**Pharmaceutical Update 20/20**

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1. Course Description
   1. Every year the FDA approves numerous pharmaceuticals (AKA “Legend Drugs”) for the management of diseases in many therapeutic categories.
   2. This course will review recently approved pharmaceuticals that are pertinent to optometric patient care.
   3. This course will review systemic and ocular complications of select pharmaceuticals.
2. Therapeutic Areas to be Covered
   1. Optometry
   2. Endocrinology
   3. Cardiology/Vascular Disease
   4. Family Medicine
   5. Hepatology (liver, pancreas, gall bladder)
   6. Neurology
   7. Dermatology
   8. Gastroenterology
   9. Miscellaneous
3. Pharmaceutical Resource Matrix
   1. Commercial/Sales
      1. Representatives
         1. On label, educational lunches, samples, discount cards, coupons
         2. Organizes the promotional dinners
   2. Medical Affairs- Medical Science Liaison (MSL)
      1. OD, MD, PharmD, PhD,…
      2. Education, education, education
      3. On label or that “reactive” off label question
      4. Where the granular discussion occurs
      5. No sales
   3. Clinical Research
      1. Company sponsored studies
   4. Marketing
      1. Assists representative on therapeutic usage
      2. Consultant, advisory board, promotional speaker
   5. Market Access
      1. Formulary access
         1. Commercial and Federal payers
4. Avaclyr (Acyclovir)
   1. Ophthalmic ointment for treatment of herpetic keratitis
   2. Comparison to Zirgan and Viroptic
   3. Clinical data
   4. ADRs
5. Vyzulta™ (latanoprostene Bunod) Ophthalmic Solution 0.024%
   1. Bausch & Lomb
   2. approved (previously Vesneo**™**)
   3. Indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension
   4. Once daily monotherapy
   5. Dual mechanism of action
   6. Uveoscleral pathway to increase aqueous humor outflow
   7. Butanediol mononitrate, which releases NO to increase outflow through the trabecular meshwork and Schlemm's canal.
   8. Ocular adverse events
   9. Conjunctival hyperemia, eye irritation, eye pain and instillation site pain
   10. Increased pigmentation of the iris and periorbital tissue and growth of eyelashes can occur
6. Xelpros™ (latanoprost ophthalmic solution 0.005%)
   1. Sun Pharmaceuticals
   2. Dosage: QD
   3. Reduce IOP in open-angle glaucoma and ocular hypertension
   4. Xelpros is the first latanoprost product not formulated with the preservative benzalkonium chloride
      1. Potassium sorbate 0.47% - preservative
   5. Reduces IOP in patients with open-angle glaucoma and ocular hypertension
   6. Up to a mean of 6 mm Hg to 8 mm Hg in randomized clinical trials
7. Rhopressa netarsudil ophthalmic solution)
   1. Aerie Pharmaceuticals
   2. Treatment of glaucoma or ocular hypertension
   3. Rho kinase inhibitor
      1. ROCK-NET Inhibitor
   4. Once daily in the evening
      1. Twice a day dosing is not well tolerated and is not recommended
   5. Side Effects
      1. Conjunctival hyperemia
      2. Corneal verticillata
      3. Instillation site pain
      4. Conjunctival hemorrhage
   6. Rhopressa (ROCK-NET Inhibitor) Triple-Action
   7. Wang SK, Chang RT. An emerging treatment option for glaucoma: Rho kinase inhibitors. *Clin Ophthal* 2014;8:883-890.
   8. Wang RF, Williamson JE, Kopczynski C, Serle JB. Effect of 0.04% AR-13324, a ROCK, and norepinephrine transporter inhibitor, on aqueous humor dynamics in normotensive monkey eyes. *J Glaucoma* 2015. 24(1):51-4.
   9. Kiel JW, Kopczynski C. Effect of AR-13324 on episcleral venous pressure (EVP) in Dutch Belted rabbits. *ARVO* 2014. Abstract 2900
