New Drug Update

Rebecca Maxson, PharmD, BCPS
July 20, 2019
Disclosure

- I have nothing to disclose regarding this presentation
- The use of brand names are purely to help the audience recognize these medications as they are marketed
Objectives

• Describe the pace of new drug approvals by the FDA over the past year
• Discuss the MOA, major ADRs, administration and clinical pearls for several new medications that are of interest to a consulting pharmacist
New Drug Approvals
June 2018 through May 2019
Drug research is NOT dead

- Roughly 150 NDAs on the FDA’s website for the timeframe
- Majority were new formulations/manufacturers, new dosage forms and new combinations
- Eighteen new cancer drugs
- Nine biosimilars
- Drugs in this presentation – more likely to be used in our geriatric population
Migraine Prevention
Calcitonin gene-related peptide (CGRP)

- Vasoconstriction/vasodilation theory of migraines disproven
- Pain is theorized to come from activity within the trigeminovascular system
- One of the neuropeptides released when the trigeminal sensory nerves are activated
  - Central and peripheral vasodilation
  - Central and peripheral nociception
- New agents block CGRP in the periphery --> fewer CNS ADRs
CGRP antagonists

- Monoclonal antibodies
- Preventative treatment of migraine in adults
- Subcutaneous injection – at home or MD office
- Common ADRs
  - Injection site reaction
  - Hypersensitivity
- Pregnancy – only animal studies, no adverse effects, long half-life
- Not studied well in geriatrics, pediatrics
- No renal, hepatic dose adjustments
- Belimumab (Benlysta) drug interaction

Ajovy [Prescribing Information]. North Wales, PA: Teva Pharmaceuticals USA, Inc. 01/2019.
Fremanezumab-vfrm (Ajovy®)

- Dosing: 225 mg monthly OR 675 mg q3 months (3 injections of 225)
- 1.5 mL single-dose prefilled syringe
- Refrigerate, remove 30 min prior to administration, protect from direct sunlight; 24 hours at room temp
- Do not freeze or shake
- Half-life ~ 31 days
- Teva Pharmaceuticals USA
Fremanezumab-vfrm (Ajovy®) - Efficacy

- Episodic migraine - Study 1
  - 875 patients, 3 months
  - Baseline ~ 9 migraine days/month
  - ~ 3.5 day decrease in migraine days/month versus 2.2 day decrease with placebo

- Study 2
  - 1130 patients, 3 months
  - Baseline ~ 20 migraine days/month
  - ~ 4.5 day decrease versus 2.5 decrease with placebo
Erenumab-aooe (Aimovig®)

- 70 mcg monthly; some need 140 mcg monthly
- Prefilled autoinjector or prefilled syringe, contains latex
- Additional ADR: constipation (1-3%)
- Half-life ~ 28 days
- Refrigerate in original carton, 7 days at room temperature
- Do not freeze or shake
- Amgen/Novartis
Erenumab-aooe (Aimovig®) - Efficacy

- **Episodic Migraine – Study 1**
  - 995 pts, 6 months, 8 migraine days/month
  - 3.2-3.7 day decrease versus 1.8 day decrease for placebo

- **Episodic Migraine – Study 2**
  - 546 patients, 3 months, 8 migraine days/month
  - 2.9 day decrease versus 1.8 day decrease for placebo

- **Chronic Migraine – Study 3**
  - 667 patients, 3 months, 18 migraine days/month
  - 6.6 day decrease versus 4.2 day decrease for placebo
Galcanezumab-gnlm (Emgality®)

- 240 mg loading dose followed by 120 mg monthly
- Prefilled pen or syringe
- Half-life ~ 27 days
Galcanezumab-gnlm (Emgality®) - Efficacy

- **Episodic Migraine – Study 1**
  - 858 pts, 6 months, ~ 9 migraine days/month at baseline
  - 4.7 day decrease versus 2.8 day decrease for placebo

- **Episodic Migraine – Study 2**
  - 915 patients, 6 months, ~ 9 migraine days/month at baseline
  - 4.3 day decrease versus 2.3 day decrease for placebo

- **Chronic Migraine – Study 3**
  - 1113 patients, 3 months, ~ 19 migraine days/month at baseline
  - 4.8 day decrease versus 2.7 day decrease for placebo
The American Headache Society

- Diagnosed with migraine and 4-7 headache days/month PLUS BOTH
  - Inability to tolerate or inadequate response at least a 6 week trial of 2 previously-known preventive therapies
  - At least moderate disability (MIDAS>11 or HIT-6>50)

- Diagnosed with migraine and 8-14 headache days/month PLUS
  - Inability to tolerate or inadequate response to a 6 week trial of 2 previously-known preventive therapies

