New Drug Update 2015

Wesley Lindsey, Pharm.D.
Associate Clinical Professor
Auburn University: Harrison School of Pharmacy

Biography
- Undergraduate: University of North Carolina at Asheville
- Pharmacy: Campbell University
- Residency: Drug Information at Campbell University
- Faculty:
  - Palm Beach Atlantic University
  - Auburn University: 2006 – Present

Objectives
- Name the major new chemical entities approved by the FDA in 2014 and early 2015
- Recognize the major therapeutic aspects of new drugs approved by the FDA in 2014 (e.g., indications, adverse reactions, drug interactions);
- Identify drugs approved by the FDA in 2014 that represent a major therapeutic advancement.
New Drug Approvals

- Approvals By Year
  - 2011: 31
  - 2012: 37
  - 2013: 27
  - 2014: 44

 Renewal of the Prescription Drug User Fee Act (PDUFA)

- Occurred in 2012
- FDA now collects fees from generic and bio-similar product companies
- Approval times are shortened
- Priority vs Standard Review
- User fees account for nearly half of the FDA's operating budget
FDA Conditional Approval

• 2013: FDA can offer approval to certain medications after Phase 1/2 testing

• Initially ~18 products were submitted for approval

• Limited success

FDA Priority Review Vouchers

• FDA can award vouchers to companies that create drugs for rare diseases

• Vouchers are transferable
  – 2 sold in 2014
  • BioMartin for $67.5M
  • Knight for $125M

NOTABLE NEW DRUGS
2014 – PRESENT
**Farxiga (dapaglifozin)**

- **Indication**
  - Glycemic control in adults with Type 2 diabetes
- **Mechanism**
  - Increases urinary glucose excretion in the urine
- **Dosing**
  - Start 5mg daily in the am w/ food
  - May increase to 10mg daily if needed

**Adverse Reactions**
- Hypotension
- Hypoglycemia
- Mycotic infections in women
- UTIs

**Drug Interactions**
- Other diabetes therapies (hypoglycemia)

**Clinical Notes**
- Has been studied as both monotherapy and add-on therapy for DM
- 0.6% to 0.8% reduction in Hgb A1C for the 5mg dose, ~1% reduction with 10mg dose
- Clinical trials noted some weight loss in patients
Jardiance (empagliflozin)

- **Indication**
  - Glycemic control in adult patients with Type 2 diabetes
- **Mechanism of Action**
  - Increases urinary glucose excretion in the urine
- **Dosing**
  - 10mg once daily in the AM
  - 25 mg once daily if needed

Jardiance (empagliflozin)

- **Adverse Reactions**
  - Hypotension
  - Hypoglycemia
  - Mycotic infections in women
  - UTIs
- **Drug Interactions**
  - Other diabetes therapies (hypoglycemia)
  - Diuretics

Jardiance (empagliflozin)

- **Clinical Notes**
  - Both doses had ~0.7% reduction in Hgb A1C
  - This reduction was seen whether as monotherapy or add-on to other medications
Trulicity (dulaglitide)

- **Indication**
  - Improve glycemic control in adult patients with Type 2 diabetes

- **Mechanism of Action**
  - Stimulates glucose dependent insulin release, slows gastric emptying

- **Dosing**
  - 0.75mg SQ once weekly
  - Up to 1.5mg SQ once weekly

Trulicity (dulaglitide)

- **Adverse Reactions**
  - BBW: thyroid tumors
  - Nausea/vomiting/diarrhea
  - Abdominal pain
  - Injection site reactions

- **Drug Interactions**
  - Secretagogues

Trulicity (dulaglitide)

- **Clinical Notes**
  - Hgb A1c Lowering over 26 weeks

<table>
<thead>
<tr>
<th>Dulaglitide 0.75mg</th>
<th>Dulaglitide 1.5mg</th>
<th>Exenatide 10mcg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.3%</td>
<td>-1.51%</td>
<td>-0.99%</td>
<td>-0.46%</td>
</tr>
</tbody>
</table>
**Tanzeum (albiglutide)**

- **Indications**
  - Glycemic control in adult patients with Type 2 diabetes

- **Mechanism of Action**
  - Stimulates glucose dependent insulin release, slows gastric emptying

