Optometric Education Consultants

Pharmaceutical Update 2024

Greg Caldwell, OD, FAAO

Optometric Education Consultants
Sunday, March 10, 2024

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Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

- Lectured for: Alcon, B&L, BioTissue, Dompé
  - Disclosure: Receive speaker honorariums
- Advisory Board: Dompé, ImmunoGen, Iveric
  - Disclosure: Receive participant honorariums
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
  - Disclosure: Non-salaried financial affiliation with Pharmanex
- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
- The content of this activity was prepared independently by me - Dr. Caldwell
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
- Optometric Education Consultants – Scottsdale, AZ, Pittsburgh, PA, Sarasota, FL , Barcelona, Spain, Orlando, FL, Mackinac Island, MI, Quebec City, Canada, and Nashville, TN- Owner

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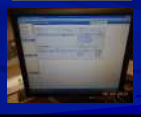
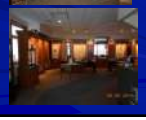
My Practice

I am a clinician first then a scientist

- Some are scientists first then clinician
- I need to simplify for patient and patient care.
- Science is great, but not good if there isn't a clinical application.
- Some lectures are science based without clinical application.
- My lecture will be a hybrid. Showing clinical applications of the science



It is wonderful to have someone who's juggling so many aspects of optometry (scientific, clinical experience, teacher & lecturer). It is refreshing and very informative. -Sarah

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"The Comfort Zone"

Confidence
Capable
Courage
Commitment

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Pharmaceutical Resource Matrix

- Commercial/Sales
  - Representatives
    - On label, educational lunches, samples, discount cards, coupons
    - Organizes the promotional dinners
- Medical Affairs- Medical Science Liaison (MSL)
  - OD, MD, PharmD, PhD,…
  - Education, education, education
  - On label or that "off label" question
  - Where the granular discussion occurs
  - No sales
- Clinical Research
  - Company sponsored studies
- Marketing
  - Assists representative on therapeutic usage
  - Consultant, advisory board, promotional speaker
- Market Access
  - Formulary access
    - Commercial and Federal payers

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If you have a glaucoma practice you have an ocular surface disease practice

Follicular Conjunctivitis

Superficial Punctuate Keratitis (SPK)

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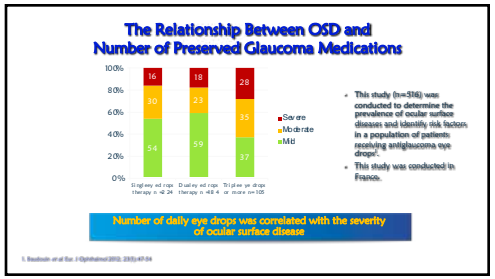
The Relationship Between OSD and Number of Preserved Glaucoma Medications
100%
80%
60%
40%
20%
0%
16
30
54
18
23
59
28
35
37
Severe
Moderate
Mild
This study (n=316) was conducted to determine the prevalence of ocular surface disease and identify risk factors in a population of patients receiving antiglaucoma eye drops[1].
This study was conducted in France.
Number of daily eye drops was correlated with the severity of ocular surface disease

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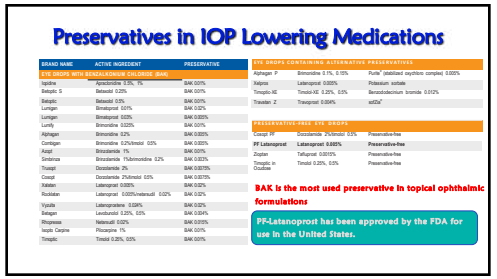
Preservatives in IOP Lowering Medications
BRAND NAME
ACTIVE INGREDIENT
PRESERVATIVE
EYE DROPS WITH BENZALKONIUM CHLORIDE (BAK)
EYE DROPS CONTAINING ALTERNATIVE PRESERVATIVES
PRESERVATIVE-FREE EYE DROPS
BAK is the most used preservative in topical ophthalmic formulations
PF-Latanoprost has been approved by the FDA for use in the United States.

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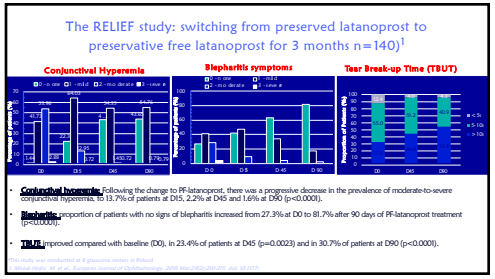
The RELIEF study: switching from preserved latanoprost to preservative free latanoprost for 3 months n=140)[1]
Conjunctival Hyperemia
Blepharitis symptoms
Tear Break-up Time (TBUT)
Conjunctival hyperemia: Following the change to PF-latanoprost, there was a progressive decrease in the prevalence of moderate-to-severe conjunctival hyperemia, to 13.7% of patients at D15, 2.2% at D45 and 1.6% at D90 (p<0.0001).
Blepharitis: proportion of patients with no signs of blepharitis increased from 27.3% at D0 to 81.7% after 90 days of PF-latanoprost treatment (p<0.0001).
TBUT: improved compared with baseline (D0), in 23.4% of patients at D45 (p=0.0023) and in 30.7% of patients at D90 (p<0.0001).

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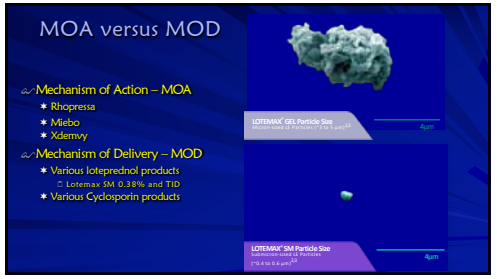
MOA versus MOD
Mechanism of Action – MOA
Rhopressa
Miebo
Xdemvy
Mechanism of Delivery – MOD
Various loteprednol products
Lotemax SM 0.38% and TID
Various Cyclosporin products
LOTEMAX® GEL Particle Size
LOTEMAX® SM Particle Size

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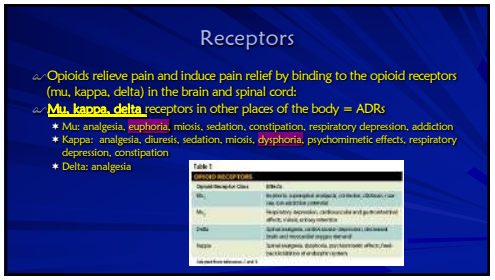
Receptors
Opioids relieve pain and induce pain relief by binding to the opioid receptors (mu, kappa, delta) in the brain and spinal cord:
Mu, kappa, delta receptors in other places of the body = ADRs
Mu: analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction
Kappa: analgesia, diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation
Delta: analgesia

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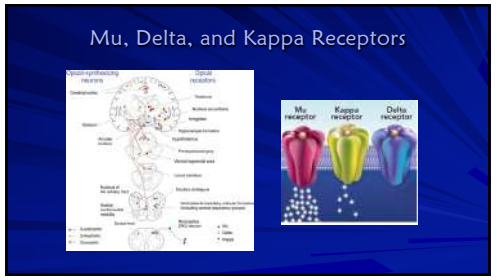
Mu, Delta, and Kappa Receptors
Mu receptor
Kappa receptor
Delta receptor

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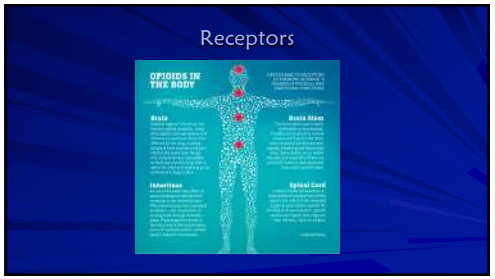

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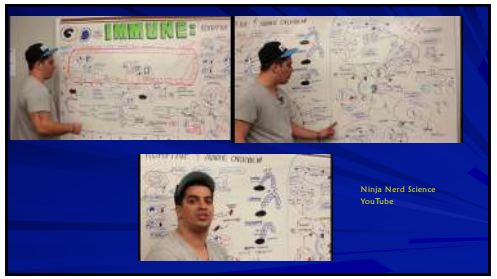

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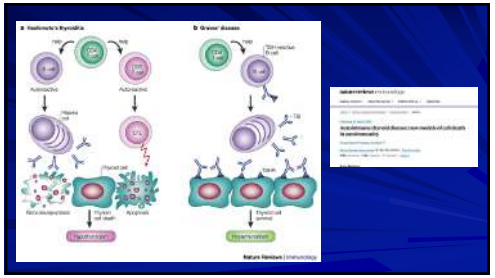

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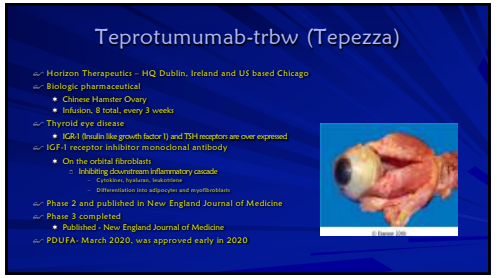

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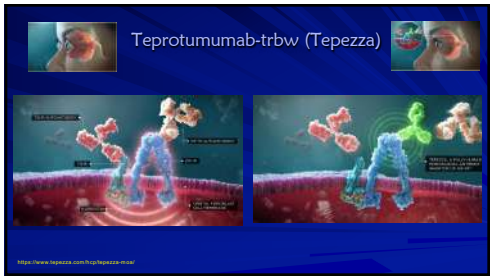

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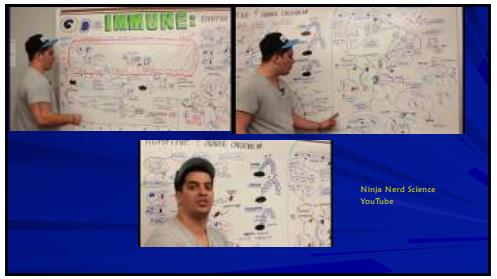

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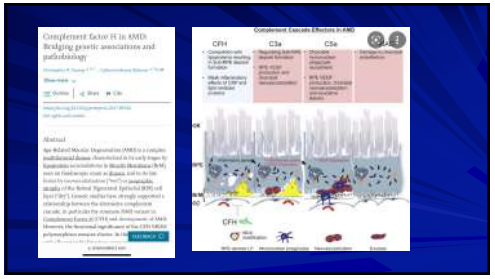

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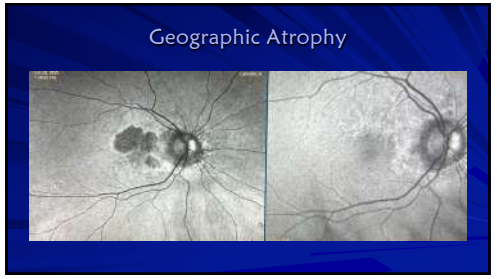

