New Drugs You Need to Know

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The Business of New Drugs

- Drug development driven by profit for new agents vs. innovation for new treatments
- JAMA study (2017): 10 cancer drugs
  - $7.2 Billion to develop
  - $67 Billion in sales
- “Me too” drugs
- Delaying release of generics
- Combinations or modifications of old drugs → patent extension!
- Who loses most?

New Drug Advertising

- Over $6.5 Billion in 2016
  - >60% increase over past 5 years
  - More spent on ads than research and development
- Return on investment!
- Where are the ads for the cheap prescriptions?
- Up to 1000% price hikes on brand name prescriptions in past 2 years
- Meanwhile
  - $300 Million spent on lobbying and campaign contributions

Are These “Diseases” or a Normal Part of Life?

- Premenstrual Dysphoric Disorder
- Shift Work Sleep Disorder
- Male Pattern Baldness
- Erectile Dysfunction
- Restless Leg Syndrome
- Social Phobia
- “Low T”

Are These New Drugs?

- Quedexy XR:
  - Long acting version of topiramide (Topamax)
  - Generic Topamax: $11/month
  - Quedexy: $360/month
- Yosprala
  - Combination of aspirin and omeprazole (Prilosec) for people who need to take aspirin but have a risk of peptic ulcer disease
  - OTC aspirin and omeprazole: $17/month
  - Yosprala: $165/month

Nuedexta® (dextromethorphan and quinidine)

- “The only FDA approved treatment for PseudoBulbar Affect”
  - Involuntary crying or laughing
  - Occurs in a small portion of patients with ALS, MS, post brain trauma including stroke
- Some evidence that dextromethorphan (DM) can reduce PBA symptoms
- Low dose quinidine added to reduce DM metabolism
Nuedexta® (dextromethorphan and quinidine)
- 283 ALS or MS patients with “clinically significant PBA”
- 2 doses of Nuedexta or placebo
- Weekly crying or episodes by day 85 as compared to start of study
  - Nuedexta: 25 fewer
  - Placebo: 15 fewer
- Conclusion: “Nuedexta reduced these episodes by 49%!"

Nuedexta® (dextromethorphan and quinidine)
- Quinidine can be toxic, even at low doses
  - QT prolongation
  - ITP
  - Lupus-like syndrome
  - Hepatic toxicity
  - Diarrhea and dizziness common

Nuedexta® (dextromethorphan and quinidine)
- Released in 2011
- Sales were slow prior to marketing campaign
  - 2012: $37 Million
  - 2016: $218 Million
- If purchased separately
  - Dextromethorphan: $30/month
  - Quinidine: $20/month
  - Nuedexta: $800/month

Linzess® (linaclotide)
- Activates receptors in the intestine
  - Increased fluid within the intestine
  - Glorious BM
- Approved for “chronic idiopathic constipation” and “irritable bowel syndrome with constipation”
- Comes in 3 doses (75 mg, 145mg and 290mg)
- Fun fact: Drug company that makes Linzess also owns Proctor and Gamble, makers of Charmin bath tissue and Pampers diapers

Linzess® (linaclotide)
- 1276 patients with constipation
- Linactlotide or placebo for 12 weeks
- Primary end point: “three or more complete spontaneous bowel movements (CSBMs) per week”

Linzess® (linaclotide)
- Less straining than placebo
- Greater “stool consistency” than placebo
- 16% developed diarrhea
- Cost for a 12 week supply: $1050
Trulance® (plecanatide)

- “Me-too” product to compete with Linzess released earlier this year
- Works by the same mechanism
- Response rate about the same
- Cost about the same
- Selling point: Less frequency of diarrhea!
  - 5% vs. 1% with placebo
  - Linzess: 16% vs. 5% with placebo

New Area of Marketing: Opioid-Induced Constipation

- Movantik® (naloxegol): AstraZeneca
- Symproic® (naldemedine): Purdue
- Both are oral derivatives of naltrexone
- Both cost $330/month
- Relistor® (methylnaltrexone): Salix
  - Injectable, oral forms
  - $1500/month

Oral Anticoagulants

- Warfarin
- Pradaxa® (dabigatran): Boeringer
- Xarelto® (rivaroxaban): Janssen
- Eliquis® (apixaban): Bristol-Myers Squibb

The new guys

Savaysa® (edoxaban)

- Once-daily Factor Xa inhibitors, just like Xarelto
- Savaysa:
  - Approved for a-fib, DVT/PE
  - Made in Japan since 2011, now sold here
- Bevyxxa:
  - Approved to reduce DVT risk (so far)
  - Made by a small company hoping to be taken over by a big company
  - IPO coming this month

Savaysa® (edoxaban) vs. warfarin

- 8200 patients with DVT
  - “Non-inferior” to warfarin in preventing recurrent DVT/PA (3.3% each)
- 21,000 patients with a-fib
  - Slightly lower rate of stroke (1.2% vs 1.5%)
  - BUT: stroke rate higher in patients with poor kidney function
  - Less major bleeding (2.8% vs. 3.4%)

Bevyxxa® (betrixaban)

- Betrixaban (5-6 weeks) vs. Lovenox (1-2 weeks) for DVT prophylaxis
- Composite outcome (DVT, PE, death, asymptomatic DVT detected on ultrasound) lower with Bevyxxa 6.0% vs 4.4%
- Conclusion: 30% reduction!
  - BUT: 80% of events were asymptomatic DVT
- Betrixaban vs. warfarin in a-fib
  - Similar rates of stroke and bleeding
Comparison Between Newer Anticoagulants

Monthly Cost
- Warfarin: $8
- Pradaxa: $385
- Xarelto: $400
- Eliquis: $400
- Savaysa: $330
- Bevyxxa: $470

Idarucizumab® (Praxbind)
- Reversal agent for dabigatran (Pradaxa)
- Monoclonal antibody ($$$$$$) that binds to dabigatran, neutralizing its anticoagulant effect
- Accelerated approval in 2015 based on one study, 90 patients
  - Demonstrated lower unbound dabigatran
  - Sample size too small to make any conclusions on bleeding reduction
  - Risk of clotting?

