Late Breakers in Pharmacotherapy, II

Wednesday, October 21, 2015
8:00 a.m. to 9:30 a.m.
Continental Ballroom 5

Moderator: Robert B. Parker, II, Pharm.D., FCCP
Professor, University of Tennessee College of Pharmacy, Memphis, Tennessee

Agenda

8:00 a.m.  Women’s Health
Nicole E. Cieri, Pharm.D.
Clinical Assistant Professor, Department of Pharmacy Practice, D’Youville College School of Pharmacy, Buffalo, New York

8:15 a.m.  Psychiatry
Stephanie Phan, Pharm.D., BCPP
Clinical Assistant Professor, Associate Department Head, Southwest Georgia Clinical Campus, University of Georgia College of Pharmacy, Albany, Georgia

8:30 a.m.  Vaccines/Immunizations
Scott J. Bergman, Pharm.D., BCPS
Southern Illinois University Edwardsville School of Pharmacy, Edwardsville, Illinois

8:45 a.m.  Geriatrics
Stephanie M. Crist, Pharm.D.
Assistant Professor of Pharmacy Practice, Division of Ambulatory Care, St. Louis College of Pharmacy, St. Louis, Missouri

9:00 a.m.  Nephrology
Mary Vilay, Pharm.D.
Associate Professor, University of New Mexico College of Pharmacy, Albuquerque, New Mexico

9:15 a.m.  Neurology
Melody Ryan, Pharm.D., MPH, FCCP, BCPS, CGP
Professor, University of Kentucky College of Pharmacy, Lexington, Kentucky

Conflict of Interest Disclosures
Scott J. Bergman: Speaker’s bureau for Sanofi-Pasteur.
Stephanie M. Crist: no conflicts to disclose.
Nicole E. Cieri: no conflicts to disclose.
Robert B. Parker: no conflicts to disclose.
Stephanie Phan: no conflicts to disclose.
Melody Ryan: no conflicts to disclose.
Mary Vilay: no conflicts to disclose.

### Learning Objectives

1. Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in pharmacogenomics.
2. Identify the limitations/controversies associated with these late-breaking trials.
3. Discuss approaches to apply and implement the new findings into practice.

### Self-Assessment Questions

Self-assessment questions are available online at [www.accp.com/qc15](http://www.accp.com/qc15).
Flibanserin: The ‘Female Viagra’
Nicole Cieri, Pharm.D., BCPS
October 21st, 2015

Learning Objectives
- Analyze and interpret the results of the most recent trials of flibanserin, the first drug approved for hypoactive sexual desire disorder (HSDD) in women this past June.
- Identify the limitations/controversies associated with these trials
- Choose an appropriate patient for use of flibanserin in practice

Background
- Hypoactive sexual desire disorder (HSDD):
  - American Psychiatric Association Definition (DSM-IV-TR):
    - Persistent or recurrent deficiency in, or absence of, sexual fantasies and desire for sexual activity that causes marked distress or interpersonal difficulty
  - Multifactorial Disorder
    - Dysregulation of excitatory/inhibitory signals in the CNS that regulate sexual response
    - Dopamine, Norepinephrine, Testosterone: stimulation of sexual desire
    - Serotonin: inhibition of sexual desire

- DSM-IV-TR: HSDD and female Sexual Arousal Disorder (FSAD) were diagnosed separately
  - DSM-5 diagnostic criteria combine HSDD and FSAD into female sexual interest/arousal disorder
- Consideration for future studies and selecting patients as candidates
  - Approval of flibanserin to treat these disorders has been studied based on now obsolete criteria

Conflict of Interests
- None
Background

- **Flibanserin**
  - Post synaptic agonist of the serotonin (5-HT) receptor-1A and antagonist of 5HT-2A
  - Induction of transient decreases in serotonin and increases in dopamine and norepinephrine
  - Approved on June 4, 2015 as the first drug for boosting female sexual desire
  - 3rd time before the FDA

