Training

PGY2 specialty residency training is an organized, directed, and accredited program that builds upon the competencies established in PGY1 residency training. The PGY2 program increases the resident's depth of knowledge, skills, and abilities and is designed to promote accountability and best practices that prepare residents to provide comprehensive medication management and clinical leadership in a specialty area.⁷

PGY2 pharmacy residency programs build on Doctor of Pharmacy education and PGY1 pharmacy residency programs to contribute to the development of clinical pharmacists in advanced or specialized practice. PGY2 residencies provide residents with opportunities to function independently as practitioners by conceptualizing and integrating accumulated experience and knowledge and incorporating both into the provision of patient care that improves medication therapy. Residents who successfully complete an accredited PGY2 pharmacy residency should possess competencies that qualify them for clinical pharmacist and/or faculty positions and situate them to be eligible for attainment of board certification in the specialized practice area (when board certification for the practice area exists).³

The PGY2 specialty residency in SOT is designed to transition PGY1 residency graduates from generalist practice to specialized practice, focused on the care of SOT recipients and, in some instances, living organ donors. Residency graduates are equipped to participate as essential members of interdisciplinary teams caring for transplant patients, assuming responsibility for the medication-related aspects of care. Team involvement includes contributing the pharmacy perspective to selection and preparation of recipients. Transplant residency graduates are proficient in the care of patients as they prepare to receive a transplant, during the acute care phase of transplantation, and in the ongoing primary care role after transplant as the pharmacist works with the patient to sustain the survival of the transplanted organ, manage diseases that occur or reoccur post transplant, and enhance the patient's general health and wellness.³

In addition to these direct patient care responsibilities, transplant residency graduates are trained to serve as authoritative resources in their health systems for the optimal use of medications in transplant recipients. In that role, they can be relied upon to lead the development and implementation of medication-related guidelines and protocols for transplant patient care, meet the health system's needs for transplant-related drug information, and

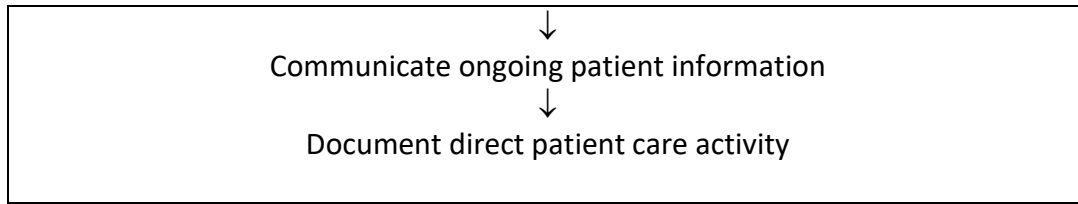
provide the transplant pharmacy perspective to organizations making technology, automation, and budgetary decisions regarding transplant medications and patient care. Graduates are also highly skilled in the design and delivery of education and training related to transplantation for a wide spectrum of potential audiences, including the patient and/or caregiver as well as health care professionals in practice or in training.

Because transplantation is such a rapidly developing field, graduates of SOT pharmacy residencies are all skilled in supporting or conducting transplant research and in outcomes analyses.

Required outcomes for PGY2 pharmacy residencies in SOT include the following³:

- Outcome R1: Serve as an authoritative resource on the optimal use of medications in recipients of a solid organ transplant
- Outcome R2: Optimize the outcomes of transplant patients by promoting and/or providing evidence-based medication therapy as an integral member of an interdisciplinary team in acute and ambulatory care settings





- Outcome R3: Manage and improve the medication-use process in transplant patient care areas
- Outcome R4: Demonstrate leadership and practice management skills
- Outcome R5: Demonstrate excellence in the provision of training or educational activities about transplant-related medications for health care professionals and health care professionals in training
- Outcome R6: Conduct transplant research

Elective educational outcomes for PGY2 pharmacy residencies in solid organ transplant include³:

- Outcome E1: Demonstrate additional leadership and practice management skills
- Outcome E2: Contribute to formulary decisions regarding transplant-related medications
- Outcome E3: Demonstrate additional skills for managing and improving the medication-use process in transplant patient care areas
- Outcome E4: Publish on transplant-related topics
- Outcome E5: Function effectively in transplant settings participating in clinical investigations
- Outcome E6: Demonstrate skills required to function in an academic setting

Fellowship Training

According to the *American College of Clinical Pharmacy (ACCP) Guidelines for Clinical Research Fellowship Training Programs*, a fellowship program is a directed, individualized postgraduate training program designed to prepare the fellow to function as an independent investigator. Fellowships typically require prior completion of a master's degree or doctoral degree in a health science discipline, completion of a residency or equivalent clinical experience, and demonstrated interest or aptitude for a career in research. Fellowship programs prepare pharmacists to be competent in the scientific research process. Training is typically composed of approximately 80% research activities and 20% advanced practice activities, although this may vary by program.

SOT fellowship programs model other fellowships and emphasize research and practice in the SOT setting. Fellowship experience is typically gained in protocol design; study design; data

acquisition, analysis, and interpretation; grant writing; manuscript preparation; implementation of institutional review board submission; and conducting clinical and laboratory research projects. Didactic and clinical training of pharmacy students and other health care professionals is also a common component of these programs. The ultimate goal of an SOT fellowship program is to provide the pharmacist with specialized practice experience and essential knowledge, skills, and abilities to conduct research and function as a primary investigator in SOT.⁸

A copy of the *ACCP Guidelines for Clinical Research Fellowship Training Programs* is attached as Appendix F-2.

GUIDELINE 3. Provide a comprehensive listing of the programs, sponsoring organizations or institutions, locations and individuals in charge.

Table F-1 lists PGY2 SOT pharmacy residency programs as of January 3, 2018, including 39 programs with 42-43 residency positions. There are also six SOT pharmacy fellowship programs, as detailed in Table F-2.

Table F-1. Postgraduate Year Two Solid Organ Transplantation Pharmacy Residency Programs as of January 3, 2018

Sponsoring Organization	Status	City	State	Program Director	Number of Residency Positions
Barnes-Jewish Hospital	Accredited	St. Louis	MO	Jennifer C. Hagopian	1
Baylor St. Luke's Medical Center	Accredited	Houston	TX	Melissa J. Manson	1
Beth Israel Deaconess Medical Center	Candidate	Boston	MA	Christin Rogers	1
Children's Healthcare of Atlanta	Accredited	Atlanta	GA	Rochelle Schmidt Liverman	1
Duke University Hospital	Accredited	Durham	NC	Matthew T. Harris	1
Emory University Hospital	Accredited	Atlanta	GA	Michael L. Hurtik	1
Hennepin County Medical Center	Accredited	Minneapolis	MN	Tracy L. Anderson-Haag	1
Henry Ford Hospital	Accredited	Detroit	MI	Nimisha Sulejmani	1
Houston Methodist Hospital	Accredited	Houston	TX	Jill C. Krisl	2
Indiana University Health	Pre-candidate	Indianapolis	IN	Erin Lushin	1
Jackson Memorial Hospital	Candidate	Miami	FL	Alexandra Centeno	1

King Faisal Specialist Hospital and Research Centre	Accredited	Riyadh	Saudia Arabia	Delal Alkortas	1-2
Mayo Clinic Florida	Candidate	Jacksonville	FL	Matthew Soto-Arenall	1
Methodist University Hospital	Accredited	Memphis	TN	Heather Snyder	1
MUSC Medical Center and College of Pharmacy	Accredited	Charleston	SC	Holly B. Meadows	2
Nebraska Medicine	Accredited	Omaha	NE	Megan H. Keck	1
New York-Presbyterian Hospital	Accredited	New York	NY	Demetra Tsapepas	2
Northwestern Memorial Hospital	Accredited	Chicago	IL	Kathleen Cunningham	1
Ochsner Clinic Foundation (Ochsner Medical Center)	Accredited	New Orleans	LA	Stephanie Anders	1
Rush University Medical Center	Accredited	Chicago	IL	Nicole R. Alvey	1
Tampa General Hospital	Accredited	Tampa	FL	Angela Logan	1
The Johns Hopkins Hospital	Accredited	Baltimore	MD	Lindsey A. Pote	1
The Mount Sinai Medical Center	Accredited	New York	NY	Leandra R. Miko	1
The Ohio State University Wexner Medical Center	Accredited	Columbus	OH	Holli A. Winters	1
University Health System	Accredited	San Antonio	TX	Barrett Crowther	1
University of Alabama at Birmingham Hospital	Accredited	Birmingham	AL	Alexandra James	1
University of California, San Diego Health	Accredited	San Diego	CA	Ashley A. Feist	1
University of California, San Francisco Medical Center	Candidate	San Francisco	CA	David Quan	1
University of Illinois at Chicago College of Pharmacy	Accredited	Chicago	IL	Mia R. Schmiedeskamp-Rahe	1
University of Kentucky Healthcare	Accredited	Lexington	KY	TrisAnn Rendulic	1
University of Maryland Medical Center	Accredited	Baltimore	MD	Brian M. Masters	1
University of Michigan Health System	Accredited	Ann Arbor	MI	Linda J. Stuckey	1
University of North Carolina Medical Center	Accredited	Chapel Hill	NC	Ruth-Ann M. Lee	1

University of Utah Hospitals and Clinics	Accredited	Salt Lake City	UT	Lonnie D. Smith	1
University of Virginia Health System	Accredited	Charlottesville	VA	Winston A. Ally	1
University of Wisconsin Hospital and Clinics	Accredited	Madison	WI	Kimberly E. Holdener	1
UPMC Presbyterian Shadyside	Accredited	Pittsburgh	PA	Michael A. Shullo	1
Vanderbilt University Medical Center	Accredited	Nashville	TN	Christie B. Truscott	1
Yale New Haven Hospital	Accredited	New Haven	CT	Elizabeth Cohen	1

Table F-2. Solid Organ Transplantation Pharmacy Fellowship Programs

Sponsoring Organization	City	State	Program Contact	Number of Fellowship Positions	Primary Specialty	Secondary Specialty
Terasaki Research Institute	Los Angeles	CA	Matt Everly	Dependent on interested candidates	Transplantation	
University of Cincinnati	Cincinnati	OH	Rita R. Alloway	1	Transplantation	N/A
University of Illinois – Chicago Medical Center	Chicago	IL	Patricia Thielke	1	Transplantation	N/A
University of Pittsburgh	Pittsburgh	PA	Chris Ensor	Dependent on interested candidates	Transplantation	
University of Washington	Seattle	WA	Mary F. Hebert	1	Immunology Therapeutics/ Solid Organ Transplantation	
Western University of Health Sciences	Pomona	CA	David I. Min	1	Transplantation	Pharmacogenomics

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- ⁸ American College of Clinical Pharmacy. *ACCP Guidelines for Clinical Research Fellowship Training Programs*. Available at: <https://www.accp.com/docs/positions/guidelines/pos15.pdf>. Accessed December 14, 2017.

CRITERION G: Transmission of Knowledge

The area of specialization shall be one in which there is an adequate transmission of specialized knowledge through professional, scientific and technical literature directly related to the specialty area. ***This criterion refers to the TRANSMISSION OF KNOWLEDGE.***

Transmission and dissemination of specialized knowledge in solid organ transplantation (SOT) pharmacy practice occurs through national standards and guidance, formal networking groups within professional practice associations, peer-reviewed publications and periodicals, live educational programming, and enduring educational resources in print- and web-based vehicles.

National Standards and Guidance

For pharmacist specialists in SOT, one of the primary mechanisms for transmission of knowledge is through rules, regulations, standards, guidelines, and position papers authored by national organizations and government entities. Examples of these documents that are foundational for SOT pharmacist specialists include the following:

- The Department of Health and Human Services Centers for Medicare & Medicaid Services regulation 42 CFR Parts 405, 482, 488, and 498 for the Medicare Program outline the hospital conditions of participation and detail the requirements for approval and re-approval of transplant centers to perform organ transplants. This final rule establishes the Medicare conditions of participation for heart, heart-lung, intestine, kidney, liver, lung, and pancreas transplant centers. This rule sets forth clear expectations for safe, high quality transplant service delivery in Medicare-participating facilities.¹
- The United Network for Organ Sharing (UNOS) is a private, non-profit organization that manages the nation's organ transplant system under contract with the federal government. The organization's bylaws govern the conduct of organ transplantation in the U.S. and specifically require the identification of one clinical transplant pharmacist.²
- The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients provide guidance to the health care team responsible for the care of heart transplant patients and recommends that transplant centers should have specialty-trained pharmacists or physicians with expertise in pharmacology as part of the multidisciplinary team.³

- The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline on the monitoring, management, and treatment of kidney transplant recipients is intended to assist practitioners, including pharmacists, caring for adults and children after kidney transplantation. The guideline specifically addresses the value of the pharmacist’s role in addressing patient nonadherence and the value of pharmacist’s contributions within the healthcare team to ensure positive patient outcomes.⁴

Formal Networking Groups

Major health care associations have formal networking sections and groups dedicated to SOT pharmacist specialists. These groups foster professional interaction and provide opportunities for practice advancement through educational programming, newsletters, research networks, and leadership. As an example, networking groups that currently exist within pharmacy practice and other health care associations are shown in Table G-1.

Table G-1. Solid Organ Transplantation Networking Groups

Organization	Networking Group	Description
American College of Clinical Pharmacy (ACCP)	Immunology/Transplantation Practice and Research Network (PRN)	The Immunology/Transplantation PRN’s mission is to improve the health of tissue, cellular, and SOT donors, as well as recipients and patients with immunologic disorders by fostering practice innovation, supporting outcomes and translational research, and providing education to patients and practitioners. ACCP’s Immunology/Transplantation PRN currently has more than 550 members.
American Society of Health-System Pharmacists (ASHP)	Section of Clinical Specialists and Scientists (SCSS)	The ASHP Section of Clinical Specialists and Scientists represents clinical experts and advocates for practice advancement and focuses on improving patient care by creating and translating scientific advances into practice. The section provides a formal mechanism for national networking among section members. This group has responsibility for planning and developing educational programming, tracks, and workshops offered at ASHP meetings. The Network Facilitator for Immunology/Transplant hosts a networking session at the ASHP Midyear Clinical Meeting and posts bi-annually on the ASHP SCSS Connect site. ASHP’s Section of Clinical Specialists and Scientists currently has 280

		members who have indicated an interest in SOT pharmacy.
American Society of Transplantation (AST)	Community of Practice (COP) – Transplant Pharmacy	The Transplant Pharmacy COP is dedicated to exchanging knowledge, offering networking opportunities, advocating for issues that are relevant to each of their constituencies, and developing resources to meet the needs of their members. AST’s Transplant Pharmacy COP has approximately 420 members.
International Society for Heart & Lung Transplantation (ISHLT)	ISHLT Connect	This platform allows members to network, share ideas, get advice and feedback, compare strategies, engage in discussions, collaborate on Committee, Council, and Workforce projects. ISHLT has xx number of SOT pharmacist specialist members.

GUIDELINE 1. Identify journals and other periodicals dealing specifically with the proposed specialty.

Journals

Issues of interest in SOT pharmacy practice span many areas of pharmacy practice and topics in SOT research, clinical care, and health promotion. Many SOT pharmacy and primary care practice journals consistently publish articles highlighting evidence, outcomes, and contributions to patient care through SOT pharmacy practice. Examples of such journals include:

- **American Journal of Transplantation** – This monthly journal serves as a forum for debate and reassessment and is a major platform for promoting understanding, improving results, and advancing science in this field. It is a resource for researchers and clinicians. Original articles, case reports, invited reviews, letters to the editor, critical reviews, news features, consensus documents, and guidelines are all published in the *American Journal of Transplantation*.
- **Clinical Transplantation** – This monthly journal aims to provide communication for those involved in the care of patients who require, or have had, organ or tissue transplants, including: kidney, intestine, liver, pancreas, islets, heart, heart valves, lung, bone marrow, cornea, skin, bone, and cartilage, viable or stored. *Clinical Transplantation* is focused on the complete spectrum of present transplant therapies, as well as those that are experimental or may become possible in the future. This journal includes the following features: clinical and translational studies, focused reviews, full-

length papers, short communications, clinical reviews, seminal papers, and cooperative surveys.

- ***Journal of Heart & Lung Transplantation*** – This monthly publication covers the field of intra-thoracic organ transplantation, support, and replacement via peer-reviewed articles on all aspects of heart and lung transplantation and end-stage heart and lung disease.
- ***Pediatric Transplantation*** – Published eight times a year, this journal highlights the most recent advances in clinical and basic science related to transplantation (SOT, stem cell transplantation, immunobiology, and infectious disease) in infants, children, and adolescents. Reviews and editorial on controversial issues are also covered.
- ***Progress in Transplantation*** – This journal is a quarterly, indexed, peer-reviewed publication. *Progress in Transplantation* reflects the multi-disciplinary team approach to procurement and clinical aspects of organ and tissue transplantation by providing a professional forum for exchange of the continually changing body of knowledge in transplantation through publication of original research, case studies, donor management issues, international papers, review articles, clinical practice issues, and policy papers related to the disciplines focused on transplantation.
- ***Transplant Infectious Disease*** – This journal was established to present the most current information on the prevention and treatment of infection complicating organ and bone marrow transplantation for clinicians and scientists. The journal includes review articles on relevant subjects, the results of clinical investigation, case reports, and two recurring features: a clinical-pathologic conference and reviews of the basic science foundation of transplant infectious disease.
- ***Transplantation*** – The official journal of The Transplantation Society and the International Liver Transplantation Society is published monthly and covers advances in transplantation. The journal publishes original research articles on original clinical science and original basic science. The Editors and Editorial Board are an international group of research and clinical leaders that include many pioneers of the field, representing a diverse range of areas of expertise. The editorial team provides peer review and delivers editorial evaluation of all manuscripts submitted to the journal.
- ***Transplantation Proceedings*** - *Transplantation Proceedings* publishes several different categories of manuscripts, all of which are peer-reviewed. The first type of manuscript consists of the current state of world transplantation biology and medicine. These manuscripts emanate from congresses of the affiliated transplantation societies, from Symposia sponsored by the Societies, as well as special Conferences and Workshops - covering related topics. *Transplantation Proceedings* also publishes several special sections, including publication of *Clinical Transplantation Proceedings*.

- ***Transplant International*** - This official, peer-reviewed journal of the European Society for Organ Transplantation (ESOT), the European Liver and Intestine Transplant Association (ELITA), and the German Transplantation Society (DTG) provides a forum for clinical and experimental research on the biology, physiology, and immunology of both tissue and organ transplantation.

Solid organ transplantation pharmacy columns and features are also published periodically in the *American Journal of Health-System Pharmacy (AJHP)*, *Annals of Pharmacotherapy*, *Journal of the American Pharmacists Association (JAPhA)*, *Journal of Pharmacy Practice (JPP)*, and *Pharmacotherapy*, as well as many other general medical journals.

- *AJHP* is the official publication of the American Society of Health-System Pharmacists (ASHP). It publishes peer-reviewed scientific papers on contemporary drug therapy and pharmacy practice innovations in hospitals and health systems.
- *Annals of Pharmacotherapy* is an independent, peer-reviewed journal that publishes evidence-based articles on practice, research, and education. Two transplantation pharmacists are on the editorial panel.
- *JAPhA* is an official publication of the American Pharmacists Association (APhA). It provides a peer-reviewed forum for original research, review, experience, and opinion articles that link science with contemporary pharmacy practice to improve patient care.
- *JPP* is a peer-reviewed journal that offers practicing pharmacists in-depth reviews and research trials, surveys of new drugs, novel therapeutic approaches, pharmacotherapy reviews and controversies, pharmacokinetics, drug interactions, drug administration, adverse drug events, medication safety, pharmacy education, and other pharmacy practice topics.
- *Pharmacotherapy* publishes peer-reviewed, scientific, and professional information and knowledge to improve patient outcomes through optimal pharmacotherapy. *Pharmacotherapy* is an official journal of the American College of Clinical Pharmacy (ACCP).

Newsletters and Online Periodicals

Professional pharmacy practice associations publish a variety of print and online media that disseminate SOT practice information. The ACCP Immunology/Transplantation PRN email list service is a mechanism for sharing, obtaining, and reporting data among SOT pharmacist members. The ASHP Section of Clinical Specialists and Scientists also hosts an email list service to facilitate communication and problem solving among members. The American Society of Transplantation Transplant Pharmacist Community of Practice also facilitates a list serve for their pharmacist members.

GUIDELINE 2. Provide a select bibliography of published abstracts, articles, position papers, and white papers in the professional literature dealing with the proposed specialty.

As of February 5, 2018, 88 relevant articles related to SOT pharmacy practice have been published in the professional literature that support the tenets of this petition. The prevalence of articles in pharmacy and medical journals focusing on SOT pharmacy practice and patient care of complex patients by SOT pharmacist specialists provides further evidence of this emerging specialty. A bibliography of all articles and resources published on specialized SOT pharmacy practice and related issues is attached as Appendix G-1.

GUIDELINE 3. Reference and summarize selected experimental and quasi-experimental, peer-reviewed articles demonstrating the value of the proposed specialty (if available and appropriate).

SOT pharmacist specialists in a variety of settings are demonstrating and publishing positive clinical and economic outcomes resulting from effective management of SOT patients. Their collective work provides support for the validity of this proposed specialty. A detailed overview of the top 54 pivotal articles, as determined by the SOT experts from the petitioning organizations, is attached as Appendix G-2.

GUIDELINE 4. Describe methods of knowledge transmission through symposia, seminars, workshops, etc., and enclose representative programs concerning these activities.

The specialized knowledge required for SOT pharmacist specialists is transmitted through a variety of methods, including symposia, live and web seminars, interactive workshops, and enduring resources. Each year, national and state health care associations, schools and colleges of pharmacy, and for-profit educational companies offer live and enduring programming to disseminate the latest evidence for managing the unique needs of SOT patients and share innovations in specialized SOT pharmacy practice. Hundreds of hours of programs are available annually to SOT pharmacists through local, regional, and national meetings and events; web-based programs; and online learning.

According to the Accreditation Council for Pharmacy Education (ACPE) Pharmacists' Learning Assistance Network (PLAN) database, providers of ACPE-approved continuing pharmacy education have collectively offered almost 650 hours of SOT programming over the past 3 years (August 23, 2014–August 23, 2017). This programming includes:

- 266 programs with 528.5 hours of live, knowledge-based programs. A complete listing of these ACPE-approved activities is provided as Appendix G-3.

- 38 programs with 77.5 hours of live, application-based programs. A complete listing of these ACPE-approved activities is provided as Appendix G-4.
- 21 programs with 26.75 hours of home study, knowledge-based programs. A complete listing of these ACPE-approved activities is provided as Appendix G-5.
- 5 programs with 14.5 hours of home study, application-based programs. A complete listing of these ACPE-approved activities is provided as Appendix G-6.

Sample program materials from select live educational activities are attached as Appendix G-7 and include programming from the following events:

- ISHLT 38th Annual Meeting and Scientific Sessions Preliminary Program; 2018
- ACCP Immunology/Transplantation PRN Focus Session – Antibody-Mediated Rejection: Are We Really Making Progress? – A Spirited Debate; 2017
- ACCP Solid Organ Transplantation in HIV- or HCV-Infected Recipients: Controversies in Patient Management; 2017
- ASHP Challenges in Transplantation: The Notorious DSA (Donor Specific Antibodies); 2017
- ASHP Updates in Transplantation 2016
- ACCP Immunology/Transplantation PRN Focus Session—Novel Approaches to Immunomodulation After Transplantation; 2015

GUIDELINE 5. Provide the number of such events, included in #4 above, which occur on an annual basis, and the average total attendance at such programs.

Live, national events are one mechanism for dissemination of knowledge to SOT pharmacist specialists. Over the last 3 years, the petitioning organizations have collectively hosted 14 live educational events with 817 certificates of credit issued across all programs. Recognizing that pharmacists attend multiple programs, the total number of certificates does not equate to the number of unique participants. The total number of certificates of credit issued reflects the strong interest in programming for SOT pharmacist specialists. Table G-2 outlines these programs.

Table G-2. Solid Organ Transplantation Pharmacist Specialist Educational Programming and Attendance

Sponsoring Organization	Solid Organ Transplant Pharmacy Programming and Attendance
American College of Clinical Pharmacy	2015 – 2 programs; 282 certificates of credit issued 2016 – 4 programs; 163 certificates of credit issued 2017 – 5 programs; 40 certificates of credit issued
American Society of Health-	2015 – 1 program; 62 certificates of credit issued

System Pharmacists	2016 – 1 program; 194 certificates of credit issued 2017 – 1 program; 76 program attendees
American Society of Transplantation	2015 – 2016 – 2017 –
International Liver Transplant Society	2015 – 2016 – 2017 –
International Society for Heart & Lung Transplantation	2015 – 3 programs; XX pharmacist attendees 2016 – 5 programs; 124 attendees; 79 certificates of credit issued 2017 – 6 programs; 134 attendees; 115 certificates of credit issued *Not all ISHLT transplantation programs offer ACPE CPE credit

Additional Mechanisms for Dissemination of Knowledge

In addition to the methods discussed in each of the guidelines above, enduring publications and professional award programs serve an important function in the dissemination of knowledge in the proposed specialty.

Nonperiodical Publications

Many enduring publications and resources have been developed to enhance the skills and knowledge SOT pharmacist specialists. Examples of such publications include:

- *Pediatric Solid Organ Transplantation, 2nd Edition* – This is a comprehensive text on all aspects of pediatric SOT. It provides a reference to the basic science and organ specific surgical technique and after care. This second edition has been updated considering recent developments in this rapidly advancing area.
- *Pharmacotherapy: A Pathophysiologic Approach, 9th Edition* – This book was written to help the clinician advance the quality of patient care through evidence-based medication therapy derived from pharmacotherapeutic principles. The scope of this book includes drug indications and dosages, initial selection, proper administration, and monitoring of drugs. There is a chapter included in the book dedicated to pharmacotherapy as it relates to SOT.
- *Pharmacotherapy Principles and Practice, 4th Edition* – This book used an evidence-based approach to teach the reader how to design, implement, monitor, and evaluate medication therapy. There is a chapter dedicated to SOT.
- *Textbook of Organ Transplantation* – This textbook (or e-book), written for the transplant team, provides a complete and comprehensive overview of modern transplantation in all its complexity, from basic science to surgical techniques to post-

operative care, and from likely outcomes to considerations for transplant program administration, bioethics, and health policy. Related chapters in the textbook include “Drugs Specifically Approved for Transplant Indications;” “Drug Interactions in Organ Transplantation;” “Nonadherence, Psychosocial Adaptation and Its Effects in Pediatric Transplantation;” and “Transplant Pharmacy Services.”

- *Transplant Immunology, 1st Edition* – Produced in association with the American Society of Transplantation and written by experts in the field, this book provides a comprehensive overview of immunology in relation to clinical transplantation, including the basic functionality of the immune system, the latest developments in immunosuppressive drugs and protocols, and emerging technologies.
- *Transplant Infections, 4th Edition* – This book is a guide for all medical professionals working with transplant patients. It covers advances in the field of transplant infections, including a review of surgical infections, treatment, prevention, and practice.

Professional Awards

In 2015, AST began the Fellow of the American Society of Transplantation program to recognize members who have demonstrated exceptional commitment to the field of transplantation as well as outstanding service to AST. Below is a list of SOT pharmacist specialists who have been recognized with this achievement (Table G-3).

Table G-3. Fellows of the American Society of Transplantation

Award Year	Recipient
2017	Ahmed Aljedai, PharmD, MBA, BCPS, FCCP Nicole Alvey, PharmD Gregory Malat, PharmD Samir Patel, PharmD Demetra Tsapepas, PharmD
2016	Marie A. Chisholm-Burns, PharmD Matthew Everly, PharmD Jillian Fose, PharmD Kathleen D. Lake, PharmD Angela Q. Maldonado, PharmD, BCPS Yasar Tasnif, PharmD Kimi Ueda, PharmD Ashley A. Vo, PharmD
2015	Barrett Crowther, PharmD Steven Gabardi, PharmD, BCPS Nicole A. Pilch, PharmD, MS, BCPS Lisa Potter, PharmD

	Christin Rogers, PharmD, FCCP, BCPS Lonnie Smith, PharmD Ignatius Tang, MD, PharmD Eric M. Tichy, PharmD, BCPS Kathleen M. Tornatore, PharmD Jennifer Trofe-Clark, PharmD, BCPS
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In addition, other professional awards have recognized SOT pharmacist specialists for their contributions to the profession and advancing clinical practice in SOT. These awards, and their recipients, are outlined in Table G-4.

Table G-4. Solid Organ Transplantation Pharmacist Specialist Recipients of National Professional Awards

Organization/Award	Description	Year/Recipient
ACCP: Clinical Practice Award	The Clinical Practice Award recognizes an ACCP member who has developed an innovative clinical pharmacy service, provided innovative documentation of the impact of clinical pharmacy services, provided leadership in the development of cost-effective clinical pharmacy services, or shown sustained excellence in providing clinical pharmacy services.	2003 Marie A. Chisholm
ACCP: Education Award	The Education Award recognizes an ACCP member who has shown excellence in the classroom or clinical training site, conducted innovative research in clinical pharmacy education, demonstrated exceptional dedication to continuous professional development, or shown leadership in the development of clinical pharmacy education programs.	2000 Marie A. Chisholm
ACCP: Paul R. Dawson Award	Since 2015, the Paul R. Dawson Award criteria include all research that has made sustained contributions to the quality of patient outcomes. The intent of the award is to annually recognize an active scientist within the ranks of pharmacy education as a leader in the broad range of research related to health services delivery directly affecting patient outcomes, including basic, clinical, translational, and health services research.	2015 Marie A. Chisholm-Burns
ACCP: Robert K. Chalmers Distinguished Pharmacy Educator Award	The Robert K. Chalmers Distinguished Pharmacy Educator Award recognizes an individual's excellence in pharmacy education.	2005 Marie A. Chisholm

ACCP: Rufus A. Lyman Award	The Rufus A. Lyman Award is presented annually to the author(s) of the best paper published in the <i>American Journal of Pharmaceutical Education</i> .	2007, 1995 Marie A. Chisholm-Burns
ACCP: Russell R. Miller Award	The Russell R. Miller Award recognizes an ACCP member who has made substantial contributions to the literature of clinical pharmacy, either in the form of a single, noteworthy contribution or sustained contributions over time.	2014 Rita Alloway
American Pharmacists Association (APhA): Daniel B. Smith Practice Excellence Award	The Daniel B. Smith Practice Excellence Award, in honor of the first president of the American Pharmaceutical Association, is APhA's premier practice award to recognize a pharmacy practitioner in any practice setting who has distinguished himself/herself and the profession by outstanding performance.	2006 Marie A. Chisholm
APhA: Research Achievement Award	The award, offered annually, is intended to recognize and encourage outstanding, meritorious achievement in any of the pharmaceutical sciences. Contributions to be recognized by this award will be in the areas of basic pharmaceutical, clinical, and economic, social, and administrative sciences (ESAS). The APhA Research Achievement Award was first established in 1961 as six separate awards, each recognizing outstanding, meritorious achievement in six disciplines of pharmaceutical sciences. Since 1995, these awards have been consolidated into a single annual award.	2014 Marie Chisholm-Burns (Clinical)
American Society of Health-System Pharmacists (ASHP): Award of Excellence	The award, established in 2005 as the successor to the ASHP Certificate of Appreciation, recognizes a specific recent contribution or achievement that has advanced the ability of hospital and health-system pharmacists in the United States to serve the needs of patients.	2011 Marie A. Chisholm-Burns
ASHP Foundation: Pharmacy Practice Research Award	The program honors original, significant contributions to biomedical literature by pharmacists.	2011 Marie Chisholm-Burns
ASHP Foundation: Award for Sustained Contributions to the Literature	This is an annual award that recognizes a pharmacist who, over the course of his/her career, has made significant contributions to the biomedical literature.	2014 University of Tennessee College of Pharmacy 2013 Marie Chisholm-Burns
ASHP Foundation	This is a nationally acclaimed awards program that	2014 Dr. Linda Awdishu

Award for Excellence in Medication-Use Safety	recognizes outstanding pharmacist leadership, teamwork, innovation, and patient outcomes that demonstrate improvements in patient safety within a medication-use system in a hospital or health system.	2010 Medical University of South Carolina
American Society of Transplantation (AST): Clinician of Distinction Award (Non-Physician Award)	This award recognizes a distinguished non-physician clinician or administrator who is considered an expert in his/her field, whose career is dedicated to transplant, and who is recognized for outstanding contributions to clinical transplantation.	2016 Christin Rogers 2015 Marie Chisholm-Burns
American Society of Transplantation (AST): Mentoring Award	The AST Mentoring Award is intended to recognize outstanding mentors in the field of transplantation. Special consideration will be given to individuals whose dedicated leadership and contribution have shaped the career path(s) of individuals who trained under their guidance.	2013 Rita Alloway
National Academies of Practice (NAP): Nicholas Andrew Cummings Award	Awarded to a member of a NAP Academy who has demonstrated outstanding or extraordinary contributions to interprofessional health care	2011 Marie Chisholm-Burns

¹ Department of Health and Human Services. Hospital conditions of participation: requirements for approval and re-approval of transplant centers to perform organ transplants. Fed Regist. 2007;72(61):15198e15280. Available at: <https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandCompliance/Downloads/Transplantfinal.pdf>. Accessed February 6, 2018.

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Appendix B-1

Letters of Support

February 1, 2018

William M. Ellis, BSPHarm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Avenue., NW
Washington DC 20037

RE: Recognition of Solid Organ Transplantation (SOT) Pharmacist Specialists

Dear Mr. Ellis,

On behalf of the American Society of Transplantation (AST), representing a majority of the nation's medical professionals engaged in the field of solid organ transplantation, we urge the Board of Pharmacy Specialties to recognize solid organ transplantation (SOT) as a specialty in the field of pharmacy. This recognition is critical to ensure that the specialized training and knowledge needed to address the complex medication needs unique to transplant patients remains a necessary component of the overall transplant team.

Transplant patients have uniquely complex pharmacological needs. SOT pharmacists require extensive post-doctoral training and experience to develop the expertise necessary to serve this patient population. They are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. Their practice is unique among other pharmacy specialties because they care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. Their role on the SOT team includes creation of a customized pharmacotherapeutic regimen that is essential to the success of organ transplantation. They provide knowledge of pharmacology, optimal dosing, appropriate monitoring, management of drug interactions, and management of medication side effects while contributing to program-wide initiatives and clinical program developments.

Just as important as the design, implementation, and monitoring of the pharmacotherapeutic plan is the SOT pharmacist specialist's understanding of the everyday challenges both socially and financially that may impact a patient's ability to comply with this plan. The SOT pharmacist specialist is key to this effort, understanding the patient's medical needs while recognizing potential challenges from both the patient and caregiver perspective in managing the often challenging routine of multiple medications at multiple times to protect the lifesaving organ graft. Transplant pharmacists are best positioned to "translate" an ideal theoretical medication regimen into one that is practical (i.e. scheduling medications for optimal outcomes considering drug interactions and pharmacology, medication adjustments per insurance/hospital formulary or affordability) and provide the corresponding medication education and training for the patient to prevent rejection and readmission.

The SOT pharmacist specialist is a valued member of the transplant team within our Society's membership and in transplant programs across the country. They bring an expertise that is critical to

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the clinical planning for an individual's transplant journey, but they also serve as an educational resource and advocate for their patients beyond the transplant event and hospitalization. They meet with recipients and donors to teach them about their medication plans before hospital discharge. They answer questions and look for opportunities to tailor regimens to individual needs as much as possible. Additionally, they serve as a trusted advocate from a regulatory perspective when patients struggle with coverage issues for their critical medications. Their understanding of FDA regulation and payer coverage is just as valuable as their clinical knowledge to the success of our patients in many cases.

The AST is keenly aware of the many facets of patient care that our SOT pharmacist specialists cover as we begin to grow into an outward facing patient resource in addition to a professional society. It has been well demonstrated that the work of transplant pharmacists increase adherence rates and improve transplant outcomes (1-5). Patients and transplant pharmacist members have openly shared their stories of working together to find a manageable and successful path for transplant recipients. A successful relationship between SOT pharmacist specialists and patients through thoughtful education and open communication is essential and pays for itself in optimal short-term and long-term patient and graft outcomes.

We believe it is critical that the Board of Pharmacy Specialties recognize SOT pharmacist specialists. Their training and knowledge with this complex patient population of all ages is a key aspect of a successful transplant program, and the ongoing training of these specialized pharmacists is integral to the field's continued advancement as we focus on maximizing graft life as the number of those waiting for a lifesaving organ transplant continues to increase.

Thank you in advance for your consideration of our request. If you have any questions or require additional information, please do not hesitate to contact either of us directly, or Shandie Covington, AST's Executive Director, at 856-316-0924.

Sincerely,



Ronald G. Gill, PhD
President



Dianne McKay, MD
President-Elect

References:

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Bruce Kaplan, MD
Raleigh R White and Vice President
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Scott & White Memorial Hospital and Clinic
2401 South 31st Street
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December 12, 2017

William M. Ellis, BS Pharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

I am writing this letter of support for recognition of Transplant Pharmacy Practice as a specialty. Over my 20 yearlong career in transplantation, I have had the pleasure to work alongside many transplant pharmacists in clinical and research realm. I have a strong belief that these uniquely trained pharmacists are of incalculable value as colleagues and of great service to transplant patients and community.

I currently serve as a Co-chair of the American Society of Transplantation Kidney and Pancreas Community of Practice. I also serve as the Executive of *Transplantation* and served as Deputy Editor of *American Journal of Transplantation* for fourteen years. I also serve as a reviewer for NIH. In my career, I mentored numerous fellows and faculty – including transplant pharmacists. I have 300 peer reviewed publications and have been Chair of several Transplant institutes.

Transplant recipients make a unique population of patients whose postoperative outcomes depend on lifelong adherence to a complex medication regimen. Transplant medications are often prescribed “off label” and active interpretation of available literature is essential to ensure medications are utilized to their best potential. Moreover, management of comorbidities and drug toxicities often requires specialized training. Transplant pharmacists are uniquely positioned to collaborate with physicians to meet and maintain complex needs of the transplant population. Consequently, transplant regulatory agencies recognize that transplant pharmacists are essential members of every transplant team today. Their participation is required in the evaluation and care of organ donors, transplant candidates and transplant recipients. They also participate in Transplant Suitability Committees, Adverse Event Analysis and Quality Assurance & Performance Improvement Committees.

Transplant pharmacists have made a significant contribution to the field of transplant research that lead to lasting and significant changes in practice. They are key members of the interdisciplinary research team. In this role, they catalyze research initiatives, organize, analyze, and interpret data in a highly regulated field. As investigators, their contribution allowed us to make considerable progress in evaluating safety and efficacy of immunosuppressant medications in transplant recipients. As the editor of major transplant publications, I can attest to their consistent and ongoing contribution in the field.

Allowing specialty designation will assure that these clinicians are recognized for their expertise. Growth in the number of transplant pharmacists involved in clinical care and research will help to ensure that we will have adequate numbers of clinicians to continue the work in the future. Recognition of transplant pharmacists as a specialty is a positive step towards supporting their work and encouraging new practitioners to consider a career in transplantation.

Sincerely,

Bruce Kaplan, MD
Raleigh J Wright Professor and Vice President
Baylor Scott and White Health
Central Division

December 1, 2017

William M. Ellis, BSPHarm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

RE: Statement of Support - Solid Organ Transplantation Pharmacist
Specialist

Director Ellis,

My name is E.M. I am writing this letter today to support the recognition of Solid Organ Transplantation ("SOT") Pharmacist Specialists. I believe SOT Pharmacists are an integral and necessary part of the complex treatment plans involved in all stages of Solid Organ Transplantation. Solid Organ Transplantation involves, from pre-transplant preparation and care to post transplant maintenance and follow up, many issues that require an entire team of medical professionals to ensure a high standard care for transplant recipients and donors. Surely, it cannot be overstated enough the benefits of having Pharmacists trained and certified in this Specialty to the transplant team and especially to patients.

First, some background to provide a context for my statement. I am a transplant recipient and beneficiary of both pre and post transplant care from a team including a Solid Organ Transplantation Pharmacist. I was the recipient of a Kidney transplant from a living related donor in 2004. My pre and post transplant care plan has been followed at a Chicago-area hospital until the present day. Certain personnel have changed since my transplant, but my transplant physician and transplant pharmacist have remained consistent over the past 10 years. I have faced a number of medical issues in the 13 years since my transplant, but I have been able to deal with them successfully

with the care and assistance of my medical team. While I could state many instances of the care provided by my medical team, today I am writing in regards to my transplant pharmacist.

From my perspective, I feel that transplant pharmacists are important to obtaining idealized outcomes for transplant patients. I have lost count of the amount of times I have had questions about my medications and their side effects therein. My transplant pharmacist has and continues to answer all of my questions regarding my medication regimen, contraindications, and potential alternatives. In my observation, they do this for not only me but for the voluminous number of patients being seen at my care center. While there are patients who may keep up with their medication information as much as or more than myself, there are also patients who do not or are not able to do this for many reasons. I think the value to patients and their caregivers speaks for itself. My transplant pharmacist also works with my transplant nurse and transplant physician to maintain a regimen that maximizes health and minimizes side effects and issues. I believe that pharmacists that have specialized training in solid organ transplantation will be vital as the number of transplant patients increases.

I have a number of experiences during my time as a patient, but one time in particular demonstrates the care and expertise of my transplant pharmacist. Approximately five years ago, I was told by my transplant physician that I had indications for diabetes. Apprehensive and worried for what this new development would have on my transplant and health, my transplant physician had me speak with my transplant pharmacist. My transplant pharmacist proceeded to go thru all of my medications and new medications, more than 15 individual scripts. She answered questions about each medication and how it would interact with other medications and my transplant. She also gave me tips on

ideal methods and best practices for taking my medications. On a late Friday afternoon near the end of clinic time as the last patient in a busy clinic, my transplant pharmacist spent over an hour helping me to adjust to these circumstances. The specialized knowledge of transplant care coupled with their pharmaceutical expertise made sure that I knew what was ahead of me. From my conversations with other members of my care team, this is not a singular instance but a standard to ensure that patients are well equipped to deal with their treatment regimen. While this is an experience regarding one transplant pharmacist and one patient, I feel it is indicative of the overarching value and care that is and can be provided by having a transplant pharmacist with specialized training in transplant. Physicians, Nurses, and other members of the care team are made better where a transplant pharmacist who has the training and specialized knowledge to deal with transplant issues is a part of the care team. My instance is probably one of many that could be spoken about by an endless list of other patients.

I feel that it is important to look towards the future and prepare for health care needs which will only grow. As advancements in medicine and technology grow, people will continue to live longer. The need for transplants by an ever growing percentage of the populace will continue to tax resources of medical providers. In order to address these needs, it is important to be proactive in preparing current and future providers with education and training that will enable them to keep with the changes. It is here where additional value can be gleaned from Pharmacists with specialties in Solid Organ Transplantation. In addition to the already rigorous educational standards involved in training Pharmacists, a specialty in Solid Organ Transplantation will enable Pharmacists to assist Doctors in developing the most ideal treatment methods to deal with

issues such as rejection, infection, and viruses such as BK. The constant adjustments of medications along with the unique challenges of a transplant require that Transplant Pharmacists be involved in all stages of treatment. Doing this will result in reduced strain on care facilities because patient health can be maintained with significantly less follow up after a patient has reached an ideal course of treatment. Transplant teams can then focus their efforts on more difficult cases while not compromising care for the entire census of patients. This will result in financial, medical, and staffing benefits for the entire transplant team.

In closing, Transplant Pharmacists provide a significant value for transplant teams and providing a specialty for Solid Organ Transplantation can only be beneficial for the Pharmacy practice as a whole. The role that Transplant Pharmacists play in the transplant team both in their individual roles and in compliment with other members of the team helps to ensure that the highest standard of care is maintained. My Chicago area care center has had transplant pharmacists on staff for nearly 40 years and as a result patients and the hospital have benefitted. My transplant pharmacist and other transplant pharmacists I have encountered there maintain high standards that only credit the profession and practice of Pharmacy. It is because of them that I believe a Specialty in Solid Organ Transplantation Pharmacy is important and why I advocate today. If their care is any example, then it is vital that this Specialty be Recognized and Certified. Thank you for your time reading this statement.

Sincerely

EM



Prabhakar K. Baliga, MD
Fitts-Raja Professor of Surgery
Chairman Department of Surgery

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CSB 420Q
MSC 613
Charleston SC 29425
Tel 843 792 4638
Fax 843 792 9005

December 12, 2017

William M. Ellis, BPharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

Re: Recognition of Transplant Pharmacy Practice as a Specialty Certification

Dear Mr. Ellis,

I am writing in support of recent efforts to recognize Transplant Pharmacy Practice as a specialty within the purview of the Board of Pharmacy Specialties.

There are several justifications behind the recognition of Transplant Pharmacy Practice as a specialty certification. These include the fact that there is a specialized body of knowledge related to pharmacotherapy in solid organ transplant donors and recipients. There are focused practice settings where relatively large numbers of solid organ transplant donor and recipient patients are seen for inpatient and/or outpatient care, and there is a growing demand for specialty certification for the purpose of supporting advanced pharmacy roles in care of these patients.

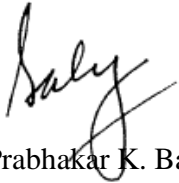
Drug therapy for solid organ transplant recipients is becoming increasingly complex. Solid organ transplant pharmacotherapy must consider the complex comorbidities of donors and recipients. Protocols and guidelines must be continually updated and adapted based on novel practice and individual center outcomes. The transplant pharmacist plays a key role in these efforts. Transplant pharmacists are involved in each phase of transplant (pre, peri, and post) and optimize transitions of care. Complex combinations of drug therapy may present special issues related to drug interactions or adverse events that are unique in the solid organ transplant population. All these and other factors argue strongly for the development of pharmacists who are expert in the knowledge and practice of pharmacotherapy in the solid organ transplant recipients and donors. Most of these complex patients are treated in inpatient or outpatient centers where a number of other similarly complex solid organ transplant patients are seen. This concentration of patients in these centers creates a demand for placement of pharmacists to help manage their drug therapy, in collaboration with other caregivers.

Solid organ transplant practitioners have long accepted pharmacists as collaborators in care of their patients. Increasingly, "advanced practice pharmacists" are being recognized by institutions in a formal manner. Some institutions are pursuing formal pathways of privileging and credentialing that are similar to those currently in place for other "mid-level" practitioners. The United Network for Organ Sharing and the Centers for Medicare/Medicaid recognize the need for solid organ transplant

pharmacists in each phase of care. During accreditation surveys the transplant pharmacist's involvement in each phase of care and credentials are verified.

Medical staff, other hospital leaders, and the public in general recognize "board certification" as an important evidence of some degree of competency. The Transplant Pharmacy Specialist credential will provide an essential credential to ensure the transplant pharmacist pedigree is not compromised; I therefore strongly encourage pursuit of this petition.

Respectfully,

A handwritten signature in black ink, appearing to read "Baliga", written in a cursive style.

Prabhakar K. Baliga, MD
Fitts-Raja Professor of Surgery
Chairman, Department of Surgery
Chief, Division of Transplant Surgery
MUSC Department of Surgery



January 9, 2018

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William M. Ellis, BSP Pharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

Dear Sir:

On behalf of the Ochsner Multi-Organ Transplant Institute, I write in support of the petition to recognize solid organ transplantation as a board certified pharmacy specialty.

Organ transplantation is a complex, multidisciplinary specialty. Our multi-disciplinary approach is mandated by UNOS and CMS and a crucial member of our team is the transplant trained specialty pharmacist. Our pharm Ds are integrated within the specific organ transplant teams and their practice is 100% dedicated to the care of pre and post-transplant patients. Drug interactions are common and our pharm Ds are necessary to ensure that we deliver effective, safe care.

Transplant recipients are among the most complex patients in our hospital. Sepsis is the most common cause of death and rejection is the most common cause of allograft dysfunction. Safely balancing immunosuppression to prevent rejection while minimizing toxicity and infection is challenging. The transplant pharmacist is necessary to help create and optimize our immunosuppression strategies and thus optimize outcomes.

Solid organ transplant programs are almost always located in academic medical centers. Beyond direct patient care, patient education and protocol development, transplant pharmacists are often involved in discovery and research.

Certification will ensure that pharmacists who want to pursue a career in transplantation understand and are prepared for the unique and complex challenges of working in this specialty. It truly is a unique set of skills that are required and it deserves special recognition.

Sincerely,

George E. Loss, Jr., M.D., Ph.D.
Chief of Surgical Services
Chairman, Department of Surgery
Chief, Multi-Organ Transplant Institute

GEL/saa

Ochsner Health System

Date: November 20, 2017

To: William M. Ellis, BSPHarm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

From: Lana Schmidt, MBA
National Kidney Patient Advocate
1636 N703rd Lane
Liberty, Illinois 62347

RE: Petition to the Board of Pharmacy Specialties (BPS) for Recognition of Solid Organ Transplantation (SOT) Pharmacist Specialists

I have had the privilege of working with a transplant pharmacist in many different capacities before, during and after my kidney transplant.

I had a very unusual situation with extremely high antibodies - many unacceptable - and the chances of getting a transplant were slim to none. I had been on dialysis 13 years and there was not a transplant surgeon in the United States who would transplant me except Dr. Benedetti from the University of Illinois in Chicago. Dr. Benedetti and his transplant pharmacist were looking at a special drug for highly sensitized patients.

The transplant pharmacist thoroughly did all the research on the novel drug and put together a comprehensive manual that we could use to try to attempt to secure funding for the drug. The information my transplant pharmacist put together was extremely useful and so specific to my situation. She would go out of her way and speak to the organization we were trying to secure funding with and explain specifics even further. Because of her outstanding work and remarkable transplant knowledge we were able to secure the funding so I could receive a kidney transplant!

She helped pave the way for this drug to be used more widely and gave hope to highly sensitized patients to be able to receive a transplant.

I trust the care, information and expertise I receive from the transplant pharmacists. The regular pharmacists lack the specialized knowledge and training to understand transplant and the unique needs of transplant patients. It is critical to have pharmacists' that understand the nuances of drugs used for transplantation. As a patient if I have a medical issue I will turn to my transplant surgeon or the transplant pharmacists. They are so helpful and knowledgeable. The transplant pharmacist would carefully go through all my medicines and make sure I had the right drug and right dosage.

Transplant is different than any other field of medicine. Many of my local doctors do want to have me as a patient because they are afraid of doing something wrong because of the transplant. At first I tried to work with my local pharmacies on getting the transplant drugs I needed. I had to go to four different pharmacies. It was clear my needs were not going to be met locally. So I ended up getting all my medications sent to me from the University of Illinois in Chicago Transplant Pharmacy. Since that time, everything has gone great.

Recently Humana said in order to keep their insurance I had to order the monthly drugs from them, not the University of Illinois pharmacy. It has been a disaster. The people I'm talking to don't know anything about the drugs, can't even pronounce them properly so I know what they are sending me nor do they know anything about transplant. They are just a call center filling scripts. I don't like it, I am very frustrated by it and want to stay with the University of Illinois transplant pharmacy. I can ask questions and they know what I'm talking about.

I support having Transplant Pharmacists Specialists and totally agree with the "Definition of Solid Organ Transplantation Pharmacist Specialist" and through my experience with my own transplant pharmacist I can clearly see the great need for this specialty.

There are not enough words in the English language to say thank you to my transplant pharmacist for her expertise and all that she has done for me!

Lana Schmidt

January 3, 2018

William M. Ellis, BSP Pharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

Dear Mr. Ellis,

I am writing to endorse establishing **Solid Organ Transplantation** as a recognized specialty within the Board of Pharmacy Specialties. I would like to support this request by providing several examples of the expertise and acumen of Transplant Pharmacists whom I have encountered in my 20 years of professional experience within the field of organ transplantation.

The role of the Transplant Pharmacist is unique and extraordinarily specialized within the field of transplantation. In no other specialty are pharmacists considered to be such a core team member, with regulatory requirements dictating not only the inclusion of their role, but also their responsibilities in rounding, patient education, and discharge planning.

At my previous organization, with the onset on the new CMS regulations in 2007, we tripled the Transplant Pharmacy support we had for all of our organ programs to remain in compliance with the regulations. At Tampa General, we are currently drafting a proposal to double the size of our Transplant Pharmacy team due to the need expressed by both patients and our teams.

As our first line of defense, I have observed Transplant Pharmacists catch errors in the ordering of immunosuppression time and time again. The presence of our pharmacists on rounds, in our clinics, and in our multidisciplinary meetings makes for *much* safer care for our patients, as we trust them to weigh in from a pharmacological viewpoint, as well as that of a patient advocate.

Speaking of patient advocacy, our Transplant Pharmacists are oftentimes the first to detect a financial barrier with a patient after transplant, and they work to ensure that patient receives needed medications. They understand what is at risk, and that the Gift of Life is a once-in-a-lifetime opportunity for most of our patients.

The Transplant Pharmacist has a vast fund of knowledge that includes not only specialty medications, but health literacy, patient adherence, assessment, and an understanding of the pharma industry. The training and expertise of our Transplant Pharmacists is absolutely irreplaceable.

Please consider recognizing the true uniqueness of the Transplant Pharmacist by granting a distinct specialty certification. We would not have such amazing long-term success nationally with organ transplant without their tremendous contributions.

Sincerely,



Melissa N. Roberts, MSN, RN, CPTC
Divisional Director, Transplant Center and MCS Program
Tampa General Hospital
mroberts@tgh.org

William M. Ellis, BSPHarm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

January 15, 2018

Dear Mr. Ellis:

It is a pleasure to write this letter in support of the Board of Pharmacy Specialties recognizing solid organ transplantation pharmacist specialists. I believe this specialty area is truly deserving of its own board certification.

The Department of Pharmacy at the University of Illinois Hospital and Clinics has provided progressive clinical pharmacy services since the late 1970s. The department's clinical pharmacist group currently numbers 62, with 22 clinical pharmacists practicing in the hospital setting and 40 in a variety of ambulatory clinics. One of the first areas that we identified the need for patient-focused clinical pharmacy services was transplant and we have had dedicated clinical pharmacists practicing in this specialty since 1977. It was also one of the first areas in which we developed a collaborative drug therapy management (CDTM) agreement; in this case with the transplant physicians which allowed our transplant clinical pharmacists the ability to provide patient care per stipulations of the agreement. More recently the CDTM agreement has been modified to a clinical care protocol which allows our transplant clinical pharmacists the ability to order/adjust medications, labs, etc. per the protocol pathway in the EHR. This was one of the first protocols developed in the hospital and approved by the Medical Staff Executive Committee, which is an indication of the value senior level leadership and the medical staff places on the services provided by our transplant clinical pharmacists.

In our department, clinical pharmacists are organized into teams (e.g., transplant, pediatrics, medicine, etc.). Of all our teams, the transplant team is the one that has the largest ambulatory footprint. The team's scope of practice spans both the inpatient and clinic settings, ensuring smooth transitions of care and minimizing the potential for medication errors to occur during these transitions. Further, the role of our transplant clinical pharmacists within the transplant group transcends clinical service provision. Our transplant clinical pharmacists are key members of and contributors to transplant's research and quality teams as well as its operations committee. When compared to our other clinical pharmacist teams, the transplant team has established a uniquely balanced practice model between acute, ambulatory and administrative duties that ensures shared experiences, responsibilities, and equitable distribution of workload between team members. Their model is one that we want our other clinical pharmacist teams to emulate to the fullest extent possible.

The transplant program at the University of Illinois is medium in size. In terms of volume, we perform approximately 150 kidney transplants, 40 liver transplants, 15 pancreas transplants and 1 small bowel transplant on an annual basis. Over the last decade, we have increased the size of our transplant clinical

pharmacist team from 2 to 5. This was driven in part by the Center for Medicare and Medicaid Services (CMS) significantly changing their conditions of participation to include mandated participation of transplant pharmacists in the evaluation of transplant candidates and donors and in their perioperative and postoperative transplant management as well as to be part of the multidisciplinary team that addresses the quality assurance and performance improvement (QAPI) efforts of the transplant program. Hospital leadership recognized the need to have a sufficient number of clinical pharmacists to comply with the conditions of participation and supported the expansion of our transplant pharmacist team by providing salary support for the new positions. With this said, with the ever evolving clinical and quality roles of our transplant clinical pharmacists, we are currently developing a proposal for an additional pharmacist to meet some of the unmet needs of this patient population.

We have been working for several years to navigate the credentialing and privileging process for our clinical pharmacists. As a testament to our transplant clinical pharmacist group's scope of practice and integration with the transplant group, we selected this group to be the first to undergo this process. This decision was fully supported by the Chair of Surgery (transplant surgeon) who offered to assist in whatever way was needed in this process. We have identified board certification, which would be transplant board certification if it was available, as one item needed for credentialing. All our transplant clinical pharmacists are board certified (BCPS), an indication of this group's understanding of the importance of board certification.

Finally, pharmacists in our department who obtain board certification have the expense of the exam paid for once passed. In addition, they receive a \$2000 salary increase as recognition for their certification. Further, as already mentioned, we have decided that a clinical pharmacist needs to be board certified to be credentialed in our organization, which is an indication of the importance that we place on board certification.

In conclusion, I fully support BPS certification in solid organ transplantation. I believe that there is an ongoing need by hospitals to have pharmacists with training in this specialty area. As already mentioned, transplant is one of the few areas in health care where pharmacists are mandated to be part of the health care team by a regulatory agency. Within my own organization, I anticipate adding another transplant clinical pharmacist soon to address the needs of this complex patient population.

Sincerely,

A handwritten signature in black ink that reads "Andrew J. Donnelly". The signature is written in a cursive, flowing style.

Andrew J. Donnelly, PharmD, MBA, FASHP
Director of Pharmacy,
University of Illinois Hospital & Health Sciences System
Clinical Professor and Associate Dean for Clinical Affairs,
University of Illinois at Chicago College of Pharmacy



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27 December 2017

William M. Ellis, BSPharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Avenue, NW
Washington, DC 20037-2985

Dear Mr. Ellis,

It is with great enthusiasm that we write to convey our support of the petition to recognize transplant pharmacists as a pharmacy specialty.

Our institution has a unique story in that we waited almost a year to hire a transplant pharmacist. We were committed to finding the right person with the experience and specialized knowledge needed to help us grow our program. It was clear that not any pharmacist can assume this role because advanced practice requires a deep understanding of transplantation and factors that affect outcomes. Our decision to hire a transplant-trained pharmacist was also influenced by the need to develop efficient pharmacy services and workflows that enhanced patient safety. While we could have easily filled the position with a non-transplant trained pharmacist, we knew that recruiting a transplant pharmacist would only enhance our growing program.

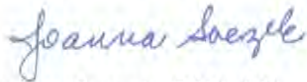
Since hiring our transplant pharmacist, we have seen an incredible benefit to our program. Our pharmacist sees virtually every transplant recipient pre- and post-transplant and makes interventions to optimize treatment in the hospital and clinic settings. By bringing a different perspective to medication management, our patients are receiving much more comprehensive care. Oftentimes drug interactions cannot be avoided and our pharmacist proactively monitors and adjusts medications to provide the best outcomes for our patients. It is evident that a transplant pharmacist's knowledge of clinically relevant drug interactions is much deeper than pharmacists who are unfamiliar with transplant medications and this makes a huge difference in complex treatment regimens. Additionally, the sharing of this knowledge has improved the understanding of transplant medications not only for patients but for our transplant staff as well. Our pharmacist is also actively involved with protocol development and quality improvement projects and elevates these initiatives with her expertise in transplant medication management.

The state of New Mexico recognizes advanced pharmacy practice as an important part of patient care and created a specific license for pharmacist clinicians. These pharmacists operate independently under the supervision of a physician and are able to expand patient access to healthcare. For us, board certification in transplant pharmacy would help us identify pharmacists who have the expertise needed to be a successful and credible transplant pharmacist clinician. As we expand our program, it is our goal to have our pharmacist obtain a pharmacist clinician license. Board certification in transplant pharmacy will

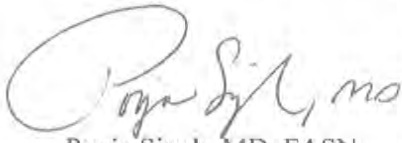
give us leverage to discuss reimbursement strategies with local insurance companies so that we can continue to provide high quality care.

In summation, we resoundingly support the petition to recognize transplant as a pharmacy specialty. It is so clear to us that a transplant pharmacist is an integral member of our team that we definitely do not want to go back to the times when we did not have one!

Sincerely,



Joanna Saczek, BSN, RN
Transplant Services Director
University of New Mexico Hospitals



Pooja Singh, MD, FASN
Associate Professor of Medicine
Division of Nephrology
Medical Director, Renal Transplant Services
University of New Mexico School of Medicine



Louis E. Ahusim, PharmD, MS
Executive Director, Pharmaceutical Services
Clinical Associate Professor, College of Pharmacy
University of New Mexico Health Sciences Center
University of New Mexico Hospitals



Charles O. Strickler Transplant Center

February 5, 2018

William M. Ellis, BSPharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

RE: Recognition of Solid Organ Transplantation (SOT) Pharmacist Specialists

Dear Mr. Ellis,

As Chief of the Division of Transplantation and Director of the Charles O. Strickler Transplant Center at the University of Virginia, it is with great enthusiasm that I support and encourage the recognition of board – certified Solid Organ Transplantation (SOT) Pharmacist Specialists.

Currently within the Commonwealth of Virginia, The University of Virginia (UVA) is the only institution where any patient - adult or child - can be transplanted with any solid organ: heart, lung, liver, kidney, and pancreas including islet cells to treat type 1 diabetes. The obvious complexities of treating the aforementioned patients would not be feasible without the team of Transplant Clinical Pharmacists. Within the Charles O. Strickler Transplant Center we are able to offer our patient’s access to six specialized SOT pharmacist.

With continued additions to the transplant waitlist, we as an institution are strategizing to double our transplant volumes. It is our responsibility to serve the community and the Commonwealth while providing quality care at its highest level. Our philosophy within the Division of Transplantation is that of teamwork and multidisciplinary care. Ensuring quality outcomes for our many patients cannot be achieved without the implementation, design, and monitoring of pharmacotherapeutic plans.

During the 14 years I spent at the University of Illinois at Chicago, the transplant center experienced a formidable increase in the quality of care PharmDs make in the transplant population. Incorporating PharmDs into daily transplant care has become a crucial part of all multidisciplinary transplant programs.

Sincerely,

JOSÉ OBERHOLZER, MD, MHCM, FACS
Professor, Surgery and Biomedical Engineering
Director, Charles O. Strickler Transplant Center
Chief, Division of Transplantation
University of Virginia School of Medicine

December 12th, 2017

William M. Ellis, BSPharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Avenue, NW
Washington, DC 20037-2985

On behalf of the UW Health Division of Transplantation, we are writing to support the petition to recognize solid organ transplantation as a board certified pharmacy specialty.

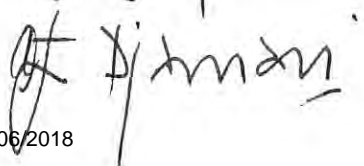
At UW Health, transplant pharmacists are involved in all phases of care, including both inpatient and outpatient settings. These pharmacists are expertly trained to provide high quality direct patient care to a very unique and challenging patient population. They are essential members of our multidisciplinary healthcare team and provide critical input by optimizing pharmacotherapeutic regimens to improve outcomes, safety, and adherence, all of which are necessary for a successful transplant. Their expertise in transplant specific drug interactions, medication adverse effects, and alternative modes of therapy is crucial and a clear indicator that specialization should be required for advanced practice. Furthermore, our pharmacists independently practice under several delegation protocols to treat specific disease states. Not only does this save us a considerable amount of time but we fully trust in their specialized training to manage these complex patients. The level of care we provide at UW Health would certainly suffer if we did not have transplant pharmacists to support our program.

Beyond patient care, our pharmacists are heavily involved in academic research, patient safety initiatives including protocol development, guideline authorship, and quality metrics analysis. These projects are often high quality, very detailed, and serve as evidence that specialized knowledge is needed to contribute to a robust transplantation program. On top of that, our pharmacists are committed to advancing the practice of transplantation medicine and are involved nationally within the American Society of Transplantation.

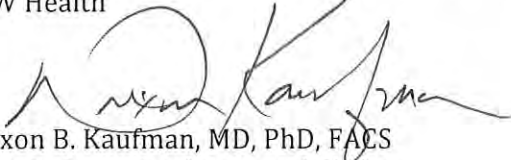
As medication therapies for solid organ transplantation become more complex and expensive, we believe that the pharmacist has a unique role on our team to ensure effective and safe medication use. With a board certified specialty in solid organ transplantation pharmacy, we can ensure that skilled pharmacists are identified to support and help expand our transplant program. Furthermore, certification will show other providers that the individual pharmacist has specialized knowledge in solid organ transplantation pharmacotherapy and continues to maintain that knowledge.

In closing, we strongly urge the Board of Pharmacy Specialties to accept the petition to recognize solid organ transplantation as a pharmacy specialty.

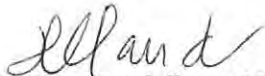
Sincerely,

Arjang Djaman


Arjang Djamali, MD, MS, FASN
Professor of Medicine and Surgery
Head, Nephrology Division
Department of Medicine
University of Wisconsin School of Medicine and Public Health
UW Health



Dixon B. Kaufman, MD, PhD, FACS
Ray D. Owen Professor and Chair
Division of Transplantation
Department of Surgery
Medical Director, Transplant Service Line
Surgical Director, Kidney Transplantation
University of Wisconsin School of Medicine and Public Health
UW Health



Didier Mandelbrot, MD
Professor of Medicine
Medical Director of Kidney and Pancreas Transplantation
Medical Director of Living Kidney Donation
Department of Medicine
University of Wisconsin School of Medicine and Public Health
UW Health

William M. Ellis, BPharm, MS
Executive Director
Board of Pharmacy Specialties
2215 Constitution Ave., NW
Washington, DC 20037

1 December 2017

Dear Director Ellis,

I had the honor of being asked to write a letter of support for the recognition of solid organ transplantation pharmacist specialist through the Board of Pharmacy Specialties. I have the unique experience of being able to write from the perspective of not just a pharmacist who will be completing a PGY-2 in transplant pharmacy from 2018-2019, but also as a previous transplant recipient myself who had the benefit of receiving care from a trained transplant pharmacist.

I first became interested in pharmacy over a decade ago when I was undergoing chemotherapy for acute myeloid leukemia in which a medication preparation/order error resulted in a pulmonary toxic dose requiring a double lung transplant for survival. My world was upturned in the matter of a few days; I was a healthy teenager (except for the AML) who was seeing the light at the end of the tunnel with chemotherapy to being intubated with the limited possibility of ever getting off of a ventilator with a poor prognosis. While I had fantastic physicians who provided excellent clinical care, there were a lot of holes in the information being relayed to me. It was the transplant pharmacist who spent the time to explain the process and what to expect and who reassured me that I could get through this experience. It was the interactions that I had with my transplant pharmacist that I truly believe helped save my life, kept me healthy throughout the past decade, and ignited my interest in the pharmacy profession.

When I first woke up after being intubated and discovered that I required the transplant, I remember feeling so incredibly scared and confused with what was happening. I remember the haze of doctors coming in and telling me so much information but nothing really processed. It wasn't until the pharmacist came in and began explaining everything to me that I really grasped what was happening. The pharmacist took the time to explain the process in terms of before, during, and after the surgery. She explained what to expect in terms of medication burden, side effects, adverse effects signs and symptoms, and sat there with me as I labored to write out my questions for her on the whiteboard. After the surgery, periodically she would stop by to check to see how things were going and if I had any questions or concerns as it came closer to my discharge date. She was a breath of fresh air for me and was a provider I could tell truly care about her patients. She opened my eyes to the world of clinical pharmacy and broke that retail pharmacist stereotype for me.

As a PGY-1 resident currently, I have had the privilege of completing an extended rotation in transplant in which I was able to learn a significant amount about transplant at one of the

largest transplant facilities in the United States. I was able to immerse myself in the team and spent a significant amount of time with the patients both in the clinic before and after the transplant and while they were inpatient. The amount of knowledge and skills that I developed during that time was truly eye opening. Learning the intricacies of balancing immunosuppression with prophylactic and treatment anti-infectives with patient specific factors is a complexity that requires time and passion to learn. Developing the skills to be able to educate patients on their extensive medications, which often go from a handful prior to transplant to over 20 after requires refining in order to not overwhelm the patient while still having an impact. All of these complexities combine to make complex patients who benefit best from trained, specialized pharmacists.

I truly believe that transplant pharmacists should be identified as a specialty through board certification because of the unique patient set that encompasses transplant, the complex medication requirements, and the extensive amount of education that is required to be given to patients in a manner that manageable for the patient. While generalized clinical pharmacists are incredibly qualified to practice, I believe that it is beneficial to identify those pharmacists who are either PGY-2 trained or have extended experience in transplant. Additionally, as more and more pharmacy departments across the United States move away from a specialist model, it is beneficial to be able to quickly identify pharmacists who are specifically trained in transplant for the benefit of the department and overall patient care.

If you have any questions or concerns, or would like to speak to me for additional information, please do not hesitate to contact me at the information below.

Sincerely,

Cassandra Votruba, PharmD
PGY1 General Clinical Practice Resident
University of Wisconsin Hospital and Clinics
600 Highland Ave, Madison WI, 53792
cvotruba@uwhealth.org
602-881-5324

Appendix C-1

Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification

Survey of Solid Organ Transplantation Pharmacists Interested in Board Certification

Dear Solid Organ Transplantation Pharmacist:

We are contacting you regarding the Board of Pharmacy Specialties' call for petition considering solid organ transplantation as a pharmacy specialty. We kindly request that you complete this 5-10 minute survey to provide the organizations petitioning BPS with essential data to support the petition to BPS.

The American College of Clinical Pharmacy (ACCP) and the American Society of Health-System Pharmacists (ASHP) have partnered to develop and submit a petition to the Board of Pharmacy Specialties (BPS) to recognize solid organ transplantation pharmacy practice as a specialty. For purposes of this petition, the definition of solid organ transplantation pharmacy practice is:

Solid organ transplantation (SOT) pharmacist specialists have the specialized training and knowledge needed to manage complex medication regimens unique to the solid organ transplantation population. Additionally, they are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. They care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. SOT pharmacist specialists provide evidence-based, patient-centered medication management. They design, implement, monitor, and modify pharmacotherapeutic plans to improve safety and efficacy, which leads to optimal short-term and long-term patient and allograft outcomes. Core responsibilities of SOT pharmacist specialists are to analyze and reevaluate multifaceted clinical and outcomes data to improve care and demonstrate ongoing quality assessment and process improvement as required by regulatory agencies. Finally, SOT pharmacist specialists are integral members of the interprofessional transplant team that facilitates medication adherence and pharmacotherapy education.