- **Dosing**
  - 30mg SQ once weekly
  - 50mg SQ once weekly if needed

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**Tanzeum (albiglutide)**

- **Adverse Reactions**
  - BBW: thyroid tumors
  - URTI
  - Nausea/vomiting/diarrhea
  - Abdominal pain

- **Drug Interactions**
  - Secretagogues

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**Tanzeum (albiglutide)**

- **Clinical Notes**
  - Reduction in Hgb A1C
    - 30mg ~0.6 to 0.7%
    - 50mg ~1.0%
Otezla (apremilast)

- **Indication**
  - Treatment of adult patients with active psoriatic arthritis

- **Mechanism of Action**
  - Inhibits phosphodiesterase 4

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Otezla (apremilast)

- **Dosing**

<table>
<thead>
<tr>
<th>Day</th>
<th>AM</th>
<th>AM</th>
<th>PM</th>
<th>PM</th>
<th>AM</th>
<th>AM</th>
<th>PM</th>
<th>PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>10mg</td>
<td>10mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td></td>
<td></td>
<td>10mg</td>
<td>20mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20mg</td>
<td>20mg</td>
<td>10mg</td>
<td></td>
</tr>
<tr>
<td>Day 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20mg</td>
<td>10mg</td>
<td></td>
</tr>
<tr>
<td>Day 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10mg</td>
<td></td>
</tr>
<tr>
<td>Day 6+</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
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Otezla (apremilast)

- **Adverse Reactions**
  - Diarrhea, nausea
  - Headache
  - Depression

- **Drug Interactions**
  - CYP 450 Inducers
    - Phenobarbital, rifampin
    - Phenytoin

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**Otezla (apremilast)**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Apremilast 20mg BID</th>
<th>Apremilast 30mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR 20</td>
<td>13%</td>
<td>27%</td>
<td>37%</td>
</tr>
<tr>
<td>ACR 50</td>
<td>4%</td>
<td>15%</td>
<td>20%</td>
</tr>
<tr>
<td>ACR 70</td>
<td>1%</td>
<td>6%</td>
<td>11%</td>
</tr>
</tbody>
</table>

ACR= American College of Rheumatology

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**Movantik (naloxegol)**

- **Indication**
  - Opioid induced constipation in patients with non-cancer pain

- **Mechanism of Action**
  - Peripherally acting mu-opioid receptor antagonist

- **Dosing**
  - 25mg once daily
  - 12.5mg once daily if needed

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**Movantik (naloxegol)**

- **Adverse Reactions**
  - Abdominal pain, diarrhea, flatulence
  - Possible opioid withdrawal

- **Drug Interactions**
  - Numerous: CYP 3A4 Inhibitor and Inducers
  - Other opioid antagonists
Movantik (naloxegol)

- Clinical Notes
  - Response defined as ≥3 spontaneous bowel movements per week or increase of ≥1 additional bowel movement per week over baseline
    - ~42% response in naloxegol
    - ~29% response in placebo

Sivextro (tedizolid)

- Indication
  - Acute bacterial infections caused by gram + organisms
- Mechanism of Action
  - Binds to the 50S subunit of bacterial ribosome and inhibits protein synthesis
- Dosing
  - 200mg once daily
  - 6 days

Sivextro (tedizolid)

- Adverse Reactions
  - Nausea, vomiting, diarrhea
  - Serotonin syndrome (rare)
- Drug Interactions
  - Antidepressants
Sivextro (tedizolid)

- Clinical Notes

<table>
<thead>
<tr>
<th>Early Clinical Response</th>
<th>JAMA</th>
<th>Lancet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linezolid (10 days)</td>
<td>79.4%</td>
<td>83%</td>
</tr>
<tr>
<td>Tedizolid (6 days)</td>
<td>79.5%</td>
<td>85%</td>
</tr>
</tbody>
</table>

Dalvance (dalbavancin)

- Indications
  - Acute bacterial infections caused by gram + organisms
- Mechanism of Action
  - It kills bacteria
- Dosing
  - 1000mg IV over 30 min
  - 500mg IV over 30 min one week later

Dalvance (dalbavancin)

- Adverse Reactions
  - Nausea, vomiting, diarrhea
  - Rash
- Drug Interactions
  - None of note
**Dalvance (dalbavancin)**