Review

- **SNOWDROP**
  - Flibanserin 100mg PO qHS vs placebo x24 weeks for naturally postmenopausal women of any age diagnosed with HSDD according to the DSM IV criteria lasting ≥6 months
  - Co-primary endpoints
    - Satisfying Sexual Events (SSE) in 28 days
    - Female Sexual Functional Index (FSFI) score
  - Secondary endpoint
    - Female Sexual Distress Scale-Revised (FSDS-R)

Results

- Significant improvement in SSE compared to placebo
  - 1.0 vs 0.6 (p=0.004)
- Significant improvement in FSFI
  - 0.7 vs 0.4 (p<0.001)
- Significant decrease in FSDS-R
  - -8.3 vs -6.3 (p=0.006)
- Most frequent adverse events:
  - Dizziness, somnolence, nausea, headache
- 12 serious AE but none deemed related to treatment
- No evidence of suicidal ideation

Interpretation/Analysis

- SNOWDROP had slightly smaller increase in SSEs compared to previous trials of flibanserin in premenopausal women
  - 1.0 vs 1.6-2.5
- Potentially high placebo effect
- List of prohibited medication greatly reduced compared to previous trials
- Limited to patient in heterosexual relationship and naturally induced menopause

BEGONIA

- Flibanserin 100mg PO qHS vs placebo x24 weeks for naturally postmenopausal women of any age diagnosed with HSDD Primary endpoints
- Co-primary endpoints
  - Satisfying Sexual Events (SSE) in 28 days
  - Female Sexual Functional Index (FSFI) score
- Secondary endpoint
  - Female Sexual Distress Scale-Revised (FSDS-R)
**BEGONIA**

- **Results**
  - Significant improvement in SSE compared to placebo
    - 2.5 vs. 1.5 (p<0.001)
  - Significant improvement in FSFI
    - 1.0 vs. 0.7 (p<0.001)
  - Significant decrease in FSDS-R
    - -9.4 vs -6.1 (p<0.001)
  - Most frequent adverse events:
    - Dizziness, somnolence, nausea
  - 6 serious AE but none deemed related to treatment
  - No evidence of suicidal ideation


**Choosing a Patient**

- **Postmenopausal**
  - Women with naturally induced menopause, at least one ovary and diagnosed with HSDD of ≥ 6 months’ duration
    - Excluded women with other sexual dysfunction, certain psychiatric d/o’s, several gynecologic and pelvic pathology d/o’s and concomitantly taking certain medications that may affect sexual function
    - Relationship criteria

- **Premenopausal (Approved Indication)**
  - Women ≥18yo diagnosed with HSDD of ≥ 6 months’ duration
    - Excluded women with other sexual dysfunction, certain psychiatric d/o’s, several gynecologic and pelvic pathology d/o’s and concomitantly taking a more extensive list of medications that may affect sexual function (compared to postmenopausal)
    - Relationship criteria
    - eDiary criteria
  - Previous extension trial: safety up to 52 weeks
  - Previous withdrawal trial: safety demonstrated

**Summary and Further Considerations**

- Flibanserin is the first pharmacotherapy option approved for the treatment of HSDD (in premenopausal women)
- Balance the safety of a chronic treatment for a non life threatening condition
- Obsolete diagnostic criteria
- Root cause
- Therapeutic lifestyle changes

**Additional References**

Learning Objectives

- Identify concerns with reportedly increasing antipsychotic use in young people
- Describe antipsychotic use among younger and older children, adolescents, and young adults in the United States

Background

- Antipsychotic risks and benefits appear to be different in young people compared to adults
  - Higher risk of metabolic adverse effects
  - Unclear impact of hyperprolactinemia on growth
  - Greater incidence of extrapyramidal symptoms
  - Unknown effects on central nervous system development, brain maturation
- Efficacy of antipsychotics is best evaluated in schizophrenia, autism spectrum disorders, and bipolar disorder