   10. 3 Identified IOP-Lowering Mechanisms
   11. Netarsudil Causes Expansion of TM in Donor Eyes, Increases TM Outflow Facility in Clinic
   12. Netarsudil Is Similarly Effective at Baseline IOPs
       1. <25 mmHg and ≥25 mmHg
   13. Most Frequently Reported Systemic TEAEs
   14. Netarsudil Once Daily Demonstrated Consistent Ocular Safety Profile with Four Phase 3 Studies
   15. Ocular AEs Leading to Discontinuations
   16. *Pooled Phase 3 Studies*
   17. Conjunctival Hyperemia Was Sporadic and Severity Did Not Increase with Continued Dosing
   18. Netarsudil Once-Daily Dosing Biomicroscopy Hyperemia Severity Did Not Increase Over Time *Netarsudil QD (N=839)*
   19. Conjunctival Hemorrhage Was Sporadic and Severity Did Not Increase with Continued Dosing
   20. Cornea Verticillata Observed in Phase 3 Studies
   21. Cornea Verticillata Due to Phospholipidosis
   22. Summary of the Most Common   
       Netarsudil Ocular TEAEs
   23. How Will I Use Netarsudil to Treat Glaucoma?
8. Rocklatan™(netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%
   1. Stay tuned
   2. Aerie pharmaceuticals
   3. Once-daily eye drop
   4. Aerie Pharmaceuticals Announces
      1. Early Notification of FDA Acceptance of NDA Submission for Roclatan™ (netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%
9. Oxervate™ (cenegermin-bkbj)
   1. Dompé farmaceutici SpA
   2. Ophthalmic solution indicated for the treatment of neurotrophic keratitis
   3. Dosing: Instill 1 drop in affected eye 6 times per day (at 2 hour intervals) for 8 weeks
   4. Storage issues: in the freezer at the pharmacy; patient keeps the individual vials in the fridge – once “actively ready” for use, then it is only stable for 12 hours
   5. ADRs: eye pain, inflammation, corneal deposits
10. Zerviate (cetirizine) ophthalmic solution 0.24%
    1. NicOx
    2. Treatment of ocular itching associated with allergic conjunctivitis
    3. Twice daily (approximately 8 hours apart)
    4. Second generation antihistamine (H1 receptor antagonist)
    5. Binds competitively to histamine receptor sites to reduce
       1. Swelling
       2. Itching
       3. Vasodilation
11. Luxturna (voretigene neparvovec)
    1. Spark Therapeutics
    2. For the treatment of vision loss due to confirmed biallelic RPE65-mediated inherited retinal disease
    3. Gene therapy for mutations in the RPE65 gene
    4. Intraocular suspension for subretinal injection
    5. Administered to each eye on separate days
       1. Within a close interval, no fewer than 6 days apart
    6. Once inside the eye, the new genetic material enables patients to produce the protein that is missing as a result of their genetic mutation
    7. *RPE65*-mediated Inherited Retinal Disease (IRD)
    8. Also known as inherited retinal dystrophies
    9. Leber’s congenital amaurosis (LCA)
    10. Autosomal recessive retinitis pigmentosa (RP).
        1. Group of rare blinding conditions caused by one of more than 220 different genes
    11. Biallelic *RPE65*gene mutations often experience
        1. Night blindness (nyctalopia)
        2. Nystagmus
        3. Loss of peripheral vision
           1. Develop tunnel vision
           2. Eventually, they may lose their central visionl
              1. Resulting in total blindness
12. Cequa™ (cyclosporine ophthalmic solution) 0.09%
    1. Dosed BID
    2. Single-use vials
    3. “New Nanomicellar Ophthalmic Solution for Treatment of Keratoconjunctivitis Sicca”
    4. Formulation technology uses micelles
       1. Gelatinous aggregates of amphipathic molecules
    5. Hydrophobic and hydrophilic molecules
    6. Ease of entry into conjunctiva and cornea
    7. High delivery of cyclosporine A (CsA)
    8. Indication and Important Safety Information
       1. A calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye)
    9. Warnings and Precautions:
       1. Potential for Eye Injury and Contamination: To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.
       2. Use with Contact Lenses: CEQUA should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution
    10. Adverse Reactions:
        1. The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%)
        2. Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection
13. Inveltys- loteprednol etabonate
    1. Kala Pharmaceuticals
    2. Nanoparticle-based Mucus Penetrating Particles (MPP)
    3. MOD
    4. 1.0% pain after ocular surgery
    5. 0.25% temporary relief of the signs and symptoms of dry eye disease
14. Ocular/Immunology/Rheumatology Meds
    1. Humira (adalimumab)
       1. Company: Abbvie
       2. Indication: uveitis
          1. Specifically indicated for the treatment of non-infectious intermediate, posterior and panuveitis
       3. Dosage: subcutaneous injection
          1. Recommended dose is 80 mg initial dose
          2. Followed by 40 mg every other week starting one week after initial dose
       4. The significance of this FDA approval is important! Many insurance companies (ex. Medicare) will not pay for “off-label” uses.