- Diagnosed with migraine PLUS EITHER
  - Inability to tolerate or inadequate response at least a 6 week trial of 2 previously-known preventive therapies
  - Inability to tolerate or inadequate response to a minimum of 2 quarterly injections of botulinum toxin
Infectious Disease
Eravacycline (Xerava®)

• Indication: complicated intra-abdominal infections (> 18 yoa), NOT indicated for complicated urinary tract infections

• Warnings and precautions
  • Hypersensitivity
  • Tooth discoloration and enamel hypoplasia
  • Inhibition of bone growth – 2nd/3rd trimester; < 8 yoa
  • C. diff

• ADRs
  • Infusion site reactions
  • N/V/D
Eravacycline (Xerava®)

- **Dosing:** 1 mg/kg IV q12h x 4-14 days, 60 minute infusion
- **Dose adjustment**
  - Strong CYP3A inducer: 1.5 mg/kg q12h
  - Severe hepatic impairment (Child Pugh C): 1 mg/kg IV q12h x 1 day then 1 mg q24h
- **IV preparation**
  - Powder: each vial 50 mg eravacycline in 5 mL sterile water
  - Swirl gently
  - Pale yellow to orange solution
  - Target dilution is 0.3 mg/mL using 0.9% NaCl
  - Infuse within 6 hours (room temp), 24 hours (fridge)

Eravacycline (Xerava®)

- **PD/PK**
  - AUC/MIC
  - Half-life – 20 hours
  - Metabolized by CYP3A4 and FMO-mediated oxidation
  - 34%/47% excretion in urine/feces

- **MOA**
  - Binds 30S ribosomal subunit thus disrupting bacterial protein synthesis
  - Bacteriostatic primarily

- **MOR**
  - Efflux pumps
  - Target site modifications
Eravacycline (Xerava®)

<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
<th>Anaerobic</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. faecalis</td>
<td>C. freundii</td>
<td>Variable activity</td>
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<tr>
<td>E. faecium</td>
<td>E. coacae</td>
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<tr>
<td>S. aureus</td>
<td>E. coli</td>
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<tr>
<td></td>
<td>K. oxytoca</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K. pneumoniae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NOT Pseudomonas aeruginosa</td>
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</tbody>
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Eravacycline (Xerava®) - Efficacy

- Two non-inferiority clinical trials with cIAI
- Compared to ertapenem or meropenem
- Micro-ITT: 846 pts
  - 56 yo, 56% male, 95% European
  - 60% intra-abdominal abscesses
- Non-inferior to carbapenems
Omadacycline (Nuzyra®)

- Indication: community acquired bacterial pneumonia and acute bacterial skin and skin structure infections

- Warnings and precautions
  - Mortality imbalance in patients with CABP
  - Tooth discoloration and enamel hypoplasia
  - Inhibition of bone growth – 2nd/3rd trimester; < 8 yoa
  - *C. diff*

- ADRs
  - Infusion site reactions
  - GI, HTN, headache
  - Increase in LFTs

Omadacycline (Nuzyra®)

- IV and PO
- 7-14 days
- No dose adjustments

<table>
<thead>
<tr>
<th>Infection</th>
<th>Loading Doses</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABP</td>
<td>200 mg IV over 60 min OR 100 mg IV over 30 min x 2 doses</td>
<td>100 mg IV over 30 min daily OR 300 mg PO daily</td>
</tr>
<tr>
<td>ABSSI</td>
<td>200 mg IV over 60 min OR 100 mg IV over 20 min x 2 doses OR 450 mg PO daily x 2 days</td>
<td>100 mg IV over 30 min daily OR 300 mg PO daily*</td>
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<tr>
<td></td>
<td></td>
<td>*day 1 if IV load, day 3 if PO load</td>
</tr>
</tbody>
</table>
Omadacycline (Nuzyra®)

- IV Reconstitution
  - 200 mg: 2 vials, 10 mL SWI, final concentration 2mg/mL
  - 100 mg: 1 vial, 5 mL SWI, final concentration 1 mg/mL
  - Gently swirl
  - Yellow to dark orange
- Within 1 hour, dilute to final concentration using 0.9% NS or D5W
- 12 hours (room), 48 hours (refrigerator)
- At room temp for 60 min before infusion
- AVOID infusing with any IV line that also contains calcium or magnesium

Omadacycline (Nuzyra®)

- Before PO administration
  - Fast for 4 hours
- Take with water
- After PO administration
  - No food/drink for 2 hours
  - No dairy, antacids or MVI for 4 hours
Omadacycline (Nuzyra®)

- **Drug-drug interactions**
  - Depress plasma prothrombin activity
  - Absorption impaired by antacids (AL, CA, Mg), bismuth subsalicylate and iron

- **PK/PD**
  - Food greatly reduced bioavailability
  - 20% PPB
  - Great penetration to lungs