Antipsychotics in Youth

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Age group, y</th>
<th>FDA-Approved Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>13-17</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td></td>
<td>10-17</td>
<td>Bipolar I, mania/mixed</td>
</tr>
<tr>
<td></td>
<td>6-18</td>
<td>Tourette’s disorder</td>
</tr>
<tr>
<td></td>
<td>6-17</td>
<td>Irritability/aggression with autistic disorder</td>
</tr>
<tr>
<td>Asenapine</td>
<td>10-17</td>
<td>Bipolar I, mania/mixed episode</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>13-17</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>Bipolar I, mania/mixed episode</td>
</tr>
<tr>
<td></td>
<td>10-17</td>
<td>Bipolar I, depression episode (with fluoxetine)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>13-17</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td></td>
<td>10-17</td>
<td>Bipolar I, mania/mixed episode</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>13-17</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Risperidone</td>
<td>13-17</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td></td>
<td>10-17</td>
<td>Bipolar I</td>
</tr>
<tr>
<td></td>
<td>5-17</td>
<td>Irritability/aggression with autistic disorder</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>10-17</td>
<td>Bipolar I, mania/mixed episode</td>
</tr>
</tbody>
</table>

Worldwide Data

- Despite study heterogeneity, the general trend is increased antipsychotic use in youth
  - European countries, Canada, United States, Australia, others
  - May include increased frequency of new use and longer duration of use
  - Conditions being addressed: ADHD, conduct and behavioral disturbances, mood disorders
Late Breaker: Psychiatry

- Treatment of Young People With Antipsychotic Medications in the United States
  - Olfson M, King M, Shoenbaum M.
  - JAMA Psychiatry 2015;72(9):867-74.
  - September 2015

- Population-level, retrospective, observational study of young people aged 1 to 24

Study Design

- Objective: To describe the national prevalence of antipsychotic use in young people

- Data Sources
  - IMS LifeLink LRx Longitudinal Prescription databases
  - Data on filled prescriptions in 2006, 2008, and 2010
  - National representation by age, sex, insurance
  - Captured 63% of all retail prescriptions in the U.S.
  - Medical Expenditure Panel Survey
    - Percentage who did not fill prescriptions
  - 2009 IMS Medical Claims Database
    - Merged with pharmacy claims from 2009 LRx database

Results

- Percentage of young people with any antipsychotic prescription by age category

<table>
<thead>
<tr>
<th>Year</th>
<th>Population with Prescription by Age, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-6 y</td>
</tr>
<tr>
<td>2006</td>
<td>0.14</td>
</tr>
<tr>
<td>2008</td>
<td>0.16</td>
</tr>
<tr>
<td>2010</td>
<td>0.11</td>
</tr>
</tbody>
</table>

- Percentage of young people, by sex, with any antipsychotic prescription by age category

<table>
<thead>
<tr>
<th>Year, by sex</th>
<th>1-6 y (%)</th>
<th>7-12 y (%)</th>
<th>13-18 y (%)</th>
<th>19-24 y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>2006</td>
<td>0.20</td>
<td>1.28</td>
<td>1.35</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>0.24</td>
<td>1.33</td>
<td>1.43</td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>0.16</td>
<td>1.20</td>
<td>1.42</td>
</tr>
<tr>
<td>Females</td>
<td>2006</td>
<td>0.08</td>
<td>0.45</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>0.09</td>
<td>0.47</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>0.06</td>
<td>0.44</td>
<td>0.95</td>
</tr>
</tbody>
</table>

- Percentage of antipsychotic users with any antipsychotic by prescription source

<table>
<thead>
<tr>
<th>Age category, y</th>
<th>Population with Prescription by Year, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatrist</td>
<td></td>
</tr>
<tr>
<td>Child/adolescent psychiatrist</td>
<td></td>
</tr>
<tr>
<td>1-6</td>
<td>51.0</td>
</tr>
<tr>
<td>7-12</td>
<td>74.7</td>
</tr>
<tr>
<td>13-18</td>
<td>79.7</td>
</tr>
<tr>
<td>19-24</td>
<td>71.1</td>
</tr>
</tbody>
</table>

- Other classes of psychotropic among young people with antipsychotics in 2008

<table>
<thead>
<tr>
<th>Prescription Medication</th>
<th>Population with Prescription by Age, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-6 y (n=96,725)</td>
</tr>
<tr>
<td>Stimulants</td>
<td>58.7</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>20.3</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>16.5</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>6.4</td>
</tr>
<tr>
<td>Antipsychotics only</td>
<td>27.8</td>
</tr>
</tbody>
</table>
Results

