Cardiovascular Medications: Something Old, Something New, Something Borrowed, Let’s Review!

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Disclosures

• No conflicts of interest to disclose
Cardiac Medications
What’s New?

- Not much........recently
FDA Cardiovascular Drug Approvals

- 2010: (4) – includes Dabigatran (Pradaxa) anticoagulant
- 2011: (4) – includes Rivaroxaban (Xarelto) an oral anticoagulant and Ticagrelor (Brilinta) – antiplatelet agent
- 2012: (3) – includes Apixaban (Eliquis) – oral anticoagulant
- 2013: (6) – none in regular use
- 2014: (2) – none in regular use
FDA Cardiovascular Drug Approvals - 2015

- **Corlanor (ivabradine):** treatment of chronic heart failure when beta blockers ineffective to lower HR
- **Entresto (sacubitril and valsartan):** treatment of chronic heart failure
- **Kengreal (cangrelor):** antiplatelet agent reducing periprocedural thrombotic events in the cath lab
- **Praluent (alirocumab):** treatment of heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease
- **Repatha (evolucumab):** treatment of high cholesterol
FDA Cardiovascular Drug Approvals - 2015

- **Savaysa (edoxaban):** treatment of deep vein thrombosis, pulmonary embolism and risk of stroke and embolism due to atrial fibrillation
- **Prestalia (perindopril and amlodipine):** treatment of hypertension
- **Kanuma (sebelipase alfa):** treatment of Lysosomal Acid Lipase (LAL) deficiency
- **Uptava (selexipag):** treatment of pulmonary arterial hypertension
FDA Cardiovascular Drug Approvals - 2016

- **Byvalson (nebivolol/valsartan):** treatment of hypertension
- **Yosprala (aspirin/omeprazole):** prevention of cardiovascular and cerebrovascular events (both OTC meds)
FDA Cardiovascular Drug Approvals - 2017

• **Bevyxxa (betrixaban)** – prophylaxis of venous thromboembolism in hospitalized, acutely medically ill patients at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE.

**Due out later 2017**
Something Old: Spironolactone for CHF

- Older medication – potassium sparing diuretic that is an aldosterone antagonist (reduces Na and water retention)
- Indicated for Class II-IV NYHA CHF patients
- Spironolactone significantly lowered risk of all-cause mortality (46% to 35%)
- Likely underutilized in CHF as studies
- Side effects/Cautions: GI issues, hyperkalemia, gynecomastia
Something New(er): Entresto (sacubitril/valsartan) for CHF

- Approved in 2015
- 2016 - Given a Class I recommendation for CHF treatment by the ACC/AHA
- PARADIGM-HF Trial showed Entresto significantly reduced deaths from cardiovascular causes and heart failure hospitalizations in patients with HFrEF when compared to standard ACE inhibitor therapy

## PARADIGM-HF: Effect of Sac/Val vs. Enalapril on the Primary Endpoint and Its Components

<table>
<thead>
<tr>
<th></th>
<th>Sac/Val (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>914 (21.8%)</td>
<td>1117 (26.5%)</td>
<td>0.80 (0.73–0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td>558 (13.3%)</td>
<td>693 (16.5%)</td>
<td>0.80 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospitalization for heart failure</strong></td>
<td>537 (12.8%)</td>
<td>658 (15.6%)</td>
<td>0.79 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
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</table>

Sac/Val = Sacubitril/Valsartan.
Potential Impact of switching to Entresto from traditional therapy

- 28000 US deaths avoided each year
- 30 year projection – estimated 220 fewer CHF hospitalizations per 1000 patient years. (Paradigm-HF)
Entresto

Why aren’t more patients on it?