<table>
<thead>
<tr>
<th>Clinical Response</th>
<th>Clinical Cure at End of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalbavancin 2 doses</td>
<td>79.7%</td>
</tr>
<tr>
<td>Vancomycin-linezolid 14 days</td>
<td>79.8%</td>
</tr>
</tbody>
</table>

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**Orbactiv (oritavancin)**

- **Indication**
  - Acute bacterial infections due to gram + organisms
- **Mechanism of Action**
  - Puts the brakes on bacterial reproduction
- **Dosing**
  - 1200mg as a single infusion

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**Orbactiv (oritavancin)**

- **Adverse Reactions**
  - Nausea, vomiting, diarrhea
  - Subcutaneous abscesses
- **Drug Interactions**
  - Warfarin
  - Heparins (?)
Orbactiv (oritavancin)

<table>
<thead>
<tr>
<th>Clinical Endpoints</th>
<th>Clinical Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oritavancin</td>
<td>82.3%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>78.9%</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>79.6%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>80%</td>
</tr>
</tbody>
</table>

Zontivity (vorapaxar)

- **Indication**
  - Reduction of thromboembolic events in patients with a history of MI or PAD
- **Mechanism of Action**
  - Inhibits thrombin induced platelet aggregation
- **Dosing**
  - 2.08mg once daily

Zontivity (vorapaxar)

- **Adverse Reactions**
  - BBW: Bleeding
  - Anemia
- **Drug Interactions**
  - Warfarin
Zontivity (vorapaxar)

- Clinical Notes
  - Primary endpoint achieved at 3 years (NEJM)
    - 9.3% vorapaxar
    - 10.5% placebo
  - Primary endpoint achieved at 3 years (Am J Cardiol)
    - 10.1% vorapaxar
    - 11.8% placebo
  - Higher incidences of bleeding

Savaysa (edoxaban)

- Indications
  - Reduce stroke and embolism in patients with NVAF
  - Treatment of DVT and PE

- Mechanism of Action
  - Factor Xa inhibitor
Savaysa (edoxaban)

- Dosing
  - NVAF: 60mg once daily
    - Patient must have CrCl between 50mL/min and 95mL/min
  - DVT/PE treatment: 60mg once daily
    - Patient must have CrCl between 50mL/min and 95mL/min

- Adverse Reactions
  - BBW: Renal function warnings
  - Ischemic stroke in patients with high renal function
  - Bleeding
  - Anemia

- Drug Interactions
  - Other anticoagulants/antiplatelets
  - Low dose ASA increased bleeding risk

- Clinical Notes
  - Compared to warfarin re: symptomatic VTE for 12 months
    - 3.2% edoxaban
    - 3.5% warfarin
  - Re: bleeding
    - 8.5% edoxaban
    - 10.3% warfarin
Rapivab (peramivir)

- **Indication**
  - Uncomplicated influenza in patients > 18 yo
- **Mechanism of Action**
  - Neuraminidase inhibitor
- **Dosing**
  - 200mg IV injection

Rapivab (peramivir)

- **Adverse Reactions**
  - Diarrhea
- **Drug Interactions**
  - Live attenuated influenza virus vaccine

Rapivab (peramivir)

- **Clinical Notes**
  - Improvement in symptoms can potentially be seen in 24 hours after administration
  - Shortens duration of symptoms and lessens severity of symptoms overall
Oral Allergy Immunotherapy

- Grastek
- Oralair
- Ragwitek

- Indicated for treatment of allergic rhinitis in patients 18-65 yo.
- Continuous vs. Seasonal therapy

Advantages of SLIT

| Safer (fewer local and systemic allergic reactions) |
| More comfortable for patients (oral vs subcutaneous) |
| More convenient of patients (self-administered at home) |

Disadvantages of SLIT

| Must start taking medication prior to allergen season |
| Benefit only seen with consistent patient adherence |
| High incidence of side effects (throat/ear pruritus, mouth edema, throat irritation) |

Random Stuff I Find Interesting

- Belsomra (suvorexant)
  - Orexin inhibitor for insomnia
- Vyvanse (lysextendamphetamine)
  - Approved for binge eating
- Contrave (naltrexone/bupropion)
  - Combo for weight loss
- Afrezza (inhaled insulin)
  - We are go again
Thank You!

Questions?