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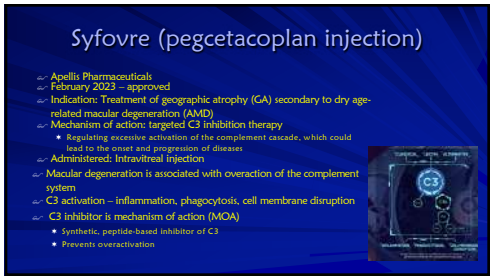

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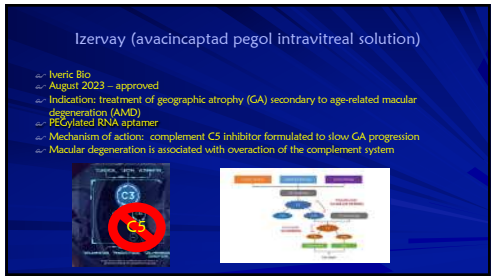

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Inflammatory Lifestyle, Genetics, Epigenetics, and Over Reactive Immune System

Evidence Based Medicine

Evidence Informed Risk Adjusted Medicine

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Aptamer versus Antibody

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Small Molecule Drugs versus Biologics

- Small molecule drugs are made by adding and mixing together known chemicals and reagents using a series of controlled and predictable chemical reactions
  - Organic chemistry
  - Inorganic chemistry
- Biologics are made by harvesting the substances produced and secreted by constructed cells
  - Genetic engineering – is the closet manufacturing process of a biologic drug

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Size and Complexity of Biologic Drugs

- Small molecule drugs can be taken orally
  - Tend to work in the body within cells
- Biologics are significantly larger in size
  - Typically injected and interact within the body in the bloodstream or on the surfaces of cells, rather than within the cells
- Small molecule drugs
  - Such as aspirin
  - Composed of only 20 to 100 atoms
- Small biologics
  - Such as hormones
  - Composed of 200 to 3000 atoms
- Large biologics
  - Such as antibodies
  - Composed of 5000 to 50,000 atoms

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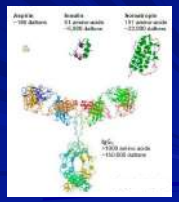
Biologic Drugs versus Small Molecule Drugs

- Biologic Drugs
  - Larger, complex, dynamic structures
  - Diverse populations of molecules
    - Not easily characterized
  - Complicated manufacturing
  - Example: Teprotumumab (Tepezza)
- Small Molecule Drugs
  - Synthetic
  - Manufactured using a defined chemical process
  - Smaller and simpler
  - Example: Aspirin



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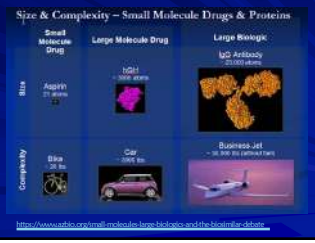
Size and Complexity of Biologic Drugs



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Making Biologics

A piece of DNA is inserted into a living cell— yeast, bacterial, viral, or mammalian cell

↓

Cell then produces a large amount of a specific molecule (e.g. protein)

↓

Desired molecular isolation (living cells/material removed - only the desired molecules are left)

↓

The isolated molecules become the active ingredient in a biologic drug

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Treatments for Choroidal Neovascularization (CNV)

- Where is all started in the eye
- Disorders of the blood vessels in the retina are responsible for some of the most common causes of blindness in the world
  - Retinopathy of prematurity
    - Important cause of blindness in children in middle-income countries
  - Diabetic retinopathy
    - Common cause of blindness in the working-age population of industrialized countries
  - Age-related macular degeneration
    - A common cause of blindness in the world
- These conditions are caused partly by over-production of a protein called vascular endothelial growth factor (VEGF)
- VEGF was discovered in the 1980s and is important in the growth and development of blood vessel in tumor growth
  - 1994 it was proven that retinal hypoxia produces VEGF

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Past Treatments for Choroidal Neovascularization (CNV)

- Current Anti-VEGF treatments
  - Pegaptanib (Macugen)
    - First FDA Approved December 2004
    - RNA aptamer
    - AMD
  - Bevacizumab (Avastin)
    - Humanized full length monoclonal antibody - 2005
    - AMD
  - Ranibizumab (Lucentis)
    - Humanized monoclonal antibody fragment – 2006
    - AMD, DME, DR, RVO
  - Aflibercept (Eylea)
    - Fusion protein – 2011
    - AMD, DME, DR
  - Brolucizumab-dbll (Beovu)
    - Humanized single-chain antibody fragment - 10-8-2019
    - Up to 3 months dosing intervals, most are 4-6 weeks
      - 50% remained 3 months after 1 year

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Beovu (brolucizumab)

- Indication: injection is used for the treatment of Neovascular (Wet) Age-related Macular Degeneration (AMD)
  - **Offers a 3-month dosing schedule in the first year of treatment**
- Warning issued by the American Society of Retinal Specialists about a series of intraocular inflammation events—some of which led to severe vision loss
- On April 8, 2020, Novartis announced its completion of the review, which included an assessment by an external, independent Safety Review Committee
- Complications: n=1098
  - Intraocular inflammation (IOI) - 4.6% (n=50)
  - IOI + retinal vasculitis – 3.3% (n=36)
  - IOI + retinal vasculitis –retinal (artery) vascular occlusion – 2.1% (n=23)
  - Vision loss of 15 letters or more - <1%

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Eylea (aflibercept)

- Regeneron Pharmaceuticals, Inc
- Eylea 2 mg versus Eylea HD 8 mg
  - November 18, 2011 – Wet AMD (BLA)
  - July 29, 2014 – Diabetic Macular Edema
  - October 6, 2014 – Macula edema from retinal vein occlusion
  - May 25, 2015 – Diabetic retinopathy
  - August 17, 2018 – New Eylea (sBLA) – wet AMD
  - May 13, 2019 – Diabetic retinopathy (sBLA)
  - February 8, 2023 – ROP
    - Treatment of retinopathy of prematurity (ROP) in preterm infants
    - First pharmacological treatment for ROP in infants
  - Mechanism of action: vascular endothelial growth factor A (VEGF-A) and placental growth factor (PlGF) antagonists that stops the growth of abnormal blood vessels and leakage in the eyes in patients diagnosed with retinal diseases

Biologics License Application (BLA) supplemental Biologics License Application (sBLA)

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Eylea (aflibercept)

August 10, 2023 at 6:58 PM EDT « Back

EYLEA HD (AFLIBERCEPT) INJECTION 8 MG APPROVED BY FDA FOR TREATMENT OF WET AGE-RELATED MACULAR DEGENERATION (WAMD), DIABETIC MACULAR EDEMA (DME) AND DIABETIC RETINOPATHY (DR)

Approval based on the pivotal PULSAR and PHOTON trials in which EYLEA® HD demonstrated clinically equivalent vision gains to EYLEA (aflibercept) injection 2 mg that were maintained with fewer injections

First and only treatment approved in wAMD and DME for immediate dosing at 8-week and up to 16-week intervals following three initial monthly doses

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Eylea (aflibercept)

- Now have five approved indications to treat retinal conditions caused by ocular angiogenesis
  - Wet AMD
  - DME
  - Macular edema following retinal vein occlusion (RVO)
  - DR
  - ROP
- Eylea HD 8 mg
  - Wet AMD
  - DME

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Vabysmo (faricimab-svoa)

- Genentech
- Indications February 2022
  - Wet age-related macular degeneration (AMD)
  - Diabetic macular edema (DME)
- Indications October 2023
  - Treat macular edema following retinal vein occlusion.
- Mechanism of action: vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) inhibitor
- Administered: Intravitreal injection
- Extended dosing 1-4 months

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Demodex Infestation

- Collarettes are pathognomonic sign of Demodex Infestation
- Collarettes are composed of mite waste products and eggs
  - Regurgitated undigested material combined with epithelial cells, keratin, and mite eggs

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Xdemvy (lotilaner ophthalmic solution) 0.25%

- Tarsus Pharmaceuticals
- Indication: Demodex blepharitis
- Mechanism of action: lotilaner works as an antiparasitic agent to target parasite-specific GABA-Chloride (Cl) channels
  - Located within the nervous system channels of the Demodex mites
- Administration: Drops
- Dosing: 1 gtt BID x 6 weeks

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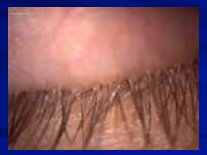
45-Year-Old White Man
Somewhat Symptomatic
October 30, 2023



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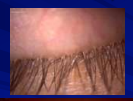
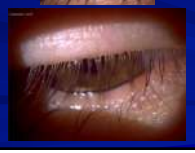
October 30, 2023 - December 4, 2023
5 weeks





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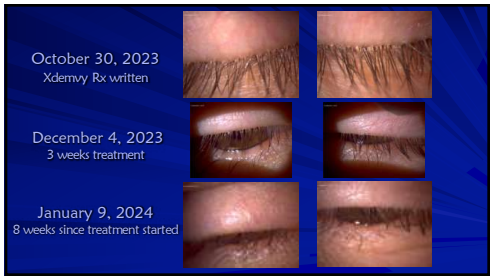

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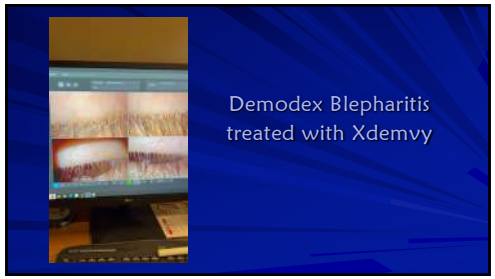

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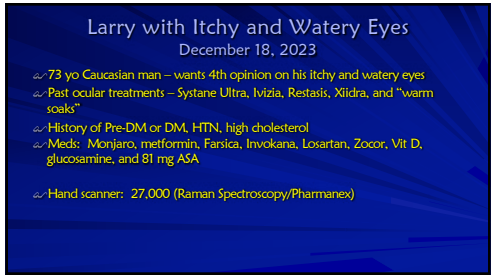

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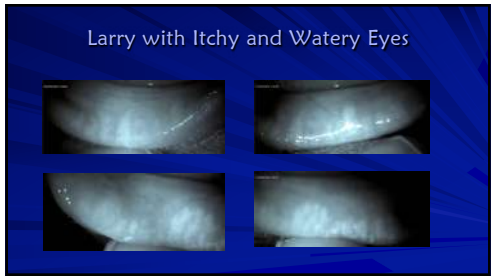