We kindly request that you complete the survey by Friday, December 8, 2017. Your individual responses will be kept confidential. Collectively, all pharmacist responses will be compiled to further document the unique elements of this specialty and provide support for this specialty in a petition to the Board of Pharmacy Specialties.

Student pharmacists and residents whose clinical service has less than 50% of time spent in the provision of care to solid organ transplantation patients should not participate in the full survey but may still sign on to support the petition. At the end of the survey, all respondents will have an opportunity to add your signature to the petition. If questions arise, contact Jann Skelton at jskelton@silverpennies.com. Thank you for taking the time to provide this valuable information.

- Stephanie Anders, PharmD, BCPS; Representing the American Society of Health-System Pharmacists
- Maya Campara, PharmD, BCPS; Representing the American College of Clinical Pharmacy
- Amanda Condon, PharmD; Representing the American College of Clinical Pharmacy

- Nicole A. Pilch, PharmD, MSCR, BCPS; Representing the American Society of Health-System Pharmacists

Practicing Solid Organ Transplant Pharmacists

* Indicates response required

* How many years have you been a licensed pharmacist?

- < 5 years
- 5-9 years
- 10-14 years
- 15-19 years
- > 19 years

* How many years have you been in solid organ transplantation pharmacy practice?

- I do not practice in solid organ transplantation pharmacy practice
- < 5 years
- 5-9 years
- 10-14 years
- 15-19 years
- > 19 years

If 'I do not practice...' link to the option to provide support for the SOT petition

*Please indicate your primary practice setting.

- Ambulatory care
- Community hospital, for profit
- Community hospital, not for profit
- Family medicine/Internal medicine/Primary care/Private office
- Federal hospital or institution
- Managed care
- Pharmaceutical industry
- University-affiliated hospital
- University hospital
- Private hospital
- School of Pharmacy or Medicine
- Specialty pharmacy
- Other

Please indicate your secondary practice setting, if applicable.

- Community hospital, for profit
- Community hospital, not for profit
- Family medicine/Internal medicine/Primary care/Private office
- Federal hospital or institution
- Managed care
- Pharmaceutical industry
- University-affiliated hospital
- University hospital
- Private hospital

- School of Pharmacy or Medicine
- Specialty pharmacy
- Other

* Do you believe that you currently practice in the area of solid organ transplantation specialization as defined by the Task Group?

- Yes
- No

If no, link to the option to provide support for the SOT petition

*Which solid organ transplantation recipients do you provide clinical care for? Please check all that apply.

- Adult heart
- Pediatric heart
- Adult lung
- Pediatric lung
- Adult liver
- Pediatric liver
- Adult kidney
- Pediatric kidney
- Pancreas
- Small bowel
- Multivisceral
- Other

*What other BPS certifications do you currently hold? Please check all that apply.

- Ambulatory Care Pharmacy
- Cardiology Pharmacy
- Critical Care Pharmacy
- Geriatric Pharmacy
- Infectious Diseases Pharmacy
- Nuclear Pharmacy
- Nutrition Support Pharmacy
- Oncology Pharmacy
- Pediatric Pharmacy
- Pharmacotherapy
- Psychiatric Pharmacy
- None

* On average, how many HOURS per week do you practice in your solid organ transplantation practice site?

- Full-time: 40 or more hours per week
- 31 - 39 hours per week
- 25 - 30 hours per week

- 21 - 24 hours per week
- 15 - 20 hours per week
- 10 - 14 hours per week
- 1 - 9 hours per week

* If yes, in an average week, what PERCENTAGE of your time do you estimate is devoted exclusively to providing direct patient care and services according to this definition? (Note: This may be the same as reported in the previous question; however, it may also be different. For example, you may provide additional services at your solid organ transplantation practice that are unrelated to direct patient care.)

- 90% - 100%
- 80% - 89%
- 70% - 79%
- 60% - 69%
- 50% - 59%
- 40% - 49%
- 30% - 39%
- 20% - 29%
- 10% - 19%
- 1% - 9%

* Please check all types of residencies/fellowships completed.

- PGY1 Residency - Pharmacy Practice
- PGY2 Residency - Solid Organ Transplant
- PGY2 Residency - Other Specialty
- Fellowship
- No residency or fellowship
- Other (please specify)

If PGY2 – Other Specialty; What PGY2 Residency Program did you complete?

- Ambulatory Care Pharmacy
- Cardiology Pharmacy
- Community Pharmacy
- Corporate Pharmacy Leadership
- Critical Care Pharmacy
- Drug Information
- Emergency Medicine Pharmacy
- Family Medicine
- Geriatric Pharmacy
- Health-System Corporate Pharmacy Administration
- Health-System Medication Management Pharmacy
- Health-System Pharmacy Administration
- Health-System Pharmacy Administration/MS
- HIV Pharmacy
- Infectious Diseases Pharmacy
- Internal Medicine Pharmacy

- Managed Care Pharmacy System
- Medication-Use Safety
- Neonatology Pharmacy
- Nephrology Pharmacy
- Neurology Pharmacy
- Nuclear Pharmacy
- Nutrition Support Pharmacy
- Oncology Pharmacy
- Palliative Care/Pain Management Pharmacy
- Pediatric Pharmacy
- Pharmacoeconomics and Outcomes Research
- Pharmacogenetics
- Pharmacotherapy
- Pharmacy Informatics
- Pharmacy Outcomes/Health care Analytics
- Psychiatric Pharmacy
- Specialized Area of Pharmacy
- Transitions of Care
- Other

* If the petition to recognize solid organ transplantation pharmacy practice as a specialty is approved, how likely would you be to pursue this specialty recognition within the next 5 years?

- Highly likely
- Likely
- Somewhat likely
- Unlikely
- Highly unlikely

* Are you directly responsible for hiring solid organ transplantation pharmacists within your organization?

- Yes
- No

Solid Organ Transplantation Pharmacist Employers

Definition of Solid Organ Transplantation Pharmacist Specialists

Solid organ transplantation (SOT) pharmacist specialists have the specialized training and knowledge needed to manage complex medication regimens unique to the solid organ transplantation population. Additionally, they are experts in meeting clinical and regulatory needs not encountered in any other pharmacy specialty. They care for patients throughout all phases of solid organ transplantation, at all ages, and in various health care settings. SOT pharmacist specialists provide evidence-based, patient-centered medication management. They design, implement, monitor, and modify pharmacotherapeutic plans to improve safety and efficacy, which leads to optimal short-term and long-term patient and allograft outcomes. Core responsibilities of SOT pharmacist specialists are to analyze and reevaluate multifaceted

clinical and outcomes data to improve care and demonstrate ongoing quality assessment and process improvement as required by regulatory agencies. Finally, SOT pharmacist specialists are integral members of the interprofessional transplant team that facilitates medication adherence and pharmacotherapy education.

*What is the total number of clinical FTEs allocated to serving patients with solid organ transplantation within your organization?

* What is the total number of administrative or management FTEs allocated to serving patients with solid organ transplantation within your organization?

*What percentage of these pharmacists do you believe are currently practicing in the area of specialization as defined above?

*What percentage of these pharmacists practicing in the area of specialization are currently required to have advanced clinical training (e.g., residency training)?

*What percentage of these solid organ transplant pharmacist positions currently require BPS specialty certification or other earned credentials?

*Do you have a credentialing and privileging program for pharmacists within your organization?

- Yes
- No

If yes - * Is BPS Board Certification currently a requirement for your credentialing and privileging program?

- Yes
- No

If no - * Do you anticipate that BPS Board Certification will become a requirement for your credentialing and privileging program within the next 3 years?

- Yes
- No

*How many solid organ transplantation pharmacist positions within your institution are currently vacant/unfilled?

*Please rank, in preferred order, the current desired level of training for pharmacists practicing in solid organ transplantation pharmacy in your organization. 1 = most desired; 5 = least desired

- PGY1 Residency - Pharmacy Practice
- PGY2 Residency - Solid Organ Transplant
- PGY2 Residency - Other
- Employer-provided training program
- None required or desired

*If BPS recognizes solid organ transplantation pharmacy as a specialty, what is the likelihood that you would require this new specialty credential for newly hired pharmacists within your organization?

- Highly likely
- Likely
- Somewhat likely
- Unlikely
- Highly unlikely

*If BPS recognizes solid organ transplantation pharmacy as a specialty, what is the likelihood that you would require this new specialty credential for currently employed solid organ transplantation pharmacists within your organization?

- Highly likely
- Likely
- Somewhat likely
- Unlikely
- Highly unlikely

*Which of the following ranges best describes your organization's anticipated growth in the number of solid organ transplant pharmacy specialists (as described above) over the next 5 years?

- Projected decrease
- 0%-5%
- 5%-10%
- 10%-20%
- >20%

*How many positions for solid organ transplantation pharmacy specialists (as defined above) has your organization recruited over the past 3 years, from November 1, 2014 to November 1, 2017?

*What percentage of these positions were filled?

*How many positions for solid organ transplantation pharmacy specialists (as defined above) do you estimate you will hire within the next 3 years?

*Please add any additional comments that would help us understand the demand for specialists in solid organ transplantation practice within your organization.

OPTIONAL: If you would like to support this recognition effort by signing the petition to BPS, please add your signature in support of this proposed specialty by completing the following information:

First Name*

Last Name*
Credentials*
Title*
Place of Employment*
Work Address*
City *
State*
Zip Code*
Work Phone Number*
Work Email Address*

Appendix D-1

Role Delineation Study for Solid Organ Transplantation Pharmacists



**Role Delineation Study for
Solid Organ Transplantation Pharmacists**

March 2017



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INTRODUCTION

The Board of Pharmacy Specialties (BPS) improves patient care by promoting the value of specialized training, knowledge, and skill in pharmacy and the specialty board certification of pharmacists. It accomplishes this mission by

1. providing leadership for the profession of pharmacy in the discussion, evolution, direction, and recognition of specialty board certification of pharmacists;
2. establishing and promoting, in collaboration with stakeholders, the value of pharmacy specialization and board certification;
3. establishing the standards for identification and recognition of pharmacy specialties;
4. establishing standards of eligibility, knowledge, and skills for pharmacists as the basis for board certification;
5. developing and administering a valid process to evaluate the knowledge and skills for recognition of board-certified pharmacists; and
6. assessing and recognizing the continued eligibility, knowledge, and skills of board-certified pharmacists through a valid recertification process.

BPS is exploring the feasibility of establishing board certification for pharmacists whose practice includes a specialty in solid organ transplantation. Solid organ transplantation pharmacists provide evidence-based, patient-centered medication therapy management and care for patients of all ages throughout all phases of solid organ transplantation in various healthcare settings. Solid organ transplantation pharmacists have the specialized knowledge and expertise needed to manage complex medication regimens unique to the solid organ transplantation population in addition to clinical and regulatory needs not encountered in any other pharmacy specialty. Solid organ transplantation pharmacists are specially trained to design, recommend, implement, monitor, and modify pharmacotherapeutic plans to optimize outcomes. They review, analyze, and reevaluate multifaceted clinical and outcomes data in order to provide quality care and assess program effectiveness. Finally, they provide education and counseling throughout the transitions of care.

BPS identified pharmacists with expertise in solid organ transplantation to meet with Castle Worldwide, Inc., for two days (August 26 and 27, 2016) in National Harbor, Maryland, to define performance domains and tasks as well as the knowledge required for the competent performance of the tasks. The group delineated these elements through intense analysis of the practice of pharmacists who include solid organ transplantation in their practice, giving particular attention to the ways that it applies in different settings and patient conditions.

As the primary process for identifying the competency and knowledge that pharmacists must have to provide solid organ transplantation pharmacy services proficiently, role delineation helps to establish content validity. Validation through systematic role delineation study helps to support the claim that a certification examination (if one is to be developed) bears a sound linkage to practice.

The role delineation study in solid organ transplantation pharmacy identified the point in time that pharmacists specializing in this area are expected to perform the tasks (Performance Expectation), the nature of harm that the inability to perform the tasks competently might bring about (Consequence), and how often they perform the tasks (Frequency). Ratings addressing these issues and provided by participants in a nationwide survey play an important role in understanding the essential knowledge base and documenting its fidelity to practice.

BPS desired to adhere to established standards for the conduct of job analysis studies, the general family of methods to which role delineation study belongs. These guidelines have their foundation in logically sound and legally defensible procedures drawn from psychometric literature and case law. Essential principles and procedures are outlined in federal regulation (*Uniform Guidelines on Employee Selection Procedures*) and manuals, such as *Standards for Educational and Psychological Testing* (published by the American Educational Research Association, 2014). Castle employed these standards as well as those of the National Commission for Certifying Agencies (NCCA, 2016) throughout the study.

In preparation for the project, Castle interviewed Angela Maldonado, PharmD, CPP, BCPS, FAST, and Christopher Ensor, PharmD, BCPS, AQ-Cardiology. Castle also reviewed several documents addressing solid organ transplantation practices, including the *Thoracic Transplant Pharmacy Professionals Core Competency Curriculum*, First Edition, prepared by the International Society for Heart and Lung Transplantation. The purpose of these preliminary activities was to acquaint Castle staff with the basic activities and terminology of solid organ transplantation pharmacy. Castle then prepared a booklet of instruction for use with the panel of experts.

The role delineation study consisted of the following major phases:

- I. Initial Development and Validation. The panel of pharmacists with expertise in solid organ transplantation identified the essential domains, tasks, and knowledge.
- II. Validation Study. Several organizations whose members include pharmacists with a specialty in solid organ transplantation sent email invitations on behalf of BPS to complete a survey based on the work of the panel. A qualified group of respondents provided data in this phase.
- III. Development of Specifications. Based on the ratings gathered from survey participants, Castle proposed specifications to provide direction for decision making about the design of a BPS assessment in solid organ transplantation, should one be developed.

The panel of experts in solid organ transplantation appointed by BPS defined the essential framework of the role delineation study. The panel and other project personnel are listed here:

Name	Employer	City
Tiffany E. Kaiser, PharmD, MS, BCPS, FACC	University of Cincinnati	Cincinnati, OH
James N. Fleming, PharmD, BCPS	Medical University of South Carolina	Charleston, SC
Barrett Crouther, PharmD, BCPS, FAST	University Health System	San Antonio, TX
Lisa Potter, PharmD, BCPS, FCCP, FAST	University of Chicago Medicine	Chicago, IL
Christopher R. Ensor, PharmD, BCPS, AQ-Cardiology	University of Pittsburgh	Pittsburgh, PA
Lyndsey J. Bowman, PharmD, BCPS	Tampa General Hospital	Tampa, FL
Angela Q. Maldonado, PharmD, CPP, BCPS, FAST	Vidant Medical Center	Greenville, NC
Lonnie Smith, PharmD, FAST	University of Utah Hospital and Clinics	Salt Lake City, UT
Nicole A. Pilch, PharmD, MSCR, BCPS, FAST	Medical University of South Carolina	Charleston, SC
Emily Benefield, PharmD, BCPS, BCPPS	Primary Children's Hospital	Salt Lake City, UT
Maya Campara, PharmD, BCPS	University of Illinois at Chicago	Chicago, IL
Cher Enderby, PharmD, BCPS, BCNSP	Mayo Clinic	Jacksonville, FL
Laura Myhre, PharmD, BCPS	Mayo Clinic	Rochester, MN
Rochelle Schmidt Liverman, PharmD	Children's Healthcare of Atlanta	Atlanta, GA
Steven Gabardi, PharmD, BCPS, FAST, FCCP	Brigham and Women's Hospital	Boston, MA

BPS Staff

Jacquelyn Kelly-Marshall, Director of Certification

Castle Staff

James P. Henderson, Ph.D.

INITIAL DEVELOPMENT AND EVALUATION

Consistent with its mission, BPS is exploring the feasibility of offering certification for pharmacists whose practice includes solid organ transplantation pharmacy. Accordingly, BPS conducted a role delineation study to determine the knowledge that pharmacists whose practice includes solid organ transplantation pharmacy must have in order to provide proficient services. The role delineation study focused on relevant elements of responsibility that apply in the variety of settings in which solid organ transplantation pharmacists work. Of particular interest in the study was the degree to which pharmacists whose practice includes solid organ transplantation are expected to be proficient in the domains and tasks in the first year of certification, assuming a program is developed.

The role delineation study began with a preliminary review of literature and preparatory discussions in the summer of 2016 and a meeting of the role delineation panel on August 26 and 27, 2016, in National Harbor, Maryland. Assisted by Castle, the panel of experts outlined domains, tasks, and knowledge that are essential to work of pharmacists working with solid organ transplantation patients. A large-scale validation study conducted in February and March 2017 provided information that was used to assess the appropriateness of the domains and tasks as delineated by the panel of experts.

Solid organ transplantation pharmacists have the specialized knowledge and expertise needed to manage complex medication regimens unique to the solid organ transplantation population in addition to clinical and regulatory needs not encountered in any other pharmacy specialty. Solid organ transplantation pharmacists are specially trained to design, recommend, implement, monitor, and modify pharmacotherapeutic plans to optimize outcomes. They review, analyze, and reevaluate multifaceted clinical and outcomes data in order to provide quality care and assess program effectiveness. Finally, they provide education and counseling throughout the transitions of care.

Early Steps in the Role Delineation Study

The first steps in conducting the role delineation study included a preliminary review of sources about solid organ transplantation, an interview with individuals who have in-depth knowledge about solid organ transplantation pharmacy, the preparation of instructional materials, and a two-day meeting with a panel of experts whose members represented a broad range of practice settings, regions, and qualifications. The purpose of the preliminary analysis was to identify the basic steps involved in solid organ transplantation pharmacy and key terminology. With this information, Castle prepared instructional materials that members of the expert panel used to inform their participation in the role delineation meeting and that Castle used to convey essential explanations. The objective of the meeting was to define the domains, tasks, and knowledge required for each task at a level commensurate with BPS certification, should a program be established (Appendix A).

Preliminary Analysis

To provide leadership for the role delineation study, Castle sought to become acquainted with the role and major responsibilities of pharmacists whose practice includes solid organ transplantation. Castle reviewed relevant material provided by BPS (see bibliography) and its leadership. Discussion with two of these leaders, Angela Maldonado, PharmD, CPP, BCPS, FAST, and Christopher Ensor, PharmD, BCPS, AQ-Cardiology, was extremely informative, particularly because of their deep knowledge and experience in solid organ transplantation. The preliminary analysis enhanced Castle's familiarity with the terminology, major responsibilities, and general scope of this practice area.

Instructional Materials

Essential to the success of the role delineation meeting were the materials used to inform panelists about key concepts (Appendix B). The instruction booklet included a draft definition of solid organ transplantation, other essential definitions, and sample language for domains, tasks, and knowledge. The instruction booklet also included a set of validation scales that are commonly used in role delineation studies as well as worksheets that were used for various purposes in the meeting.

Instructional materials were used during the meeting of the panel of experts as a means of building understanding among participants about concepts and terms and to orient their essential thought processes and activities.

Role Delineation Meeting

The panel of experts reviewed the draft definition of solid organ transplantation pharmacy and then reached consensus on suggestions for its revision. After this discussion, panelists expressed clear understanding that the level of proficiency expected for the program, as indicated by the typical BPS eligibility criteria, is high but appropriate for pharmacists at the time they would first qualify for board certification. The panel then focused on developing an outline of domains, tasks, and requisite knowledge that likely would be adequate for the upcoming five-year period and appropriate for the newly certified pharmacist. The domains are as follows:

- Domain I: Clinical Skills and Therapeutic Management
- Domain II: Administration and Practice Development
- Domain III: Information Management and Education
- Domain IV: Public Health

For each domain, panel experts worked in focus groups to draft tasks, which the whole group then reviewed and refined through a consensus process. The participants' diversity led to discussions that challenged terminology, phrasing, and every aspect of the draft statements, with the resulting agreement representing a statement that all members of the panel believed to be valid. The panel also developed a set of knowledge statements for each task in the domains, making refinements and reaching consensus through whole-group discussion.

At the end of the meeting, all panelists evaluated several scales that are commonly used in certification-related role delineation studies: Performance Expectation, Consequence, and Frequency. The panel refined the scales to ensure their applicability to pharmacists whose practice includes solid organ transplantation pharmacy.

BPS arranged for the review of the draft content outline by solid organ transplantation pharmacists who had not participated in the panel in order to gather suggestions for refinement and to determine if anything had been left out. After the comments of these individuals were assimilated, BPS and Castle held a conference call of the panel on January 4, 2017, to consider the suggestions and make decisions about incorporating them in the outline.

Based on the work of the expert panel and in consultation with BPS staff, Castle developed an electronic validation survey. The process of review informed revisions to the survey. Data were then collected from a large sample of pharmacists whose practice includes solid organ transplantation. The results of the validation survey are the major focus of this report.

VALIDATION STUDY

Questionnaire Design and Distribution

Castle developed an online questionnaire to be completed by pharmacists who include solid organ transplantation pharmacy as part or all of their practice. The purpose of the questionnaire was to collect data on the domains and tasks as developed by the panel of experts. The questionnaire phase of the role delineation study was important because pharmacists who provide services for solid organ transplantation patients should have input into the delineation of this work. Such input is critical because the panel of experts, although highly qualified and representative in many key ways, constituted only a small sample of the population. Evaluation by the larger professional community is essential in order to make well-founded generalizations. The questionnaire also was designed to solicit demographic information to describe the group of respondents and document their qualifications as members of the population.

Given that no certification program exists for solid organ transplantation pharmacists, the sampling plan required the cooperation of three organizations outside of BPS to send survey invitations to their members (Appendix C). Perhaps the best source of contact information regarding survey participants was the American Society of Transplantation Community of Practice, which sent the survey invitation to 412 individuals. The American College of Clinical Pharmacy (ACCP) sent the survey invitation to 553 individuals, of whom 394 were full ACCP practitioner members and the remainder were students, residents, or fellows. The American Society of Health-System Pharmacists (ASHP) also sent invitations to its members who conceivably could have a solid organ transplantation specialty as part of their practice, but the number of individuals is not known. The link included in the invitation sent by each organization allowed Castle to associate the responses received to the organization. Castle monitored responses, and BPS requested that the organizations send follow-up correspondence as appropriate.

There is a high probability that many individuals received invitations from several organizations. As a result, the total number of individuals invited to participate is not known, making it impossible to compute a response rate. Ultimately, Castle received 220 qualified, usable responses. To be included in the data set for analysis, respondents had to provide at least 15% of the task ratings requested. The survey was long and complex—30 minutes were required to complete it. Not all individuals responded to every question, so the total number of responses per question varies.

Who Responded to the Survey?

The survey (Appendix D) included 17 demographic questions, consistent with previous BPS surveys but with questions specifically designed for the solid organ transplantation pharmacy investigation. There were several reasons for collecting and analyzing demographic data. One was to determine the degree of diversity among respondents along dimensions that may be seen as influencing practice, and another was to assess the degree to which respondents were qualified to provide data for an analysis of solid organ transplantation pharmacy. Demographic data are summarized in the tables and graphs on the following pages. Based on a review of these statistics, it is reasonable to conclude that respondents represented the diverse population to a reasonable degree.

The first demographic question in the survey asked respondents to indicate the highest level of education they have achieved in pharmacy. Almost all of the respondents who answered the question have a doctor of pharmacy degree (PharmD).

Table 1. What is the HIGHEST pharmacy-related degree you have earned?

Response	Count	Percent
Bachelor's degree	3	1.5%
Master's degree	0	0.0%
PharmD	192	97.5%
Ph.D.	1	0.5%
Other	1	0.5%
Total	197	100.0%

Generally speaking, respondents are reasonably new practitioners. Just about half of the respondents achieved their first licensure as pharmacists in 2010 or after. Only about 5% were first licensed prior to 1995.

Table 2. In what year were you first licensed as a pharmacist?

Response	Count	Percent
2015-2017	15	7.5%
2010-2014	84	42.2%
2005-2009	52	26.1%
2000-2004	26	13.1%
1995-1999	11	5.5%
1990-1994	8	4.0%
1985-1989	1	0.5%
1980-1984	2	1.0%
Total	199	100.0%

One of the pathways by which applicants can satisfy the eligibility requirements to take a BPS examination is to complete a residency program. Over half of the respondents completed a two-year residency focused on solid organ transplantation pharmacy, and most of the 24 Other responses indicated that the respondent had completed a two-year pharmacy residency in one of the BPS specialty pharmacy areas.

Table 3. Have you completed a residency training program? If so, what is the HIGHEST program completed?

Response	Count	Percent
Yes, Postgraduate Year One (PGY1) Pharmacy Residency	52	26.0%
Yes, Postgraduate Year Two (PGY2) Pharmacy Residency in Solid Organ Transplantation	111	55.5%
No	13	6.5%
Other	24	12.0%
Total	200	100.0%

Fewer than 10% of the respondents reported completion of a fellowship training program. Of the small number that have this qualification, most focused on solid organ transplantation pharmacy. See Table 4.

Table 4. Have you completed a fellowship training program?

Response	Count	Percent
No	186	93.5%
Yes, in solid organ transplantation pharmacy	10	5.0%
Yes, in other area (please specify)	3	1.5%
Total	199	100.0%

Respondents were asked next to indicate which BPS specialties they hold. By far, the largest group of respondents reported current certification in pharmacotherapy. Because respondents could mark more than a single response, Table 5 reports only the frequency (Count) for each response option.

Table 5. Are you certified in a BPS specialty? (Select all that apply.)

Response	Count
No	47
Ambulatory Care Pharmacy	3
Critical Care Pharmacy	1
Geriatric Pharmacy	0
Nuclear Pharmacy	0
Nutrition Support Pharmacy	3
Oncology Pharmacy	0
Pediatric Pharmacy	6
Pharmacotherapy	147
Psychiatric Pharmacy	0

Just over half of the respondents indicated that they have worked in solid organ transplantation pharmacy for five years or less. Only about 10% of the respondents have provided services in this area for 15 or more years.

Table 6. In total, how long have you worked full time and/or part time in solid organ transplantation?

Response	Count	Percent
Less than 3 years	57	28.6%
3 to 5 years	49	24.6%
6 to 8 years	32	16.1%
9 to 11 years	27	13.6%
12 to 14 years	13	6.5%
15 to 17 years	14	7.0%
18 to 20 years	4	2.0%
More than 20 years	3	1.5%
Total	199	100.0%

The overwhelming majority of respondents (over 70%) reported that they devote 90% or more of their pharmacy practice to solid organ transplantation pharmacy.

Table 7. What percentage of time do you spend in solid organ transplantation pharmacy practice?

Response	Count	Percent
Less than 10%	3	1.5%
10-19%	4	2.0%
20-29%	10	5.0%
30-39%	3	1.5%
40-49%	2	1.0%
50-59%	10	5.0%
60-69%	4	2.0%
70-79%	12	6.0%
80-89%	9	4.5%
90-100%	143	71.5%
Total	200	100.0%

Consistent with the responses reported in Table 7 about the percentage of practice devoted to solid organ transplantation pharmacy, a roughly similar percentage reported working 40 or more hours per week in solid organ transplantation pharmacy.

Table 8. On average, what number of hours do you work in solid organ transplantation pharmacy weekly?

Response	Count	Percent
Less than 10	10	5.0%
10-19	10	5.0%
20-29	20	10.0%
30-39	15	7.5%
40-49	83	41.5%
50-59	40	20.0%
60 or more	22	11.0%
Total	200	100.0%

Respondents were asked to report the number of medication orders they verify on average each day. About three-fourths of the respondents reported none to 20 or fewer.

Table 9. On average, how many medication orders do you verify per day?

Response	Count	Percent
None	84	42.2%
1-20	65	32.7%
21-100	40	20.1%
More than 100	10	5.0%
Total	199	100.0%

The next question in the demographic survey was about the allocation of the respondents' practice to patients in three age groups. It may be seen in Table 10 that most respondents devote only a small portion of their practice to pediatric patients and that the adult (18-65) group generally constitutes a larger share of practice than the adult (65+) patient population.

Table 10. During the past 12 months, considering the patients for whom you provided solid organ transplantation pharmacy services, what percentage of time do you spend with the following population groups?

Description	Pediatric (< 18)		Adult (18-65)		Adult (65+)	
	Count	Percent	Count	Percent	Count	Percent
Less than 10%	126	76.4%	8	4.1%	14	7.4%
10-19%	12	7.3%	4	2.0%	25	13.2%
20-29%	8	4.8%	2	1.0%	62	32.6%
30-39%	1	0.6%	8	4.1%	24	12.6%
40-49%	1	0.6%	12	6.1%	33	17.4%
50-59%	1	0.6%	25	12.7%	21	11.1%
60-69%	0	0.0%	43	21.8%	6	3.2%
70-79%	1	0.6%	46	23.4%	5	2.6%
80-89%	3	1.8%	33	16.8%	0	0.0%
90-100%	12	7.3%	16	8.1%	0	0.0%
Total	165	100.0%	197	100.0%	190	100.0%

Just under 25% of the respondents classified their primary practice setting as an academic institution. Other common practice settings were university-affiliated hospitals, university hospitals, and acute care/inpatient. The responses are summarized in Table 11.

Table 11. What is your PRIMARY practice setting?

Response	Count	Percent
Academic institution	47	23.5%
Acute care/inpatient	37	18.5%
Ambulatory care	12	6.0%
Community hospital, for profit	1	0.5%
Community hospital, not for profit	12	6.0%
Family medicine/Internal medicine/Primary care/Private office	0	0.0%
Federal hospital or institution	1	0.5%
Managed care	0	0.0%
Pharmaceutical industry	2	1.0%
University-affiliated hospital	42	21.0%
University hospital	41	20.5%
Private hospital	3	1.5%
Specialty pharmacy	0	0.0%
Other	2	1.0%
Total	200	100.0%

One of the respondents who marked Other reported a combined practice setting, and the second respondent marking Other practices primarily in a semi-academic institution.

Many respondents do not have a secondary practice setting. Of those who do, the largest portion reported it to be ambulatory care. The responses are summarized in Table 12.

Table 12. What is your SECONDARY practice setting?

Response	Count	Percent
Academic institution	13	6.5%
Acute care/inpatient	19	9.5%
Ambulatory care	57	28.5%
Community hospital, for profit	0	0.0%
Community hospital, not for profit	3	1.5%
Family medicine/Internal medicine/Primary care/Private office	0	0.0%
Federal hospital or institution	1	0.5%
Managed care	1	0.5%
Pharmaceutical industry	0	0.0%
University-affiliated hospital	13	6.5%
University hospital	16	8.0%
Private hospital	1	0.5%
Specialty pharmacy	1	0.5%
Other	4	2.0%
No secondary setting reported	71	35.5%
Total	200	100.0%

The Other responses included a combination of the above and research.

The largest group of respondents reported that they work with two to five other solid organ transplantation pharmacists at their primary practice setting, although a large group reported working with six or more solid organ transplantation specialists.

Table 13. How many solid organ transplantation specialists are employed at your primary practice setting?

Response	Count	Percent
1	27	13.6%
2 to 5	132	66.7%
6 or more	39	19.7%
Total	198	100.0%

As was the case with the number of solid organ transplantation pharmacists who work in the primary practice setting, the most common response for those who answered the question was 2 to 5.

Table 14. How many solid organ transplantation technicians are employed at your secondary practice setting?

Response	Count	Percent
1	27	13.5%
2 to 5	72	36.0%
6 or more	22	11.0%
No response	79	39.5%
Total	200	100.0%

Next, respondents were asked if they initiate orders for drug therapy, and if so, with what authority. Over 80% of the respondents reported that they initiate orders, and most frequently with the co-signature of a physician or physician designee.

Table 15. Within your practice, do you initiate orders for drug therapy?

Response	Count	Percent
Yes, under a collaborative practice agreement	36	18.0%
Yes, under a specific protocol	29	14.5%
Yes, under an independent prescribing authority	2	1.0%
Yes, under other prescribing privilege	4	2.0%
Yes, with physician (or other physician designee) co-signature	93	46.5%
No, pharmacists may have the authority, but I do not initiate orders	7	3.5%
No, pharmacists do not have authority to initiate orders	29	14.5%
Total	200	100.0%

As detailed in Table 16, the most common job title for respondents in their primary practice setting is clinical pharmacists, followed distantly by clinical coordinator.

Table 16. What position do you hold at your primary practice site?

Response	Count	Percent
Staff pharmacist	3	1.5%
Clinical pharmacist	155	77.5%
Clinical coordinator	17	8.5%
Pharmacy manager	9	4.5%
Regional manager	0	0.0%
Corporate position	1	0.5%
Educator	3	1.5%
Researcher	4	2.0%
Other	8	4.0%
Total	200	100.0%

Over one-third of the respondents practice pharmacy in the Midwest region of the United States. The next largest group practices in the South.

Table 17. In which geographic region do you practice pharmacy?

Response	Count	Percent
Northeast (ME, NH, VT, MA, RI, CT, NY, NJ, PA)	32	16.0%
South (DE, MD, DC, VA, WV, NC, SC, GA, FL, KY, TN, AL, MS)	54	27.0%
Midwest (IN, OH, MI, IL, WI, IA, NE, MN, SD, ND, MO, KS, AR, LA, OK, TX)	80	40.0%
West (MT, ID, WY, CO, NM, AZ, UT, NV, WA, OR, CA, AK, HI)	29	14.5%
Outside of the United States (please specify)	5	2.5%
Total	200	100.0%

Four of the “Other” responses were Saudi Arabia. One respondent reported Canada.

Validation of the Domains and Tasks

Validation Scales

Respondents were asked to evaluate each task by using scales for Performance Expectation, Consequence, and Frequency. A three-point scale was used for Performance Expectation, with the most desired response being “1” (immediately upon engaging in solid organ transplantation). The Consequence scale employed five units (1 to 5), with a “5” indicating the potential for extreme harm. A five-point scale (1 to 5) was used for the Frequency scale, with a response of “5” representing the highest rating. The scales are listed below as a reference:

Performance Expectation: At what point in time are specialists in solid organ transplantation pharmacy first expected to perform the domain or task?

- 1 = Not at all
- 2 = Within the first 6 months of work as a specialist (includes exactly 6 months)
- 3 = After the first 6 months of work as a specialist (does not include exactly 6 months)

Consequence: To what degree would the inability of specialists in solid organ transplantation pharmacy to perform duties in each domain or task be seen as causing harm to stakeholders? (Harm may be seen as physical, psychological, emotional, legal, financial, etc.)

- 1 = No harm
- 2 = Minimal harm
- 3 = Moderate harm
- 4 = Substantial harm
- 5 = Extreme harm

Frequency: How often do specialists in solid organ transplantation pharmacy perform duties in each of the domains or tasks, considering a one-year period?

- 1 = Never
- 2 = Rarely (once per year)
- 3 = Sometimes (once per month)
- 4 = Often (once per week)
- 5 = Repeatedly (daily)

Castle’s analysis for Performance Expectation responses addressed the number and percentage of respondents selecting each option. Castle determined the number and percentage of respondents who selected the various options for Frequency and Consequence as well, but in addition computed several descriptive statistics for these responses, which may be considered ordinal in nature. The descriptive statistics include means, which are the simple arithmetic average of the scale values given by the respondents. The standard errors of the mean describe the theoretical range within which the means of other samples drawn from this population would lie. The standard deviation statistics describe the spread of the response distributions, with small estimates indicating tight groupings and agreement among the respondents. Medians are the rating found in the center of the distribution of ratings when they are ranked from high to low.

Clinical Skills and Therapeutic Management

There are six tasks in the first domain, Clinical Skills and Therapeutic Management. The tasks indicate the work pharmacists do when engaged in activities related to the domain. The tasks in this domain, which are abbreviated with key words in tables 18-22, are presented in full below:

1. Evaluate patients for living donation or transplantation using appropriate assessment methods and resources in order to identify pharmacologic risks, contraindications, and other considerations.
2. Interpret pertinent health-related information in accordance with evidence, standards, and guidelines throughout all phases of transplant-related care in order to determine if and when modifications to therapy are warranted.
3. Individualize treatment plans in accordance with evidence, standards, and guidelines.
4. Facilitate continuity of care by communicating pertinent patient information during transitions of care in order to avoid medication-related errors and complications.
5. Advocate for access to medications using prescription drug plans and other resources.
6. Implement a plan to overcome patient-specific barriers to care using continuous assessment.

As may be seen in Table 18, respondents' Performance Expectation for the tasks in Clinical Skills and Therapeutic Management indicate strongly that pharmacists are expected to perform all of them immediately upon engaging in solid organ transplantation pharmacy. The level of support is overwhelming for several tasks, with more than 90% expecting performance for the newly certified.

Table 18. Counts and Percentages for Performance Expectation for Tasks in Clinical Skills and Therapeutic Management

Task (Key Words)	N	1	2	3
Evaluate patients	220	5 (2.3%)	199 (90.5%)	16 (7.3%)
Interpret health-related information	220	0 (0.0%)	210 (95.5%)	10 (4.5%)
Individualize treatment plans	220	0 (0.0%)	206 (93.6%)	14 (6.4%)
Facilitate continuity of care	219	0 (0.0%)	214 (97.7%)	5 (2.3%)
Advocate for access to medications	218	13 (6.0%)	166 (76.1%)	39 (17.9%)
Plan to overcome patient barriers	219	2 (0.9%)	190 (86.8%)	27 (12.3%)

Ratings: 1 = Not at all, 2 = In first 6 months, 3 = After 6 months

There also is substantial support for the hypothesis that tasks in Clinical Skills and Therapeutic Management must be performed proficiently (Consequence scale), in that well over half of respondents indicated that at least moderate and up to extreme harm would result from poor performance (Table 19). The Consequence means (Table 20) for all tasks in Clinical Skills and Therapeutic Management are above the scale midpoint of 3.0, indicating that harm resulting from poor performance would be of at least moderate intensity.

Table 19. Counts and Percentages for Consequence for Tasks in Clinical Skills and Therapeutic Management

Task (Key Words)	N	1	2	3	4	5
Evaluate patients	205	8 (3.9%)	48 (23.4%)	87 (42.4%)	45 (22.0%)	17 (8.3%)
Interpret health-related information	205	3 (1.5%)	8 (3.9%)	38 (18.5%)	99 (48.3%)	57 (27.8%)
Individualize treatment plans	205	3 (1.5%)	6 (2.9%)	54 (26.3%)	91 (44.4%)	51 (24.9%)
Facilitate continuity of care	204	3 (1.5%)	8 (3.9%)	51 (25.0%)	81 (39.7%)	61 (29.9%)
Advocate for access to medications	204	13 (6.4%)	50 (24.5%)	64 (31.4%)	54 (26.5%)	23 (11.3%)
Plan to overcome patient barriers	204	7 (3.4%)	21 (10.3%)	95 (46.6%)	55 (27.0%)	26 (12.7%)

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Table 20. Descriptive Statistics for Consequence for Tasks in Clinical Skills and Therapeutic Management

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Evaluate patients	205	3	3.1	0.1	1.0
Interpret health-related information	205	4	4.0	0.1	0.9
Individualize treatment plans	205	4	3.9	0.1	0.9
Facilitate continuity of care	204	4	3.9	0.1	0.9
Advocate for access to medications	204	3	3.1	0.1	1.1
Plan to overcome patient barriers	204	3	3.4	0.1	0.9

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

The Frequency scale addressed the question of how the tasks are performed, given that newly certified specialists perform them and that they are consequential. The modal Frequency rating was 5 for the first four tasks, indicating that it is performed daily. The fourth and fifth tasks are also performed often, about once per week. Counts and percentages for each response option bear out these findings (Table 21). Descriptive statistics as given in Table 22 indicate that the second, third, fourth tasks have average ratings that exceed 4.5 on the five-point scale and that the other tasks have means close to 4.

Table 21. Counts and Percentages for Frequency for Tasks in Clinical Skills and Therapeutic Management

Task (Key Words)	N	1	2	3	4	5
Evaluate patients	204	3 (1.5%)	4 (2.0%)	16 (7.8%)	67 (32.8%)	114 (55.9%)
Interpret health-related information	204	0 (0.0%)	0 (0.0%)	4 (2.0%)	16 (7.8%)	184 (90.2%)
Individualize treatment plans	204	0 (0.0%)	0 (0.0%)	4 (2.0%)	19 (9.3%)	181 (88.7%)
Facilitate continuity of care	203	0 (0.0%)	0 (0.0%)	7 (3.4%)	35 (17.2%)	161 (79.3%)
Advocate for access to medications	202	5 (2.5%)	25 (12.4%)	60 (29.7%)	56 (27.7%)	56 (27.7%)
Plan to overcome patient barriers	202	1 (0.5%)	5 (2.5%)	46 (22.8%)	71 (35.1%)	79 (39.1%)

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Table 22. Descriptive Statistics for Frequency for Tasks in Clinical Skills and Therapeutic Management

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Evaluate patients	204	5	4.4	0.1	0.8
Interpret health-related information	204	5	4.9	0.0	0.4
Individualize treatment plans	204	5	4.9	0.0	0.4
Facilitate continuity of care	203	5	4.8	0.0	0.5
Advocate for access to medications	202	4	3.7	0.1	1.1
Plan to overcome patient barriers	202	4	4.1	0.1	0.9

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Administration and Practice Development

The second domain is Administration and Practice Development. The five tasks are presented in full here, and they are abbreviated in tables 23-27.

1. Establish sustained, collaborative, professional relationships with members of the interdisciplinary transplant team and consultant services in order to promote patient care across the continuum.
2. Establish institutional guidelines, policies, procedures, and formularies that are consistent with evidence, regulation, and/or current practice guidelines and standards in collaboration with other stakeholders in order to facilitate patient care.
3. Perform quality improvement activities in order to enhance the safety and effectiveness of medication-use processes in solid organ transplantation.
4. Monitor compliance with guidelines, policies, procedures, and formularies in partnership with institutional leadership in order to identify shortcomings and implement performance improvement initiatives.
5. Implement processes for cost effective care focusing on continuous quality improvement, patient safety, and outcomes in order to justify modifications in transplantation pharmacy services.

The first task in Administration and Practice Development is regarded overwhelmingly as work that pharmacists who specialize in solid organ transplantation are expected to perform (Table 23); however, the majority of respondents expect only experienced pharmacists to be responsible for the others.

Table 23. Counts and Percentages for Performance Expectation for Tasks in Administration and Practice Development

Task (Key Words)	N	1	2	3
Establish professional relationships	211	0 (0.0%)	188 (89.1%)	23 (10.9%)
Establish institutional policies, etc.	211	0 (0.0%)	92 (43.6%)	119 (56.4%)
Perform quality improvement activities	211	1 (0.5%)	97 (46.0%)	113 (53.6%)
Monitor compliance	211	1 (0.5%)	104 (49.3%)	106 (50.2%)
Implement cost effective care	211	1 (0.5%)	82 (38.9%)	128 (60.7%)

Ratings: 1 = Not at all, 2 = In first 6 months, 3 = After 6 months

Respondents view the potential for harm if the tasks are performed improperly (Consequence) differently than they do Performance Expectation. The most frequent response was 3, indicating moderate harm; however, responses are spread across the scale options. The tasks all have an average rating near the scale midpoint, indicating moderate harm as well.

Table 24. Counts and Percentages for Consequence for Tasks in Administration and Practice Development

Task (Key Words)	N	1	2	3	4	5
Establish professional relationships	199	8 (4.0%)	24 (12.1%)	82 (41.2%)	59 (29.6%)	26 (13.1%)
Establish institutional policies, etc.	199	7 (3.5%)	24 (12.1%)	86 (43.2%)	60 (30.2%)	22 (11.1%)
Perform quality improvement activities	199	8 (4.0%)	37 (18.6%)	89 (44.7%)	49 (24.6%)	16 (8.0%)
Monitor compliance	198	8 (4.0%)	44 (22.2%)	90 (45.5%)	41 (20.7%)	15 (7.6%)
Implement cost effective care	198	8 (4.0%)	60 (30.3%)	88 (44.4%)	30 (15.2%)	12 (6.1%)

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Table 25. Descriptive Statistics for Consequence for Tasks in Administration and Practice Development

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Establish professional relationships	199	3	3.4	0.1	1.0
Establish institutional policies, etc.	199	3	3.3	0.1	0.9
Perform quality improvement activities	199	3	3.1	0.1	0.9
Monitor compliance	198	3	3.1	0.1	0.9
Implement cost effective care	198	3	2.9	0.1	0.9

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

The Frequency ratings presented in tables 26 and 27 indicate that specialists in solid organ transplantation perform the first task repeatedly, on a daily basis, and that the others are performed once per week, or at least monthly.

Table 26. Counts and Percentages for Frequency for Tasks in Administration and Practice Development

Task (Key Words)	N	1	2	3	4	5
Establish professional relationships	198	0 (0.0%)	1 (0.5%)	2 (1.0%)	24 (12.1%)	171 (86.4%)
Establish institutional policies, etc.	199	0 (0.0%)	6 (3.0%)	53 (26.6%)	85 (42.7%)	55 (27.6%)
Perform quality improvement activities	199	0 (0.0%)	7 (3.5%)	73 (36.7%)	71 (35.7%)	48 (24.1%)
Monitor compliance	198	0 (0.0%)	9 (4.5%)	79 (39.9%)	63 (31.8%)	47 (23.7%)
Implement cost effective care	198	0 (0.0%)	11 (5.6%)	89 (44.9%)	60 (30.3%)	38 (19.2%)

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Table 27. Descriptive Statistics for Frequency for Tasks in Administration and Practice Development

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Establish professional relationships	198	5	4.8	0.0	0.4
Establish institutional policies, etc.	199	4	3.9	0.1	0.8
Perform quality improvement activities	199	4	3.8	0.1	0.8
Monitor compliance	198	4	3.7	0.1	0.9
Implement cost effective care	198	3	3.6	0.1	0.9

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Information Management and Education

There are five tasks in Information Management and Education. They are presented in their entirety below and in abbreviated form in the tables.

1. Evaluate biomedical literature with regard to study design, statistical analysis, and applicability of results to the solid organ transplantation population.
2. Contribute to the body of transplant knowledge for the purpose of improving patient outcomes and medication use.
3. Educate solid organ transplant candidates, recipients, donors, and caregivers on issues related to medications and medication adherence.
4. Disseminate information regarding public health initiatives in order to promote health, safety, and wellness in transplant patients.
5. Educate healthcare professionals, trainees, and other stakeholders concerning medication-related issues associated with the care of transplant patients.

Data indicate that the pharmacists are expected to perform all tasks in Information Management and Education immediately upon engaging in specialty practice in solid organ transplantation pharmacy except for the second (Contribute to the body of transplant knowledge), for which respondents indicate that at least six months of experience is expected (Table 28).

Table 28. Counts and Percentages for Performance Expectation for Tasks in Information Management and Education

Task (Key Words)	N	1	2	3
Evaluate literature	207	0 (0.0%)	183 (88.4%)	24 (11.6%)
Contribute to knowledge	207	5 (2.4%)	61 (29.5%)	141 (68.1%)
Educate patients and caregivers	207	0 (0.0%)	203 (98.1%)	4 (1.9%)
Disseminate information	206	13 (6.3%)	121 (58.7%)	72 (35.0%)
Educate healthcare professionals	207	0 (0.0%)	161 (77.8%)	46 (22.2%)

Ratings: 1 = Not at all, 2 = In first 6 months, 3 = After 6 months

Ratings for Consequence indicate that moderate to substantial harm would result from the poor performance of most tasks in this domain. Respondents indicate that the least amount of harm would result from poor performance of the second task. Tables 29 and 30 summarize the Consequence ratings.

Table 29. Counts and Percentages for Consequence for Tasks in Information Management and Education

Task (Key Words)	N	1	2	3	4	5
Evaluate literature	197	18 (9.1%)	49 (24.9%)	71 (36.0%)	42 (21.3%)	17 (8.6%)
Contribute to knowledge	196	43 (21.9%)	88 (44.9%)	42 (21.4%)	17 (8.7%)	6 (3.1%)
Educate patients and caregivers	197	3 (1.5%)	10 (5.1%)	39 (19.8%)	74 (37.6%)	71 (36.0%)
Disseminate information	197	27 (13.7%)	77 (39.1%)	58 (29.4%)	26 (13.2%)	9 (4.6%)
Educate healthcare professionals	197	9 (4.6%)	39 (19.8%)	69 (35.0%)	52 (26.4%)	28 (14.2%)

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Table 30. Descriptive Statistics for Consequence for Tasks in Information Management and Education

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Evaluate literature	197	3	3.0	0.1	1.1
Contribute to knowledge	196	2	2.3	0.1	1.0
Educate patients and caregivers	197	4	4.0	0.1	1.0
Disseminate information	197	2	2.6	0.1	1.0
Educate healthcare professionals	197	3	3.3	0.1	1.1

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

The task in Information Management and Education that is performed most frequently is Educate patients and caregivers, for which the clear majority of ratings correspond to repeatedly (that is, on a daily basis). The others are performed monthly or weekly.

Table 31. Counts and Percentages for Frequency for Tasks in Information Management and Education

Task (Key Words)	N	1	2	3	4	5
Evaluate literature	196	0 (0.0%)	5 (2.6%)	35 (17.9%)	81 (41.3%)	75 (38.3%)
Contribute to knowledge	196	1 (0.5%)	45 (23.0%)	79 (40.3%)	42 (21.4%)	29 (14.8%)
Educate patients and caregivers	197	0 (0.0%)	1 (0.5%)	5 (2.5%)	15 (7.6%)	176 (89.3%)
Disseminate information	197	5 (2.5%)	44 (22.3%)	74 (37.6%)	41 (20.8%)	33 (16.8%)
Educate healthcare professionals	197	0 (0.0%)	4 (2.0%)	55 (27.9%)	64 (32.5%)	74 (37.6%)

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Table 32. Descriptive Statistics for Frequency for Tasks in Information Management and Education

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Evaluate literature	196	4	4.2	0.1	0.8
Contribute to knowledge	196	3	3.3	0.1	1.0
Educate patients and caregivers	197	5	4.9	0.0	0.5
Disseminate information	197	3	3.3	0.1	1.1
Educate healthcare professionals	197	4	4.1	0.1	0.9

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Public Health

Two tasks were identified in Public Health for pharmacists whose practice includes a specialty in solid organ transplantation. They are presented in their entirety below and in abbreviated form in the tables.

1. Use population-level data to develop, implement, and assess practices or strategies for addressing health promotion and disease prevention.
2. Provide information and guidance to the public regarding organ donation and allocation.

The data presented in Table 33 indicate that the specialists in solid organ transplantation pharmacy are expected to perform both tasks in Public Health only after they have at least 6 months of experience.

Table 33. Counts and Percentages for Performance Expectation for Tasks in Public Health

Task (Key Words)	N	1	2	3
Use population-level data	204	20 (9.8%)	49 (24.0%)	135 (66.2%)
Provide information and guidance	203	36 (17.7%)	52 (25.6%)	115 (56.7%)

Ratings: 1 = Not at all, 2 = In first 6 months, 3 = After 6 months

Ratings for Consequence indicate that at least minimal harm, if not moderate harm, would result from the poor performance of the first task in Public Health, with slightly less harm seen if information provided to public was not done proficiently. Tables 34 and 35 summarize the Consequence ratings.

Table 34. Counts and Percentages for Consequence for Tasks in Public Health

Task (Key Words)	N	1	2	3	4	5
Use population-level data	200	26 (13.0%)	83 (41.5%)	72 (36.0%)	15 (7.5%)	4 (2.0%)
Provide information and guidance	199	60 (30.2%)	85 (42.7%)	43 (21.6%)	8 (4.0%)	3 (1.5%)

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Table 35. Descriptive Statistics for Consequence for Tasks in Public Health

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Use population-level data	200	2	2.4	0.1	0.9
Provide information and guidance	199	2	2.0	0.1	0.9

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Generally speaking, the tasks in Public Health are performed rarely or sometimes (approximately once per year or once per month), with averages hovering just below the scale midpoint for both tasks.

Table 36. Counts and Percentages for Frequency for Tasks in Public Health

Task (Key Words)	N	1	2	3	4	5
Use population-level data	200	16 (8.0%)	52 (26.0%)	86 (43.0%)	29 (14.5%)	17 (8.5%)
Provide information and guidance	199	23 (11.6%)	70 (35.2%)	78 (39.2%)	19 (9.5%)	9 (8.5%)

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Table 37. Descriptive Statistics for Frequency for Tasks in Public Health

Task (Key Words)	N	Median	Mean	SE Mean	Std Dev
Use population-level data	200	3	2.9	0.1	1.0
Provide information and guidance	199	3	2.6	0.1	1.0

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Domain Ratings

After rating the tasks, participants in the survey were asked to evaluate the domains as a whole, considering all tasks in the domain taken together. The evidence that pharmacists with a specialty in solid organ transplantation are expected to perform the domains immediately when engaging in the specialty is very strong for two of the domains. But two domains, Administration and Practice Management as well as Public Health are seen by the majority of respondents as requiring experience.

Table 38. Counts and Percentages for Performance Expectation for Domains

Domain	N	1	2	3
Clinical Skills and Therapeutic Management	219	0 (0.0%)	210 (95.9%)	9 (4.1%)
Administration and Practice Development	211	0 (0.0%)	102 (48.3%)	109 (51.7%)
Information Management and Education	205	0 (0.0%)	177 (86.3%)	28 (13.7%)
Public Health	201	18 (9.0%)	57 (28.4%)	126 (62.7%)

Ratings: 1 = Not at all, 2 = In first 6 months, 3 = After 6 months

Consequence ratings suggest that the first domain (Clinical Skills and Therapeutic Management) has the greatest criticality. For two of the other domains, Administration and Practice Development and Information Management and Education, the degree to which harm might result from the improper performance of pharmacists with a specialty in solid organ transplantation is slightly lower but still is between moderate and substantial. Consequence ratings for Public Health indicate minimal harm to moderate harm. Domain-level responses for Consequence are summarized in tables 39 and 40.

Table 39. Counts and Percentages for Consequence for Domains

Domain	N	1	2	3	4	5
Clinical Skills and Therapeutic Management	206	3 (1.5%)	7 (3.4%)	48 (23.3%)	92 (44.7%)	56 (27.2%)
Administration and Practice Development	201	8 (4.0%)	41 (20.4%)	99 (49.3%)	39 (19.4%)	14 (7.0%)
Information Management and Education	197	7 (3.6%)	44 (22.3%)	82 (41.6%)	53 (26.9%)	11 (5.6%)
Public Health	199	27 (13.6%)	111 (55.8%)	48 (24.1%)	9 (4.5%)	4 (2.0%)

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Table 40. Descriptive Statistics for Consequence for Domains

Domain	N	Median	Mean	SE Mean	Std Dev
Clinical Skills and Therapeutic Management	206	4	3.9	0.1	0.9
Administration and Practice Development	201	3	3.0	0.1	0.9
Information Management and Education	197	3	3.1	0.1	0.9
Public Health	199	2	2.3	0.1	0.8

Ratings: 1 = No harm, 2 = Minimal harm, 3 = Moderate harm, 4 = Substantial harm, 5 = Extreme harm

Consistent with the findings for Consequence, ratings for Frequency (tables 46 and 47) indicate that specialists in solid organ transplantation provide services related to Clinical Skills and Therapeutic Management on a routine basis. Work related to Administration and Practice Development and Information Management and Education is performed monthly to weekly, while work related to Public Health is performed a little less often, averaging less than but close to monthly.

Table 46. Counts and Percentages for Frequency for Domains

Domain	N	1	2	3	4	5
Clinical Skills and Therapeutic Management	205	0 (0.0%)	0 (0.0%)	3 (1.5%)	38 (18.5%)	164 (80.0%)
Administration and Practice Development	201	0 (0.0%)	4 (2.0%)	71 (35.3%)	77 (38.3%)	49 (24.4%)
Information Management and Education	197	0 (0.0%)	3 (1.5%)	46 (23.4%)	40 (40.6%)	68 (34.5%)
Public Health	198	11 (5.6%)	67 (33.8%)	86 (43.4%)	84 (12.1%)	10 (5.1%)

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

Table 47. Descriptive Statistics for Frequency for Domains

Domain	N	Median	Mean	SE Mean	Std Dev
Clinical Skills and Therapeutic Management	205	5	4.8	0.0	0.4
Administration and Practice Development	201	4	3.9	0.1	0.8
Information Management and Education	197	4	4.1	0.1	0.8
Public Health	198	3	2.8	0.1	0.9

Ratings: 1 = Never, 2 = Rarely (once per year), 3 = Sometimes (once per month), 4 = Often (once per week), 5 = Repeatedly (daily)

RELIABILITY ANALYSIS FOR DOMAINS

The reliability of the scales for domains was assessed in order to determine how consistently the tasks performed as measures. Reliability refers to the degree to which tests or surveys are free from measurement error. With inconsistency (i.e., unreliability), it would be difficult to interpret the results of the study. Reliability analysis expresses the adequacy of data reported for the Consequence and Frequency ratings for each performance domain based on the tasks in that area of responsibility. (Reliability for Performance Expectation, a categorical variable, was not assessed.)

Reliability, reported in Table 48, was measured by estimating internal consistency (Cronbach's alpha) using the respondents' ratings for Consequence and Frequency for the tasks in each domain. This procedure calculates the extent to which the task ratings within a domain consistently measure what other tasks within that performance domain measure. Reliability coefficients range from 0 to 1 and should be at or above 0.70 to be judged as adequate. Most reliability coefficients obtained for this study were strong, especially for Administration and Practice Management. The coefficients for Frequency for Clinical Skills and Therapeutic Management, just under the threshold, and Information Management and Education are acceptable.

Table 48. Reliability

Domain	Consequence	Frequency
Clinical Skills and Therapeutic Management	0.88	0.69
Administration and Practice Development	0.91	0.86
Information Management and Education	0.85	0.70
Public Health	0.82	0.77

CONCLUSION

BPS conducted the role delineation study in order to characterize the role and responsibilities of pharmacists whose practice includes a specialty in solid organ transplantation. BPS relies on this methodology to establish the basis for its examinations' content validity, but in this case the role delineation study served to determine if a specialized body of knowledge could be identified. Because there is no database that contains everyone who specializes in solid organ transplantation pharmacy, BPS cooperated with three organizations to invite potentially qualified participants to respond to the survey, and Castle received 220 usable responses. Responses to items in the demographic portion of the survey support the conclusion that participants constitute a reasonable and qualified sample.

Tasks and domains were evaluated using scales for Performance Expectation, Consequence, and Frequency. The Performance Expectation scale offered insight into whether specialists in solid organ transplantation pharmacy are expected to perform the tasks within the first 6 months of their specialty practice. Frequency (how often) and Consequence (potential for harm) also supplied information about the validity of the role delineation, which should be considered when making decisions about the certification examination. Respondents were provided the standards for other BPS certification programs. Because there is not currently a certification program in solid organ transplantation and the scales, especially for Performance Expectation, were worded without specific reference to assumptions about the completion of training, respondents provided ratings that may not have been based on certifiable specialists, even given the BPS standards. Consequently, the possibility that respondents applied the scale differently should be considered during interpretation of Performance Expectation.

Data collected in the validation study are reliable and validate that the domains and tasks are appropriate elements of responsibility in the practice of solid organ transplantation pharmacy. Several tasks, notably the following, should be evaluated prior to development of test specifications, in the event that specialty certification is established in this area of practice.

Information Management and Education:

2. Contribute to the body of transplant knowledge for the purpose of improving patient outcomes and medication use.

Public Health

1. Use population-level data to develop, implement, and assess practices or strategies for addressing health promotion and disease prevention.
2. Provide information and guidance to the public regarding organ donation and allocation.

As a result, several specific recommendations may be useful to BPS:

1. The content outline for the certification examination for the specialty should be based on the role delineation, given consideration of the tasks listed above, if BPS proceeds with development of the program.
2. A multiple-choice examination may be developed in accordance with psychometric and test development principles as an effective assessment of knowledge required by the newly certified specialist in solid organ transplantation.
3. A single examination program is appropriate.

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APPENDIX A: CONTENT OUTLINE

BOARD OF PHARMACY SPECIALTIES

Content Outline for SOLID ORGAN TRANSPLANTATION PHARMACY

Definition and Target Audience

Solid Organ Transplantation Pharmacists provide evidence-based, patient-centered medication therapy management and care for patients throughout all phases of solid organ transplantation at all ages and in various healthcare settings.

Solid Organ Transplantation Pharmacists have the specialized knowledge and expertise needed to manage complex medication regimens unique to the solid organ transplantation population in addition to clinical and regulatory needs not encountered in any other pharmacy specialty. Solid Organ Transplantation Pharmacists are specially trained to design, recommend, implement, monitor, and modify pharmacotherapeutic plans to optimize outcomes. They review, analyze, and reevaluate multifaceted clinical and outcomes data in order to provide quality care and assess program, process, and protocol effectiveness. Finally, they provide education and counseling throughout the transitions of care.

Domain 1: Clinical Skills and Therapeutic Management

1. Evaluate patients for living donation or transplantation using appropriate assessment methods and resources in order to identify pharmacologic risks, contraindications, and other considerations.

Knowledge of:

- a. Organ-specific criteria for living donation
- b. Organ-specific criteria for transplant listing
- c. Pharmacologic risks (e.g., anticoagulation, drug interactions, adherence, intolerance)
- d. Non-pharmacologic risks (e.g., comorbid diseases, immunologic risk, social support)

2. Interpret pertinent health-related information in accordance with evidence, standards, and guidelines throughout all phases of transplant-related care in order to determine if and when modifications to therapy are warranted.

Knowledge of:

- a. Diseases leading to end-stage organ failure
- b. Common comorbid conditions
- c. Medication history
- d. Medication reconciliation
- e. Allergy and drug intolerance history
- f. Pertinent clinical data (e.g., laboratory and microbiologic data, pathology results)
- g. Immunologic risk
- h. Organ function
- i. Integrity of drug absorption, distribution, metabolism, and elimination processes

3. Individualize treatment plans in accordance with evidence, standards, and guidelines.

Knowledge of:

- a. Immunomodulation
- b. Evidence-based regimens for desensitization
- c. Evidence-based regimens for induction
- d. Evidence-based regimens for maintenance
- e. Evidence-based regimens for management of rejection
- f. Immunologic event monitoring
- g. Drug-related safety, efficacy, and tolerability monitoring
- h. Pre- and post-transplantation infections
- i. Pre- and post-transplantation malignancies
- j. Allograft-specific complications
- k. Non-immunologic post-transplantation complications
- l. Nonadherence
- m. Pharmacogenetics and pharmacogenomics
- n. Medication management in special populations

4. Facilitate continuity of care by communicating pertinent patient information during transitions of care in order to avoid medication-related errors and complications.

Knowledge of:

- a. Role and responsibilities of healthcare team members
- b. Errors during transition
- c. Challenges with transition between programs (e.g., pediatric to adult, one transplant center to another)
- d. Challenges with transition between settings (e.g., inpatient to outpatient, facility to facility)
- e. Challenges with co-management (e.g., multi-organ transplant recipients, community v. transplant providers)

5. Advocate for access to medications using prescription drug plans and other resources.

Knowledge of:

- a. Barriers in the prescription process (e.g., prior authorization, formulary)
- b. Prescription coverage
- c. Patient assistance programs (e.g., grants, free drugs, copay cards, vouchers)
- d. Role of specialty pharmacies in transplantation

6. Implement a plan to overcome patient-specific barriers to care using continuous assessment.

Knowledge of:

- a. Strategies for assessing patients' readiness and willingness to participate in their own care
- b. Strategies for assessing adherence
- c. Patient and caregivers' health literacy
- d. Cultural competence and how it may affect the care of patients (e.g., culture, belief systems)
- e. Humanistic factors (e.g., quality of life, end of life) and how they may affect the care of patients
- f. Barriers to care (e.g., language, vision/hearing impaired, support)
- g. Medical insurance plans and coverage (e.g., provider networks, ancillary services)

Domain 2: Administration and Practice Development

1. Establish sustained, collaborative, professional relationships with members of the interdisciplinary transplant team and consultant services in order to promote patient care across the continuum.

Knowledge of:

- a. Regulations, strategies, and resources surrounding collaborative practice agreements
 - b. Principles in establishing a scope of practice protocol
 - c. Identifying interprofessional roles and relationships
 - d. Strategies for implementing effective collaborative relationships
 - e. Strategies for communicating healthcare-related recommendations
 - f. Steps involved in continuity of care within healthcare systems
 - g. Appropriate documentation of patient care activities and recommendations in accordance with policies and guidelines
2. Establish institutional guidelines, policies, procedures, and formularies that are consistent with evidence, regulation, and/or current practice guidelines and standards in collaboration with other stakeholders in order to facilitate patient care.

Knowledge of:

- a. Evidence-based standards of care and clinical pathways
 - b. Cost effective treatment protocols and alternative and therapeutic interchange options
 - c. Considerations for evaluating the need for protocol development
 - d. Considerations for institutional drug use (e.g., formulary management, Pharmacy and Therapeutics Committee, special order drug systems)
 - e. Organizations, agencies, and accrediting bodies and their requirements (e.g., Centers for Medicare and Medicaid Services, United Network for Organ Sharing)
 - f. Policy and procedure utilization in practice settings
3. Perform quality improvement activities in order to enhance the safety and effectiveness of medication-use processes in solid organ transplantation.

Knowledge of:

- a. Quality improvement opportunities, activities, and tools
 - b. Metrics for evaluating medication use
 - c. Medication safety principles pertinent to patients
 - d. Quality measures
4. Monitor compliance with guidelines, policies, procedures, and formularies in partnership with institutional leadership in order to identify shortcomings and implement performance improvement initiatives.

Knowledge of:

- a. Regulatory standards (e.g., Centers for Medicare and Medicaid Services, United Network for Organ Sharing/Organ Procurement and Transplantation Network, Scientific Registry for Transplant Recipients)
- b. Metrics and tools (e.g., plan-do-study-act, root cause analysis, medication use evaluation)
- c. Development and implementation of monitoring strategies
- d. Methods used in performing data audits
- e. Strategies for reporting data

5. Implement processes for cost effective care focusing on continuous quality improvement, patient safety, and outcomes in order to justify modifications in transplantation pharmacy services.

Knowledge of:

- a. Components of sustainable business models and related metrics (e.g., cost benefit analysis, cost effectiveness analysis, return on investment, clinical outcomes analyses)
- b. Continuous quality improvement processes
- c. Literature evaluating medication errors and patient safety (e.g., Institute of Medicine report, Beers criteria)
- d. Principles of medication use evaluation
- e. Process for reporting adverse drug reactions, medication errors, and incidents
- f. Quality measures

Domain 3: Information Management and Education

1. Evaluate biomedical literature with regard to study design, statistical analysis, and applicability of results to the solid organ transplantation population.

Knowledge of:

- a. Biomedical search strategies
- b. Implications of study design, methodology, and statistical analysis on generalizability
- c. Transplant study endpoints
- d. Clinical application and limitations of published data and reports

2. Contribute to the body of transplant knowledge for the purpose of improving patient outcomes and medication use.

Knowledge of:

- a. Institutional review board requirements
- b. Research study design
- c. Publication and review process
- d. Drug development and approval process

3. Educate solid organ transplant candidates, recipients, donors, and caregivers on issues related to medications and medication adherence.

Knowledge of:

- a. Education-related considerations (e.g., age, health literacy, culture)
- b. Education-related techniques (e.g., teach-back, participatory)
- c. Risk factors for non-adherence
- d. Strategies for improving adherence
- e. Interviewing strategies
- f. Home monitoring
- g. Pregnancy and contraception
- h. Proper drug storage, handling, and disposal

4. Disseminate information regarding public health initiatives in order to promote health, safety, and wellness in transplant patients.

Knowledge of:

- a. Principles and practices of disease prevention (e.g., immunization, tobacco cessation)
- b. Clinical practice guidelines and national initiatives (e.g., Healthy People 2020)
- c. Clinical practice guidelines for health maintenance and screenings

5. Educate healthcare professionals, trainees, and other stakeholders concerning medication-related issues associated with the care of transplant patients.

Knowledge of:

- a. Pertinent literature, evidence-based treatment guidelines, and consensus statements
- b. Publications by professional societies (e.g., American Society of Health-System Pharmacists, The International Society for Heart and Lung Transplantation, American College of Clinical Pharmacy, American Society of Transplantation)
- c. Principles and methods for educating pharmacists, trainees, and other healthcare professionals on transplantation-related issues
- d. Risk evaluation and mitigation strategies

Domain 4: Public Health

1. Use population-level data to develop, implement, and assess practices or strategies for addressing health promotion and disease prevention.

Knowledge of:

- a. Immunization guidelines (e.g., Advisory Committee on Immunization Practices, Infectious Diseases Society of America, American Society of Transplantation)
- b. Population health data repositories (e.g., Scientific Registry of Transplant Recipients)
- c. Principles and practices of wellness, disease prevention, and treatment (e.g., smoking cessation, cancer screening, sexually transmitted infections)

2. Provide information and guidance to the public regarding organ donation and allocation.

Knowledge of:

- a. Scientific Registry of Transplant Recipients data trends (e.g., waitlist mortality, living vs deceased donor outcomes)
- b. Transplant disparities (e.g., age, race, distance from transplant center, socioeconomic)
- c. Allocation scoring systems
- d. Community outreach (e.g., dispelling myths surrounding donation, living donor education)
- e. Cultural competence



Role Delineation Study for Solid Organ Transplantation Pharmacy

INSTRUCTION BOOKLET



Facilitator: James P. Henderson, Ph.D.

Agenda

Friday, August 26

- 8:00 a.m. Meeting begins**
- Introduce participants
 - Review role delineation study processes and objectives
 - Discuss the target audience
 - Review draft domains

9:20 a.m. Morning break

- 9:30 a.m. Meeting resumes**
- Reach consensus on domains
 - Review procedures and considerations for evaluating and modifying task statements
 - Review and suggest revisions to task statements, working in small groups

12:00 p.m. Working lunch

- 1:00 p.m. Meeting resumes**
- Review task statements and suggested revisions as a whole group

2:50 p.m. Afternoon break

- 3:00 p.m. Meeting resumes**
- Continue reviewing task statements and suggested revisions as a whole group

5:00 p.m. Adjourn for the day

Saturday, August 27

- 7:00 a.m. Meeting resumes**
- Review procedures and considerations for evaluating and modifying knowledge statements
 - Review and suggest revisions to knowledge statements, working in small groups

9:00 a.m. Morning break

- 9:10 a.m. Meeting resumes**
- Review knowledge statements and suggested revisions as a whole group

12:00 p.m. Working lunch

- 1:00 p.m. Meeting resumes**
- Continue reviewing knowledge statements and suggested revisions as a whole group

4:00 p.m. Validation exercise

4:30 p.m. Meeting adjourns

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OVERVIEW OF MEETING ACTIVITIES

The Board of Pharmacy Specialties (BPS) improves patient care by promoting the recognition and value of specialized training, knowledge, and skills in pharmacy and specialty board certification of pharmacists. It accomplishes this mission by:

1. Providing leadership for the profession of pharmacy in the discussion, evolution, direction, and recognition of specialty board certification of pharmacists;
2. Establishing and promoting, in collaboration with stakeholders, the value of pharmacy specialization and board certification;
3. Establishing the standards for identification and recognition of pharmacy specialties;
4. Establishing standards of eligibility, knowledge, and skills for pharmacists as the basis for board certification;
5. Developing and administering a valid process to evaluate the knowledge and skills for recognition of board-certified pharmacists; and
6. Assessing and recognizing the continued eligibility, knowledge, and skills of board-certified pharmacy specialists through a valid recertification process.