- Use of any psychotherapy in 2009 among young people with antipsychotic prescriptions, by age:
  - 1-6 years (n=925): 13.5%
  - 7-12 years (n=5,939): 20.4%
  - 13-18 years (n=8,198): 24.8%
  - 19-24 years (n=5,353): 18.8%

- Diagnoses in 2009 among young people with antipsychotic prescriptions, following slide

Results – By Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis (2009)</th>
<th>Population with Diagnosis by Age, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-6 y</td>
</tr>
<tr>
<td>ADHD</td>
<td>52.5</td>
</tr>
<tr>
<td>Autism or mental</td>
<td>23.1</td>
</tr>
<tr>
<td>retardation</td>
<td></td>
</tr>
<tr>
<td>Disruptive behavioral</td>
<td>20.6</td>
</tr>
<tr>
<td>disorders</td>
<td></td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>8.1</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.9</td>
</tr>
<tr>
<td>Depression</td>
<td>1.8</td>
</tr>
<tr>
<td>Adjustment-related</td>
<td>0.8</td>
</tr>
<tr>
<td>disorders</td>
<td></td>
</tr>
<tr>
<td>Substance use</td>
<td>0.3</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>23.5</td>
</tr>
<tr>
<td>Other mental disorder</td>
<td>13.5</td>
</tr>
</tbody>
</table>

Limitations

- Prescription database captures purchased medications
- Data not available on antipsychotic safety and/or efficacy
- Population denominator was a possibly imprecise estimate
- Service claims data were not available for all patients
- Diagnostic data were not validated by an expert
- Current practices may be different

Conclusions

- Antipsychotic use in younger and older children decreased, but increased in young adults between 2008 and 2010
- Peak antipsychotic use is in adolescents; higher for males
- Antipsychotic prescriptions are more likely to come from a psychiatrist than a child and adolescent psychiatrist
- Stimulants are most often co-prescribed in younger and older children; more likely to have ADHD diagnosis
- Psychotherapy use may be underutilized
Learning Objectives

1. Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in vaccines/immunizations.
2. Identify the limitations/controversies associated with these late-breaking trials.
3. Discuss approaches to apply and implement the new findings into practice.

The Impact of Age on the Efficacy of 13-valent Pneumococcal Conjugate Vaccine in Elderly


Pneumococcal conjugate polysaccharide vaccine

- PCV - Prevnar 13
  - Produces memory B-cells
  - Subsequent exposure boosts response
  - FDA-approved: 50 years and up, 2011
  - CDC-recommended:
    - All infants & children, 2010
    - Immunocompromised adults, 2012
    - Everyone 65 years and up, 2014

Pneumococcal polysaccharide vaccine

- PPSV – Pneumovax 23 (1983)
  - Still recommended for adults ≥ 65 years old
    - 1 year after PCV13
  - Ages 2-64 years with risk factors
  - T-cell dependent response
  - Decreases invasive pneumococcal disease (IPD)
    - Reduction in pneumonia and mortality not compelling

Community-acquired Pneumonia Immunization Trial in Adults (CAPITA)

- Randomized, double-blind, placebo-controlled efficacy trial of PCV13
  - Adults ≥65 years old
  - The Netherlands
  - Limited use of PPSV
- Primary endpoint: community-acquired pneumonia (CAP) from vaccine serotypes
- N=84,492 subjects

**CAPITA results**

**Primary endpoint:**
- 45.6% efficacy for confirmed CAP
  - CI: 21.8 to 62.5%

**Secondary endpoints:**
- 75% efficacy for IPD due to vaccine serotype
  - CI: 41.4-90.8%
- 5% overall reduction in pneumonia (NS)