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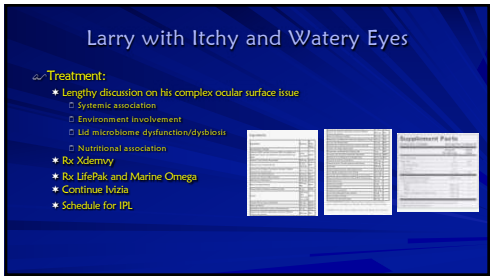

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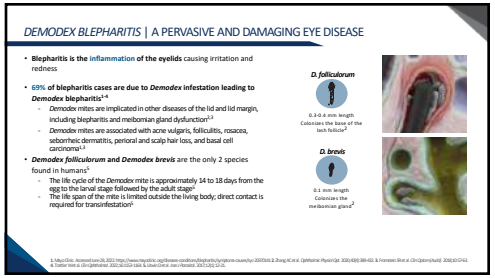

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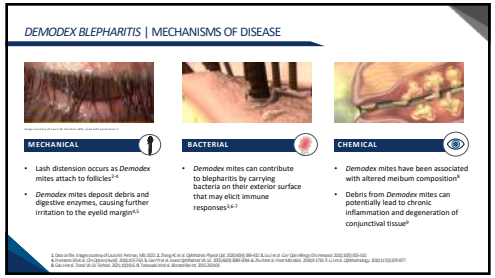

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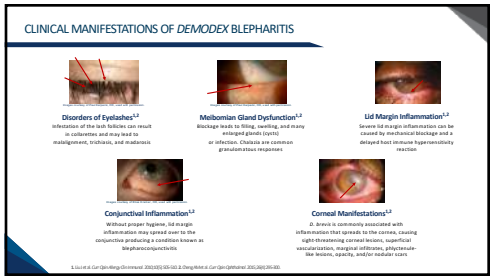

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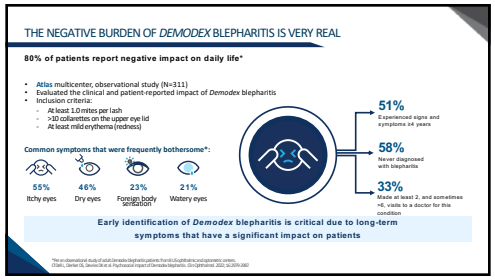

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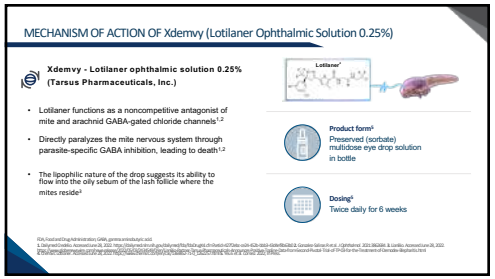

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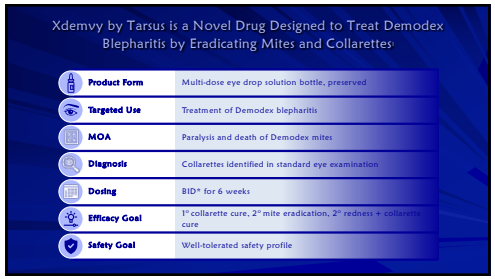

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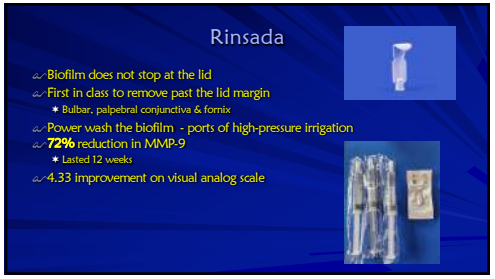

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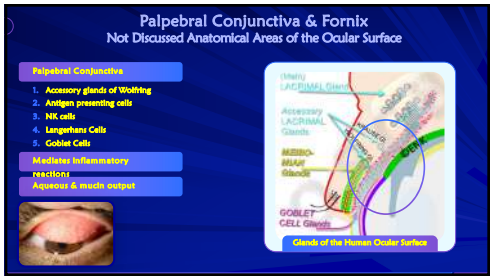

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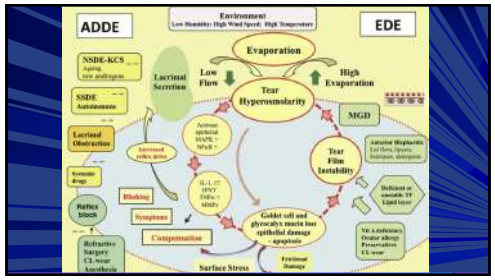

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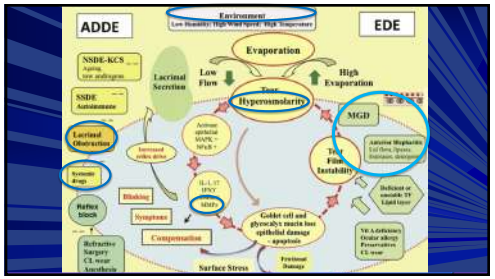

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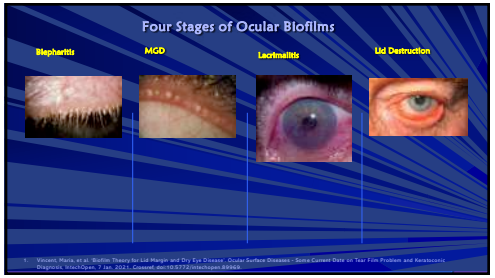

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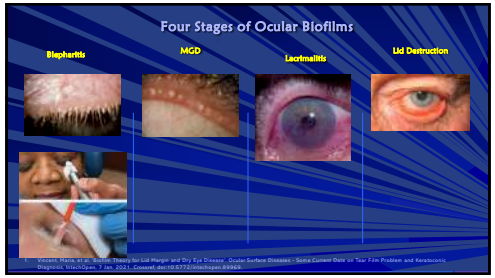

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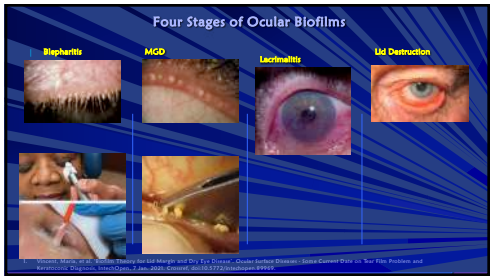

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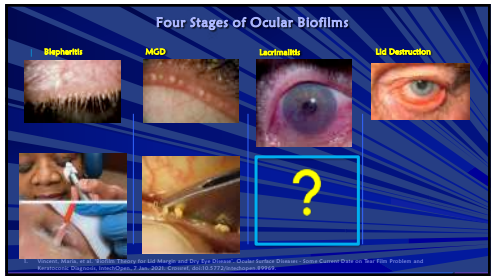

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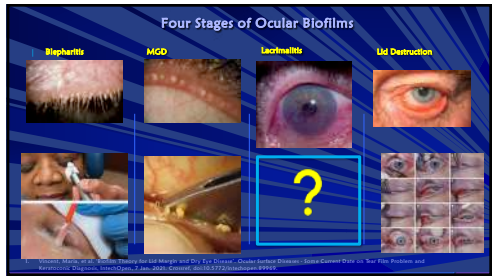

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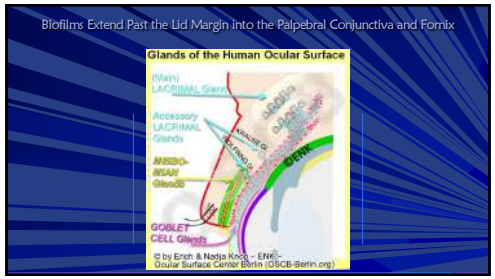

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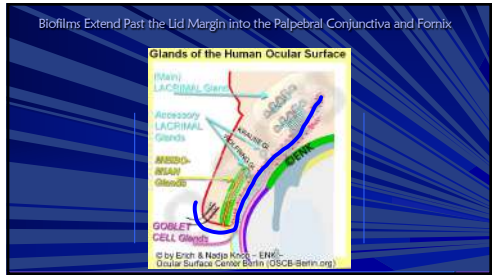

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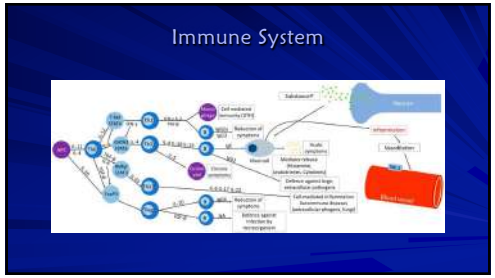

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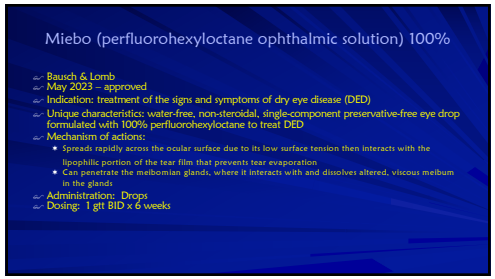

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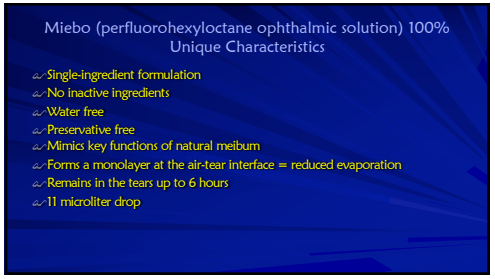

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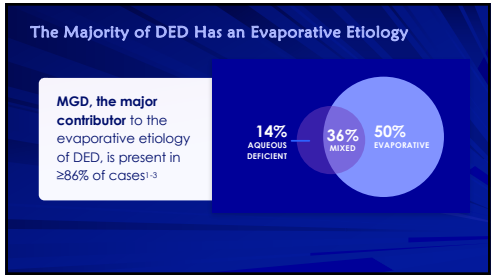

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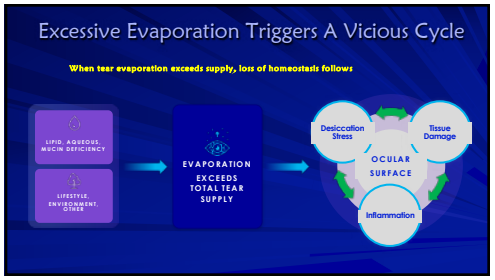