- **MOA**
  - Binds 30S ribosomal subunit thus disrupting bacterial protein synthesis
  - Bacteriostatic primarily
  - ACTIVE against Gram + bacteria with tet K and tet L efflux pumps and ribosomal protection proteins, tet M
<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td><em>Haemophilus</em></td>
<td>Atypical</td>
</tr>
<tr>
<td><em>S. pyogenes</em></td>
<td><em>Klebsiella</em></td>
<td></td>
</tr>
<tr>
<td>MSSA/MRSA</td>
<td><em>Enterobacter</em></td>
<td></td>
</tr>
<tr>
<td><em>E. faecalis</em></td>
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<td></td>
</tr>
</tbody>
</table>

- Not pseudomonas
Omadacycline (Nuzyra®) – Efficacy CABP

CABP
• Compared to moxifloxacin 400 mg IV/PO daily x 7-14 days
• 774 pts
  • 62 yoa, 55% male, 92% white

ABSSSI
• Compared to linezolid 600 mg IV/PO q12h
• 1390 pts in 2 trials
  • Trial 1: 655 pts, 47 yoa, 65% male, 92% white
  • Trial 2: 735 pts, 44 yoa, 63% male, 91% white, all in US
Plazomicin (Zemdri®)

- **Indication**: aminoglycoside for complicated urinary tract infections including pyelonephritis (> 18 yoa)
  - Neoglycoside
  - Structural modifications increase the traditional spectrum of aminoglycosides to include MDR gram negative organisms

- **Black Box warning**
  - Nephrotoxicity
  - Ototoxicity
  - Neuromuscular blockade
  - Fetal harm

- **Other Warnings/Precautions**
  - Hypersensitivity
  - *C. diff*
### Plazomicin (Zemdri®)

- **ADRs**
  - Decreased renal function
  - Diarrhea/N/V
  - Hypertension/hypotension
  - Headache

<table>
<thead>
<tr>
<th>CLcr (mL/min)</th>
<th>Dosing</th>
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<tbody>
<tr>
<td>≥ 90</td>
<td>15 mg/kg IV q24h x 4-7 days</td>
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<tr>
<td>&lt; 90 and ≥ 60</td>
<td>15 mg/kg IV q 24h</td>
</tr>
<tr>
<td>&lt; 60 and ≥ 30</td>
<td>10 mg/kg IV q 24h</td>
</tr>
<tr>
<td>&lt; 30 and ≥ 15</td>
<td>10 mg/kg IV q 48 h</td>
</tr>
</tbody>
</table>

- No dosing recommendations for RRT
- Dosing weight: TBW unless TBW > IBW by > 25% then adjusted BW
- Therapeutic drug monitoring
  - Trough < 3 mcg/mL, check before 2nd dose
  - Adjust interval 1.5 fold if trough ≥ 3 mcg/mL
Plazomicin (Zemdri®)

- **IV preparation**
  - Single-dose 10 mL vial
    - 500 mg plazomicin in 10 mL SWI
  - Dilute to final volume of 50 mL in 0.9% NaCl OR LR
  - Stable for 24 hrs at room temp at concentrations ranging from 2.5 mg/mL to 45 mg/mL

- **PK/PD**
  - AUC/MIC
  - Half-life 3.5 h with normal renal function
  - No metabolism
  - 20% PPB
Plazomicin (Zemdri®)

• **MOA**
  - Binds 30S ribosomal subunit thus disrupting bacterial protein synthesis
  - Concentration dependent bactericidal activity
  - Post-antibiotic effect from 0.2-2.6 hours at 2x MIC against enterobacteriaceae

• **MOR**
  - Aminoglycoside modifying enzymes – NOT inhibited
  - Alteration of targets site
  - Efflux pump upregulation
  - Loss of membrane porins decreased permeability
Plazomicin (Zemdri®)

• Spectrum of Activity
  • Gram-negative organisms, including Pseudomonas and ESBL producing pathogens
  • Staphylococcus aureus
  • Variable or no activity
    • Most gram-positive organisms
    • Obligate anaerobes A
Plazomicin (Zemdri®) - Efficacy

- Patients hospitalized with cUTI (including pyelonephritis)
- Compared to meropenem 1g IV q8h (30 min infusion)
- Micro-ITT: 388 pts (162 with pyelonephritis)
  - 64 yo, 53% female, 99.5% white
  - Median treatment duration 6 days
- Non-inferior at day 5 and test of cure visit
Baloxavir (Xofluza®)

- **Indication:** treatment of acute uncomplicated influenza (> 12 yoa), symptomatic for ≤ 48 hours

- **MOA**
  - Baloxavir marboxil is a prodrug, hydrolysis to baloxavir
  - Inhibits endonuclease activity of the polymerase acidic (PA) protein
  - PA is required for influenza virus replication
  - Active against influenza virus A and virus B