Solid Organ Transplantation Pharmacists provide evidence-based, patient-centered medication therapy management and direct care for solid organ transplant patients, with a focus on the identification, resolution, and prevention of drug-related problems experienced by solid organ transplant patients, including assessment and monitoring for potential adverse drug reactions and interactions. In the event that BPS develops a specialty certification program in solid organ transplant pharmacy, the role delineation study serves one major purpose: to provide the basis for demonstrating the practice-relatedness of the solid organ transplantation pharmacy specialty examination that would be used in the program. The role delineation study documents that the information to be tested is relevant to the care of patients.

We anticipate a substantial amount of group interaction and activity. It is important for each member of the panel to be realistic, cooperative, and focused on teamwork. We hope panelists will appreciate the common goal of collaboration concerning the various elements of the study.

DEFINITION OF TERMS

Target Audience Statement

Target audience statements describe the basic characteristics of the group that is expected to seek certification in the specialty, if one is developed. The characteristics include the prerequisites and other qualifications that distinguish solid organ transplantation pharmacy as a unique professional specialty.

Target Audience

The solid organ transplantation pharmacist has the advanced knowledge and experience needed to manage transplant-related drug-therapy. Solid organ transplantation pharmacists coordinate the development and implementation of drug therapy protocols, assist in ensuring protocol adherence, and measure outcomes with the protocols. Further, they provide medication reconciliation, medication therapy management, and discharge counseling.

The following eligibility criteria are typical for BPS specialty certification:

- Graduation from a pharmacy program accredited by the Accreditation Council for Pharmacy Education (ACPE) or a program outside the U.S. that qualifies the individual to practice in the jurisdiction.
- Current, active license to practice pharmacy in the U.S. or another jurisdiction.
- Completion of four (4) years of practice experience (**post-pharmacist licensure**) with at least 50% of time spent in specialized pharmacy activities as defined by the [content outline for the program](#).*

OR

Completion of a PGY1 residency* plus two (2) additional years of practice (**post-pharmacist licensure**) with at least 50% of time spent in specialized pharmacy activities as defined by the [content outline for the program](#).

OR

- Completion of a specialty (PGY2) residency** in the pharmacy specialty.
- Achieving a passing score on the BPS specialty certification examination.

* *Practice experience should not be more than seven years prior to the application date.*

** *Effective January 1, 2013, only residency programs accredited by the American Society of Health-System Pharmacists (ASHP) or new residency programs granted Candidate Status for accreditation by ASHP are creditable for this purpose.*

Domains

Domains are the major responsibilities or duties that characterize the practice of a specialty. Domains are denoted as major headings in an outline format and may include brief behavioral descriptions. The domains listed below are examples, and they are intended to be illustrative of the scope and generality intended for the study. In developing your own list of domains during the meeting, you may use any from this list, if they are appropriate, or devise your own.

Domain 1: Phases of Transplantation, Including Pre-, Peri-, and Post-Transplantation

Domain 2: Therapeutics, Patient Management, and Adherence Education

Domain 3: Practice Management

Domain 4: Patient Advocacy

Domain 5: Research, Quality Assurance, and Process Improvement

Task Statements

A task statement defines an activity that elaborates on a domain. The set of task statements for a domain offers a comprehensive and detailed description of the domain. In particular, task statements should answer the following questions:

- What activity is performed? (active verb)
- To whom or to what is the activity directed? (direct object or another phrase clarifying who or what receives the activity or how it is performed)
- How is the activity performed? (if helpful)
- Why is the activity performed? (if helpful)

Sample Task Statements

1. Review patients' medication in accordance with evidence, rational mechanism-based decision making, standards, and guidelines in order to establish and/or modify drug therapies.
2. Counsel patients and caregivers regarding solid organ transplantation pharmacotherapy using appropriate educational methods and resources in order to promote compliance and adherence.
3. Document all patient care activities (e.g., patient-specific findings, detailed treatment recommendations and communications with patients and other healthcare providers) using established procedures and regulations in order to maximize the quality of care.
4. Provide education and consultation to healthcare professionals and other stakeholders concerning issues related to the care of solid organ transplantation patients based on evidence and other appropriate literature in order to improve general understanding about medication therapies pertaining to transplantation.
5. Perform quality improvement activities using appropriate systems and checklists in order to enhance the safety and effectiveness of medication use in solid organ transplantation patient care.

How to Write Task Statements

1. Make sure that the task statements are complete.
1. What? 2. To whom/what? 3. How (if helpful)? 4. Why (if helpful)?
2. Begin the task statements with active verbs: assess, collect, identify, diagnose, document, plan, manage, collaborate, consult, etc.
3. Please avoid using verbs that are not as definitive as others: be responsible for, help, assist, keep, participate, or handle. Please avoid the use of such verbs.
4. Record task statements on the worksheet provided or in a word processing document.
5. We anticipate developing approximately 5 to 12 task statements for each domain.

Knowledge Statements

For each domain, it is valuable to understand what knowledge is required for proficient performance. The set of knowledge statements clarifies the expectations for pharmacists working with solid organ transplantation patients. Each knowledge statement should be coded to the task(s) to which it pertains most closely.

Sample Knowledge Statements

1. Pharmacotherapies, including transplantation immunosuppression, infectious disease, critical care, and internal medicine
2. Medication use evaluation
3. Research design and methodology, including clinical trial methodology
4. Risk factors for development of rejection

VALIDATION RATING SCALES

Please consider specialists in solid organ transplantation pharmacy when evaluating the domains and tasks using the following scales.

Performance Expectation: At what point in time are specialists in solid organ transplantation pharmacy first expected to perform the domain or task?

- 0 = Not at all
- 1 = Within the first six months of work as a specialist (includes exactly six months)
- 2 = After the first six months of work as a specialist (does not include exactly six months)

Example: *Certified Public Accountants are expected to conduct financial audits in the first six months after certification, but client management would be performed later in the career.*

Consequence: To what degree would the inability of specialists in solid organ transplantation pharmacy to perform duties in each domain or task be seen as causing harm to stakeholders? (Harm may be seen as physical, psychological, emotional, legal, financial, etc.)

- 0 = No harm
- 1 = Minimal harm
- 2 = Moderate harm
- 3 = Substantial harm
- 4 = Extreme harm

Example: *It is consequential that workers on high-rise buildings maintain a grip on their hammers. (Failure injures the public walking below and impacts other stakeholders such as employers, insurers, etc.)*

Frequency: Frequency refers to how often specialists in solid organ transplantation pharmacy perform duties in each of the domains or tasks, considering a one-year period. The following scale is used to record frequency:

- 0 = Never
- 1 = Rarely (once per year)
- 2 = Sometimes (once per month)
- 3 = Often (once per week)
- 4 = Repeatedly (daily)

Example: *Flight attendants open soft drinks for passengers repeatedly, yet this job duty is neither important nor consequential.*

WORKSHEET FOR DOMAINS

The domains listed below are provided for illustrative purposes only. In developing your own list of domains during the meeting, you may use any from this list, if they are appropriate, or devise your own.

- Domain 1: Phases of Transplantation, Including Pre-, Peri-, and Post-Transplantation
- Domain 2: Therapeutics, Patient Management, and Education
- Domain 3: Practice Management
- Domain 4: Patient Advocacy
- Domain 5: Research, Quality Assurance, and Process Improvement

Please list below the domains that you believe characterize the work of specialists in solid organ transplantation pharmacy.

WORKSHEET FOR TASK STATEMENTS

Domain: _____

Task Statement #1: _____

Task Statement #2: _____

Task Statement #3: _____

Task Statement #4: _____

Task Statement #5: _____

Task Statement #6: _____

Task Statement #7: _____

Task Statement #8: _____

Task Statement #9: _____

Task Statement #10: _____

Task Statement #11: _____

Task Statement #12: _____

Task Statement #13: _____

Task Statement #14: _____

Task Statement #15: _____

WORKSHEET FOR KNOWLEDGE STATEMENTS

Task: _____

KNOWLEDGE STATEMENTS

Knowledge Statement #1: _____

Knowledge Statement #2: _____

Knowledge Statement #3: _____

Knowledge Statement #4: _____

Knowledge Statement #5: _____

Knowledge Statement #6: _____

Knowledge Statement #7: _____

Knowledge Statement #8: _____

Knowledge Statement #9: _____

Knowledge Statement #10: _____

Knowledge Statement #11: _____

Knowledge Statement #12: _____

Knowledge Statement #13: _____

Knowledge Statement #14: _____

Knowledge Statement #15: _____

Knowledge Statement #16: _____

Knowledge Statement #17: _____

Knowledge Statement #18: _____



6001 Hospitality Court, Suite 100, Morrisville, North Carolina 27560

APPENDIX C (1): SURVEY INVITATIONS

Dear Colleague:

With the cooperation of the AST Transplant Pharmacy Community of Practice, the Board of Pharmacy Specialties (BPS) is conducting a survey about solid organ transplantation pharmacy. The survey is part of our evaluation of solid organ transplantation pharmacy as a potential pharmacy specialty. If your pharmacy practice includes solid organ transplantation, we would greatly appreciate your input.

A panel of experts identified the major areas of responsibility (domains) and tasks that are generally performed by pharmacists whose practice includes solid organ transplantation. Additionally, a set of knowledge statements for each task delineates what solid organ transplantation pharmacists must know in order to perform proficiently. The purpose of the survey is to request feedback regarding these proposed domains and tasks from all pharmacists who include solid organ transplantation in their practice. In the event that BPS decides to establish a specialty certification program, the domains and tasks will play a foundational role in the certification examination.

We estimate it will take approximately 25 minutes to complete the survey. *All responses are kept confidential, and your individual responses will not be released. All results will be reported in the aggregate. Individual responses will **NOT** be identified, although we request that you provide your name solely for survey management purposes. **We ask that you complete the entire survey in one sitting.***

Your participation in this effort is invaluable. **Individuals who complete the survey will be entered into a random drawing to receive one of four \$50 Amazon gift cards.**

The survey will close on **March 6, 2017**.

Please click https://www.research.net/r/BPS_AST to complete the survey.

This survey is being administered with the assistance of Castle Worldwide, Inc., a company that specializes in the development and validation of high-stakes tests. If you encounter any issues with the survey or if the survey link is inactive, please contact the survey administrator at surveyadmin@castleworldwide.com.

Thank you for your participation,

William Ellis, RPh, MS
Executive Director
Board of Pharmacy Specialties
Washington, DC

APPENDIX C (2): SURVEY INVITATIONS

Dear Colleague:

With the cooperation of the American College of Clinical Pharmacy (Immunology/Transplantation PRN), the Board of Pharmacy Specialties (BPS) is conducting a survey about solid organ transplantation pharmacy. The survey is part of our evaluation of solid organ transplantation pharmacy as a potential pharmacy specialty. If your pharmacy practice includes solid organ transplantation, we would greatly appreciate your input.

A panel of experts identified the major areas of responsibility (domains) and tasks that are generally performed by pharmacists whose practice includes solid organ transplantation. Additionally, a set of knowledge statements for each task delineates what solid organ transplantation pharmacists must know in order to perform proficiently. The purpose of the survey is to request feedback regarding these proposed domains and tasks from all pharmacists who include solid organ transplantation in their practice. In the event that BPS decides to establish a specialty certification program, the domains and tasks will play a foundational role in the certification examination.

We estimate it will take approximately 25 minutes to complete the survey. *All responses are kept confidential, and your individual responses will not be released. All results will be reported in the aggregate. Individual responses will **NOT** be identified, although we request that you provide your name solely for survey management purposes. **We ask that you complete the entire survey in one sitting.***

Your participation in this effort is invaluable. **Individuals who complete the survey will be entered into a random drawing to receive one of four \$50 Amazon gift cards.**

The survey will close on **March 6, 2017**.

Please click https://www.research.net/r/BPS_ACCP to complete the survey.

This survey is being administered with the assistance of Castle Worldwide, Inc., a company that specializes in the development and validation of high-stakes tests. If you encounter any issues with the survey or if the survey link is inactive, please contact the survey administrator at surveyadmin@castleworldwide.com.

Thank you for your participation,

William Ellis, RPh, MS

Executive Director

Board of Pharmacy Specialties

Washington, DC

APPENDIX C (3): SURVEY INVITATIONS

Dear Colleague:

With the cooperation of the American Society of Health System Pharmacists (Section of Clinical Specialists and Scientists), the Board of Pharmacy Specialties (BPS) is conducting a survey about solid organ transplantation pharmacy. The survey is part of our evaluation of solid organ transplantation pharmacy as a potential pharmacy specialty. If your pharmacy practice includes solid organ transplantation, we would greatly appreciate your input.

A panel of experts identified the major areas of responsibility (domains) and tasks that are generally performed by pharmacists whose practice includes solid organ transplantation. Additionally, a set of knowledge statements for each task delineates what solid organ transplantation pharmacists must know in order to perform proficiently. The purpose of the survey is to request feedback regarding these proposed domains and tasks from all pharmacists who include solid organ transplantation in their practice. In the event that BPS decides to establish a specialty certification program, the domains and tasks will play a foundational role in the certification examination.

We estimate it will take approximately 25 minutes to complete the survey. *All responses are kept confidential, and your individual responses will not be released. All results will be reported in the aggregate. Individual responses will **NOT** be identified, although we request that you provide your name solely for survey management purposes. **We ask that you complete the entire survey in one sitting.***

Your participation in this effort is invaluable. **Individuals who complete the survey will be entered into a random drawing to receive one of four \$50 Amazon gift cards.**

The survey will close on **March 6, 2017**.

Please click https://www.research.net/r/BPS_ASHP to complete the survey.

This survey is being administered with the assistance of Castle Worldwide, Inc., a company that specializes in the development and validation of high-stakes tests. If you encounter any issues with the survey or if the survey link is inactive, please contact the survey administrator at surveyadmin@castleworldwide.com.

Thank you for your participation,

William Ellis, RPh, MS

Executive Director

Board of Pharmacy Specialties

Washington, DC

APPENDIX D: SURVEY

Appendix F-1

Required Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2) Pharmacy Residencies in Solid Organ Transplant



Required Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2) Pharmacy Residencies in Solid Organ Transplant

Overview of PGY2 Solid Organ Transplant Pharmacy Residencies

PGY2 pharmacy residencies in solid organ transplant are designed to transition PGY1 residency graduates from generalist practice to specialized practice focused on the care of solid organ transplant recipients and, in some instances, living organ donors. Residency graduates are equipped to participate as essential members of interdisciplinary teams caring for transplant patients, assuming responsibility for the medication-related aspects of care. Team involvement includes contributing the pharmacy perspective to selection and preparation of recipients. Transplant residency graduates are proficient in the care of patients as they prepare to receive a transplant, during the acute care phase of transplantation, and in the ongoing primary care role after transplant as the pharmacist works with the patient to sustain the survival of the transplanted organ, manage diseases that occur or reoccur post transplant, and enhance the patient's general health and wellness.

In addition to these direct patient care responsibilities, transplant residency graduates are trained to serve as authoritative resources in their health systems for the optimal use of medications in transplant recipients. In that role, they can be relied upon to lead the development and implementation of medication-related guidelines and protocols for transplant patient care, meet the health system's needs for transplant-related drug information, and provide the transplant pharmacy perspective to organizations making technology and automation decisions. Graduates are also highly skilled in the design and delivery of education and training related to transplantation for a wide spectrum of potential audiences, including the patient and/or caregiver as well as health care professionals in practice or in training.

Because transplantation is such a rapidly developing field, graduates of solid organ transplant pharmacy residencies are all skilled in supporting or conducting transplant research and in outcomes analyses.

Explanation of the Contents of This Document:

Each of the document's objectives has been classified according to educational taxonomy (cognitive, affective, or psychomotor) and level of learning. An explanation of the taxonomies is available elsewhere.¹

The order in which the required educational outcomes are presented in this document does not suggest relative importance of the outcome, amount of time that should be devoted to teaching the outcome, or sequence for teaching.

The educational outcomes, goals, and objectives are divided into those that are required and those that are elective. Required outcomes, including all of the goals and objectives falling under them, must be included in the design of all programs. Elective outcomes are provided for those programs that wish to add to the required outcomes. Programs selecting an elective outcome are not required to include all of the goals and objectives falling under that outcome. In addition to the potential elective outcomes contained in this document, programs are free to create their own elective outcomes with associated goals and objectives. Other sources of elective outcomes may include elective educational outcomes in the list provided for PGY1 pharmacy residencies and educational outcomes for training in other PGY2 areas. Each of the goals falling under the program's selection of program outcomes (required and elective) must be evaluated at least once during the resident's year.

Educational Outcomes (Outcome): Educational outcomes are statements of broad categories of the residency graduates' capabilities.

Educational Goals (Goal): Educational goals listed under each educational outcome are broad sweeping statements of abilities.

Educational Objectives (OBJ): Resident achievement of educational goals is determined by assessment of the resident's ability to perform the associated educational objectives below each educational goal.

Instructional Objectives (IO): Instructional objectives are the result of a learning analysis of each of the educational objectives. They are offered as a resource for preceptors encountering difficulty in helping residents achieve a particular educational objective. The instructional objectives falling below the educational objectives suggest knowledge and skills required for successful performance of the educational objective that the resident may not possess upon entering the residency year. Instructional objectives are teaching tools only. They are not required in any way nor are they meant to be evaluated.

¹ Nimmo, CM. Developing training materials and programs: creating educational objectives and assessing their attainment. In: Nimmo CM, Guerrero R, Greene SA, Taylor JT, eds. Staff development for pharmacy practice. Bethesda, MD: ASHP; 2000.

Required Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2) Pharmacy Residencies in Solid Organ Transplant

Outcome R1: Serve as an authoritative resource on the optimal use of medications in recipients of a solid organ transplant.

Goal R1.1 Establish oneself as an expert for transplant pharmacy-related information and resources.

OBJ R1.1.1 (Synthesis) Develop a strategy for earning credibility within the organization to be an authoritative resource on the pharmaceutical care of transplant patients.

IO Identify barriers to the transplant pharmacist for earning credibility with members of the transplant team.

IO Identify barriers to the transplant pharmacist for earning credibility within the organization.

Goal R1.2 Lead the modification or development and implementation of medication-related guidelines or protocols for transplant patient care.

OBJ R1.2.1 (Analysis) Identify the need for a new or modified medication-related guideline/protocol for transplant patient care.

OBJ R1.2.2 (Synthesis) Modify or develop a medication-related guideline/protocol for transplant patient care based on best evidence and analyses of the organization's transplant patient data.

OBJ R1.2.3 (Synthesis) Formulate a strategy to successfully implement a medication-related guideline/protocol for transplant patient care.

OBJ R1.2.4 (Evaluation) Assess the results of implementing a medication-related guideline/protocol for transplant patient care.

IO Explain how a medication-use evaluation can be utilized to measure the effects of implementing a guideline/protocol on clinical processes or outcomes.

IO Explain how a medication-use evaluation can be utilized to measure adherence to a guideline/protocol.

Goal R1.3 Provide concise, applicable, comprehensive, and timely responses to formal or informal drug information requests pertaining to the care of transplant patients.

OBJ R1.3.1 (Analysis) Discriminate between the requester's statement of need and the actual drug information need by clarifying any additional and appropriate defining questions.

OBJ R1.3.2 (Synthesis) Formulate a systematic, efficient, and thorough procedure for retrieving drug information.

IO Identify various sources of transplant-related biomedical literature and the nature and caliber of information each is likely to provide.

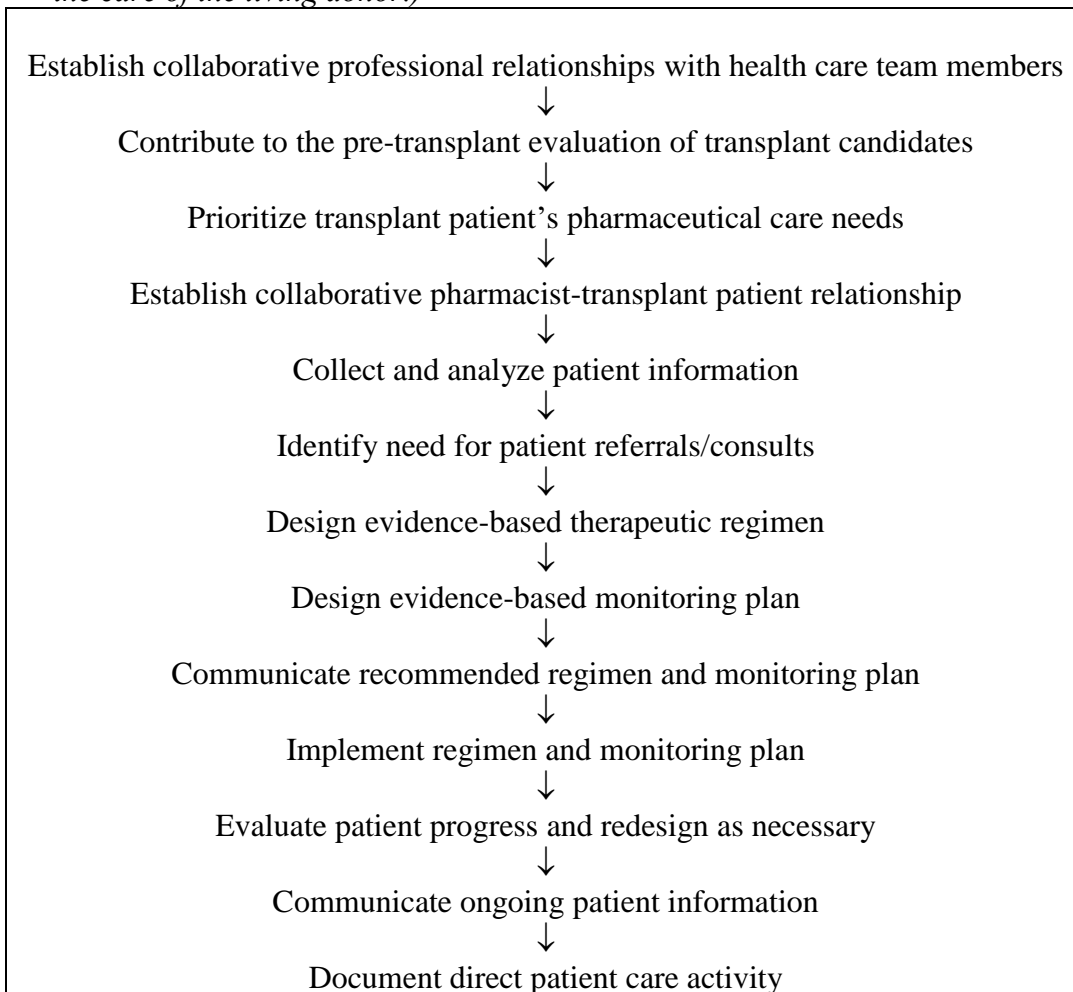
IO Explain the potential need for increased reliance on alternate sources (e.g., abstracts from national meeting presentations, industry-authored medical information responses, expert opinion, clinical practice guidelines, transplant registries or databases) when researching transplant-related medication questions.

- OBJ R1.3.3 (Analysis) Determine from all retrieved biomedical literature the appropriate information to evaluate.
- OBJ R1.3.4 (Evaluation) Evaluate the usefulness of biomedical literature gathered.
- OBJ R1.3.5 (Evaluation) Determine whether a study's conclusions are supported by the study results.
- OBJ R1.3.6 (Synthesis) Formulate responses to formal drug information requests based on analysis of the literature.
- OBJ R1.3.7 (Synthesis) Provide appropriate responses to informal drug information questions that require the pharmacist to draw upon his or her knowledge base.
- OBJ R1.3.8 (Evaluation) Assess the effectiveness of drug information recommendations.
 - IO Explain all factors that must be assessed to determine the effectiveness of a response.*
- Goal R1.4 Develop a core library appropriate for transplant pharmacy practice.
 - OBJ R1.4.1 (Application) Use a knowledge of standard transplant-related resources to develop and maintain a core library of primary, secondary, and tertiary references appropriate for transplant pharmacy practice, education, and research.
 - IO Explain how to access and withdraw information from national transplant databases (e.g., The United Network for Organ Sharing).*
- Goal R1.5 Contribute the transplant pharmacy perspective to the organization's technology and automation systems decisions.
 - OBJ R1.5.1 (Synthesis) When appropriate, contribute to the organization's design of its technology and automation systems.
 - IO Explain the transplant pharmacist's potential contributions to the design of technology (e.g., CPOE, databases, pharmacy systems, PDAs) for the organization.*
 - IO Explain the transplant pharmacist's potential role in contributing to decisions regarding automation.*
- Goal R1.6 Contribute to clinical, humanistic and/or economic transplant outcomes research.
 - OBJ R1.6.1 (Evaluation) Contribute to a prospective or retrospective clinical, humanistic and/or economic outcomes analysis.
 - IO Explain the purposes of prospective and of retrospective clinical, humanistic and economic outcomes analyses.*
 - IO Explain the principles and methodology of basic outcomes analyses.*
 - IO Explain study designs appropriate for prospective and for retrospective clinical, humanistic and economic outcomes analyses.*
 - IO Explain the types of data that must be collected in prospective and in retrospective clinical, humanistic and economic outcomes analyses.*
 - IO Explain possible reliable sources of data for clinical, humanistic and economic outcomes analyses.*
 - IO Explain methods for analyzing data in prospective and in retrospective clinical, humanistic and economic outcomes analyses.*
 - IO Explain the impact of limitations of retrospective data on the interpretation of results.*

- IO Explain how results of prospective and of retrospective clinical, humanistic and economic outcomes analyses can be applied to clinical practice decisions.*
- IO Explain the regulatory process when trying to implement prospective or retrospective clinical, humanistic, and economic outcomes analyses.*

Outcome R2: Optimize the outcomes of transplant patients by promoting and/or providing evidence-based medication therapy as an integral member of an interdisciplinary team in acute and ambulatory care settings.

(In those settings where the transplant pharmacist provides care to both the transplant recipient and a living donor, the following educational goals and objectives also apply to the care of the living donor.)



- Goal R2.1** Establish collaborative professional relationships with members of interdisciplinary health care teams involved in the care of transplant patients.
- OBJ R2.1.1** (Synthesis) Implement a strategy that effectively establishes cooperative, collaborative, and communicative working relationships with members of the interdisciplinary health care team involved in the care of a transplant patient.
- IO Explain the training and expected areas of expertise of the members of the interdisciplinary transplant team with which one works.*

- IO *For each of the professions with which one interacts on the interdisciplinary transplant team, explain the profession's view of its role and responsibilities in collaborations on patient-centered care.*
 - IO *Explain the expectations of the pharmacist's role on the transplant team from the viewpoint of different collaborating professions.*
 - IO *Explain the professional dynamics of the different services that contribute to the care of transplant patients.*
 - IO *Identify the interpersonal dynamics of each member of the transplant team.*
- Goal R2.2 Contribute to the pre-transplant evaluation of transplant candidates.
- OBJ R2.2.1 (Evaluation) Contribute the pharmacy perspective to the selection process and listing of transplant patients.
 - IO *Explain factors to consider when determining those patients who are medically, surgically, and socially suitable for transplantation.*
 - IO *Explain factors to consider when determining the most appropriate immunosuppressive/immunomodulatory approach for a given transplant recipient-donor combination (living or cadaveric).*
- Goal R2.3 Prioritize the pharmaceutical care needs of transplant patients.
- OBJ R2.3.1 (Synthesis) Devise a strategy for prioritizing pharmaceutical care activities given practical time constraints and multiple practice responsibilities.
 - IO *Explain factors to consider when determining priorities of care among transplant patients.*
 - IO *Explain how priorities of pharmaceutical care may be mandated or influenced by the complexity or urgency of a given transplant patient's problems.*
 - IO *Explain the importance to transplant pharmacy practitioners of maintaining proficiency in the management of general medical problems in immunocompromised patients.*
- Goal R2.4 Establish collaborative relationships between the pharmacist and transplant patients and/or caregivers.
- OBJ R2.4.1 (Synthesis) Formulate a strategy that effectively establishes a patient-centered relationship between the pharmacist and transplant patient and/or caregiver.
 - IO *Explain unique characteristics of transplant patients that may influence the pharmacist-patient relationship.*
 - IO *Explain social and pharmacoeconomic issues encountered frequently in transplant recipients.*
 - IO *Explain how pharmacist-patient interactions may differ when the organ is from a living donor versus when the organ is from a deceased donor.*
- Goal R2.5 Collect and analyze patient information.
- OBJ R2.5.1 (Analysis) Collect and organize all patient-specific information needed by the transplant pharmacist to anticipate, prevent, detect, and/or resolve medication-related problems and to make appropriate evidence-based, patient-centered therapeutic recommendations as part of the interdisciplinary transplant team.

- IO *Explain the types of information that are typically available regarding a transplant patient and donor, prior to direct pharmacist-patient involvement.*
 - IO *Identify the types of patient-specific information, including complementary and alternative medicines, the pharmacist requires to anticipate, prevent, detect, and/or resolve medication-related problems and to make appropriate evidence-based, patient-centered medication therapy recommendations for transplant patients.*
 - IO *Explain the functions of the immune system and how they relate to transplantation and design of immunosuppressive therapies.*
 - IO *Explain how to interpret and apply the various diagnostic and laboratory tests commonly performed in transplant patients.*
 - IO *Explain pharmacokinetic and pharmacodynamic alterations that occur between pre- and post-transplantation, and how these might influence drug dosing strategies for transplant patients.*
 - IO *Explain the signs and symptoms, epidemiology, etiology, risk factors, pathogenesis, natural history, pathophysiology, clinical course, prevention, and pre-transplant management of diseases or conditions that frequently underlie an indication for transplantation as listed in the appendix.*
 - IO *Explain the management of end-stage organ disease in recipients awaiting transplant.*
 - IO *Explain signs and symptoms, epidemiology, etiology, risk factors, pathogenesis, natural history, pathophysiology, clinical course, prevention, and treatment of diseases or conditions that frequently occur or reoccur after transplantation as listed in the appendix.*
 - IO *Explain signs and symptoms, epidemiology, etiology, risk factors, pathogenesis, pathophysiology, clinical course, prevention, and treatment of the types of rejection that may occur after transplantation as listed in the appendix.*
 - IO *Explain the mechanism of action, pharmacokinetics, pharmacodynamics, pharmacogenomics, pharmacoeconomics, usual regimen (dose, schedule, form, route, and method of administration), indications, contraindications, interactions, adverse reactions, and therapeutics of immunosuppressive agents.*
 - IO *Explain transplant-specific or unique mechanisms of action, pharmacokinetics, pharmacodynamics, pharmacogenomics, pharmacoeconomics, usual regimen (dose, schedule, form, route, and method of administration), indications, contraindications, interactions, adverse reactions, and therapeutics of medications used to prevent and treat diseases commonly occurring in transplant recipients.*
- OBJ R2.5.2 (Analysis) Determine the presence of any of the following medication therapy problems in a transplant recipient's or living organ donor's current medication therapy:
1. Medication used without medical indication

2. Medical conditions for which medication therapy is warranted but not prescribed
3. Inappropriate medication selection for a given medical condition
4. Immunization regimen is incomplete or inappropriate
5. Current medication therapy regimen contains something inappropriate (dose, dosage form, duration, schedule, route of administration, method of administration)
6. Unnecessary therapeutic duplication
7. Medication to which the patient is allergic has been prescribed
8. Adverse drug- or device-related events are highly suspected, or potential for such events is detected
9. Clinically significant drug-drug, drug-disease, drug-nutrient, or drug-laboratory test interactions or potential for such interactions
10. Medical therapy has been compromised by social, recreational, nonprescription, complementary, or alternative drug use by the patient
11. Patient not receiving full benefit of prescribed medication therapy
12. Problems arising from the financial impact of medication therapy on the patient
13. Patient lacks understanding of medication therapy
14. Patient not adhering to medication regimen

IO Explain why the transplant pharmacist needs to anticipate therapeutic dilemmas and formulate appropriate alternatives.

IO Explain the potential impact of transplant-related medication side effects, costs, and scheduling on the adherence and persistence of transplant patients.

IO Explain how optimization of pre-transplant therapies may impact post-transplantation outcomes.

IO Describe common long-term post-transplant complications and their implication(s) regarding indication for initiation or modification of therapy.

OBJ R2.5.3 (Analysis) Using an organized collection of patient-specific information, summarize the transplant patient's health care needs.

Goal R2.6 Identify patients in need of a referral or consult.

OBJ R2.6.1 (Evaluation) When presented with a transplant patient with health care needs that cannot be met by the transplant interdisciplinary team, contribute to the team's decision to make a referral or request a consult.

IO Explain the role of non-pharmacologic approaches in addressing post-transplant complications or patient care needs.

Goal R2.7 Design evidence-based therapeutic regimens for transplant patients.

OBJ R2.7.1 (Synthesis) Specify therapeutic goals for a transplant patient incorporating the principles of evidence-based medicine that integrate patient-specific data, center-specific experience, disease and medication-specific information, ethics, and quality-of-life considerations.

IO Explain various genetic, race, gender-related, age-related, and disease-related factors that influence the establishment of therapeutic goals and their achievement in transplant patients.

OBJ R2.7.2 (Synthesis) Design a patient-centered regimen that meets the evidence-based therapeutic goals established for a transplant patient; integrates patient-specific, disease, and medication information; ethical and quality-of-life issues; and considers pharmacoeconomic principles.

IO Identify various sources of disease management and drug-use guidelines potentially applicable to transplant populations.

IO Explain how to assess a transplant candidate's immunologic risk and how it would influence the patient's medication regimen.

IO Evaluate organization-specific protocols or patient management strategies versus external guidelines and reported experience when deciding which to use with a specific patient.

IO Explain the rationale underlying various immunosuppressive strategies utilized in transplant patients.

IO Explain screening approaches for identification of transplant patients eligible for research protocols based on protocol inclusion and exclusion criteria.

IO Explain additional concerns with adherence/persistence and cost when designing or implementing medication regimens for transplant patients.

IO Explain various payer mechanisms for coverage of transplant-related medications, particularly the interplay between Medicare, Medicaid, commercial insurers, and medication assistance programs.

IO Explain medication therapy considerations for those who have served as living organ donors.

Goal R2.8 Design evidence-based monitoring plans for management of transplant patients.

OBJ R2.8.1 (Synthesis) Design a patient-centered, evidence-based monitoring plan for a medication regimen that effectively evaluates achievement of transplant patient-specific goals.

IO State customary monitoring parameters for medication regimens commonly prescribed for transplant patients that assess for safety and efficacy.

IO Explain the effect of transplant-related medication therapies on the interpretation of clinical parameters.

IO Explain various approaches to assessing immunologic response to medication therapy (e.g., therapeutic drug monitoring, functional immunologic assays, biopsies, clinical complications [i.e., certain viral infections]).

OBJ R2.8.2 (Synthesis) Design a patient-centered, evidence-based monitoring plan for non-pharmacologic therapy that effectively evaluates achievement of transplant patient-specific goals.

IO Describe the relative role of surgical or non-pharmacologic interventions in managing post-transplant complications.

IO Describe the implications of surgical or technical complications of transplant upon the pharmacologic plan of therapy.

Goal R2.9 Communicate medication regimen recommendations and monitoring plans for transplant patients to relevant persons.

- OBJ R2.9.1 (Application) Communicate recommendations for a patient-centered, evidence-based therapeutic regimen and corresponding monitoring plan to other members of the interdisciplinary team in a manner that is systematic, logical, accurate, timely, system-appropriate, and secures consensus from the team.
- OBJ R2.9.2 (Application) Communicate recommendations for a patient-centered, evidence-based therapeutic regimen and corresponding monitoring plan to the transplant patient in a way that is sensitive, accurate, matched to the patient's level of comprehension, and fosters adherence and persistence by the patient and/or caregiver.
- IO Explain the kinds of issues that require particular sensitivity when discussing medication treatment plans with transplant patients and/or caregivers.*
- IO Explain to the patient and/or caregiver the special obligations (or monitoring requirements) of patients participating in research protocols and the rights of patients to withdraw from protocols.*
- Goal R2.10 Implement regimens and monitoring plans.
- OBJ R2.10.1 (Application) When appropriate, initiate the patient-centered, evidence-based therapeutic regimen and monitoring plan for a transplant patient according to the organization's policies and procedures for pharmacist or research-related privileging.
- IO Explain the organization's policies and procedures for ordering diagnostic or monitoring tests.*
- IO Explain the organization's policies and procedures for issuing medication orders.*
- OBJ R2.10.2 (Application) When necessary, contribute to the work of the team to facilitate patient access to necessary medications.
- IO Explain the general framework of patient assistance programs available for transplant-related drugs.*
- IO Explain the pharmacist's role relative to other interdisciplinary team members in securing payer coverage or patient assistance for transplant-related drugs, within the context of the training program.*
- IO Explain circumstances in which it may be appropriate to redesign a patient's medication regimen in order to ensure that a patient will have financially viable access to the prescribed medications.*
- IO Explain various approaches used to adjust medication regimens in order to facilitate patient access to medications.*
- OBJ R2.10.3 (Application) Use effective patient education techniques to provide counseling to transplant patients and caregivers, including information on medication therapy, interactions, adverse effects, adherence, persistence, appropriate use, handling, storage, and medication administration.
- IO Explain the imperative that patients learn they must check with the transplant team before adding any prescribed, OTC, or alternative medication to their regimen.*
- IO Explain the critical role of adherence and persistence in the short and long-term success of transplantations.*

IO Explain potential strategies for educating patients who present educational challenges (e.g., language barriers, blind, deaf, illiterate, immature).

Goal R2.11 Evaluate transplant patients' progress and redesign medication regimens and monitoring plans as indicated by their clinical course.

OBJ R2.11.1 (Evaluation) Accurately assess the transplant patient's progress toward short and long-term therapeutic goals.

IO Explain potential long-term complications in transplant recipients and the importance of monitoring for such complications.

IO Explain the interplay between management of short-term post-transplant complications and potential implications for longer-term management goals or approaches.

IO Explain the role of the pharmacist in ongoing management of transplant patients for maximizing survival of a transplanted organ and its recipient.

IO Explain the transplant organization's systematic plan for routine patient follow-up and monitoring.

IO Assess the need of an individual patient to modify the organization's routine approach to patient follow-up and monitoring.

OBJ R2.11.2 (Synthesis) Based on evaluation of monitoring data, therapeutic outcomes, and the evolution of standards of care within transplantation, redesign a transplant patient's medication regimen and monitoring plan as necessary.

IO Explain the impact of evolving transplant research and its potential application to ongoing therapy of transplant recipients.

Goal R2.12 Communicate ongoing patient information to relevant persons.

OBJ R2.12.1 (Application) Ensure that accurate and timely information regarding a specific transplant patient reaches those who need it at the appropriate time, according to the organization's established or innovative approaches.

IO Explain how to recognize instances in which there is urgency in communicating the results of monitoring to the appropriate members of the transplant team.

OBJ R2.12.2 (Application) When given a transplant patient who is transitioning from one health care setting to another, facilitate continuity of care by communicating pertinent patient information to the receiving health care professionals.

IO Explain what information will be critical to ongoing implementation or monitoring of a specific plan of pharmaceutical care.

IO Explain how to identify the key recipients of critical information and the most effective means of communicating such information for a given care setting.

Goal R2.13 Document direct patient care activities appropriately.

OBJ R2.13.1 (Analysis) Select for documentation the appropriate direct patient-care activities for transplant patients.

OBJ R2.13.2 (Application) Use effective communication practices when documenting a direct patient-care activity for a transplant patient.

Outcome R3: Manage and improve the medication-use process in transplant patient care areas.

- Goal R3.1 Serve as an organizational resource for knowledge about the proper preparation, distribution, and administration of transplant-related medications.
 - OBJ R3.1.1 (Comprehension) Explain aspects of the preparation, distribution, and administration of medications unique to transplantation.
- Goal R3.2 Identify potential opportunities for improvement relating to aspects of the organization's medication-use system affecting transplant patients.
 - OBJ R3.2.1 (Comprehension) Explain those aspects of the organization's medication-use system affecting transplant patients and any vulnerabilities to adverse drug events (ADEs).
 - OBJ R3.2.2 (Analysis) Analyze the structure and process of the medication-use system and, when called for, measure outcomes in the transplant environment.
 - OBJ R3.2.3 (Evaluation) Identify opportunities for improvement in aspects of the organization's medication-use system affecting transplant patients by comparing the medication-use system to relevant best practices.
 - OBJ R3.2.4 (Application) Participate in the organization's system for reporting medication errors and adverse drug reactions.

Outcome R4: Demonstrate leadership and practice management skills.

- Goal R4.1 Exhibit the ongoing development of essential personal skills of a practice leader.
 - OBJ R4.1.1 (Characterization) Practice self-managed continuing professional development with the goal of improving the quality of one's own performance through self-assessment and personal change.
 - IO State criteria for judging one's performance of tasks that are critical in one's own practice.*
 - IO Explain the role of participation in transplant and pharmacy professional organization meetings in the ongoing development of expertise in transplantation.*
 - OBJ R4.1.2 (Characterization) Demonstrate commitment to the professional practice of transplant pharmacy through active participation in the activities of local, state, and/or national transplant and pharmacy professional organizations.
 - IO Assess the relevance of membership or participation in various professional associations associated with transplant or pharmacy practice.*
 - IO Explain the importance of contributing to the work of transplant professional organizations in advancing the visibility of the pharmacist's role in transplantation.*
 - OBJ R4.1.3 (Characterization) Demonstrate the ability to make rational but rapid decisions in intense situations where time is at a minimum.
 - OBJ R4.1.4 (Organization) Demonstrate sensitivity to the perspective of the patient, caregiver, or health care colleague in all communications.
 - IO Explain the importance of adjusting one's communications according to the level of health literacy of the patient.*
 - IO Explain common situations in the practice of transplant pharmacy which can present challenges to effective communication.*

- IO Explain potential communication strategies that could be used to overcome difficulties in communication, including the use of active listening.*
- IO Explain the meaning of cultural competence in health care practice.*
- IO Explain communication strategies that are appropriate for patients who are non-English speakers or who are impaired.*
- IO Explain the importance of adjusting one's communications for different types of health professionals (e.g., nurses, physicians, respiratory therapist).*
- OBJ R4.1.5 (Characterization) Demonstrate enthusiasm and passion for the profession of transplant pharmacy.
 - IO Explain the roles of transplant pharmacists in various practice areas including clinical practice, academia, and industry (e.g., medical science liaison, clinical research scientist, study coordinator).*
- Goal R4.2 Contribute to the leadership and management activities within the transplant pharmacy practice area.
 - OBJ R4.2.1 (Application) Use effective negotiation skills to resolve conflicts.
 - OBJ R4.2.2 (Synthesis) Use group participation skills when leading or working as a member of a formal or informal work group.
- Goal R4.3 Exercise practice leadership.
 - OBJ R4.3.1 (Characterization) Demonstrate a commitment to advocacy for the optimal care of transplant patients through the assertive and persuasive presentation of patient care issues to members of the health care team, the patient, and/or the patient's representative(s).
 - OBJ R4.3.2 (Comprehension) Explain the nature of mentoring in pharmacy, its potential connection with achievement, and the importance of being willing to serve as a mentor to appropriate individuals.
 - OBJ R4.3.3 (Comprehension) Explain the general processes of establishing and maintaining a transplant pharmacy residency program.
 - OBJ R4.3.4 (Comprehension) Explain the potential benefits, to the practitioner and the profession, of contributing to the transplant literature.
 - OBJ R4.3.5 (Characterization) Demonstrate a caring attitude toward transplant patients and their representative(s).
 - IO Explain potential emotional issues surrounding both donation of an organ and receipt of an organ from a living or deceased donor.*
 - IO Explain initiatives to increase organ donation awareness and potential means of supporting such efforts on a personal or professional basis.*
 - OBJ R4.3.6 (Synthesis) Promote health improvement and wellness of the transplant patient.

Outcome R5: Demonstrate excellence in the provision of training or educational activities about transplant-related medications for health care professionals and health care professionals in training.

- Goal R5.1 Provide effective education or training about transplant-related medications to health care professionals and those in training.

- OBJ R5.1.1 (Application) Use effective educational techniques in the design of all educational activities.
- IO Identify issues in transplant pharmacy practice that would be suitable for interdisciplinary educational sessions.*
 - IO Explain the differences in effective educational strategies when teaching colleagues versus residents versus students versus health professionals in other disciplines.*
 - IO Design instruction that meets the individual learner's needs.*
 - IO Explain the concept of learning styles and its influence on the design of instruction.*
 - IO Construct appropriately worded educational objectives.*
 - IO Explain the match between instructional delivery systems (e.g., demonstration, written materials, videotapes) and the specific types of learning each facilitates.*
 - IO Design instruction that utilizes strategies, methods, and techniques congruent with the objectives for education or training.*
 - IO Explain effective teaching approaches for the various types of learning (e.g., imparting information, teaching psychomotor skills, inculcation of new attitudes).*
- OBJ R5.1.2 (Synthesis) Design an assessment strategy that appropriately measures the specified objectives for education or training and fits the learning situation.
- IO Explain appropriate assessment techniques for assessing the learning outcomes of educational or training programs.*
- OBJ R5.1.3 (Application) Use skill in the four preceptor roles employed in practice-based teaching (direct instruction, modeling, coaching, and facilitation).
- IO Explain the stages of learning that are associated with each of the preceptor roles.*
- OBJ R5.1.4 (Application) Use skill in case-based teaching.
- IO Explain the importance of identifying key teaching points for a case before attempting to construct it.*
 - IO Explain factors to consider when selecting which patient data to present in a case*
- OBJ R5.1.5 (Application) Use public speaking skills to speak effectively in large group situations.
- IO Explain techniques that can be used to enhance audience interest.*
 - IO Explain techniques that can be used to enhance audience understanding of one's topic.*
 - IO Explain speaker habits that distract the audience.*
- OBJ R5.1.6 (Application) Use public speaking skills to speak effectively in small group situations.

Outcome R6: Conduct transplant research.

Goal R6.1 Conduct a transplant research project using effective project management skills.

- OBJ R6.1.1 (Synthesis) Identify a topic of significance for a transplant research project.

- IO Explain the types of research projects (e.g., prospective, retrospective, clinical trials) that will meet residency program project requirements and timeframe.*
- IO Explain factors to consider in assessing the relevance or significance of a potential project idea to a particular practice setting.*
- IO Explain how to conduct an efficient and effective background literature search for a project.*
- IO Explain how to generate a research question(s) to be answered by an investigation.*
- OBJ R6.1.2 (Synthesis) Formulate a feasible design for a transplant research project.
 - IO Explain the elements of a project proposal.*
 - IO Explain how to identify those individuals who will be affected by the conduct of the project and strategies for gaining their cooperation.*
 - IO Explain how to determine a timeline with suitable milestones that will result in project completion by an established target date.*
 - IO Explain the ethics of research on human subjects and the role of the IRB in monitoring research.*
 - IO Explain various methods for constructing data collection tools.*
- OBJ R6.1.3 (Synthesis) Secure any necessary approvals, including IRB and funding, for one's design of a project.
 - IO Explain how to identify those key stakeholders who must approve a particular project.*
 - IO Explain the components that make up a budget for various types of research projects.*
 - IO Explain the role of the organization's IRB in the approval process.*
- OBJ R6.1.4 (Synthesis) Implement a transplant research project as specified in its design.
 - IO Explain strategies for keeping one's work on a project at a pace that matches with the projected timeline.*
 - IO When given a particular approved residency project, explain methods for organizing and maintaining project materials and documentation of the project's ongoing implementation.*
 - IO Explain methods for data analysis.*
- OBJ R6.1.5 (Synthesis) Effectively present the results of a transplant research project at a meeting outside of the organization.
 - IO Explain the process of submitting a research abstract for presentation at an appropriate pharmacy or transplant association meeting.*
- OBJ R6.1.6 (Synthesis) Successfully utilize accepted manuscript style to prepare a final report of a transplant research project.
 - IO When given a particular residency project ready for presentation, explain the type of manuscript style appropriate to the project and criteria to be met when using that style.*
- OBJ R6.1.7 (Evaluation) Accurately assess the impact, including sustainability if applicable, of the residency project.

<p style="text-align: center;">Elective Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2) Pharmacy Residencies in Solid Organ Transplant</p>
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Outcome E1: Demonstrate additional leadership and practice management skills.

- Goal E1.1 Develop a proposal for a new or revised transplant-related pharmacy service.
- OBJ E1.1.1 (Synthesis) Write a proposal for a transplant-related service that meets a perceived need of the organization and its patients.
 - IO Explain the effect of resource limitations on realistic designs for new or improved transplant-related pharmacy services.*
 - OBJ E1.1.2 (Application) Use effective presentation skills to present a proposal for a new or revised transplant-related service to the various concerned entities within the organization.
 - OBJ E1.1.3 (Evaluation) Utilize effective strategies for implementing a new or revised transplant-related pharmacy service.
 - OBJ E1.1.4 (Evaluation) Appraise a new or revised transplant pharmacy service for adequacy in meeting the stated goals.

Outcome E2: Contribute to formulary decisions regarding transplant-related medications.

- Goal E2.1 Contribute to the organization's formulary decision-making process for transplant-related medications.
- OBJ E2.1.1 (Evaluation) Make recommendations for additions or deletions to the organization's formulary for a transplant-related medication based on literature, organizational protocols, and/or comparative reviews.
 - IO Explain off-label usage patterns of transplant medications and their potential impact on formularies and medication-use policies.*
 - IO State the elements of a comparative formulary review including consideration of efficacy, safety, and cost.*
 - IO State key sources to consult, including prescribers, in the preparation of a comparative review and recommendation(s) for a given organization.*
 - IO Explain the importance of including consideration of efficacy, safety, and cost in the preparation of reviews.*
 - OBJ E2.1.2 (Synthesis) Formulate effective strategies for communicating formulary restrictions to providers.
 - IO Explain routes of communication of formulary information within the organization and any peculiarities in the transplant setting.*
 - IO Identify instances when formulary changes should be communicated immediately.*
 - OBJ E2.1.3 (Evaluation) When presented with a real or hypothetical drug shortage, identify appropriate alternative medications.
 - IO State resources for identifying medications in short supply.*
 - IO Explain the organization's system for communicating information regarding drug shortages.*
 - IO Explain a strategy for making optimal choices for alternative medications.*
 - IO Explain strategies for allocating existing supplies of a drug in short supply.*

Outcome E3: Demonstrate additional skills for managing and improving the medication-use process in transplant patient care areas.

- Goal E3.1 Prepare and dispense medications for transplant patients following existing standards of practice and the organization's policies and procedures.
- OBJ E3.1.1 (Evaluation) Interpret the appropriateness of a transplant-related medication order before preparing or permitting the distribution of the first dose.
 - OBJ E3.1.2 (Application) Follow the organization's policies and procedures to maintain the accuracy of the patient's medication profile.
 - OBJ E3.1.3 (Application) Prepare transplant-related medications following appropriate standards of practice and the organization's policies and procedures.
 - OBJ E3.1.4 (Application) Dispense transplant-related medications following the organization's policies and procedures.
- Goal E3.2 Design and implement quality improvement changes to aspects of the organization's medication-use system affecting transplant patients.
- OBJ E3.2.1 (Synthesis) Contribute to the design and implementation of pilot interventions to change problematic or potentially problematic aspects of the medication-use system with the objective of improving quality of care for transplant patients.

Outcome E4: Publish on transplant-related topics.

- Goal E4.1 Write for publication pertinent medication-use information on transplant-related topics for health care professionals and/or the public.
- OBJ E4.1.1 (Synthesis) Use a knowledge of the purpose of a particular publication to write pertinent transplant-related information for health care professionals and/or the public.
 - IO (Analysis) Identify transplant-related topics that would be suitable for a particular audience.*
 - OBJ E4.1.2 (Synthesis) Submit a suitably formatted article on a transplant-related topic for peer-reviewed publication.
 - OBJ E4.1.3 (Evaluation) Provide peer review of a pharmacy or transplant-related article for a publication.

Outcome E5: Function effectively in transplant settings participating in clinical investigations.

- Goal E5.1 Contribute to the operation of a system that prepares and distributes investigational transplant-related medications.
- OBJ E5.1.1 (Evaluation) Evaluate relevant aspects of a transplant-related investigational drug study.
 - IO Explain factors to consider (e.g., impact on pharmacy budget, personnel) when determining the feasibility of a proposed transplant-related investigational drug study.*
 - IO Explain drug procurement, storage, preparation, administration, and accountability considerations for investigational or other research-related drugs.*

- IO Explain the phases of the investigational drug development process and the objectives for each phase as it applies to gaining FDA approval of transplant-related drugs.*
- IO Explain the steps in the investigational drug protocol approval process.*
- IO Explain the purposes of standard sections of investigational protocols for transplant-related therapy.*
- IO Explain factors to consider when judging the adequacy of the informed consent document.*
- IO Explain the laws and regulations governing informed consent (and, in pediatric patients, assent) and conduct of clinical research.*
- OBJ E5.1.2 (Application) Manage the use of transplant-related investigational drugs according to established protocols and the organization's policies and procedures.
- OBJ E5.1.3 (Comprehension) Compare and contrast record-keeping requirements of various agencies regulating transplant-related clinical research studies.
 - IO Explain the process for reporting adverse reactions to drugs used in a transplant-related investigational protocol.*

Outcome E6: Demonstrate skills required to function in an academic setting.

- Goal E6.1 Understand faculty roles and responsibilities.
 - OBJ E6.1.1 (Comprehension) Explain variations in the expectations of different colleges/schools of pharmacy for teaching, practice, research, and service.
 - IO Discuss how the different missions of public versus private colleges/schools of pharmacy can impact the role of faculty members.*
 - IO Discuss maintaining a balance between teaching, practice, research and service.*
 - IO Discuss the relationships between scholarly activity and teaching, practice, research and service.*
 - OBJ E6.1.2 (Analysis) Explain the role and influence of faculty in the academic environment.
 - IO Explain the responsibilities of faculty in governance structure (e.g. the faculty senate, committee service).*
 - IO Describe the responsibilities of faculty (e.g. curriculum development and committee service) related to teaching, practice, research, and service roles.*
 - OBJ E6.1.3 (Comprehension) Describe the academic environment.
 - IO Describe how the decisions by university and college administration impact the faculty.*
 - IO Discuss outside forces (e.g. change in the profession, funding source, accreditation requirements) that impact administrator and faculty roles.*
 - OBJ E6.1.4 (Comprehension) Describe the types and ranks of faculty appointments.
 - IO Explain the various types of appointments (e.g. non-tenure, tenure-track, and tenured faculty).*
 - IO Differentiate among the various ranks of faculty (e.g. instructor, assistant professor, associate professor, full professor).*
 - IO Discuss the role and implications of part-time and adjunct faculty as schools continue to expand and faculty shortages occur.*

- OBJ E6.1.5 (Comprehension) Discuss the promotion and tenure process for each type of appointment.
IO Identify the types of activities that are considered in the promotion process.
IO Identify the types of activities that are considered for tenure.
- OBJ E6.1.6 (Application) Identify resources available to help develop academic skills.
IO Explain the role of academic-related professional organizations (e.g. AACP) in faculty professional development.
IO Identify resources to help develop teaching skills and a teaching philosophy.
- OBJ E6.1.7 (Comprehension) Explain the characteristics of a typical affiliation agreement between a college of pharmacy and a practice site (e.g., health system, hospital, clinic, retail pharmacy).
IO Explain how the political environments of either a college or a practice site may affect the other.
- Goal E6.2 Exercise teaching skills essential to pharmacy faculty.
- OBJ E6.2.1 (Synthesis) Develop an instructional design for a class session, module, or course.
IO Construct a student-centered syllabus.
IO Construct educational objectives for a class session, module, or course that is appropriate to the audience.
IO Identify appropriate instructional strategies for the class session, module, or course to achieve the objectives.
IO Consider assessment tools that measure student achievement of the educational objectives.
- OBJ E6.2.2 (Synthesis) Prepare and deliver didactic instruction on a topic relevant to the specialized area of pharmacy residency training.
IO Identify educational technology that could be used for a class session, module, or course (e.g., streaming media, course management software, audience response systems).
IO Create instructional materials appropriate for the topic and audience.
IO Identify strategies to deal with difficult learners.
IO Given feedback from teaching evaluations (e.g. student and or peer), devise a plan to incorporate improvements in future instruction.
- OBJ E6.2.3 (Application) Develop and deliver cases for workshops and exercises for laboratory experiences.
IO Identify the appropriate level of case-based teachings for small group instruction.
IO Identify appropriate exercises for laboratory experiences.
IO Provide appropriate and timely feedback to improve performance.
- OBJ E6.2.4 (Application) Serve as a preceptor or co-preceptor utilizing the four roles employed in practice-based teaching (direct instruction, modeling, coaching and facilitation).
IO Assess the learner's skill level to determine the appropriate preceptor strategy for providing practice-based teaching.

- IO* Given performance-based criteria, identify ways to provide constructive feedback to learners.
 - IO* Develop strategies to promote professional behavior.
 - IO* Identify strategies to deal with difficult learners in the practice setting.
 - IO* Given a diverse learner population, identify strategies to interact with all groups with equity and respect.
- OBJ E6.2.5 (Analysis) Develop a teaching experience for a practice setting (e.g., introductory or advanced pharmacy experience).
- IO* Create educational goals and objectives to be achieved.
 - IO* Develop activities that will allow achievement of identified educational goals and objectives.
 - IO* Identify how and when feedback should be provided.
 - IO* Identify other preceptors for the experience, if appropriate.
 - IO* Determine training that might be needed for the preceptors to deliver student education.
 - IO* Identify potential challenges of precepting and providing patient care services simultaneously.
- OBJ E6.2.6 (Synthesis) Design an assessment strategy that appropriately measures the specified educational objectives for the class session, module, course, or rotation.
- IO* Identify appropriate techniques for assessing learning outcomes in various educational settings [e.g., written examinations, oral examinations, practical examinations, Objective Structured Clinical Examination (OSCE)].
 - IO* Develop examination questions to assess the knowledge, skills, attitudes and behaviors that are appropriate to the learner's level and topic.
 - IO* Discuss the various methods for administering examination questions (e.g., computerized testing, paper testing).
- OBJ E6.2.7 (Evaluation) Create a teaching portfolio.
- IO* Define the concept of a teaching portfolio and describe its primary purpose
 - IO* Outline the steps in building a teaching portfolio.
 - IO* Develop a personal teaching philosophy to guide one's teaching efforts and facilitate student learning.
- OBJ E6.2.8 (Evaluation) Compare and contrast methods to prevent and respond to academic and profession dishonesty.
- IO* Evaluate physical and attitudinal methods to prevent academic dishonesty.
 - IO* Discuss methods of responding to incidents of academic dishonesty.
 - IO* Discuss the role of academic honor committees in cases of academic dishonesty.
 - IO* Identify examples and methods to address unprofessional behavior in learners.
- OBJ E6.2.9 (Comprehension) Explain the relevance of copyright laws to developing teaching materials.
- IO* Discuss copyright regulations as related to reproducing materials for teaching purposes.

IO Discuss copyright regulations as related to linking and citing on-line materials.

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The effective date for implementation of these educational outcomes, goals and objectives is July 1, 2008.

Appendix

PGY2 Pharmacy Residencies in Solid Organ Transplant

PGY2 pharmacy residencies in solid organ transplant may vary according to the types of transplantation performed by the organization's transplant program. However, learning experiences in direct patient care occurring in both acute and ambulatory practice settings are expected. A pharmacy residency in solid organ transplant must provide direct clinical experience and build core didactic knowledge in a minimum of two of the following types of transplantation:

- Heart
- Intestine
- Kidney
- Liver
- Lung
- Pancreas/islet

Other learning experiences may be tailored to the specific needs and interests of the resident. Solid organ transplant pharmacy residency programs that are able to offer experience with any of the following should consider their inclusion in core or elective learning experiences:

- Advanced critical care
- Bone marrow/stem cell transplant
- Clinical research
- Corneal transplant
- Pediatric transplant
- Transplant infectious disease

The following is an extensive listing of diagnoses leading to transplant, as categorized by the United Network for Organ Sharing (UNOS). While this is provided as a resource, it is left to the discretion of the program director to select the particular disease states and aspects of management most relevant to their program goals. In this sense, it is anticipated that those disease states comprising a larger fraction of transplant indications and those with implications for recipient preparation or post-transplant management (i.e., due to recurrence or other complications requiring management) would receive greater emphasis.

I. Diseases or conditions that frequently underlie and indication for:

A. Kidney transplantation

1. Congenital, rare familial, and metabolic disorders
2. Diabetes
3. Glomerular disease
4. Hypertensive nephrosclerosis
5. Neoplasms
6. Polycystic kidneys
7. Renovascular and other vascular diseases
8. Tubular and interstitial diseases
9. Retransplant/graft failure

10. Other renal diseases
 - B. Pancreas and/or islet cell
 1. Diabetes mellitus, type 1 or 2
 2. Diabetes secondary to chronic pancreatitis or cystic fibrosis without pancreatectomy
 3. Pancreatectomy prior to pancreas transplant
 4. Pancreatic, bile duct or other cancer
 5. Graft failure/retransplantation
 - C. Liver transplantation
 1. Acute hepatic necrosis
 2. Biliary atresia
 3. Cholestatic liver disease/cirrhosis
 4. Malignant neoplasms
 5. Metabolic diseases
 6. Non-cholestatic cirrhosis
 7. Other hepatic diseases
 - D. Intestine transplantation
 1. Functional bowel problem
 2. Short gut syndrome
 3. Graft failure/retransplant
 4. Other intestinal disorders
 - E. Heart transplantation
 1. Cardiomyopathy
 2. Congenital heart disease
 3. Coronary artery disease
 4. Valvular heart disease
 5. Retransplant/graft failure
 6. Other cardiac diseases
 - F. Lung transplantation
 1. Congenital disease
 2. Emphysema/COPD
 3. Cystic fibrosis
 4. Idiopathic pulmonary fibrosis
 5. Primary pulmonary hypertension
 6. Alpha-1-antitrypsin deficiency
 7. Retransplant/graft failure
 8. Other pulmonary diseases
- II. Diseases or conditions that frequently occur or reoccur after transplantation:
- A. Post-transplant infection considerations
 1. Central venous catheter infections and treatment options
 2. Dental procedure prophylaxis
 3. HBV prophylaxis and treatment
 4. HCV prophylaxis and treatment
 5. Herpes simplex and zoster
 6. Immunization recommendations
 - a) Pre-transplant

- b) Post-transplant
- 7. Infection prophylaxis monitoring and treatment
 - a) CMV and EBV
 - b) Anti-fungal
 - c) PCP
- 8. Infectious exposure management
 - a) Measles
 - b) Varicella (chicken pox)
- 9. Parvovirus
- 10. Polyoma virus nephropathy (screening and treatment)
- 11. Surgical infectious prophylaxis
- 12. Sepsis
- 13. Timing of post-transplant infections (0-30 days, 30-180 days, >180 days)
- 14. Tuberculosis
- 15. Urinary tract infections/pyelonephritis
- B. Post-transplant malignancy considerations
 - 1. Kaposi's sarcoma
 - 2. Lymphoma
 - 3. Post-transplant lymphoproliferative disease (PTLD)
 - 4. Risk of new malignancy or recurrent malignancy
 - 5. Skin cancer
- C. Other organ-specific considerations
 - 1. Cardiovascular
 - a) Cardiac allograft vasculopathy (CAV)
 - b) Cardiovascular risk management
 - c) Congestive heart failure (CHF)
 - d) Coronary artery disease (CAD)
 - e) Hemodynamic conditions
 - f) Hyperlipidemia
 - g) Hypertension
 - h) Orthostatic hypotension
 - 2. Endocrine
 - a) New onset diabetes mellitus after transplantation (NODAT)
 - b) Metabolic diseases (metabolic syndrome)
 - c) Hyperparathyroidism
 - d) Osteoporosis/bone disease
 - e) Gout
 - f) Pancreatitis
 - 3. Erectile dysfunction
 - 4. Gastrointestinal
 - a) Malnutrition/anorexia
 - b) Nausea/vomiting/diarrhea

5. Hematologic
 - a) Bone marrow suppression (leukopenia, anemia, thrombocytopenia)
 - b) Post transplant erythrocytosis (PTE)
 6. Hepatic
 - a) Biliary complications and management
 - b) Hepatotoxicity
 - c) Vanishing bile duct syndrome
 7. Neurological
 - a) CNI neurotoxicity
 - b) Depression
 - c) Headache
 - d) Neurogenic bladder
 8. Pulmonary
 - a) Bronchiolitis obliterans organizing pneumonia (BOOP)
 - b) Interstitial pneumonitis
 - c) Pulmonary edema
 9. Renal
 - a) Acute tubular necrosis
 - b) Chronic allograft nephropathy
 - c) CNI nephrotoxicity
 - d) Dehydration
 - e) Electrolyte imbalances
 - f) HUS/TTP (CNI/rapa-related versus other etiologies)
 - g) Proteinuria
 - h) Renal tubular acidosis
- D. Surgical/technical complications
1. Bleeding
 2. Hydronephrosis
 3. Ischemia/reperfusion Injury
 4. Lymphocele
 5. Obstruction/leak
 6. Pain
 7. Primary graft non-function
 8. Technical graft loss
 9. Thrombosis
- E. Common recurrent diseases
1. Liver
 - a) Autoimmune hepatitis
 - b) Biliary cirrhosis
 - c) Hepatitis viral infection
 - d) Hepatocellular carcinoma (HCC)
 - e) Non-alcoholic steatohepatitis (NASH)

2. Kidney
 - a) Focal segmental glomerulosclerosis (FSGS)
 - b) IgA nephropathy
 - c) Membranous glomerulonephritis (GN)
 - d) Systemic lupus erythematosus (SLE)
 - e) Other autoimmune diseases
3. Pancreas/Islet
 - a) Diabetes mellitus type I
 - b) Diabetes mellitus type II

III. Types of rejection that may occur after transplantation:

- A. Antibody mediated (acute humoral)
- B. Chronic (immunologic and non-immunologic causes)
- C. Hyper-acute
- D. T-cell mediated (acute cellular)

Appendix F-2

ACCP Guidelines for Clinical Research Fellowship Training Programs

GUIDELINES FOR CLINICAL RESEARCH FELLOWSHIP TRAINING PROGRAMS

A research fellowship is a directed, highly individualized postgraduate training program designed to prepare the participant to function as an independent investigator.

Introduction

The purpose of fellowship training programs is to develop competency and expertise in the scientific research process, including hypothesis generation and development, study design, protocol development, grantsmanship, study coordination, data collection, analysis and interpretation, technical skills development, presentation of results, and manuscript preparation and publication. A fellowship candidate is expected to possess appropriate practice skills relevant to the knowledge area of the fellowship. Such skills may be obtained through prior practice experience or completion of a residency program.

Under the close direction, instruction, and supervision of a qualified investigator-preceptor, the fellow receives a highly individualized learning experience, using the fellow's research interests and knowledge needs as a focus for his/her education and training. Fellowships are typically offered through schools/colleges of pharmacy, academic health centers, the pharmaceutical industry, and/or specialized care institutions. A fellowship graduate should be capable of conducting independent and collaborative research and functioning as principal investigator.