CI = 95% Confidence Interval, NS=Not significant

**CAPITA population**

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Subjects (n)</th>
<th>% of study participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-69</td>
<td>32,933</td>
<td>39.0</td>
</tr>
<tr>
<td>70-74</td>
<td>25,145</td>
<td>29.8</td>
</tr>
<tr>
<td>75-79</td>
<td>15,758</td>
<td>18.7</td>
</tr>
<tr>
<td>80-84</td>
<td>7,715</td>
<td>9.1</td>
</tr>
<tr>
<td>≥85</td>
<td>2,941</td>
<td>3.5</td>
</tr>
</tbody>
</table>

**CAPITA results by age**

Vaccine efficacy against first episode of VT-CAP or VT-IPD in mITT population

<table>
<thead>
<tr>
<th>Age range</th>
<th>Total number of episodes</th>
<th>Number of episodes in PCV13 group</th>
<th>Number of episodes with Placebo</th>
<th>Vaccine Efficacy (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>184</td>
<td>68</td>
<td>116</td>
<td>41.4% (21.4;57.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;75</td>
<td>113</td>
<td>38</td>
<td>75</td>
<td>49.3% (26.2;67.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥75</td>
<td>71</td>
<td>30</td>
<td>41</td>
<td>26.8% (−15.2;55.1)</td>
<td>0.094</td>
</tr>
</tbody>
</table>

**Discussion**

- Overall results indicate benefit of PCV13 in those 65 years and older
- No difference detected in preventing pneumonia and IPD if ≥75 years
- Antibody response did not differ by age
- Phagocyte function may decline over time
- Booster could have some benefit
Limitations

- Post-hoc analysis combining CAP and IPD
- Small number of patients enrolled ≥85 years
- Population had not received previous PPSV
- PCV only recently recommended for children in The Netherlands
- 13% of CAP caused by vaccine serotypes

Conclusion

- Efficacy of PCV13 declines with age
- May not be worth giving PCV after 75 or 80 years of age
- Cost-effectiveness to be determined
- Future studies needed with PPSV as “booster”
Late Breakers in Pharmacotherapy II: Geriatrics
Stephanie M. (Seaton) Crist, Pharm.D., BCACP, CGP
October 21, 2015

Conflict of Interests
- None to disclose

Learning Objectives
- Identify patient care trends affecting pharmacotherapy and health outcomes in geriatrics
- Identify risks associated with opioid use in patients with dementia
- Discuss approaches to applying these new data into evidence-based practice

Article Citation

Background
- Opioid use among older adults continues to rise
- Neuropathologic findings in young drug abusers similar to those seen in Alzheimer’s disease (AD)
- Unanswered question: do opioids have long-term effects on cognition?

Study Objective
To determine whether prescription opioid use is associated with higher dementia risk or greater cognitive decline
Methods

Population-based, prospective cohort study within Group Health (Seattle area)
- Data from Adult Changes in Thought (ACT) Study
- Opioid use identified from computerized pharmacy claims data
- Patient visits every two years
- Opioid exposure converted to morphine equivalent doses → total standard doses (TSD)
  - 1 TSD = morphine 30 mg

Inclusion Criteria

- Age ≥ 65 years
- Community-dwelling
- No baseline dementia
- At least 10 years of membership within Group Health

Exclusion Criteria

- < 1 follow-up visit
- Invalid cognitive score (CASI) at baseline
- Consent withdrawn

Cognitive Abilities Screening Instrument (CASI)

- Potential uses:
  - Screening tool for identifying dementia
  - Monitoring parameter for disease progression
  - Providing a profile of impairment among various cognitive domains
- Nine cognitive domains
- Total score range 0-100 (lower is worse)

Outcomes

- Primary
  - CASI (cut-point for cognitive analysis: ≤86)
- Secondary
  - CASI-IRT (Item Response Theory)
  - Nonsteroidal anti-inflammatory drug (NSAID) use

Study Participation

4,724 participants in original ACT study
- After exclusions:
  - 3,434 in the dementia analyses
  - 3,993 in CASI analyses

Results

- Baseline characteristics, n = 3,434:
  - Mean age: 74 years
  - 40% male
  - 72% regular exercise
  - 48% treated for HTN
  - 25% obese
  - 18% CAD
  - 10% depression
  - <5% current smoker
- 92% had at least one opioid fill:
  - 39%: codeine
  - 26%: oxycodone
  - 23%: hydrocodone
Results, continued