- **Dosing**
  - 40 to < 80 kg: 40 mg PO x 1
  - ≥ 80 kg: 80 mg PO x 1

Baloxavir (Xofluza®)

- AVOID taking with poly-valent cation contain laxatives, antacids or oral supplements
- Warnings and precautions: secondary bacterial infections
- ADRs
  - Diarrhea
  - Bronchitis
  - Nasopharyngitis
  - Headache
  - Nausea
- Pregnancy – no risks seen with animals
Baloxavir (Xofluza®)

- **PK**
  - 94% PPB
  - Metabolised by UGT1A3 and CYP3A4

- **Drug interactions**
  - Tested with itraconazole, probenecid, oseltamivir, midazolam, digoxin and rosvastatin
  - Chelate with polyvalent cations, decreases absorption


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Baloxavir (Xofluza®) - Efficacy

• Trial 1 – Japan only
  • 400 adults, 38 yoa, 62% male, predominately A/H1N1 strain
  • Compared to placebo
  • Time to alleviation of symptoms: 50 hours Xofluza 40 mg vs 78 hours placebo

• Trial 2 – Japan and US
  • 1436 pts, 34 yoa, 54% male, predominately A/H3N2 strain
  • Compared to oseltamivir, xofluza dosed on weight
  • Time to alleviation of symptoms: 54 hours Xofluza vs 54 hours oseltamivir
Unique Dosage Forms
Midazolam (Nayzilam®)

• Acute treatment by non-healthcare professional of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures)
  • Single-use treatment that the patient can carry

• Seizure cluster
  • Acute episodes of consecutive seizures that occur within a short period of time with a patient regaining consciousness during the interictal period
  • Distinguishable for patient’s normal seizure pattern
  • ~150,000 US citizens with uncontrolled epilepsy also experience seizure clusters
  • Can lead to status epilepticus

Midazolam (Nayzilam®)

- **Dosing**
  - Single-dose nasal spray unit containing 5 mg midazolam per 0.1 mL
  - One spray in one nostril
  - May repeat one dose in opposite nostril after 10 minutes if no response to first dose
  - No more than 2 doses per seizure cluster
  - No more than 1 episode every three days
  - No more than 5 episodes per month

- **ADRs**
  - Somnolence, headache, nasal discomfort, throat irritation, rhinorrhea
Midazolam (Nayzilam®)

- Nasal administration
  - Open blister pack ONLY when ready to use
  - Do NOT prime
Clobazam (Sympazan®)

- Clobazam in an oral film
- For adjunctive treatment of seizures associated with Lenno-Gastaut Syndrome (LGS) in patients > 2 yoa
- Same dosing as oral clobazam
- Dosage forms: 5 mg, 10 mg and 20 mg oral films as package of 60
- Store at room temp
- Place on top of the tongue
- With or without food
- Do NOT take liquid with the oral film

Colchicine (Gloperba®)

- **PROPHYLAXIS** of gout flares in adults
- Oral solution
  - 0.6 mg/5 mL
  - 30 day prescription in 150 mL bottle
  - Cherry flavor profile (red liquid)
  - Room temperature

- **Dosing**
  - 0.6 mg daily to twice daily

- **Contraindications**
  - Renal or hepatic impairment with CYP3A4 or P-gp inhibitors
  - Patients with both renal and hepatic impairment

### Colchicine Dosing Adjustments

- **Geriatric**
  - Reduce prophylactic daily dose by 50% if ≥ 70 yoa

<table>
<thead>
<tr>
<th>Gout prophylaxis</th>
<th>Gout Flare Tx</th>
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<tr>
<td><strong>CrCl (ml/min)</strong></td>
<td><strong>Colcrys®</strong></td>
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<tr>
<td>30-80</td>
<td>None</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>0.3 mg daily</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>0.3 mg 2x/week</td>
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</tbody>
</table>
Levodopa inhalation powder (Inbrija®)

- Treatment for “Off” periods in Parkinson’s disease (PD) patients
- Orally inhaled powder – bypasses GI absorption
- Dosing
  - Inhale two capsules (84 mg total) as needed for OFF symptoms
  - Maximum of 5 times per day
- ADRs
  - Cough, URI, discolored sputum
  - nausea

Levodopa inhalation powder (Inbrija®)

- **Contraindications**
  - Nonselective monoamine oxidase (MAO) inhibitors

- **Warnings**
  - Fall asleep during ADLs
  - Sudden discontinuation/rapid dose reduction can cause hyperpyrexia and confusion
  - Hallucinations/exacerbation of psychosis
  - Decrease impulse control/compulsive behaviors
  - Can cause or exacerbate dyskinesia
  - Avoid in patients with asthma, COPD and other chronic lung disease
Levodopa inhalation powder (Inbrija®)

• Drug Interactions
  • Nonselective monoamine oxidase (MAO) inhibitors
  • Selective MAO-B inhibitors
  • Dopamine D2 receptor antagonists and isoniazid
  • Iron salts