Training Program Requirements

1. A minimum of 3,000 hours of the fellowship training time devoted to research-related activities over a minimum period of two years
2. Administrative institutional support for the preceptor's research program and the fellowship training program
3. Availability of advanced educational opportunities (e.g., graduate level coursework) in research-related topics. Such coursework may include, but is not limited to, courses in research design and methods, biostatistics, ethical issues, pharmacokinetics, pharmacodynamics, pharmacoconomics, and others as appropriate to the specific fellow and program.
4. Availability of appropriate facilities (e.g., laboratory and/or clinical) to conduct research
5. Availability of qualified personnel to teach clinical, laboratory, and/or computer technology-based research skills
6. Ready access to scientific literature and computer facilities

Preceptor Qualifications

1. A clinical scientist with an established and ongoing record of independent research accomplishments and expertise in the area of specialization related to the fellowship, which may be exemplified by:
 1. receiver of fellowship training, a graduate degree, and/or equivalent experience;
 2. experience as principal or primary investigator on research grants and/or projects; and
 3. a record of published research papers in peer-reviewed scientific literature on which the preceptor is the primary or senior author.
2. Active collaborative research relationships with other scientists

Fellowship Applicant Criteria

1. Master's or doctoral degree in a health science discipline required
2. Residency or equivalent clinical experience preferred
3. Demonstrated interest in or an aptitude for a career in research required

Fellowship Experiences

Ideally, a research fellow should initiate and complete at least one original research project. However, it is recognized that this may not be possible in every case. Whether through the completion of one project from start to finish or through participation in multiple projects, the fellow should obtain extensive experience in:

1. Development of at least one scientific hypothesis
2. Development of experimental methods to test the developed hypothesis
3. Preparation of a protocol and submission of the protocol to the appropriate institutional review committee
4. Grantsmanship, including identification of appropriate funding sources for specific projects and preparation and submission of a grant for extramural funding consideration
5. Study design and coordination and data collection
6. Statistical analysis of data
7. Data analysis and interpretation
8. Development of clinical, laboratory, and/or computer-based research skills as appropriate to the specific training program
9. Abstract preparation and submission
10. Presentation of research at peer-reviewed scientific meetings
11. Manuscript preparation and submission for publication in peer-reviewed journals
12. Participation in journal clubs, research workshops, and/or seminar series
13. Instruction in biomedical science ethics

Approved by the ACCP Board of Regents, October 22, 2004

Appendix G-1

Solid Organ Transplantation Pharmacy Bibliography

Solid Organ Transplantation Pharmacy Bibliography

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Appendix G-2

Annotated Literature Review

APPENDIX G-2
Annotated Literature Review
Solid Organ Transplantation Pharmacist Specialists

Citation	Summary	Conclusion	Relevance to BPS Petition
<p>Organ Procurement and Transplantation Network. Bylaws. September 2017. Available at: https://optn.transplant.hrsa.gov/media/1201/optn_bylaws.pdf. Accessed February 5, 2018.</p>	<p>The Organ Procurement and Transplantation Network (OPTN) is a unique public-private partnership that links all professionals involved in the U.S. donation and transplantation system. OPTN has personnel requirements for certain personnel, with their bylaws requiring that “each transplant program identify at least one clinical transplant pharmacist on staff who will provide pharmaceutical expertise to transplant recipients. The clinical transplant pharmacist should be a member of the transplant team, providing comprehensive pharmaceutical care to transplant recipients.” The bylaws further state that “the transplant pharmacist will work with patients and their families, and members of the transplant team, including physicians, surgeons, nurses, clinical coordinators, social workers,</p>	<p>Solid organ transplantation (SOT) pharmacist specialists are a vital member of the transplant team.</p>	<p>OPTN’s Bylaws require a transplant pharmacist to be on staff for transplant programs and details the job functions of the transplant pharmacist, providing evidence for Criterion A.</p>

	<p>financial coordinators and administrative personnel. The transplant pharmacist should be a licensed pharmacist with experience in transplant pharmacotherapy.”</p>		
<p>Carthon CE, Hall RC, Maxwell PR, Crowther BR. Impact of a pharmacist-led vaccine recommendation program for pediatric kidney transplant candidates. <i>Pediatr Transplant</i>. 2017 Jul 4. [Epub ahead of print].</p>	<p>This retrospective study of 47 pediatric patients evaluated the impact of transplant pharmacist interventions on the completion rate of vaccination schedules at the time of kidney transplant.</p>	<p>The median percentage of up-to-date vaccinations at time of transplant was significantly higher in intervention group (91%) vs. control group (80%). The median change in up-to-date vaccinations from time of evaluation to time of transplant was also significantly higher in the intervention group (7.5%) compared to the control group (0%). With pharmacist intervention, significantly more patients were up-to-date with vaccination schedules at the time of transplant.</p>	<p>These results suggest that a transplant pharmacist may serve as a valuable resource to increase vaccination schedule compliance between time of evaluation and transplantation and provides evidence to support Criterion A.</p>
<p>Cajita MI, Baumgartner E, Berben L, Denhaerynck K, Helmy R, et al; BRIGHT Study Team. Heart transplant centers with multidisciplinary team show a higher level of chronic illness management - Findings from the International BRIGHT Study. <i>Heart Lung</i>. 2017 Jun 14. pii: S0147-9563(17)30108-5. doi:</p>	<p>This article describes a secondary analysis of the BRIGHT study, a cross-sectional study in 11 countries assessing multidisciplinary in 36 heart transplant centers. A multidisciplinary team was defined as having a team that was composed of physician(s), nurse(s), and another healthcare professional (either a social</p>	<p>While the composition of the follow-up teams in heart transplant centers varied, the majority of centers met the ISHLT recommendation of having a multidisciplinary team, and this was associated with higher levels of chronic illness management.</p>	<p>This article discusses the importance of deploying a multidisciplinary team, including pharmacists, when caring for patients following heart transplant. The data provides evidence to support Criterion A.</p>

<p>10.1016/j.hrtIng.2017.05.006. [Epub ahead of print].</p>	<p>worker, psychiatrist, psychologist, pharmacist, dietician, physical therapist, or occupational therapist).</p>		
<p>Maldonado AQ, Bowman LJ, Szempruch KR. Expanding transplant pharmacist presence in pretransplantation ambulatory care. <i>Am J Health Syst Pharm.</i> 2017;74(2):22-5.</p>	<p>This article supports the need for transplant pharmacists in the ambulatory care setting to provide pre-transplantation care for patients.</p>	<p>As the role of the multidisciplinary team in transplantation evolves, continued opportunity for pharmacist-provided patient education and support at all phases should be evaluated. Implementing universal prospective pharmacist involvement before transplantation allowed greater insight into each transplant candidate's history and the pharmacologic and nonpharmacologic risks that may need to be addressed before, during, and after transplantation.</p>	<p>This article provides case study evidence supporting the need for transplant pharmacist expertise in the pre-transplantation phase. This article provides support for Criterion A.</p>
<p>Sin JH, Li H, Jandovitz N, King M, Tsapepas DS. Dynamic interplay of pharmacy learners during a solid organ transplantation learning experience. <i>J Pharm Pract.</i> 2017 Jan 1:897190017715392. doi: 10.1177/0897190017715392. [Epub ahead of print].</p>	<p>By utilizing the dynamic interplay and collaboration between pharmacy learners through direct and non-direct patient care activities, experiential and educational opportunities may be improved and enhanced for each learner. A tiered learning approach engages individuals in areas such as direct patient care,</p>	<p>An experience during a solid organ transplantation learning experience, using a layered learning practice model that included a clinical pharmacy specialist, a postgraduate year 2 specialty pharmacy resident, a postgraduate year 1 pharmacy resident, and a pharmacy student, is described.</p>	<p>This article describes the development of a layered learning practice model and provides support for Criteria A and F.</p>

	patient education, presentations, research projects, career development, and the feedback process.		
Covert KL, Mardis CR, Fleming JN, et al. Development of a predictive model for drug-related problems in kidney transplant recipients. <i>Pharmacotherapy</i> . 2017 Feb;37(2):159-69.	This prospective, observational study of 237 adults developed a model to predict which patients are at highest risk of drug-related problems (DRPs) to streamline pharmacists' workflow in a chronic kidney transplant clinic.	This study demonstrated that a straightforward, 5-minute survey completed by renal transplant recipients prior to their clinic visit may be capable of effectively determining those at risk of having six or more DRPs, potentially allowing use as a screening tool for transplant pharmacists' workflow prioritization.	This article provides a screening tool for transplant pharmacists to determine patients at highest risk for DRPs. This article provides support for Criterion A.
Griffin SP, Nelson JE. Impact of a clinical solid organ transplant pharmacist on tacrolimus nephrotoxicity, therapeutic drug monitoring, and institutional revenue generation in adult kidney transplant recipients. <i>Prog Transplant</i> . 2016 Dec;26(4):314-21.	This retrospective review evaluates the impact of a clinical SOT pharmacist on nephrotoxicity, therapeutic drug monitoring, and revenue generation in adult kidney patients on tacrolimus.	There was no significant difference in the incidence of acute nephrotoxicity in adult kidney patients on tacrolimus after the inclusion of a full-time clinical SOT pharmacist on the abdominal transplant team. However, there was a significant increase in the rate of appropriately drawn tacrolimus troughs and prescription capture rates.	This article provides support for Criterion A and highlights potential benefits of engaging SOT pharmacists in the care of kidney transplant patients.
Doyle IC, Maldonado AQ, Heldenbrand S, Tichy EM, Trofe-Clark J. Nonadherence to therapy after adult solid organ	The purposes of this paper are to provide a comprehensive literature review that identifies factors associated with medical	Medication nonadherence and its contributing factors evolve, necessitating initial, ongoing, and consistent assessment by	This article outlines the evidence of the critical importance of nonadherence for patients following adult

<p>transplantation: A focus on risks and mitigation strategies. <i>Am J Health Syst Pharm.</i> 2016;73(12):909-20.</p>	<p>and immunosuppressant nonadherence in the adult solid organ transplantation population and to describe associative interventions and resultant outcomes.</p>	<p>the health care team. Evaluation of individual risk factors for nonadherence may aid in the formulation of mitigation strategies to improve outcomes in adult solid organ transplant recipients.</p>	<p>solid organ transplantation and provides support for Criterion A.</p>
<p>Byrns JS, Pilch NW, Taber DJ. Impact of Pharmacist Involvement in Early Identification and Enrollment in Patient Assistance Programs on CMV Outcomes in Transplantation. <i>J Pharm Pract.</i> 2016;29(2):97-102.</p>	<p>The purpose of this study was to determine whether the utilization of patient assistance programs (PAPs) helps to prevent cytomegalovirus (CMV) infection when compared to those do not receive valganciclovir prophylaxis in lieu of CMV preemptive monitoring. This retrospective analysis of patients at risk of CMV reactivation who received kidney and/or pancreas transplants, determined whether early identification and enrollment in PAP can prevent CMV-related events. The incidence of CMV viremia was lower in the PAP group (12.8% vs 36.2%, respectively). Cost benefit analysis found that hiring a full-time pharmacy employee for enrolling patients in PAPs was cost beneficial for the institution/health care system.</p>	<p>Early identification and enrollment of patients in patient assistance programs reduces the incidence of cytomegalovirus viremia. Pharmacists play a crucial role in this process.</p>	<p>This article outlines the role of transplant pharmacists in the early identification and enrollment of patients into patient assistance programs and provides support for Criterion A.</p>

<p>Potter LM, Tichy EM, Horwedel TA, et al. Impact of the pharmacy practice model initiative on clinical pharmacy specialist practice: an alternative viewpoint. <i>Pharmacotherapy</i>. 2016 Nov;36(11):e195-7.</p>	<p>This viewpoint clearly and expertly articulates how the role and value of transplant pharmacist specialists may exceed the patient-centered Pharmacy Practice Model Initiative that has been developed. The article also highlights that the transplant regulatory environment demands recognition of specialist roles in transplantation.</p>	<p>The practice of SOT pharmacist specialists calls for a patient-centered approach throughout the life of a patient and often transcends traditional practice setting delineations.</p>	<p>The information contained in this viewpoint provides evidence for the demand for SOT pharmacist specialists and provides support for Criterion A.</p>
<p>Williams A, Low JK, Manias E, Crawford K. The transplant team's support of kidney transplant recipients to take their prescribed medications: a collective responsibility. <i>J Clin Nurs</i>. 2016 Aug;25(15-16):2251-61.</p>	<p>This exploratory qualitative study evaluated results of five focus groups comprised of members of kidney transplant teams to obtain an understanding of how health professionals support the kidney transplant patient to take their medications as prescribed long-term.</p>	<p>Analysis revealed that adherence was a collective responsibility involving the whole of the transplant team and the patient via education blitz in hospital, identifying and managing nonadherence, promotion of self-advocacy, and the partnership between the patient and health professional. Patients were directed how to take their complex medications and be self-empowered, yet the partnership between the patient and health professional limited the patient's voice.</p>	<p>The information described provides support for the pharmacist's role in supporting medication adherence in kidney transplant patients and provides support for Criterion A.</p>
<p>Covert KL, Fleming JN, Staino C, et al. Predicting and preventing readmissions in</p>	<p>The primary outcome of this retrospective, case-controlled study in 384 adult kidney</p>	<p>This study concluded that readmission rates were only independently predicted by</p>	<p>This study provides evidence as to the critical role of SOT pharmacist specialists in</p>

<p>kidney transplant recipients. <i>Clin Transplant</i>. 2016 Jul;30(7):779-86.</p>	<p>transplant patients was to identify and assess patient and process-level risk factors that contribute to 30-day readmission rates in kidney transplant recipients.</p>	<p>pharmacist identification of patient lack of understanding or adherence regarding post-transplant medications and dialysis exposure for more than three years (OR 2.3, 95% CI 1.10–4.71, p = 0.026 and OR 2.1, 95% CI 1.22, 3.70, respectively), both of which were significantly modified by history of diabetes.</p>	<p>predicting patient medication adherence within kidney transplant patients and provides support for Criterion A.</p>
<p>Ah YM, Lee JY, Moon MR, et al. Clinical and economic evaluation of pharmacists' contribution to patient care on a multi-disciplinary liver transplant team. <i>Int J Clin Pharmacol Ther</i>. 2016;54(2):102-9.</p>	<p>This retrospective cost-benefit analysis described and evaluated the clinical and economic implications of pharmacists' interventions as members of the liver transplant team for hospitalized liver recipients.</p>	<p>The study documented 1,880 interventions for 420 liver transplant recipients. The most common drug therapy problem was "need additional drug therapy" (42.6%) followed by "dosage problems" (23.5%). The study showed a clear cost-benefit of the pharmacists' activities with a cost-benefit ratio of 3.8.</p>	<p>The study demonstrated the positive impact of clinical pharmacists on the care of hospitalized liver transplant patients in terms of both clinical and economic outcomes and provides support for Criterion A.</p>
<p>Staino C, Pilch N, Patel S, Trobaugh K, Fleming J, et al. Optimizing finite resources: Pharmacist chart reviews in an outpatient kidney transplant clinic. <i>J Am Pharm Assoc</i>. 2015;55(6):613-20.</p>	<p>This retrospective longitudinal, cross-sectional study of 219 individual kidney transplant patients determined if a pharmacist-executed comprehensive chart review could serve as sufficient substitution for direct participation during outpatient clinic visits in the post-discharge follow-up treatment of kidney</p>	<p>The results of this study suggest that comprehensive chart review by pharmacists prior to patient clinic visits may not be as effective as in-person consultation in communicating recommendations to providers. Providers accepted a greater percentage of recommendations that were delivered directly compared</p>	<p>This article describes the role of the pharmacist in comprehensive chart reviews and provides support for Criteria A and B.</p>

	transplant recipients.	with recommendations presented via a note in the patient folder following chart review (92% vs. 28%, respectively). Directly provided recommendations were also associated with higher severity scores.	
Migliozzi DR, Zullo AR, Collins C, Elsaid KA. Achieving blood pressure control among renal transplant recipients by integrating electronic health technology and clinical pharmacy services. <i>Am J Health Syst Pharm.</i> 2015;72(22):1987-92.	This case study describes the implementation and outcomes of a program combining electronic home blood pressure monitoring (HBPM) and pharmacist-provided medication therapy management (MTM) services in a renal transplantation clinic.	Implementation of electronic HBPM and pharmacist-provided MTM services implemented in a renal transplant clinic was associated with sustained improvements in blood pressure control. Incorporation of a pharmacist in the renal transplant clinic resulted in the detection and resolution of medication-related problems.	This article describes the pharmacist's role and associated outcomes in managing blood pressure among renal transplant recipients and provides evidence for Criterion A.
Taber DJ, Pilch NA, Trofe-Clark J, Kaiser TE. A National Survey Assessing the Current Workforce of Transplant Pharmacists Across Accredited U.S. Solid Organ Transplant Programs. <i>Am J Transplant.</i> 2015 Oct;15(10):2683-90.	There is a median of 1.4 pharmacist full-time equivalents (FTEs) (range 0.1–7.1) for every 100 transplants. The predominant activities performed by pharmacists during the transplant phase include medication review (95%), lab review (92%), allergy review (88%), medication therapy management (92%), bedside rounds (87%), medication	The involvement of dedicated transplant pharmacists within multidisciplinary care has become standard at many centers, although expansion is still needed to ensure core pharmaceutical care components are provided to all transplant recipients across all centers. These results inform on the typical responsibilities of pharmacists practicing within the field of	This national survey provides evidence outlining the day-to-day roles and responsibilities that support Criterion A. Specific data on the number of transplant pharmacists and the time they spend allocated to specific tasks provides relevant data for Criterion C. The survey also details the educational background and experience of transplant pharmacists and provides

	<p>education (79%), documentation (71%), and coordinating discharge medications (58%). The results of this national workforce survey demonstrate the majority of transplant pharmacists are routinely providing direct patient care during the initial transplant hospitalization (e.g. transplant phase), which includes medication therapy management coupled with interaction and education of patients/caregivers and providers.</p>	<p>transplantation and illustrate that the level of pharmacist involvement significantly varies across transplant centers and the phases of transplantation.</p>	<p>evidence for Criterion F.</p>
<p>Maldonado AQ, Tichy EM, Rogers CC, et al. Assessing pharmacologic and nonpharmacologic risks in candidates for kidney transplantation. <i>Am J Health Syst Pharm.</i> 2015 May;72(10):781-93.</p>	<p>This feature article discusses pharmacotherapy concerns and other factors with a bearing on patient selection for kidney transplantation. The process of selecting appropriate candidates for kidney transplantation involves multidisciplinary assessment to evaluate a patient’s mental, social, physical, financial, and medical readiness for successful surgery and good post-transplantation outcomes.</p>	<p>Consensus opinions of practitioners in transplantation pharmacy regarding the pharmacologic and nonpharmacologic factors that should be considered in assessing candidates for kidney transplantation are presented.</p>	<p>Transplantation pharmacists can play important roles in the recognition and stratification of pharmacologic and nonpharmacologic risks in prospective kidney transplant recipients and the identification of issues that require a mitigation strategy. This article reviews these issues in detail and provides support for Criterion A.</p>
<p>Trofe-Clark J, Kaiser T, Pilch N, Taber D. Value of solid organ</p>	<p>Advances in organ transplantation have led to</p>	<p>The transplant pharmacist is a consistent member of the</p>	<p>This article provides both a historical overview and a</p>

<p>transplant-trained pharmacists in transplant infectious diseases. <i>Curr Infect Dis Rep</i>. 2015 Apr;17(4):475.</p>	<p>improved graft and patient survival. Transplant pharmacist's education and training uniquely position them to contribute knowledge and skills to the management of these highly complex patients.</p>	<p>transplant team that can add value to the multidisciplinary approach of prevention and treatment of transplant infectious diseases through all phases of transplant care.</p>	<p>current narrative outlining the roles and responsibilities of transplant pharmacists and supports Criterion A. The information also provides support to Criterion F, Education and Training, and Criterion G, Transmission of Knowledge.</p>
<p>United Network for Organ Sharing. Bylaws. February 1, 2015. Available at: https://www.unos.org/wp-content/uploads/unos/UNOS_Bylaws.pdf. Accessed July 27, 2017.</p>	<p>The United Network for Organ Sharing (UNOS) Bylaws state that each transplant program should identify at least one Clinical Transplant Pharmacist on staff who will provide pharmaceutical expertise to transplant recipients. The Clinical Transplant Pharmacist should be a member of the transplant team, providing comprehensive pharmaceutical care to transplant recipients.</p>	<p>The UNOS Bylaws direct transplant pharmacists to work with patients and their families and members of the transplant team, including physicians, surgeons, nurses, clinical coordinators, social workers, financial coordinators and administrative personnel.</p>	<p>The Bylaws of this international organization specifically outlines the expectation for the role of SOT pharmacist specialists and provides support for both Criterion A and Criterion B.</p>
<p>Pinelli NR, Clark LM, Carrington AC, Carrington JL, Malinzak L, Patel A. Pharmacist managed diabetes and cardiovascular risk reduction clinic in kidney transplant recipients: bridging the gap in care transition. <i>Diabetes Res Clin Pract</i>. 2014 Dec;106(3):e64-7.</p>	<p>This feasibility study describes clinical outcomes for patients receiving the care transition intervention delivered through a pharmacist managed diabetes and cardiovascular risk reduction clinic (PMDC) during the first year of service implementation.</p>	<p>This feasibility study showed evidence that embedding an endocrinology trained provider improves the care transition of kidney transplant recipients with diabetes from the inpatient to ambulatory care setting. Readmission rates were reduced at 30- and 90-days but not following completion of the intervention period.</p>	<p>This article provides evidence that a pharmacist-managed diabetes and cardiovascular risk reduction clinic was associated with improved patient outcomes and reduced health care resource utilization and provides support for Criterion A.</p>

<p>Israni A, Dean CE, Salkowski N. Variation in structure and delivery of care between kidney transplant centers in the United States. <i>Transplantation</i>. 2014 Sep 15;98(5):520-8.</p>	<p>Results of a survey of directors of 156 transplant centers demonstrated significant variation between centers in several domains, one domain being that 65% of transplant centers do not have a dedicated transplant pharmacist in outpatient care.</p>	<p>This study showed that there was significant variation on the structure and process of care in kidney transplantation, including frequency of follow-up and coordination of care between kidney transplant centers.</p>	<p>Vast disparities were revealed between transplant programs concerning the availability of a dedicated transplant pharmacist. This article provides support for Criterion A and Criterion B.</p>
<p>Joost R, Dörje F, Schwitulla J, Eckardt KU, Hugo C. Intensified pharmaceutical care is improving immunosuppressive medication adherence in kidney transplant recipients during the first post-transplant year: a quasi-experimental study. <i>Nephrol Dial Transplant</i>. 2014 Aug;29(8):1597-607.</p>	<p>A prospective study with 74 renal transplant recipients using a sequential control group design was performed to investigate the impact of a pharmaceutical intensified care program led by a clinical pharmacist on daily drug adherence during the first year after renal transplantation.</p>	<p>Intensified pharmaceutical care improved patients' medication adherence remarkably, suggesting that the applied additional care program has the potential to improve outcomes after organ transplantation.</p>	<p>This article highlights the role and value of clinical pharmacists in improving medication adherence in kidney transplant patients and provides support for Criterion A.</p>
<p>Tichy EM, Pilch NA, Smith LD, et al. Building a business plan to support a transplantation pharmacy practice model. <i>Am J Health Syst Pharm</i>. 2014;71(9):751-7.</p>	<p>This article describes business planning aspects that can be used by pharmacy clinicians, managers, and leaders to implement new or expanded transplantation pharmacy service opportunities.</p>	<p>Recognition of the role of the transplantation pharmacist by governing bodies such as CMS and UNOS has transitioned the role of the transplantation pharmacist from a novelty to a necessary member of the multidisciplinary transplantation team. Transplantation recipients are among the most pharmacologically complex patients in health care today, and business plans should</p>	<p>This key article reviews the evidence to support the creation of a business plan to support transplantation pharmacy. The information provided lends support to Criteria A and B.</p>

		be created to justify the development of robust pharmacy teams at transplantation centers.	
Hahn L. A solid organ transplant elective course for pharmacy students. <i>Am J Pharm Educ.</i> 2014;78(1):15.	To develop and implement a solid organ transplant elective course for second and third year pharmacy students, and assess its impact on students' knowledge in the management of medications, adverse effects, and complications in organ transplantation patients. Students' solid organ transplantation knowledge was assessed using examinations, quizzes, a group presentation, and class participation. Most students felt that their knowledge increased significantly regarding the course objectives.	Students who completed the elective course significantly improved their confidence and knowledge regarding solid organ transplantation, felt more prepared than their peers who did not complete the course, and became open to exploring careers or residencies in this area.	This key article to pharmacist transplant literature discusses the development of an elective course in solid organ transplant. The information provided lends support to Criteria A, B, and F.
Chisholm-Burns MA, Spivey CA, Graff Zivin J, Lee JK, Sredzinski E, Tolley EA. Improving outcomes of renal transplant recipients with behavioral adherence contracts: a randomized controlled trial. <i>Am J Transplant.</i> 2013 Sep;13(9):2364-73.	This randomized controlled trial assessed the effects of a 1-year behavioral contract intervention on immunosuppressant therapy adherence and health care utilizations and costs among 150 adult renal transplant recipients. All interventions were conducted by a study clinical pharmacist.	The Intervention group renal transplant recipients (n = 76) had higher adherence than control group renal transplant recipients (n = 74) over the study period (p < 0.01). 76.1% of the intervention group compared with 42.7% of the control group was not hospitalized during the 1-year study period (RR = 1.785; 95%	This study demonstrates the value of SOT pharmacist specialists in improving adherence in renal transplant patients and provides support for Criterion A.

		CI: 1.314, 2.425), resulting in cost savings. Evidence supports using behavioral contracts as an effective adherence intervention that may improve health care outcomes and lower costs.	
Maldonado AQ, Weeks DL, Bitterman AN, et al. Changing transplant recipient education and inpatient transplant pharmacy practices: a single-center perspective. <i>Am J Health Syst Pharm</i> . 2013 May 15;70(10):900-4.	This retrospective observational analysis evaluates the pharmacists' contributions to improved inpatient medication practices and educational services for kidney transplant recipients at a community hospital.	The participation of pharmacists on the kidney transplant team enhanced a hospital's medication management, discharge planning, and patient education services for transplant recipients, helping to reduce their average length-of-stay (LOS) (from 7.8 days in 2007 to 3.4 days in 2011, $p < 0.001$), with no adverse effect on all-cause 30-, 90-, and >90-day readmission rates (all $p > 0.09$). The pharmacists also yielded substantial cost savings, with annual cost savings attributable to the reduction in LOS were estimated at \$279,180.	This article provides clinical and economic evidence to support the role of the clinical pharmacist in caring for kidney transplant patients and supports Criterion A.
Maldonado AQ, Bray BS, Woodard LJ, et al. Impact of participation on a solid organ transplant team on student pharmacists' perceptions of interprofessional roles. <i>Am J Pharm Educ</i> . 2013 May	This article examines student pharmacists' perceptions of inter professional roles before and after completing an advanced pharmacy practice experience on solid organ transplantation. Student	Student pharmacist participation in interprofessional clinical APPEs can positively influence their professional development as they prepare to become members of multi-disciplinary	This article discusses the value and importance of interprofessional roles on the solid organ transplant team and provides support for Criteria A and F.

13;77(4):74.	pharmacists' scores on interprofessionalism increased significantly on 17 of 22 items. Positive changes were seen in the interprofessional education core competency areas of roles and responsibilities, interprofessional communication, and teams and teamwork.	teams in the health care workforce.	
Taber DJ, Pilch NA, McGillicuddy JW, et al. Improving the perioperative value of care for vulnerable kidney transplant recipients. <i>J Am Coll Surg.</i> 2013 Apr;216(4):668-76.	This retrospective analysis determined the impact of the development and implementation of a quality improvement initiative aimed at improving perioperative outcomes in all transplant patients, focusing efforts on the highly vulnerable delayed graft function (DGF) patient population.	Health care value can be significantly improved in kidney transplant recipients, particularly in DGF patients, by implementing a multidisciplinary initiative (including PharmDs) aimed at safely and efficiently discharging patients.	This article highlights how a multidisciplinary team that includes pharmacists can improve clinical outcomes in kidney transplant patients and provides support for Criterion A.
Taber DJ, Pilch NA, McGillicuddy JW, et al. Improved patient safety and outcomes with a comprehensive interdisciplinary improvement initiative in kidney transplant recipients. <i>Am J Med Qual.</i> 2013 Mar-Apr;28(2):103-12.	A multidisciplinary quality improvement initiative was developed that targeted eliminating medication use and safety issues in kidney transplant patients. The team developed key initiatives, including improved medication reconciliation, development of a diabetes management service, and improved discharge medication dispensing, delivery,	Follow-up analysis demonstrated reduced medication discrepancies by >2 per patient and obtaining 100% adherence with reconciliation. Pharmacists reviewed discharge medications, reaching 100% by study end, leading to a 40% reduction in medication safety issues. Length of stay remained short, and delayed discharges were	A multidisciplinary quality improvement initiative, including pharmacists, can improve medication safety in kidney transplant patients, which can lead to improved clinical outcomes and provides support for Criterion A.

	education, and scrutiny.	reduced by 14%; 7-day readmission rates decreased by 50%. Acute rejection and infection rates also significantly decreased.	
Musgrave CR, Pilch NA, Taber DJ, et al. Improving transplant patient safety through pharmacist discharge medication reconciliation. <i>Am J Transplant</i> . 2013 Mar;13(3):796-801.	Greater than 50% of medication errors are estimated to occur during transitions of care, and solid-organ transplant recipients are at an increased risk for errors due to significant changes in their medication regimen following transplantation. This prospective, observational study was conducted to evaluate the discharge process for transplant recipients and determine if transplant pharmacist involvement would improve safety.	The results of this study demonstrate that transplant patients are at very high risk for medication errors at the time of discharge and that the formalized involvement of transplant pharmacists in the medication reconciliation process, particularly at the time of discharge, leads to improved medication safety through the significant reduction of medication errors.	This study demonstrates that transplant recipients are at a high risk for medication errors and that transplant pharmacist involvement leads to improved safety through the significant reduction of medication errors, providing evidence for Criterion A.
Staino C, Lewin JJ 3rd, Nesbit TW, Sullivan B, Ensor CR. Survey of transplant-related pharmacy services at large comprehensive transplant centers in the United States. <i>Prog Transplant</i> . 2013 Mar;23(1):23-7.	This article identifies characteristics of transplant-related pharmacy services at comprehensive transplant centers.	Large comprehensive transplant centers use multiple transplant pharmacists to perform patient care in the inpatient and outpatient environments. 71% of centers surveyed plan to expand transplant pharmacist staff by a mean of 1.4 FTEs.	This article speaks to the clinical role of the transplant pharmacist and provides evidence to support the demand for these roles. The information provided lends support for Criterion A and Criterion B.

<p>Bangash HK, Colegio OR. Management of non-melanoma skin cancer in immunocompromised solid organ transplant recipients. <i>Curr Treat Options Oncol.</i> 2012 Sep;13(3):354-76.</p>	<p>The management of non-melanoma skin cancers (NMSCs) in solid organ transplant recipients (OTRs) presents a variety of clinical challenges for physicians. OTRs are at a 65-fold increased risk for developing cutaneous squamous cell carcinomas (SCC), the most common NMSC that develops after transplantation.</p>	<p>Organ transplant recipients should be carefully educated about the benefits of UV protection, sunscreen use, self-skin examinations and regular dermatological evaluations. Patient follow-up can be tailored according to the individual risk factors. Additionally, patients should be started on vitamin D and calcium supplements to prevent any side effects associated with vitamin D deficiency. Close multidisciplinary collaboration is essential for the successful medical care of these patients.</p>	<p>This article describes the roles and responsibilities of transplant pharmacists in managing non-melanoma skin cancer in SOT recipients and provides support for Criterion A.</p>
<p>Harrison JJ, Wang J, Cervenko J, et al. Pilot study of a pharmaceutical care intervention in an outpatient lung transplant clinic. <i>Clin Transplant.</i> 2012 Mar-Apr;26(2):E149-57.</p>	<p>This study assessed drug therapy problems (DTPs), pharmacist recommendations, and patient satisfaction with pharmacist services for 43 lung transplant patients.</p>	<p>The most common DTPs identified by the pharmacist were adverse drug effect (27%) and untreated indication (25%). Overall, 62% of pharmacist recommendations were rated very significant or significant. Pharmacists can make valuable contributions in a lung transplant clinic setting by identifying DTPs and making recommendations with a positive impact on patient outcomes and satisfaction.</p>	<p>This article provides evidence of how engagement of SOT pharmacists improves patient safety and outcomes and provides support for Criterion A.</p>
<p>Taber DJ, Pilch NA, Bratton CF,</p>	<p>This retrospective observational</p>	<p>Patient-induced medication</p>	<p>The high likelihood of</p>

<p>McGillicuddy JW, Chavin KD, Baliga PK. Medication errors and adverse drug events in kidney transplant recipients: incidence, risk factors, and clinical outcomes. <i>Pharmacotherapy</i>. 2012;32(12):1053–60.</p>	<p>study in 476 kidney transplant recipients determined the incidence, risk factors, and clinical outcomes associated with clinically significant medication errors or adverse drug events in kidney transplant recipients. Thirty-seven (8%) of the 476 patients developed a clinically significant medication-related problem (MRP). Patients with MRPs had significantly higher rates of acute rejection (11% vs 30%, p=0.004), cytomegalovirus infection (15% vs 30%, p=0.033), and 30-day readmissions (5% vs 16%, p=0.018). Graft survival was also significantly lower in patients who had MRPs (p<0.001).</p>	<p>errors and associated adverse drug events were common in kidney transplant recipients. General and transplant- specific risk factors were associated with the development of these MRPs, and MRPs were associated with increased risk of rejection and graft loss.</p>	<p>medication related problems in kidney transplant patients supports the need for SOT pharmacist specialists and provides evidence for Criterion A.</p>
<p>Hlubocky JM, Stuckey LJ, Schuman AD, et al. Evaluation of a transplantation specialty pharmacy program. <i>Am J Health-Syst Pharm</i>. 2012;69:340-7.</p>	<p>A study of 290 kidney transplant patients evaluated the value of a transplantation specialty pharmacy (TSP) program, including its impact on patient and health care provider satisfaction, selected clinical outcomes, and the institution's financial margin. Most patients (84%) reported being satisfied with the program, and 98% would recommend it to others. Ninety-six percent of providers believed the pharmacy</p>	<p>A transplantation specialty pharmacy (TSP) program provided a high level of satisfaction to patients and health care providers, may have influenced some clinical outcomes, and served as a source of positive margin for its institution.</p>	<p>This article provides evidence for value of the role of SOT pharmacist specialists to patients and other health care providers and supports Criterion A.</p>

	<p>improved continuity of care, and 91% reported spending less time on pharmacy-related problems after the program's initiation. Medication adherence appeared to be higher in patients enrolled in the TSP program compared with historical controls. Hospital readmissions and length of stay did not significantly differ between groups. The TSP program generated \$7.5 million in revenue during its first fiscal year. Roughly \$5.5 million was spent on incremental operating expenses, resulting in over \$2 million in margin.</p>		
<p>Maldonado AQ, Seiger TC, Urann CL, et al. Billing for outpatient transplant pharmacy services. <i>Am J Health-Syst Pharm.</i> 2012;69:144-7.</p>	<p>The economic impact of outpatient pharmacy services in a kidney transplant program was evaluated. Overall, pharmacist visits accounted for 22% of the outpatient kidney transplant visits in 2010, with pharmacists billing at a higher level of acuity compared with nursing for the same patient encounter 48% of the time. This translated to an approximate increase of \$100 per patient visit. For the one-year study period, pharmacists utilizing facility-fee billing increased outpatient reimbursement by</p>	<p>By utilizing outpatient facility-fee billing for pharmacy services, the transplant program increased reimbursement in the outpatient setting.</p>	<p>This article provides evidence for the improvement of economic outcomes as a result of SOT pharmacist engagement and provides support for Criterion A.</p>

	approximately \$10,000.		
Alloway RR, Dupuis R, Gabardi S, et al. Evolution of the role of the transplant pharmacist on the multidisciplinary transplant team. <i>Am J Transplant</i> . 2011 Aug;11(8):1576-83.	This article describes the training and role of a transplant pharmacist on the patient care team and provides a roadmap to implementation of novel transplant pharmacy services.	Transplant pharmacists are uniquely positioned to aid the transplant team in patient education, patient transition between levels of care and medication therapy management. Broader expansion of transplant pharmacy services into the pediatric and ambulatory care settings has the potential to impact both patient and center specific outcomes.	This key article to pharmacist transplant literature discusses the value and importance of interprofessional roles on the solid organ transplant team and provides support for Criteria A, B, F and G.
Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. <i>J Heart Lung Transpl</i> . 2010;29(8):914-56.	The 2010 International Society for Heart and Lung Transplantation (ISHLT) convened experts in all areas of heart transplantation to develop practice guidelines for the care of heart transplant recipients.	Guidelines state that transplant centers should strive to have specialty-trained pharmacists or physicians with expertise in pharmacology as part of the multidisciplinary team.	These international guidelines reinforce the need for SOT pharmacist specialists in the care of patients with heart and lung transplants and provides support for Criterion A.
Stemer G, Lemmens-Gruber R. Clinical pharmacy services and solid organ transplantation: a literature review. <i>Pharm World Sci</i> . 2010 Feb;32(1):7-18.	This study summarizes the available evidence regarding the role and impact of clinical pharmacy services in the care of solid organ transplantation patients. Interventions performed in these studies consisted of routine clinical pharmacy services with a focus on identifying, resolving and	High quality evidence that supports the benefit of clinical pharmacy services in the care of solid organ transplantation patients is rare. Nevertheless, all of the included studies showed that clinical pharmacy services had a positive impact. Furthermore, all included studies showed that patients	This review article highlights the benefits of SOT pharmacists in the care of transplantation patients and provides support for Criterion A.

	<p>preventing drug related problems; clinical pharmacy services with a focus on therapeutic drug monitoring; and those with a focus on compliance enhancement and educational interventions. Acceptance rates were generally above 95%, and most studies reported that clinical pharmacy services had a positive impact on the care of solid organ transplantation patients. Positive perceptions of patients and health care professionals are also reported.</p>	<p>and physicians appreciated clinical pharmacists. The various outcome measures used in these studies were improved by interactions with clinical pharmacists.</p>	
<p>Klein A, Otto G, Kramer I. Impact of a pharmaceutical care program on liver transplant patients' compliance with immunosuppressive medication: a prospective, randomized, controlled trial using electronic monitoring. <i>Transplantation</i>. 2009;87:839-47.</p>	<p>This prospective, randomized, controlled trial examined the influence of this program on liver transplant patients' compliance with immunosuppressive therapy. Pharmaceutical care of liver transplant patients led to a significant increase in compliance with the immunosuppressive therapy. The mean dosing compliance of the intervention group was 90% ± 6% compared with 81% ± 12% in the control group (P=0.015). Furthermore, patients in the intervention group were more likely to achieve target blood</p>	<p>Patients who received pharmaceutical care with traditional patient care showed significantly better compliance with their immunosuppressive medication than patients who received only traditional patient care. Pharmaceutical care proved to be an effective intervention that should be implemented in posttransplant care.</p>	<p>This randomized controlled trial demonstrates the value of pharmacist engagement in the care of liver transplant patients and provides support for Criterion A.</p>

	levels.		
De Bleser L, Matteson M, Dobbels F, Russell C, De Geest S. Interventions to improve medication-adherence after transplantation: a systematic review. <i>Transplant Int.</i> 2009;22:780-97.	This systematic review of interventions to improve adherence to medical regimens in solid organ transplant recipients and determined that no single intervention proved to be superior at increasing medication-adherence in organ transplantation, but a combination of interventions in a team approach for the chronic disease management of organ transplant patients may be effective in a long-term perspective.	Finding the most effective combination of interventions to enhance adherence is vital. Utilizing a randomized controlled trial design and adhering to the CONSORT guidelines can lead to higher quality studies and possibly more effective intervention studies to enhance medication-adherence.	This review highlights the value of the team approach to managing solid organ transplant patients and provides support for Criterion A.
Eisenhart A, Dupuis RE. Pursuing a career in transplant pharmacy. <i>Am J Health Syst Pharm.</i> 2008 Dec 15;65(24):2331-3.	This viewpoint describes the process for pharmacists pursuing a career in transplant pharmacy, highlights the importance of recognition for pharmacists in these roles, and describes the process for becoming an SOT pharmacist specialist.	Pharmacists have played an important role in the care of transplant patients since at least the mid-1970s, and there are now increased opportunities for transplant pharmacists.	The information and perspectives provided in this viewpoint provide support for Criterion A and Criterion F.
Chisholm-Burns MA, Spivey CA, Garrett C, McGinty H, Mulloy LL. Impact of clinical pharmacy services on renal transplant recipients' adherence and outcomes. <i>Patient Prefer Adherence.</i> 2008	The purpose of this article is to provide a description of a clinical pharmacy services program implemented in a renal transplant clinic to improve medication access and adherence as well as health and	Clinical pharmacy services have a positive impact on renal transplant recipients' medication adherence, health and economic outcomes, and health-related quality of life.	This article reviews the clinical and economic benefits of clinical pharmacist engagement on the renal transplant team and provides support for Criterion A.

Feb 2;2:287-92.	economic outcomes among renal transplant recipients.		
Burckart GJ. Transplant pharmacy: 30 years of improving patient care. <i>Ann Pharmacother.</i> 2007;41(7):1261-3.	This article discusses the historical contribution of transplant pharmacists over the last three decades and outlines future opportunities for SOT pharmacists.	Pharmacy has contributed to both basic research on immunosuppressive agents and applied research on caring for organ transplant patients. Cyclosporine and tacrolimus were uniquely difficult drugs to manage, and pharmacy provided research into pharmacokinetics, drug interactions, metabolites, and therapeutic drug monitoring. More recently, pharmacy has been able to document ways to improve patient adherence, improve blood pressure control, provide economically sound drug therapy, and provide patient education on their medications.	This historical reflection demonstrates the growth of SOT pharmacy and highlights the critical role and expertise required to enhance patient outcomes. This article provides support for Criterion A.
Chisholm MA, Kwong WJ, Spivey CA. Associations of characteristics of renal transplant recipients with clinicians' perceptions of adherence to immunosuppressant therapy. <i>Transplantation.</i> 2007;84:1145-50.	This retrospective analysis evaluated 53,997 patients to determine surveillance criteria for renal transplant recipients at highest risk for immunosuppressant therapy nonadherence.	Renal transplant recipients (RTRs) who were male, nonwhite, or used mycophenolate mofetil or tacrolimus were more likely to be nonadherent than recipients who used cyclosporine, steroids, azathioprine, or had Medicare. Nonadherent RTRs were more likely to experience graft failure.	This article outlines the risks of nonadherence for renal transplant patients, the critical role of the transplant pharmacist, and the importance of targeted interventions to patient population at the highest risks of nonadherence. The information provides support for Criterion A.

<p>Chisholm MA, Spivey CA, Mulloy LL. Effects of a medication assistance program with medication therapy management on the health of renal transplant recipients. <i>Am J Health Syst Pharm.</i> 2007 Jul 15;64(14):1506-12.</p>	<p>This article details the effects of a medication assistance program with medication therapy management (MTM) on the clinical outcomes and health-related quality of life (HQOL) of renal transplant recipients.</p>	<p>A medication assistance program that included MTM services improved medication access, clinical outcomes, and HQOL in renal transplant recipients.</p>	<p>This study underscores the importance of MTM and guided support to ensure access to transplant medications. The role of the SOT pharmacist is discussed and provides evidence for Criterion A.</p>
<p>Department of Health and Human Services. Hospital conditions of participation: requirements for approval and re-approval of transplant centers to perform organ transplants. <i>Fed Regist.</i> 2007;72(61):15198e15280. Available at: https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandCompliance/Downloads/Transplantfinal.pdf. Accessed January 22, 2018.</p>	<p>This final rule establishes Medicare conditions of participation for heart, heart-lung, intestine, kidney, liver, lung, and pancreas transplant centers. This rule sets forth clear expectations for safe, high quality transplant service delivery in Medicare-participating facilities.</p>	<p>This final rule requires transplant centers to employ individuals with expertise in different relevant areas, including pharmacology.</p>	<p>This federal rule outlines the requirements for approval and re-approval of transplant centers to perform organ transplants and requires expertise within pharmacology on the transplant teams. This information provides support for Criterion A.</p>
<p>American Society of Health-System Pharmacists. Required educational outcomes and objectives for postgraduate year two (PGY2) pharmacy residencies in solid organ transplant. August 18, 2007. Available at: https://www.ashp.org/-/media/assets/professional-</p>	<p>These Required Educational Outcomes, Goals, and Objectives for Postgraduate Year Two (PGY2) Pharmacy Residencies in Solid Organ Transplant are designed to transition PGY1 residency graduates from generalist practice to specialized practice focused on the care of solid</p>	<p>Residency graduates are equipped to participate as essential members of interdisciplinary teams caring for transplant patients, assuming responsibility for the medication-related aspects of care.</p>	<p>These requirements for PGY2 pharmacy residencies outline the educational outcomes, goals and objectives for accredited residency programs and provide support for Criterion A and Criterion F.</p>

<p>development/residencies/docs/pgy2-solid-organ-transplant-pharmacy.ashx?la=en&hash=C58DB55C931525BE4252A28E1EE0E9932D31FC8D. Accessed August 10, 2017.</p>	<p>organ transplant recipients and, in some instances, living organ donors.</p>		
<p>Chisholm MA. A renal transplantation advanced pharmacy practice experience. <i>Am J Pharm Educ.</i> 2006;70(1):3.</p>	<p>This article describes the establishment and evaluation of an ambulatory care renal transplantation clinic advanced pharmacy practice experience. Students spent 5 weeks performing pharmaceutical care activities for renal transplant patients, presenting health-related topics, and conducting research.</p>	<p>Students found this APPE enjoyable and believed that it increased their knowledge concerning transplant medicine and patient care. With the recommendation that all transplant programs have clinical pharmacy services, it is imperative to train students to care for transplant patients.</p>	<p>Information in this manuscript can be used as a guide for utilizing the combined resources from schools of pharmacy and transplantation centers to implement a renal transplant ambulatory care APPE and provides support for Criterion F.</p>
<p>Ohler L, Lo A. Transplant pharmacists: key to a successful transplant program. <i>Prog Transplant.</i> 2004 Jun;14(2):80-1.</p>	<p>Every transplant program should include a dedicated clinical pharmacist with specialized knowledge about transplantation to optimize patient outcomes. Although their role in transplantation is often understated, transplant pharmacists fill a tremendous void on a multidisciplinary transplant team.</p>	<p>The contribution of the pharmacist enables the transplant team to have a more in-depth and comprehensive perspective when designing and implementing drug regimens for each transplant recipient.</p>	<p>This editorial reviews key factors that support success of a transplant pharmacist and highlights the role of the pharmacist. This editorial provides support for Criterion A.</p>
<p>Chisholm MA, Mulloy LL, Jagadeesan M, DiPiro JT. Impact of clinical pharmacy services on renal transplant</p>	<p>This randomized, controlled trial evaluates the impact of clinical pharmacy services on renal transplant patients' compliance</p>	<p>Patients who received clinical pharmacy services with traditional patient care services had better compliance with</p>	<p>This study demonstrates the value of clinical pharmacist involvement in the care of post-transplant patients and</p>

patients' compliance with immunosuppressive medications. <i>Clin Transplant</i> . 2001 Oct;15(5):330-6.	with immunosuppressive agents.	immunosuppressants than patients who only received traditional patient care services. Results of this study suggest a multidisciplinary team that includes a clinical pharmacist as part of the care for post-transplant patients is beneficial for enhancing medication compliance.	provides support for Criterion A.
Chisholm MA, Vollenweider LJ, Mulloy LL, Jagadeesan M, Wade WE, DiPiro JT. Direct patient care services provided by a pharmacist on a multidisciplinary renal transplant team. <i>Am J Health Syst Pharm</i> . 2000 Nov 1;57(21):1994-6.	This study (1) documented the number and types of recommendations made by a pharmacist to the multidisciplinary renal transplant team, (2) determined the rate of acceptance of the recommendations, and (3) determined the potential impact of the recommendations on patient care.	A pharmacist's services in a renal transplant clinic were well received by the team and had a positive potential impact on patient care.	This article highlights the positive role of the pharmacist on a renal transplant team and provides evidence for Criterion A.
Chisholm MA, Vollenweider LJ, Mulloy LL, Wynn JJ, Wade WE, DiPiro JT. Cost-benefit analysis of a clinical pharmacist-managed medication assistance program in a renal transplant clinic. <i>Clin Transplant</i> . 2000 Aug;14(4 Pt 1):304-7.	This study determined the cost savings resulting from a clinical pharmacist-managed patient medication assistance program that involved the renal transplant clinical pharmacist assisting patients to procure immunosuppressants from pharmaceutical manufacturers.	A clinical pharmacist-managed medication assistance program in a renal transplant clinic produced substantial cost savings over this 1-year study period. For each dollar spent in pharmacist's time, a minimum of \$4 was returned to the institution.	This study supports the economic value of clinical pharmacist care to transplant patients and provides support for Criterion A.
Ciminelli AM, Dupuis R, Williams D, et al. Patient	Recipients of solid organ transplants face many	A posttransplant teaching program has been widely	This letter supports the role of the transplant pharmacist

<p>education role of a pharmacist on a transplant service. <i>Am J Health Syst Pharm.</i> 2000 Apr 15;57(8):767-8.</p>	<p>challenges, including daily self-care needs and complex medication regimens that must be continued for life. The role of drug therapy is not limited to immunosuppression; transplant recipients may have infections, hypertension, diabetes, osteoporosis, hyperlipidemia, and many other conditions that require additional drug therapy. The complexity, duration, and adverse effects of these regimens can contribute to noncompliance— the rate of which ranges from 4.7% to 18% in this patient population. Ensuring appropriate patient education to help address these issues is the focus of this letter.</p>	<p>accepted by staff and patients. The program allows for appropriate patient education to be completed despite the shortened time of hospitalization. Along with building patient knowledge and confidence, the program allows the pharmacist to participate in the development of rational medication regimens and to monitor for effectiveness, adverse effects, drug interactions, and compliance.</p>	<p>in patient education and provides support for Criterion A.</p>
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Appendix G-3

ACPE PLAN Programming Live Forum Knowledge Activity

Title	UAN	Hrs (CEUs)	City	Activity Type	Provider Description
2015 Mississippi Transplant Symposium	0032-9999-15-051-L01-P	13.5	Jackson	Knowledge	0032 - University of Mississippi School of Pharmacy
2016 Pediatric Transplant Symposium at Texas Children's Hospital	0514-9999-16-012-L01-P	6.5	Houston	Knowledge	0514 - Texas Children's Hospital Pharmacy
2017 Mississippi Transplant Symposium	0032-9999-17-015-L01-P	12	Jackson	Knowledge	0032 - University of Mississippi School of Pharmacy
2nd Annual Digestive Diseases: New Advances - Clinical Case Conundrums Day 2	0374-9999-15-012-L01-P	0.75	Philadelphia	Knowledge	0374 - Rutgers Biomedical and Health Sciences
2nd Annual Digestive Diseases: New Advances - Hepatology Session	0374-9999-15-010-L01-P	4	Philadelphia	Knowledge	0374 - Rutgers Biomedical and Health Sciences
3rd Annual Digestive Diseases: New Advances - Clinical Case Conundrums	0374-9999-16-005-L01-P	0.75	Philadelphia	Knowledge	0374 - Rutgers Biomedical and Health Sciences
3rd Annual Digestive Diseases: New Advances - Hepatology Session	0374-9999-16-003-L01-P	4	Philadelphia	Knowledge	0374 - Rutgers Biomedical and Health Sciences
A Balancing Act: Immunosuppression in Transplant Medicine	0376-0000-16-019-L01-P	1	Boston	Knowledge	0376 - CME Outfitters, LLC
Advanced Immunology Updates for Basic and Clinical Scientists	0453-9999-15-034-L04-P	3.5	Philadelphia	Knowledge	0453 - Amedco, LLC
ALIGNING FINANCIAL INCENTIVES IN NEW SYSTEMS OF ALLOCATION, PAIRED-EXCHANGE, AND EXPANDED DONATION	0530-9999-15-202-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Allied Health Symposium 1: Identifying Opportunities to Incorporate Quality Improvement and Research Into Your Day	0453-9999-16-125-L04-P	2.75	Boston	Knowledge	0453 - Amedco, LLC
Allied Health Symposium 2	0453-9999-16-173-L04-P	2.75	Boston	Knowledge	0453 - Amedco, LLC
Assessing the Need for Antifungal Prophylaxis in Solid Organ Transplant Recipients with Cytomegalovirus	0112-9999-17-327-L01-P	1	Ann Arbor	Knowledge	0112 - Michigan Pharmacists Association
Cardiopulmonary Stress Testing: Beyond Transplant Evaluation	0453-9999-17-067-L04-P	0.75	Lake Geneva	Knowledge	0453 - Amedco, LLC
CASE STUDIES: REAL LIFE DONOR HEART OFFERS	0530-9999-15-208-L04-P	1.25	Phoenix	Knowledge	0530 - Global Education Group

Clinical Pearls for the Care of the Transplant Recipient for the Non-Transplant Pharmacist	0032-9999-15-026-L01-P	1	Biloxi	Knowledge	0032 - University of Mississippi School of Pharmacy
Controversies - Reenacting the Civil War - Geographic Disparities in Transplantation	0453-9999-16-159-L04-P	0.75	Boston	Knowledge	0453 - Amedco, LLC
Controversies in Transplantation - Clinical: Using the Hepatitis C Infected Donor Organ in the Era of Direct Acting Antivirals: Access for All or Only for Some?	0453-9999-17-117-L01-P	0.75	Chicago	Knowledge	0453 - Amedco, LLC
Current and Future Strategies in Kidney Transplant Immunosuppression	0228-0000-15-115-L01-P	1	Amelia Island	Knowledge	0228 - Georgia Society of Health-System Pharmacists, Inc.
Current Challenges in HPB and Liver Transplant Surgery	0453-9999-15-032-L04-P	3.75	Philadelphia	Knowledge	0453 - Amedco, LLC
DISCUSSION ON THE NEW UNOS HEART ALLOCATION PROPOSAL	0530-9999-15-206-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Donor Heart Selection	0530-9999-15-197-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Don't Go Rejecting My Heart: Management Considerations in Heart Transplantation	0256-0000-14-731-L01-P	1.25	Chicago	Knowledge	0256 - American Heart Association
Drug interactions with Transplant Medications	0163-9999-17-046-L01-P	1	Weston	Knowledge	0163 - Florida Society of Health System Pharmacists, Inc.
Engineering Organ Repair and Regeneration	0530-9999-15-008-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Exciting Updates in Transplant ID: Case-based Learning	0453-9999-15-033-L04-P	4.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Featured Allied Health Symposia III: Beyond the "BENEFIT:" How Do You Use Belatacept?	0453-9999-17-103-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Featured Allied Health Symposia III: Breaking News in Transplant Pharmacology: Reviewing the Year's Top Publications Involving Pharmacotherapy	0453-9999-17-105-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Featured Allied Health Symposia III: What's Your Protocol? Show Me the Data!	0453-9999-17-104-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Featured Allied Health Symposium I - Case-Based Approach to the Multidisciplinary Management of Complex Chronic Disease States Post-Transplantation: Management of Metabolic Complications Post-Transplant	0453-9999-17-150-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC

Featured Allied Health Symposium II: Balancing Quality & Risk: MPSC: Friend Or Foe? Current Status And The Future Of Transplant Program Oversight	0453-9999-17-129-L05-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
GETTING THE MESSAGE ACROSS INCREASED INFECTIOUS RISK DONORS	0530-9999-15-205-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
HIV PRN Focus Session -- HIV in Special Populations	0217-0000-16-129-L02-P	1.5	Hollywood, www.accp.com /am	Knowledge	0217 - American College of Clinical Pharmacy
How Are Organs Allocated in Europe/ Eurotransplant	0530-9999-15-201-L04-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
Immune Monitoring in Thoracic Organ Transplantation	0453-9999-15-029-L04-P	4.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Immunology/Transplantation PRN -- Post-transplant Malignancy: Managing our BIG Problem	0217-0000-16-143-L01-P	1.5	Hollywood, www.accp.com /am	Knowledge	0217 - American College of Clinical Pharmacy
Immunology/Transplantation PRN Focus Session—Novel Approaches to Immunomodulation After	0217-0000-15-129-L01-P	1.5	San Francisco, www.accp.com /gc	Knowledge	0217 - American College of Clinical Pharmacy
Immunology/Transplantation PRN Focus Session—The Development of Clinical Pharmacists in Transplantation and the Expansion of Clinical Pharmacy Services Within Immunology and Transplantation	0217-0000-14-123-L04-P	2	Austin, www.accp.com /am	Knowledge	0217 - American College of Clinical Pharmacy
Immunosuppressants: Introducing the New Agents and Reviewing Alternate Administrations Options	0163-0000-15-170-L01-P	1	Orlando	Knowledge	0163 - Florida Society of Health System Pharmacists, Inc.
Improving Outcomes Through Proactive Monitoring of Transplant Patients	0376-0000-16-030-L01-P	1.5	www.cmeoutfitters.com	Knowledge	0376 - CME Outfitters, LLC
Increasing the Donor Heart Pool	0530-9999-15-194-L04-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
Infection, Immunity and the Microbiome	0453-9999-15-037-L04-P	1.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Infections - Fungal	0299-9999-15-025-L01-P	0.5	Austin	Knowledge	0299 - Syntaxx Communications, Inc.
Innovators in Transplantation	0453-9999-16-181-L04-P	1	Boston	Knowledge	0453 - Amedco, LLC
Keep Calm and Transplant On: A Guide to the Basic Management of Solid Organ Transplant Recipients	0108-0000-17-013-L01-P	1	Portsmouth	Knowledge	0108 - Virginia Society of Health-System Pharmacists
Kidney Transplantation	0016-9999-15-117-L01-P	0.5	Minneapolis	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Kidney Transplantation	0845-0000-16-023-L01-P	1	ce.unthsc.edu	Knowledge	0845 - University of North Texas Health Science Center

Kidney Transplantation	0845-0000-16-023-L01-P	1	Fort Worth	Knowledge	0845 - University of North Texas Health Science Center
Kidney Transplantation 2015	0016-9999-15-019-L01-P	7.5	Dallas	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Kidney Transplantation in the Elderly	0453-9999-15-047-L04-P	1.5	Philadelphia	Knowledge	0453 - Amedco, LLC
Kidney Transplantation: Optimizing Access & Outcomes in 2016	0016-9999-16-006-L01-P	1.5	Boston	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Literature Review	0016-9999-15-062-L01-P	1.5	Dallas	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Liver Allocation	0530-9999-15-196-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Liver Allocation: Strengths, Problems and Pitfalls with Current Future Issues	0453-9999-15-048-L04-P	1.5	Philadelphia	Knowledge	0453 - Amedco, LLC
Long-Term Outcomes in Kidney Transplantation	0016-9999-15-028-L01-P	1.5	Dallas	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
LONG-TERM RISKS TO LIVING KIDNEY DONORS	0530-9999-15-204-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Lunch Workshop: Swinging for the Fences	0530-9999-17-079-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Lung Transplantation the Second Time Around - Considerations in Re-do Lung Transplantation	0453-9999-15-039-L04-P	1.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Management of the Brain Dead Organ Donor	0294-9999-15-132-L04-P	1	Richmond	Knowledge	0294 - VCU School of Pharmacy, Office of Continuing Education
Measure Twice, Cut Once: Medication Safety in Transplantation	0377-0000-17-001-L05-P	1	New York	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
Mechanisms of Immunoregulation in Response to Liver Allografts	0453-9999-15-038-L04-P	1.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Medical Care of the Kidney Transplant Recipient	0453-9999-15-030-L04-P	4	Philadelphia	Knowledge	0453 - Amedco, LLC
Medication Needs of Transplant Recipients: Protecting the Gift of Life	0837-9999-15-042-L01-P	1	Newton	Knowledge	0837 - University of New England College of Pharmacy
Midday Didactic #1: Allo-induced Autoimmunity: The Perfect and Underappreciated Storm in Transplantation	0453-9999-17-137-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #1: Cardiac Function in Liver Transplantation: Assessing and Mitigating Risk Across the Continuum of Care	0453-9999-17-163-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #1: Donors Should Not Have to Pay to Donate - Towards Financial Neutrality for Living Donors	0453-9999-17-116-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC

Midday Didactic #10: Together Everyone Achieves More: The Multidisciplinary Approach To Generating Revenue, Increasing Transplant Referrals, Improving Outcomes, And Performing Research	0453-9999-17-107-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #2: Chronic Antibody Mediated Rejection? When Should We Intervene and Does It Matter?	0453-9999-17-138-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #2: Transplant Therapeutics Consortium Update	0453-9999-17-115-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #2: Understanding ESRD After Live Kidney Donation	0453-9999-17-164-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #3: Alternatives to Liver Redistricting to Improve Fairness in Liver Allocation	0453-9999-17-114-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #3: Delayed Allograft Function - What is the Impact and What Therapeutics are the Most Promising?	0453-9999-17-165-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #4: Beta-cell Replacement - Choices, Choices, Choices	0453-9999-17-113-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #4: Integration of APOL-1 into Kidney Transplantation: Summary of the AST Expert Workshop	0453-9999-17-166-L05-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #5: Infected Donors: Expanding the Donor Pool & the Risk of Avoiding All Risk	0453-9999-17-112-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #5: Strategies for Extending the Cardiac Donor Pool	0453-9999-17-141-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #5: What's Hot in Deceased Organ Donation - Normothermic Perfusion	0453-9999-17-167-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #6: Liver Transplant for HCC in the Next Decade	0453-9999-17-168-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #6: Strategies for Expanding the Donor Pool in Lung Transplantation	0453-9999-17-142-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #7: Parenthood After Transplantation	0453-9999-17-110-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #8: Bench to Bedside- Mechanisms and Approaches to Reduce Organ Injury	0453-9999-17-109-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #8: CMV in 2017: What's Hot, What's New?	0453-9999-17-144-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC

Midday Didactic #8: HIV Positive Transplantation	0453-9999-17-134-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #9: Bench to Bedside - B cells	0453-9999-17-145-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Didactic #9: Cellular Alchemy- Engineering Functional Cell Types and Whole Organs from Progenitors	0453-9999-17-108-L05-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Interactive #1: Advances of Laparoscopic Technique in Living Donor Hepatectomy	0453-9999-17-135-L04-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Interactive #1: Debates In Mechanical Circulatory Support and Cardiac Transplantation	0453-9999-17-162-L01-P	1.5	Chicago	Knowledge	0453 - Amedco, LLC
Midday Symposium: A Year Following the New Kidney Allocation System (KAS) - What's Working, What's Not!	0453-9999-16-116-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Advances in Treg Biology	0453-9999-16-113-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: AMR in Liver Transplantation	0453-9999-16-117-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Cross-Disciplinary Understanding of the Risk of Frailty in Transplantation	0453-9999-16-165-L05-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Developing New Therapy for Transplant Recipients: What are the Barriers?	0453-9999-16-122-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Donor Derived Infections: New Insights on the Use of Infected Donors	0453-9999-16-119-L05-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: ESRD Attributable to Kidney Donation	0453-9999-16-167-L05-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Far from the Madding Crowd: Best Practices in OPO and Transplant Center Leadership	0453-9999-16-144-L04-P	15	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Frontiers in Inflammation Relevant to Transplantation	0453-9999-16-114-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Increasing Deceased Donor Organs: Overcoming Barriers to Donor Intervention Research	0453-9999-16-168-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Innate and Adaptive Immune Memory	0453-9999-16-162-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Kidney Transplantation - Technical Challenges	0453-9999-16-123-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC

Midday Symposium: Liver Disease in the Non-Liver Transplant Patient	0453-9999-16-170-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Liver Transplantation for Malignancy? State of the Art and Future Directions	0453-9999-16-121-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Novel Solutions to Geographic Disparities in Kidney Transplantation	0453-9999-16-171-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Predictors of Survival after Lung Transplant	0453-9999-16-118-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Rapid Fire State-of-the-Art in Xenotransplantation	0453-9999-16-115-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Subclinical TCMR and ABMR in Kidney Transplantation: Pathogenesis and Management	0453-9999-16-172-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Technical Challenges in Liver Transplantation	0453-9999-16-145-L01-P	15	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Toward Adopting Molecular Diagnostics as standard of care in Transplantation	0453-9999-16-163-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Updates in Thoracic and Combined Thoracic/Abdominal Organ Allocation	0453-9999-16-169-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: Viral Hepatitis Pre-, Peri- and Post-Liver Transplantation	0453-9999-16-141-L01-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: What's New for the Organ Procurement and Transplantation Network and Scientific Registry of Transplant Recipients?	0453-9999-16-120-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Midday Symposium: New Avenues for Developing Biomarkers	0453-9999-16-146-L04-P	1.5	Boston	Knowledge	0453 - Amedco, LLC
Mississippi Transplant Forum	0032-9999-14-053-L01-P	12.25	Jackson	Knowledge	0032 - University of Mississippi School of Pharmacy
MPhA Annual Meeting: Transplant Patient in Primary Care? What does a Pharmacist Need to Know?	0102-0000-14-022-L01-P	0.25	St Paul	Knowledge	0102 - Minnesota Pharmacists Association
Not all in fun & games: Fungal Infections and the Solid Organ Transplant Recipient	0163-9999-17-026-L01-P	1	Gainesville	Knowledge	0163 - Florida Society of Health System Pharmacists, Inc.
Novel Immunosuppression in Solid Organ Transplantation	0377-0000-15-003-L01-P	1	Columbia University Medical Center, NY	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy

Novel Immunosuppression in Solid Organ Transplantation	0377-0000-15-003-L01-P	1	Weill Cornell Medical Center NY	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
Opening Plenary Session	0453-9999-17-009-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Organogenesis and Regenerative Medicine	0530-9999-15-009-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Pearls for Safe Medication Use in Transplant Patients	0120-9999-15-006-L01-P	1	Fort Wayne	Knowledge	0120 - Indiana Pharmacists Alliance
Pediatric Symposium 1: Antibodies and Pediatric Transplantation - What, When, Why, (and How)?	0453-9999-17-149-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Pediatric Symposium 1: Improving long-term Outcomes in Pediatric Transplantation	0453-9999-16-126-L04-P	2.25	Boston	Knowledge	0453 - Amedco, LLC
Pediatric Symposium 2: Antibodies: Good, Bad and Customized	0453-9999-16-174-L04-P	2.5	Boston	Knowledge	0453 - Amedco, LLC
Pediatric Symposium II: Transitions in Care in Pediatric Transplantation	0453-9999-17-101-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Pediatric/Allied Health Symposium: Adherence in Transplantation: Applying Findings from the MALT and BRIGHT Studies	0453-9999-16-149-L04-P	3	Boston	Knowledge	0453 - Amedco, LLC
Pediatric/Allied Health Symposium: Promoting Adherence in the 21st Century	0453-9999-17-130-L01-P	3.25	Chicago	Knowledge	0453 - Amedco, LLC
Pharmacologic Management of Acute agitation and Aggression in Youth	0008-9999-17-130-L01-P	1	Aurora	Knowledge	0008 - University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences
Plenary Session 1	0453-9999-15-044-L04-P	1.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #1: HLA Antibody Diagnostics and Management: Allorecognition and Transplant Immunodiagnostics	0453-9999-17-048-L01-P	4.25	Chicago	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #2: Advanced Immunology Updates for Basic and Clinical Scientists	0453-0000-16-097-L04-P	3.5	Boston	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #2: The State of the Art in Kidney Transplantation - An Update for the Busy Clinician: Expect the Unexpected: Complications	0453-9999-17-049-L01-P	4.25	Chicago	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #3: Basic Immunology and Transplant Immunology for the Clinician	0453-9999-16-098-L01-P	4	Boston	Knowledge	0453 - Amedco, LLC

Pre-Meeting Symposium #3: Exciting Updates in Transplant ID 2017: Case-based learning with Audience Response	0453-9999-17-050-L01-P	4.25	Chicago	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #4: Best Practices in the Peri-Operative Care of the Liver Transplant Patient - Post-Transplant: Optimizing Early Patient Liver Graft Survival	0453-9999-16-099-L05-P	4	Boston	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #4: Preserving Native Renal Function in Liver Transplantation: Case Focused Session: Evaluation and Management of Renal Dysfunction in Patients with Cirrhosis (Case Based) ? Audience Response	0453-9999-17-051-L01-P	4.25	Chicago	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #5: Kidney	0453-9999-16-100-L01-P	5.25	Boston	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium #6: Transplant Program Leadership	0453-9999-16-101-L04-P	4	Boston	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 07: the Future is Here: Emerging Issues in Infectious Disease	0453-9999-16-032-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 12: It's All in the Translation: CMV from Bedside to Bench and Back Again	0453-9999-16-033-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 13: Child's Play: Infectious Risk After Transplant During Every-day Life	0453-9999-16-034-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 14: Genomics: What Do I Have to Know and How Will It Affect My Practice?	0453-9999-16-035-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 17: The Biology of Aging and Lung Transplantation	0453-9999-16-037-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 21: Unraveling "Chronic Rejection" in the Heart	0453-9999-16-038-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 23: A 2016 Focused Update on AMR in Cardiac Transplantation: Immunologic Diagnostics and the Treatment of Refractory AMR	0453-9999-16-039-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 26: Hanging in the Balance: Minimizing Risk and Maximizing Benefit with Donor Derived Infection	0453-9999-16-040-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC
Pre-Meeting Symposium 28: Lifecycle Journey of Hepatitis C Heart Failure Patient in 2016	0453-9999-16-041-L04-P	2	Washington	Knowledge	0453 - Amedco, LLC

Pretransplant Immunological Risk Assessment for Successful Transplantation of Sensitized Patients	0453-9999-15-043-L04-P	1.25	Philadelphia	Knowledge	0453 - Amedco, LLC
Promising New Drugs in Other Fields: How Do You Address Immune Response in Your Area? Can We Use These in Transplant?	0530-9999-15-006-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Rejection got you down? A closer look at novel agents for antibody-mediated rejection.	0008-9999-15-112-L01-P	1	Aurora	Knowledge	0008 - University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences
Removing Disincentives and Exploring Controversies of Incentives	0530-9999-15-195-L04-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Renal Replacement Therapy: Options and Choices	0016-9999-15-114-L01-P	0.5	Minneapolis	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Role of the Transplant Pharmacist in the Ambulatory Clinic	0837-9999-16-087-L01-P	1	Portland	Knowledge	0837 - University of New England College of Pharmacy
Safety and Efficacy of Biologic Use Post Liver Transplantation	0112-9999-17-312-L01-P	1	Ann Arbor	Knowledge	0112 - Michigan Pharmacists Association
Session 1: Time to Refocus from Early to Late Outcomes	0530-9999-17-080-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 10: Donor Specific Antibody: Should We Avoid or Confront?	0530-9999-17-095-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Session 2: Challenges to Therapeutic Innovation in Transplant: Multiple Perspectives	0530-9999-17-081-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Session 3: Option 1: No Transplantable Organ Left Behind	0530-9999-17-082-L01-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
Session 3: Option 2: Antibodies Pre Heart Transplantation	0530-9999-17-083-L01-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
Session 3: Option 3: Antibodies Pre-Lung Transplantation	0530-9999-17-084-L01-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
Session 4: Historical Perspectives on the Failure to Enact the Immunosuppression Bill and why this Goal Remains	0530-9999-17-085-L01-P	1.25	Phoenix	Knowledge	0530 - Global Education Group
Session 5: Option 1: Recipient Candidacy: Do the Right Thing!	0530-9999-17-086-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 5: Option 2: Antibodies Post Heart Transplantation	0530-9999-17-087-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 5: Option 3: The Challenges of Post Lung Transplantation Antibodies	0530-9999-17-088-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 6: Option 1: Transplant Value - How to Survive the Next Decade	0530-9999-17-089-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 6: Option 2: Antibody Case Studies in Heart Transplantation	0530-9999-17-090-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group

Session 6: Option 3: Case Studies In Lung Transplantation: Challenges in Treatment	0530-9999-17-091-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Session 7: Post - Transplant Infections: Jeopardizing Long-Term Success	0530-9999-17-092-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Session 8: Lunch Workshop - Hepatitis C - Death of an Old foe	0530-9999-17-093-L01-P	1.5	Phoenix	Knowledge	0530 - Global Education Group
Session 9: Biomarkers and Personalized Medicine: Why Can't I Order It?	0530-9999-17-094-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
Solid Organ Transplantation in Pediatrics	0377-0000-14-020-L01-P	1	Columbia University Medical Center, NY	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
Solid Organ Transplantation in Pediatrics	0377-0000-14-020-L01-P	1	Weill Cornell Medical Center, NY	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
Solid Organ Transplantation: A Review of Immunosuppression	0008-9999-17-095-L01-P	1	Aurora	Knowledge	0008 - University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences
STRATEGIES TO EXPAND THE LIVER DONOR POOL	0530-9999-15-203-L04-P	2	Phoenix	Knowledge	0530 - Global Education Group
Student Program: The Science, The Art, and The Allure of Transplantation	0453-9999-16-127-L04-P	2.5	Boston	Knowledge	0453 - Amedco, LLC
Sunrise 12: Precision Medicine in Transplantation: Drug Levels and Beyond	0453-9999-16-047-L04-P	1	Washington	Knowledge	0453 - Amedco, LLC
Sunrise 6: The Fly in the Ointment: Nosocomial Infections	0453-9999-16-043-L04-P	1	Washington	Knowledge	0453 - Amedco, LLC
Sunrise 9: Lung Transplant Benefit is More Than just Survival	0453-9999-16-045-L04-P	1	Washington	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #1: Fine-tuning Immunosuppression in Liver Transplantation	0453-9999-17-126-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #2: DCD Liver Transplantation: Current Controversies and Future Directions	0453-9999-17-155-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #3: New Concepts in Immune Monitoring	0453-9999-17-156-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #3: Special Deliveries: Pregnancy and Transplantation	0453-9999-17-124-L05-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #4: Social Media and Organ Donation - The Next Frontier	0453-9999-17-123-L04-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #4: Updates on Women's Health in Solid Organ Transplant	0453-9999-17-157-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Didactic #5: Emerging Infections in the Age of Global Warming - Implications for Transplantation	0453-9999-17-158-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC

Sunrise Didactic #8: Dendritic Cells in Solid Organ Transplant	0453-9999-17-119-L04-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Interactive #1: Expanding the Liver Donor Pool: The Art of Allocation	0453-9999-17-128-L04-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Interactive #2: Clinical Xenotransplantation - Perpetual Myth or Potential Reality?	0453-9999-17-127-L05-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Interactive #2: Simultaneous Liver Kidney Transplantation - Where are we and where are we going?	0453-9999-17-152-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Interactive #2: Transplantation in the Elderly: Is 80 the New 60?	0453-9999-17-089-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Interactive #3: Maintaining Minimal-Volume Solid Organ Pancreas Transplant Programs ? PRO/CON	0453-9999-17-153-L01-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Repairing Organs Ex-Vivo	0453-9999-16-111-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 12 HIV and Transplantation: It Isn't Going Away	0453-9999-17-030-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 15 Extracorporeal Photopheresis: Shedding Light on Rejection	0453-9999-17-036-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 16 Pregnant: Scared? So Are We...Management of Pregnancy in Our Complex Patients	0453-9999-17-037-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 17 Living in a 'Bacterial' World: Microbiome in Thoracic Transplantation	0453-9999-17-038-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 2 Chagasic Cardiomyopathy: Lessons To Be Learned	0453-9999-17-011-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 3 Lifecycle Journey of Thrombosis in Mechanical Circulatory Support Patients	0453-9999-17-012-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 4 Completing the Picture: Patient Reported Outcomes (PROs) as an Essential Source of Information in Evaluating Transplantation Outcomes	0453-9999-17-013-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 5 Upcoming Opportunities and Challenges in Pediatric Lung Transplantation	0453-9999-17-014-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 6 "Those Darn CARVs": Respiratory Viruses in Lung Transplant	0453-9999-17-015-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium 8 Live Long and Prosper: Thriving After Pediatric Transplantation	0453-9999-17-027-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC

Sunrise Symposium 9 Mixed Rejection (MR) of the Cardiac Allograft: The Next Frontier	0453-9999-17-028-L04-P	1	San Diego	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Advancing Transplant Care Using Pharmacogenomics	0453-9999-16-177-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: BK Virus and the Renal Allograft: A 360 Degree View	0453-9999-16-156-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Clinical Transplant Tolerance - Molecular and Cellular Biomarkers	0453-9999-16-105-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Controversies & Strategies Surrounding Substance Use in Transplant Candidates	0453-9999-16-104-L05-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Do High-Risk Transplant Recipients take Higher Risk when treated with Generic Tacrolimus?	0453-9999-16-131-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Ethical Dilemmas Related to the Internet and Transplant	0453-9999-16-154-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Fat and Inflammation Basic	0453-9999-16-151-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Imminent Death Donation	0453-9999-16-153-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Informed Decision Making in Living Organ Donation	0453-9999-16-112-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Leveling the Playing Field - How to Minimize Racial and Ethnic Disparities in Access to Transplantation	0453-9999-16-176-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Molecular Microscopic Approach to Chronic Allograft Injury	0453-9999-16-150-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: New Roles for Macrophages	0453-9999-16-106-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Obesity and NASH in Transplant	0453-9999-16-130-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Organ Donor Management: Maximizing Quality and Quantity of Donated Organs	0453-9999-16-134-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Pregnancy Donors, Recipients, and a Link to Tolerance	0453-9999-16-129-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Renal Controversies in Liver Transplantation	0453-9999-16-107-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC

Sunrise Symposium: Telemedicine: Excite, Engage, and Enhance Patient Centered Care in Transplantation and Living Donation	0453-9999-16-178-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: The KPD Plateau: What We Can Do About It	0453-9999-16-180-L05-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: The Nuts and Bolts of PHS Increased Risk Donors	0453-9999-16-179-L05-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Top New Papers In Transplant Infectious Disease	0453-9999-16-110-L01-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Sunrise Symposium: Women in Transplant - Networking Breakfast	0453-9999-16-155-L04-P	1.25	Boston	Knowledge	0453 - Amedco, LLC
Symposium 10 Antibodies in Mechanical Circulatory Support: The Phantom Menace	0453-9999-17-016-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 11 Not CAVing to CLADtastrophe: Emerging Mechanisms of Chronic Heart and Lung Allograft Disease	0453-9999-17-017-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 15 HLA, AMR and DSA – Approaching Antibodies in Kids	0453-9999-17-019-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 16 "Around the World in 80 Days": Infectious Challenges in Cardiothoracic Transplantation	0453-9999-17-020-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 18 Weeding Out Fact from Fiction: The Highs and Lows of Marijuana Use in Transplant	0453-9999-17-022-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 19 Cardiogenic Shock: Types, Teams and Tactics	0453-9999-17-023-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 2 When Should We Call It Quits? – The Efficacy of Interventions to Ameliorate Psychosocial Risk Factors	0453-9999-17-003-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 20 ECMO in Lung Transplantation: Sensational Success or Fantastic Failure?	0453-9999-17-024-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 22 Let's Get Personal! Precision Diagnostics in Thoracic Transplantation	0453-9999-17-025-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 23 Taming of the Shrew: Mycobacterium Abscesses in Lung Transplantation	0453-9999-17-026-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 24 Aiming Off Target: Non-Cardiac Consequences of LVAD Support	0453-9999-17-031-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC

Symposium 25 Dealing with Antibodies Before and After Heart Transplant: Do We Have New Arrows in our Quiver?	0453-9999-17-032-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 27 Bench to Bedside: How Advances in Immunology Shape the Care of Today's Lung Transplant Recipients	0453-9999-17-033-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 28 Great Debates in Pulmonary Hypertension	0453-9999-17-034-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 3 PGD and Vasoplegia After Heart Transplantation – Sink or Swim	0453-9999-17-004-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 30 E-health, Wearables, Social Media and Big Data in Transplantation: Fancy Toys or True Care Innovations?	0453-9999-17-035-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 30: JHLT at ISHLT: The Year in a Capsule	0453-9999-16-044-L04-P	1.5	Washington	Knowledge	0453 - Amedco, LLC
Symposium 4 Thinking Outside the Box: Extra-Pulmonary Management in Lung Transplantation	0453-9999-17-005-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 6 The Failing Fontan – Where Do We Go From Here?	0453-9999-17-007-L04-P	2	San Diego	Knowledge	0453 - Amedco, LLC
Symposium 9 JHLT at ISHLT: The Year in a Capsule	0453-9999-17-010-L04-P	1.5	San Diego	Knowledge	0453 - Amedco, LLC
The Art of Drug Dosing in Solid Organ Transplant	0377-0000-17-012-L01-P	1	New York	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
The Immunosuppression Balancing Act: Preserving Long-Term Allograft Function for Optimal Patient Outcomes	0376-0000-17-018-L01-P	1.25	Chicago	Knowledge	0376 - CME Outfitters, LLC
The Mystery of Transplant: Mangement of the Transplant Patient in the Primary Care Setting Organ Transplant	0120-0000-16-022-L01-P	1	Indianapolis	Knowledge	0120 - Indiana Pharmacists Alliance
The New Era of Kidney Allocation	0530-9999-15-193-L04-P	2.25	Phoenix	Knowledge	0530 - Global Education Group
The Unplenary	0530-9999-15-010-L01-P	1	Phoenix	Knowledge	0530 - Global Education Group
Therapeutic Drug Monitoring in Solid Organ Transplantation	0377-0000-16-008-L01-P	1	New York	Knowledge	0377 - New York Presbyterian Hospital Department of Pharmacy
Through the Lens of a Primary Care Professional	0016-9999-15-118-L01-P	0.5	Minneapolis	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Transplant by the Bay	0230-0000-17-001-L01-P	11.25	Tampa	Knowledge	0230 - USF Health
Transplant Pharmacotherapy from Donation to Transplantation	0134-0000-17-006-L04-P	1	Westbury Manor 1100 Jericho Turnpike	Knowledge	0134 - New York State Council of Health-System Pharmacists
Transplantation in Depth: B Cells	0453-9999-16-124-L04-P	3	Boston	Knowledge	0453 - Amedco, LLC
Transplantation...Start to Finish	0016-9999-15-055-L01-P	1.5	Dallas	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy

UHC Rapid Diffusion Innovation in Specialty Pharmacy: Improving Outcomes with a Better Understanding of the Patient Journey for Those Who Have a Lung Transplant	0022-9999-15-123-L01-P	1.75	Orlando	Knowledge	0022 - University of Kentucky College of Pharmacy
Update on Cardiac Transplantation	0530-9999-15-198-L04-P	1	Phoenix	Knowledge	0530 - Global Education Group
Updates on Tacrolimus Dosing: Once Vs. Twice Daily Administration	0389-0000-14-008-L01-P	0.5	Waltham	Knowledge	0389 - Lahey Hospital & Medical Center
Western CE: cardiology topics	0134-0000-17-052-L04-P	2.5	D'Youville College School of Pharmacy	Knowledge	0134 - New York State Council of Health-System Pharmacists
What Is the Promise of Cell Therapy Today? What's Around the Corner? What Will You See in Your Lifetime?	0530-9999-15-005-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
What's Trendy in Transplant: Clinical Pearls for Pharmacists	0217-9999-15-164-L01-P	1	Shady Grove	Knowledge	0217 - American College of Clinical Pharmacy
Whatever Happened to Gene Therapy?	0530-9999-15-007-L01-P	2	Phoenix	Knowledge	0530 - Global Education Group
What's Hot - What's New: Overview of Top Presented Abstracts	0453-9999-16-182-L04-P	1	Boston	Knowledge	0453 - Amedco, LLC
What's Hot, What's New: Overview of Top Presented Abstracts	0453-9999-17-099-L04-P	1.25	Chicago	Knowledge	0453 - Amedco, LLC
When Transplanting a Heart is Not Enough - The Role of Dual Organ Transplantation	0453-9999-15-052-L04-P	1.5	Philadelphia	Knowledge	0453 - Amedco, LLC
Where Are We Going With Kidney Paired Donation	0530-9999-15-207-L04-P	1.25	Phoenix	Knowledge	0530 - Global Education Group
Workshop: Hypertension in the CKD Population – Case-Based Presentation	0016-9999-15-033-L01-P	2	Dallas	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy
Workshop: Treatment of Blood Pressure in Special Populations	0016-9999-16-009-L01-P	1.5	Boston	Knowledge	0016 - University of Illinois at Chicago College of Pharmacy

266 Programs

528.5 hours

Appendix G-4

ACPE PLAN Programming Live Forum Application Activity

Title	UAN	Hrs (CEUs)	City	Activity Type	Provider Description
2017 Pediatric Pharmacy Preparatory Review and Recertification Course—Pediatric Transplantation, Cardiology, and Pulmonary	0217-0000-17-047-L01-P	3.5	Jacksonville/www.updatesintherapeutics.com	Application	0217 - American College of Clinical Pharmacy
Advancements in Immunotherapy and the Microbiome: Principles and Patient Outcomes	0217-0000-16-133-L01-P	1.5	Hollywood, www.accp.com/am	Application	0217 - American College of Clinical Pharmacy
Infectious Diseases Update: A Focus on the Immunocompromised Patient	0299-9999-16-006-L01-P	1	Honolulu	Application	0299 - Syntax Communications, Inc.
Midday Didactic #3: Why are Kidneys Discarded and What Can Be Done about It?	0453-9999-17-139-L05-P	1.5	Chicago	Application	0453 - Amedco, LLC
Midday Didactic #4: Management of Viral Hepatitis Before and After Solid Organ Transplantation	0453-9999-17-140-L01-P	1.5	Chicago	Application	0453 - Amedco, LLC
Midday Didactic #6: Risky business - BK Infection: Diagnosis, Treatment, & Immunosuppression Reduction	0453-9999-17-111-L01-P	1.5	Chicago	Application	0453 - Amedco, LLC
Midday Didactic #7: Keeping the High MELD/PELD Patient Alive On the List	0453-9999-17-169-L01-P	1.5	Chicago	Application	0453 - Amedco, LLC
Midday Symposium: Cutting Edge Topics in CMV and Transplant	0453-9999-16-143-L04-P	1.5	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Detecting and Dealing with Non-adherence in Transplant Recipients	0453-9999-16-148-L01-P	1.5	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Heart - Controversies in Immunosuppression	0453-9999-16-142-L01-P	1.5	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Impact of Belatacept in the Clinic	0453-9999-16-147-L01-P	1.5	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Liver Allocation	0453-9999-16-166-L04-P	1.25	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Pancreas Transplantation - How I Do It!	0453-9999-16-139-L01-P	1.5	Boston	Application	0453 - Amedco, LLC
Midday Symposium: Understanding and Minimizing the Costs of Living Kidney Donation	0453-9999-16-140-L04-P	1.5	Boston	Application	0453 - Amedco, LLC
Optimizing the Use of Marginal Organs	0530-9999-15-192-L04-P	2	Phoenix	Application	0530 - Global Education Group
Pediatric Pharmacy Preparatory Review and Recertification Course—Pediatric Transplantation, Cardiology, and Pulmonary	0217-0000-16-040-L01-P	3.5	Phoenix, www.updatesintherapeutics.com	Application	0217 - American College of Clinical Pharmacy
Pediatric Pharmacy Preparatory Review Course—Pulmonary, Pediatric Transplant and Neonatology	0217-0000-15-038-L01-P	3.5	Rosemont	Application	0217 - American College of Clinical Pharmacy

Pediatric Symposium II: Transplant Strategies for Pediatric Recipients	0453-9999-17-100-L01-P	3.25	Chicago	Application	0453 - Amedco, LLC
Pre-Meeting Symposium #1: Theoretical and Practical Aspects of HLA Antibodies as a Basis for Clinical Decision Making: Bringing the Lab to the Clinic	0453-9999-16-096-L01-P	4	Boston	Application	0453 - Amedco, LLC
Pre-Meeting Symposium #5: Challenges in Transplant Listing and Organ Allocation: Impact of the New Kidney Allocation System on Transplant Program Workflow	0453-9999-17-052-L01-P	4.25	Chicago	Application	0453 - Amedco, LLC
Pre-Meeting Symposium #7: Exciting Updates in Transplant ID: Case-based Learning - Treatment: Keeping the Wolves at Bay	0453-9999-16-102-L01-P	4.25	Boston	Application	0453 - Amedco, LLC
Pre-Meeting Symposium #8: Collaboration At Its Finest: A Case-Based Approach Highlighting The Significance Of The Multi-Disciplinary Team	0453-9999-16-103-L05-P	4	Boston	Application	0453 - Amedco, LLC
Preparative Regimens: Dosing Considerations in Special Populations	0299-9999-15-016-L01-P	1	San Diego	Application	0299 - Syntaxx Communications, Inc.
Student Program - The Science, The Art, And The Allure Of Transplantation: Fundamental Concepts of Transplantation	0453-9999-17-148-L04-P	3.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Didactic #2: Antifungal Testing, Prevention, and Treatment Stewardship in SOT	0453-9999-17-125-L01-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Didactic #6: Getting the Most Bang for Your Buck: Creative Ways to Expand Pharmacy Services to Meet Regulatory Requirements	0453-9999-17-159-L03-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Didactic #6: Transplant Team Leadership: Leading a Multidisciplinary Transplant Team	0453-9999-17-121-L04-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Didactic #7: Opioids and Opioid Substitution Therapy in Transplant Candidates	0453-9999-17-120-L01-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Didactic #8: Interspecies Chimeric Complementation for the Generation of Functional Human Organs in Large Animal Hosts	0453-9999-17-161-L04-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Interactive #1: The CKDPC Web-based "Lifetime ESRD Risk Calculator"	0453-9999-17-088-L05-P	1.25	Chicago	Application	0453 - Amedco, LLC
Sunrise Interactive #3: Pushing Boundaries for Recipient Selection in Lung Transplant	0453-9999-17-090-L01-P	1.25	Chicago	Application	0453 - Amedco, LLC

Sunrise Symposium: Heart - Does My Patient Have AMR and How Do I Treat It?	0453-9999-16-132-L04-P	1.25	Boston	Application	0453 - Amedco, LLC
Sunrise Symposium: Management of Urologic Issues and Complications with Renal Transplant	0453-9999-16-136-L01-P	1.25	Boston	Application	0453 - Amedco, LLC
Sunrise Symposium: Reaching Consensus on AMR in Lung Transplantation	0453-9999-16-109-L01-P	1.25	Boston	Application	0453 - Amedco, LLC
Sunrise Symposium: Sex and Drugs In Transplantation	0453-9999-16-108-L01-P	1.25	Boston	Application	0453 - Amedco, LLC
Sunrise Symposium: The Current Status Of The US Workforce Of Transplant Surgeons And New Paradigms In Transplant Training	0453-9999-16-157-L04-P	1.25	Boston	Application	0453 - Amedco, LLC
Sunrise Symposium: You Can't Always Get What You Want: Multidrug Resistant Organisms	0453-9999-16-133-L04-P	1.25	Boston	Application	0453 - Amedco, LLC
Third Annual Interprofessional Forum on Ethics and Religion in Health Care: Challenges in Organ Donation and Transplantation	0025-0000-16-120-L04-P	6	Baltimore	Application	0025 - University of Maryland School of Pharmacy

38 Programs

77.5 hours

Appendix G-5

ACPE PLAN Programming Home Study Knowledge Activity

Title	UAN	Hrs (CEUs)	Activity Type	Provider Description
Biomarkers and Diagnostics for Assessment of Renal Allograft Function and Prognosis	0027-9999-11-054-H01-P	0.5	Knowledge	0027 - Northeastern University Bouve College of Health Sciences School of Pharmacy
Case Study in Hepatitis C: Patient with Chronic Hepatitis C Genotype 3 Virus Infection Who Has Undergone Orthotopic Liver Transplantation (2235.62)	0052-0000-15-110-H01-P	0.75	Knowledge	0052 - Projects In Knowledge, Inc.
Cutting Edge of Transplantation Optimizing Long-Term Transplant Survival: Therapeutics, Targets & Technologies	0530-9999-15-055-H01-P	1.5	Knowledge	0530 - Global Education Group
Demystifying the Methodology of the SRTR Program-specific Reports (And How It Affects Your Center)	0522-9999-13-006-H05-P	1	Knowledge	0522 - Dannemiller, Inc.
Device Therapy in Heart-failure Patients	0860-0000-17-019-H01-P	0.75	Knowledge	0860 - OptumHealth Education
Diagnosing Your Center's Strengths and Weaknesses: Using the SRTR Survival Estimate Worksheets	0522-9999-13-007-H05-P	0.5	Knowledge	0522 - Dannemiller, Inc.
Ethical Principles in the Allocation of Organs	0860-0000-17-009-H01-P	1	Knowledge	0860 - OptumHealth Education
Immune Globulin: Considerations of the Transplant Specialty Pharmacist	0535-0000-16-020-H01-P	0.5	Knowledge	0535 - Specialty Pharma Education Center
Improving Medication Adherence and Outcomes in Transplant Recipients	0027-9999-13-068-H01-P	0.5	Knowledge	0027 - Northeastern University Bouve College of Health Sciences School of Pharmacy
Kidney Transplantation: A Pharmacist-Focused Discussion of Common Clinical Issues Related to Comorbidities, Renal Function, and Organ Rejection	0290-0000-13-108-H01-P	3	Knowledge	0290 - Pharmacy Times Office of Continuing Professional Education
Lecture of the Month: Obesity: Implications for Liver Disease and Transplantation	0216-0000-15-068-H01-P	1.5	Knowledge	0216 - American Society for Parenteral and Enteral Nutrition, Inc.
Maintenance Immunosuppressive Therapy: Taming the Immune Response	0175-0000-14-040-H01-P	1	Knowledge	0175 - Pharmacy Society of Wisconsin
Managed Care's Role in Improving Adherence and Outcomes in Solid Organ Transplantation	0290-9999-15-002-H01-P	3	Knowledge	0290 - Pharmacy Times Office of Continuing Professional Education
Managing Patients Receiving Transplant Medications	0422-0000-16-213-H01-P	1	Knowledge	0422 - Pharmacist's Letter Therapeutic Research Center

Psychosocial Impact of Transplant in Children	0860-0000-17-013-H01-P	0.75	Knowledge	0860 - OptumHealth Education
The Immunology Report - Summer 2013	0027-9999-13-067-H01-P	3	Knowledge	0027 - Northeastern University Bouve College of Health Sciences School of Pharmacy
The Pharmacist's Role in Improving Outcomes in Renal Transplantation	0430-0000-16-110-H01-P	2	Knowledge	0430 - Postgraduate Healthcare Education, LLC
Transplant Medications: Outpatient ?What the pharmacist needs to know.	0401-0000-12-011-H01-P	2	Knowledge	0401 - Drug Store News
Using Telehealth to Enable Patient-centered Care for Transplant	0860-0000-17-010-H01-P	0.75	Knowledge	0860 - OptumHealth Education
Walking the Thin Line with Transplant Medications	0422-0000-13-212-H01-P	1	Knowledge	0422 - Pharmacist's Letter Therapeutic Research Center
Working with Patients Before and After Transplants	0239-0000-12-022-H01-P	0.75	Knowledge	0239 - American Diabetes Association

21 Programs

26.75 hours

Appendix G-6

ACPE PLAN Programming Home Study Application Activity

Title	UAN	Hrs (CEUs)	Activity Type	Provider Description
ACSAP 2013 Book I -- Pulmonary and Preventive Care III	0217-0000-13-009-H01-P	6	Application	0217 - American College of Clinical Pharmacy
Kidney Transplantation: Case 1. Patient With End-Stage Renal Disease Secondary to Interstitial Nephritis Presenting for Cadaveric Renal Transplantation	0290-0000-13-119-H01-P	1	Application	0290 - Pharmacy Times Office of Continuing Professional Education
Kidney Transplantation: Case 2. Patient Presenting 3 Months Post Living Donor Transplant	0290-0000-13-120-H01-P	1	Application	0290 - Pharmacy Times Office of Continuing Professional Education
Pediatric Pharmacy Preparatory Review Course—Pulmonary, Pediatric Transplant and Neonatology	0217-0000-15-038-H01-P	3.5	Application	0217 - American College of Clinical Pharmacy
The Ambulatory Care Preparatory Review and Recertification Course? Gastrointestinal Disorders, Immunizations, and Solid Organ Transplantation	0217-0000-13-020-H01-P	3	Application	0217 - American College of Clinical Pharmacy

5 programs

14.5 Hours

Appendix G-7

Sample Educational Program Materials

ACCP

Immunology/Transplantation PRN Focus
Session – Antibody-Mediated Rejection:
Are We Really Making Progress? – A
Spirited Debate

Immunology/Transplantation PRN Focus Session—Antibody-Mediated Rejection: Are We Really Making Progress?—A Spirited Debate

Activity Number: 0217-0000-17-136-L01-P, 1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Saturday, October 7, 2017

1:45 p.m. to 3:15 p.m.

Phoenix Convention Center North Bldg. Street Level: Meeting Room 122

Moderator: Amanda Condon, Pharm. D.

Clinical Pharmacy Specialist, Solid Organ Transplantation, University of New Mexico Hospitals, Albuquerque, New Mexico

Agenda

- 1:45 p.m. Novel Endpoints for Measuring the Effectiveness of Antibody-Mediated Rejection
Matthew J. Everly, Pharm.D., BCPS
Interim Director, Terasaki Research Institute, Los Angeles, California; Adjunct Assistant Professor of Medicine, Nephrology Division, David Geffen School of Medicine, University of California, Los Angeles, California
- 2:05 p.m. Antibody-Mediated Rejection: Yes, Novel Agents Are Worthy of Use—Pro Point and Rebuttal
Christopher R. Ensor, Pharm.D., BCPS
Assistant Professor of Pharmacy and Medicine; Medical Director of Lung Transplant Outcomes Research Program, University of Pittsburgh, Pittsburgh, Pennsylvania
- 2:30 p.m. Antibody-Mediated Rejection: No, the Risks and Costs of Novel Agents Outweigh Their Benefit—Con Counterpoint and Rebuttal
Lisa Potter, Pharm.D., FCCP, BCPS
Clinical Coordinator, Transplant Pharmacy Services, University of Chicago Medicine, Chicago, Illinois
- 2:55 p.m. Antibody-Mediated Rejection Panel Discussion
Steven Gabardi, Pharm.D., FCCP, BCPS
Abdominal Organ Transplant Specialist, Program Director, PGY2 Organ Transplant Pharmacology Residency Program, Brigham and Women's Hospital, Boston, Massachusetts; Assistant Professor of Medicine, Harvard Medical School, Boston, Massachusetts

Conflict of Interest Disclosures

Amanda Condon: No conflicts to disclose

Christopher R. Ensor: Grants: (Amgen, CSL Behring)

Matthew J. Everly: No conflicts to disclose

Steven Gabardi: No conflicts to disclose

Lisa Potter: Clinical Investigator: (Organ Recovery Systems, Astellas, Cinkate, BMS)

Learning Objectives

1. Define AMR in various solid organ transplant populations.
2. Discuss the limitations of current clinical endpoints for AMR.
3. Analyze the literature behind novel clinical endpoints for AMR treatment.
4. Describe early phase investigational treatments for AMR.
5. Describe current and novel agents and treatment regimens for AMR.
6. Compare the costs, effectiveness, and risk associated with each agent/regimen used in AMR treatment based upon the point-counterpoint debate.
7. Design a treatment regimen, using the specifics of your institution, transplant population, and ability to take risk based upon the point-counterpoint debate.
8. Review key AMR debate points.
9. Justify costs associated with AMR consequences and therapeutics.
10. Describe future direction of AMR therapies.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/am.

Novel Endpoints for measuring the effectiveness of Antibody Mediated Rejection



Matthew J. Everly, PharmD, BCPS, FAST

Learning Objectives

1. Define AMR in various solid organ transplant populations.
2. Discuss the limitations of current clinical endpoints for AMR.
3. Analyze the literature behind novel clinical endpoints for AMR treatment.
4. Describe early phase investigational treatments for AMR

and Disclosures

Work with Bristol-Myers Squibb (Grant), Astellas (Advisory Board), Veloxis (Grant), Octapharma (Grant), CSL Behring (Grant), and BiologicTx (Advisory board).

Defining Antibody Mediated Rejection (ABMR) and Chronic antibody mediated rejection (cABMR)

Diagnostic Criteria for Acute ABMR in Renal Allograft Biopsies

(L.C. Racusen et al, Am J Transplant 3: 1-7, 2003)

1. Morphologic evidence
 - a. Neutrophils and/or monocytes/macrophages in PTC and/or glomeruli (peritubular capillaritis; glomerulitis)
 - b. Arterial fibrinoid necrosis
 - c. Thrombi in glomerular capillaries, arterioles, and/or small arteries
 - d. Acute tubular injury, without other apparent causes
2. Immunohistologic evidence
 - a. Diffuse C4d in PTC
 - b. Immunoglobulin and/or complement in arterial fibrinoid necrosis
3. Serologic evidence
 - a. Circulating antibodies to donor HLA or other specific anti-donor antibodies at the time of biopsy

Banff 2013 Classification of Antibody-Mediated Rejection (ABMR) in Renal Allografts (continued)

Chronic, Active ABMR; all three features must be present for diagnosis¹

1. Morphologic evidence of chronic tissue injury, including 1 or more of the following:
 - Transplant glomerulopathy (cg >0)⁹, if no evidence of chronic TMA
 - Severe peritubular capillary basement membrane multilayering (requires EM)^h
 - Arterial intimal fibrosis of new onset, excluding other causes
2. Evidence of current/recent antibody interaction with vascular endothelium, including at least one of the following:
 - Linear C4d staining in peritubular capillaries (C4d2 or C4d3 by IF on frozen sections, or C4d > 0 by IHC on paraffin sections)
 - At least moderate microvascular inflammation ([g + ptc] ≥2)¹
 - Increased expression of gene transcripts in the biopsy tissue indicative of endothelial injury, if thoroughly validated
3. Serologic evidence of donor-specific antibodies (HLA or other antigens)

¹ In the absence of evidence of current/recent antibody interaction with the endothelium (those features in section 2), the term active should be omitted; in such cases DSA may be present at the time of biopsy or at any previous time post-transplantation.

⁹ Includes GBM duplication by electron microscopy only (cg1a) or GBM double contours by light microscopy

^h ≥7 layers in 1 cortical peritubular capillary and ≥5 in 2 additional capillaries, avoiding portions cut tangentially

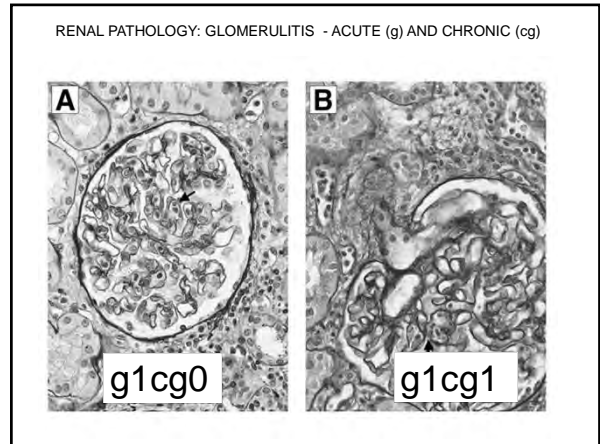
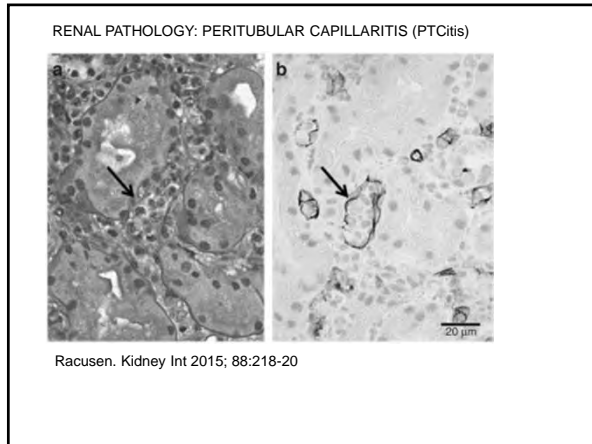
¹ In the presence acute T cell-mediated rejection, borderline infiltrates, or evidence of infection, ptc ≥2 alone is not sufficient to define moderate microvascular inflammation and g must be ≥1.

Banff 2013 Classification of Antibody-Mediated Rejection (ABMR) in Renal Allografts (continued)

C4d Staining without Evidence of Rejection; all 3 features must be present for diagnosis¹

1. Linear C4d staining in peritubular capillaries (C4d2 or C4d3 by IF on frozen sections, or C4d>0 by IHC on paraffin sections)
2. g = 0, ptc = 0, cg = 0 (by LM and by EM if available), v = 0; no TMA, no peritubular capillary basement membrane multilayering, no acute tubular injury (in the absence of another apparent cause for this)
3. No acute cell-mediated rejection (Banff 97 type 1A or greater) or borderline changes

¹ The clinical significance of these findings may be quite different in grafts exposed to anti-blood-group antibodies (ABO-incompatible allografts), where they do not appear to be injurious to the graft and may represent accommodation, and anti-HLA antibodies where more clinical outcome data is needed.



Revised (Banff 2013) definitions and scoring system for Glomerulitis (g) and Chronic Glomerulopathy (cg)

- Glomerulitis is defined as intra-capillary mononuclear inflammatory cell infiltration **AND** endothelial cell enlargement **with complete or partial occlusion of 1 or more capillary lumens**.
The extent of glomerulitis is scored based on percentage using PAS and/or silver sections (with or without CD68 immunostain) as follows:
 - g0 - no glomerulitis (0%)
 - g1 - segmental or global glomerulitis in 1-25% of glomeruli
 - g2 - segmental or global glomerulitis in 25-75% of glomeruli
 - g3 - segmental or global glomerulitis in >75% of glomeruli
- Chronic glomerulopathy (transplant glomerulopathy) is defined as presence of glomerular basement membrane duplications observed using PAS and/or silver stained sections in the absence of significant IC deposits along capillary walls by IF and/or EM studies.
Double contours scored as follows:
 - cg0 - NO double contours of the GBM (0%) in any glomeruli using LM PAS/silver or EM.
 - cg1 - double contours of the GBM in 1-25% of capillaries in the most involved glomerulus by LM (cg1b) or EM (cg1a - see criteria below)
 - cg2 - double contours of the GBM in 26-50% of capillaries in the most involved glomerulus
 - cg3 - double contours of the GBM in >50% of capillaries in the most involved glomerulus

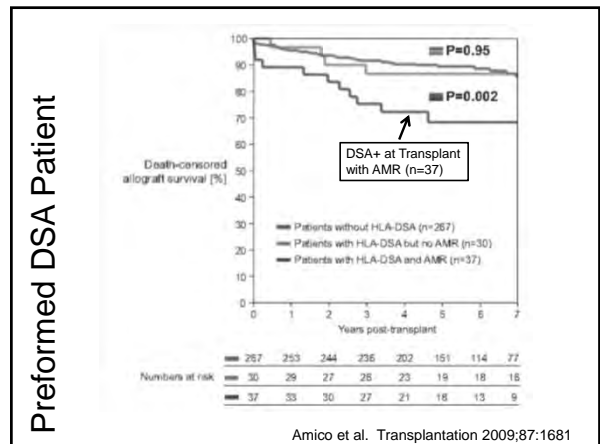
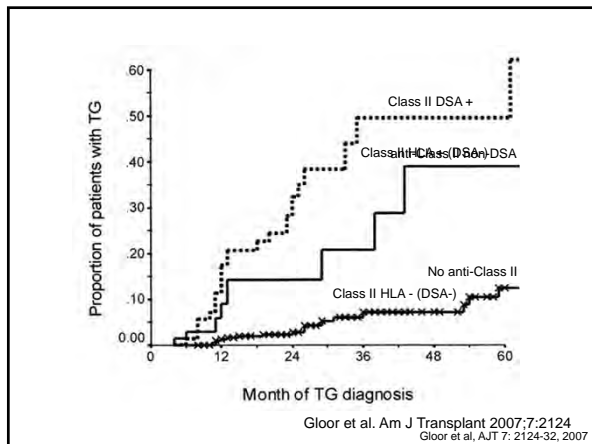
American Journal of Transplantation 2007; 7:2124-2132
Journal of Clinical Investigation 2007; 117:1111-1118

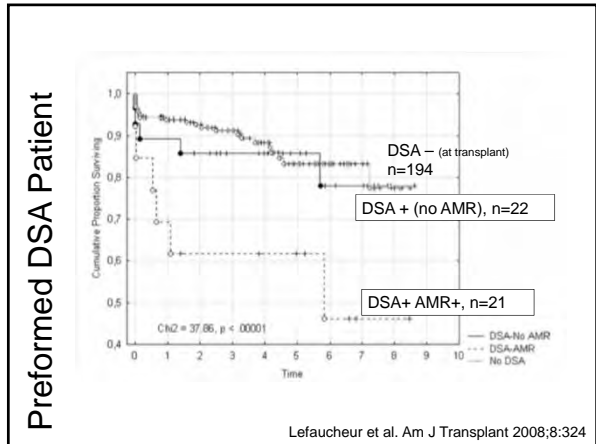
Transplant Glomerulopathy: Subclinical Incidence and Association with Alloantibody

J. M. Gloor^{a,*}, S. Sethi^b, M. D. Stegall^c, W. D. Park^d, S. B. Moore^e, S. DeGoey^f, M. D. Griffin^g, T. S. Larson^h and F. G. Cosio^a

Introduction
Transplant glomerulopathy (TG) is a condition associated with poor outcome, characterized by duplication of glomerular basement membranes, mesangial matrix expansion, and mesangial cell interposition (1,2). Originally identified as a variant of chronic allograft nephropathy of unknown etiology, TG is now recognized with increased frequency in patients with a prior history of humoral rejection, and is also associated with deposition of the complement degradation product C4d, suggesting that TG may be one manifestation of antibody-mediated injury (3-5).

Gloor et al. *Am J Transplant* 2007;7:2124





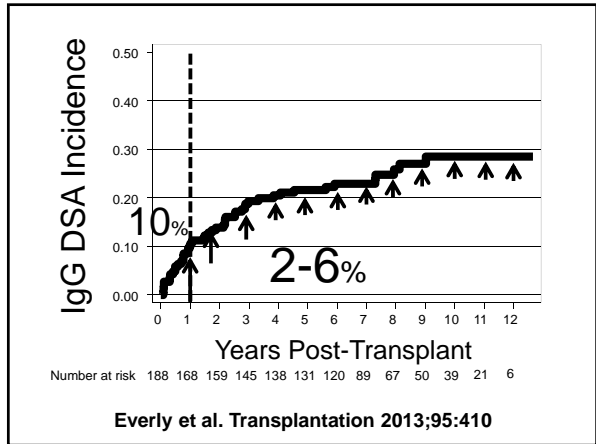
We are still learning how to identify ABMR and cABMR...

de novo DSA

How big is the de novo DSA problem in transplantation?

Adult Kidney Transplants

Study	Pre-tpx MFI cutoff	dnDSA MFI cutoff	Samples size	Percent of patient with dnDSA overall	Median follow-up post transplant	1 year incidence of dnDSA	5 year incidence of dnDSA
Cooper et al. Transplantation 2011	500 MFI	500 MFI	N=244	27%	24 months	Not reported	Not reported
Devos et al. Kidney Int 2012	2000 MFI	2000 MFI	N=347	18%	26 months	Not reported	Not reported
Everly et al. Transplantation 2013	1000 MFI	1000 MFI	N=189	25%	8 years	11%	20%
Heliman et al. Transplantation 2013	1000 MFI	1000 MFI	N=245	18%	21 months	8.2%	Not reported
Weibe et al AJT 2015	300 MFI	500 MFI	N=508	13%	6.25 years	2%	10%

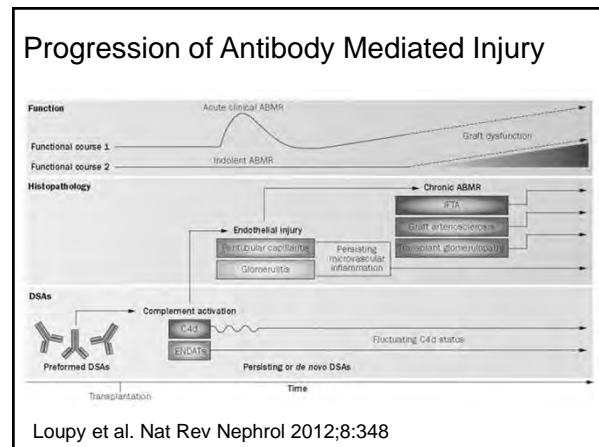
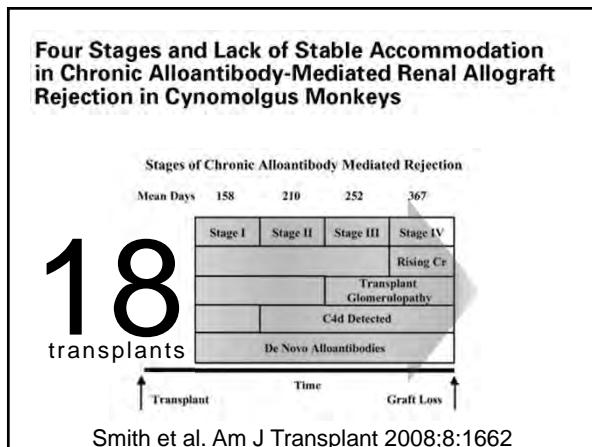
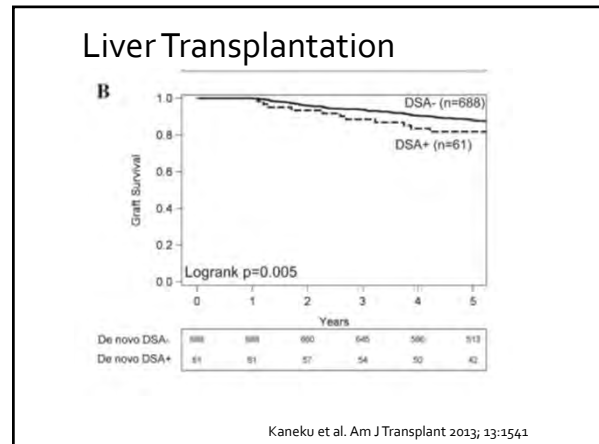
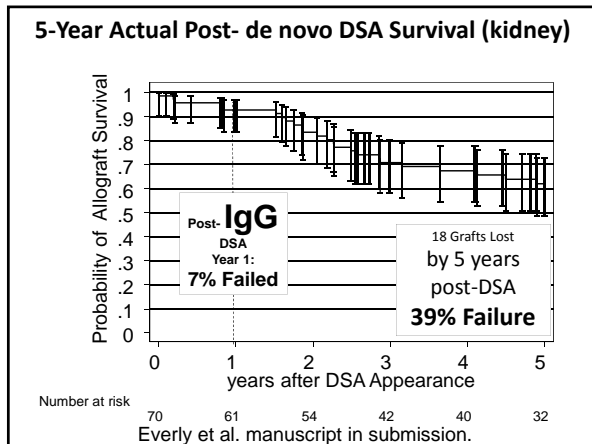


Liver Transplant and de-novo DSA dnDSA MFI cutoff 5000

Table 2: Frequency of de novo DSA by HLA class and locus

All patients (n = 749)	
DSA positive, n (%)	61 (8.1%)
By HLA class	
DSA class I, n (%)	3 (5%)
DSA class II, n (%)	58 (95%)
DSA class I+II, n (%)	0
By HLA locus	
HLA-A, n (%)	0
HLA-B, n (%)	3 (5%)
HLA-DRB1, n (%)	7 (12%)
HLA-DRB345, n (%)	8 (13%)
HLA-DQ, n (%)	52 (85%)

Kaneku et al. Am J Transplant 2013; 13:1541



Thymoglobulin			
Rituximab	cyclophosphamide		
	Increase mycophenolate		
	Increase tacrolimus		
		Anti-IL6	
NONE ARE APPROVED FOR AMR TREATMENT			
IVIG	IgG endopeptidase (IdeS)		Eculizumab
Pheresis		BAFF/APRIL inhibitors	C1-inhibitors
	bortezomib		

23

Where are we with endpoints for ABMR?



Transplant Therapeutics Consortium

Overview

TTC
TRANSPLANT THERAPEUTICS
CONSORTIUM
CRITICAL PATH INSTITUTE

TTC

Introduction

Tucson, Ariz., April 26, 2017 –Critical Path Institute (C-Path) is pleased to announce the launch of the Transplant Therapeutics Consortium (TTC), co-founded by the two leading US organizations in organ transplantation: the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS). The TTC is a collaboration within the transplant community including clinicians, surgeons, industry scientists, and others. The overall objective of the TTC is to collaborate on the development and regulatory endorsement of new drug development tools applicable in kidney transplant, with the hope of expanding to other solid organ transplantation in the future.

In the United States, there are currently 600,000 patients receiving dialysis every year; with more than 105,000 patients on the kidney transplant waiting list. In 2016, there were 19,000 kidney transplants in the US, and the failure rates for living donor kidney transplants at 1, 5, and 10 years are approximately 3%, 15%, and 40%, respectively. Deceased donor kidney transplant failure rates are even higher, with 6%, 27%, and 52% of these transplants failing at 1, 5, and 10 years, respectively. @http://www.critpath.org/2016/04/26/ttc-1/

What are some possible endpoints for ABMR?

**ClinicalTrials.gov listing
Of Phase III trials for ABMR**

phase III | antibody mediated rejection

Search Details

Row	Save	Status	Study Title	Conditions	Interventions
1	<input type="checkbox"/>	Recruiting	Efficacy and Safety of Human Plasma-derived C1-esterase Inhibitor as add-on to Standard of Care for the Treatment of Refractory Antibody Mediated Rejection (AMR) in Adult Renal Transplant Recipients	Antibody-mediated Rejection	Drug: C1-esterase inhibitor; Drug: Placebo
2	<input type="checkbox"/>	Recruiting	A Multicenter Study to Evaluate the Efficacy and Safety of Givproph for the Treatment of Acute Antibody-mediated Rejection in Patients With Kidney Transplant	Acute Antibody-Mediated Rejection (AMR)	Biological: Givproph; Drug: Placebo
3	<input type="checkbox"/>	Recruiting	Effect of Proxigen Against Graft Loss	Kidney Transplantation	Drug: Proxigen (human normal immunoglobulin G (IgG + 96 % purity))
4	<input type="checkbox"/>	Unknown	Induction Therapy Study in Live Donor Kidney Transplant Recipients With a Positive Crossmatch	Kidney Failure, Chronic	Drug: Thymoglobulin

Efficacy and Safety of Human Plasma-derived C1-esterase Inhibitor as add-on to Standard of Care for the Treatment of Refractory Antibody Mediated Rejection (AMR) in Adult Renal Transplant Recipients

This study is currently recruiting participants. **ClinicalTrials.gov Identifier:** NCT03221962

See [Contents and Locations](#)

Verified September 2017 to US; Being

Sponsor: CSL, Behring

Information provided by (Responsible Party): CSL, Behring

Full Text View | Tabular View | No Study Results Posted | Download | How to Read a Study Record

Purpose

This is a double-blind, randomized-withdrawal, placebo-controlled study in kidney transplant patients with AMR to measure the efficacy and safety of human plasma-derived C1-esterase inhibitor as add-on to standard of care (SOC).

Estimated Primary Completion Date: July 16, 2020 (Final data collection date for primary outcome measure)

Current Primary Outcome Measures: ^{1,2,3,4}

Time to loss of response during Treatment Period 2 | Time Frame: Up to approximately 25 weeks | Loss of response is defined as 1 of the following, whichever occurs first:

- Decline in Estimated Glomerular Filtration Rate (eGFR), or
- Allograft failure, or
- Subject death by any cause.

Current Secondary Outcome Measures: ^{5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100}

- Time to all-cause allograft failure after randomization into Treatment Period 2 | Time Frame: Up to approximately 105 weeks | Allograft failure is defined as 1 of the following, whichever occurs first:
 - Allograft nephropathy
 - Permeable dialysis
 - Return to the transplant waitlist
- Percentage of subjects with response to treatment at the end of Treatment Period 1 | Time Frame: Up to approximately 13 weeks | Response is defined as an increase in eGFR.
- Percentage of subjects with sustained improvement of eGFR during Treatment Period 2 | Time Frame: Up to approximately 25 weeks | Sustained improvement is defined as an increase in eGFR.
- Change from screening in Banff category scores at up to 38 weeks | Time Frame: Screening and up to approximately 38 weeks | Banff category scores are used to grade the histopathology of kidney allograft biopsies using a scoring system of 0 (best possible) to 3 (worst possible).
- Percentage of subjects with new or worsening chronic active AMR during Treatment Period 2 | Time Frame: Up to approximately 25 weeks | New or worsening chronic active AMR during Treatment Period 2, as defined by the Banff 2015 criteria (Lupaj et al, 2017)
- Percentage of subjects with remission during Treatment Period 1 and during Treatment Period 2 | Time Frame: Up to approximately 38 weeks |
- Percentage of subjects surviving at the end of Treatment Period 2 | Time Frame: Up to approximately 38 weeks |
- Percentage of subjects with a surviving allograft at the end of Treatment Period 2 | Time Frame: Up to approximately 38 weeks |
- Time to subject death after randomization into Treatment Period 2 | Time Frame: Up to approximately 105 weeks |
- Percentage of subjects with any adverse event (AE) assessed as related to investigational product | Time Frame: Up to approximately 42 weeks after the time of first investigational product administration |
- Pre-dose C1-INH Functional activity | Time Frame: Day 1, approximately Week 12, and approximately Week 38 |
- Time to maximum plasma concentration (C_{max}) for C1-INH functional activity | Time Frame: Up to 72 hours after dose |
- Area under the plasma concentration time curve (AUC₀₋₇₂) for C1-INH functional activity | Time Frame: Up to 72 hours after dose |

A Multicenter Study to Evaluate the Efficacy and Safety of Cytzeo® for the Treatment of Acute Antibody-mediated Rejection in Patients With Kidney Transplant

This study is currently recruiting participants.
[View Details and Locations](#)

Verified August 2017 by Site
 Sponsor: **Amgen**
 ID: **NCT03454720**
 Information provided by (Responsible Party): **Amgen**

Purpose
 To evaluate the efficacy of Cytzeo® given for the treatment of acute antibody-mediated rejection (AMR) in kidney transplant recipients, as measured by the proportion of subjects with new or worsening transplant glomerulopathy (TG) at 6 months after treatment initiation.

Current Primary Outcome Measures #14
 (submitted: January 26, 2017)
 Evaluate efficacy for the treatment of acute AMR of renal allograft in kidney transplant recipients as measured by the proportion of subjects with new or worsening transplant glomerulopathy (TG) at 6 months after treatment initiation using Banff criteria (Time Frame: Screening to Month 6)

Original Primary Outcome Measures #14
 (submitted: September 16, 2015)
 Proportion of subjects with new or worsening transplant glomerulopathy (TG) within 6 months post-treatment as determined by Banff criteria (Time Frame: Screening to Month 6)

Other related proposed endpoint measures:
 Prevention of de novo DSA (by 24 months post transplant)

To Compare the Effects of Immediate-release Tacrolimus and Astagraf XL on Donor-Specific Antibody (DSA) Formation and the Development of Immune Activation (IA) in de Novo Kidney Transplant Recipients (ASTOUND)

This study is currently recruiting participants.
[View Details and Locations](#)

Verified July 2017 by Amgen Pharma Inc | Amgen Pharma Global Development, Inc. |
 Sponsor: **Amgen Pharma Global Development, Inc.**
 ID: **NCT02222091**
 Information provided by (Responsible Party): **Amgen Pharma Inc | Amgen Pharma Global Development, Inc. |**

Purpose
 This study will compare the incidence of a two-part composite endpoint consisting of de novo donor specific antibody formation or a designation of "immune activation" (an peripheral blood molecular profiling in patients maintained on twice daily, immediate-release tacrolimus versus those maintained on Astagraf XL, in the first two years post-transplant.

Condition	Intervention	Phase
Kidney Transplantation	Drug: Astagraf XL Drug: Tacrolimus immediate release	Phase 4

Primary Outcome Measures:
 • Combined incidence of DSA or IA (Time Frame: At 1 year post-transplant or EOS up to 2 years post-transplant)
 DSA considered as a binary variable (positive or negative), with positivity based on a threshold criteria of mean Fluorescence Intensity approaching 1000. Immune Activation (IA) considered as a binary variable (present or absent) based on updated molecular signatures. End of Study (EOS)

Summary

1. ABMR and cAMBR Diagnosis

We are improving the diagnostic criteria but there is still more needed (especially in organs other than kidney).

2. Risk of de novo DSA

7-10% fail in first post-dnDSA year
40% fail in 5 year post-dnDSA

Liver 20% fail by 5 years (post-DSA analysis has not been conducted)

3. Current ABMR Endpoints

None exist!

4a. Potential ABMR Endpoints

Composite endpoint

- Decline in eGFR, or
- Allograft failure, or
- Subject death

4b. Potential ABMR Endpoints

Single endpoint
Proportion of new or worsening
transplant glomerulopathy after
treatment (6months)

4c. Other Endpoints

Prevention of dnDSA by 24
months post-transplant.

Thank You

Antibody-Mediated Rejection: *Novel Agents Are Worthy of Use*

Christopher R. Ensor, PharmD, BCPS
Assistant Professor of Pharmacy and Medicine
Medical Director, Lung Transplant Outcomes Research Program
Associate Member, Thomas E. Starzl Transplantation Institute

October 7 2017, Phoenix AZ

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Relevant Financial Relationship Disclosure Statement

I will discuss investigational use of the following drugs:
carfilzomib, cinryze, tocilizumab

The following relevant financial relationships exist related to my role in this session:
Grant Funding: CSL Behring Inc.; Amgen Inc.

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Objectives

- Describe current and novel agents and treatment regimens for AMR
- Compare the costs, effectiveness, and risk associated with each agent/regimen used in AMR treatment based upon the point-counterpoint debate
- Design a treatment regimen using the specifics of your institution, transplant population and ability to take risk based upon the point-counterpoint debate

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What does "Novel" Mean in AMR Anyway?!

Novel (adj): new and not resembling something formerly known or used; original or striking especially in conception or style. (Merriam-Webster)

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Novel Therapeutic Paradigm Shift in AMR

Current paradigm: AMR treatment is episodic and only targeted at DSA and supporting cellular infrastructure

Novel paradigm: AMR is both an acute and chronic disease requiring long-term therapy targeted at DSA, arresting injury, and preventing fibrosis

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Targeting DSA with Novel Therapies

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DOI: 10.1111/ajt.14226

Proteasome Inhibitor Carfilzomib-Based Therapy for Antibody-Mediated Rejection of the Pulmonary Allograft: Use and Short-Term Findings

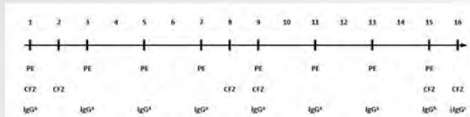
C. R. Ensor^{1,2*}, S. A. Yousem³, M. Marrani⁴, M. R. Morrell⁵, M. Mangiola⁶, J. M. Pilewski⁷, J. D'Onofrio⁸, S. R. Wosnitowski⁹, R. Venkataramanan¹⁰, A. Zeevi¹¹ and J. F. McDyer¹²

Am J Transplant 2017;17:1260-68.

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CFZ-Based Regimen

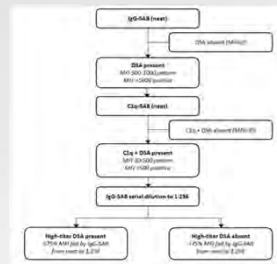


Am J Transplant 2017;17:1380-88.

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DSA Testing Regimen



Am J Transplant 2017;17:1380-88.

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Patient Characteristics	%
Patients / Courses of CFZ (n)	19 / 23
Age in years, mean (SD)	51.1 (12.3)
Caucasian	75
ILD	44
COPD	38
Tacrolimus	55
Mycophenolate	80
Everolimus/Sirolimus	20
Alemtuzumab	60
CLAD prior to CFZ	33
Advanced BOS (grade ≥ 2) prior to CFZ	25
Days to AMR therapy	560
Antibody responsiveness	67
Completed regimen	74
CFZ dose-reduced for ADE	11

Am J Transplant 2017;17:1380-88.

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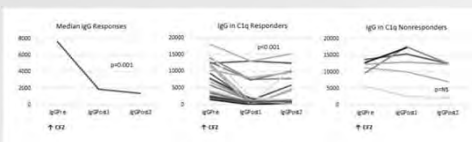
DSA and AMR Characteristics	%
Immunodominant DSA (n)	34
DQ	74.2
DR	16.1
DQ+DR	9.7
2016 AMR Criteria	
Definite	43.8
Probable +	12.4
Probable	43.8
Pathologic Characteristics	
≥ A3	25
Acute lung injury	56.3
Bronchitis	43.8
Capillaritis or endothelialitis	31.3
C4d +	43.8

Am J Transplant 2017;17:1380-88.

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IgG-Based Responsiveness

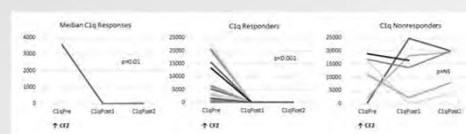


Am J Transplant 2017;17:1380-88.

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C1q-Based Responsiveness

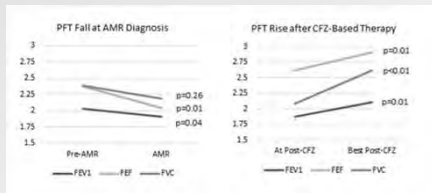


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PFT Responsiveness

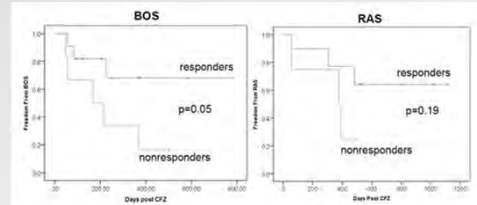


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Freedom From CLAD



Am J Transplant 2017;17:1380-88.

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Arresting Injury with Novel Therapies

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doi: 10.1111/ajt.12877

Plasma-Derived C1 Esterase Inhibitor for Acute Antibody-Mediated Rejection Following Kidney Transplantation: Results of a Randomized Double-Blind Placebo-Controlled Pilot Study

R. A. Montgomery¹*, B. J. Grand¹, L. Racusen², A. M. Jackson³, J. M. Garonzik⁴, Wang⁵, T. Shah⁶, E. S. Woodie⁷, C. Sommerer⁸, D. Fitts⁹, K. Rookich⁹, P. Zhang⁹ and M. E. Ukeles⁹

Am J Transplant 2016;16:3468-78.

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C1 Esterase (Cinryze) Regimen

- Randomization 1:1 C1e vs. placebo
- Severe AMR excluded
- C1-esterase regimen
 - 5000 units of C1e on day 1
 - 2500 units of C1e on days 3, 5, 7, 9, 11, 13
- Hopkins enrolled 14/18 patients
 - Plasma exchange every-other-day 100 mg/kg IVIG

Am J Transplant 2016;16:3468-78.

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Parameter	Treatment group		
	Placebo (n = 7)	C1 INH (n = 7)	All patients (n = 14)
Age (years)			
Mean ± SD	52.3 ± 11.4	46.4 ± 10.9	49.4 ± 11.2
Sex, n (%)			
Female	5 (71)	5 (71)	10 (71)
Male	2 (29)	2 (29)	4 (29)
Weight (kg)—female			
Mean ± SD	66.6 ± 19.2	79.5 ± 22.2	73.1 ± 20.7
Weight (kg)—male			
Mean ± SD	87.4 ± 9.8	84.1 ± 8.3	85.8 ± 7.7
Race, n (%)			
Black or African American	1 (14)	3 (43)	4 (29)
White	6 (86)	4 (57)	10 (71)
Primary cause of renal failure, n (%)			
Glomerulonephritides	3 (43)	3 (43)	6 (43)
Hypertension	1 (14)	2 (29)	3 (21)
Congenital defect	2 (29)	0	2 (14)
Diabetes (type 1 or type 2)	0	1 (14)	1 (7)
Unknown	1 (14)	0	1 (7)
Unknown—presumed chronic pyelonephritis	0	1 (14)	1 (7)

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Total number of lifetime kidney transplants, n (%)	3 (43)	0	3 (21)
1	1 (14)	7 (100)	8 (57)
2	2 (29)	0	2 (14)
3	1 (14)	0	1 (7)
4	1 (14)	0	1 (7)
Total number of PP sessions in the 14 days before transplant through 14 days posttransplant			
Mean ± SD	10.7 ± 4.0	11.7 ± 3.2	11.2 ± 3.5
Subjects with prior splenectomy, n	0	0	0
Day since current transplant, n (%)			
-30	6 (86)	7 (100)	13 (93)
90-365	1 (14)	0	1 (7)
Type of current transplant, n (%)			
Living donor	6 (86)	6 (86)	12 (86)
Deceased donor	1 (14)	1 (14)	2 (14)
Subjects with ABO-incompatible transplant	4 (57)	3 (43)	7 (50)
Lowest serum creatinine (mg/dL) value within 30 days after transplant (before qualifying episode of AMR)			
Mean ± SD	0.9 ± 0.4	1.3 ± 0.5	1.1 ± 0.5
Highest serum creatinine (mg/dL) value on day of qualifying renal allograft biopsy (± 2 days)			
Mean ± SD	1.5 ± 0.8	1.7 ± 0.4	1.6 ± 0.6
Subjects needing dialysis within 14 days before the first dose of study drug, n (%)	0	3 (43)	3 (21)
Subjects needing dialysis within 14 days after transplant, n (%)	1 (14)	0	1 (7)
Specificity of DSA closest to and within ± 7 days of the qualifying biopsy			
HLA class I, n (%)	6 (86)	7 (100)	13 (93)
HLA class II, n (%)	6 (86)	5 (71)	11 (79)

Am J Transplant 2016;16:3468-78.

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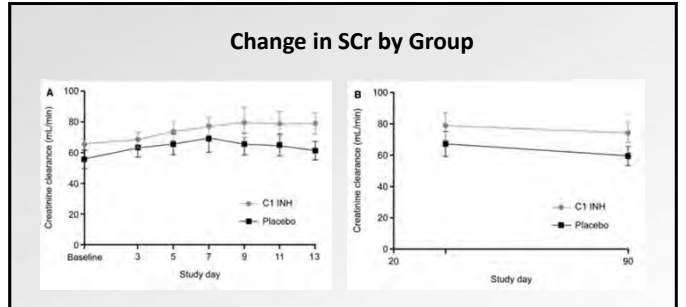


Table 4: Change in histopathology scores from qualifying biopsy to day-20 biopsy

Histopathology end point	Placebo (n = 9)			C1 INH (n = 9)			p-value for treatment difference ¹
	Qualifying biopsy	Day-20 biopsy	Change	Qualifying biopsy	Day-20 biopsy	Change	
C4d score							
Mean ± SD	60.8 ± 41.2	15.8 ± 32.9	-45.0 ± 46.9	68.7 ± 41.8	32.6 ± 39.1	-36.1 ± 33.4	0.6498
Margination score							
Mean ± SD	23.0 ± 24.8	17.0 ± 25.8	-6.0 ± 14.0	9.2 ± 15.2	21.8 ± 29.3	12.6 ± 25.9	0.0768
Glomerulitis score							
Mean ± SD	17.0 ± 24.9	23.7 ± 30.9	6.7 ± 26.6	16.3 ± 23.4	19.0 ± 28.8	2.7 ± 13.6	0.6928
Vasculitis score							
Mean ± SD	3.9 ± 7.8	0 ± 0.0	-3.9 ± 7.8	0 ± 0.0	3.2 ± 6.4	3.2 ± 6.4	0.0508
Glomerulosclerosis score							
Mean ± SD	4.2 ± 6.8	2.8 ± 3.6	-1.4 ± 7.8	8.9 ± 9.6	2.6 ± 4.3	-6.3 ± 7.9	0.2042
Chronic glomerulopathy score							
Mean ± SD	0.3 ± 1.0	0.6 ± 1.7	0.2 ± 0.7	0 ± 0.0	0 ± 0.0	0 ± 0.0	0.3322
Interstitial fibrosis score							
Mean ± SD	3.2 ± 6.6	9.1 ± 14.1	5.9 ± 9.8	0.7 ± 1.3	12.2 ± 20.4	11.6 ± 20.9	0.4723
Chronic vasculitis score							
Mean ± SD	8.3 ± 12.8	6.7 ± 11.7	-1.7 ± 18.2	2.6 ± 4.5	5.4 ± 7.7	2.9 ± 9.0	0.5103

Am J Transplant 2016;16:3468-78.

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6 Month Punch Biopsy in Hopkins Cohort

- C1e group 0/7 TG+
- Placebo group 3/7 TG+

Am J Transplant 2016;16:3468-78.

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Preventing Fibrosis with Novel Therapies

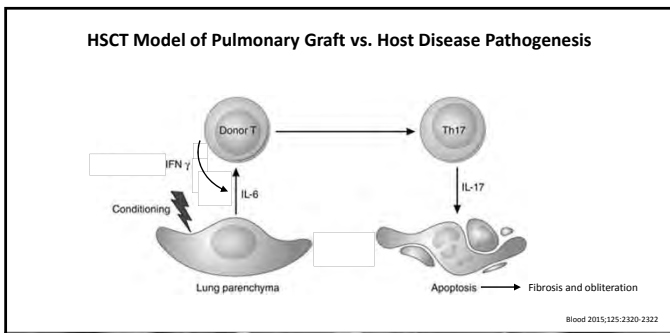
© 2017 The American Society of Transplantation and Kidney Disease. In part of Transplant Surgery. doi: 10.1111/1365-3113.14278

Assessment of Tocilizumab (Anti-Interleukin-6 Receptor Monoclonal) as a Potential Treatment for Chronic Antibody-Mediated Rejection and Transplant Glomerulopathy in HLA-Sensitized Renal Allograft Recipients

J. Chai¹*, O. Aubert², A. Vo³, A. Loupy⁴, M. Haast⁵, D. Paliyanda¹, J. Kim¹, S. Louie¹, A. Kang¹, A. Peng¹, J. Kahwaji¹, N. Reinsmoen⁶, M. Toyoda⁷ and S. C. Jordan¹

Am J Transplant 2017;17:2381-9.

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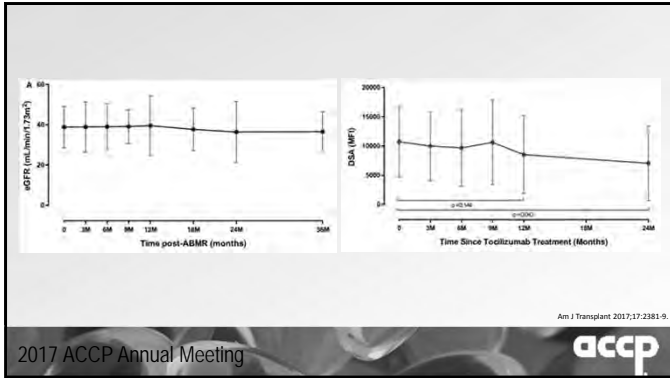
Table 1: Characteristics of chronic active antibody-mediated rejection patients with tocilizumab treatments

	N	Patients
Recipient characteristics		
Age (yr), mean (SD), year	36	45.66 (16.64)
Gender male, No. (%)	36	19 (52.78)
Graft age <1, No. (%)	36	17 (47.22)
Donor characteristics		
Deceased donor, No. (%)	36	20 (55.56)
Extended-criteria (donor, No. (%)	36	1 (2.78)
Cold ischemia time >24 hr, No. (%)	36	2 (5.56)
Delayed graft function ¹ , No. (%)	36	6 (16.67)
Immunology at the time of transplantation		
HLA mismatches, mean (SD)	26 ²	4.07 (1.46)
Anti-HLA DSA positive, No. (%)	26 ²	18 (69.23)
Time from transplantation to treatment, mean (SD), year	39	6.72 (4.63)
Immunology at the time of AMR		
Anti-HLA DSA ³ , No. (%)	36	33 (91.67)
Anti-angiotensin type 1 receptor antibody ⁴ /DSA ³ , No. (%)	36	3 (8.33)
Number of anti-HLA DSAs, mean (SD)	33 ²	1.91 (1.26)
Number of class 1, mean (SD)	33 ²	0.43 (0.60)
Number of class 2, mean (SD)	33 ²	1.45 (0.94)
Renal function at the time of AMR		
eGFR, mean (SD), mL/min/1.73 m ²	36	48.43 (34.58)
eGFR for adult patients, mean (SD), mL/min/1.73 m ²	32	36.82 (10.37)
eGFR for pediatric patients, mean (SD), mL/min/1.73 m ²	4	77.63 (25.88)
Follow-up (yr), mean (SD), year	36	3.26 (2.04)
Graft loss, No. (%)	36	4 (11.11)
Received >2 AMR treatment sessions before tocilizumab, No. (%)	36	33 (91.67)

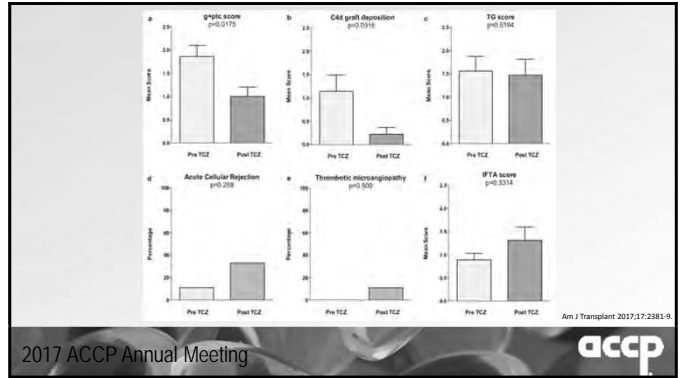
Am J Transplant 2017;17:2381-9.

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Novel Therapeutic Paradigm Shift in AMR

Current paradigm: AMR treatment is episodic and only targeted at DSA and supporting cellular infrastructure

Novel paradigm: AMR is both an acute and chronic disease requiring long-term therapy targeted at DSA, arresting injury, and preventing fibrosis

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Questions

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Antibody-Mediated Rejection: No! The Risks and Costs of Novel Agents Outweigh Their Benefit

Lisa Potter, PharmD, BCPS, FCCP, FAST
Clinical Coordinator, Transplant Pharmacy Services
University of Chicago Medicine
October 7, 2017

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No! Risks and Costs Outweigh the Benefit

Objectives

- Compare the effectiveness, risks, and costs associated with each agent/regimen used in AMR treatment
- Design a treatment regimen, using the specifics of your institution, transplant population, and ability to take risk

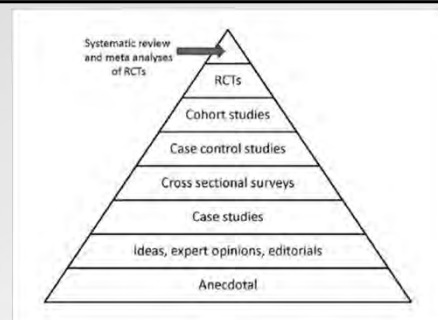
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Plasmapheresis, IVIG, rituximab,
bortezomib, carfilzomib, eculizumab...

How hard have you looked?
(i.e. How good is your evidence?)

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KDIGO Clinical Practice Guidelines (2009)

6.4: We suggest treating antibody-mediated acute rejection with one or more of the following alternatives, with or without corticosteroids (2C):

- Plasma exchange
- Intravenous immunoglobulin
- Anti-CD20 antibody
- Lymphocyte depleting antibody

6.5: For patients who have a rejection episode, we suggest adding mycophenolate if the patient is not receiving mycophenolate or azathioprine, or switching azathioprine to mycophenolate (2D)

Kasiske BL, et al. *Kidney Int* 2009; 100: 391-399.

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Table 1 | KDIGO nomenclature and description for grading recommendations

Grade*	Patients	Implications	Policy
Level 1 We recommend†	Most people in your situation would want the recommended course of action and <small>with a small exception would not</small>	Most patients should receive the recommended course of action.	The recommendation can be adopted as a policy in most situations.

Level 2 We suggest†	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require debate and involvement of stakeholders before policy can be determined.
------------------------	---	---	---

Table 2 | Final grade for overall quality of evidence

A: High quality of evidence. We are confident that the true effect lies close to that of the estimate of the effect.

B: Moderate quality of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially

C: Low quality of evidence. The true effect may be substantially different from the estimate of the effect.

D: Very low quality of evidence. The estimate of effect is very uncertain, and often will be far from the truth.

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ISHLT Heart Transplant Guidelines (2010)

- Initial therapy of AMR can include immunoadsorption and corticosteroid (CS) or plasmapheresis/low dose of IVIg and CS. (Class IIa, LOE C)
- Rituximab can be added to reduce the risk of recurrent rejection. (Class IIa, LOE C)
- Changes in therapy, which can be considered for maintenance immunosuppression in patients who experience AMR, can include switch to tacrolimus in patients receiving cyclosporine, increased doses of mycophenolate, and CS. (Class IIa, LOE C)

Costanzo MR, et al. *J Heart Lung Transpl* 2010; 29: 914-956.