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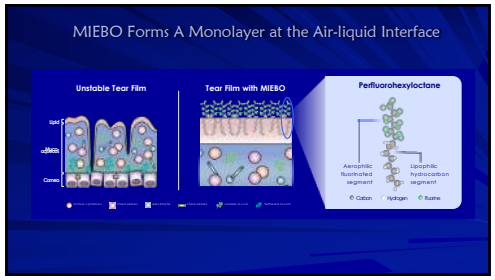

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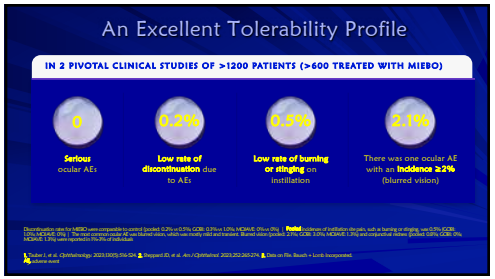

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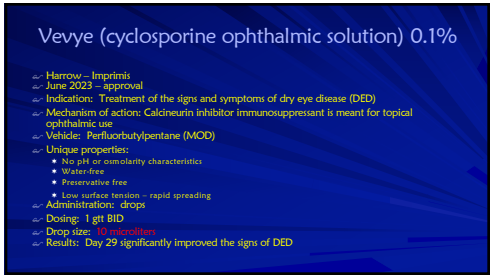

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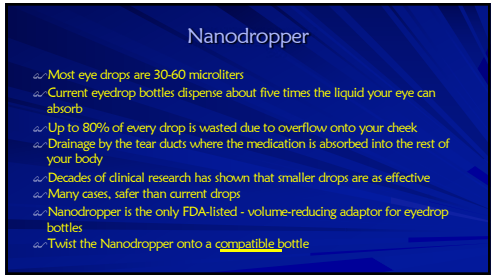

89

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Cequa™ (cyclosporine ophthalmic solution) 0.09%
Indication and Important Safety Information

Indication:

A calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye)

Warnings and Precautions:

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.

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

Adverse Reactions:

The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%)

Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection

92

Cequa™ Formulation

- Novel, aqueous, nanomicellar formulation of cyclosporine A 0.09%[1-4]
- Unpreserved, isotonic, neutral pH fluid that is supplied in unit dose vials
- Well tolerated in a 12-week phase 2b/3 study[5]

93

Effect of Cequa Cyclosporine Ophthalmic Solution 0.09% in Patients With Dry Eye Disease That Is Inadequately Controlled on Cyclosporine 0.05% Ophthalmic Emulsion
Phase 4 Study Results

- Objective: To evaluate improvement in DED signs and symptoms following use of CsA 0.09% in patients whose DED is inadequately controlled on CsA 0.05%
- A total of 124 patients were included in the ITT population (received ≥1 dose of study drug and had ≥1 postbaseline assessment)
- Mean ± SD patient age was 65.6 ± 11.54 years
- Most enrolled patients were female (109; 87.9%)

CsA 0.09% elicited statistically significant improvement from baseline in total CFS (corneal fluorescein score) score by 4 weeks of treatment
CsA 0.09% elicited statistically significant improvement from baseline in mSANDE (symptoms) score by 4 weeks of treatment
CsA 0.09% elicited statistically significant improvement from baseline in central CFS score by 4 weeks of treatment
CsA 0.09% elicited statistically significant improvement from baseline in total conjunctival staining score by 4 weeks of treatment
CsA 0.09% elicited statistically significant improvement from baseline in Schirmer's score at Weeks 4 and 12 of treatment
CsA 0.09% elicited statistically significant improvement from baseline in frequency of artificial tear use by 4 weeks of treatment

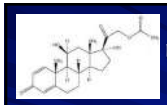
94

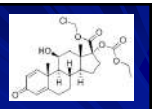
Effect of Cequa Cyclosporine Ophthalmic Solution 0.09% in Patients With Dry Eye Disease That Is Inadequately Controlled on Cyclosporine 0.05% Ophthalmic Emulsion
Phase 4 Study Results

- CsA 0.09% was generally well tolerated, consistent with its established safety profile
- Overall, 58 patients (43.3%) reported ≥1 TEAE
- Most AEs (73.8%) were mild in severity
- The most common treatment-related AEs were instillation site irritation (12.7%) and instillation site pain (2.2%)
  - All other treatment-related AEs occurred in <2% of patients
- Conclusion
  - Twice-daily administration of CsA 0.09% elicited statistically significant improvement in both total CFS and mSANDE scores in patients whose DED was inadequately controlled on CsA 0.05%
  - Improvements were evident as early as Week 4 and continued to increase in magnitude through Week 12
  - CsA 0.09% was well tolerated in this patient population

95

Steroids
Ketones versus Esters





- Prednisolone acetate molecule modified to undergo predictable degradation to inactive metabolites by local esterases
- Corticosteroids, C-20 ketone replaced with a C-20 ester
- C-20 ester steroids are associated with a lower incidence of IOP elevations vs. C-20 ketone steroids
  - IOP and cataracts
- Retrometabolic drug design of loteprednol aims to improve safety while maintaining efficacy

96

Loteprednol Etabonate Products
Ester Steroids

- Lotemax suspension 0.5%
- Alrex suspension 0.2%
- Lotemax gel 0.5%
- Lotemax SM gel 0.38%
- Inveltys suspension 1.0%
- Eysuvis suspension 0.25%

97

Eysuvis- loteprednol etabonate 0.25%

- Kala Pharmaceuticals, now Alcon
- Approved October 27, 2020
- Nanoparticle-based Mucus Penetrating Particles (MPP)
- Dry eye flares
- First prescription therapy – Specifically for the Short-Term treatment of Dry Eye Disease
  - Short term = "up to two weeks"
  - Dry eye flares - dry eye disease characterized by acute exacerbations "flares"

98

Eysuvis - loteprednol etabonate suspension 0.25%

- Mechanism of Action – "AMPPLIFY Technology"
  - Allows drug to penetrate through tear mucins
    - Increased penetration into tissues, 3-fold to original loteprednol
- Nanoparticle-based Mucus Penetrating Particles (MPP)
  - Mucus is a barrier for topical ophthalmic drug delivery
  - AMPPLIFY utilizes two proprietary attributes
    - Nanoparticles to allow penetration into mucus pores
      - Particles smaller than 500 nm
    - Mucus penetrating surface coating
      - Prevents adherence to mucus
  - Allows rapid and enhanced ocular
    - Distribution
    - Penetration

99

Lotemax SM (loteprednol etabonate) 0.38%

- Indicated for the treatment of post-operative inflammation and pain following ocular surgery
- SubMicron - *Particle size* reduced to facilitate ocular penetration
  - Allowing for a decrease in drug concentration and dosing frequency (TID)
  - Increase intraocular penetration
  - Median particle diameter size reduced 5 to 12.5-fold:
    - LE gel 0.38% ≈ 0.4-0.6 µm
    - Lotemax gel 0.5% ≈ 3-5 µm
  - Potential for a ~10-fold increase in rate of drug dissolution
    - Based on a 10-fold increase in relative surface area with smaller particles

100

Lotemax SM (loteprednol etabonate) 0.38%

- Increased concentrations demonstrated in ocular tissues
  - Cornea and aqueous humor
  - Following single topical ocular instillation of Lotemax SM 0.38% vs Lotemax gel 0.5% in rabbits
- Compared to Lotemax Gel 0.5%
  - Single topical instillation of Lotemax SM 0.38% were greater in the aqueous humor and cornea
  - Concentrations in the conjunctiva remain the highest out of the ocular tissues, with ample drug to mediate anti-inflammatory effects at the ocular surface
- Formulation advancement while maintaining a low BAK
  - Lowest concentration of BAK, 0.003% among the commercially available corticosteroid ocular drops
    - Inveltys is 0.01%

101

Lotemax SM (loteprednol etabonate) 0.38%

- **Submicron formulation is designed to reduce the Lotemax Gel drug concentration 0.38% vs. 0.5%)**
- **Dosing frequency TID vs. QID**
- **Formulation builds on the heritage and advantages of Lotemax gel 0.5%:**
- **Retrometabolically designed corticosteroid**
  - Retains potent anti-inflammatory activity
  - Minimal potential for class Aes
- **Mucoadhesive, non-settling, shear-thinning gel**
  - A gel in the bottle: transitions to a liquid upon instillation
  - Becomes mucoadhesive liquid on dilution with tears
  - No need to shake - uniform dosing
  - Non-blurring

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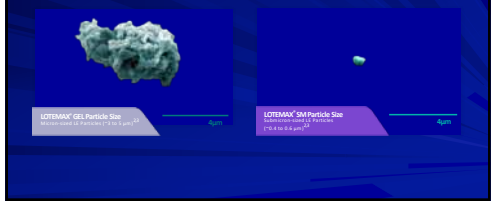
Submicron Formulation



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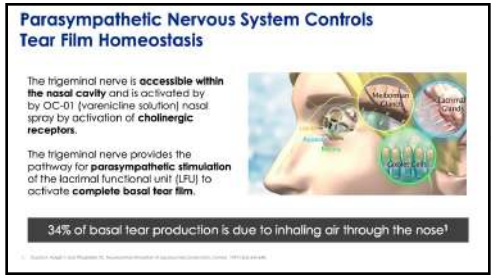

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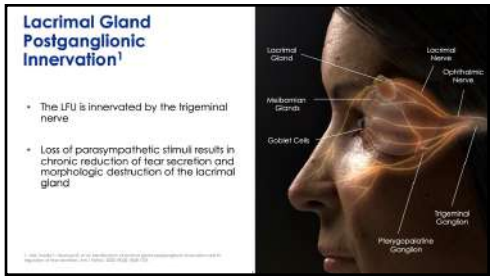

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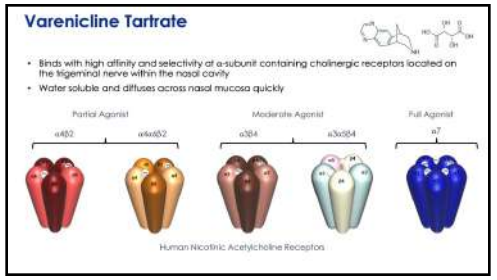

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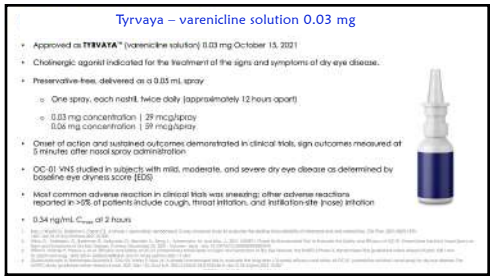