• Administration

• Supplied as
  • 60 capsules (15 blister cards with 4 capsules each) + 1 inhaler
  • 92 capsules (23 blister cards of 4 caps each) + 1 inhaler
  • Store in blister packaging at room temp

Dexamethasone ophthalmic insert (Dextenza®)

- One time ophthalmic insert that releases 0.4 mg dexamethasone for up to 30 days
  - Inserted by surgeon in the lower lacrimal punctum into the canaliculus
- Replace the ~ 70 steroid eye drops required after cataract surgery
- Delayed approval
- Cost/coverage???
- Similar warnings/ADRs to steroid eye drops
Revafenacin (Yulperi®)

- Once daily, nebulized, anti-muscarinic for COPD maintenance
- Dosing: 175 mcg/3 mL nebulized daily
  - Not recommended with any degree of hepatic impairment
- ADRs
  - Cough, nasopharyngitis, URI
  - Headache
  - Back pain
- Drug interactions
  - Other anticholinergic medications
  - OATP1B1 and OATP1B3 inhibitors – increases exposure to active metabolite


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Revefenacin (Yulperi®)

- **Metabolism**
  - Rapid hydrolysis to major active metabolite
  - Plasma levels of metabolites are 4-6 fold greater than parent

- **Other PK**
  - Protein binding: 71% parent, 42% metabolite
  - Terminal half-life: 22 hours parent, 70 hours metabolite

- **Storage and how supplied**
  - Room temp in protective foil pouch
  - 30 individually pouched unit-dose vials or 7 vials


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Revefenacin (Yulperi®) – Clinical Trials

- 52-week open-label trial versus tiotropium
  - 1,055 patients
  - ADRs consistent with those in placebo trials and similar to tiotropium
- Two, 12-week efficacy trials versus placebo
  - 812 patients with moderate to very severe COPD
  - 37% on concomitant LABA or ICS/LABA therapy that was continued
  - Yupelri showed significant improvement in FEV$_1$ versus placebo
Prucalopride (Motegrity®)

• Selective serotonin-4 (5-HT$_4$) agonist to treat adults with chronic idiopathic constipation (CIC)

• Dosing
  • Adults: 2 mg PO daily
  • CrCl < 30 mL/min: 1 mg PO daily
  • Avoid in patients requiring dialysis
  • With or without food

• Contraindications and warnings
  • Intestinal perforation/obstruction/ileus/Crohn’s, UC or toxic megacolon – avoid
  • Suicidal ideation and behavior
Prucalopride (Motegrity®)

- **ADRs**
  - Abdominal pain, nausea, diarrhea, abdominal distention, vomiting, flatulence
  - Dizziness
  - Fatigue
  - Headache

- **How supplied**
  - HDPE bottle of 30 tablets
  - Room temperature
  - Store in original container to protect from moisture
Prucalopride (Motegrity®)

- **PK**
  - Single dose increased # of high amplitude propagating contractions in 1st 12 hours when compared to an osmotic laxative treatment
  - Mean colonic transit time reduced from 65 hours to 53 hours
  - Terminal half-life ~ 24 h
  - Bioavailability > 90%
  - 30% plasma protein binding
  - Renal excretion is main route of elimination
Prucalopride (Motegrity®) – Clinical Trials

- Six, double-blind, placebo control trials
- 2,484 pts
- All were 12 weeks except trial 6 was 24 weeks
- Responder: 3 or more complete spontaneous bowel movement (CSBM)/week
- All studies, motegrity better than placebo
- Improvement seen as early as week 1 and maintained through week 12
Amlodipine and celecoxib (Consensi®)

- Combination of amlodipine and celecoxib
- Available doses amlodipine/celecoxib
  - 2.5 mg/200 mg
  - 5 mg/200 mg
  - 10 mg/200 mg
- Warnings/precautions, PK, PD – similar to individual agents
Amlodipine and celecoxib (Consensi®)

- 2 weeks, UK, 152 patients
- Amlodipine/celecoxib 10/200 mg vs amlodipine 10 mg vs celecoxib 200 mg vs placebo (1.5:1.5:1.5:1)
- 95% white, 67% male, 56 yoa
- Noninferior BP reduction between combo and amlodipine alone group
- More nighttime BP reduction with amlodipine (non-significant for non-inferiority)
- Mean 24-hour ambulatory diastolic BP, combination was superior for combination
  - 7.1 ± 5.6 mmHg combo vs 4.8 ± 4.8 mm Hg amlodipine, superiority p=0.038
- Similar ADR profile in this 2 week study between active arms
Baricitinib (Olumiant®)