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Plasmapheresis, IVIG, rituximab, bortezomib, carfilzomib, eculizumab...

How reliable are these treatments?

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Rituximab in Kidney Transplantation: Systematic Reviews of Efficacy for AMR

Author	Study Details	Outcomes	Limitations
Macklin et al.	AAMR: 18 records relating to 9 studies (2 syst reviews), 1 RCT, 6 retrospect comp CAMR: 10 records relating to 7 retrospective comparative studies	5/7 report improved graft outcomes 2/7 report no difference 1/7 report improved graft outcomes 3/7 report no difference 3/7 report inferior outcomes	Positive results were limited to studies w/multiple doses 1/14 report more AEs
Roberts et al.	AAMR: 5 RCT 7 nonrandomized controlled trials	Limited by marked heterogeneity in definition of AMR, severity of AMR, and treatment regimen	Data is of low or very low quality
Hychko et al.	AMR: 10 studies (94 of 114 studies were excluded)	OR 3.16 (95%CI: 1.75-5.70)	Positive results AEs include BK nephropathy, CMV viremia, pneumonia, HZV, septic shock

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Bortezomib in Kidney Transplantation: Role for AMR

	Group 1 (n=10): Bortez 1.3 mg/m ² x4	Group II (n=9): Rituximab 500 mg x1
Acute / Chronic AMR (n)	7 / 3	6 / 3
Mean SCr at 9 months (mg/dL)	2.5 ± 0.6	5.1 ± 2.1
Mean eGFR at 9 months (ml/min)	31.1 ± 9.5	12.3 ± 4.7
Proteinuria >1 g/day at baseline	50%	44%
Proteinuria >1 g/day at 9 months	No change	No change
Graft loss at 18 months	40% (4/7 acute, 0/3 chronic)	89% (5/6 acute, 3/3 chronic)

Waiser J, et al. *Nephrol Dial Transpl* 2012; 27: 1246-1251.

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Bortezomib in Kidney Transplantation: Role for late AMR

	Group 1 (n=10): PE + rituximab	Group 2 (n=8): bortezomib	Group III (n=10): Optimized maintenance
Mean time to rejection (yr)	5.7	5.0	6.8
Mean MFI for immunodominant DSA	9,162 ± 4,877	10,054 ± 5,286	10,410 ± 5,381
Mean eGFR at baseline (ml/min)	29.1 ± 10.1*	38.3 ± 12.7	36.8 ± 18.4
Mean eGFR at 12 months (ml/min)	24.8 (ACR-); (ACR+)	32.2	25.2
Proteinuria at baseline (g/day)	1.28 ± 1.4	1.2 ± 1	2.62 ± 2.3
Proteinuria at 12 months (g/day)	1.33	0.83 ± 0.59	2.84 ± 2.48
Graft loss at 12 months	50% (ACR+)	0%	20%

Touzot M, et al. *Transplantation* 2015; 99: 63-68.

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Bortezomib in Kidney Transplantation: An Upcoming Trial

STUDY PROTOCOL

Open Access

Bortezomib in late antibody-mediated kidney transplant rejection (BORTEJECT Study): study protocol for a randomized controlled trial

Farsad Iskandary¹, Gregor Bond¹, Elisabeth Schwaiger², Zeljko Kikic³, Christine Winer², Markus Wahmann¹, Lena Mannova¹, Helmut Haslacher⁴, Heinz Regele⁵, Rainer Oberbauer⁴ and Georg A Böhmig⁷

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Carfilzomib in Lung Transplantation

Zeevi A, et al <i>Clin Transpl</i> 2013: 399-405	Case report, n=1 Plasma exchange, IVIG, carfilz	
Ensor C, et al. <i>Am J Transplant</i> 2017; 17: 1380-8	Observational study, n=14 Plasma exchange, IVIG, carfilz	10 (71%) responded DSA MFI fell 7664 -> 1878 -> 1400 DSA C1q MFI fell 3596 -> <30 -> <30 50% mortality due to graft failure

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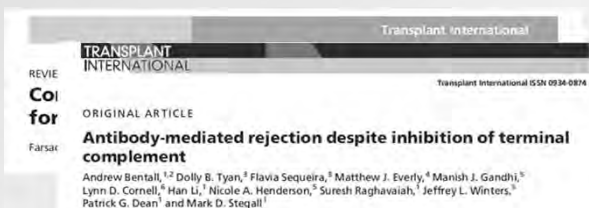
Eculizumab



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Eculizumab



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IVIg, plasmapheresis, rituximab, bortezomib, carfilzomib, eculizumab...

Finding the risk/benefit balance

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Risks and Toxicities

Plasmapheresis		
Plasma exchange	Increases bleeding risk due to nonselective protein removal	
Double-filtration plasmapheresis	Increases bleeding risk due to nonselective protein removal	
Immunoadsorption	Does not remove circulating cytokines, which may play a role	
Rituximab	Possible increase in infectious outcomes	
Bortezomib	Risk for neuropathy	
Carfilzomib		
Eculizumab		

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IVIg, plasmapheresis, rituximab, bortezomib, carfilzomib, eculizumab...

What are the costs? What is the value?

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AMR Treatment Costs

- Plasmapheresis: \$5875 per session
- Gammagard: \$1567.56 per 10g; \$3135.12 per 20g; etc.
- Rituximab: \$1042.36 per 100 mg
- Bortezomib: \$1923.60 per 3.5 mg
- Carfilzomib: \$1229.03 per 30 mg; \$2458.06 per 60 mg
- Eculizumab: \$7696.80 per 300 mg (10 mg/ml x30 ml)

Pricing data is from Lexi-Comp*. Accessed Sept 4, 2017. Updated monthly.

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Variable	Estimate (CI)	Range	% Occurrence	Source (Reference number)
Plasma Exchange Costs				
1 Exchange	2980			University of Rochester Billing Office
1 Hour Apheresis	1119			University of Rochester Billing Office
Cofactor	520			University of Rochester Billing Office
Cofactor Placement	850			University of Rochester Billing Office
Plasma Lab Test	44			University of Rochester Billing Office
Cofactor Removal	323			University of Rochester Billing Office
Plasma Exchange				
Death	4700000	0-82%	0.02	16,14
Side Effect % and Costs				
Bleeding	443		4.9	% The University of Rochester Billing Office
Cofactor Depletion	1713		2.4	% University of Rochester Billing Office
Nausea	466		2.4	% Lexi-Comp
Hypotension	14.9		4.8	% Lexi-Comp
DVT	4100		2.4	% Lexi-Comp, The University of Rochester Billing Office
Infection	1506		4.9	% Lexi-Comp, The University of Rochester Billing Office
Plasma Exchange Hospital Days				
ICU	17.4	10-17.4		8,11,12
Non-ICU	8.3			8,11,12
Number of Exchanges Required				
ICU cost	2463			University of Rochester Billing Office
Hospital Cost/Day				
ICU professional fee	755			University of Rochester Billing Office
Non-ICU hospital cost	1010			University of Rochester Billing Office
Non-ICU professional fee	280			University of Rochester Billing Office

Heatwole Cet al. J Clin Neuromuscul Dis 2011; 13: 85-94.

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Bortezomib in Kidney Transplantation: Role for late AMR

	Group I (n=10): Bortez 1.3 mg/m2 x4	Group II (n=9): Rituximab 500 mg x1
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Mean eGFR at 9 months (ml/min)		
Proteinuria >1 g/day at baseline		
Proteinuria >1 g/day at 9 months	No change	No change
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\$7,694 **\$5,212**

Waiser J, et al. Nephrol Dial Transpl 2012; 27: 1246-1251.

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Carfilzomib

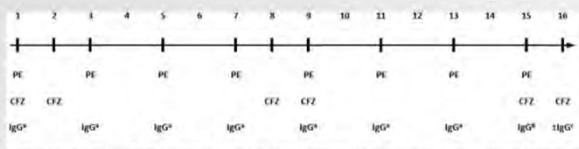
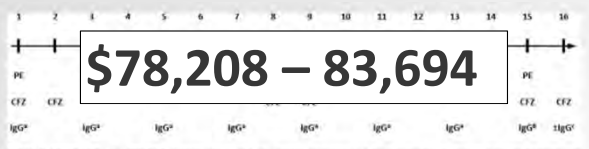


Figure 2. CFZ-based AMR regimen. Sixteen-day course. PE, plasma exchange (1.5 plasma volume exchanges/session) replaced with 5% albumin and/or fresh frozen plasma; CFZ, carfilzomib 20 mg/m²; IgG, intravenous immunoglobulin G (Gammagard Liquid, 10%); *100 mg/kg; †500 mg/kg; ‡500 mg/kg if serum IgG level <700 mg/dL. Order of therapy: PE, CFZ, intravenous immunoglobulin G on days where all three are administered. CFZ doses were administered over 10-30 min and premedicated with sodium chloride 0.9% 250 mL bolus, acetaminophen 650 mg, diphenhydramine 25-50 mg, ondansetron 4 mg, and prednisone 40 mg. IgG doses were premedicated with acetaminophen 650 mg and diphenhydramine 25-50 mg. AMR, antibody-mediated rejection.

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Carfilzomib



\$78,208 – 83,694

Figure 2. CFZ-based AMR regimen. Sixteen-day course. PE, plasma exchange (1.5 plasma volume exchanges/session) replaced with 5% albumin and/or fresh frozen plasma; CFZ, carfilzomib 20 mg/m²; IgG, intravenous immunoglobulin G (Gammagard Liquid, 10%); *100 mg/kg; †500 mg/kg; ‡500 mg/kg if serum IgG level <700 mg/dL. Order of therapy: PE, CFZ, intravenous immunoglobulin G on days where all three are administered. CFZ doses were administered over 10-30 min and premedicated with sodium chloride 0.9% 250 mL bolus, acetaminophen 650 mg, diphenhydramine 25-50 mg, ondansetron 4 mg, and prednisone 40 mg. IgG doses were premedicated with acetaminophen 650 mg and diphenhydramine 25-50 mg. AMR, antibody-mediated rejection.

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In Sum

- One size does not fit all!
- The data is all over the place
 - Inconsistent definitions, inconsistent diagnosis
 - Inconsistent treatment regimens / doses / durations
 - Small and varied studies
- It's time to collaborate
 - Treatment consortia
 - One question at a time, and replicate

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ACCP

Solid Organ Transplantation in HIV- or HCV-Infected Recipients: Controversies in Patient Management

Solid Organ Transplantation in HIV- or HCV-Infected Recipients: Controversies in Patient Management

Activity Number: 0217-0000-17-132-L02-P, 1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Saturday, October 7, 2017

9:45 a.m. to 11:15 a.m.

Phoenix Convention Center North Bldg. Street Level: Meeting Room 122

Moderator: Maya Campara, Pharm.D., BCPS

Clinical Pharmacist, Solid Organ Transplant, University of Illinois Hospital and Health Science System, Chicago, Illinois

Agenda

- 9:45 a.m. HIV/HCV-Infected Donors—The New Frontiers in Solid Organ Transplantation
Lindsey A. Pote, Pharm.D., BCPS
Liver Transplant Clinical Pharmacy Specialist; Solid Organ Transplantation Residency Program Director, The John Hopkins Hospital, Baltimore, Maryland
- 10:15 a.m. Organ Transplantation in HIV-Positive Patients
Shellee A. Grim, Pharm.D., BCPS
Adjunct Clinical Associate Professor, University of Illinois at Chicago; Clinical Pharmacy Specialist, Loyola University Medical Center, Chicago, Illinois
- 10:45 a.m. The New Frontier: HCV Treatment and Management Following Organ Transplantation
Juliana Chan, Pharm. D., FCCP, BCACP
Clinical Associate Professor, University of Illinois at Chicago, College of Pharmacy; Clinical Pharmacist, University of Illinois Medical Center, Chicago, Illinois

Conflict of Interest Disclosures

Maya Campara: No conflicts to disclose

Juliana Chan: Consultancies: (OptumRx)

Shellee A. Grim: Consultancies: (Astellas Pharma US, Inc.)

Lindsey A. Pote: No conflicts to disclose

Learning Objectives

1. Describe the use of HIV/HCV infected donors as a method to alleviate the growing demand for organ donors (HIV Organ Policy Equity (HOPE) Act, various HCV donor protocols).
2. Define the criteria for use of HIV-infected donors in solid organ transplantation and describe efficacy/safety outcomes.
3. Define the criteria for use of HCV-infected donors in solid organ transplantation and describe efficacy/safety outcomes.
4. Describe safety and efficacy outcomes SOT in HIV-infected recipients.
5. Review considerations for management of antiretroviral therapy in transplant patients with HIV.
6. Discuss complications of solid organ transplantation in patients with HIV.
7. Describe safety and efficacy outcomes SOT in HCV-infected recipients.
8. Discuss HCV management following solid organ transplantation.

9. Describe advantages and disadvantages of HCV treatment options in SOT recipients, including cost and reimbursement issues.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/am.

HIV/HCV Infected Donors – The New Frontiers in Solid Organ Transplantation

Lindsey A. Pote, PharmD, BCPS
Clinical Pharmacist Specialist, Solid Organ Transplantation
The Johns Hopkins Hospital

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Financial Disclosures

- I have no relevant financial relationships or commercial interests to disclose for this presentation.
- This continuing education activity contains discussion of published and/or investigational uses that are not indicated by the FDA.

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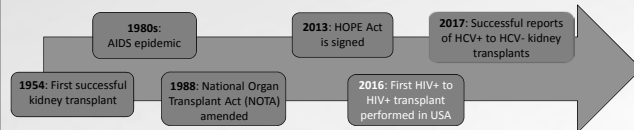
Objectives

- Describe the use of HIV/HCV infected donors as a method to alleviate the growing demand for organ donors
- Define the criteria for use of HIV-infected donors in solid organ transplantation
 - Describe efficacy and safety outcomes
- Define the criteria for use of HCV-infected donors in solid organ transplantation
 - Describe efficacy and safety outcomes

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History of HIV and HCV in Transplantation



<https://www.unos.org/transplantation/history>
<https://www.aids.gov/hiv-aids/basics/hiv-aids-101/aids-timeline/>

<https://pub.jhu.edu/2016/07/31/first-hiv-to-hiv-transplant-hiv-positive/>
<http://www.philly.com/philly/health/health-news/Penn-Medicine-Hopkins-UNOS-transplant-hepatitis-Dopacer-Merck-Gilead-harvoni-dialysis.html>

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HIV New Frontier

- Antiretroviral therapy (ART) significantly improved life expectancy of patients with HIV
- Chronic illnesses cause more death than opportunistic infections
- HIV+ transplant candidates have higher waitlist mortality than HIV- transplant candidates



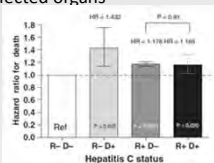
Stock PG, et al. N Engl J Med 2010; 363: 2004-14.
Rodriguez RA. J Am Soc Nephrol 2003; 14 1307-1313.

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HCV New Frontier

- Good outcomes demonstrated in HCV+ recipients receiving HCV+ infected organs
- Significant improvement in sustained viral response (SVR) with direct acting antivirals (DAA)
 - Pre-transplant treatment:
 - SVR12 approximately 95%
 - Post-transplant treatment:
 - SVR range from 70-96%



Curry MP. Gastroenterology 2015; 148 (100-107): e1.
Northrup PG. Transl Int 2010; 23:1038-1044.

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The Need Continues to Grow

Year	Waiting at year end	Transplants performed	Donors recovered
2003	83,731	25,473	13,285
2006	94,441	28,940	14,750
2009	105,567	28,459	14,632
2012	117,040	28,053	14,010
2015	122,071	30,975	15,068

<https://optn.transplant.hrsa.gov/need-continues-to-grow/>

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Expansion of the Donor Pool in America

Historical Advancements

- Expanded criteria donors (ECD)
- Donation after cardiac death (DCD)
- Public Health Service (PHS) increased risk donors
- Hepatitis B virus core antibody positive (HBcAb+) donors

Current Initiatives

- Increase use of HCV-infected organs
 - HCV negative recipients
 - Utilization in non-liver transplant recipients
- Increase use of HIV+ donors in HIV+ recipients
- Strategies for safely using organs from persons who inject drugs (PWID)

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Development of Criteria for Use of HIV-Infected Donors

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Thinking Outside the Box

- South Africa's HIV to HIV Transplant Experience
 - HIV associated nephropathy (HIVAN) - primary cause of end stage renal disease (ESRD)
 - Limited dialysis resources
 - ↓ availability of deceased donors and ↑ rates of HIV infection among donors
 - Safety and effectiveness of HIV+ to HIV+ kidney transplant was unknown
- In 2008, performed 4 kidney transplants involving HIV infected donors and HIV infected recipients

Muller E, et al. N Engl J Med 2010; 362 (24): 2336-2337.

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Considering HIV+ to HIV+ Transplants in America

Table 1: Key differences in epidemiology of HIV infection between South Africa and United States

	South Africa	United States
Population	53 million	316 million
Estimated living with HIV infection	5.6 million	1.1 million
HIV prevalence (15-49 years old)	17.8%	0.6%
Predominant subtype	HIV-1, Group M, Subtype C	HIV-1, Group M, Subtype B
Estimated annual deaths among HIV+	310,000	17,000
Transmitted drug resistance*	<5%	10-18%
Transplant waiting list†	4300	123,992
Kidney transplants performed 2013	229	16,696

HIV, human immunodeficiency virus; HIV+ = HIV-infected; HIV-, HIV-uninfected.

*Transmitted drug resistance in newly infected individuals.

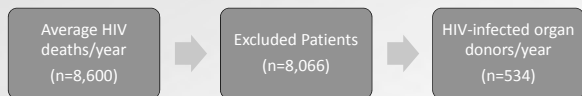
†These statistics include both HIV- and HIV+ patients. In the United States, the number of HIV+ patients on the waiting list is unknown.

Boyersky BI, et al. Am J Transplant 2015; 15: 2023-2030.

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Potential Resource of HIV-Infected Donors

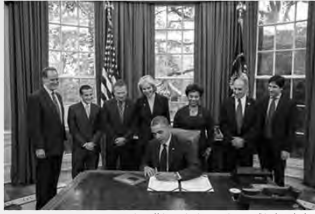


Boyersky BI, et al. Am J Transplant 2011; 11: 1209-1217.

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HIV Organ Policy Equity (HOPE) Act



<https://obamawhitehouse.archives.gov/blog/2013/11/21/hiv-organ-policy-equity-hope-act-now-law>

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Using HIV-Infected Donors in Solid Organ Transplantation

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South African Experience: 3-5 Year Outcomes

Characteristic	Patients (N=27)
Age—yr	
Median	43
Interquartile range	28-43
Male sex—no (%)	13 (48)
Race—no (%)	
Black	26 (96)
Mixed race	1 (4)
ART regimen—no (%)	
Protease inhibitor-based therapy	11 (41)
NRTI-based therapy	16 (59)
Anti-HIV induction therapy†	
ATC	
No. of patients (%)	10 (37)
Cumulative dose—mg	
Median	413
Interquartile range	406-750
Thymoglobulin	
No. of patients (%)	17 (63)
Cumulative dose—mg	
Median	600
Interquartile range	450-1000

- HIV-positive recipients
 - CD4 T-cell counts $\geq 200/\text{mm}^3$
 - Undetectable plasma HIV RNA level
 - Antiretroviral therapy (ART)
- HIV-positive deceased donors
 - Test positive for HIV at time of referral using 4th generation enzyme-linked immunosorbent assay
 - No previous ART or only first line ART

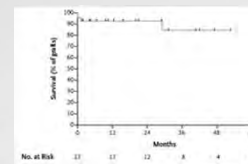
Muller E, et al. N Engl J Med 2015; 372 (7): 613-620.

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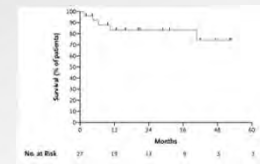


South African Experience: Results at 3-5 Years

Graft Survival



Patient Survival



Muller E, et al. N Engl J Med 2015; 372 (7): 613-620.

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South African Experience: CD4 Results at 3-5 Years

- 8 episodes of biopsy-proven acute rejection
 - Occurred in 5 patients
- Rejection rates
 - 8% at 1 year
 - 22% at 3 years
- Majority of cases were reversed with treatment

Muller E, et al. N Engl J Med 2015; 372 (7): 613-620.

Time from Transplantation to Rejection Episode	Treatment	Outcome
	Medication or Other Treatment	Total Dose
Patient 5	Methylprednisolone	200 mg
7 yr	ATC	750 mg
Patient 7	Methylprednisolone	200 mg
1 yr 7 mo	Methylprednisolone	200 mg
Patient 9	Methylprednisolone	200 mg
4 mo	Methylprednisolone	200 mg
1 yr 9 mo	Methylprednisolone	200 mg
Patient 17	Thymoglobulin and plasmapheresis	800 mg
1 wk	Thymoglobulin and plasmapheresis	100 mg
Patient 27	Thymoglobulin and plasmapheresis	100 mg
1 wk	Thymoglobulin and plasmapheresis	100 mg

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Pharmacologic Considerations

Immunosuppression:

- Induction therapy
 - Rabbit antithymocyte globulin or Equine antithymocyte globulin
- Maintenance regimen
 - Tacrolimus
 - Mycophenolate mofetil
 - Prednisone

Antiretroviral Therapy:

- NNRTI*-based regimens switched to boosted protease inhibitor-based regimens
 - To further suppress the donor-virus replication
 - To lower cost of antirejection medications based on drug-drug interaction
- Due to concerns of tacrolimus nephrotoxicity, this practice was discontinued

Muller E, et al. N Engl J Med 2015; 372 (7): 613-620.

*NNRTI = Nonnucleoside Reverse-Transcriptase Inhibitor

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Current Practice in America

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HOPE in Action

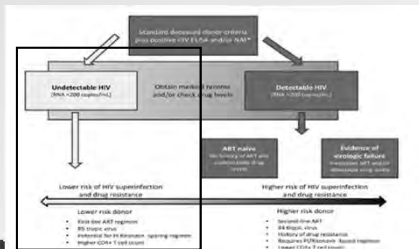
- New York Presbyterian Hospital/Weill Cornell Medical Center
- University of Colorado Hospital/Health Science Center
- Duke University Hospital
- Montefiore Medical Center
- VCU Medical Center
- University of Minnesota
- New York Presbyterian Hospital/Columbia University Medical Center
- Johns Hopkins Hospital
- Hahnemann University Hospital
- Mount Sinai Medical Center
- University of California San Francisco Medical Center
- University of Alabama Hospital
- Yale New Haven Hospital
- Emory University Hospital
- Indiana University Health
- Georgetown University Medical Center
- Rush University Medical Center
- Massachusetts General Hospital
- Methodist Dallas Medical Center
- University of Maryland Medical System

<https://optn.transplant.hrsa.gov/learn/professional-education/hope-act/>

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HIV+ Deceased Donor Selection Criteria



Boyarsky BJ, et al. Am J Transplant 2015; 15: 2023-2030.

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Clinical Experience

	Patient #1	Patient #2
Age at time of transplant, years	49	62
Sex	Female	Female
Cause of end stage disease	Hepatitis C Virus	Hepatitis C Virus
Type of organ transplant	Liver	Simultaneous Liver-Kidney
Donor information	35 year old, HIV Ab+, NAT negative	37 year old, HIV Ab+, NAT negative
HIV labs prior to transplant	CD4 - 1183; Viral load undetectable	CD4 - 588; Viral load undetectable
HIV regimen prior to transplant	Etravirine, Raltegravir, Abacavir-Lamivudine	Darunavir, ritonavir, raltegravir

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HIV+ to HIV+ Liver Transplant Experience

	Patient #1	Patient #2
HIV Regimen after Transplant	Emtricitabine-tenofovir alafenamide, dolutegravir	Emtricitabine-tenofovir alafenamide, dolutegravir
Induction Therapy	None	Basiliximab
Maintenance Immunosuppression Regimen	- Tacrolimus - Mycophenolate mofetil - Prednisone	- Tacrolimus - Mycophenolate mofetil - Prednisone
Recent HIV labs	April 2017 CD4 592; Undetectable Viral Load	August 2017 CD4 548; Undetectable Viral Load
Liver Function Tests	August 2017 Tbili < 0.2; AlkPhos 156 AST/ALT 20/17	August 2017 Tbili < 0.2; AlkPhos 66 AST/ALT 8/10

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Development of Criteria for Use of HCV-Infected Donors

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American Journal of Transplantation 2017; 17: 1421-1431
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doi: 10.1111/ajt.14281

Meeting Report

The American Society of Transplantation Consensus Conference on the Use of Hepatitis C Viremic Donors in Solid Organ Transplantation

J. Levitsky^{1,2*}, R. N. Formica^{3,4}, R. D. Bloom⁵, M. Charlton⁶, M. Curry⁷, J. Friedewald⁸, J. Friedman⁹, D. Goldberg¹⁰, S. Hall¹¹, M. Ison¹², T. Kaiser¹³, D. Klassen¹⁴, G. Klitnalm¹⁵, J. Kobashigawa¹⁶, A. Liapakis¹⁷, K. O'Connor¹⁸, P. Reese¹⁹, D. Stewart²⁰, N. Terrault²¹, N. Theodoropoulos²², J. Trotter²³, E. Verina²⁴ and M. Volk²⁵

need for scientific study and consensus, the American Society of Transplantation convened a meeting of experts to review current data and develop the framework for the study of using HCV viremic organs in solid organ transplantation.

Abbreviations: CDC, Centers for Disease Control and Prevention; ChIA, chemiluminescence assay; CKD, chronic kidney disease; DAA, direct-acting antiviral agent; EIA, enzyme immunoassay; ESRD, end-stage renal disease; FDA, Food and Drug Administration.

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HCV Testing in Relation to Exposure

Levitsky J, et al. Am J Transplant 2017. [epub ahead of print].

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Redefining Hepatitis C “Positive” Donor

Donor HCV Serostatus	Donor NAT Status	Clinical Implication
Positive	Negative	<ul style="list-style-type: none"> Non-viremic Spontaneously cleared, successfully treated, or false positive antibody
Positive	Positive	<ul style="list-style-type: none"> Viremic Acute infection with high risk of HCV transmission
Negative	Positive	<ul style="list-style-type: none"> Viremic Usually indicates acute infection with high risk of HCV transmission
Negative	Negative	No HCV infection

Levitsky J, et al. Am J Transplant 2017. [epub ahead of print].

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Using HCV-Viremic Donors in Solid Organ Transplantation

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Proposed Donor Management Strategies

Levitsky J, et al. Am J Transplant 2017. [epub ahead of print].

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Selection of Candidates for HCV-Viremic Donors

Type of Candidate	Definition of Candidate's HCV Status	Advantages of Accepting HCV-Viremic Donor	Disadvantages of Accepting HCV-Viremic Donor
HCV Naïve	No history of being infected with HCV	<ul style="list-style-type: none"> May shorten time to transplant Reduce death on waitlist 	<ul style="list-style-type: none"> Financial constraints of DAA costs and insurance approval Risk versus benefit
HCV Resolved/Cured	Prior history of HCV infection, but now HCV NAT negative		
HCV Viremic	Currently, HCV NAT positive	<ul style="list-style-type: none"> Already an acceptable practice 	<ul style="list-style-type: none"> Minimal ethical concerns

Levitsky J, et al. Am J Transplant 2017. [epub ahead of print].

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Advancements in HCV-Infected Kidney Donation

Trial	THINKER (n=10)	EXPANDER-1 (n=8)
Organ	Kidney	Kidney
Donors	- HCV genotyping during allocation - Genotypes 1a or 1b only	HCV NAT positive
Recipients	HCV negative	HCV serostatus & NAT negative
Treatment	When HCV NAT was detected in the recipient, grazoprevir/elbasvir for 12 weeks	- Grazoprevir/elbasvir started pre-op and continued for 12 weeks - Sofosbuvir added for genotype 2 or 3
Outcomes	- SVR in all patients - Excellent allograft function in all patients - No adverse events related to treatment	- No HCV infection observed in recipients - No graft failure; 3 patients with DGF - Antivirals were well tolerated

Goldberg DS, et al. N Engl J Med 2017. [epub ahead of print]. Durand C, et al. Am J Transplant 2017; 17 (Supplement S3), Abstract 2.

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Results of THINKER Trial (n=10)

- 58 day median time from activation on the waitlist
- All 10 patients had detectable HCV RNA at post-op day 3
 - Undetectable within 4 weeks of HCV therapy
- All patients had excellent renal function

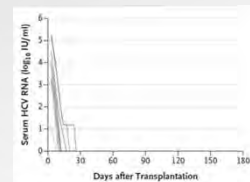


Figure 1. Hepatitis C Viral Load in 10 Kidney-Transplant Recipients.

Goldberg DS, et al. N Engl J Med 2017. [epub ahead of print].

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Results of EXPANDER-1 Trial (n=8)

- HCV RNA detected in four recipients on post-op day 1, but not after
 - Never detected in 4 recipients
- No graft failure observed
 - 3 patients with delayed graft function

Donor HCV Genotypes	Number of Patients
1a	2
Mixed 1a/3	1
3	1
Insufficient HCV	3

Durand C, et al. Am J Transplant 2017; 17 (Supplement S3), Abstract 2.

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Conclusions from THINKER and EXPANDER-1

- HCV treatment was well-tolerated by kidney transplant recipients
 - No adverse events related to HCV treatment in either study
- Both trials showed successful treatment of HCV infection after transplant
- Strategy appears to safely expand donor options
- Next steps:
 - Larger study sample size
 - Long-term outcomes

Goldberg DS, et al. N Engl J Med 2017. [epub ahead of print]. Durand C, et al. Am J Transplant 2017; 17 (Supplement S3), Abstract 2.

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Case Report: 57 YOF with HCV Cirrhosis (1a)

- HCV Treatment History
 - Previous non-responder to peginterferon based triple therapy with boceprevir
 - Completed 12 weeks course of sofosbuvir/simeprevir
 - Achieved SVR
- MELD 12
 - Decompensation caused by ascites
 - Waitlisted for approx. 3 years
- Disease Progression
 - Diagnosed with hepatopulmonary syndrome (HPS)
 - Granted MELD exception points (22)
 - No living donor candidates
 - Consideration of HCV RNA+ donors
 - Risks and benefits of allograft reviewed by transplant team
 - Extensive education provided to patient
 - Informed consent obtained

Saberi B, et al. Liver Transplant – Accepted manuscript online: 5 August 2017.

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HCV-Viremic Donor & Treatment Plan

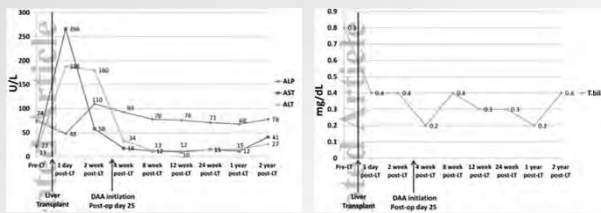
- 18 YOM high risk donor
 - Death from IV heroin overdose
 - HCV Ab negative
 - HCV RNA NAT+
- Liver biopsy showed
 - Moderate portal inflammation
 - Mild interface hepatitis
 - Minimal fibrosis without evidence of cirrhosis, micro- or macro-vesicular steatosis
- Genotype not reported
- Post-Liver Transplant Day #3
 - HCV genotype reported as 1a
 - HCV RNA quantified at 5,170,000 IU/mL
- HCV Treatment
 - Ledipasvir/Sofosbuvir x 24 weeks
 - Avoided ribavirin due to anemia
 - Initiated on post-operative day #25 after obtaining insurance approval
 - HCV RNA undetectable at 8 weeks
 - Achieved SVR

Saberi B, et al. Liver Transplant – Accepted manuscript online: 5 August 2017.

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Case Report: 2 Year Outcomes



Saberi B, et al. Liver Transplant – Accepted manuscript online: 5 August 2017.

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Final Thoughts...

- Use of HIV and HCV-infected donors has the potential to increase the supply of organs in the United States
- More clinical research is needed:
 - Larger study populations
 - Longer follow-up periods
 - Studies involving heart & lung transplant recipients
- Access to DAAs after transplant with HCV-viremic donors

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HIV/HCV Infected Donors – The New Frontiers in Solid Organ Transplantation

Lindsey A. Pote, PharmD, BCPS
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 The Johns Hopkins Hospital

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SOLID ORGAN TRANSPLANTATION IN HIV-POSITIVE PATIENTS

SHELLEE A. GRIM, PHARM.D, MS-CTS, BCPS

DISCLOSURES

- Shellee Grim, PharmD, MS-CTS has recently served on an advisory board for Astellas Pharma US, Inc.
- This presentation will include discussion of unapproved or "off-label" usage of commercial products and/or devices.

LEARNING OBJECTIVES

- Describe the safety and efficacy outcomes of solid organ transplant (SOT) in HIV-infected recipients
- Review considerations for management of antiretroviral (ARV) therapy in SOT recipients with HIV
- Discuss complications of SOT in patients with HIV

BACKGROUND

- Introduction of HAART in 1996 drastically changed epidemiology of HIV infection
 - Patients with HIV are living longer
 - Decrease in HIV-associated complications and opportunistic infections (OIs)
 - Increase in chronic diseases such as HIV nephropathy and cirrhosis
- Solid organ transplantation
 - In the early 2000s, first reports of successful SOT with ARVs
 - NIH study from 2003-09 for renal/liver SOT
 - Introduction of integrase inhibitors in 2008

Roland ME, Am J Transplant 2007;7:1; Volberding PA, Lancet 2010;376:49; Miro JM, Clin Microbiol Infect 2014;20(Suppl 7):119

OUTCOMES

- Patient and graft survival
- Allograft rejection
- Safety
 - HIV control
 - OI recurrence
 - AIDS-defining illness

SURVIVAL RENAL TRANSPLANTATION

Study	Population	N	Patient survival	Graft survival
Roland 2007	HIV+	18	94%	83%
Stock 2010	HIV+	150	88%	74%
Mazuecos 2011	HIV+	20	95%*	74%*
	HIV-	40	100%*	91%*
Locke 2015	HIV+/HCV-	362	92%	83%
	HIV-/HCV-	3620	94%	84%
	HIV+/HCV+	105	77%	63%
	HIV-/HCV+	1050	86%	77%

*5 year survival reported for Mazuecos study; other studies reported 3 year survival

Roland ME, Am J Transplant 2007;7:1; Stock PG, N Engl J Med 2010;363:2004; Mazuecos A, Nephrol Dialysis Transplant 2011;26:1401; Locke JE, J Am Soc Nephrol 2015;26:2222

SURVIVAL LIVER TRANSPLANTATION

Study	Population	N	Patient survival	Graft survival
Roland 2007	HIV+	11	64%	64%
Coffin 2010	HIV+/HBV+	22	85%	85%
	HIV-/HBV+	20	100%	100%
Terrault 2012	HIV+/HCV+	89	60%	53%
	*High risk	25	29%	20%
	Low risk	64	72%	65%
Sawinski 2015	HIV-/HCV+	235	79%	74%
	HIV-/HCV-	22926	76%	76%
	HIV+/HCV+	20829	66%	69%
*High-risk: BMI <21, combined liver/kidney transplant, HCV+ donor	HIV+/HCV-	72	67%	69%
	HIV+/HCV+	160	47%	55%

SURVIVAL

- Observational cohort comparison between HIV-infected patients undergoing transplant compared to HIV-infected SOT candidates
- Renal transplantation does not confer survival benefit
- Liver transplantation confers survival if the MELD score is 15 or greater

Roland ME, AIDS 2016;30:435.

OUTCOMES: REJECTION

- Rejection rates 2- to 3-fold higher than HIV-uninfected patients
- Etiology unclear
 - Innate immune system dysregulation from HIV infection
 - Decreased exposure to immunosuppressants secondary to drug interactions with ARVs
 - Less aggressive immunosuppression protocols given HIV infection

Roland ME, Am J Transplant 2007;7:1; Stock PG, N Engl J Med 2010;363:2004; Coffin CS, Am J Transplant 2010;10:1268; Terrault NA, Liver Transplantation 2012;18:716.

OUTCOMES: SAFETY

- Progression of HIV disease
 - Transient declines in CD4+ cell count post-transplant
 - HIV viral load generally well controlled with occasional transient episodes of HIV viremia (and less frequent persistent HIV viremia)
- Opportunistic infection/AIDS-defining illnesses uncommon when standard prophylaxis used
- Post-transplant bacterial infections occur similarly to HIV-uninfected patients

Roland ME, Am J Transplant 2007;7:1; Stock PG, N Engl J Med 2010;363:2004; Coffin CS, Am J Transplant 2010;10:1268; Terrault NA, Liver Transplantation 2012;18:716.

CONSIDERATIONS FOR TRANSPLANTATION IN HIV-INFECTED

- Consider NIH inclusion criteria prior to determining transplant candidate status
- Optimal immunosuppression
- Optimal ARV regimen
- Drug interactions
- Prophylaxis
- Management considerations

CRITERIA FOR SOT AMONG RENAL RECIPIENTS

- Undetectable HIV viral load on ARV regimen
- CD4+ cell count > 200 cells/mm³ for 3 months prior to transplantation
- History of adherence with stable ARV regimen
- Lack of active opportunistic infections, malignancy, and severe malnutrition
- If HBV/HCV-infected, lack of progression to advanced fibrosis/cirrhosis
- HCV-infected donors may be considered for HCV-infected recipients (RT and LTRs) on an individual basis
- Acceptance of lifelong PCP prophylaxis
- Appropriate follow up with HIV providers
- Access to immunosuppressive medication TDM

Stock PG, N Engl J Med 2010;363:2004

CRITERIA FOR SOT AMONG LIVER RECIPIENTS

- Same as renal transplant candidates with the following exceptions:
- Undetectable HIV viral load on ARV regimen **OR detectable viral load due to ARV intolerance related to ESLD but with HIV genotypic/phenotypic testing that is predictive of viral suppression with ARV therapy**
- CD4⁺ cell count > 200 cells/mm³ for 3 months prior to transplantation in patients with history of AIDS-defining illness **OR CD4⁺ cell count >100 cells/mm³ patients without history of opportunistic infection**

Coffin CS, Am J Transplant 2010;10:1268;
Terrault NA, Liver Transplantation 2012;18:716.

IMMUNOSUPPRESSION: USE OF ATG

- Carter et al. described the use of ATG among 20 consecutive renal transplant recipients
 - 11 patients received ATG for acute rejection or delayed graft function
 - 1 case *Candida* esophagitis
 - 10 bacterial infections in 6 patients
 - 9 patients did not receive ATG
 - 1 case each of bacterial and viral infection
- Use of ATG associated with increased risk of renal allograft loss in NIH study (MV model, HR 2.5, 95% CI 1.1-5.6, p=0.03)

Carter JT, Am J Transplant 2006;6:753; Stock PG, N Engl J Med 2010;363:21; Blumberg EA, Am J Transplant 2013;13:169

INDUCTION IMMUNOSUPPRESSION

- Renal transplant database to compare HIV-seropositive renal transplant recipients who received ATG (n=189), an IL-2 receptor blocker (n=268), both (n=80), or no induction immunosuppression (n=252)
- Receipt of induction immunosuppression
 - Shorter hospitalization, lower rates of delayed graft function, decreased graft loss
 - No increased risk of infection (pooled or by individual agent)
- Receipt of ATG
 - Lower rates of acute rejection

Kucirka LM, Am J Transplant 2016;16:2368

MAINTENANCE IMMUNOSUPPRESSION

- Cyclosporine has antiviral activity, but based on NIH kidney study, tacrolimus is preferred
 - Cyclosporine use associated with 2.1-fold increased risk of rejection compared to tacrolimus
- MMF may suppress HIV replication (especially in combination with NRTIs) and is more potent antimetabolite
- Sirolimus has been shown to enhance in-vitro antiviral activity of enfuvirtide, efavirenz, and CCR5 inhibitor
 - Sirolimus is associated with 2.2-fold increased risk of rejection compared to CNI-based regimen

Margolis DM, JAIDS 2002;31:45; Stock PG, N Engl J Med 2010;363:2004; Blumberg EA, Am J Transplant 2013;13:169; Locke JE, Transplantation 2014;97:446; Stock PG, Am J Transplant 2014;14:1136

DRUG INTERACTIONS

Antiretroviral	Effect on immunosuppressant Levels
NRTIs	
All	No change
NNRTIs	
EFV, NVP, ETR	↓FK, CSA, SRL, EVL: No change MMF
RPV	No change
PIs	
All	↑FK, CSA, SRL, EVL: No change MMF
INSTIs	
EVG/c or EVG/r	↑FK, CSA, SRL, EVL: No change MMF
DTG, RAL	No change

Jain AKB, Transplant Proc 2002;34:1540; Vogel M, Liver Transplant 2004;10:939; Barau C, Fund Clin Pharmacol 2009;23:423; van Maarseveen EM, AIDS Patient Care 2012;26:568; Frassetto L, Biopharm Drug Dispos

RECOMMENDED REGIMENS FOR ARV-NAÏVE PATIENTS

- PI-based
 - Darunavir/rilonavir plus TDF/FTC or TAF/FTC
- INSTI-based
 - Dolutegravir plus 3TC/FTC or TDF/FTC or TAF/FTC
 - Elvitegravir/cobicistat plus TDF/FTC or TAF/FTC
 - Raltegravir plus TDF/FTC or TAF/FTC

Guidelines for the use of Antiretroviral Agents in Adults and Adolescents. Department of Health and Human Services. July 14, 2016: 1-288.

ARV THERAPY IN HIV

ARV regimen	N	Graft survival
INSTI-based	9	100%
Non-INSTI-based	4	25%
INSTI and PI-based	1	0%
NNRTI-based	2	0%
PI-based	1	100%

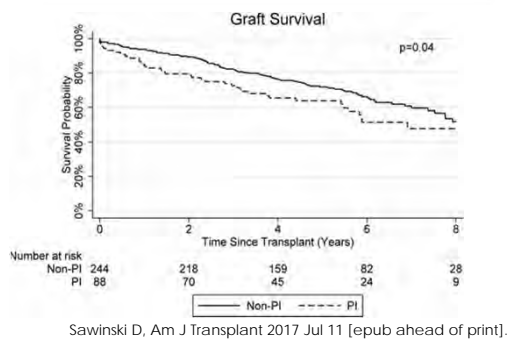
Azar MM, Int J STD AIDS 2017;28:447.

ARV THERAPY IN HIV

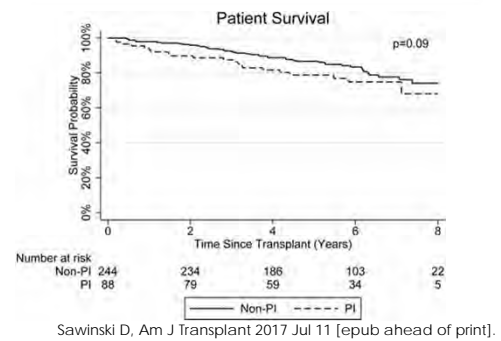
- Patients given ARV regimens that inhibit CYP450 systems have higher rates of rejection
- Sawinski et al. used renal transplant database to identify 332 HIV patients who underwent renal transplant
 - 88 PI-based
 - 244 non-PI based
- No difference in rejection rates
- Significant difference in allograft and patient survival

Tricot L, Am J Transplant 2009;9:1946; Moreno A, Liver Transpl 2010;16:530; Rosa R, F1000Research 2016;5:2893; Stock PG, Am J Transplant 2017 Aug 31 [epub ahead of print]; Sawinski D, Am J Transplant 2017 Jul 11 [epub ahead of print].

GRAFT SURVIVAL BY ARV REGIMEN



PATIENT SURVIVAL BY ARV REGIMEN



RALTEGRAVIR PK IN OLT

PK parameter	HIV+ OLT recipients (n=17)	HIV+ control group (n=65)
C _{through} (ng/mL)	492 (179-819)	292 (153-670)
C _{1h} (ng/mL)	2302 (1097-3045)	1246 (588-2861)
C _{2h} (ng/mL)	2813 (1646-3696)	1318 (686-2565)
C _{3h} (ng/mL)	2960 (1730-4395)	1224 (603-1913)
C _{4h} (ng/mL)	1789 (988-2543)	676 (401-1408)
C _{max} (ng/mL)	3922 (2846-4764)	2223 (1240-3970)
AUC ₀₋₄ (ng*h/mL)	8890 (6022-10676)	5243 (2887-8515)
AUC ₀₋₁₂ (ng*h/mL)	14314 (11627-19998)	8795 (5218-12954)
Cl (L/h)	26 (17-34)	45 (31-77)

Cattaneo D, J Antimicrob Chemother 2016;71:1341.

ARV THERAPY: TENOFOVIR

- Tenofovir disoproxil fumarate (TDF) can cause nephrotoxicity and reduce bone mineral density
 - TDF is metabolized to tenofovir, then intracellularly to tenofovir-diphosphate (active)
 - Higher levels of tenofovir associated with toxicity
- Tenofovir alafenamide fumarate (TAF) is another prodrug
 - ~4-times tenofovir-diphosphate concentrations
 - ~90% lower tenofovir exposure
- Use of TDF (n=23) compared to renal transplant recipients on non-TDF ARV (n=81)
 - Trend toward worse allograft survival among recipients of TDF but not significant

Ray AS, Antiviral Res 2016;125:63; Boyle SM, Transplant Infect Dis 2017;19:e12727

ARV THERAPY: MARAVIROC

- CCR5 antagonism may reduce allograft rejection
- Enhanced antiretroviral activity in combination with sirolimus
- Role: TBD

Li J, J Immunol 2011; 186:3753, Latinovic O, Antiviral Res 2009;83:86.

ARV THERAPY

- Initiate therapy as soon as patient is reliably taking oral medications post-transplantation
- For HBV-infected recipients, ARV therapy should include tenofovir and emtricitabine or lamivudine
- Dose adjust for renal function (if necessary)
- Check *HLA-B*5701* if using abacavir
- Manage drug interactions

Blumberg EA, Am J Transplant 2013;13:169: Guidelines for the use of Antiretroviral Agents in Adults and Adolescents. Department of Health and Human Services. July 14, 2016: 1-288.

PROPHYLAXIS

Opportunistic infection	Primary prophylaxis	Regimen
PCP	Indicated for life	SMX/TMP 1 DS or SS daily
Toxoplasma gondii	Toxo IgG+ recipients with CD4+ less than 200 cells/mm ³ or donor seropositive	SMX/TMP 1 DS daily
MAC	CD4+ less than 75 cells/mm ³	Azithromycin 1200 mg weekly
CMV	CMV IgG+ donors or recipients for at least 3 months	Valganciclovir 900 mg daily
Histoplasma	CD4+ less than 150 cells/mm ³ and at high risk given geography	Itraconazole 200 mg daily
Tuberculosis	+latent TB or close contact	Isoniazid 300 mg daily for 9 months
Coccidioidomycosis	IgG or IgM+ in recipient from endemic area and CD4+ less than 250 cells/mm ³ : lifelong	Fluconazole 400 mg daily

MANAGEMENT CONSIDERATIONS

- Administer vaccines prior to transplantation
 - Hepatitis A and B if non-immune
 - Pneumococcal
 - Influenza
 - Varicella if CD4+ cell count >200 cells/mm³ if non-immune
 - HPV if 15-26 years of age
- Monitor HIV RNA and CD4+ T-cell counts 1 month post-transplant and every 2-3 months thereafter
- In the presence of persistent HIV viremia, resistance testing should be performed

Blumberg EA, Am J Transplant 2013;13:169: Guidelines for the use of Antiretroviral Agents in Adults and Adolescents. Department of Health and Human Services. July 14, 2016: 1-288.

COMPLICATIONS

- Posttransplant period complicated by risk of infection and rejection
- PK/PD drug interactions between ARVs, immunosuppressives, and anti-infective agents
- Increased rate of acute graft rejection
- HCV infection
- AIDS-defining illnesses
- Infectious complications
- Medication safety

Blumberg EA, Am J Transplant 2013;13:169.

AIDS-DEFINING ILLNESSES

- No increase in OIs with standard prophylaxis
 - Kaposi's sarcoma (4)
 - Esophageal (5) and bronchial (1) candidiasis
 - *Pneumocystis jirovecii* pneumonia (2)
 - Cryptosporidiosis (1)
- No recurrent OIs in recipients with a pre-transplant history
- OI history not associated with survival
- Most often experience similar infections to non-HIV infected persons

Stock PG, N Engl J Med 2010;363:2004; Roland ME, AIDS 2016;30:435.

INFECTIOUS COMPLICATIONS

- Infection rate similar to HIV-uninfected
- Most often experience similar infections to non-HIV infected persons
 - ~69% bacterial
 - ~9% fungal
 - 6-14% viral
- Risk factors
 - HCV infection and low CD4⁺ cell count in kidney and liver transplant recipients
 - Receipt of ATG in kidney recipients
 - Caucasian race in liver recipients

Stock PG, N Engl J Med 2010;363:2004;
Allioaie O, Int J STD AIDS 2017;Jan 1 [Epub ahead or print].

MEDICATION MONITORING/TOXICITY

- Overlapping toxicities between immunosuppressives and ARVs
 - Insulin resistance/Diabetes mellitus
 - Dyslipidemia
 - Vitamin D deficiency

Primeggia J, Infect Dis Clin N Am 2013;473: Guidelines for the use of Antiretroviral Agents in Adults and Adolescents. Department of Health and Human Services. July 14, 2016: 1-288; Pham P-IT, Diabetes Metab Syndr Obes 2011;4:175

DOLUTEGRAVIR CASE REPORT

- 56-yr-old M with HIV underwent RT
- ARVs: NRTIs plus ritonavir-boosted darunavir and raltegravir
- Maintenance IS: tacrolimus, MMF, and prednisone
- Prophylaxis: TMP/SMX and valganciclovir
- SCr stabilized at 1.5 mg/dL
- ARVs changed to dolutegravir/abacavir/lamivudine
- Two weeks later, SCr up to 1.9 mg/dL
- Workup negative for infection, obstruction, or rejection
- SCr remained stable at 1.8 mg/dL: attributed to dolutegravir

Lee DH, Transplant Infect Dis 2016;18:625.

Thank you!

The New Frontier: HCV Treatment and Management Following Solid Organ Transplantation

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Objectives

- 1 Describe safety and efficacy outcomes following solid organ transplantation in HCV-infected recipients.
- 2 Discuss HCV management following solid organ transplantation.
- 3 Describe advantages and disadvantages of HCV treatment options in solid organ transplantation recipients, including cost and reimbursement issues.

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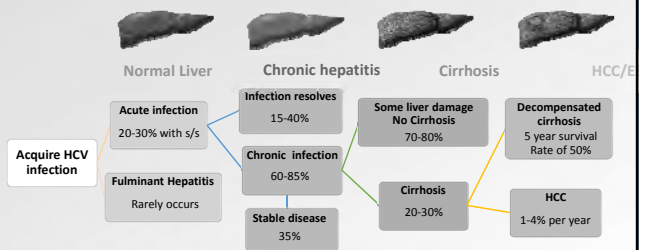
Abbreviations

HCV	Hepatitis C virus	LDV	Ledipasvir
LT	Liver transplant	GZP/EBR	Grazoprevir/elbasvir
IVDU	Intravenous drug use	DCV	Daclatasvir
HCC	Hepatocellular carcinoma	VEL	Velpatasvir
SVR	Sustained virologic response	PROD	Paritaprevir/ritonavir/ombitasvir
DAA	Direct-acting antivirals	VOX	Voxilaprevir
SIM	Simeprevir	GLE/PIB	Glecaprevir/pibrentasvir
SOF	Sofosbuvir	FCH	Fibrosing cholestatic hepatitis
CTP	Child-Turcotte-Pugh	RAS	Resistance associated substitutions

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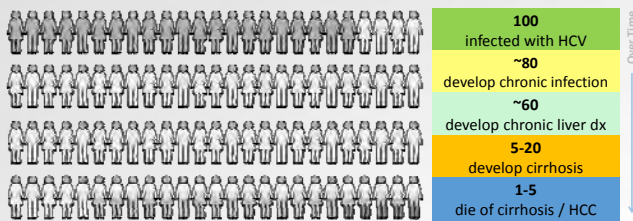
Natural History of HCV



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Progression of liver disease 2nd to HCV

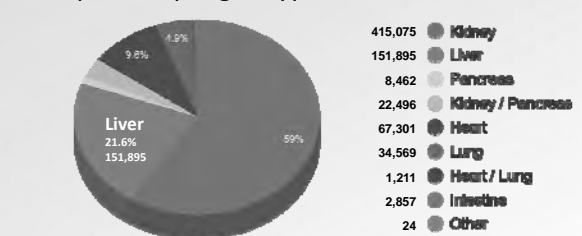


Adapted CDC hepatitis C general fact sheet

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Transplants by organ type (1/1/88 – 6/30/17)

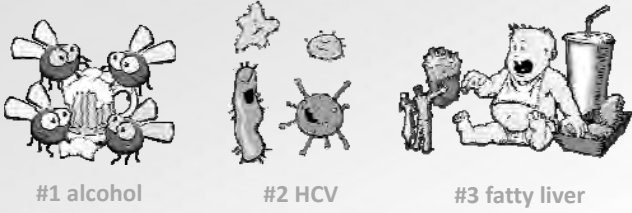


OPTN: Organ Procurement and Transplantation Network: <https://www.optn.org/data/>, last accessed July 20, 2017

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Reasons for a liver transplant



#1 alcohol

#2 HCV

#3 fatty liver

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Case: Mr. Larry Liver

- 59-YOM with GT1a HCV cirrhosis and HCC, naïve to HCV treatment
- PMH: esophageal varices with no bleeding, HTN, gout
- ROS: No ascites, hepatic encephalopathy
- Imaging: CT of the abdomen show a 3.5-mm nodule confirmed to be HCC
- Labs:
 - WBC 3.7, Hgb 11.4, Plat 73, INR 1.5
 - Na 139, Alb 3.1, T bili, 1.6, AST 40, ALT 26, Cr 0.95
 - HCV RNA: 10,451,261 IU/mL



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Getting a new liver is not a 'cure'

Recurrent HCV

- Elevated LFTs
- Detectable HCV RNA levels
- Histologic changes → Fibrosis



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Factors promoting fibrosis progression/HCV recurrence post liver transplantation

Donor	Transplant	Recipient
<ul style="list-style-type: none"> • Older donor age • Nonblack • Prolong cold ischemia time • Graft steatosis • Interleukin-28B (IL-28B) 	<ul style="list-style-type: none"> • Acute rejection • CMV • Diabetes post transplant • Immunosuppressive therapy 	<ul style="list-style-type: none"> • HIV • Females • Blacks • HCV RNA level at time of surgery • IL - 28B

Burns P, De Martin E, Zanetto A, et al., Hepatitis C virus and liver transplantation: where do we stand? Transpl Int. 2016 Feb;29(2):135-52.

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Will HCV treatment improve outcomes?



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Eradicating HCV prior to transplant minimize risk of HCV recurrence post transplant

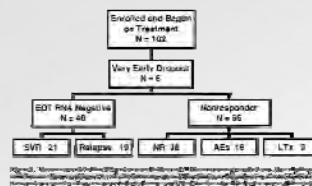


Table 2. Recurrent HCV after LT with HCV treatment

HCV RNA Pre LT	HCV RNA Post LT	
	RNA - positive	RNA - negative
Positive	22	0
Negative	0	9

Note: All of the pts reported have a minimum of 6 mo of post LT follow-up. Three of the 9 pts who were RNA negative were on treatment at the time of LT

Everson GT. Treatment of patients with hepatitis C virus on the waiting list. Liver Transpl. 2003;9:S90-S94.

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Treating HCV in liver transplant patient improves survival

	Treated (n=89)	Not treated (n=75)
3 years	94 %	81 %
5 years	85 %	72 %
7 years	74 %	62 %

Survival (p=0.04)

Patient survival from transplantation in treated compare to untreated matched controls

Berenguer M, Palau A, Aguilera V et al. Clinical benefits of antiviral therapy in patients with recurrent hepatitis C following liver transplantation. Am J Transplant. 2008;8(3):679-87.

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Achieving SVR in the liver transplant patient improves survival

	SVR12 (n=33)	Nonresponders (n=56)
1 years	100 %	98 %
3 years	93 %	80 %
5 years	93 %	69 %

Survival (p=0.032)

Patient survival since treatment initiation (n=89)

Berenguer M, Palau A, Aguilera V et al. Clinical benefits of antiviral therapy in patients with recurrent hepatitis C following liver transplantation. Am J Transplant. 2008;8(3):679-87.

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Past and Present HCV treatments pre and post transplant

Prior to 2011

- PegIFN ± ribavirin
- Issues:
 - Low SVR
 - Multiple adverse effects
 - Graft failure
 - Death

From 5/11 - 10/13

- Boceprevir or telaprevir + PegIFN + Ribavirin
- Issues similar to PegIFN + Ribavirin
- More adverse effects
- More dosage reductions
- More blood monitoring
- Drug interactions

From 11/13 - present

- 2nd generation direct acting antiviral agents (DAA)
- Drug interactions
- PegIFN free regimens
- May require Ribavirin for cirrhotic pts
- High SVR rates

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3rd Generation HCV Medications

	Brand name	Generic name	FDA approval date	\$\$\$ course of treatment	Duration of Tx(weeks)
Past	Pegasys/Peginteron	Pegylated interferon	2000	33,600 - 37,000	48
	Rebetol/Copegus	Ribavirin	2000	1100-17,000	48
	Victreks	Boceprevir	5/13/2011	26,400 - 48,400	24-44
	Inciev	Telaprevir	5/23/2011	49,200	12
Now	Olysio	Simeprevir	11/22/2013	66,360	12
	Sovaldi	Sofosbuvir	12/06/2013	84,000	12
	Harvoni	Ledipasvir/Sofosbuvir	10/01/2014	94,500	12
	Olysio + Sovaldi	Sofosbuvir + Simeprevir	11/05/2014	150,000	12
	Viekira Pak	Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir	12/19/2014	83,319	12
	Viekira XR	Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir	07/25/2016	83,000	12
	Daklinza	Daclatasvir	07/24/2015	63,000	12
	Zepatier	Elbasvir/Grazoprevir	01/28/2016	54,600-72,800	12-16
	Technivie	Ombitasvir/Paritaprevir/ Ritonavir	07/24/2015	76,653	12
	Eplclusa	Sofosbuvir/Velpatasvir	06/28/2016	74,760	12
Vosevi	Sofosbuvir/Velpatasvir/Voxilaprevir	07/18/2017	74,760	12	
Mavyret	Glecaprevir/Pibrentasvir	08/03/2017	26,400	8	

SVR rates with DAA regimens for HCV in the pre/post liver transplant setting

	# of pts	Genotype	Duration (wks)	SVR	CTP	Pre/Post	Trial
SIM + SOF ± RBV	42	1	12	74-100%	B, C	Pre	Modi et al.
SIM + SOF ± RBV	325	1	12	88%	-	Post	Nguyen et al.*
LVD/SOF + RBV	108 229	1, 4	12 or 24	86-89% 96-98%	B, C A,B,C	Pre Post	SOLAR-1
LVD/SOF + RBV	107 226	1, 4	12 or 24	78-96% 50-100%	B, C A,B,C	Pre Post	SOLAR-2
PROD + RBV	34	1	24	97%	-	Post	CORAL-1
DCV + SOF + RBV	60 53	1-6	12 to 24	83% 94%	B, C	Pre Post	ALLY-1
GZP/EBR	10 30	1,4,6	12	90% 100%	≤ A B	Pre	C-SALT part A
VEL/SOF ± RBV	87	1	12	94%	-	Pre	ASTRAL-4
VEL/SOF	90	1-6	12	83%	A,B,C	Pre	ASTRAL-4
VEL/SOF	90	1-6	24	86%	A,B,C	Pre	ASTRAL-4

*Meta-analysis of 8 studies of post liver transplant patients who received SIM + SOF with or without RBV. SVR, sustained virologic response; DAA, direct acting antiviral; SIM, simeprevir; SOF, sofosbuvir; RBV, ribavirin; LVD/SOF, ledipasvir/sofosbuvir; GZP/EBR, grazoprevir/elbasvir; DCV, daclatasvir; VEL/SOF, velpatasvir/sofosbuvir; CTP, Child Turcotte Pugh; PROD, postoperative/orthotopic liver transplantation; Harvoni/SOF, sofosbuvir/ledipasvir; Vosevi/SOF, sofosbuvir/velpatasvir/voxilaprevir; ASTRAL-4, AASLD Hepatitis C Virus and Liver Transplantation: Guidelines for the Practice of Medicine. 2017 Apr 3;14(2):244-50.

Most common mild to moderate adverse effects with DDAs

Fatigue

may be related to ribavirin

Dermatological

itching, dermatitis, photosensitivity reaction

Gastrointestinal

nausea, vomiting, diarrhea, constipation, upset stomach

Pyrexia

fevers, chills, aches, joint pain

Headaches

Asthenia

Arthralgia

Insomnia

Anemia

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Rare, but severe adverse effects with DDAs

Elevated serum bilirubin

- Simeprevir

Elevated ALT level

- Elbasvir/Grazoprevir
- Ombitasvir Paritaprevir Ritonavir Dasabuvir
– Ethinyl estradiol containing birth control

Decompensated liver disease → death

- Elbasvir/Grazoprevir
- Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir
- Simeprevir

Renal

- Sofosbuvir / Ledipasvir
- Sofosbuvir / Velpatasvir
- Sofosbuvir + Daclatasvir

Contraindicated in patient's with
Child-Pugh class B or C

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Drug interactions with DDAs

	SIM	LVD/SOF	VEL/SOF	DCV	PROD	GZP/EBR	SOF/VEL/VOX
CYP3A				X		X	
CYP1A2	X						X
CYP3A4	X		X		X		X
CYP2B6			X				X
CYP2C8			X		X		X
OATP1B1	X			X	X	X	X
OATP1B3	X			X	X	X	X
P-glycoprotein	X	X	X	X		X	X
BCRP	X	X	X	X	X		X
UGT1A1					X		

SIM, simeprevir; SOF, Sofosbuvir; LED, Ledipasvir; GZP/EBR, Grazoprevir/elbasvir; DCV, Daclatasvir; VEL, Velpatasvir; PROD, Paritaprevir/ritonavir/ombitasvir; VOX, Voxilaprevir; GLE/PIB, Glecaprevir/pibrentasvir

Drug interactions with DDAs in the transplant setting

	Azathioprine	Mycophenolate	Cyclosporine	Tacrolimus	Sirolimus	Everolimus
PROD						
SIM						
GZP/EBR						
GLE/PIB						
LVD/SOF						
VEL/SOF						
DCV						
SOF/VEL/VOX						
SOF						

Key: Avoid May require dosage adjustment No interaction expected

SIM, simeprevir; SOF, Sofosbuvir; LED, Ledipasvir; GZP/EBR, Grazoprevir/elbasvir; DCV, Daclatasvir; VEL, Velpatasvir; PROD, Paritaprevir/ritonavir/ombitasvir; VOX, Voxilaprevir; GLE/PIB, Glecaprevir/pibrentasvir

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Summary of the new era of HCV therapies

SVR is approximately 50 - 90% in pre-transplant

Dependent on Child – Pugh and MELD score

SVR is approximately 80 - 90% in post-transplant

Dependent on Child – Pugh and MELD score

Minimal adverse effects

Fatigue, headaches, nausea, upset stomach

MUST consider drug-drug interactions

Pre-transplant: polypharmacy

Post-transplant: immunosuppressive therapy

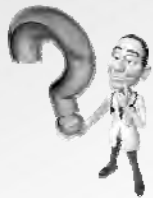
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Now what do I do since I have the basics down?

Questions to consider

- When to treat, pre or post transplant?
How long to treat for?
- Which DAA regimen to consider?
Should ribavirin be used or not?
- What do adverse outcomes are expected?



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When to treat, pre or post transplant?

Recurrent HCV infection in ALL LT

- As early as 72 hours post surgery
- Develop cirrhosis
5 yrs: 10-30%
10 yrs: ~50%
- Fibrosing cholestatic hepatitis (FCH)
10% of LT within 6 months
Death within 1-2 yrs if not treated

<https://billboardmonthlight.blogspot.com/2010/09/cartoon-saturday.html>

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Pre-transplant DAA treatment while waiting for a liver transplant

61 pts with HCV and CTP ≤7 and MELD ≤17

46 underwent a LT

43 achieved a HCV RNA level < 25 IU/mL at time of LT (n; %)

30 (70) achieved post LT SVR12	10 (23) recurrent HCV infection	3 (7) died [2: graft failure; 1: hepatic artery thrombosis]
--------------------------------	---------------------------------	---

- Design: Open-label, multicenter, international, phase 2 trial on waitlist for LT secondary to HCC
- Excluded: Decompensated liver disease
- Treatment: SOF + RBV up to 48 weeks
- Primary end point: SVR 12 post transplant

Curry MP, Forns X, Chung RT, et al. Gastroenterology. 2015;148:100-7.

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Does timing of treatment and severity of liver disease affect SVR rates? (SOLAR -1, SOLAR -2)

Design

- SOLAR-1 (USA), SOLAR-2 (international)
- Open-label, phase 2, multicenter trial, GT 1 and 4
- Cohort A: **pre-liver transplant**: CTP-B, CTP-C
- Cohort B: **post-liver transplant**: no cirrhosis, CTP-A, CTP-B, CTP-C, FCH

Treatment

- LDV/SOF + RBV 12 or 24 weeks

Primary end point

- SVR 12

Charlton M, Everson GT, Flamm SL, et al. Gastroenterology. 2015; 149: 649-59. Manns M, Samuel D, Gane EJ, et al. Lancet Infect Dis. 2015: 685-97

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Does timing of treatment and severity of liver disease affect SVR rates? (SOLAR -1, SOLAR -2)

SVR 12 among genotype 1 patients

		12 weeks of LDV/SOF + RBV (n; %)		24 weeks of LDV/SOF + RBV (n; %)	
		SOLAR-1	SOLAR-2	SOLAR-1	SOLAR-2
Pre-transplant	Cohort A CTP B	26/30 (87)	20/23 (87)	24/27 (89)	22/23 (96)
	Pre-transplant CTP C	19/22 (86)	17/20 (85)	20/23 (87)	18/23 (78)
	Cohort B No cirrhosis	53/55 (96)	42/45 (93)	55/56 (98)	44/44 (100)
Post-transplant	CTP A	25/26 (96)	30/30 (100)	24/25 (85)	27/28 (96)
	CTP B	22/26 (85)	19/20 (95)	23/26 (88)	20/20 (100)
	CTP C	03/05 (60)	01/02 (50)	03/04 (75)	04/05 (80)
	FCH	4/04 (100)	03/3 (100)	2/02 (100)	02/2 (100)

Charlton M, Everson GT, Flamm SL, et al. Gastroenterology. 2015; 149: 649-59. Manns M, Samuel D, Gane EJ, et al. Lancet Infect Dis. 2015: 685-97

Does timing of treatment and severity of liver disease affect SVR rates? (ALLY 1)

Design

- Open-label, phase 2, multicenter trial, GT 1 - 6
- Cohort A: **pre-liver transplant**: CTP A, CTP-B, CTP-C, MELD ≥ 8 and ≤ 40
- Cohort B: **post-liver transplant**: no cirrhosis, CTP-A, CTP-B, CTP-C, FCH

Treatment

- DCV + SOF + RBV 12 weeks (± 12 weeks in some cases)

Primary end point

- SVR 12

Poordad F, Schiff ER, Vierling JM, et al. Hepatology. 2016; 63: 1493-1505

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Does timing of treatment and severity of liver disease affect SVR rates? (ALLY 1)

SVR 12

		12 weeks of DAC + SOF + RBV (n; %)
Pre-transplant	Cohort A CTP A	11/12 (92)
	CTP B	30/32 (94)
	CTP C	09/16 (56)
Post-transplant	Cohort B All patients	50/53 (94)

60 pts with HCV, CPT A, B, C and treated with DCV + SOF + RBV

60% CTP improved, 25% CTP unchanged, 15% CTP worsened

CTP B (30) → CTP A (15)
CTP C (13) → CTP B (6)

Poordad F, Schiff ER, Vierling JM, et al. Hepatology. 2016; 63: 1493-1505

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Recommendation when to treat with a DAA in the liver transplant setting

Treat all pre and post LT patient

Goal of therapy

- Pre LT: at least 1 month prior to LT, HCV RNA level LLOQ. NOT a reason to delay LT if treatment course is not completed
- Post LT: SVR12

Duration of therapy

12 or 24 weeks

- Post LT: Initiate treatment early (3-6 months) to minimize progression to cirrhosis

Poordad F, Schiff ER, Vierling JM, et al. Hepatology. 2016; 63: 1493-1505

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Things to consider when deciding which DAA regimen to use in the transplant setting

Genotype	Treatment experience	Severity of liver disease	Drug interactions	Resistance	Special populations
<ul style="list-style-type: none"> • 2 Easy to tx • 1 • 1b • 1a • 3 Hard to tx 	<ul style="list-style-type: none"> • Naive • Relapser • Partial responder • Null responder 	<ul style="list-style-type: none"> • Cirrhosis or no cirrhosis • CTP score • MELD score 	<ul style="list-style-type: none"> • CYP3A • CYP2C8 • OATP1B1/3 • Acid suppressing agent • P-gp 	<ul style="list-style-type: none"> • NS5A test 	<ul style="list-style-type: none"> • HIV • Renal impairment • Liver impairment

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Which DAA regimen* to consider: Pre-liver transplant ?

AASLD/IDSA recommendations	Genotype					
	1	2	3	4	5	6
LDV/SOF + RBV ¹ x12 wks ²	x				x	x
LDV/SOF x 24 wks ³	x				x	x
VEL/SOF + RBV ⁴ x 12 wks ²	x	x	x	x	x	x
VEL/SOF + RBV ⁴ x 24 wks ²	x				x	x
DCV/SOF + RBV ¹ x 12 wks	x	x	x	x		
DCV/SOF x 24 wks ³	x				x	



¹ 600mg, increase as tolerated
² 24 wks for patients who failed SOF or NS5A
³ regimen for patients who can not tolerate ribavirin therapy
⁴ for CTP C, RBV 600mg, increase as tolerated, otherwise use weight base RBV for CTP A and B

*For most up to date recommendation, please go to www.hcvguidelines.com

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Which DAA regimen* to consider: Post-liver transplant ?

AASLD/IDSA recommendations	Genotype					
	1	2	3	4	5	6
LDV/SOF + RBV ^{1,4} x 12 wks	x			x		
LDV/SOF x 24 wks ³	x			x		
VEL/SOF + RBV ⁴ x 12 wks ²	x	x	x	x	x	x
VEL/SOF + RBV ⁴ x 24 wks ²	x			x	x	x
DCV/SOF + RBV ² x 12 wks	x	x	x	x		
DCV/SOF x 24 wks ³	x	x	x	x		
SOF + RBV ¹ x 24 wks ⁴		x				



¹ weight base
² 600mg, increase as tolerated
³ regimen for patients who can not tolerate ribavirin therapy
⁴ 600mg, increase as tolerated for CTP B or CTP C

*For most up to date recommendation, please go to www.hcvguidelines.com

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Why should ribavirin be used with a DAA?