• $4500/year prior to discounts
• Some issues with insurance authorizations
• Providers still gaining experience with the drug
Coumadin – Something Old

• Chemical entity discovered in 1930s with cattle bleeding to death after eating moldy sweet clover (contained coumarin)
• Warfarin (name derived from the Wisconsin Alumni Research Foundation (WARF) started to be used as rat poison
• Safety in humans determined after farm worker overdosed on it and they were saved with vitamin K administration (1951)
• Approved for human use in 1955
Coumadin – Something Old

• Still widely used (though less than before)
• Inexpensive
• Reversible with vitamin K, FFP, Kcentra etc.
• Requires regular lab testing
• Lots of drug interactions
• Narrow Therapeutic Index
New Oral Anticoagulants

- Pradaxa (dabigatran)
  - **Has reversal agent (Praxbind)**
- Xarelto (Rivaroxaban) – most common in the community
- Eliquis (apixaban) – maybe safer in renal patients
- Savaysa (edoxaban) – can’t use if kidney function is too good
- Bevyxxa (betrixaban) – indicated for VTE proph in hospital patients
Benefits of the Newer Anticoagulants

- Equal or more effective vs Warfarin
- Adverse effects equal or better vs Warfarin
- No/Less lab testing
- Less drug interactions
- More consistent blood levels and less variability in effects
- More atrial fibrillation patients now getting appropriately prophylaxis for strokes
“Old” Cholesterol Lowering Agents
The Statins

• Still very effective agents to decrease cholesterol levels
• More affordable since most are generic
• Recommended post MI
• Recommended to improve CV outcomes especially with other risk factors ie. Diabetes, smoking, hyperlipidemia and hypertension
• Side effects can be limiting to some patients
New Cholesterol Lowering Agents

Praluent (alirocumab):

• Indicated for the treatment of heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease

• Increases LDL clearance by inhibiting PCSK9 binding to LDL receptors

• 75-150 mg q2 weeks or 300 mg q4 weeks

• $14,000 per year!!

• If LDL goals unable to be reached with standard therapy
New Cholesterol Lowering Agents
Repatha (evolucumab)

- treatment of high cholesterol
- 140 mg q2 weeks or 420 mg q4 weeks
- Increases LDL by binding to PCSK9 which increases clearance of LDL
- $14,000 per year
- If LDL goals unable to be reached with standard therapy
What’s New in Pharmacy?

Pharmacists as Providers
Pharmacists as Providers in the Community

• Clinical Pharmacists have been in place for over 30 years in the inpatient setting
• Do not necessarily replace other caregivers ie. Physicians, NP’s, PA’s
• Are the Drug Experts
• May be more accessible – easier to get an appointment
Pharmacists as Providers
Services May Include

- Furnish Nicotine Replacement Therapy
- Furnish Naloxone
- Travel Medications
- Immunizations
- Order/Interpret Lab tests
- Administer Drugs/Biologics
- Furnish Hormonal Contraceptives

http://www.cpha.com/Advocacy/Expanding-Pharmacist-Services
An **Advance Practice Pharmacist (APP) partners** together with patients’ primary care physicians around taking care of patient’s health, to make sure all meds are **optimized** at safe and effective doses; ensure no **drug-drug interactions** exists, and may, when appropriate, stop medications. The Advance Practice Pharmacist **empowers** the patient with knowledge of his/her medications. They help **personalize** medication therapy to patient’s lifestyle and **coordinate** help to reduce out-of-pocket **costs** for medications.
Medication Therapy Management Clinic

Goals of the Clinic:

1) Reduce 30 day readmissions
2) Achieve quality metrics
3) Build lasting relationships with our patients
Advanced Practice Pharmacist- Authorized Activities

- Perform patient assessments,
- Order and interpret drug therapy-related tests in coordination with a patient’s primary care provider or diagnosing prescriber to monitor patient progress,
- Refer patients to other health care providers

http://apppharmacist.com/benefits/
Advanced Practice Pharmacist-Authorized Activities

• Participate in the evaluation and management of diseases and health conditions in collaboration with other health care providers,

• Pharmacist may initiate, adjust, and discontinue drug therapy upon referral from a patient’s treating prescriber when necessary and medically appropriate.