       5. Monitoring parameters:
       6. Must place PPD before initiating = if PPD+, then initiation of Humira may convert latent TB to ACTIVE tuberculosis
       7. Once Humira is initiated, watch for any signs or symptoms of infection…if the patient has a “cold”, “flu”, or is taking antibiotics, then Humira dose must be HELD until the patient is healthy.
          1. Non-infectious intermediate, posterior and panuveitis
          2. Reason for reduced acuity?
    2. Actemra™ (tocilizumab)- Genetec
       1. First innovative therapy for GCA in more than 50 years
       2. Design to speed the development for treatments of serious diseases such as GCA and certain cancers
       3. Patients were randomized to receive tocilizumab 162 mg weekly injections plus a 6-month and 12-month prednisone-taper compared to controls receiving placebo plus similar steroid taper
       4. The preliminary results indicate that patients receiving high dose tocilizumab had superior disease remission at 1 year compared to the steroid-only taper
       5. Further investigation from this study will attempt to identify the lowest therapeutic dose of prednisone that can be used in patients also using tocilizumab, the amount of tocilizumab needed to induce remission, and how long patients stay in remission on this therapy
       6. Tocilizumab does not directly treat GCA
       7. Reduces steroid load after disease has been adequately treated by steroids and enhances disease remission
       8. Steroids are main therapy
       9. Studies are ongoing to see:
       10. What is the lowest steroid tapering dose that can be used with tocilizumab
       11. Future studies may show tocilizumab as steroid replacement
    3. Biosimilars
       1. Hadlima (Adalimumab-bwwd)
          1. Biologic agent SIMILAR to Humira
          2. What is a “biosimilar”agent?
    4. Olumiant™ (baricitinib); Rinvoq (upadacitinib)
       1. Janus Kinase inhibitor
       2. Indicated for the treatment of adult patients with moderate/severe active rheumatoid arthritis
       3. Must have failed 1 or more TNF-alpha inhibitors (e.g. Remicade, Humira)
       4. THE HUB-BUB? It is an orally administered medication, as opposed to MOST of the others that are injectables!
       5. Known as “un-jections”
15. Endocrinology
    1. Incretin System
    2. New/updated Type 2 diabetes guidelines suggest use of insulin and/or agents that act as agonists on the incretin system!
    3. Many, MANY manufacturers are starting to make new combination drugs that contain both
       1. Benefit? Fewer injections per day!
       2. Risk? The patient’s wallet, and increased risk of hypoglycemia!
    4. Qternmet XR (dapagliflozin/saxagliptin/metformin), Ozempic (semaglutide), etc.
       1. Combination medications
       2. Type 2 diabetes
    5. Soliqua 100/33 (insulin glargine and lixisenatide injection)
       1. Long-Acting insulin + GLP-1 Agonist
       2. Inadequately controlled type 2 diabetes
    6. Synjardy (empagliflozin and metformin hydrochloride)
       1. SGLT-2 inhibitor + biguanide (ORAL)
       2. Type 2 diabetes
    7. ALERT! Watch for even NEWER guideline updates to include the “flozins” (above and Invokana/canagliflozin) due to new data that shows improvement in CV risks in HIGH RISK patients!
16. Cardiology/Vascular Disease
    1. Consensi™ (amlodipine and celecoxib)
       1. New combination of a calcium-channel blocker (CCB) and specific COX-2 inhibitior
       2. Indicated for patients with hypertension and osteoarthritis
    2. Repatha™(evolocumab)
       1. Heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease
    3. Praluent™ (alirocumab)
       1. Heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease
    4. Both subcutaneous injections…used when “statins” don’t work!
       1. Stay tuned for myopathy issues…
       2. “statins on steroids” – diplopia, etc.
17. Family Medicine
    1. Evenity (Romosozumab-aqqg)
       1. A sclerostin inhibitor for treatment of postmenopausal osteoporosis
       2. Used in patients at high risk for fracture
       3. Dosing considerations
    2. Lucemyra™ (Lofexidine)
       1. Central alpha-2 adrenergic agonist
       2. Indicated for the mitigation of opioid withdrawal symptoms; helps facilitate abrupt opioid discontinuation in adults
       3. Usually taken PO, 4 times a day
       4. ADRs
    3. Vaccines…
       1. Zostavax™ – SQ, live vaccine; 60 years and older
          1. “the only game in town…”