Design

Observational retrospective study by the UK National Health Service in England evaluated HCV pts "at significant risk of death or irreversible damage within 12 months due to hepatic or extrahepatic manifestations"

- Cohort 1: Receive HCV treatment in Decompensated pts Post-LT recurrent HCV Extrahepatic patients
- Cohort 2: Did not receive HCV treatment

Foster GR, Irving WL, Cheung CM, et al. J of Hepatology. 2016; 64: 1224-1231

Treatment

Selected by the clinician

- 12 weeks with or without ribavirin SOF/LDV SOF+DCV

Primary end point

SVR 12

Secondary end point

Adverse outcomes or event

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Why should ribavirin be used with a DAA?

		SVR 12 (n,%)			
		SOF/DCV	SOF/DCV + RBV	SOF/LDV	SOF/LDV + RBV
Decompensated patient	GT 1	2/4 (50)	30/34 (88.2)	11/13 (84.6)	136/149 (91.3)
	GT 3	3/5 (60)	75/105 (71.4)	2/5 (40)	37/57 (64.9)
	Non GT 1,3	3/3 (100)	9/11 (81.8)	0 (0)	21/23 (91.3)
Post LT Recurrent infection without decompensation	GT 1	1/1 (100)	5/6 (83.3)	5/5 (100)	14/14 (100)
	GT 3	0 (0)	8/10 (80)	0/2 (0)	1/2 (50)
	Non GT 1,3	0 (0)	1/1 (100)	0 (0)	3/3 (100)

Foster GR, Irving WL, Cheung CM, et al. J of Hepatology. 2016; 64: 1224-1231

Treatment adverse effects and functional outcomes

Discontinued therapy: 26 (5.6%)

- Deaths: 7

Primarily associated with RBV

- Required RBV dosage adjustments: 18.7%
- Discontinue RBV: 9.6%
- Hemoglobin < 8 g/dL: 23 (5.4%)

Develop acute kidney injury

- Creatinine increase ≥ 1.5-fold: 13/467 (2.8%)

Increase MELD score

- Untreated (38%) vs treated (23%), p=0.05

Development of 're-compensation'

- untreated (10%) vs treated (3.7%), p=0.0009

Increase MELD score occurred less in treatment group achieving SVR12

- SVR 12 (11.9%) vs did not SVR (68.8%)

Foster GR, Irving WL, Cheung CM, et al. J of Hepatology. 2016; 64: 1224-1231

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Ribavirin adverse effects and contraindications

Anemia

- Hemolytic
 - May require dosage adjustments

Dermatological side effects

- Dry skin, rash, itching

Pregnancy

- Category X
- Causes birth defects
- Confirmed teratogenic and / or embryocidal effect in animals
- Must use 2 forms of effective contraception during treatment and 6 months post-treatment
 - Applies to males and females



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Treatment recommendations for pre-LT

	Pt with HCC on LT wait list	Decompensated liver disease	Pt with HCC on LT wait list	Decompensated liver disease	Pt with HCC on LT wait list	Decompensated liver disease
Severity of liver disease	CPT-A; MELD <15		CPT-B; MELD 15-25		CPT-C; MELD ≥ 25	
Initiate treatment	Yes		Yes	Maybe	Maybe	No
Goal of treatment	Simplify post LT treatment management	Delist from transplant list	Simplify post LT treatment management	Delist from transplant list	Prevent mortality	Obtain transplant

www.hcvguidelines.org, last accessed, July 25, 2017
 Belli LS, Douvrou C, Berenguer M, et al. J of Hepatology. DOI: <http://dx.doi.org/10.1016/j.jhep.2017.03.006>.

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Treatment recommendations for post-LT

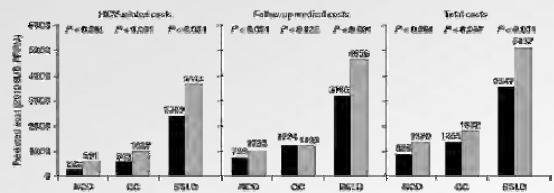
Patient with recurrent HCV infection	
Severity of liver disease	All, FCH
Initiate treatment	Yes, within 3 to 6 months post LT
Goal of treatment	Prevent cirrhosis Minimize risk of developing extra hepatic manifestations (e.g., diabetes, renal impairment)



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Health care cost associated with HCV treatment



Mean per pt per month (PPPM) follow-up costs by tx history and disease severity (2010)

NCD = non-cirrhotic disease; CC = compensated cirrhosis; ESLD = end-stage liver disease

Gordon SC, Hainath FM, Pockros PJ, et al. *Aliment Pharmacol Ther*. 2013;38:784-793.

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Cost effective to treat before or after LT?

Design: Cost analysis to determine if treating 1000 patients with HCV decompensated disease or HCC is less than after liver transplant.

	Treat pre LT	Treat post LT
Per patient QALY (quality-adjusted life per year)	9.27	8.69
Per patient LYs (life years)	11.19	10.9
Patient lifetime cost	\$304,800	\$283,789

The incremental cost-effective ratio was \$36,583 when compare to post LT.

Treating HCV pre LT is cost effective.

Ahmed A, Gonzalez SA, Cholanterti G, et al. *Hepatology*. 2017;1:46-56.

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HCV treatment and PRE-liver transplantations: what we know...

Advantages

- Achieve high SVR rate
- Slow the progression of liver disease
- Reverse decompensation
- Prevent HCV recurrence
- MELD score improvement
- Clinical improvement

Disadvantages

- "MELD purgatory"
 - May delist off transplant list
- Reduced achieving SVR in decompensated cirrhotic
- Drug interactions
- Adverse effects (ribavirin)

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HCV treatment and POST-liver transplantations: what we know...

Advantages

- High SVR rate
- Reduce liver disease progression
- Improve graft survival
- Improve QOL and patient survival
- Minimize extrahepatic manifestation

Disadvantages

- Drug interactions with immunosuppressive therapy
- SVR rates reduced in those who developed decompensated graft cirrhosis

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Case: Mr. Larry Liver

- 59-YOM with GT1a HCV cirrhosis and HCC, naïve to HCV treatment
- PMH: esophageal varices with no bleeding, HTN, gout
- ROS: No ascites, hepatic encephalopathy
- Imaging: CT of the abdomen show a 3.5-mm nodule confirmed to be HCC
- Labs:
 - WBC 3.7, Hgb 11.4, Plat 73, INR 1.5
 - Na 139, Alb 3.1, T bili, 1.6, AST 40, ALT 26, Cr 0.95
 - HCV RNA: 10,451,261 IU/mL



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ASHP


Challenges in Transplantation: The Notorious DSA (Donor Specific Antibodies)



**Challenges in Transplantation:
The Notorious DSA (Donor Specific Antibodies)**

Moderator: Christina Teeter Doligalski, Pharm.D., BCPS, CPP
Clinical Pharmacist, Ambulatory Care Clinical Services
UNC Solid Organ Transplant Clinics
UNC Medical Center Department of Pharmacy






Disclosure

All planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.

- Off-label uses will be discussed.




Housekeeping

- Please silence all cell phones and pagers
- We will have 10 minutes at the completion of all 3 presentations for questions

Objectives

- Describe the impact of costimulatory pathways in the development of Donor Specific Antibodies (DSA) and evaluate the role costimulatory blockade has in prevention of DSA development.
- Assess the utility of mTOR inhibitors in the prevention of DSA development.
- Using the data provided, recommend a role in therapy for IVIG in the treatment of donor specific antibodies.



ashp MIDYEAR 2017
Clinical Meeting & Exhibition


Belatacept and the role of the costimulatory pathway in the development of DSAs

Elizabeth Cohen, Pharm.D., BCPS
Clinical Pharmacist Specialist II, Solid Organ Transplant
Yale New Haven Hospital
New Haven, CT




Objectives

- Describe the mechanism of belatacept and its use in solid organ transplant
- Discuss the role of costimulation blockade in preventing donor specific antibody (DSA) formation after solid organ transplant



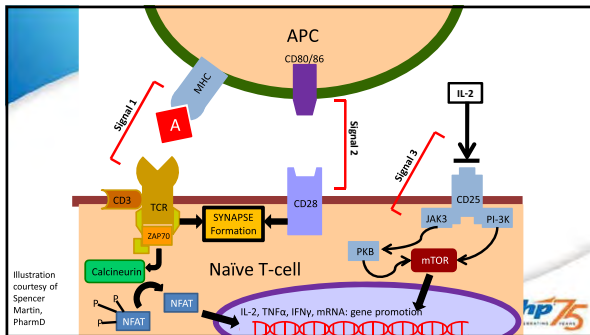
Belatacept (Nulojix®)

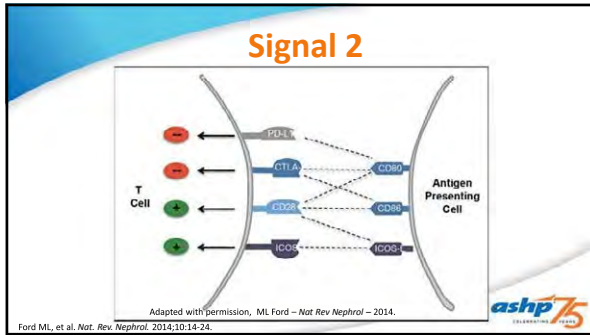
- Novel immunosuppressant approved in 2011
- FDA approved for *de novo* use for prevention of kidney transplant rejection in combination with:
 - Induction: basiliximab
 - Maintenance: mycophenolate mofetil and prednisone
- Once monthly, weight based, IV infusion
- No drug level monitoring

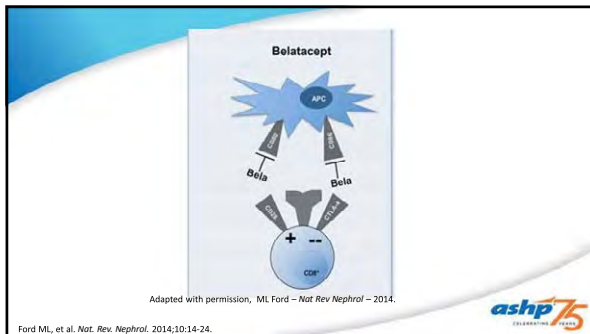


HOW DOES BELATACEPT WORK?









Mechanism of Belatacept


- Co-stimulation blockade
- Fusion protein
 - Fc fragment of human IgG1
 - Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4)
- Prevents binding of CD80/86 on Antigen Presenting Cells (APC) to CD28 on T-cells → inhibiting T-cell activation

ashp 75

BENEFIT 7 year data

- Patients on belatacept vs. cyclosporine had:
 - Decreased rates of composite end point of death and graft loss
 - Improved glomerular filtration rates (GFR)
 - Similar rates of serious adverse events
 - Lower development of donor-specific antibodies (DSA)


Vincenzi F, et al. *N Engl J Med.* 2016;374(4):333-343.



DSAs: BENEFIT 7 year data

- Less DSA development with belatacept
- Lower rates of Class II DSAs with belatacept
- What's the big deal?


Vincenzi F, et al. *N Engl J Med.* 2016;374(4):333-343.



Donor Specific Antibodies (DSA)

- Average kidney graft loss at ~10 years
- ~2/3 of losses are due to antibody mediated rejection (AMR)
- 15-30% of recipients develop *de novo* DSA
- Treatment once DSA is formed is not perfect


Thaunat O, et al. *J Am Soc Nephrol.* 2016;27:1890-1900.
Kim EJ, et al. *Am J Transplant.* 2014;14:59-69.



Donor Specific Antibodies (DSA)

- High affinity IgG against protein antigen
- Binding of DSA to graft epithelium triggers complement cascade → cellular damage and AMR
- Non-complement binding DSA → allograft vasculopathy
- Decreases the life of the graft


Thaunat O, et al. J Am Soc Nephrol. 2016;27:1890-1900.



Creating DSA


- B cells are activated through antigen binding with B cell receptors (BCR)
- Internalized antigen is processed and presented by MHC to T follicular helper (Tfh) cells
- Second activation of B cells through costimulation
- B cells then proliferate in the germinal center

Thaunat O, et al. J Am Soc Nephrol. 2016;27:1890-1900.
Kim EJ, et al. Am J Transplant. 2014;14:59-69.




Prevent DSA formation

GOAL

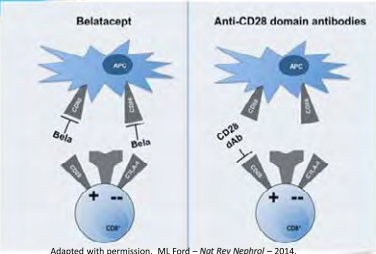


Costimulation and DSA Development

- Primarily animal data
- Complete mechanism is unknown
- Promising data




The slide features a blue and white background with a curved top edge. The title is in orange, and the list items are in black. The logo is in the bottom right corner.



Belatacept
APC
Bela
CD28

Anti-CD28 domain antibodies
APC
CD28
gAb
CD28


Adapted with permission, ML Ford - Not Rev Nephrol - 2014.



The diagram shows two scenarios of T cell activation. On the left, an Antigen Presenting Cell (APC) presents an antigen to a T cell. The interaction is mediated by B7-1 on the APC and CD28 on the T cell. Belatacept (Bela) is shown as a blue Y-shaped molecule that binds to B7-1, preventing it from interacting with CD28. On the right, an Anti-CD28 domain antibody (gAb) is shown as a blue Y-shaped molecule that binds to CD28 on the T cell, preventing it from interacting with B7-1. The T cell is depicted with a plus sign and a minus sign, indicating its activation state.

Preventing DSA with Belatacept

- Nonhuman primate kidney transplant model
- Induced AMR with:
 - Anti-CD3 immunotoxin
 - Tacrolimus
 - Alefacept
- Goal: prevent DSA formation with belatacept and anti-CD40 mAb




The slide features a blue and white background with a curved top edge. The title is in orange, and the list items are in black. The logo is in the bottom right corner.

Preventing DSA with Belatacept

- Theory: Two pathways of costimulation blockade (CoB) will prevent DSA formation
- 4 animals received belatacept and 4 animals received anti-CD40 mAB in addition to AMR induction regimen (CoB-treated)
- Serum creatinine at 60 days significantly lower in CoB treated animals
- CoB prevented AMR on biopsy
- CoB prevented early *de novo* DSA


Kim EJ, et al. *Am J Transplant.* 2014;14:59-69.



Preventing DSA with Belatacept

- Suppressed re-population of B cells
- Decreased percentages of central memory T cells
- Suppressed germinal center reconstruction after T cell depletion
- Suppressed Tfh cells and B cell expansion


Kim EJ, et al. *Am J Transplant.* 2014;14:59-69.



Reverse Signaling Using Belatacept

- *In vivo* studies demonstrate that belatacept (CTLA4-Ig) induces indoleamine 2,3 dioxygenase (IDO)
- IDO inhibits
 - Dendritic cell function
 - T cell responses
 - B cell antibody production


Thaunat O, et al. *J Am Soc Nephrol.* 2016;27:1890-1900.
Chen L. *Nat Rev Immunol.* 2004;4:336-347.



Using Belatacept to Prevent DSAs

- 14 belatacept patients matched to 56 cyclosporine patients with 10 year follow-up
- Belatacept patients had higher GFR
- Identical patient and graft survival (71%)
- 0 belatacept patients with DSA vs. 35% of cyclosporine patients


Schwarz C, et al. *Transpl Int.* 2015;28:820-827.



Converting to Belatacept


- 6 patients converted to belatacept ~ 4 months post transplant
 - 2/6 with rejection history
- Significantly improved GFR
- No new rejection
- No new DSA development
- Improvement in DSA in patient with AMR after treatment completed

Gupta G, et al. *Am J Transplant.* 2015;15:820-2726-2731.




What is the mechanism of belatacept?

- A. Calcineurin inhibitor
- B. mTOR inhibitor
- C. Co-stimulation blocker
- D. IL-2 receptor antagonist




What's the primary proposed mechanism of preventing DSA formation with belatacept?

- A. Tfh cell inhibition
- B. CD40 inhibition
- C. IL-2 inhibition
- D. B cell inhibition



Key Takeaways


- Belatacept is a novel immunosuppressant with a unique mechanism of blocking costimulation in the immune cascade
- Understanding belatacept and DSA formation is still being researched, but with promising results



ashp MIDYEAR 2017
Clinical Meeting & Exhibition


**Prevention of Donor Specific Antibody Development:
Is there a Role for mTOR inhibitors in Renal Transplant?**

Megan Goetz, Pharm.D., BCPS
Solid Organ Transplant Clinical Pharmacist
University of Kentucky HealthCare
Lexington, KY




Audience Poll

- Are any centers currently utilizing mammalian target of rapamycin inhibitors for the prevention of donor specific antibodies for any organ population?
- Renal transplant?




Objectives

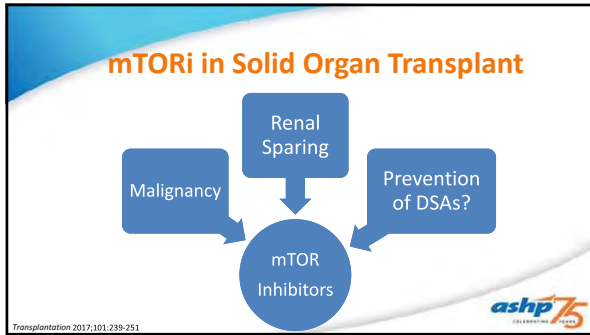
- Describe the pharmacologic properties and current roles of mammalian target of rapamycin inhibitors (mTORi)
- Identify the mechanism mTORi for the prevention of DSA
- Determine the use of mTORi prevention for DSA to the renal transplant recipient



mTORi Review

	Sirolimus (SRL)	Everolimus (EVR)
Typical Dosing	1-5 mg daily	0.75-1.5 mg twice daily
Trough Concentration	5-15 ng/ml (24 hour)	3-8 ng/ml (12 hour)
Major ADRs	Hyperlipidemia, Cytopenias, Proteinuria, Impaired wound healing, Peripheral edema, Pneumonitis	
Half-life	~ 60 hours	~ 30 hours
Drug Interactions	CYP3A4, P-glycoprotein	





Assessment Question #1

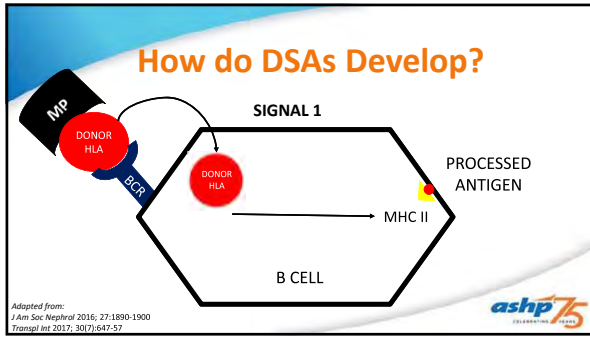
Based on current uses of mTORi, which of the following patients would be most appropriately indicated for use of mTORi in maintenance immunosuppression?

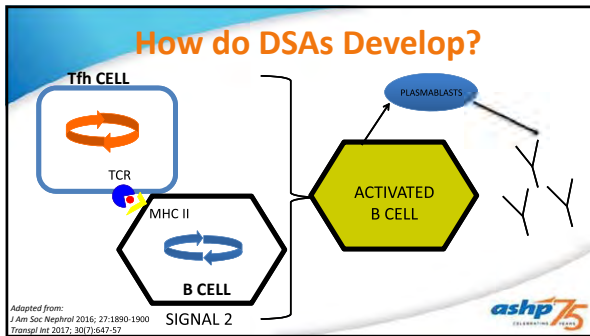
- A. 57 YOF s/p liver transplantation approximately 2 months ago due to hepatitis C virus and hepatocellular carcinoma
- B. 65 YOM POD#1 bilateral lung transplant due to chronic obstructive pulmonary disease
- C. 72 YOF stable serum creatinine 5 years post renal transplant
- D. 41 YOM 1 year s/p liver transplantation with baseline triglycerides greater than 500 mg/dL

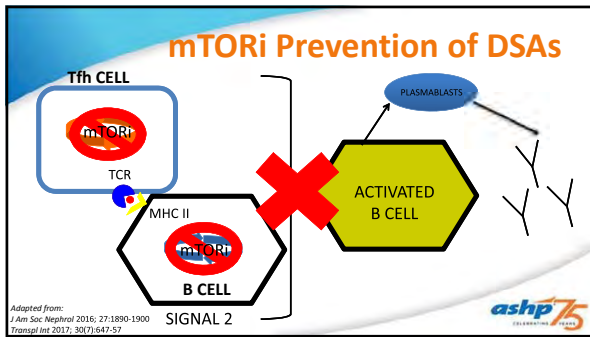
Antibody Mediated Rejection (AMR)

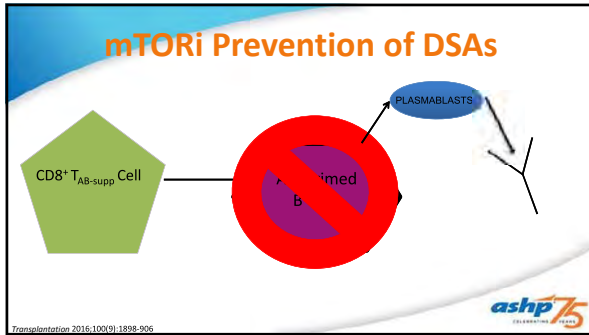
- AMR typically starts with the generation of DSAs
 - Reduced graft survival
 - 2/3 of renal allograft loss
 - Leading cause of late transplant failure

J Am Soc Nephrol 2016; 27:1890-1900
Transpl Int 2017; 30(7):647-57
Transplantation 2016;100(3):1898-906









Assessment Question #2

- Which of the following is a proposed mechanism in which mTOR inhibitors are thought to prevent DSA production?

A. Via restriction of Tfh cell secondary signals for B cell activation

B. Via inhibition of B cell proliferation and differentiation to plasma cells, thus decreasing antibody production

C. Lack of depletion CD8⁺ T_{AB-supp} Cell, thus depleting alloprimed B cells

D. All of the above

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mTOR Inhibition Suppresses Post-transplant Alloantibody Production

Purpose

- To determine the relative efficacy of mTORi and CNI for suppression of in vivo humoral alloimmunity
- To determine if CNI + mTORi produced additive or synergistic effects on humoral alloimmunity

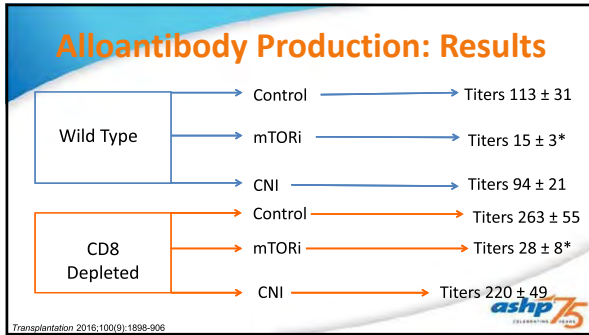
Methods

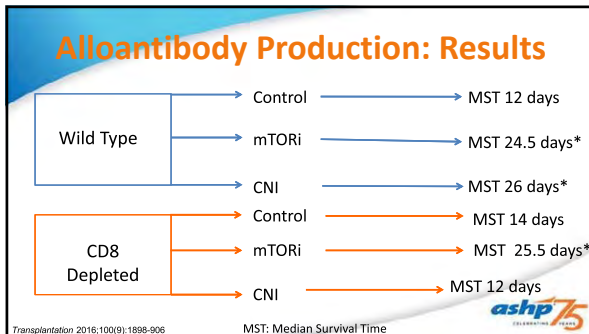
- Wild type or CD-8 depleted mice were transplanted with allogeneic *hepatocytes*
- Recipients were treated with a mTORi and/or CNI

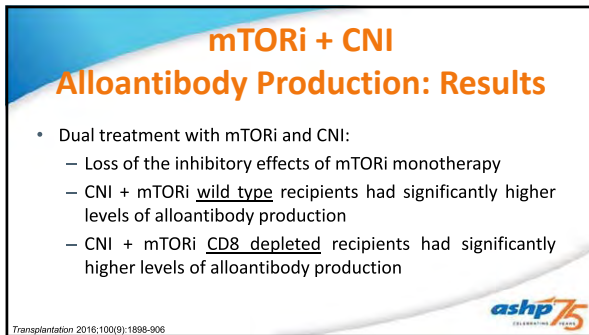
CNI: Calcineurin inhibitor

ashp 75

Transplantation 2016;100(9):1898-906








CD8⁺ Killing of Alloprimed B Cells: Results

- CNI Therapy
 - Significant suppression of CD8 mediated killing of B cells compared to controls (P= 0.009) and mTORi treated recipients (P= 0.005)


Transplantation 2016;100(9):1898-906



Conclusions

- Results support the efficacy of mTORi for suppression of humoral alloimmunity in part through direct effects on alloprimed B cell function


Transplantation 2016;100(9):1898-906



**mTORi Prevention of DSA:
Liver Transplant**

Purpose	<ul style="list-style-type: none">• To investigate the prevalence of DSA development in a large cohort of liver transplant patients, and to define predictive and protective factors
Methods	<ul style="list-style-type: none">• 400 liver transplant recipients were retrospectively screened for DSAs• Patients treated with FK monotherapy, FK + MMF, or FK + EVR

Clin Transplant 2017;31e12874



Results: Immunosuppressive Therapy Influences on DSA Development

Immunosuppression	DSA + (no., %)	OR (95% CI)	P
FK (N = 151)	31 (20.5)		
FK + MMF (N= 146)	33 (22.6)		
FK + EVR (N = 94)	10 (10.6)	0.45 (0.22 – 0.92) P =0.028	0.025

Clin Transplant 2017;31e12974

mTORi and De novo DSA (DnDSA)

Study	Time to mTORi	mTORi	Control	DnDSA % (n/N)		
				mTORi	Control	P Value
SPIESSER	De novo	SRL MMF +/- CS	CSA MMF +/- CS	13 (9/69)	10.9 (8/73)	0.52
CENTRAL	7 weeks	EVR MPS CS	CSA MPS CS	15 (9/60)	21.1 (12/57)	0.6
ELEVATE	10-14 weeks	EVR MPS CS	FK or CSA MPS CS	I: 8.3 (10/120) II: 6.3 (6/95)	I: 2.4 (4/168) II: 7 (9/138)	---

MMF: Mycophenolate mofetil FK: Tacrolimus
 Adapted from: *Transpl Int* 2017; 30(7):647-57

mTORi and DnDSA

Study	Time to mTORi	mTORi	Control	DnDSA % (n/N)		
				mTORi	Control	P
De Sanders-Freitas	3 mo.	SRL MPA CS	Reduced FK MPA CS	17.8 (8/45)	7.3 (3/45)	0.2
CERTITEM	3 mo.	EVR LD MPS CS	CSA MPS CS	27.2 (22/81)	4.9 (4/82)	0.001
Liefeldt et al	3-4.5 mo.	EVR MPS CS	CSA MPS CS	23 (14/61)	10.8 (7/65)	0.048

Adapted from: *Transpl Int* 2017; 30(7):647-57

De Novo Donor Specific Antibody Formation: Mycophenolate versus mTORi

Primary Objective	Define the risk of DSA development based on immunosuppression regimen	
Secondary Objectives	DSA formation associated with: Acute Rejection Glomerular Filtration Rate (GFR) Proteinuria	
Matched cohorts	2:1 Mycophenolate (132): mTORi (66)	
	FK Mycophenolate Prednisone	FK mTORi Prednisone

Exp. Clin. Transplant 2017 [ePub ahead of print]

Results

	mTORi (N=66)		Mycophenolate (N=132)		P value	
	6m	1y	6m	1y	6m	1y
Overall DnDSA	20 (30.3%)		37 (28.0%)		0.73	
Mean FK Trough (ng/ml)	7.4	5.4	7.6	6.5	0.78	0.02
Median Proteinuria (mg/g Creatinine)	0.1	0.1	0.1	0.1	0.3	0.4
Acute Rejection (AR) (N, %)	6 (9.1)	6 (9.1)	12 (9.1)	15 (11.4)	1	0.64

Exp. Clin. Transplant 2017 [ePub ahead of print]

Results


		Everolimus (N = 36)	Sirolimus (N= 30)	P value
DSA	Overall	14 (38.9%)	6 (20%)	0.11
AR	6 months	5 (13.9%)	1 (3.3%)	0.21
	1 year	5 (13.9%)	1 (3.3 %)	0.21

Exp. Clin. Transplant 2017 [ePub ahead of print]

Results

Graft Survival (3 year)	Patient Survival (3 year)
<ul style="list-style-type: none">• mTORi: 88.6%• MPA: 85.7%– P value : 0.41	<ul style="list-style-type: none">• mTORi: 90.9%• MPA: 90.3 %– P value : 0.63


Exp Clin Transplant 2017 [ePub ahead of print]



Conclusions

- In the setting of tacrolimus based immunosuppression (in conjunction with low-dose corticosteroids)
 - mTORi did not provide a differential effect upon de novo DSA formation compared to mycophenolate


Exp Clin Transplant 2017 [ePub ahead of print]



Audience Poll


- Would anyone currently recommend implementing the use of mTORi for the prevention of DSA development in renal transplant?


Exp Clin Transplant 2017 [ePub ahead of print]



mTOR Inhibitor Role in Renal Transplant
Key Takeaways


- No studies have shown a benefit to decreased de novo DSA production in renal transplant as in liver transplantation
- Can still be considered for prevention of CNJ nephropathy, malignancy






**Prevention of Donor Specific Antibody Development:
Is there a Role for mTOR inhibitors in Renal Transplant?**


Megan Goetz, Pharm.D., BCPS
Solid Organ Transplant Clinical Pharmacist
University of Kentucky HealthCare
Lexington, KY






**Donor Specific Antibodies: Role of
Intravenous Immunglobulin**

Arin Jantz, Pharm.D., BCPS
Pharmacy Specialist – Solid Organ Transplant
Henry Ford Hospital
Detroit, MI



Objectives


- Summarize the background, mechanism, and common adverse effects with intravenous immunoglobulin therapy
- Analyze available data for the use of intravenous immunoglobulin in antibody-mediated rejection
- Evaluate data of intravenous immunoglobulin use for positive donor specific antibodies post-transplant



Patient Case

AG is a 45 year old patient who received a deceased donor kidney transplant approximately 6 months ago.


- End stage renal disease: focal segmental glomerulosclerosis
- Creatinine was elevated at 2.2 mg/dL (baseline: 1.2 - 1.4 mg/dL)



Patient Case

- Kidney biopsy findings:
 - *Minimal signs of acute cellular rejection*
 - *Histologic damage suspicious for antibody-mediated rejection and positive C4d staining in the peritubular capillaries*
- Donor specific antibody (DSA): positive DQ2 at high intensity


Diagnosis: acute antibody-mediated rejection (AMR)



Patient Case

- The kidney transplant team would like to treat AG. What would you recommend?
 - A. Intravenous immunoglobulin alone
 - B. Intravenous immunoglobulin + plasmapheresis + rituximab
 - C. Rituximab + plasmapheresis + anti-thymocyte globulin
 - D. Intravenous immunoglobulin + plasmapheresis

Are there other options?




Practice Surveys

Intravenous immunoglobulin is a commonly used AMR treatment

	Kidney Transplant
Responses from:	28 centers
DSA evaluation	96% (26 of 27 centers)
IVIg	Most common treatment: 96% -With PP in 24 cases

Burton et al. *Clin Transplant* 2015. PP: Plasmapheresis




Practice Surveys

Intravenous immunoglobulin is a commonly used AMR treatment


	Kidney Transplant	Heart Transplant
Responses from:	28 centers	184 clinicians
DSA evaluation	96% (26 of 27 centers)	First year: 49%
IVIg	Most common treatment: 96% -With PP in 24 cases	Most common: IV MP Second most common treatment: IVIG or PP

Burton et al. *Clin Transplant* 2015.
 Chih et al. *Am J Transplant* 2013. PP: Plasmapheresis
 IV MP: intravenous methylprednisolone




Intravenous Immunoglobulin (IVIG)

- Antibodies pooled from thousands of donors
 - Main component: IgG
 - Can contain other isotypes (IgA or IgM)
- IV formulation introduced in 1980 for treatment of immune deficiencies
 - Mechanism soon applied to other inflammatory conditions

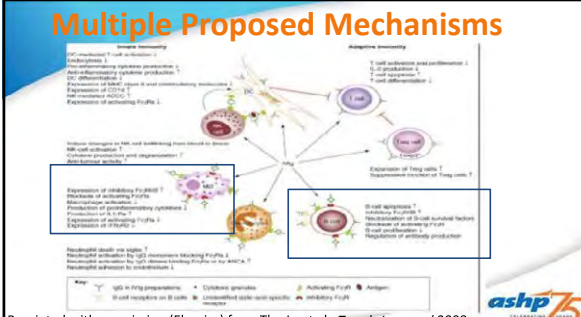
Jordan et al. *Am J Transplant* 2011.
 Schwab et al. *Nat Rev Immunol* 2013. 


Indications for IVIG Use

- Current FDA-approved indications include:
 - Autoimmune diseases like primary immune deficiency disorders, idiopathic thrombocytopenic purpura (ITP), and chronic inflammatory demyelinating polyneuropathy
 - Prophylaxis of viral and bacterial infections
- Approximately 50% of use remains off-label

Jordan et al. *Am J Transplant* 2011.
 Schwab et al. *Nat Rev Immunol* 2013.
 Immune globulin. Micromedex Solutions. Accessed August 15, 2017. 

Multiple Proposed Mechanisms



Reprinted with permission (Elsevier) from Tha-In et al. *Trends Immunol* 2008. 

Mechanism: B Cells and Antibodies

- Anti-idiotypic antibodies: block interactions of DSAs due to IgG binding
- B cell binding may downregulate antibody production

Reprinted with permission (Elsevier) from Tha-In et al. *Trends Immunol* 2008. Jordan et al. *Expert Rev Clin Immunol* 2011.

Mechanism: Complement inhibition

- Prevention of complement activation and scavenging of active complement components
- Many actions are dependent on binding to the Fc receptors

Reprinted with permission (Elsevier) from Tha-In et al. *Trends Immunol* 2008. Watanabe et al. *Am J Transplant* 2005. Jordan et al. *Expert Rev Clin Immunol* 2011.

IVIg Formulations

• Carimune® NF	• Gamunex-C®
• Gammagard S/D® and liquid®	• Gammaplex®
• Bivigam®	• Octagam®
• Flebogamma®	• Privigen®
• Gammaked®	• Cytogam®


Immune globulin. Micromedex. Accessed on August 21, 2017.

Adverse Effects

IVIG is generally well tolerated, but increased adverse events seen with high doses and certain formulations

- Infusion reactions: pre-medications to minimize risk
- Hemolytic anemia – due to anti-blood group antibodies
 - Patients with non-type O blood type
 - Liquid formulations: Gamunex-C®, Gammaked®, Privigen®


Jordan et al. *Am J Transplant* 2011. Dalakas et al. *Pharmacol Ther* 2004.



Adverse Effects

- Renal failure – typically in formulations containing sucrose
 - Carimune® NF, Cytogam®
- Thrombotic events – related to higher osmolality
 - Gammagard S/D®, Flebogamma®, Bivigam®
- Headache – all formulations

Jordan et al. *Am J Transplant* 2011. Gupta et al. *Am J Hematol* 2004.




Cost

- Depends on formulation and dose:


	Vial Size and Cost	Cost/gram	Total Cost (70 kg patient)
IVIG	5 gram: \$535 to \$1,012	\$107 to \$202	<u>2 gram/kg dose</u> \$ 14,980 to \$28,336
			<u>100 mg/kg dose</u> \$ 4,626
CMV-IVIG	2.5 gram: \$1,542	\$617	\$ 4,626

CMV-IVIG: cytomegalovirus immune globulin

Immune globulin. Lexi-Drugs. Lexicomp. Accessed August 21, 2017.
 Cytomegalovirus immune globulin. Lexi-Drugs. Lexicomp. Accessed August 21, 2017.



Efficacy of IVIG: Acute AMR




Early IVIG Use


1981: First autoimmune IVIG use (2 gm/kg in ITP)

1998: First report of IVIG use post-transplant

Early – mid 1990s: First IVIG use in pre-transplant patients




Imbach et al. *Lancet* 1981. Tyan et al. *Transplantation* 1994.
 Glotz et al. *Transplantation* 1993. Jordan et al. *Transplantation* 1998.



Early AMR Case Reports

	Patients	Treatment	Results
Jordan 1998	Case series: 7 kidney and 3 heart recipients	High dose (HD): IVIG 2 gm/kg x at least 1 dose	Rejection 'reversed' in all patients
Montgomery 2000	Retrospective review: kidney patients receiving PP/IVIG	Low dose (LD): IVIG or CMV immune globulin 100 mg/kg IV after PP	All 3 had (-) DSAs at end of treatment

Jordan et al. *Transplantation* 1998. Montgomery et al. *Transplantation* 2000.



AMR Treatment: Overall Outcomes

AMR: 5.6% (n=16)
DSA (+): 7

• **Combination therapy:** PP + IVIG (2 gm/kg average) + MP

MP: methylprednisolone; ACR: acute cellular rejection

Bocha et al. *Transplantation* 2003.

ACR: 15% (n=43)


• MP ± anti-lymphocyte therapy for severe or resistant

Graft survival at 1 year:

- AMR: 81% vs. ACR: 84%
- No rejection: 94%

AMR response: all treated immediately responded

Post-transplant DSAs: 2 (class II) out of 3 total




National Institute of Health Workgroup: Assessing Efficacy

High dose IVIG alone vs. Low dose IVIG (or CMVig) + PP

- Conclusions: both modalities are effective for AMR treatment, but need to be studied further

Takemoto et al. *Am J Transplant* 2004.




Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines

Category 2C recommendation: Treat antibody-mediated acute rejection with one or more:

- Plasma exchange (plasmapheresis/PP)
- **Intravenous immunoglobulin**
- Anti-CD20 antibody
- Lymphocyte-depleting antibody


KDIGO Transplant Work group. *Am J Transplant* 2009.



HD IVIG vs. Combination Therapy

Group A: 12 patients	• HD IVIG: 2 gm/kg every 2 weeks x 4 doses	36 month graft survival: 50 vs. 91.7% (p = 0.02) 3 month mean DSA MFI and total MFI: lower in B Infectious complications: similar between groups
Group B: 12 patients	• Combination therapy: PP (4 sessions) + IVIG + rituximab	


MFI: mean fluorescence intensity
Lefaucheur et al. *Am J Transplant* 2009



IVIG Therapy for Patients Undergoing Solid Organ Transplantation Guidelines

- II-3/B recommendation: Give **IVIG** after PP for patients who have received a living donor or deceased kidney donor transplant and who have **acute antibody-mediated rejection** to improve graft survival
 - Insufficient data to recommend IVIG without PP and no data that CMV immune globulin is superior

Shehata et al. *Transfus Med Review* 2010.




Systematic Review of AMR Treatment in Kidney Transplant Recipients

- More common use of IVIG in recent years (starting 2002)
 - PP popularity increased at same time
- Supporting evidence for IVIG was deemed 'very low'
 - No randomized controlled trials available

Optimal AMR treatment is unknown


Roberts et al. *Transplantation* 2012.



Lung Transplant: AMR Treatment

- No randomized controlled trials or head to head studies
- Case reports and small studies have extrapolated data from other organs and utilized various combinations of PP, IVIG, and rituximab
 - No recommendations for treatment regimen


Levine et al. *J Heart Lung Transplant* 2016.
Morrell et al. *J Heart Lung Transplant* 2009. Roux et al. *Am J Transplant* 2016.



Heart Transplant: AMR Treatment

- Guidelines for the care of heart transplant recipients (2010)
 - Category C recommendation: Initial therapy to remove circulating anti-HLA antibodies can include (1) plasmapheresis, (2) immunoabsorption and (3) **IVIG**
 - Based on heart desensitization data


Costanzo et al. *J Heart Lung Transplant* 2010.
Leech et al. *Clin Transplant* 2006. Coutance et al. *J Heart Lung Transplant* 2015.



Heart Transplant: AMR and DSA Treatment

- American Heart Association statement on AMR (2015)
 - Class IIa/B recommendation: It is reasonable for primary therapy to include **IVIG**, PP, anti-lymphocyte antibodies, and high dose corticosteroids
 - Class IIb/C recommendation: Consideration may be given to **treatment of rising DSAs** in early post-transplant period as may represent amnestic response.


Colvin et al. *Circulation* 2015.



Liver Transplant: AMR Treatment


- Case reports of combination therapy for DSA (+) AMR
- Banff Working Group on Liver Allograft Pathology:
 - (+) DSA is necessary criteria for diagnosis
 - Recommendation: moderate to severe AMR requires early intervention, typically with PP + **IVIG** ± B cell therapy

O'Leary et al. *Am J Transplant* 2014.
De Bello et al. *Transpl Int* 2015. Demetrius et al. *Am J Transplant* 2016.




Clinical Application

- Optimal IVIG regimen for AMR has not been defined
- Majority of data is in kidney transplant and has been extrapolated to other organ types
- Combination therapy with IVIG + PP ± B cell-directed agent appears to be most effective




**Efficacy of IVIG:
Chronic AMR**

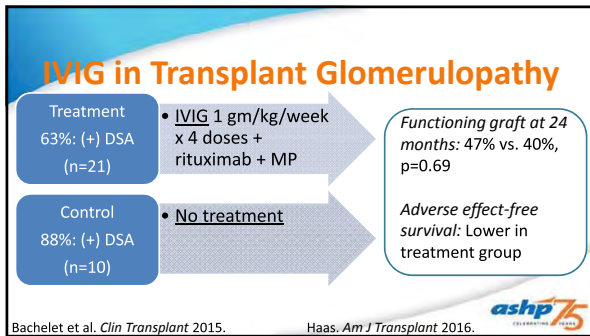


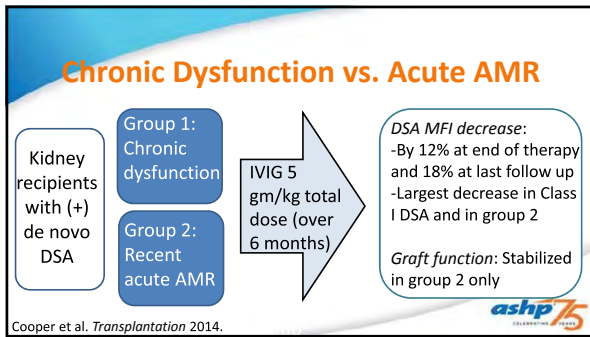
IVIg Use in Chronic AMR

	Fehr et al	Billing et al
Patients	3 adult patients	20 pediatric patients
Treatment	IVIg 400 mg/kg/day on days 2 - 5 + rituximab + MP	IVIg 1 gm/kg/week x 4 doses + rituximab
Results	Graft function improved in all 3 patients at 3 and 6 months	14 (70%) patients responded to treatment - Only 45% of those with chronic glomerulopathy

MP = Methylprednisolone
 Fehr et al. *Transplantation* 2009. Billing et al. *Transplant Int* 2009.









Clinical Application

- IVIG ± rituximab ± methylprednisolone does not appear to reverse or stabilize chronic AMR
 - More adverse effects were seen in treatment group
- Would not recommend IVIG or IVIG-containing regimens for treatment of chronic AMR




Efficacy of IVIG: Induction and Pre-emptive Therapy



IVIG as Induction Therapy

	Patients	Treatment	Results (6 Months)
Bachler 2010	Review: 104 kidney recipients with low-level (+) DSA • 37 patients received treatment	IVIG 400 mg/kg prior to reperfusion and on days 1 - 4 + anti-thymocyte globulin	Clinical/subclinical AMR: 38% vs. 55%, p=0.03 Clinical rejection: 38% vs. 72%, p=0.002 Subclinical AMR: No significant difference

Bachler et al. *Am J Transplant* 2010.



IVIG vs. Combination Therapy

Kidney recipients with positive pre-formed DSA

Group 1: IVIG 2 gm/kg

Group 2: IVIG + PP + rituximab

IVIG on post-operative days 21, 42, and 63

At one year:
 Acute AMR: 19.4 vs. 16.6%, p=NS
 DSA decrease: 44 vs. 80%, p=0.02
 Mean GFR: 43±16 vs. 54±16 mg/dL, p=0.04

Loupy et al. *Transplantation* 2010.

Consensus Guidelines: Management of Antibodies in Transplant

	Biopsy (+)	Biopsy (-)
High risk (desensitization) or Intermediate risk (DSA +)	Treat	Consider initiating therapy if rapidly increasing DSA level
Low risk	Treat	Additional DSA monitoring

Tait et al. *Transplantation* 2013.

Early IVIG Treatment in Lung Transplant

Lung transplant recipients with (+) DSA

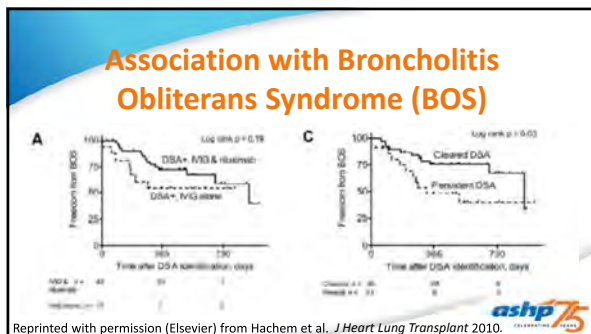
65 patients (56%) developed DSA
 - Class I: 10, class II: 41, and both: 14

IVIG 500 mg/kg monthly x at least 6

± rituximab

- IVIG + rituximab: 44 patients and IVIG: 17 patients
- DSA clearance:
 - 27 (61%) of those with combination
 - 11 (65%) of those with IVIG alone

Hachem et al. *J Heart Lung Transplant* 2010.



Comparison of Early Treatment for DSA in Lung Transplant

<p>Group A: 57 patients</p> <ul style="list-style-type: none"> • IVIG 2 gm/kg + rituximab followed by monthly IVIG if DSA (+) 	<p>Group B: 56 patients</p> <ul style="list-style-type: none"> • PP-based DSA treatment 	<p>Group C: 180 patients</p> <ul style="list-style-type: none"> • Control group without early DSA
---	---	---

Survival at 6 and 12 months: Group A was better than group B and similar to control

DSA clearance at treatment end: 92% in group A vs. 64% in group B

lus et al. *Transplantation* 2016.


Clinical Application

- Kidney transplant recipients
 - IVIG at time of transplant resulted in decreased clinical rejection
 - Combination therapy was more effective at decreasing DSA than HD IVIG
- Lung transplant recipients
 - Regimen of IVIG ± rituximab can clear DSA and was more effective than PP-based therapy

Assessment Question 1

Based on a diagnosis of AMR, the transplant team wants to treat AG. What would you recommend?


- A. IVIG 2 gm/kg alone
- B. Plasmapheresis (4 sessions) + IVIG 100 mg/kg after PP and 2 gm/kg at end + rituximab 375 mg/m²
- C. Plasmapheresis (4 sessions) + anti-thymocyte globulin 1.5 mg/kg x 3 doses + Rituximab 375 mg/m²
- D. Plasmapheresis (4 session) + anti-thymocyte globulin 1.5 mg/kg x 3 doses



Assessment Question 2

AG is going to be started on AMR therapy with PP and IVIG followed by rituximab. She wants to know what adverse events she should be expecting. She is being given Gammaked® formulation. What do you tell her?


- A. Increased risk of viral infections
- B. Tachycardia
- C. Headache
- D. Elevated liver function tests



Assessment Question 3

BD is a 55 year old male that is 7 years out from a kidney transplant. He did well initially, but was lost to follow-up for the last 2 years.


- Creatinine is 6 mg/dL (baseline a year ago: 2 to 2.2 mg/dL).
- A biopsy was done and DSA was drawn.
 - Biopsy showed *diffuse C4d in peritubular capillaries and transplant glomerulopathy*
 - DSA was positive for intermediate level DR8; past DSAs have all been negative



Assessment Question 3


How would you recommend to treat BD's DSA?

- A. No treatment – therapy has not been proven to be beneficial in chronic AMR
- B. IVIG alone – trials have shown that it can improve renal function in kidney transplant patients with chronic AMR
- C. No treatment – patient should have received IVIG alone when DSAs first became positive without dysfunction as pre-emptive therapy is standard of care
- D. IVIG + PP + rituximab – this regimen is standard of care for both acute and chronic AMR



Key Takeaways

- #1: Acute AMR treatment should utilize a multi-modal approach, including PP + IVIG ± B cell modifying agent
- #2: IVIG therapy does not appear effective in chronic AMR, but may be beneficial for DSAs if used prior to graft dysfunction
- #3: Current IVIG formulations are better tolerated than original agents, but adverse effects and overall cost are still a concern



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Questions?





**Challenges in Transplantation:
The Notorious DSA (Donor Specific Antibodies)**

Moderator: Christina Teeter Doligalski, Pharm.D., BCPS, CPP
Clinical Pharmacist, Ambulatory Care Clinical Services
UNC Solid Organ Transplant Clinics
UNC Medical Center Department of Pharmacy



Donor Specific Antibodies: Role of Intravenous Immunoglobulin

Clinical Pearls for Use of Intravenous Immunoglobulin (IVIg)

- Various mechanisms of action proposed; dose of 1 to 2 gm/kg for anti-inflammatory action
- Multiple formulations
 - No true head-to-head studies, but efficacy considered to be equivalent
 - Differences in safety and cost
- Adverse events occur in between 2 and 25% of patients and include
 - Infusion reactions: Pre-medications are often used. Recommended infusion rate and titration regimen depends on formulation.
 - Hemolytic anemia: Most often seen in patients with non-type 0 blood and liquid formulations (Gammaked®, Privigen®)
 - Renal dysfunction: 90% of cases have occurred in sucrose-containing formulations (Carimune®, Cytogam®)
 - Thrombotic events: Ensure adequate hydration. More common in higher osmolality and lyophilized formulations (Carimune® NF, Gammagard® S/D)
 - Other considerations: headache, contraindicated in IgA deficiency, amount of volume and salt content

For more formulation information: 1) Jordan SC, Toyoda M, Kahwaji J, Vo AA. Clinical aspects of intravenous immunoglobulin use in solid organ transplant recipients. *Am J Transplant* 2011 Feb; 11(2): 196-202. 2) Siegel J. The product: All intravenous immunoglobulins are not equivalent. *Pharmacotherapy* 2005 Nov; 25(11 Pt 2); 78S-84S.

IVIg as DSA treatment: Summary

<i>Pre-emptive treatment</i>	<i>Acute AMR</i>	<i>Chronic AMR</i>
<p><u>Kidney</u> Combination therapy with IVIG/plasmapheresis (PP)/anti-CD20 vs. high dose IVIG resulted in lower incidence of chronic AMR and higher GFR level (Loupy et al.)</p> <p><u>Lung</u> Depletion of DSA using IVIG ± rituximab had greater bronchiolitis obliterans syndrome (BOS)-free and overall survival than those with persistent DSA (Hachem et al.)</p> <p>IVIg + rituximab vs. PP-based therapy had better DSA clearance (Ius et al.)</p> <p><u>Evidence-based guidelines</u>: consider IVIG for rapidly increasing DSA level</p>	<p><u>Kidney</u> Combination therapy with IVIG/PP/anti-CD20 vs. high dose IVIG resulted in better graft survival and lower DSA levels (Lefaucheur et al.)</p> <p><u>Evidence-based guidelines for kidney, heart, and liver</u>: recommend IVIG as one of possible AMR treatments</p>	<p><u>Kidney</u> Combination therapy with IVIG/anti-CD20/steroid vs. no treatment in transplant glomerulopathy resulted in no difference in graft outcomes at 24 months (Bachelet et al.)</p> <p>IVIg over 4 to 6 months did not stabilize graft function and did not appear to be beneficial (Cooper et al.)</p> <p><u>Evidence-based guidelines</u>: N/A</p>

AMR=antibody mediated rejection

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Updates in Transplantation 2016



Updates in Transplantation 2016

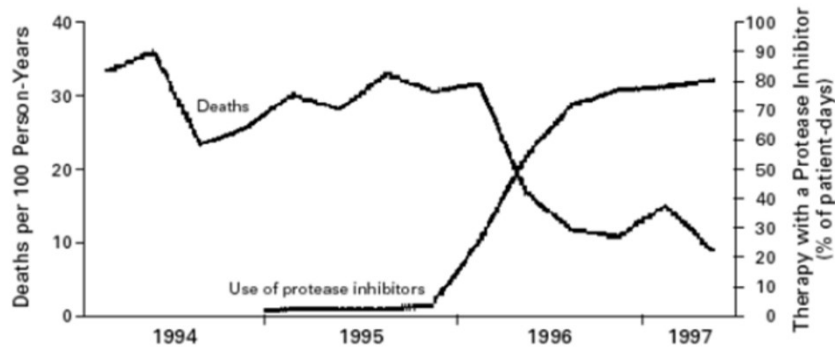
Lindsey A. Pote, Pharm.D., BCPS
Clinical Pharmacy Specialist, Solid Organ Transplantation
The Johns Hopkins Hospital

Objectives

- Summarize the major updates in transplantation in the past year, including the rising prevalence of transplantation in HIV+ recipients
- Assess the advantages and limitations of HIV pharmacotherapy in the pre-, peri-, and post-transplant settings
- Evaluate immunosuppression and opportunistic infection prophylaxis regimens specific to the HIV+ transplant recipient
- Create an effective post-transplant immunosuppressive regimen for an HIV+ transplant recipient



Introduction of HAART in 1996



Palella et al. N Engl J Med. 1998.



Development of ESRD & ESLD in HIV Patients

- Increased life expectancy of patients with HIV
- Development of long-term complications
 - Risk of end stage renal disease (ESRD)
 - HIV associated nephropathy
 - ART related kidney damage
 - Risk of end stage liver disease (ESLD)
 - Co-infection with HCV or HBV

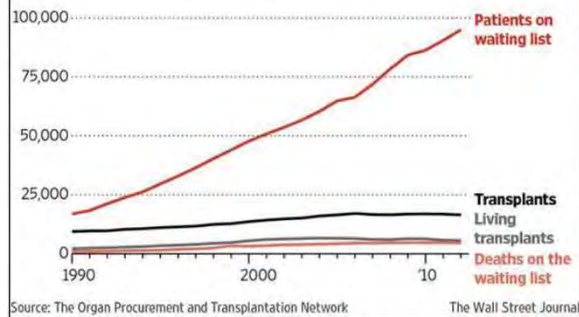
Roland et al. Transplantation. 2003.



Organ Supply & Demand

A Long Wait for a Kidney

Since 1990, the number of people on the waiting list for a kidney transplant has grown sharply, while the number of transplants has increased only slightly.



Source: The Organ Procurement and Transplantation Network

The Wall Street Journal

Becker et al. Wall Street Journal. 2014.



HIV Organ Policy Equity (HOPE) Act

- Will allow for research into transplanting organs from HIV-positive donors into HIV-positive recipients
- Enacted on November 21, 2013
- In 2016, first HIV-to-HIV kidney and liver transplant in US was performed



Image courtesy of www.livingbank.com





Updates in Transplantation 2016

Janessa M. Smith, Pharm.D., BCPS
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The Johns Hopkins Hospital

Objectives

- Assess advantages and limitations of HIV pharmacotherapy in the pre-, peri-, and post-transplant setting



Who Should Get Antiretroviral Therapy?

- DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents recommend initiating ART in **ALL** HIV-infected patients, regardless of CD4 cell count (AI)
- Initiation at any CD4 cell count may delay or prevent HIV-associated morbidity (e.g., HIV-associated nephropathy (HIVAN), liver disease, cardiovascular disease, neurologic complications and malignancies), mortality and transmission

Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Updated: 7/14/16.; NEJM. 2015;373:795-807;NEJM. 2015;373:808-22.



What to Start

- Three drugs from at least 2 classes (i.e., two mechanisms of action)
 - NRTI – nucleos(t)ide reverse transcriptase inhibitor
 - NNRTI – non-nucleoside reverse transcriptase inhibitor
 - PI – protease inhibitor
 - INSTI – integrase strand transfer inhibitor
 - EI – entry inhibitor
- Usually 2 from the NRTI class and a 3rd agent from NNRTI, PI, INSTI or EI class



What to Start

NRTI	NNRTI	PI	INSTI	EI
Abacavir Didanosine Emtricitabine Lamivudine Stavudine Tenofovir Zidovudine	Efavirenz Etravirine Nevirapine Rilpivirine	Atazanavir Darunavir Fosamprenavir Indinavir Lopinavir Nelfinavir Saquinavir Tipranavir	Dolutegravir Elvitegravir Raltegravir	Enfuvirtide Maraviroc



DHHS Recommended Regimens

- INSTI-based Regimen
 - Dolutegravir/Abacavir/Lamivudine
 - Dolutegravir PLUS Tenofovir/Emtricitabine
 - Elvitegravir/cobicistat/Tenofovir/Emtricitabine
 - Raltegravir PLUS Tenofovir/Emtricitabine
- PI-based Regimen
 - Darunavir PLUS ritonavir PLUS Tenofovir/Emtricitabine

Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.
Updated: 7/14/2016



Considerations When Selecting ART for Transplant Patients

Pre-transplant

Comorbidities
HIV resistance
HIV viral load, CD4 cell count

Peri-transplant

Rapidly changing renal function
Oral intake

Post-transplant

Pill burden
Dosing frequency
Drug interactions
Graft effects



Comorbidity Considerations

- Cardiovascular disease
 - Abacavir associated increased risk of myocardial infarction
 - PI-based therapy associated with dyslipidemia
- Co-infection with hepatitis B
 - Lamivudine and tenofovir can be used to treat HIV and HBV co-infected patients
- Co-infection with hepatitis C
 - Drug interactions
- Chronic kidney disease
 - Avoid tenofovir disoproxil fumarate (CrCl <70 mL/min)
 - Avoid tenofovir alafenamide (CrCl <30 mL/min)
- Severe liver disease
 - Avoid abacavir
 - Use PI with caution (dose adjustments, some contraindicated)



Immediate Peri-transplant Considerations

- Kidney transplant
 - NRTIs (except abacavir) require renal dose adjustment and dose should be modified during peri-transplant period as renal function improves
 - Avoid single tablet regimens and NRTI fixed-dose combination products until renal function improves/stabilizes
- Liver transplant
 - Avoid ART that requires high calorie intake (e.g., rilpivirine) or acid environment for absorption (e.g., atazanavir)



Pill Burden

- Pill burden
 - Single-tablet regimens preferred
 - Associated with increased adherence (OR 1.98, $p < 0.001$), virologic suppression (OR 1.21, $p < 0.001$) and reduced hospitalizations (HR 0.69, $p < 0.001$) as compared to multiple-tablet regimens (based on prescription data)
- Dosing frequency
 - Once-daily dosing preferred
 - Associated with increased adherence compared with twice-daily dosing in randomized controlled trials

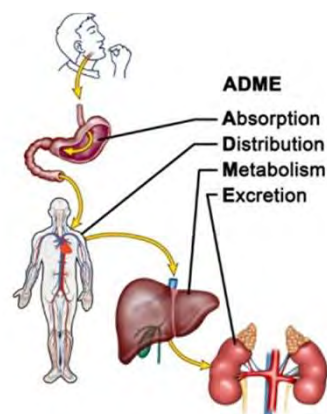
Nachega JB. Clin Infect Dis. 2014. 58:1297-1307.; Sutton SS. Pharmacotherapy. 2016; 36:385-401.; Sutton SS. Am J Manag Care. 2016;22:242-8.



Combination Products	
NRTI Combinations	
Combivir®	Lamivudine/zidovudine
Descovy®	Emtricitabine/tenofovir alafenamide
Epzicom®	Abacavir/lamivudine
Trizivir®	Abacavir/lamivudine/zidovudine
Truvada®	Emtricitabine/tenofovir disoproxil fumarate
PI/Booster Combinations	
Evotaz®	Atazanavir/cobicistat
Kaletra®	Lopinavir/ritonavir
Prezcobix®	Darunavir/cobicistat
Single Tablet Regimens	
Atripla®	Efavirenz/emtricitabine/tenofovir disoproxil fumarate
Complera®	Rilpivirine/emtricitabine/tenofovir disoproxil fumarate
Genvoya®	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Odefsey®	Rilpivirine/emtricitabine/tenofovir alafenamide
Stribild®	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Triumeq®	Dolutegravir/abacavir/lamivudine

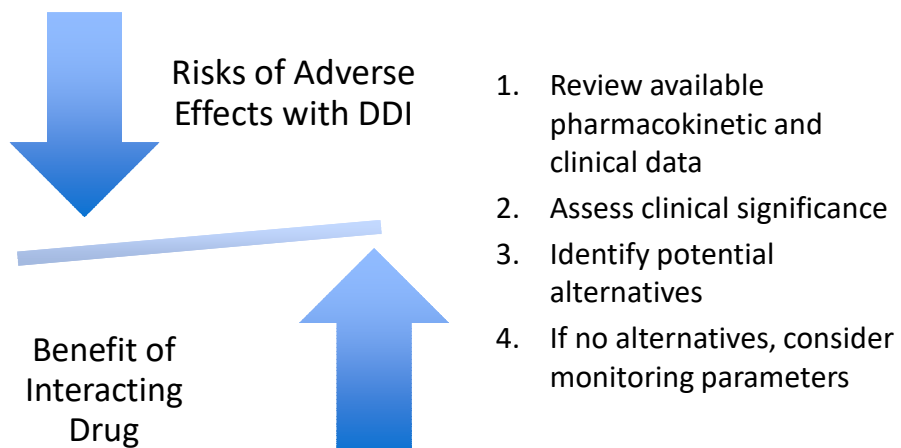
Drug Interactions with ART

- **Absorption**
 - E.g. chelation, gastric acid, P-gp
- **Distribution**
 - E.g. competition for protein binding
- **Metabolism**
 - E.g. CYP450 enzymes
- **Elimination**
 - E.g. inhibition of renal clearance



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Managing Drug Interactions



Overview Drug Interaction Concerns

- Calcineurin inhibitors (CNI) and mTOR inhibitors with PI, ritonavir, cobicistat and NNRTI
- INSTI with oral electrolyte repletion
- Acid suppression with atazanavir and rilpivirine



CNI and ART

- Cyclosporine and tacrolimus are major substrates of CYP3A4 and P-gp
- Interactions with PI, ritonavir, or cobicistat (inhibitors of CYP3A4) can result in increased exposure of CNI and increased toxicity
- Interactions with NNRTIs (inducers of CYP3A4) may result in decreased exposure of CNI and loss of efficacy
 - Note: rilpivirine is not an inducer of 3A4



Management of CNI with ART

- Tacrolimus
 - Ritonavir-boosted therapy can result in a 5- to 10-fold increase in AUC and >10-fold increase in half-life
 - Cobicistat is expected to have the same effect as ritonavir
 - Variability amongst PI and interpatient variability exists
 - Consider initial dose of 0.5-1 mg once weekly with close monitoring and adjustments based on tacrolimus levels
- Cyclosporine
 - Protease inhibitors/cobicistat can result in 5-fold increase in trough concentrations and prolong elimination half-life by 2-fold
 - Consider reducing initial daily dose by 80% with close monitoring of cyclosporine A levels



Frassetto L. Biopharm Drug Dispos. 2013;34:442-51.; Mertz D. Am J Kidney Dis. 2009;54:e1-4.; Schonder KS. Ann Pharmacother. 2003;37:1793-6.; Vogel M. Liver Transplantation. 2004;10:939-44.

Management of CNI with NNRTI Therapy

- Efavirenz, etravirine and nevirapine are moderate inducers of 3A4 and may result in significant reductions of CNI concentrations
- Interaction not well studied – if co-administration required close monitoring of trough concentrations should guide dose adjustments
 - Muller *et al.* reported a median tacrolimus dose was 8.5 mg Q12H in patients on efavirenz or nevirapine
 - Frassetto *et al.* reported similar doses of cyclosporine with efavirenz and nevirapine as non-HIV-infected patients
- Full induction (or de-induction) of CYP3A4 enzymes may take up to 2-4 weeks when starting (or stopping) NNRTI therapy

Frassetto L. *Biopharm Drug Dispos.* 2013;34:442-51.; Mertz D. *Am J Kidney Dis.* 2009;54:e1-4.; Muller E. *NEJM.* 2015;372:613-620; Frassetto L. *Transplantation.* 2005;80:13-7.



m-TOR Inhibitors with ART

- Sirolimus and everolimus are major substrates of CYP3A4 and P-gp
- Interactions with protease inhibitors may lead to significant increases in AUC
 - Jain *et al.* reported 60% increase in AUC and 9-fold increase in trough levels even with 80% empiric dose reduction
 - Barau *et al.* reported once weekly sirolimus dosing (1.5 mg) to maintain sirolimus troughs of 8-10 ng/mL
- Interaction with NNRTI not well studied – if co-administration required close monitoring of trough concentrations should guide dose adjustments
 - Full induction/de-induction of CYP3A4 enzymes may take up to 2-4 weeks when starting or stopping NNRTI therapy

Jain AK. *Liver Transplant.* 2002;8:838.; Barau C. *Fundam Clin Pharmacol.* 2009;23:423-5.



INSTI and Oral Electrolyte Replacement

- INSTI form a metal-drug complex with polyvalent cations resulting in impaired oral absorption
 - Al, Mg, Ca-containing antacids (e.g., Maalox, Tums), supplements (MVI, PhosLo) or Fe products
 - Only applies to oral products – IV electrolytes are not an issue
- Degree of interaction and management varies with INSTI

Roberts JL. Pharmacotherapy. 2011;31(10):298e-302e.



Raltegravir and Oral Electrolyte Replacement

- **Avoid** Mg-containing products with twice daily raltegravir
- **CaCO₃: Use with CAUTION**
 - Manufacturer states that the interaction did not lead to clinically meaningful changes to raltegravir concentrations
 - Case report of virologic failure with reduced raltegravir serum levels in a patient on CaCO₃ and raltegravir

	Simultaneous	2 hr before	2 hr after	6 hr before	6 hr after
RAL + Mg-Al	Cmax: ↓46% AUC: ↓49% Cmin: ↓63%	Cmax: ↓51% AUC: ↓51% Cmin: ↓56%	Cmax: ↓22% AUC: ↓30% Cmin: ↓57%	Cmax: ↓10% AUC: ↓13% Cmin: ↓50%	Cmax: ↓10% AUC: ↓11% Cmin: ↓49%
RAL + CaCO ₃ (3 g)	Cmax: ↓52% AUC: ↓55% Cmin: ↓32%	-	-	-	-

Roberts JL. Pharmacotherapy. 2011;31(10):298e-302e.
Isentress. [Package Insert]. Merck & Co. Updated 2/2015.



Dolutegravir and Oral Electrolyte Replacement

- **Space** Mg-Al-containing products
- **CaCO₃: Use with CAUTION**
 - Give simultaneously with food OR space administration
- Space administration: 2 hr before or 6 hr after dolutegravir

	Simultaneous	2 hr after/Fed*		Simultaneous	2 hr after/Fed*
DTG + Mg-Al	Cmax: ↓72% AUC: ↓74% Cmin: ↓74%	Cmax: ↓18% AUC: ↓26% Cmin: ↓30%	DTG + FeSO ₄ (324 mg)	Cmax: ↓57% AUC: ↓54% Cmin: ↓56%	Cmax: no effect AUC: no effect Cmin: no effect
DTG + CaCO ₃ (1.2 g)	Cmax: ↓37% AUC: ↓39% Cmin: ↓39%	Cmax: no effect AUC: no effect Cmin: no effect	DTG + MVI	Cmax: ↓35% AUC: ↓37% Cmin: ↓32%	-

*Mg-Al not studied under fed conditions

Tivicay. [Package Insert]. ViiV Healthcare. Updated 8/2015.



Elvitegravir and Oral Electrolyte Replacement

- Data on the effect of polyvalent cations on elvitegravir concentrations is limited
 - No data on simultaneous administration
 - Spacing by 2 and 4 hours did not affect elvitegravir
- Manufacturer recommends to space antacids (Mg-Al or CaCO₃) by 2 hours

Viteka. [Package Insert]. Gilead Sciences, Inc. Updated 9/2014.



Acid Suppression

- Not limited to transplant patients
- Atazanavir and rilpivirine are more soluble and best absorbed at lower gastric pH
- Management
 - Atazanavir: Space administration of all acid-suppressing medications (e.g., PPI, H2RA, antacids)
 - Rilpivirine: **avoid** PPI, space administration of other acid-suppressing medications (e.g., H2RA, antacids)



Optimal ART Regimens

NRTI	NNRTI	PI	INSTI	EI
Abacavir	Efavirenz	Atazanavir	Dolutegravir	Enfuvirtide
Didanosine	Etravirine	Darunavir	Elvitegravir	Maraviroc
Emtricitabine	Nevirapine	Fosamprenavir	Raltegravir	
Lamivudine	Rilpivirine	Indinavir		
Stavudine		Lopinavir		
Tenofovir		Nelfinavir		
Zidovudine		Saquinavir		
		Tipranavir		



Optimal ART Regimens

NRTI

Abacavir Didanosine	<ul style="list-style-type: none">• Lamivudine or emtricitabine preferred• Abacavir if HLA-B5701 negative and low cardiac risk• Tenofovir alafenamide preferred over tenofovir disoproxil fumarate given less renal and bone toxicity• Tenofovir/emtricitabine NRTI backbone preferred in patients co-infected with hepatitis B virus
Emtricitabine	
Lamivudine	
Stavudine	
Tenofovir Zidovudine	



Optimal ART Regimens

NNRTI

Efavirenz	<ul style="list-style-type: none">• Avoid efavirenz, nevirapine, etravirine given significant and complicated drug interactions with CNI
Etravirine	
Nevirapine	<ul style="list-style-type: none">• Avoid rilpivirine in patients that require acid suppression or unable to intake at least 500 calories with each dose
Rilpivirine	



Optimal ART Regimens

PI

Atazanavir
Darunavir
Fosamprenavir
Indinavir
Lopinavir
Nelfinavir
Saquinavir
Tipranavir

- Avoid PI-based therapy given significant and complicated drug interactions with CNI, m-TOR inhibitors



Optimal ART Regimens

INSTI

Dolutegravir
Elvitegravir
Raltegravir

- Dolutegravir preferred
- Avoid raltegravir in patients that require oral magnesium for repletion
- Avoid elvitegravir since requires cobicistat or ritonavir for PK enhancement



Optimal ART Regimens

EI	
Enfuvirtide Maraviroc	<ul style="list-style-type: none">• Maraviroc if R5 trophic virus – potential additive benefit of graft protection



Key Takeaways

- Optimal management strategy is to avoid PI-, EVG-, and NNRTI-based therapy when possible
 - If co-administration is required, closely monitor CNI and m-TOR serum levels initially and when changing ART
- Many other drug interactions with ART to consider outside immunosuppressants
- Dolutegravir with an NRTI-backbone is preferred





Updates in Transplantation 2016

Erin H. Ticehurst, Pharm.D.