- Mean follow-up: 7.3 years
- 797 (23%) developed dementia
  - 637 with “possible” or “probable” dementia
- Slightly higher risk of all-cause dementia
  - Heaviest opioid use (≥ 91 TSDs), aHR 1.29 (1.02-1.62)
  - Heaviest NSAID use (≥ 541 TSDs), aHR 1.31 (1.07-1.62)
    - Cumulative heaviest NSAID use categorized as 1200 mg of ibuprofen daily for 1.5 years
- Recent opioid use was not associated with increased rate of cognitive decline

Critical Appraisal

- Overall younger population
- Insurance claims data does not account for medication adherence
- May under- or over-report NSAID use
- Higher opioid and/or NSAID use may represent poorer overall health compared to little or no opioid/NSAID use
- Conflicting results for risk of dementia with NSAID use
- Measures of pain lacking
- Relatively weak association, not causation

Application to Practice

- Caution use of opioids (and NSAIDs) in individuals who are:
  - Older
  - Female
  - Obese
  - Report fair or poor rate of health
  - Depression
  - Little exercise
- Opioid use (and/or NSAID use) does not equal long-term cognitive harm
- More studies necessary to further conclude risk

Self-Assessment Question 1

For the primary outcome, what does the HR = 1.29 represent?

a. There is a 1.29% chance of developing dementia when taking an opioid
b. A person is 1.29 times more likely to develop dementia with opioid use
c. Roughly 98% of patients who take an opioid will develop dementia
d. There is a 29% chance of developing dementia

Self-Assessment Question 2

Opioid use is associated with increased risk of all-cause dementia.

a. True
b. False

Thank you for attending.

QUESTIONS?
"The Association of Chronic Kidney Disease with the Use of Renin-Angiotensin System Inhibitors After Acute Myocardial Infarction"

Wetmore JB, Tang F, Sharma A, Jones PG, and Spertus JA


Background

- Renin-angiotensin system (RAS) inhibitors ↓ CV morbidity and mortality
- ACC/AHA recommend ACEI post MI/stable IHD (particularly if systolic HF present)
- ACEIs and ARBs used interchangeably
- RAS inhibitor use post AMI with EF <40% = quality performance measure
- Concerns of RAS inhibitor ADE
  - Renal effects
  - Hyperkalemia

Study Objective

- Determine current practice pattern of prescribing RAS inhibitors in patients with impaired renal function at time of AMI
  - Specifically interested in association of CKD, AKI and LV function on treatment patterns

TRIUMPH Study Patients from 24 US Hospitals

Inclusion
- ≥18 years old
- MI, biomarker evidence myocardial necrosis and prolonged ischemia or ST-wave changes on ECG
- Admission SCR and subsequent in-hospital SCR
- Alive at discharge

Exclusion
- Documented RAS inhibitor contraindication
### Data Collected & Definitions

- RAS inhibitor Rx at discharge recorded
- CKD-EPI equation used to calculate eGFR
- ESRD = chronic dialysis
- AKI = 0.3 mg/dL or 50% ↑ SCR during hospitalization vs admission value

### Baseline Characteristics

#### Use of RAS Inhibitors at Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>ESRD (N=81)</th>
<th>eGFR &lt;30 (N=146)</th>
<th>eGFR 30-59 (N=818)</th>
<th>eGFR 60-89 (N=1958)</th>
<th>eGFR ≥90 (N=1220)</th>
<th>Total (N=4223)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>60.5%</td>
<td>50.0%</td>
<td>72.6%</td>
<td>76.9%</td>
<td>78.4%</td>
<td>78.4%</td>
<td>&lt;0.001</td>
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<td>70%</td>
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<td>Hx MI/PCI/CABG</td>
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<tr>
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</tbody>
</table>

* Mantel-Haenszel trend test across eGFR categories, excludes ESRD

**Interaction EF and eGFR p=0.4**
**Interaction AKI and eGFR p<0.01**
**Interaction AKI and EF p=0.25**

### Use of RAS Inhibitors at Discharge

#### Weight ratio for discharge prescription of a RAS inhibitor

- Age/10y increment
- Female
- Race
- Black vs White
- Other vs White
- Uninsured
- Obesity
- Smoking

