Overview of the GI/Liver/Nutrition PRN

Overview of the PRN

The GI/Liver/Nutrition (GILN) PRN was founded on October 25, 1999, to establish a network of clinical pharmacists interested in promoting and advancing practice, research, and education in the areas of gastrointestinal (GI) disease, liver disease, and nutrition. The founding officers, Rosemary R. Berardi (chair), William R. Garnett (secretary/treasurer), Rex O. Brown (Nominations Committee chair), and Susan Sorrells (Communications/Newsletter Committee chair), together with 25 participants, helped lay the foundation for the GILN PRN, which was officially recognized 84 days later, on January 17, 2000. The first official meeting of the GILN PRN reported 56 members.

The GILN membership is a tight-knit group of over 220 members, which include practitioners, fellows, residents, and students. Members of the GILN PRN have significantly contributed to the profession by through papers, book chapters, and posters and presentations at professional meetings. In addition, many of its members hold certifications, including BCPS, BCACP, BCNSP, and BCCCP certifications. Many GILN PRN members have also received various honors, awards, and grants toward GILN-related research.

Focus Session Highlights

The GILN PRN has a diverse membership, making it challenging to find educational topics that will appeal to all of its members. This year, the PRN is excited for its focus session at the 2018 ACCP Global Conference on Clinical Pharmacy to be held October 20–23 in Seattle, Washington, because the PRN believes it will appeal to a wide audience with a variety of interests. The focus session explores the topic of intestinal failure–associated liver disease (IFALD).

IFALD is a cholestatic disorder that develops in up to 66% of children receiving prolonged parenteral nutrition (PN). The epidemiology of IFALD in adults is less clear. Within the past 2 years, new guidelines have been developed for IFALD in adults, new lipid products have come onto the market to prevent IFALD, and data surrounding the importance of microbiota in IFALD have been published. The GILN PRN's focus session at the Global Conference will address this new information so that attendees can better prevent and treat both adult and pediatric patients receiving prolonged PN.

Opportunities for Resident and Fellow Members

The GILN PRN offers many opportunities for practitioners, residents, fellows, and students, including two travel awards. Travel award recipients are invited to present their research project at the ACCP Annual Meeting/Global Conference PRN networking and business meeting. The PRN also encourages networking with experienced practitioners and involvement in the PRN leadership.

Clinical Issue:

End of the Anti-TNF Inflammatory Bowel Disease Treatment Monopoly

Gregory Zumach, Pharm.D., BCPS

August 1998 marked the beginning of the anti–tumor necrosis factor (anti-TNF) revolution for inflammatory bowel disease (IBD) with the FDA approval of Remicade (infliximab) for the treatment of moderate to severe Crohn disease (CD). In 1998–2014, four anti-TNF agents were approved for the treatment for CD and/or ulcerative colitis (UC). These anti-TNFs supplanted previous immunomodulatory and corticosteroid treatments, largely because of their clinical remission rates[1] and success in repairing fistulizing tissue.[1,2] The enormous benefits of the anti-TNFs are weighed against their cost burden, parenteral administration, and adverse effect profile. Anti-TNFs are considered to have a favorable adverse effect profile compared with prior therapies such as the thiopurines and

corticosteroids; however, serious concerns exist for the use of anti-TNFs in patients with congestive heart failure[3] and demyelinating disease such as multiple sclerosis.[1] In addition, anti-TNFs are linked with the development of serious infections, often of the upper respiratory tract.[2] Before 2014, patients with moderate to severe IBD who had contraindications to anti-TNF therapy had few nonsurgical options.