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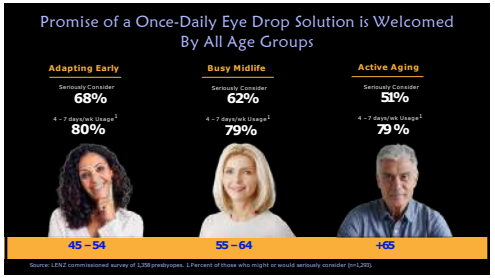

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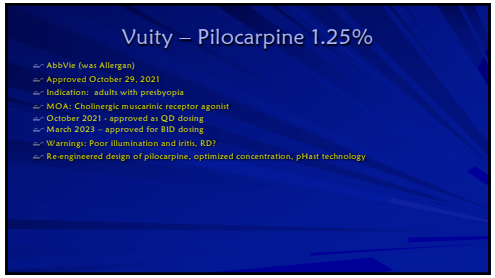

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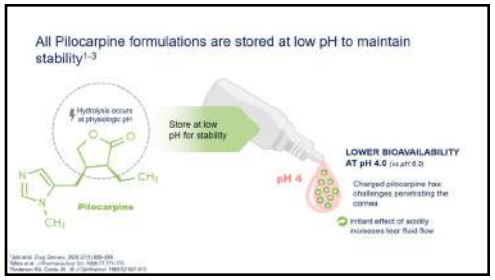

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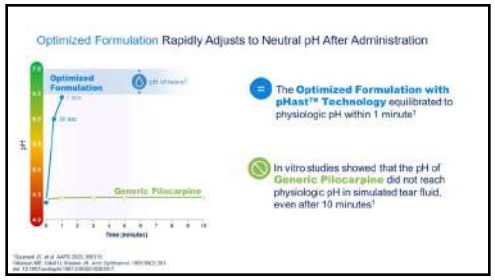

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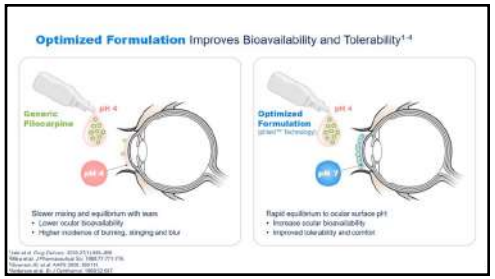

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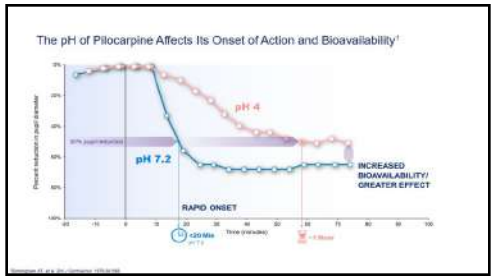


117

Qlosi (pilocarpine hydrochloride ophthalmic solution) 0.4%

- Orasis Pharmaceuticals
- October 2023 – approval
- Pronounced: CLOH-see
- Indication: Treatment of presbyopia
- Dosing: one drop in each eye can be used daily or as needed
  - Dosing up to twice a day, 2 to 3 hours apart
- Low dose pilocarpine

118

Aceclidine-Based Eye Drop

- **Lenz – Therapeutics- Late stage** exclusive **aceclidine-based eye drop** with potential of providing **all day** seamless vision for the **vast majority of presbyopes**
- **Not on the market**

Unique MOA Profile	Only miotic shown to achieve pupil sweet spot <2mm w/o myopic shift
Best-in-class clinical data	79%3-line and 92%2-line Near Vision improvement at 30min with >10hr duration
Late Stage	Ongoing Phase 3 trials for LNZ100 and LNZ101
Market Exclusivity	Broad IP protection and NCE status provide strong protection
Proven successful team	Experienced team backed by RA Capital, Alpha Wave Ventures, Versant Ventures, Sectoral Asset Management, Point 72, RTW and others

119

Mycombi
Tropicamide 1% and Phenylephrine Hydrochloride 2.5% Ophthalmic Spray

- Eyenovia, Inc.
- May 2023 - approval
- Spray
- Indication: For inducing mydriasis
- First-in-class, fixed-dose combo product of tropicamide and phenylephrine
  - Designed to induce mydriasis during in-office diagnostic procedures and conditions that call for short-term pupil dilation

120

Ryzumvi (phentolamine ophthalmic solution) 0.75%

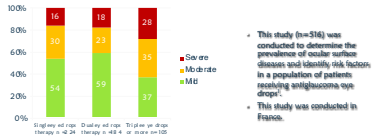
- Viatris
- September 2023 – approval
- Indication: treatment of pharmacologically induced mydriasis produced by adrenergic agonists
- Dosing: 1-2 gtts in the dilated eyes after the exam, 12 years or older
- Dosing: 1 gtt in the dilated eyes after the exam, 3-11 years old
- Mechanism of action: alpha adrenergic blocker, non-selected alpha-1 and alpha-2 adrenergic agonist – iris dilator muscle
- "Rev-Eyes 2.0" - no brow ache and improved redness

121

If you have a glaucoma practice you have an ocular surface disease practice

122

The Relationship Between OSD and Number of Preserved Glaucoma Medications

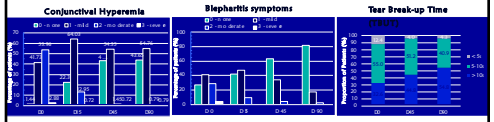


- This study (n=516) was conducted to determine the prevalence of ocular surface diseases and identify risk factors in a population of patients receiving antiglaucoma eye drops[1].
- This study was conducted in France.

Number of daily eye drops was correlated with the severity of ocular surface disease

123

The RELIEF study: switching from preserved latanoprost to preservative free latanoprost for 3 months (n = 140)[a1]



- **Conjunctival hyperemia:** Following the change to PF-latanoprost, there was a progressive decrease in the prevalence of moderate-to-severe conjunctival hyperemia, to 13.7% of patients at D15, 2.2% at D45 and 1.6% at D90 (p<0.0001).
- **Blepharitis:** proportion of patients with no signs of blepharitis increased from 27.3% at D0 to 81.7% after 90 days of PF-latanoprost treatment (p<0.0001).
- **TBUT:** improved compared with baseline (D0), in 23.4% of patients at D45 (p=0.0023) and in 30.7% of patients at D90 (p<0.0001).

124

Iyuzeh (latanoprost ophthalmic solution) 0.005% Preservative Free

- Thea Pharma Inc
- December 2022 – approval
- Indication: treatment of elevated intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) and ocular hypertension (OHT)
- First and only clinically proven formulation of preservative-free latanoprost currently available in the U.S.
- Dosage: single dosage to be placed in the eye(s) once daily in the evening
- Mechanism of action: prostaglandin F2α analogue

125

Iyuzeh (latanoprost ophthalmic solution) 0.005% Preservative Free

- Launched in Europe as the first preservative-free latanoprost formulation in 2013
- Available in 46 countries including Canada
- PF-Latanoprost formulation approved in the US is the same formulation used in Europe
- Can be stored at room temperature (15C -25C, or 59F - 77F)

126

Background of Topical Ophthalmic Preservatives

- Preservatives provide important and necessary antimicrobial activity
- Crucial in maintaining sterility and extending the shelf-life of multi-dose formulations of topical ophthalmic medications
- Preservatives are toxic to the ocular surface, particularly in the setting of chronic, prolonged exposure
- As in patients with glaucoma who may have therapeutic regimens that involve multiple eye drops and frequent instillation
- Of all ophthalmic preservatives, benzalkonium chloride (BAK) is the most used and widely studied demonstrating significant ocular surface toxicity
- Although several classes of alternative preservatives have been developed
- All have varying degrees of ocular surface toxicity as well as efficacy profiles

127

Cytotoxic Effects of BAK on Ocular Tissues

- Can occur at 0.005%, much lower than many of commercially used concentrations of BAK
- Cause tear Film Disruption
  - Acting as a detergent of the lipid layer of the tear film; decreases mucin production
- Induce inflammation and cause damage to
  - Trabecular meshwork
  - Conjunctival tissue and Corneal nerve
  - Goblet cells and decrease its density
- Compromise glaucoma filtration surgery outcomes
  - For each additional BAK-preserved eyedrop, the risk of early surgery failure increased by 21%
- Dose-dependent with cumulative burden of exposure
  - Number of preserved medications, variable BAK concentration in each drop, dosing frequency per day and duration of therapy has been shown to correlate with ocular surface disease prevalence and severity in glaucoma patients and worse quality of life

128

Preservatives in IOP Lowering Medications

BRAND NAME	ACTIVE INGREDIENT	PRESERVATIVE
EYE DROPS WITH BENZALKONIUM CHLORIDE (BAK)		
Iopidine	Apraclonidine 0.5%, 1%	BAK 0.01%
Betoptic S	Betaxolol 0.25%	BAK 0.01%
Betoptic	Betaxolol 0.5%	BAK 0.01%
Lumigan	Bimatoprost 0.01%	BAK 0.02%
Lumigan	Bimatoprost 0.03%	BAK 0.0003%
Lumify	Brimonidine 0.025%	BAK 0.01%
Alphagan	Brimonidine 0.2%	BAK 0.005%
Combigan	Brimonidine 0.2%/timolol 0.5%	BAK 0.005%
Azopt	Brinzolamide 1%	BAK 0.01%
Simbrinza	Brinzolamide 1%/brimonidine 0.2%	BAK 0.002%
Trusopt	Dorzolamide 2%	BAK 0.0075%
Cosopt	Dorzolamide 2%/timolol 0.5%	BAK 0.0075%
Xalatan	Latanoprost 0.005%	BAK 0.02%
Rocklatan	Latanoprost 0.005%/netarsudil 0.02%	BAK 0.02%
Vyzulta	Latanoprostene 0.024%	BAK 0.02%
Xelpros	Levobunolol 0.25%, 0.5%	BAK 0.004%
Rhopressa	Netarsudil 0.02%	BAK 0.015%
Isopto Carpine	Pilocarpine 1%	BAK 0.01%
Timoptic	Timolol 0.25%, 0.5%	BAK 0.01%

EYE DROPS CONTAINING ALTERNATIVE PRESERVATIVES		
Alphagan P	Brimonidine 0.1%, 0.15%	Purite® (stabilized oxychloro complex) 0.005%
Xalpros	Latanoprost 0.005%	Potassium sorbate
Timoptic-XE	Timolol-XE 0.25%, 0.5%	Benzalkonium bromide 0.012%
Travatan Z	Travoprost 0.004%	sofZia®
PRESERVATIVE-FREE EYE DROPS		
Cosopt PF	Dorzolamide 2%/timolol 0.5%	Preservative-free
PF Latanoprost	**Latanoprost 0.005%**	**Preservative-free**
Zioptan	Tafluprost 0.0015%	Preservative-free
Timoptic in Ocudose	Timolol 0.25%, 0.5%	Preservative-free

BAK is the most used preservative in topical ophthalmic formulations

PF-Latanoprost has been approved by the FDA for use in the United States.