### Baseline Characteristics

1-way ANOVA (continuous); X² or Fisher’s exact (categorical)

<table>
<thead>
<tr>
<th>Variable</th>
<th>ESRD (N=81)</th>
<th>eGFR &lt;30 (N=146)</th>
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<th>eGFR 60-89 (N=1958)</th>
<th>eGFR ≥90 (N=1220)</th>
<th>Total (N=4223)</th>
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</tbody>
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**Interaction EF and eGFR p=0.4**
**Interaction AKI and eGFR p<0.01**
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**Interaction EF and eGFR p=0.4**
**Interaction AKI and eGFR p<0.01**
**Interaction AKI and EF p=0.25**
**Take Home Message**

- ↓ RAS inhibitor use with ↓ eGFR
- RAS inhibitor prescribing may be influenced more by presence of CKD than ↓ EF
- AKI and CKD were barriers to RAS inhibitor prescribing post AMI
- Possibly patients who would benefit from RAS inhibitors are not receiving them
- More work is needed

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**Limitations**

- Use of admission SCr to estimate eGFR
- Information on hypotension missing
- Extensive collection of patient-level data
  - Risk of unmeasured confounding variable may still be present
- Few follow-up data available to better define adverse renal consequences for using/not using RAS inhibitors at discharge
Conflicts of Interest

- Melody Ryan has no conflicts of interest

Learning Objectives

- Identify/discuss new and emerging clinical data or patient care trends affecting pharmacotherapy and/or health outcomes in the area of neurology.
- Identify the limitations/controversies associated with this late-breaking trial.
- Discuss approaches to apply and implement the new findings into practice.

FDA approves first 3-D printed medicine!

- Spritam™ - rapidly disintegrating oral tablet of levetiracetam
- Approved 7/31/15
- 250 mg, 500 mg, 750 mg, and 1000 mg tablets
- Dissolves within 10 seconds with a sip of water; still must be swallowed
- Indicated for adjunctive therapy in the treatment of partial onset, myoclonic, and primary generalized tonic-clonic seizures

3-D Printing

- First 3-D (additive manufacturing) performed in 1981 with plastics
- Computer-aided design is used to create a computerized model of a real object, it is converted into code, the printer head distributes layers of material (powder, liquid, metal, etc) until the item is printed
- Since that time, used for a wide variety of items from food to weapons

3-D Medical Printing

- Titanium jaw replacement March 2012
- Facial reconstruction with titanium replacements and 3-D modeling March 2014
- Printing skin directly into wounds July 2014
- Experiments with living cells on a cellulose matrix to produce cartilage and liver tissue August 2013
- FDA approves bone tether plate February 2015
3-D Printed Medicine

- First reported samples printed in 2000
- Able to make high-concentration tablets; up to 68% of tablet weight may be drug
- Controlled-release properties can be attained through mixtures or coatings
- No molding or compression needed
- Different tablet shapes are possible (sphere, pyramid, cube)


Zip-dose Technology
- Layer of powder
- Liquid in certain areas to hold tablet together
- Layer of powder...

3-D Printed Medicines

Future Applications

- Individualized doses
- Multiple medicines in one dosage form
- Multiple release properties in one dosage form
  - Captopril, nifedipine, glipizide
- Distribution and access, especially in developing countries
  - Printers ~$150-300
- Imbed medicines into implants

http://3dprint.com/87977/3d-printed-drugs-2/

Potential Problems

- Durability of tablets
- Degradation of medicine from printer heat
- Dose uniformity
- Different strengths could be many different weights; problems with automated dispensing
- Will pharmacies be needed?
- Patent protection
- Hacking, if software widely distributed
- Illicit drug printing

With permission of Mohamed Alhnan, PhD, MRPharmS
School of Pharmacy and Biomedical Sciences, University of Central Lancashire

https://www.youtube.com/watch?v=FGpbiJxkkak