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**Rejection is more common in HIV+ kidney
transplant recipients than HIV- recipients?**

A YES

B NO



KTX Key Trial

Methods	Prospective, multi-center KTX performed 2003 – 2009 (n=150)		
Findings	Patient survival	Graft survival	Rejection
	1 year 94.6±2%	90.4%	31%
	3 years 88.2±3.8%	73.7%	41%
	Only half of rejection episodes responded to steroids		
Higher tacrolimus levels associated with decreased rejection risk			
Anti-thymocyte globulin induction associated with increased risk of graft loss			

Stock PG et al. NEJM 2010;363:2004-14

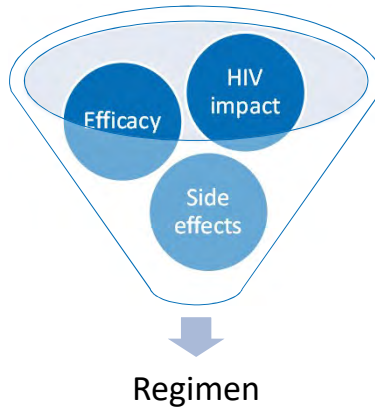


Objectives

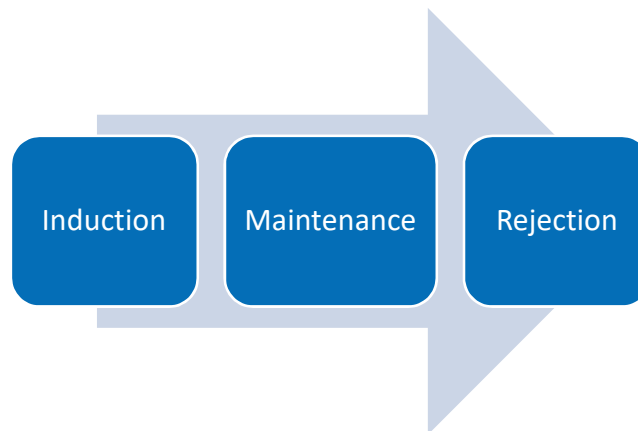
- Evaluate immunosuppression and opportunistic infection prophylaxis regimens specific to the HIV+ transplant recipient
- Create an effective post-transplant immunosuppressive regimen for an HIV+ transplant recipient



Immunosuppression Considerations



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KTX Induction

Methods	Scientific Registry of Transplant Recipients KTX performed 2000 – 2014 (n=830)
Findings	Induction reduced hospital stay and lowered rates of delayed graft function as well as graft loss without increasing infection rate
	Anti-thymocyte globulin associated with lowered rates of acute rejection (wRR 0.59, 95% CI 0.35-0.99) compared to other strategies
	Induction did not increase infection rate

Kurcirka LM et al. Am J Trans 2016;16:2368-76



KTX Anti-Thymocyte Globulin Induction

Methods	Single center KTX performed 2006 – 2013 and received anti-thymocyte globulin (n=38)
	Baseline CD4+ count > 350 versus < 350 cells/mm ³
Findings	Median follow-up 2.6 years
	Increased rate of severe CD4+ lymphopenia & higher serious infection rate in patients with pre-transplant CD4+ count < 350 cells/mm ³

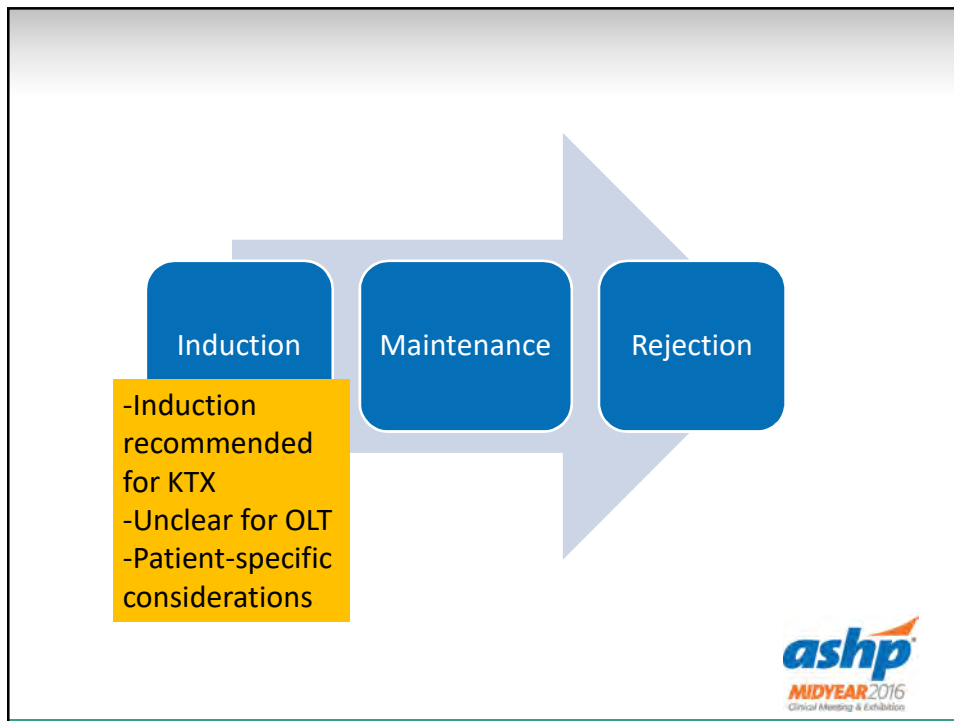
Suarez JF et al. Am J Trans 2016;16:2463-72



KTX Basiliximab Induction

Methods	Multi-center KTX performed 2005 – 2009 (n=27)	
	Basiliximab Cyclosporine or tacrolimus Mycophenolate mofetil Methylprednisolone/prednisone taper	
Findings	Patient survival	Graft survival
	1 year 100%	1 year 98%
	2 years 98%	2 years 96%
15% had acute cellular rejection		

Touzot M et al. Am J Trans 2010;10:2263-9



Calcineurin Inhibitors

- Cyclosporine has theoretical anti-HIV and anti-HCV activity
- Tacrolimus preferred over cyclosporine due to lower rejection rates
- C_0 correlates well with AUC for tacrolimus but not for cyclosporine

Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Stock PG et al. N Engl J Med 2010;363:2004-14
Frassetto LA et al. Transplantation 2014;97:702-7



KTX Calcineurin Inhibitors

Methods	National observational study (UK) KTX performed 2005 – 2013 without primary graft failure (n=78)
Findings	Acute rejection rate at 1 year (p=0.003): Cyclosporine 58% Tacrolimus 21%

Gathogo E et al. Transplantation 2016;100(4):871-18



Antiproliferatives

- Mycophenolate products may suppress HIV replication particularly in a NRTI regimen
- Mycophenolate products are more potent and preferred over azathioprine

Margolis DM et al. J Acquir Immune Defic Syndr 2002;31:45-9



Belatacept

- Belatacept potential advantages
 - Fewer drug-drug interactions
 - Side effect profile



KTX De Novo Belatacept

- Case report of de novo belatacept, mycophenolate mofetil and prednisone
- No rejection or graft loss with 18 months of follow-up
- Complications
 - E. faecalis bacteremia & bacteriuria

Cohen EA et al. Am J Trans 2016;16:2753-7



KTX Belatacept Conversion

- Case report
- Initial immunos were basiliximab, mycophenolate, tacrolimus and prednisone taper
- Conversion from tacrolimus at week 14 due to delayed graft function
- Dialysis was no longer indicated at 21 weeks
- One borderline rejection episode treated with prednisone boluses

Ebcioğlu Z et al. Am J Trans 2016 (accepted for publication)



Sirolimus

- Sirolimus inhibits HIV-1 progression via
 - Reducing CCR5-gene transcription
 - Blocking interleukin-2 intracellular secondary messenger (mTOR)
 - Up-regulating the β -chemokine macrophage inflammatory protein
- Possibly reservoir-modifying activity
- Associated with lower post-transplant HIV DNA levels
- May have anti-HHV8 activity so possible role with Kaposi's sarcoma

Stock PG et al. Am J Trans 2014;14:1136-41
 Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
 Di Benedetto FD et al. Transplantation 2010;89(6):733-8



OLT Sirolimus Conversion

Methods	Single-center OLT performed since 2003 (n=14)
	Initial immunos were tacrolimus (n=2) or cyclosporine (n=12) plus steroids
	Cyclosporine was changed to sirolimus for 6 patients due to renal dysfunction or Kaposi's sarcoma
Findings	Lower rejection rate with sirolimus Reduced HIV viral load but not CD4+ count Sirolimus associated with improved HCV viral load

Di Benedetto FD et al. Transplantation 2010;89(6):733-8



KTX Early Steroid Withdrawal

Methods	Single-center KTX performed 2006 – 2010 (n=11)
	9 anti-thymocyte globulin, 2 basiliximab Methylprednisolone days 0-4 Tacrolimus Mycophenolate mofetil
Findings	1 year outcomes: Acute rejection 9% Patient survival 100% Graft survival 91% (primary non-function)

Muthukumar T et al. Transplantation 2013;95(5):711-20



KTX Early Steroid Withdrawal

Methods	Single-center KTX performed 2007 – 2012 (n=13)
	Basiliximab, methylprednisone taper x 5 days, calcineurin inhibitor, & mycophenolic acid
Findings	61.5% patients had acute rejection with half resuming steroids
	4 year outcomes: Patient survival 100% Graft survival 89%
	eGFR 58±40 ml/min if patient had acute rejection versus 76±6 ml/min if no rejection

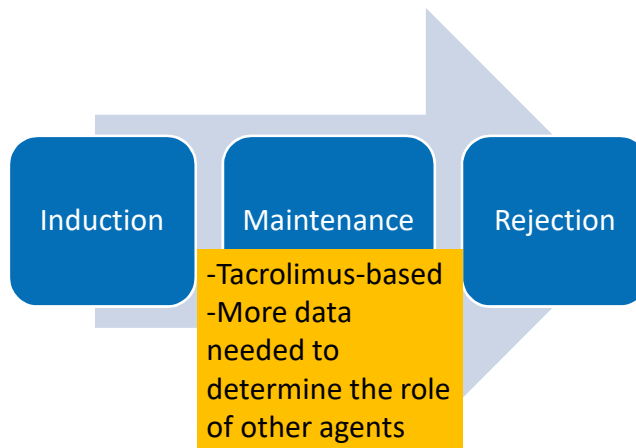
Bossini N et al. Transplant Int 2014;27:1050-9



OLT Steroid Avoidance

Methods	Single-center OLT performed 2007 – 2012 (n=4)
	Basiliximab Cyclosporine Mycophenolate mofetil added if elevated creatinine necessitated lower cyclosporine levels
Findings	Median follow-up of 17±8 (8-27 months) with 100% patient & graft survival 1 acute rejection episode treated with pulse steroids No infections

Rafecas A et al. Liver Transplant 2004;10(10):1320-3



Induction Maintenance Rejection

- Steroid boluses (low vs high)
- Maximize mycophenolate and calcineurin inhibitor
- Sirolimus
- Avoid anti-thymocyte globulin unless refractory

Fox AM, Vagefi PA, Stock PG. J Semin Liver Dis 2012;32:177-85
Carter JT et al. Am J Trans 2006;6:753-60

Opportunistic infections are more common in HIV+ kidney transplant recipients than in HIV- recipients?

A YES

B NO

OI Prophylaxis Recommendations

Infection	Agent of Choice	Criteria & Duration for Primary Prophylaxis
Pneumocystis pneumonia	Sulfamethoxazole/trimethoprim	Lifelong
Cytomegalovirus	Valganciclovir	CMV IgG+ donor or recipients x \geq 3 months

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
 Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
 Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25



OI Prophylaxis Recommendations (cont'd)

Infection	Agent of Choice	Criteria & Duration for Primary Prophylaxis
Toxoplasma gondii	Sulfamethoxazole/trimethoprim	Toxoplasmosis IgG+ donor or IgG+ recipient with CD4+ count \leq 200 cells/mm ³
Mycobacterium avium complex	Azithromycin	CD4+ count \leq 50-75 cells/mm ³ . Continue until $>$ 100 cells/mm ³ x 6 months

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
 Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
 Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25



OI Prophylaxis Recommendations (cont'd)

Infection	Agent(s) of Choice	Criteria & Duration for Primary Prophylaxis
Histoplasma capsulatum	Itraconazole	CD4+ count < 150 cells/mm ³ plus occupational or residential risk factors
Coccidioidomycosis	Fluconazole or itraconazole	IgG or IgM+ if from an endemic area when CD4+ count < 250 cells/mm ³ Lifelong if donor history of coccidioides

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25



Key Takeaways

- More experience is needed to determine patient-specific optimal immunosuppression
- Opportunistic infection prophylaxis strategies differ from standard organ transplant protocols so close attention needs to be paid



Patient Case

JR is a 43 yo male with past medical history significant for HIV, hypertension and ESRD secondary to HIV-associated nephropathy on hemodialysis three times a week. He is being considered for a kidney transplant and presents to clinic today for antiretroviral therapy modification in preparation for transplant.

His HIV has been well controlled for the past 3 months on darunavir 800 mg once daily, ritonavir 100 mg once daily, raltegravir 400 mg twice daily and tenofovir disoproxil fumarate 300 mg once weekly. He reports missing 1-2 doses per month. His most recent CD4 436 cells/mm³ and HIV RNA <20 copies/mL. He has no HIV resistance detected.



Patient Case

Current medications:
Nifedipine XL 90 mg once daily
Atorvastatin 20 mg daily
Aspirin 81 mg daily
Cinacalcet 90 mg daily
Sevelamer 800 mg three times daily with meals
Darunavir 800 mg daily
Ritonavir 100 mg daily
Raltegravir 400 mg twice daily
Tenofovir DF 300 mg once weekly

Labs:
Na: 135 mEq/L
K: 4.7 mEq/L
Cl: 100 mEq/L
Ca: 9.7 mg/dL

Scr: 7.8 mg/dL
BUN: 45 mg/dL

Gluc: 147 mg/dL

AST: 20 U/L
ALT: 18 U/L
Alk phos: 60 U/L
T. bilirubin: 0.5 mg/dL

HLA-B5701: negative



How would you modify his ART today?

- A** Discontinue raltegravir and change to dolutegravir 50 mg once daily. Continue tenofovir DF 300 mg once weekly, darunavir 800 mg once daily, ritonavir 100 mg once daily
- B** Discontinue all current antiretrovirals and start dolutegravir 50 mg once daily and Descovy® (tenofovir AF/emtricitabine 25/200 mg) once daily
- C** Discontinue all current antiretrovirals and start dolutegravir 50 mg once daily, lamivudine 50 mg x 1 dose then 25 mg daily after HD, and abacavir 600 once daily
- D** Discontinue all current antiretrovirals and start Triumeq® (dolutegravir/abacavir/lamivudine 50/600/300 mg) once daily



What information about your recommended ART should you relay to his inpatient team for peri-transplant management ?

- A** Dolutegravir inhibits metabolism of tacrolimus, empirically reduce tacrolimus dose to 0.5 mg once weekly and monitor levels
- B** Lamivudine dose should be adjusted as the patient's renal function improves post-kidney transplant
- C** Abacavir dose should be adjusted as the patient's renal function improves post-kidney transplant
- D** Can start single-tablet regimen of Triumeq® (dolutegravir/abacavir/lamivudine 50/600/300 mg) once daily on post-op day 1



Patient Case

Current medications:

Nifedipine XL 90 mg once daily

Atorvastatin 20 mg daily

Aspirin 81 mg daily

Cinacalcet 90 mg daily

Sevelamer 800 mg three times daily with meals

- Consider other medications that may need dose adjustments when changing ART
- Consider increasing atorvastatin to 40-80 mg with discontinuation of darunavir/ritonavir



JR has a KTX offer. Current PRA is 80% and CD4+ count is 450 cells/mm³. What is your recommendation for induction?

- A** No induction
- B** Anti-thymocyte globulin
- C** Basiliximab



What maintenance immunosuppression regimen do you recommend?

- A** Tacrolimus, prednisone
- B** Tacrolimus, mycophenolate mofetil, prednisone
- C** Cyclosporine, mycophenolate mofetil, prednisone
- D** None of the above



Acknowledgements

- Emily Blumberg, MD
- Christine Durand, MD
- ASHP Section of Clinical Specialists & Scientists



ACCP

Immunology/Transplantation PRN Focus Session – Novel Approaches to Immunomodulation After Transplantation

Immunology/Transplantation PRN Focus Session—Novel Approaches to Immunomodulation After Transplantation

Activity Number: 0217-0000-15-129-L01-P, 1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Monday, October 19, 2015

3:15 p.m. to 4:45 p.m.

Plaza Room B

Moderator: Christopher R. Ensor, Pharm.D., BCPS

Assistant Professor of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania

Moderator: Reed Hall, Pharm.D., BCPS

Clinical Pharmacy Specialist, UT Health Sciences Center, San Antonio, Texas

Agenda

- | | |
|-----------|--|
| 3:15 p.m. | Extending Immunosuppression: Once Daily Tacrolimus
<i>Patricia West-Thielke, Pharm.D., BCPS</i>
Assistant Director of Transplant Research, University of Illinois at Chicago, Chicago, Illinois |
| 3:35 p.m. | Belatacept: Beyond De-Novo Renal Transplantation
<i>Rita R. Alloway, Pharm.D., FCCP, BCPS</i> Research Professor, Director, Transplant Clinical Research, University of Cincinnati, Cincinnati, Ohio |
| 3:55 p.m. | Finding a 'Home' for mTOR Inhibitors
<i>Matthew J. Everly, Pharm.D., BCPS</i>
Interim Director, Terasaki Research Institute, Los Angeles and Adjunct Assistant Professor of Medicine, Nephrology Division, David Geffen School of Medicine, University of California, Los Angeles, California |
| 4:15 p.m. | The Future of Immunosuppression is Now!
<i>Jennifer Trofe-Clark, Pharm.D., FCCP, FAST, BCPS</i>
Adjunct Associate Professor of Medicine, Renal Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania; Kidney Transplant Clinical Pharmacy Specialist, Department of Pharmacy Services, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania |
| 4:35 p.m. | Panel Discussion |

Conflict of Interest Disclosures

Rita R. Alloway: Consultant/member of advisory board for Veloxis Pharmaceuticals, Astellas, Sanofi, and Amgen; Speaker's bureau for Sanofi.

Christopher R. Ensor: no information provided.

Matthew J. Everly: no conflicts to disclose.

Reed Hall: no conflicts to disclose.

Jennifer Trofe-Clark: Clinical investigator for Veloxis Pharmaceuticals and Agency for Healthcare Research and Quality; Received grant funding for Veloxis Pharmaceuticals and Agency for Healthcare Research and Quality..

Patricia West-Thielke: Received grant funding for Veloxis Pharmaceuticals and Astellas.

Learning Objectives

1. Evaluate the pharmacokinetics and clinical utility of novel once daily tacrolimus formulations.
2. Compare and contrast the two available once daily tacrolimus formulations.
3. Recognize the evolving role of belatacept in transplant immunosuppression.
4. Design a transplant immunosuppression regimen incorporating the non-traditional use of belatacept.
5. Distinguish the role for mammalian target of rapamycin (mTOR) inhibitors in transplant recipients.
6. Describe the pros and cons of mTOR inhibitor use for transplant immunosuppression.
7. Discuss the future of immunosuppression management, including pharmacogenomic assessments.
8. Describe the transplant immunosuppression pipeline opportunities and challenges.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/gc15.

Extending Immunosuppression: Once Daily Tacrolimus

Patricia M. West-Thielke, PharmD, BCPS
Director of Clinical Research
University of Illinois Health
Department of Surgery

Conflict of Interests

- Received grant funding for Veloxis Pharmaceuticals and Astellas.

Objectives

- Evaluate the pharmacokinetics and clinical utility of novel once daily tacrolimus formulations
- Compare and contrast the two available once daily tacrolimus formulations

PK Background

- Bioavailability - % of the total dose administered that is absorbed and available in the circulation
- Bioequivalence – the absence of a significant difference in the bioavailability of 2 drugs administered at the same dose
- Narrow therapeutic index drug – a drug with a narrow therapeutic range = tacrolimus

PK background

- AUC, Cmax, Cmin – we are all familiar with these
- Measures of variation:
 - Fluctuation $\rightarrow 100 \times (C_{max} - C_{min}) / C_{avg}$; peak trough exposure normalized to average concentration
 - Swing $\rightarrow 100 \times (C_{max} - C_{min}) / C_{min}$; peak trough exposure normalized to trough

Tacrolimus Formulations

- Three branded formulations are currently available on the market:
 - Once-daily Envarsus XR
 - Approved July 10, 2015
 - 80% reduction in dose from immediate release
 - Once-daily Astagraf XL
 - Approved July 19, 2013
 - 1:1 conversion with immediate release
 - Twice-daily Prograf or generic – immediate release

Astagraf

- Extended-release formulation of tacrolimus
 - Tacrolimus is mixed with ethylcellulose, hypromellose and lactose to form immediate-sustained-release granules
 - Ethylcellulose controls the rate of permeation of water into the granules giving it the sustained release character
- Similar safety and non-inferior efficacy vs. twice-daily tacrolimus capsules (Prograf)

Envarsus XR

- Utilizes MeltDose technology to reduce the size of the drug particles to individual molecules
 - Creates a solid dispersion, or "solid solution," of the drug
 - A patented nozzle sprays the drug onto a carrier which becomes a granulate which is then compressed into tablets
- Delivers the tacrolimus throughout the GI tract → stable consistent absorption over the whole day
- ↑ bioavailability, ↓ peak, ↓ peak-to-trough fluctuation
- Similar safety and non-inferior efficacy vs. twice-daily tacrolimus capsules (Prograf)

ASTCOFF

- ASTCOFF is an open label, randomized, crossover study
- Stable renal transplant recipients were randomized to receive Prograf for one week and then either
 - Envarsus for one week then Astagraf for one week or
 - Astagraf for one week then Envarsus for one week
 - Conversion factor of 1:1:0.80mg (Prograf: Astagraf: Envarsus)
- Tacrolimus levels analyzed by tandem mass spectrometry
- No dose titrations were allowed (MMF, prednisone, tacrolimus)
- 24-hour PK collections performed at the end of one-week periods

Results

- Thirty-one patients were randomly assigned to and dosed with study drug
 - 16 in Prograf:Envarsus:Astagraf
 - 15 in Prograf:Astagraf:Envarsus
- Baseline characteristics were similar across the groups
 - P→E→A vs. P→A→E
 - Mean age 50.1 vs 46.3 years;
 - 56 vs 60% male;
 - 81.3 vs 66.7% Caucasian

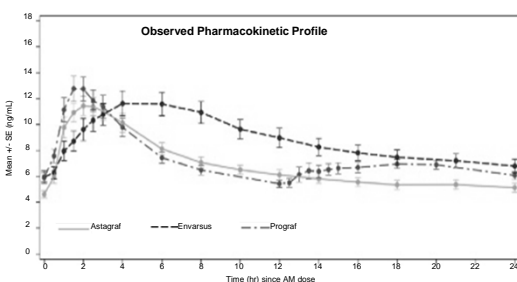
Results

Observed PK Parameters and Summary Comparisons Between Tacrolimus Formulations						
	Envarsus (E)	Astagraf (A)	Prograf (P)	P-Value		
	Once-daily	Once-daily	Twice-daily	E vs P	A vs P	E vs A
Total daily dose (mg/day) [mean]	4.9	6.1	6.1			
AUC ₂₄ (hr*ng/mL) [geometric mean]	199.3	158.6	170.3	0.002	0.149	<0.001
C _{max} (ng/mL) [geometric mean]	12.9	12.5	13.6	0.354	0.150	0.638
C _{min} (ng/mL) [geometric mean]	6.3	4.9	5.9	0.223	0.001	<0.001
Fluctuation (%) [mean]	83.6	118.9	112.6	0.004	0.518	<0.001
T _{max} (hr) [median]	5.90	1.93	1.48	<0.001	0.669	<0.001

Results

	Observed PK parameters		
	Ratio of Geometric Means, RGM (90% CI)		
	E/P	A/P	E/A
AUC ₂₄ (hr*ng/mL) [geometric mean]	117.0 (107.9, 127.0)	93.1 (85.8, 101.0)	125.7 (114.1, 138.5)
C _{max} (ng/mL) [geometric mean]	94.7 (85.8, 104.4)	91.8 (83.3, 101.3)	103.1 (92.4, 115.0)
C _{min} (ng/mL) [geometric mean]	107.0 (97.6, 117.2)	83.0 (75.7, 90.9)	128.9 (117.4, 141.6)

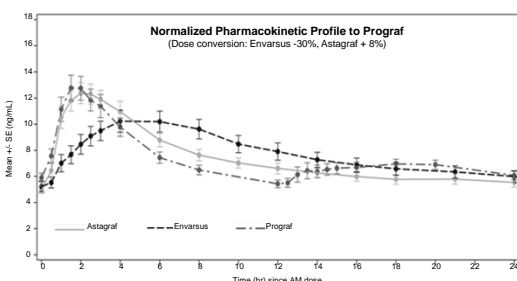
Results



Results

	Exposure-Normalized PK parameters		
	Ratio of Geometric Means, RGM (90% CI)		
	E/P	A/P	E/A
AUC ₂₄ (hr*ng/mL) [geometric mean]	102.4 (94.4, 111.1)	100.6 (92.7, 109.1)	100.6 (91.3, 110.8)
C _{max} (ng/mL) [geometric mean]	82.8 (75.1, 91.4)	99.2 (89.9, 109.4)	82.5 (73.9, 92.0)
C _{min} (ng/mL) [geometric mean]	93.6 (85.4, 102.6)	89.6 (81.8, 98.2)	103.1 (93.9, 113.2)

Results



Results

- **Observed data**
 - Envarsus presents a flatter PK profile than Astagraf and Prograf respectively
 - ↓ 30% intra-day peak-to-trough fluctuations (p=0.004 and <0.001)
 - ↑ median time to maximal concentration (T_{max}) to 6 hours for Envarsus compared to 1.93 hour and 1.48 hour (p<0.001)
 - Conversion strategy used yielded 17% ↑ exposure for Envarsus vs Prograf (p=0.002) and 25.7% higher exposure vs Astagraf (p<0.001)
 - Astagraf provided non statistically significantly ↓ (6.9%) exposure vs Prograf (p=0.149)
- **Data normalized to Prograf exposure (AUC) data**
 - When normalized to Prograf exposure, Envarsus ↓ C_{max} by ~17% when compared to Astagraf and Prograf (p=0.006 and p=0.002, respectively)
 - When normalized to Prograf exposure, Astagraf had similar C_{max} and T_{max} to Prograf (p=0.887)

Take Home Points from ASTCOFF

- Envarsus PK parameters tended to differ significantly from Astagraf and Prograf, while Astagraf and Prograf tended to be similar to each other.
- Dose conversion analysis supports the following recommended total daily dose conversions rates.
 - Prograf : Astagraf + 8%
 - Prograf : Envarsus -30%
 - Astagraf : Envarsus -36%
- Significant PK differences between tacrolimus formulations → the formulations are NOT interchangeable or substitutable.

Questions?

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**2015 ACCP Global
Conference on Clinical Pharmacy**

Belatacept: Beyond De-Novo Renal Transplantation
Rita R. Alloway, PharmD, FCCP
Research Professor of Medicine
Director, Transplant Clinical Research
University of Cincinnati

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Clinical Pharmacy

Conflict of Interests

- I have financial relationships with BMS as an investigator and Director Coordinating Center
- I have financial relationships within the last 12 mo
 - Clinical Research Grants - Novartis, Astellas, Veloxis, Takeda, Onyx, GSK, Prolong, Bristol-Myers Squibb, Chiltern, Sanofi, and FDA
 - Advisory Board - Veloxis, Astellas, Sanofi, Amgen
 - Speakers Bureau- Sanofi
- This presentation DOES include discussion of off-label use
- ACCP provided travel support

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Learning Objectives

- Recognize the evolving role of belatacept in transplantation immunosuppression
- Design a transplant immunosuppression regimen incorporating the non-traditional use of belatacept

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Learning Objective 1

- Recognize the evolving role of belatacept in transplantation immunosuppression

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Belatacept Current Role

- First FDA approved CNI free regimen
 - Approved combination with basiliximab induction, mycophenolate mofetil [MMF], and corticosteroids in adult kidney transplants based upon 1 yr noninferiority endpoint

Parameter	BELA N=226 n (%)	CYA N=221 n (%)
Efficacy Failure Month 36 Components	58 (25.7)	57 (25.8)
BPAR ^b	50 (22.1)	31 (14.0)
Graft loss	9 (4.0)	10 (4.5)
Death	10 (4.4)	15 (6.8)
Lost to follow-up	2 (0.9)	5 (2.3)

3 year results Am J Transplant. 2012 Jan;12(1):210-7. doi: 10.1111/j.1600-6143.2011.03785.x. Epub 2011 Oct 12.
5 year results J Am Soc Nephrol. 2010 Sep; 21(9): 1587-1596.

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Belatacept Cochrane Review

- No evidence of any difference in the effectiveness of belatacept and CNI in preventing acute rejection, graft loss and death.
- Belatacept is associated with
 - Less chronic kidney scarring and better kidney transplant function
 - Better blood pressure and lipid profile
 - Lower incidence of diabetes versus treatment with a CNI.
 - Harms related to PTLD remain unclear
 - Longer-term studies comparing belatacept versus tacrolimus are needed to help clinicians decide which patients might benefit most

Cochrane Database Syst Rev. 2014 Nov 24;11:CD010699. doi: 10.1002/14651858.CD010699.pub2
Transpl Int. 2015 May 12. doi: 10.1111/tni.12605. [Epub ahead of print]

Evolving Role of Belatacept

- Phase 3 study regulatory limitations required concomitant and control immunosuppression that was outdated.
- Detriments to rapid clinical uptake include
 - Increase rate and severity of acute rejection episodes
 - Unknown rates of PTLD in seropositive recipients
 - Annual costs of belatacept based regimen compared to generic alternatives is cost prohibitive for many
 - REMS
 - Lack of pediatric use due to EBV black box
 - Lack of available infusion sites willing to accept risks

Rita Alloway, Personal communication

Evolving Role of Belatacept

- Combination regimens which reduce rate and severity of acute rejection
 - T-cell depleting induction
 - Alternative combinations with tacrolimus, mTor, etc.
- Alternative regimen various CNI toxicities or diagnoses
 - Bridging regimens during DGF or AKI
 - Conversion for chronic CNI nephrotoxicity
 - Conversion for acute or chronic neurotoxicity, seizure, tremors, posterior reversible encephalopathy syndrome(PRES)
 - Recurrent disease
 - Thrombotic microangiopathy
- Non renal transplant uses, ie OLT, VCA, panc, etc

Learning Objective 2

- Design a transplant immunosuppression regimen incorporating the non-traditional use of belatacept

ACCP

- Compared to CNI containing regimens
 - Stable longterm eGFR
 - Lower acute rejection episodes after 1 year
 - Lower rate of DSA formation
 - Adherence known

Brannon et al [abstract]. *AJT* 2015; 15 (suppl 3). <http://www.atcmeetingabstracts.com/abstract/>. Accessed August 20, 2015

Belatacept – Denovo

Simultaneous CNI and Steroid Withdrawal


Design	Prospective, open label, multi-center			
Population	Low-moderate immunologic risk EBV recipients seropositive			
Intervention	Antithymocyte globulin(rabbit) 1.5mg/kg x 4, Bela , MPA, CSWD Antithymocyte globulin(rabbit) 1.5mg/kg x 4, Siro , MPA, CSWD			
Comparator	Antithymocyte globulin(rabbit) 1.5mg/kg x 4, Tacro , MPA, CSWD			
Outcomes of Interest	Variable	Bela (n=33)	Siro (n=36)	Tacro (n=30)
	BPAR	12%	4%	4%
	Graft Survival	94%	92%	100%
	Patient Survival	97%	100%	100%
	Mean eGRF (1yr/4yr) ml/min	64/60	62/72	54/56

Ferguson et al. *AJT* 2011;1(1):66-76
4 year results: Grinyo et al [abstract]. *AJT* 2014; 14 (suppl 3). <http://www.atcmeetingabstracts.com/abstract/>. Accessed August 20, 2015.

Belatacept – Denovo


Design	Prospective, single center
Population	12 kidney transplants ePRA 0% EBV recipients seropositive
Intervention	Antithymocyte globulin 2-5mg/kg, 5-7 doses Enteric coated MPA Chronic steroids
Comparator	None, Proof-of-concept
Outcomes of Interest	2/12 acute rejection treated with steroids 6/12 infections with 5 pts admitted No PTLD 100% patient and graft survival @6mo Good renal function

Transpl Immunol, 2015 Jan;32(1):35-9. doi: 10.1016/j.trim.2014.10.002. Epub 2014 Oct 20

Belatacept – Denovo 


Design	Prospective, randomized, multi-center
Population	315 kidney transplants cPRA ≤25% EBV recipient seropositive
Intervention	Belatacept 10mg/kg @ POD 1,5,15,28,56,84, then 5mg/kg monthly OR Tacrolimus targets POD 0-30 8-12ng/mL, >30 5-10ng/mL
Comparator	Antithymocyte globulin(rabbit) 4-6mg/kg OR alemtuzumab 30mg x1 dose MPA CSWD at 5 days
Outcomes of Interest	Renal function >45ml/min Patient and Graft Survival Rate, Type and Severity of Rejection

ClinicalTrials.gov Identifier: NCT01729494

Belatacept – Denovo 


- University of Cincinnati Sponsor and Coordinating Center
- 218 out of 315 enrolled
- DSMB has allowed enrollment to continue based upon 150pts enrolled with 2 months followup
- FDA IND precludes reporting any results by group until enrollment complete

ClinicalTrials.gov Identifier: NCT01729494
Rita Alloway, Personal communication

Belatacept – Denovo 


- Clinical Pearls - Efficacy
 - Expect lower baseline SrCr values thus recalibrate your trigger for biopsy
 - Consider treating steroids resistant rejections with high dose tacrolimus
 - Continue belatacept when treating rejection with tacrolimus
 - Maintain MPA at target AUCs
 - Once baseline SrCr achieved, do NOT expect “creatinine creep”
 - Diagnosis of rejection does NOT require tacrolimus maintenance conversion

Transplantation, 1996 Sep 15;62(5):594-9.
Rita Alloway, Personal communication

Belatacept – Denovo 


- Clinical Pearls - Toxicity
 - Monitor MPA AUCs, may witness suprathereapeutic MPA AUCs in tacrolimus, steroid free regimen.
 - Dose adjust MPA, but tolerate absolute neutrophil counts = 1500, if stable.
 - Aggressively dose decrease MPA in cases of viral infections, ie CMV, BKV, etc.
 - If no response in viral titers, discontinue MPA.
 - If no response, may extend belatacept dosing interval.

Rita Alloway, Personal communication
American Journal of Transplantation, 2014; 14: Suppl 3:549.
American Journal of Transplantation, 2014; 14: Suppl 3:550.

Belatacept – Conversion 

- If immediate CNI discontinuation, initiate bela at denovo dosing.
- If patient is switched to bela
 - Belatacept 5 mg/kg IV on days 1, 15, 29, 43, and 57, and then every 28 days thereafter.
 - CNI dose was tapered as follows:
 - 100% on day 1,
 - 40 to 60% on day 15,
 - 20 to 30% on day 23, and
 - none on day 29 and beyond.

Clin J Am Soc Nephrol, 6 (2011), pp. 430-439

Belatacept – Monitoring 

- Upper limit of therapeutic window defined, but not lower limit
- PK and PD (CD86-saturation) markers have limited interpatient variability
- No commercially available monitoring assay
- Authors state TDM may not be necessary, except to minimize adverse events
- TDM needed to monitor patients with viral infections and potentially breakthrough rejections

Ther Drug Monit, 2014 Dec 30. [Epub ahead of print]

Future Directions



- True pharmacoeconomic evaluation is complex
 - Multiplicity of payors over the lifetime of a transplanted graft
 - Evaluating drug costs in the context of potential savings
 - Lab costs, coordinator time??, extended graft and patient survival, etc
 - Ease administration
 - Facilitate administration via home infusion
 - Unlimited infusion centers
 - Expand label or allow for off-label uses
 - True adherence known
-

Questions?



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**2015 ACCP Global
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Finding a 'Home' for mTOR Inhibitors

Matthew Everly, BCPS
Terasaki Research Institute, Los Angeles

1

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Conflict of Interests

- I have no relevant financial relationship for the presented material

2

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Learning Objectives

- Distinguish the role for mammalian target of rapamycin (mTOR) inhibitors in transplant recipients.
- Describe the pros and cons of mTOR inhibitor use for transplant immunosuppression.

3

Bringing mTOR inhibitors to transplantation

1983: Cyclosporine
100 mg

1983: tacrolimus
1 mg
617

Calcineurin Inhibitors (CNIs)

+

- Improved 1 year survival rates to 90%
- Improved 1-year acute rejection rates to less than 20%

-

- Did not improve long term allograft survival
- Calcineurin inhibitor nephrotoxicity
- Lack of impact on B-cell/humoral rejection

4

Preventing early acute rejection does not dramatically impact long term outcomes

A

Year	Rate (%)
1995	40
1996	45
1997	35
1998	25
1999	20
2000	15

B

Year of Tx	Year of Tx	Survival (%)
1995	8.0	100
1994	7.6	100
1993	7.9	100
1992	7.7	100
1991	8.0	100
1990	8.0	100
1989	7.9	100
1988	7.9	100

Years to 51.8% survival (maximum follow-up reached)
Tx = Transplant

Salvadori et al. World J transplant 2013; 7.

5

CYCLOSPORINE-INDUCED ACUTE RENAL DYSFUNCTION IN THE RAT

EVIDENCE OF ARTERIOLAR VASOCONSTRICTION WITH PRESERVATION OF TUBULAR FUNCTION¹

JAN ENGLISH,² ANDREW EVAN,³ DONALD C. HOUGHTON,⁴ AND WILLIAM M. BENNETT^{2,5}

¹Departments of Medicine and Pathology, Oregon Health Sciences University, Portland, Oregon, and ²Department of Anatomy, ³University of Indiana Medical Center, Indianapolis, Indiana

Transplantation 1987;44:135

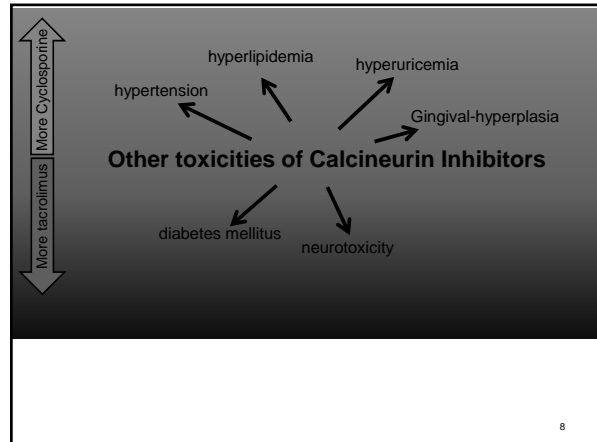
- ↓ in vasodilators (PGE2, NO)
- ↑ in vasoconstrictors (thromboxane, endothelin, and more)

6

Hypothesis:

Calcineurin inhibitors hinder long-term allograft function

7



8

CNI withdrawal & conversion studies

Study (yr)	Intervention arm	Control arm	CNI sparing strategy	Study length (mo)
RMR (2004)	SRL, Steroids, C ₆ A--Withdrawal by 3 mo (n = 215)	SRL, Steroids, C ₆ A (n = 215)	Withdrawal by 3 mo	48
Spare the Nephron (2011)	MMF, S, CNI--SRL (30-180 d) (n = 148)	MMF, S, CNI (n = 151)	Conversion by 30-180 d	24
CONCEPT (2009)	MMF, S, C ₆ A--SRL by 3 mo (n = 95)	MMF, S, C ₆ A (n = 97)	Conversion by 3 mo	12
SMART (2010)	MMF, S, C ₆ A--SRL 10-24 d (n = 70)	MMF, S, C ₆ A (n = 71)	Conversion by 10-24 d	12
ZEUS (2012)	EC-MPS, S, C ₆ A--EVR by 4.5 d (n = 154)	EC-MPS, S, C ₆ A (n = 146)	Conversion by 4.5 mo	36
HERAKLES (2012)	EC-MPS, S, C ₆ A--EVR by 3 mo (n = 171)	EC-MPS, S, C ₆ A (n = 166)	Conversion by 3 mo	12

CNI: Calcineurin inhibitor; C₆A: Cyclosporine; EVR: Everolimus; MMF: Mycophenolate mofetil; EC-MPS: Enteric coated mycophenolate sodium; SRL: Sirolimus; S: Steroids.

Salvadori et al. World J transplant 2013; 3:7.

CNI withdrawal & conversion studies

Study (yr)	Drugs	F-up (mo)	Patient survival		Graft survival		Biopsy proven acute rejection		Glomerular filtration rate (mL/min)	
			SRL/EVR	CNI	SRL/EVR	CNI	SRL/EVR	CNI	SRL/EVR	CNI
RMR (2004)	SRL (SRL+C ₆ A)	48	95.3%	92.1%	91.5%	84.2%	10.2	4.5	58.3	43.8
Spare the Nephron (2011)	SRL/CNI	24	100%	97.5%	100%	98.7%	9.5	11.3	99.5	58.8
CONCEPT (2009)	SRL/C ₆ A	12	100%	100%	100%	99.0%	16.8	8.2	69.6	64.8
SMART (2010)	SRL/C ₆ A	12	99.0%	99%	99.0%	97.0%	17.4	15.5	64.5	53.4
ZEUS (2012)	EVR/C ₆ A	36	98.1%	97.9%	98.7%	98.6%	13.0	4.8	67.9	63.6
HERAKLES (2012)	EVR/C ₆ A	12	99.4%	98.8%	99.4%	99.4%	10.0	8.4	68.6	63.0

CNI: Calcineurin inhibitor; C₆A: Cyclosporine; EVR: Everolimus; SRL: Sirolimus.

HERAKLES had a high rate of study discontinuation due to adverse events in treatment arm.

Salvadori et al. World J transplant 2013; 3:7.

- Early conversion of could be seen as efficacious from the collective trials.
- However, higher acute rejection rates, appearing just after conversion, and adverse events to mTOR inhibitor were a problem.

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CNI avoidance studies

Study (yr)	Drugs	F-Up (mo)	Patient survival		Graft survival		Biopsy proven acute rejection		Glomerular filtration rate (mL/min)	
			SRL	CNI	SRL	CNI	SRL	CNI	SRL	CNI
Flechner (2004)	SRL/C ₆ A	24	93.50%	100%	93.50%	93.60%	16.50%	16.60%	69.7	59.2
Flechner (2007)	SRL/C ₆ A	60	87.10%	90%	83.90%	76.70%	12.90%	23.30%	66.7	50.7
Lavon (2006)	SRL/TAC	12	96.00%	96%	94%	92%	13%	10%	83	41
SYMPHONY (2007)	SRL/C ₆ A	36	95%	94%	85%	87%	39%	27%	71.1	67.1
Handy (2008)	SRL/TAC	60	98.50%	93.80%	88%	83%	NA	NA	89	93
Lo (2004)	SRL/TAC	12	100%	98%	89%	80%	7%	10%	72.4	50.5
Buggenies (2007)	SRL/C ₆ A	24	NA	NA	NA	NA	NA	NA	82	49.8
Spiessner Group (2007)	SRL/TAC	12	97%	97%	85.90%	95.70%	14.30%	8.60%	69	60
Clote (2010)	SRL/TAC	12	95.80%	97.10%	88.9%	93.4%	13.8%	12.3%	56.1	58.4
ORION (2011)	SRL/TAC	24	94.5%	97%	88.9%	93.4%	13.8%	12.3%	63.4	66.7

CNI: Calcineurin inhibitor; SRL: Sirolimus; C₆A: Cyclosporine; TAC: Tacrolimus; NA: Not available.

Reasonable outcomes but a high rate of subject discontinuation seen due to mTOR related adverse effects

Salvadori et al. World J transplant 2013; 3:7.

Table 1
Incidence of adverse events of interest in pivotal transplantation studies of everolimus or sirolimus (18–30).

Adverse event	Everolimus (0.75 or 1.0 mg BID with reduced- or standard-dose TAC or CSA) ^a	Sirolimus (2 or 5 mg with CSA ± corticosteroids)
Dermatologic disorders		
Acne	5%–14%	10%–25%
Stomatitis/oral ulcers	2%–3%	0%–4%
Rash	NR	5%–10%
Wound-healing disorders		
Any wound-healing event	11%–15%	3%–8%
Wound dehiscence	1.5%	NR
Incisional hernia	3%	18%
Metabolic disorders		
Hyperglycemia	12%–14%	NR
New-onset diabetes	5%–32%	20%–27%
Lipid disorders		
Hyperlipidemia	21%–24%	30%–64%
Hypertriglyceridemia	4%	21%–57%
Lipoproteinemia	16%–17%	20%–6%
Dyslipidemia	15%	NR
Other disorders		
Hypertension	3%–30%	0%–10%
Nephrotic syndrome	NR	2%
Pulmonary disorders		
Interstitial pneumonia	0%–2%	0%–4%
Blood and lymphatic disorders		
Anemia	8%–26%	11%–27%
Leucopenia	3%–12%	5%–12%
Thrombocytopenia	5%	6%–23%
Hemodynamic disorders		
Hypertension	17%–30%	21%–38%

Abbreviations: BID, twice daily; CSA, cyclosporine; NR, not reported; TAC, tacrolimus.

Kaplan et al. Transplantation Rev 2014; 28:126.

Conversion From Calcineurin Inhibitors to Sirolimus Maintenance Therapy in Renal Allograft Recipients: 24-Month Efficacy and Safety Results From the CONVERT Trial

Francesco P. Schena,^{1,11} Michael D. Pascoe,² Josefina Alberu,³ Maria del Carmen Rial,⁴ Rainer Oberbauer,⁵ Daniel C. Brennan,⁶ Josep M. Campistol,⁷ Lorraine Racusen,⁸ Martin S. Polinsky,⁹ Robert Goldberg-Alberts,⁹ Huihua Li,⁹ Joseph Scarola,⁹ and John F. Neylan,⁹ for the Sirolimus CONVERT Trial Study Group¹⁰

Transplantation 2009;87:233.

	All patients		Stratum with baseline glomerular filtration rate 20 to 40 mL/min		Stratum with baseline glomerular filtration rate >40 mL/min		Subgroup with baseline glomerular filtration rate >40 mL/min and baseline U _{crea} ≤0.11	
	SRL (n=555)	CNI (n=275)	SRL (n=58)	CNI (n=29)	SRL (n=497)	CNI (n=246)	SRL (n=195)	CNI (n=102)
Composite safety endpoint ^a								
12 mo	36 (6.5)	11 (4.0)	14 (24.1)	3 (10.3)	22 (4.4)	8 (3.3)	6 (3.1)	4 (3.9)
24 mo	89 (16.0)	40 (14.5)	24 (41.4)	12 (41.4)	65 (13.1)	28 (11.4)	17 (8.7)	12 (11.8)
BCR ^b								
12 mo	17 (3.1)	4 (1.5)	4 (6.9)	0 (0)	13 (2.6)	4 (1.6)	5 (2.6)	2 (2.0)
24 mo	44 (7.9)	19 (6.9)	5 (8.6)	1 (10.3)	39 (7.8)	16 (6.5)	13 (6.7)	9 (8.8)
Graft survival								
12 mo	328 (95.1)	267 (97.1)	47 (81.0)	26 (89.7)	481 (96.8)	241 (98.0)	191 (97.9)	99 (97.1)
24 mo	497 (89.5)	249 (90.5)	38 (65.5)	18 (62.1)	439 (92.4)	231 (93.9)	188 (96.4)	98 (96.1)
Patient survival								
12 mo	541 (97.5)	273 (99.3)	55 (94.8)	29 (100)	486 (97.8)	244 (99.2)	191 (97.9)	100 (98.0)
24 mo	523 (94.2)	263 (95.6)	48 (82.8)	26 (89.7)	475 (95.6)	237 (96.3)	189 (96.9)	99 (97.1)

Donor-Specific HLA Antibodies in a Cohort Comparing Everolimus With Cyclosporine After Kidney Transplantation

L. Liefeldt^{1,2,3,4}, S. Brakemeier^{5,1}, P. Glander⁶, J. Wäisser⁷, N. Lachmann⁸, C. Schönemann⁹, B. Zukunff¹⁰, P. Illigens¹¹, D. Schmidt¹², K. Waa¹³, B. Rudolph¹⁴, H.-H. Neumayer¹⁵ and K. Budde¹⁶

Everolimus trials:
ZEUS sub-study and
CRAD001ADE13 sub-study

Liefeldt et al. Am J Transplant 2012; 12:1192

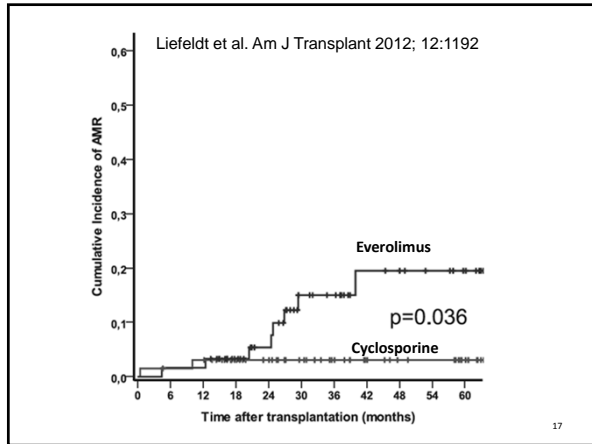
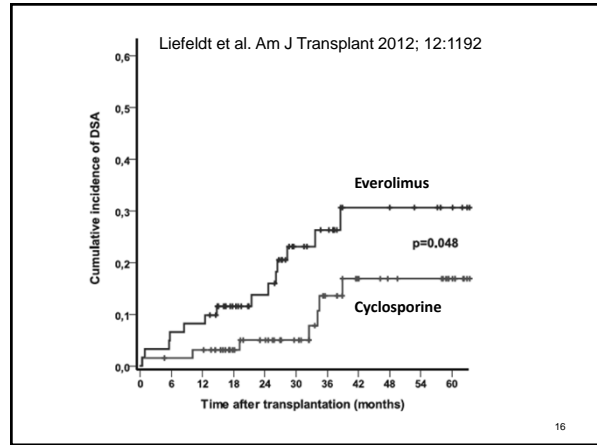
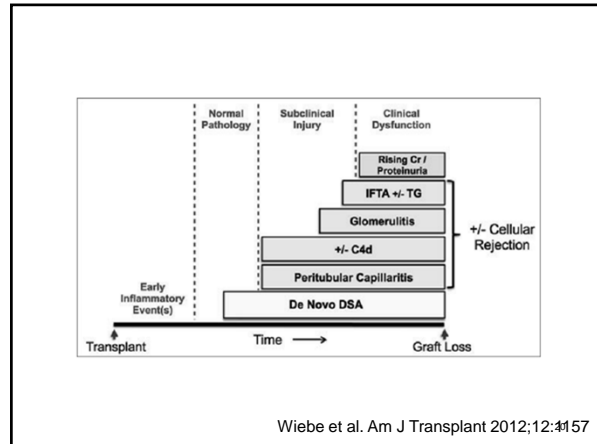
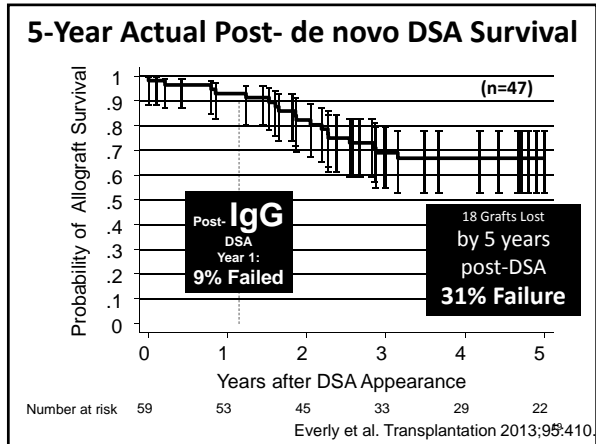


Table 3: Outcome after KTX in patients randomized to receive cyclosporine- or everolimus-based immunosuppression

Parameter	Cyclosporine (n = 66)	Everolimus (n = 61)	
Patient survival number (%)	Month 12	65 (98.5%)	61 (100.0%)
	Month 24	64 (97.0%)	60 (98.4%)
Death censored graft survival number (%)	Month 12	63 (95.4%)	60 (98.4%)
	Month 24	65/65 (100.0%)	60/61 (98.4%)
Creatinine (mg/dL)	Month 12	61/65 (98.8%)	65/60 (91.7%)
	Month 24	1.48 ± 0.61 (n = 65)	1.31 ± 0.57 (n = 60)**
Proteinuria (mg/day)	Month 12	1.69 ± 0.57 (n = 49)	1.31 ± 0.84 (n = 44)*
	Month 24	1.73 ± 0.70 (n = 40)	1.45 ± 1.06 (n = 36)*
Proteinuria >1 g/day	Month 12	179 ± 172 (n = 60)	258 ± 183 (n = 40)**
	Month 24	150 ± 97 (n = 39)	380 ± 608 (n = 34)***
Proteinuria >1 g/day	Month 12	132 ± 185 (n = 35)	278 ± 608 (n = 33)**
	>24 Months	Proteinuria >1 g/day: n = 1	Proteinuria >1 g/day: n = 7

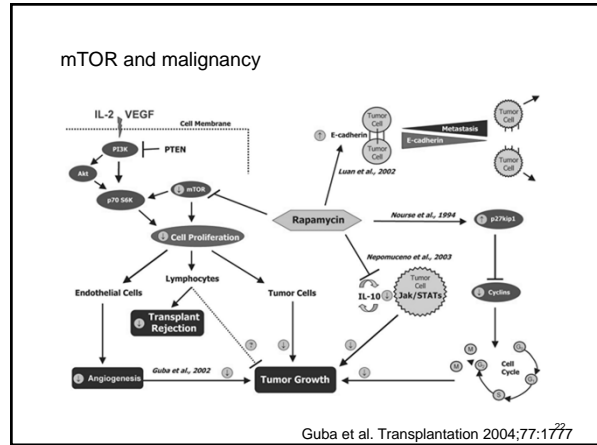
*p < 0.05, **p < 0.01, ***p < 0.001, #p = 0.075 (Wilcoxon-Mann-Whitney test).
*median follow-up: 1094 (372–2107) days, **median follow-up: 1108 (372–2107) days

Liefeldt et al. Am J Transplant 2012; 12:1192



What is the "home" for mTOR inhibitors?

21



The immunosuppressive macrolide RAD inhibits growth of human Epstein-Barr virus-transformed B lymphocytes *in vitro* and *in vivo*: A potential approach to prevention and treatment of posttransplant lymphoproliferative disorders

Mirosław Majewski*, Magdalena Korecka*, Plamen Kosshev*, Shiyong Li*, June Goldman*, Jonni Moore*, Leslie E. Silberstein*, Peter C. Nowell*, Walter Schuler*, Leslie M. Shaw*, and Mariusz A. Wasik*

*Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA 19104; and †Novartis Pharma, Basel CH-4002, Switzerland

Majewski et al. PNAS 2000;97:4285

Low Incidence of Malignancy among Sirolimus/Cyclosporine-Treated Renal Transplant Recipients

Barry D. Kahan,^{1,2} Yarkin K. Yakupoglu,¹ Linda Schoenberg,¹ Richard J. Knight,¹ Stephen M. Katz,¹ Dejian Lai,² and Charles T. Van Buren¹

Background. Malignancies, a well-known complication of immunosuppressive therapy in renal transplant recipients, represent an important cause of long-term morbidity and mortality. One approach to addressing this problem is identifying agents that display antineoplastic properties concomitant with their immunosuppressive effects.

Methods. We examined the neoplasms among 1008 renal transplant recipients treated at a single center with sirolimus-cyclosporine ± prednisone.

Results. Clinical and laboratory data, including 62.3 ± 26.1 months follow-up (range 27.1–131), revealed 36 tumors in 35 patients (3.6%) presenting at 32.5 ± 29.8 months. The 2.4% incidence of all tumors, the most common neoplasms, was 1.58-fold greater than the general U.S. population. In addition to the 0.4% incidence of posttransplant lymphoproliferative disorders (PTLD) and a 0.2% incidence of renal cell carcinoma, we observed single cases of breast, bladder, endometrial, lung, and brain neoplasms as well as leukemia. The mean trough drug concentrations at the time of diagnosis in affected recipients were within our putative target ranges. In addition to eleven graft losses due to death with a functioning kidney, two were related to chronic rejection following reduced immunosuppression, and one therapeutic nephrectomy for PTLD. Five of twelve deaths were caused by malignancies; four others among 1008 patients over the entire follow-up were attributed to cardiovascular events; one, to respiratory failure; and two, at distant locations to unknown causes.

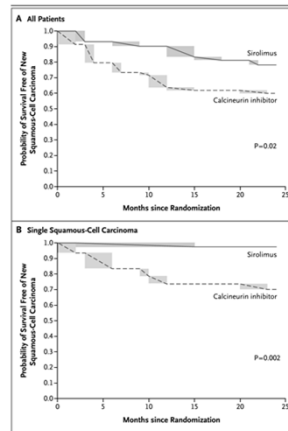
Conclusions. The sirolimus-cyclosporine ± prednisone combination appears likely to be associated with a reduced incidence of tumors.

(Transplantation 2005;80: 749–758)

Sirolimus and Secondary Skin-Cancer Prevention in Kidney Transplantation

Sylvie Euvrard, M.D., Emmanuel Morelon, M.D., Ph.D.,
 Lionel Rostaing, M.D., Ph.D., Eric Goffin, M.D., Anabelle Brocard, M.D.,
 Isabelle Tromme, M.D., Nilufer Broeders, M.D.,
 Veronique del Marmol, M.D., Ph.D., Valérie Chatelet, M.D.,
 Anne Dompmartin, M.D., Ph.D., Michèle Kessler, M.D., Andreas L. Serra, M.D.,
 Günther F.L. Hofbauer, M.D., Claire Pouteil-Noble, M.D., Ph.D.,
 Josep M. Campistol, M.D., Ph.D., Jean Kanitakis, M.D., Adeline S. Roux, M.Sc.,
 Evelyne Decullier, Ph.D., and Jacques Dantal, M.D., Ph.D.,
 for the TUMORAPA Study Group*

NEJM 2012; 367:329



NEJM 2012; 367:329

mTOR in malignancy:

- Conversion from CNI to mTOR inhibitor may have a lower rate of malignancy development
- May be most beneficial in in patients at risk of skin cancer development

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Regression of Left Ventricular Hypertrophy in Kidney Transplant Recipients: The Potential Role for Inhibition of Mammalian Target of Rapamycin

E. Paoletti and G. Cannella

Transplant Proc 2010;42:S41

28

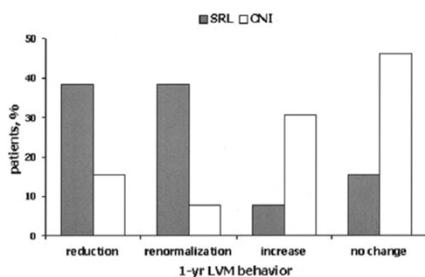


Fig 1. One-year left ventricular hypertrophy behavior in 13 renal transplant recipients converted from calcineurin inhibitor (CNI) to sirolimus (SRL) as compared to 26 continuing CNI ($P = .0125$, chi-square analysis). LVM, left ventricular mass.

Transplant Proc 2010;42:S41

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Summary

30

1. CNI-free, mTOR inhibitor based regimens have higher rates of rejection

31

2. More information is needed regarding donor specific antibodies with mTOR inhibition

32

3. Conversion to mTOR late post-transplant is not recommended in those with poor renal function and/or proteinuria

33

4. The benefit of mTOR-inhibitor based regimen in renal transplant is reduced CNI nephrotoxicity and a lower incidence of malignancy

34


5. Greatest renal transplant function benefit from mTOR conversion in 1-6 months

35

Thank You


meverly@terasakilab.org

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**2015 ACCP Global
Conference on Clinical Pharmacy**

The Future of Immunosuppression is Now!
Jennifer Trofe-Clark, Pharm D, FAST, FCCP, BCPS
Adjunct Associate Professor of Medicine
Renal, Electrolyte and Hypertension Division
Perelman School of Medicine, University of Pennsylvania
October 19, 2015


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Conflict of Interests

- Veloxis Pharmaceuticals where institution received grant/funding research support(co-PI)
- Agency for Healthcare Research and Quality where institution received grant/funding research support (clinical investigator)
- NIH/NIAID/Immune Tolerance Network funded research where institution received grant funding/research support (regulatory coordinator)
- ACCP assistance to attend this meeting


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Learning Objectives

- **Discuss the future of immunosuppression management, including pharmacogenomic assessments**
- **Describe the transplant immunosuppression pipeline opportunities and challenges**


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Learning Objective 1


- **Discuss the future of immunosuppression management, including pharmacogenomic assessments**


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**Pharmacogenomic Challenges
in Transplant**

- Limited implementation of pharmacogenomics in transplant practices to date
 - Lack of strong data supporting improved outcomes with pre-emptive testing
- Timing of sample
 - Obtain at evaluation visit or transplant admission?
 - Consider lab availability and turn-around time for results

Van Gelder T, van Schaik RH, Hesselink DA. Pharmacogenetics and immunosuppressive drugs in solid organ transplantation. Nat Rev Nephrol 2014; 10: 725-31.


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**Pharmacogenomic
Challenges in Transplant**

- Documentation of results in electronic record
 - Establish infrastructure for reporting
 - Include interpretation of results in report
 - Consider inclusion of dosing recommendations
- Economic impact undefined
 - Will pre-emptive testing decrease cost of transplant care?

Van Gelder T, van Schaik RH, Hesselink DA. Pharmacogenetics and immunosuppressive drugs in solid organ transplantation. Nat Rev Nephrol 2014; 10: 725-31.

Question 1 for the Audience



- Please answer yes or no using your participant response cards.
- Are you familiar with the ASHP Statement on the Pharmacist's Role in Clinical Pharmacogenomics?

ASHP Statement:



Pharmacist's Role in Clinical Pharmacogenomics

- Pharmacist's Responsibilities
 - Promote optimal use and time of testing
 - Interpret results
 - Educate health care providers, patients and public
- Pharmacist's Functions
 - All pharmacists should have basic pharmacogenomics understanding

American Society of Health-System Pharmacists. ASHP statement on the pharmacist's role in clinical pharmacogenomics. Am J Health-Syst Pharm. 2015; 72:579-81.

Question 2 for the Audience



- Do you know which of the following transplant immunosuppressants has Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines associated with it?
 - A. Cyclosporine
 - B. Sirolimus
 - C. Tacrolimus
 - D. Belatacept

CPIC Guidelines: CYP3A5 genotyping and tacrolimus



Table 2
Dosing recommendations for tacrolimus based on CYP3A5 phenotype

CYP3A5 phenotype*	Implications for tacrolimus pharmacokinetic parameters	Therapeutic recommendations†	Classification of Recommendation‡
Extensive Metabolizer (CYP3A5 expressor)	Lower dose-adjusted trough concentrations of tacrolimus and decreased chance of achieving target tacrolimus concentrations.	Increase starting dose 1.5 to 2 times recommended starting dose*. Trough starting dose should not exceed 0.5 mg/kg/day. Use therapeutic drug monitoring to guide dose adjustment.	Strong
Intermediate Metabolizer (CYP3A5 non-expressor)	Lower dose-adjusted trough concentrations of tacrolimus and decreased chance of achieving target tacrolimus concentrations.	Increase starting dose 1.5 to 2 times recommended starting dose*. Trough starting dose should not exceed 0.5 mg/kg/day. Use therapeutic drug monitoring to guide dose adjustment.	Strong
Poor Metabolizer (CYP3A5 non-expressor)	Higher ("normal") dose-adjusted trough concentrations of tacrolimus and increased chance of achieving target tacrolimus concentrations.	Reduce therapy with standard recommended dose. Use therapeutic drug monitoring to guide dose adjustment.	Strong

*Typically with other CYP3A substrates, an extensive metabolizer would be classified as a "normal" metabolizer, and therefore the drug dose would not change based on the person's genotype. However, in the case of CYP3A5 and tacrolimus, a CYP3A5 expressor (i.e. CYP3A5 extensive metabolizer or extensive metabolizer) would require a higher recommended starting dose and the CYP3A5 non-expressor (i.e. poor metabolizer) would require the standard recommended starting dose.

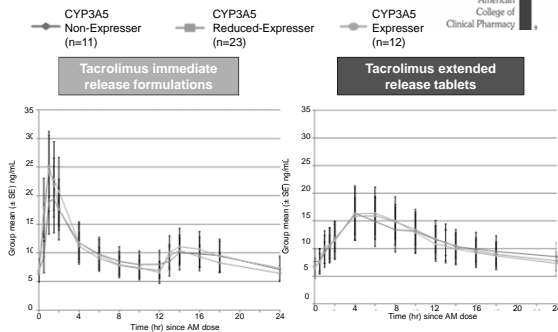
†The recommendations include the use of tacrolimus as follows: short, long and bioparameter (non-renal transplant patients, and liver transplant patients where the donor and recipient genotypes are identical).

‡Further dose adjustment or selection of alternative therapy may be necessary due to other clinical factors (e.g., underlying infections, or hepatic function).

*Starting release is described in Supplementary Data online.

Birdwell KA, Decker B, Barbarino JM, et al. Clinical pharmacogenetics implementation consortium (CPIC) guidelines for CYP3A5 genotyping and tacrolimus dosing. Clin Pharmacol Ther 2015; 98: 19-24 and HHS Public Access available in PMC 2015 July 01-Accessed August 7, 2015.

ASERTAA Trial Results



Trofe-Clark J, Brennan D, West-Theilke P, Milone M, Lim M, Bloom R. Comparison of Pharmacokinetics and Pharmacogenomics of Once-Daily Extended-Release MeltDose® Tacrolimus Tablets (Envarsus® XR) Vs. Twice-Daily Tacrolimus Capsules in Stable African American Kidney Transplant Patients: A Randomized Cross-Over Study [abstract]. Am J Transplant. 2015; 15 (suppl 3) [abstract].

Genotyping Guided Dosing of Tacrolimus in African American Kidney Transplant Recipients



- Tacrolimus clearance [CL/F (L/h)] = 48.9 L/hr x [(1.33, if days less than 9 post-transplant) x [(0.488, if CYP3A5*3/*3 or CYP3A5*3/*7 genotype) or (0.628, if CYP3A5*3/*6 or CYP3A5*6/*7 genotype)] x (0.866, if CYP3A5*1/*3 or CYP3A5*1/*6 or CYP3A5*1/*7 genotype) x (1.24, if receiving a steroid) x (1.09 if not receiving an antiviral) x (1.26 if recipient age between 18-25 yrs)

- Tacrolimus dose to achieve any given trough calculated by: total daily dose = CL/F x trough goal x 24 hrs /1000

Sanghani K, Brundage R, Miller M, et al. Development and Validation of a Genotype Guided Tacrolimus Dosing Equation for African American (AA) Kidney Transplant Recipients [abstract]. Am J Transplant. 2015; 15 (suppl 3) [abstract].

Pharmacogenomics and Immunosuppression



Drug	Recommendations
Tacrolimus	CYP3A5 expressers: increase dose recommended Other gene polymorphisms of unknown significance
Cyclosporine	Genotype guided dosing not recommended
M-TOR inhibitors	Genotype guided dosing not recommended
Azathioprine	Determine TPMT status prior to therapy initiation
Mycophenolic Acid Products	Genotype guided dosing not recommended yet
Belatacept	No information available on genotype guided dosing

Murray B, Hawes E, Lee RA, Watson R, Roederer MW. Genes and beans: pharmacogenomics of renal transplant. *Pharmacogenomics* 2013;14: 783-98. Birdwell KA, Decker B, Barbarino JM, et al. Clinical pharmacogenetics implementation consortium (CPIC). Guidelines for CYP3A5 genotyping and tacrolimus dosing. *Clin Pharmacol Ther* 2015; 98: 19-24

Future Pharmacogenomic Directions



- Develop novel approaches to examine the interaction of genetic polymorphisms involved in drug metabolism with transporter proteins and drug mechanisms
- Further define the role of pharmacogenomic donor/recipient variations

Learning Objective 2



- **Describe the transplant immunosuppression pipeline opportunities and challenges**

Immunosuppressive Pipeline Challenges



- Mainstay of immunosuppression in 2015 is...
 - Drugs developed 15 or more years ago!
- By search criteria “new drugs with immune targets”
 - 436 trials are registered with ClinicalTrials.gov
 - Less than 20% are being investigated in transplant

<https://www.clinicaltrials.gov/> Accessed August 13, 2015

Question 3 for the Audience



- *Please answer true or false using your participant response cards.*
- All immunosuppressants that are FDA approved to prevent rejection are approved to be used in all organ transplant populations

Immunosuppressive Pipeline Opportunities



- Off label use of approved agents
 - Anti-rejection agents approved for use in select transplant populations
 - Drugs approved for alternative indications
 - Alemtuzumab, rituximab, bortezomib, eculizumab
- New formulations of existing immunosuppressants
 - Modified cyclosporine, tacrolimus extended release capsules, enteric coated mycophenolic acid and tacrolimus extended release tablets

Immunosuppression Current Clinical Trial Endpoints



- Composite efficacy endpoint for short term outcomes
 - Rejection, graft, and patient survival at one year
- Non-inferiority versus superiority to current standard of care
- Long term clinical trial feasibility limited

US Food and Drug Administration. Endpoints for Clinical Trials in Kidney Transplantation; Public Workshop. <http://www.fda.gov/Drugs/NewsEvents/ucm305308.htm>. Accessed August 7, 2015.

Immunosuppression Clinical Trial Endpoints for the Future



- Validated immunologic profiling, monitoring, genomics
- Measurement of reduction in metabolic complications
- Preservation of graft function in addition to prevention of rejection in kidney transplant recipients
- Patient-reported outcomes

US Food and Drug Administration. Endpoints for Clinical Trials in Kidney Transplantation; Public Workshop. <http://www.fda.gov/Drugs/NewsEvents/ucm305308.htm>. Accessed August 7, 2015. Srinivas TR, Oppenheimer F. Identifying endpoints to predict the influence of immunosuppression on long-term kidney graft survival. Clin Transplant 2015; 29:644-53. Fleming TR, Powers JH. Biomarkers and surrogate endpoints in clinical trials. Statist Med 2012; 31: 2973-84.

Words of Wisdom from a Transplant Pharmacy Mentor



- *If anyone ever questions the value of clinical research, ask the patient.*
- *When you get frustrated, remember the patient.*

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