- Janus kinase (JAK) inhibitor for treatment of rheumatoid arthritis
  - Inadequate response to 1 or more tumor necrosis factor (TNF) antagonist therapies
  - Do NOT combine with biologic DMARDs, other JAK inhibitors or potent immunosuppressants
  - Similar to tofacitinib (Xeljanz)

- Black box warning
  - Serious infections
  - Lymphoma and other malignanices
  - thrombosis


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Baricitinib (Olumiant®)

• Warnings and precautions
  • In addition to BBW
  • GI perforations
  • Avoid with live vaccines
  • Increased LFTs

• ADRs
  • URI
  • Nausea
  • Herpes simplex and herpes zoster
Baricitinib (Olumiant®)

• Dosing
  • 2 mg PO daily
  • With or without food
  • AVOID with
    • Severe hepatic impairment
    • Moderate or severe renal impairment (GFR < 60 mL/min/1.73m²)
    • Strong OAT3 inhibitors (probenecid)
  • Avoid with live vaccines
  • Increased LFTs

• Dose adjustments
  • Lymphopenia, neutropenia, anemia
Romosozumab-aqqg (Evenity®)

- Sclerostin inhibitor for treatment of osteoporosis in postmenopausal women at high risk for fracture
  - h/o osteoporotic fracture
  - Multiple risk factors for fracture
  - Failed or intolerant to other available therapies
- Humanized monoclonal antibody (IgG2)
- Dosing/administration
  - 210 mg SQ monthly x 12 months
  - Given by healthcare provider
  - Two separate injection for entire dose
Romosozumab-aqqg (Evenity®)

- **BBW**
  - Major Adverse Cardiac Events (MACE)
- **Contraindications**
  - Hypocalcemia
- **Warnings**
  - Hypocalcemia
  - Osteonecrosis of the jaw
  - Atypical femoral fracture
- **ADRs**
  - Arthralgia
  - Headache

Romosozumab-aqgg (Evenity®) Clinical data

Study 1

- Evenity vs placebo x 12 mos then open-label denosumab for 12 mos
- 500-1000 mg calcium and 600-800 international units Vit D
- Age 55-90 with BMD T-score ≤ -2.5 at total hip or femoral neck
- New vertebral fracture at month 12
  - 0.5% vs 1.8%, p < 0.001, NNT = 77
- New vertebral fracture at month 24
  - 0.6% vs 2.5%, p < 0.001, NNT = 53

Romosozumab-aqqg (Evenity®) Clinical data

Study 2

• Evenity vs alendronate x 12 mos then open-label alendronate for 12 mos

• 500-1000 mg calcium and 600-800 international units Vit D

• Age 55-90 with
  • BMD T-score ≤ -2.5 + 1 mod-severe or 2 mild vertebral fractures
  • BMD T-score ≤ -2 + 2 mod-severe vertebral fractures or h/o proximal femur fracture

• New vertebral fracture at month 24
  • 4.1% vs 8%, p < 0.001, NNT = 25
Esketamine (Spravato®)

- Non-competitive NMDA receptor antagonist for the treatment-resistant depression in adults
  - Must also be on an oral antidepressant
  - NOT an anesthetic
  - CIII

- Dosing

<table>
<thead>
<tr>
<th>Induction Phase</th>
<th>Weeks 1-4</th>
<th>Twice per week</th>
<th>Day 1: 56 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Subsequent doses: 56 or 84 mg</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Weeks 5-8</td>
<td>Once weekly</td>
<td>56 or 84 mg</td>
</tr>
<tr>
<td>Weeks 9 +</td>
<td></td>
<td>Once weekly OR every 2 weeks</td>
<td>56 or 84 mg</td>
</tr>
</tbody>
</table>
Esketamine (Spravato®)

- Contraindications
  - Aneurysmal vascular disease or AV malformations
  - h/o intracerebral hemorrhage
- Warnings
  - Increase in BP
  - Sedation
  - Dissociation
  - Abuse and misuse
  - Suicidal thoughts and behaviors
  - Cognitive impairment
  - Impaired ability to drive and operate machinery
  - Ulcerative or interstitial cystitis
  - Embryo-fetal toxicity
Esketamine (Spravato®)

- **SPRAVATO REMS**
  - Healthcare setting must be certified
  - ONLY dispensed in health care settings
  - Only to patients enrolled in the program
  - Administered under direct observation of health care provider
  - Monitored by healthcare provider for at least 2 hours after administration
  - Pharmacies must be certified in the program and can only dispense to facilities certified by the REMS
Esketamine (Spravato®)

- ADRs
  - All the warning/precautions
  - Dissociation, dizziness, sedation, vertigo, hypoesthesia
  - Anxiety, lethargy, feeling drunk
  - Nausea, vomiting
  - Increased BP

- Metabolism
  - Noresketamine via CYP2B6 and CYP3A4

Esketamine (Spravato®) Administration

Before treatment

• Check BP
• If < 140/90 assess risk of short term BP inc
• No food for 2 hours prior
• No liquid for 30 min prior
• No nasal corticosteroid or nasal decongestant at least 1 hour prior
Esketamine (Spravato®) Administration

Administration

2. Expiration date, remove device from blister pack, check indicator shows 2 green dots, hand to patient
3. Recline head 45 degrees, hold with fingers on blue part and thumb gently supporting plunger
4. Spray into first nostril. Switch hands and repeat into second nostril
5. Check for no dots on indicator. Rest semi-reclined for 5 min after each device.