• Required to communicate any drug initiation or discontinuation promptly to the diagnosing prescriber.

http://apppharmacist.com/benefits/
Patient Story – CHF

- 66 y M hospitalized for CHF, EF 48%.
  - HR 40s, but denied symptoms bradycardia
  - On Metoprolol succinate 150 mg po BID, confirmed this was hospitalist plan
  - S/W cardiologist, decreased metoprolol succinate to 100 mg po BID
  - Called pt in 5 days, HR 50-60s, followed up w/ cardiologist
Pharmacist Ambulatory Care Clinic
Readmission Data – CHF Patients

Patients with Face-to-Face (F2F) Therapy Sessions by Day Post-Discharge
Count & 30-Day Unplanned Readmission Rate

- F2F - Not readmitted
- F2F - Readmitted
- Other - Not Readmitted
- Other - Readmitted
- F2F Readmit Rate
- Other Readmit Rate

Post-Discharge Day

# Patients

Readmission Rate

0% 2% 4% 6% 8% 10% 12% 14% 16%

1 2 3 4 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
<table>
<thead>
<tr>
<th>Appointment Status</th>
<th>Patients meeting criteria</th>
<th>Observed Readmit</th>
<th>Readmit Rate</th>
<th>O/E Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Candidates</td>
<td>1041</td>
<td>106</td>
<td>10.18%</td>
<td>0.89</td>
</tr>
<tr>
<td>Face-to-Face Completed</td>
<td>328</td>
<td>14</td>
<td>4.27%</td>
<td>0.42</td>
</tr>
<tr>
<td>No Face-to-Face</td>
<td>713</td>
<td>92</td>
<td>12.90%</td>
<td>1.06</td>
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All Diagnoses
Discharges: 2/1/16 – 7/31/17
Impact of a Pharmacy-Run Clinic in Heart Failure Patients

Presented by: Weihan Cao, Pharm.D.
PGY-1 Resident
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Background – Heart Failure Rehospitalizations

- Nearly 24% of patients discharged from a heart failure hospitalization are readmitted within 30 days\(^1\)
- Over 1 million patients with heart failure hospitalization accounting for Medicare expenditure >\$ 17 billion\(^2\)
- ACA Hospital Readmissions Reduction Program aimed to reduce 30-day hospital readmissions\(^3\)

\(^3\) "CMS to Improve Quality of Care during Hospital Inpatient Stays." CMS.gov. The Centers for Medicare & Medicaid Services
Background – Role of Pharmacists

Hospital
- Medication Reconciliation
- Drug Therapy Evaluation

Outpatient Pharmacy
- Medication Education
- Communication with patient’s PCP

Outpatient Clinic Service
- Education on Heart Failure
- Drug Therapy Evaluation Management
- Follow up appointments

Outcomes
- Reduce medication discrepancies and errors
- Improve compliance
- Improve in target dose achievement
- Fewer heart failure readmission

Study Objectives

• To determine the correlation between pharmacy clinical services and readmission rate of heart failure patients

• To describe the number and types of interventions provided by pharmacists

• To identify the challenges and opportunities for growth and development of the clinic
Methodology: Interventions

CDTM Pharmaceutical Care Management Protocol

- Recommend add/titrate CHF drug to PCP
- Identify medication error
- Monitor for ADR events
- Patient education

Telephonic follow-up
Methodology: Endpoints

• Primary Endpoints:
  – 30-day readmission
  – Number of pharmacy interventions

• Assessment measures:
  – Post-discharge days to clinic appointment
  – Dosage of medications
  – Adherence assessment
Results: Patient Selection

Patients with CDTM clinic appointments

48 Patients with systolic heart failure

23 Showed to appointment

25 Did not show to appointment
Results: 30-Day Readmission

<table>
<thead>
<tr>
<th>Readmission on Post Discharge Day 30</th>
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<tbody>
<tr>
<td>Show Group – no. (%)</td>
<td>1 (4.4%)</td>
</tr>
<tr>
<td>No Show Group – no. (%)</td>
<td>8 (32%)</td>
</tr>
</tbody>
</table>
What does all this mean?

• New ”Useful” medications are difficult to develop/produce and adopt into practice
• Drug Cost may impact accessibility
• Drug therapy is very complicated and patients may benefit from additional professional visits to get more education and assistance with adherence
• Pharmacists and other caregivers ie. NPs, PA’s etc. can supplement physicians to improve care.
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