Anti-integrin: Vedolizumab

The anti-integrin class was the only non–anti-TNF biologic to gain approval for the treatment of IBD in 1998–2016. The first anti-integrin, natalizumab, was highly successful in treating moderate to severe CD; however, it was soon discovered to be associated with a rare but often fatal condition known as progressive multifocal leukoencephalopathy (PML).[1] Natalizumab is a monoclonal antibody against the integrin α4 subunit, which is responsible for leukocyte trafficking. The α4 subunit is found not only in the gut, but also the central nervous system. Natalizumab is still featured in guidelines because of its efficacy,[1] but its use has dropped off considerably, largely because of concerns for PML.[4]

In 2014, a more gut-specific anti-integrin, vedolizumab, was developed. Vedolizumab's target to the α4β7 integrin subunit blocks the binding of the mucosal addressin cell adhesion molecule-1 (MAdCAM-1), which decreases the migration of T lymphocytes across the endothelium into inflamed tissue of the intestines.[4,5] This high selectivity comes without the perceived risk of PML, and to date, no reported cases have been associated with vedolizumab.[1] Because of the results of the GEMINI trials, vedolizumab was approved for the induction and maintenance of remission of moderate to severe UC and CD.[4,5] According to the most recent CD guidelines released in April 2018, vedolizumab is now recommended as an appropriate first-line option for patients with moderate to severe CD.[1] Updated UC guidelines are expected in summer 2018; however, the most recent guidelines from 2015 recommend vedolizumab for patients with moderate to severe disease whose anti-TNF therapies have failed.[2] Vedolizumab has a very favorable adverse effect profile.[6]

IL-12/23 Inhibitor: Ustekinumab

Ustekinumab is a monoclonal antibody designed to block a shared subunit (p40) of both interleukin 12 and interleukin 23, which are responsible for T-cell activation.[1] In 2016, ustekinumab was approved for moderate to severe CD. Through the UNITI studies, use of ustekinumab increased the number of patients who experienced clinical response and clinical remission compared with placebo, regardless of prior exposure to anti-TNFs.[7] Phase III studies are actively evaluating ustekinumab in UC.[8] Although ustekinumab is the newest biologic agent approved for IBD, it has demonstrated a strong safety profile after several years of use in psoriasis.[9] Prescribers are quickly adopting ustekinumab into their treatment armamentarium. According to research presented at the inaugural Crohn's & Colitis Congress in January 2018, a retrospective chart review noted that 19% of patients with CD who change from one biologic to another are changed to ustekinumab.[10]

Anti-TNFs have dominated the biologic market for IBD since their release. Anti-TNFs still present a significant benefit for moderate to severe IBD because of their high ceiling of mucosal healing and repair of fistulizing tissue. However, patients with moderate to severe IBD now have additional treatment options, and several drug classes in the pipeline show significant promise. Both vedolizumab and ustekinumab offer true first-line treatment potential. The roles of both will be determined as more data are presented; however, for the first time in almost two decades, treatment for these patients is no longer an anti-TNF monopoly.

References

1. Lichtenstein G, Loftus E, Isaacs K, et al. ACG clinical guideline: management of Crohn's disease in adults. Am J Gastroenterol 2018;113:481-517.

2. Bressler B, Marshall J, Feagan B, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: the Toronto consensus. Gastroenterology 2015;148:1035-1058.e3.
3. Page RL II, O'Bryant CL, Cheng D, et al.; American Heart Association Clinical Pharmacology and Heart Failure and Transplantation Committees of the Council on Clinical Cardiology; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Drugs that may cause or exacerbate heart failure: a scientific statement from the American Heart Association [published correction appears in Circulation 2016;134:e261]. Circulation 2016;134:e32-e69.
4. Sandborn W, Feagan B, Parikh A, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2013;369:711-21.
5. Feagan B, Rutgeerts P, Parikh A, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med 2013;369:699-710.
6. Colombel JF, Sands BE, Rutgeerts P, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut 2017;66:839-51.
7. Feagan B, Sandborn W, Rutgeerts P, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2016;375:1946-60.
8. ClinicalTrials.gov. A Study to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Participants with Moderately to Severely Active Ulcerative Colitis (UNIFI). Available at https://clinicaltrials.gov/ct2/show/NCT02407236. Accessed June 1, 2018.
9. Papp K, Gottlieb AB, Naldi L, et al. Safety surveillance for ustekinumab and other psoriasis treatments from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). J Drugs Dermatol 2015;14:706-14.
10. Kane S, Price L. Perceptions and use of ustekinumab in Crohn's disease: results from a national patient chart audit. Abstract presented at: Crohn's & Colitis Congress; January 19, 2018; Las Vegas, NV.