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Alternative Preservatives in Glaucoma Medications

- To reduce the cytotoxicity of BAK, several 'alternative preservatives' have been developed for antiglaucoma medications.
  - Benzododecinium bromide: a quaternary ammonium compound
  - PURITE®: S.O.C (Stabilized Oxychloro Complex)
  - sofZia®: ionic-buffered system (combination of boric acid, zinc, sorbitol, borate and propylene glycol) and functions as an oxidizing preservative
- Although these alternates are considered less toxic than BAK, they still may exert negative impact on ocular surface
  - PURITE (used in Alphagan® P) was shown to induce less corneal and conjunctival inflammatory damage[1].
  - sofZia (used in Travatan Z®): study showed less toxicity compared to BAK[2]

130

Iyuzeh (latanoprost ophthalmic solution) 0.005% Preservative Free

PF-Latanoprost had a similar IOP lowering efficacy to Xalatan in patients with POAG or OHT. The most common adverse reactions (5% to 35%) were conjunctival hyperemia, eye irritation, eye pruritus, abnormal sensation in eye, foreign body sensation in eyes, vision blurred, and lacrimation increased.

PF-Latanoprost has demonstrated similar IOP lowering efficacy to Xalatan in patients with POAG or OHT with a decade long clinical experience

PF Latanoprost has been approved by the FDA, providing US eyecare professionals with another treatment option in their glaucoma treatment armamentarium

131

Vyzulta™ (latanoprostene Bunod) Ophthalmic Solution 0.024%

- Bausch & Lomb
- November 2, 2017: approved
- Indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension
- Only nitric oxide releasing agent that targets both the trabecular meshwork and uveoscleral pathway to reduce IOP
- Once daily monotherapy
- Dual mechanism of action
  - Uveoscleral pathway to increase aqueous humor outflow
  - Butanediol mononitrate, which releases NO to increase outflow through the trabecular meshwork and Schlemm's canal.
- Ocular adverse events
  - Conjunctival hyperemia, eye irritation, eye pain and instillation site pain
  - Increased pigmentation of the iris and periorbital tissue and growth of eyelashes can occur

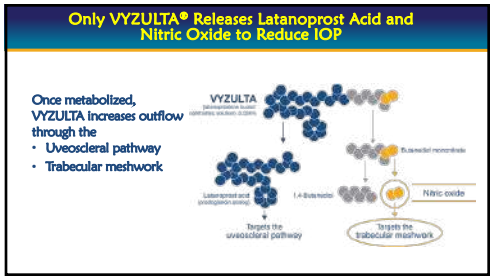
132

Nitric Oxide Plays Important Roles Throughout the Body and the Eye

Physiological functions of nitric oxide

Nitric oxide is a key regulator of numerous physiological functions in the body, including those in the eye

133



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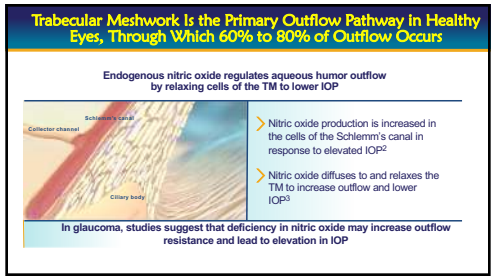

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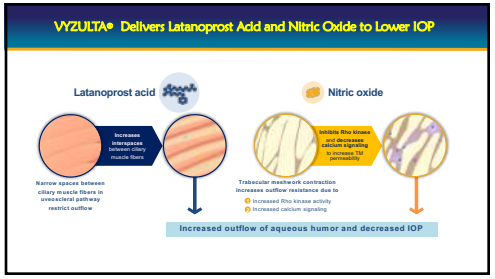

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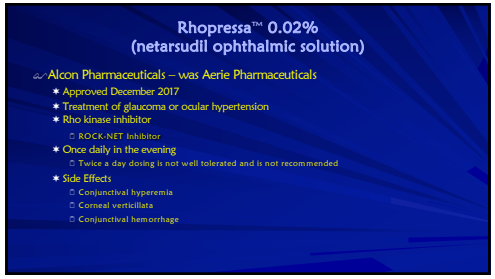

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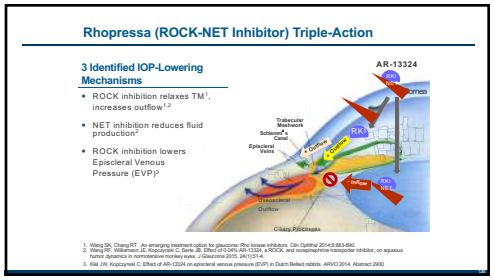

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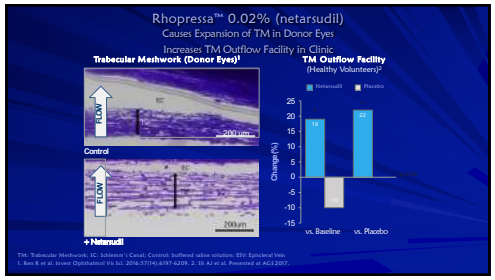
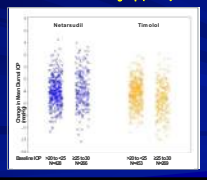


139

Netarsudil is Similarly Effective at Baseline IOPs <25 mmHg and ≥25 mmHg

Pooled Analysis Rocket 1, Rocket 2, Rocket 4

Day 90: Change from Baseline IOP by Baseline Subgroup (Pooled)



Baseline IOP ≥20 to <25 mmHg

	Netarsudil QD	Timolol BID
Median	-4.2	-4.3
Mean	-4.1	-4.3
Max	-10.7	-10.8

Baseline IOP ≥25 to <30 mmHg

	Netarsudil QD	Timolol BID
Median	-4.0	-5.3
Mean	-3.7	-5.3
Max	-12.3	-12.0

140

Rhopressa™ 0.02%

- No labeled contraindications for Rhopressa™
- No clinically relevant effects on vital signs
  - Blood Pressure
    - Changes were generally small and not clinically relevant in both groups
  - Heart Rate
    - Timolol caused statistically significant reduction in the phase 3 studies by an average of 2-3 beats per month

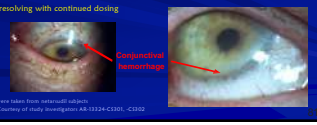
141

Conjunctival Hemorrhage was Sporadic and Severity did not Increase with Continued Dosing

Adverse Events	Netarsudil 0.02% QD (N=839) n (%)	Timolol 0.5% BID (N=839) n (%)
TEAE Conjunctival Hemorrhage	144 (17.2)	15 (1.8)
AE Resulting in Discontinuation	8 (1.0)	0

Majority 92.4% (133/144) of the conjunctival hemorrhage in netarsudil QD group was mild, 6.3% (9/144) was moderate and 1.4% (2/144) was severe

Self-resolving with continued dosing



Images were taken from netarsudil subjects
Source: Courtesy of study investigators AR-13324-C1301, -C1302

142

Cornea Verticillata Observed in Phase 3 Studies

- Cornea verticillata refers to a whorl-like pattern of deposits typically localized to the basal corneal epithelium
- Subjects are asymptomatic
- The onset was ~6 to 13 weeks (netarsudil QD)

Images were taken from netarsudil subjects
Source: Courtesy of study investigators AR-13324-C1302

143

Cornea Verticillata Due to Phospholipidosis

Medications known to cause verticillata: amiodarone, chloroquine, naproxen, phenothiazine, ocular gentamicin and tobramycin*

Due to phospholipidosis where the parent drug is complexed with phospholipids in the lysosomes

Literature review suggested it is an adaptive response by the body rather than an adverse pathology*

Data on File Based on AR-13324-IPH07
* Bateman MB et al. Surv. Ophthalmol. 2017;62:286-301

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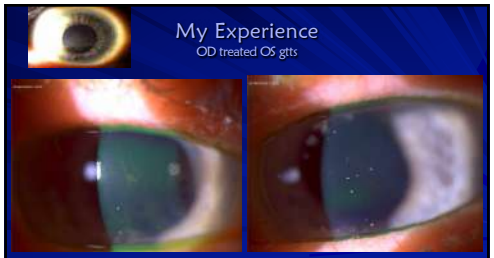
My Experience

OD treated OS gtts



145

Summary of the Most Common Netarsudil Ocular TEAEs

Conjunctival Hyperemia	Cornea Verticillata	Conjunctival Hemorrhage
54.4% TEAE	20.9% TEAE	17.2% TEAE
Severity did not increased with continued dosing	Asymptomatic	Mild in severity and transient
Sporadic	7.4% experienced reduced visual acuity	Self-resolving with continued dosing
	Not clear to a directly associated	
	All resolved after 13 weeks of D/C	

146

Honeycomb Epithelial Edema Associated With Rho Kinase Inhibition

- Thank you, Charles McBride, O.D., Beaverton, OR (12-23-2020 OGS – Google Groups)
- Sample of Rocklatan yesterday to lower his IOP of 46mmHg
- IOP today was 34
- Didn't measure corneal thickness
- The eye is blind and pretty sure it is neovascular glaucoma
- He's not been seen in three years and recently relocated from Missouri

147

Honeycomb Epithelial Edema Associated With Rho Kinase Inhibition Graft Patient

Thank you! Joe Shovlin, OD, FAAO

148

Rocklatan™

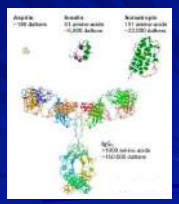
(netarsudil/latanoprost ophthalmic solution) 0.02%/0.005%

- Alcon Pharmaceuticals – was Aerie pharmaceuticals
  - March 14, 2019
- Once-daily eye drop
- First PGA combination approved
  - Superiority versus inferiority
- Refrigeration
  - Storage and after opening

149

Biologic Drugs versus Small Molecule Drugs

- Biologic Drugs
  - Larger, complex, dynamic structures
  - Diverse populations of molecules
    - Not easily characterized
  - Complicated manufacturing
  - Example: Teprotumumab (Tepezza)
- Small Molecule Drugs
  - Synthetic
  - Manufactured using a defined chemical process
  - Smaller and simpler
  - Example: Aspirin



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Why Your Patients Are on ELAHERE

Eye Care Considerations for Patients Treated With ELAHERE

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Optometry's role with Elehere - Mirvetuximab Soravtansine gynx (MIRV)