Type 2 Diabetes
- 29 million patients in the US
- Annual Cost: $245 Billion
- #7 case of death

Drugs to Treat Type 2 Diabetes
- Metformin
- Sulfonylureas: glyburide, glipizide, etc.
- Insulin
- Meglinitides: Prandin, Starlix
- Bunch of newer agents, various mechanisms: Januvia, Byetta, Victoza, Actos, Avandia, Trulicity, Invokana, Farxiga, etc.
  - Most evidence limited to reducing Hemoglobin A1-C vs. placebo

New Drugs Mechanisms of Action
- GLP-1 Receptor Agonists
  - Enhance glucose-dependent insulin secretion
  - “…glutide” “natide”
- DPP-4 Inhibitors
  - Enhance glucose-dependent insulin secretion
  - “…gliptin”
- SGLT2 Inhibitors
  - Work in the kidney to prevent glucose resorption
  - “…gliflizolin”
Drugs to Treat Type 2 Diabetes
- Generic, older drugs: <$10/month
- Newer, on patent drugs: ~$400-600/month
- The new rage: combination products: ~$400+/month (+ patent extension)

Some Combination Products
- Qtern (dapagliflozin and saxagliptin)
- Synjardy (empagliflozin and metformin)
- Invokamet (canagliflozin and metformin)
- Jentadueto (linagliptin and metformin)
- Janumet (sitagliptin and metformin)
- Prandimet (repaglinide and metformin)
- Xultophy (insulin and lixisenatide)
- Soliqua (insulin and lixisenatide)
- Kazano (alogliptin and metformin)

Atopic Dermatitis (i.e., eczema)
- Often an allergic phenomenon
- Usually managed well with topical steroids, moisturizers
- An annoyance for most
- Can be persistent/severe in some
  - Immunosuppressives: methotrexate, cyclosporine, etc.
- Big Pharma to the rescue!

Eucrisa® (crisaborole)
- New topical cream for atopic dermatitis
- Inhibits inflammatory modulators in the skin
- Clinical Trials
  - Improvement in 33% vs. 25% with placebo
  - Cost for a 60g tube: $600

Dupixent® (dupilumab)
- Subcutaneously injected human monoclonal antibody for uncontrolled eczema
- Used weekly
- Binds to receptors, blunting the production of inflammatory mediators that drive the development of eczema

Dupixent® (dupilumab): Clinical Trials
- Better “Eczema Area and Severity Index” scores than placebo
- Greater “Investigator Global Assessment” scores than placebo (37% vs. 10%)
- Side effects:
  - Ocular: conjunctivitis, keratitis
  - Oral herpes simplex flare
- Single dose: $1423
- Yearly cost: $37,000
Cosentyx® (secukinumab)
- Injectable treatment for plaque psoriasis
- Standard treatment: steroids → phototherapy → immunosuppressives, others including Otelza® ("show more of me" commercial)
- Monoclonal antibody which inhibits a specific inflammatory mediator (IL-17A) by binding to it
- Given weekly X 5 weeks, then monthly
- Four studies, 2400 patients, "≥75% reduction in Psoriasis Area and Severity Index score"
  - Secukinumab: 75%
  - Placebo 5%
  - Rhinitis, diarrhea common side effects
  - Exacerbates Crohn’s and tuberculosis
  - Probably reduces ability to fight infection
  - Cost: $10,000 dose
  - $50,000 for initial treatment, $10,000/mo thereafter
  - "$0 copay savings": $16,000 annual cap
  - Another new one just approved: Siliq® (bridalumab)
    - Works the same, costs the same but may increase risk of suicide!

Hyperkalemia
- We all know how bad this is
- ED treatmants
  - D50 (SHORTAGE) + insulin
  - HCO3 (SHORTAGE)
  - Calcium (SHORTAGE)
  - Albuterol (doesn’t do much)
- Kayexelate: slow to act, doesn’t do much, can cause severe hypernatremia, bowel necrosis

Veltassa® (patiromer)
- Approved Oct 2015
- An oral potassium binder, just like Kayexelate
  - Exchanges potassium for calcium in the gut
- NOT for emergency treatment of hyperkalemia
- 2 studies, 549 patients:
  - Drops K by 0.2 mEq/L in 8 hours, 0.75 in 48 hours
  - Need to stay on it or potassium goes back up
- Can cause constipation, hypomagnesemia
- One month supply: $950

2016-2017 Influenza Season
- Hit later than usual
- Thousands of hospitalizations, deaths
- Antivirals are of modest benefit
  - Need to be started <48 hours of symptoms
  - 5 days of treatment needed

Peramivir® (rapivab)
- Injectable neuraminidase inhibitor
  - Same class as Tamiflu, Relenza
  - Single-dose
  - Effect:
    - Symptoms reduced from an average of 3.3 days to 2.5 days
    - No effect on hospitalizations, mortality
  - Costs
    - Generic oseltamivir: $60
    - Rabivab: $950