          2. 50-ish% effective; 1 dose
          3. Efficacy wanes after 4-5 years
       2. Shingrix™ – has replaced Zostavax™
          1. We are moving in the right direction!
          2. Recommended for 50 years and older
          3. 90+% effective?; 2 doses; IM; recombinant vaccine
          4. Efficacy *seems* solid up to 7-8 years
          5. Recombinant vaccine with adjuvant for added immunogenicity
          6. VERY difficult to get right now
          7. Post-shingles:
             1. Wait until acute episode and symptoms are resolved
             2. Post-Zostavax™ patient:
             3. Wait 8 weeks after Zostavax vaccine before giving Shingrix
    4. Apadaz ™ (benzhydrocodone/acetaminophen)
       1. INITITIAL approval = 1982; this is for change in formulation!
       2. BLACK BOXED: addiction, abuse, respiratory depression, hepatotoxicity, drug interactions
    5. Benzhydrocodone = prodrug of hydrocodone
       1. 6.12mg benzhydrocodone = 4.54mg hydrocodone (plain) or 7.5mg hydrocodone bitartrate
    6. Indicated for the short-term treatment of acute pain that is severe enough to require an opioid
    7. Cassipa™(buprenorphine/naloxone)
       1. HIGHER strength SL film for maintenance treatment of opioid dependence
       2. Other choices: Suboxone, Methadone
18. Hepatology (liver, pancreas, gall bladder)
    1. Vemlidy™ (tenofovir alafenamide)
       1. Chronic hepatitis B
    2. Epclusa™ (sofosbuvir and velpatasvir)
       1. Hepatitis C
    3. You will see many new hepatitis B and C meds, as now these patients can be CURED!
19. Neurology
    1. Spravato™ (Esketamine)
       1. Nasal spray used in treatment-resistant depression
       2. Mechanims of efficacy and toxicity
       3. ADRs
    2. Epidiolex™ (Cannabidiol oil)
       1. Oral solution: twice per day dosing
       2. Indicated for the treatment of seizures in people > 2 years old (with Lennox-Gastaut syndrome or Dravet syndrome)
       3. ADRs
       4. DEA is working on “scheduling” this product!
    3. Abilify MyCite
       1. Aripiprazole plus sensor: new drug device combination
       2. Tablet is embedded with a tracking sensor to verify compliance
       3. IEM: ingestible event marker
       4. Indicated for adult patients with schizophrenia, certain types of bipolar disorder, adjunctive therapy with major depressive disorder
    4. Aimovig™ (erenumab-aooe)
    5. Ajovy ™ (fremanezumab-vfrm)
       1. Indicated for the PREVENTIVE treatment of migraine in adult patients
       2. Calcitonin gene-related receptor antagonist
       3. SQ injection
       4. Once per month for either product
       5. Once every three months for Ajovy™
       6. ADRs
       7. Would be used ALONG WITH “triptans”
20. Dermatology
    1. Doxycycline
       1. Doryx™ (enteric coated hyclate pellet), Adoxa™ (monohydrate), Oracea™ (monohydrate – 75% immedidate release + 10% delayed release)
       2. Approved 2005
       3. Good ‘ol doxy…being reborn AGAIN!
       4. Did you know?
       5. At normal doses, the monohydrate and hyclate salts have equal efficacy?
       6. At normal dose, the monohydrate salt MIGHT have a decrease in GI side effects.
       7. ALL doxy products can generally be taken with food to decrease GI upset.
       8. Don’t get caught in the web of “sexy doxy” formulations
    2. Delafloxacin™ (Baxdela)
       1. A fluoroquinolone antibiotic for acute bacterial skin and skin structure infections
       2. Available orally and intravenously
       3. Adverse effects: SO NEW…but in clinical trials, the only ophthalmic side effects that were noted = blurred vision!
       4. Only time will tell if retinal detachment is something to worry about with this new FQ!
    3. Nuzyra™(omadacycline)
       1. Tetracycline antibiotic
       2. Approved for PO/IV treatment of patients with bacterial skin infections or community-acquired bacterial pneumonia
       3. Chelation issues JUST like other tetracyclines!
       4. ADRs
    4. Seysara™ (sarecycline)
       1. Tetracycline drug
       2. Indicated for the treatment of inflammatory acne in non-nodular, moderate to severe acne vulgaris
       3. Can be taken WITH or WITHOUT food!
       4. ADR
    5. Xerava™ (eravacycyline)
       1. Tetracycline antibiotic
       2. Indicated for the treatment of intra-abdominal infections in adults
       3. IV ONLY
21. Gastroenterology
    1. Symproic™ (naldemedine)
       1. Approved 2017
       2. Opioid antagonist in the GUT
       3. Opioid-induced constipation
22. Thank You!
    1. Questions