- Antibody-drug conjugate (ADC) comprising an FR-binding antibody, cleavable linker, and maytansinoid DM4 payload
- Primary ocular events with MIRV include corneal disorder, corneal epithelial defect, keratitis, keratopathy, corneal deposits, and punctuate keratitis
- Exam and clear patient for treatment

152

Elehere - Mirvetuximab Soravtansine

Mirvetuximab soravtansine (MIRV) is the first biomarker-directed agent showing antitumor activity in patients with FRα-positive[a] platinum-resistant ovarian cancer (PROC)[1]

- MIRV is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and maytansinoid DM4 payload
- A phase 3 clinical study, SORAYA, evaluated MIRV in patients with FRα-high PROC who had received 1 to 3 prior therapies, including required bevacizumab

153

Why Your Patients Are on ELAHERE

ELAHERE is a therapy approved to treat certain patients with advanced ovarian cancer

- ELAHERE is indicated for the treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Who have received one to three prior systemic treatment regimens
- This indication is approved under accelerated approval based on tumor response rate and durability of response

154

Why Eye Care Is Important for Patients Receiving ELAHERE™

You play a critical role in patient management as ocular adverse events have been observed in patients treated with ELAHERE

BOXED WARNING: OCULAR TOXICITY

- ELAHERE can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.
- Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of ELAHERE, every other cycle for the first 8 cycles, and as clinically indicated.
- Administer prophylactic artificial tears and ophthalmic topical steroids.
- Withhold ELAHERE for ocular toxicities until improvement and resume at the same or reduced dose.
- Discontinue ELAHERE for Grade 4 ocular toxicities.

155

Proposed MOA for Ocular Events Associated With MIRV

- The underlying mechanisms of ocular toxicities remain poorly understood, but it is hypothesized to be an off-target effect on the corneal epithelium due to the lack of FRα receptors in that part of the eye
- Anti-microtubule payloads such as DM4 have been previously associated with resolvable ocular toxicity, such as blurred vision, dry eye, and keratopathy
- One hypothesis for toxicity seen with anti-microtubule payloads is that symptoms arise from a change in curvature of the cornea due to transient alterations in corneal epithelial thickness or corneal biomechanical properties, associated with the presence of microcysts
- Additionally, prolonged retention in circulation associated with MIRV's stable linker may lead to enhance exposure in normal tissues

The ocular AE profile of MIRV is a dose-dependent toxicity limited to the corneal epithelium of the eye, with resolvability observed in both non-clinical and human studies

156

Microscopic Analysis of the Corneal Epithelium

Non-clinical Microscopic Analysis (Control and MIRV 12-mg/kg Dose)[1]

Key Observations With MIRV 12-mg/kg Dose

- **Fewer and larger** epithelial cells
- Overall **thinner** epithelial layer
- Basal layer appearing disorganized as **gaps** noted between visible nuclei
- **No visible nuclei** in places across the thickness of the epithelial layer, suggesting no cells other than those of the basal layer were present[1]
- **Lesions only at the periphery** of the cornea

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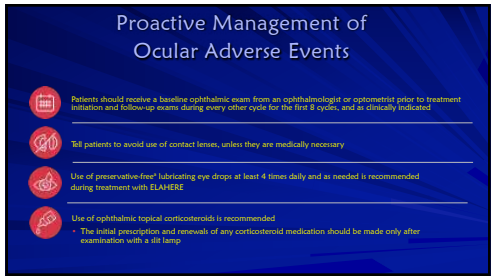

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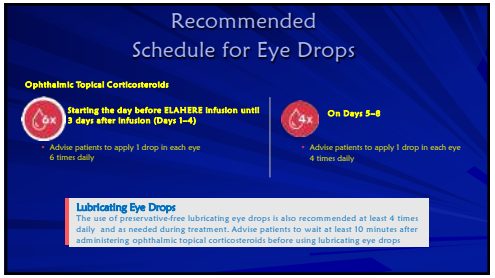

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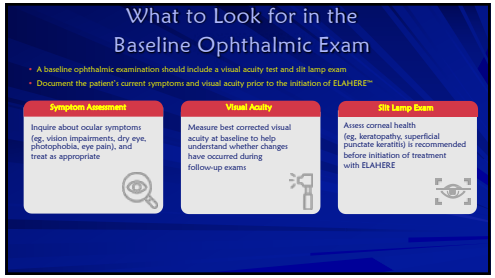

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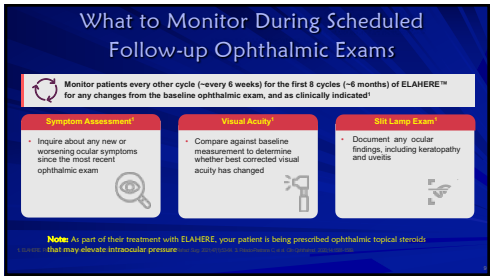

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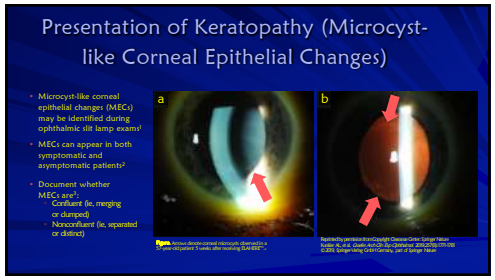

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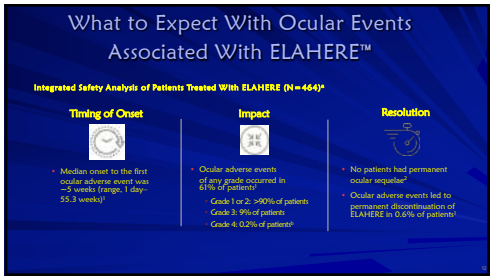

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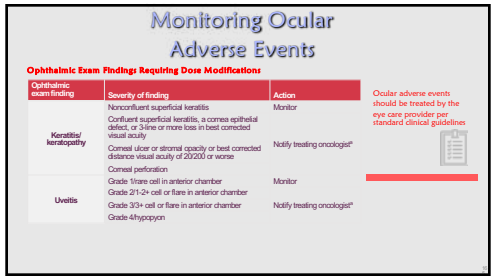

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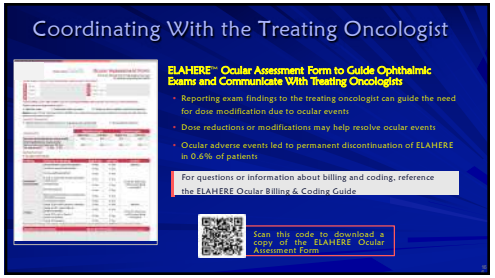

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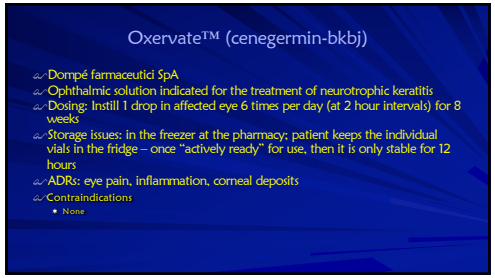

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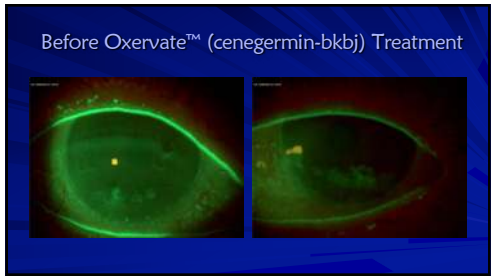

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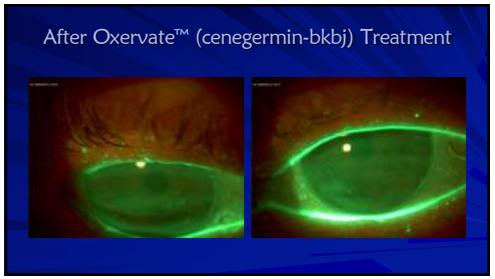

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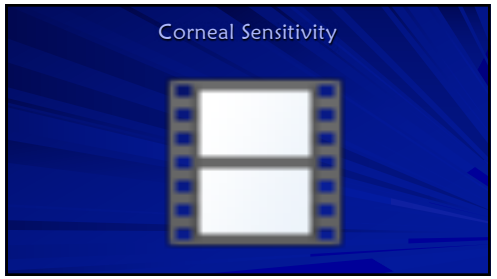

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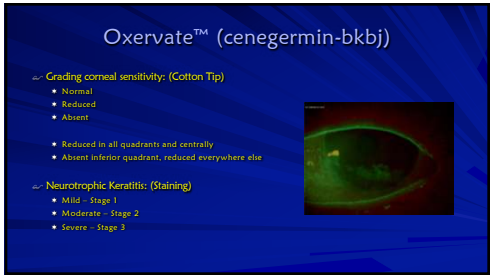

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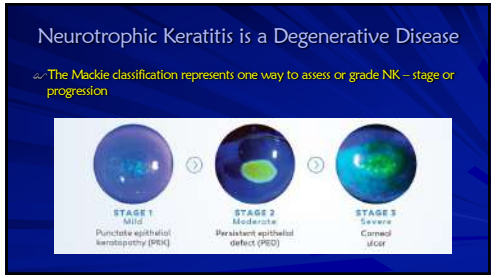

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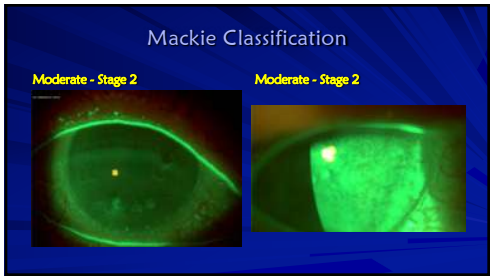

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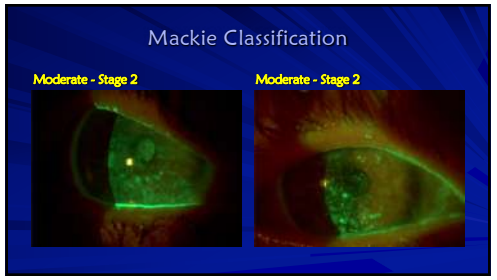

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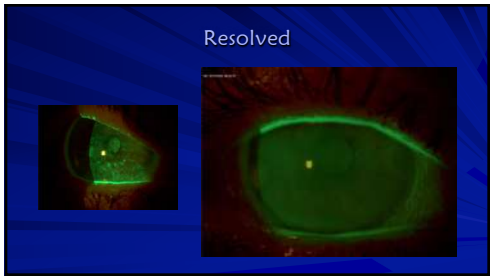