After treatment

- Observe for at least 2 hours
- Check BP ~ 40 minutes after dose and as needed clinically
- If BP decreasing and pt appears clinically stable for at least 2 hours, can discharge after 2 hours
Sodium Zirconium cyclosilicate (Lokelma®)

• Latest potassium binder
• Non-absorbed zirconium silicate that preferentially captures potassium in exchange for hydrogen and sodium

• Dosing:
  • Acute hyperkalemia: 10 g TID for up to 48 hours
    • Not for emergent hyperkalemia
  • Chronic/maintenance: 10 g daily, usual dose 5 g QODay to 15 g daily

• Warnings and precautions
  • GI in patients with motility disorders
  • Edema
Sodium Zirconium cyclosilicate (Lokelma®)

- ADRs
  - Mild to moderate edema
- Onset within 1 hours
- MUST separate from other oral medications at least 2 hours before or after
- Preparation
  - At least 3 tablespoons of water
  - Add packet and stir well
  - Get all the powder – add water, stir, repeat
New Drug Update

Rebecca Maxson, PharmD, BCPS

July 20, 2019
Other new medications

For your reference
<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivosidenib (Tibsovo)</td>
<td>AML (new or refractory)</td>
<td>First in class IDH1 inhibitor</td>
</tr>
<tr>
<td>Mogalulizumab-kpjc (Poteligeo)</td>
<td>NHL (MF &amp; SS)</td>
<td>First in class CCR4 inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>First to treat SS</td>
</tr>
<tr>
<td>Moxetumomab pasudotox-tdfk (Lumoxiti)</td>
<td>HCL</td>
<td>First in class anti-CD22</td>
</tr>
<tr>
<td>Duvelisib (Copiktra)</td>
<td>CLL, SLL, FL</td>
<td>PJP and CMV prophylaxis recommended</td>
</tr>
<tr>
<td>Cemiplimab-rwlc (Libtayo)</td>
<td>CSCC</td>
<td>First to treat advanced CSCC</td>
</tr>
</tbody>
</table>
## Oncologic agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dacomitinib (Vizimpro)</td>
<td>NSCLC</td>
<td>May cause ILD</td>
</tr>
<tr>
<td>Talazoparib (Talzenna)</td>
<td>Breast cancer</td>
<td>P-gp drug interactions</td>
</tr>
<tr>
<td>Lorlatinib (lobrena)</td>
<td>Metastatic NSCLC</td>
<td>Crosses BBB CYP3A4 interactions</td>
</tr>
<tr>
<td>Glasdegib (Daurismo)</td>
<td>AML</td>
<td>&gt; 75 yoa or significant comorbidities</td>
</tr>
<tr>
<td>Larotrectinib (vitrakvi)</td>
<td>Solid tumor with NTRK genes</td>
<td>Second tissue-agonistic cancer drug</td>
</tr>
</tbody>
</table>
# Oncologic agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giltertinib (Xospata)</td>
<td>AML</td>
<td>Rare cases of PRES Endocrine abnormalities</td>
</tr>
<tr>
<td>Tagraxofusp-erzs (Elzonris)</td>
<td>BPDCN</td>
<td>Albumin $\geq 3.2$ g/dL prior to C1 (due to CLS)</td>
</tr>
<tr>
<td>Calaspargase pegoi-mknl (Asparlas)</td>
<td>ALL (1mo-21 yrs)</td>
<td>Must be refrigerated Clotting abnormalities</td>
</tr>
<tr>
<td>Erdaftinib (Balversa)</td>
<td>Bladder cancer</td>
<td>Restrict phosphate intake to 600-800 mg/day</td>
</tr>
<tr>
<td>Alpelisib (Piqray)</td>
<td>Breast cancer</td>
<td>Risk for drug-induced ketoacidosis</td>
</tr>
</tbody>
</table>
# Anti-infective agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifamycin (Aemcolo)</td>
<td>Traveler’s diarrhea</td>
<td>Cannot be complicated by fever or blood in stool</td>
</tr>
<tr>
<td>Doravirine (Pifeltro)</td>
<td>HIV-1</td>
<td>Avoid CYP3A4 inducers</td>
</tr>
<tr>
<td>Tafenoquine (Krintafel)</td>
<td>Malaria</td>
<td>G6PD and pregnancy test prior to initiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If vomiting occurs within 1 hour, redoes</td>
</tr>
</tbody>
</table>
## Anti-infective agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecovirimat (TPOXX)</td>
<td>Smallpox</td>
<td>First product to be awarded a Material Threat Medical Countermeasure Priority Review Voucher</td>
</tr>
</tbody>
</table>
| Triclabendazole (Egaten) | Parasitic infection     | QTc prolongation  
                                        Take with food                                                         |
### Dermatologic Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarecycline (Seysara)</td>
<td>Acne</td>
<td>Administer with fluids to decrease risk of esophageal irritation and ulceration</td>
</tr>
<tr>
<td>PrabotuinumtoxinA-xvfs (Juveau)</td>
<td>Glabellar lines</td>
<td>Must be refrigerated BBW: toxin spread</td>
</tr>
<tr>
<td>Risankizumab-rzaa (Skyrizi)</td>
<td>Plaque psoriasis</td>
<td>Administer injections at two different anatomic sites</td>
</tr>
</tbody>
</table>
## Neurologic Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amifampridine (Firdpase)</td>
<td>Lamber-Eaton myasthenic syndrome</td>
<td>Contraindicated if history of seizures</td>
</tr>
<tr>
<td>Simponimod (Mayzent)</td>
<td>MS</td>
<td>Dose by CYP2C9 genotype</td>
</tr>
<tr>
<td>Stirpentol (Diacomit)</td>
<td>Darvet syndrome</td>
<td>Not appropriate as monotherapy</td>
</tr>
<tr>
<td>Solriamfetol (Sunosi)</td>
<td>Narcolepsy, OSA</td>
<td>Just scheduled as C-IV Not yet marketed</td>
</tr>
</tbody>
</table>
## Women’s Health Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brexanolone (Zulresso)</td>
<td>Post-partum depression</td>
<td>Continuous infusion over 60 hours REMS program</td>
</tr>
<tr>
<td>Segestron acetate and ethinyl estradiol (Ancovera)</td>
<td>Contraception</td>
<td>Intravaginal ring</td>
</tr>
<tr>
<td>Elagolix (Orlissa)</td>
<td>Pain associated with endometriosis</td>
<td>High risk of OP (minimize duration of use)</td>
</tr>
<tr>
<td>Drug (brand)</td>
<td>Indication/Clinical role</td>
<td>Interesting fact</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Inotersent (Tegsedi)</td>
<td>Polyneuropathy of hereditary transthyretin-mediated amyloidosis</td>
<td>REMS (glomerulonephritis, thrombocytopenia) SQ</td>
</tr>
<tr>
<td>Patisiran (Onpattro)</td>
<td>Repeatedly reduced with Vitamin A levels IV</td>
<td></td>
</tr>
<tr>
<td>Lanadelumab-fiy (Takhzyro)</td>
<td>Hereditary angioedema prophylaxis</td>
<td>≥ 12 yoa SQ</td>
</tr>
<tr>
<td>Migalastat (Galafold)</td>
<td>Fabry disease</td>
<td>Pharmacologic chaperone</td>
</tr>
</tbody>
</table>
# Hematologic and Immunologic Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lusutrombopaq (Mulpleta)</td>
<td>Thrombocytopenia</td>
<td>7 day procedure window after treatment</td>
</tr>
<tr>
<td>Elapegademase-lvrl (Revcovi)</td>
<td>ADA-SCID</td>
<td>IM Dosing formula Refrigerate in original carton</td>
</tr>
<tr>
<td>Emapalumab (gamifant)</td>
<td>HLH</td>
<td>Monitor for TB, adenovirus, EBV and CMV q 2wks</td>
</tr>
<tr>
<td>Ravulizumab-cwva (Ultomiris)</td>
<td>PNH</td>
<td>REMS IV</td>
</tr>
</tbody>
</table>
# Hematologic and Immunologic Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caplacizumab-yhdp (Calbibi)</td>
<td>aTTP</td>
<td>IV With plasma exchange and immunosuppression</td>
</tr>
</tbody>
</table>

## Nutritional Agent

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid emulsion (fish oil-based) (Omegaven)</td>
<td>Pediatric parenteral nutrition</td>
<td>Baseline TG</td>
</tr>
</tbody>
</table>
## Cardiac and Ophthalmologic Agents

<table>
<thead>
<tr>
<th>Drug (brand)</th>
<th>Indication/Clinical role</th>
<th>Interesting fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cenegermin (Oxervate)</td>
<td>Neurotrophic keratitis</td>
<td>First in class rhGNF Dispensed as weekly carton of multt-dose vials</td>
</tr>
<tr>
<td>Tafamidis meglumine (Vydaqel)</td>
<td>ATTR-CM</td>
<td>Currently unavailable First treatment for this disease state</td>
</tr>
</tbody>
</table>