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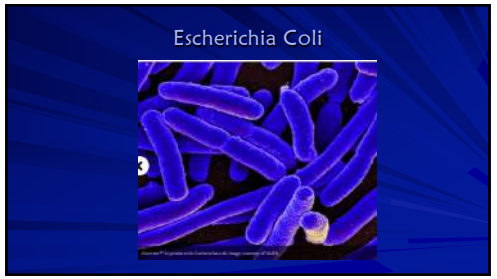

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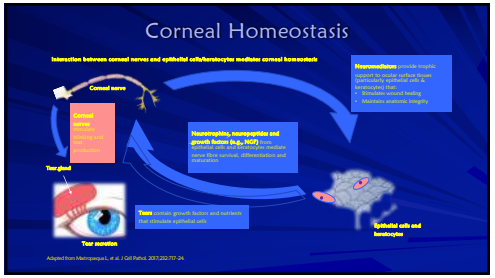

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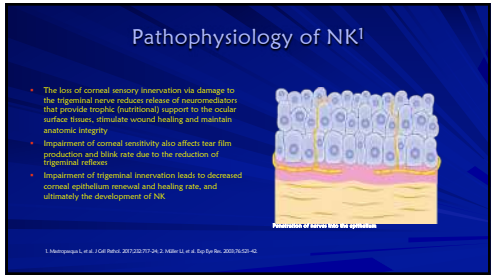

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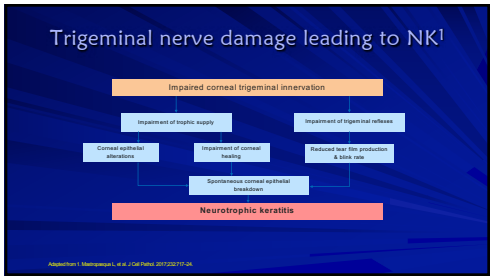

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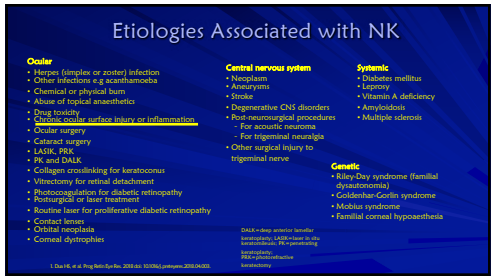

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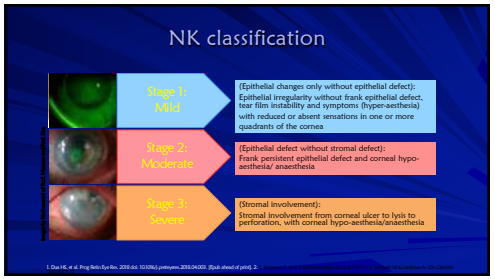

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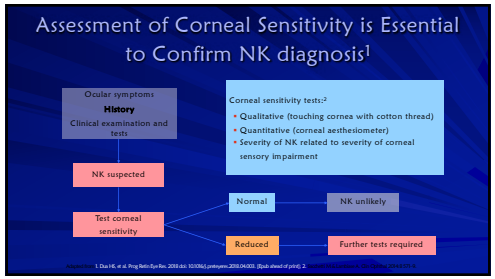

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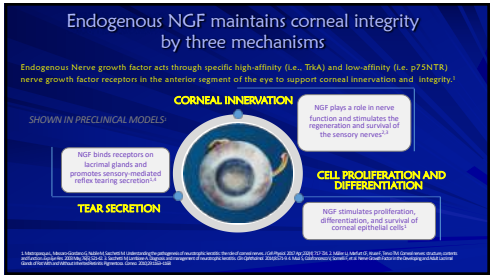

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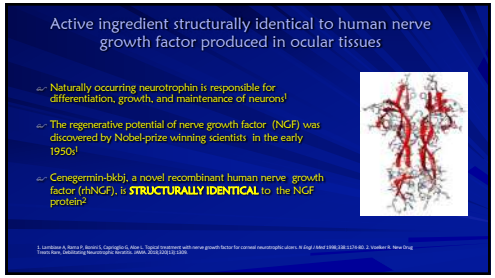

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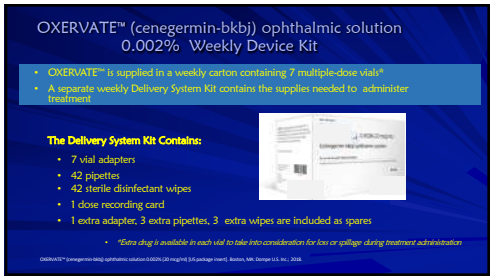

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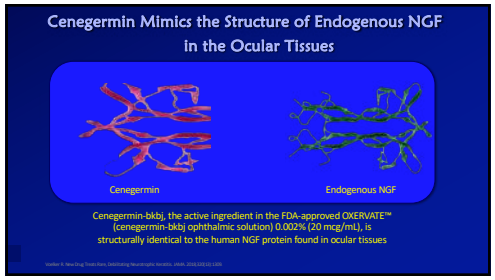

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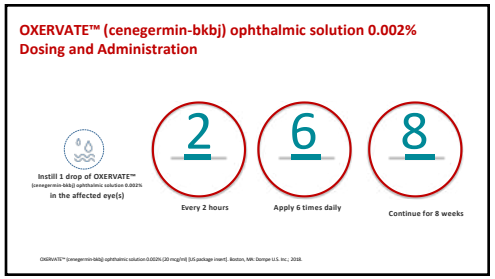

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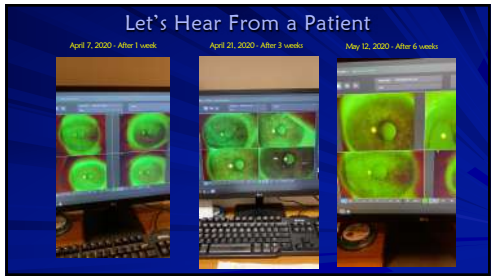

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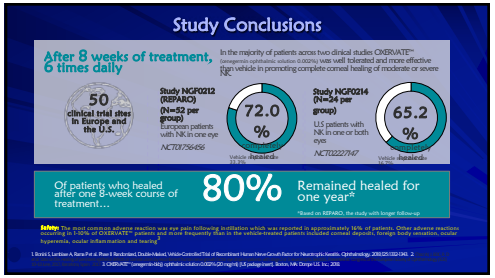

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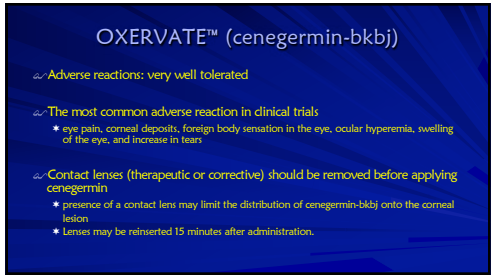

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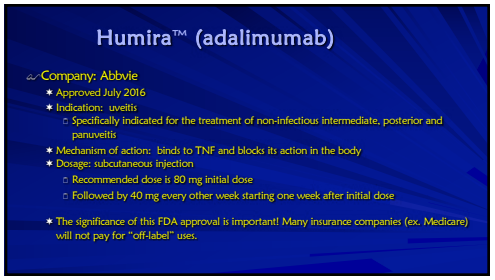

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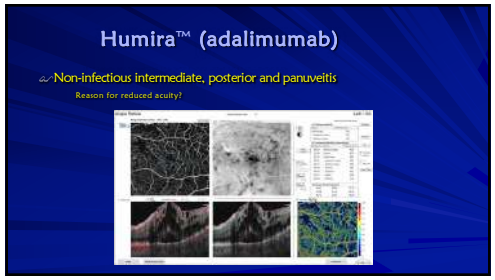


193

Humira™ (adalimumab)

- Monitoring parameters:
  - Must place PPD before initiating = if PPD+, then initiation of Humira may convert latent TB to ACTIVE tuberculosis
  - 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.

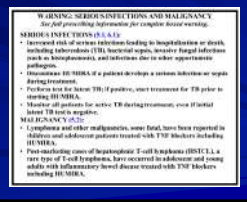
194

Hadlima™ (adalimumab-bwwd)

- Biosimilars
  - Hadlima (Adalimumab-bwwd)
    - Biologic agent SIMILAR to Humira
    - What is a "biosimilar" agent?
      - Remember what the FDA say about "biosimilars"

195

Humira™ (adalimumab)
Hadlima™ (adalimumab-bwwd)



WARNING: SERIOUS INFECTIONS AND MALIGNANCY
See full prescribing information for complete boxed warning.

SERIOUS INFECTIONS (5.1, 6.1)

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections such as histoplasmosis, and infections due to other opportunistic pathogens.
- Discontinue HUMIRA if a patient develops a serious infection or sepsis during treatment.
- Perform test for latent TB; if positive, start treatment for TB prior to starting HUMIRA.
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

MALIGNANCY (5.2)

- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including HUMIRA.
- Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescent and young adults with inflammatory bowel disease treated with TNF blockers including HUMIRA.

196

Actemra™ (tocilizumab)

ACTEMRA is indicated for the treatment of giant cell arteritis (GCA) in adult patients.

Let's qualify this statement

197

From: http://www.actemra.com/actemra/rheumatoid-arthritis/ra.html

198

Actemra™ (tocilizumab)

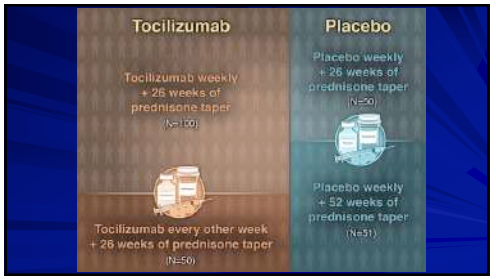
- Actemra™ (tocilizumab)- Genetec
  - First innovative therapy for GCA in more than 50 years
  - Design to speed the development for treatments of serious diseases such as GCA and certain cancers

199

Actemra™ (tocilizumab)

- 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
- The preliminary results indicate that patients receiving high dose tocilizumab had superior disease remission at 1 year compared to the steroid-only taper
- 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

200



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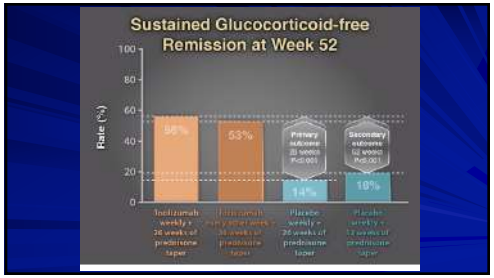

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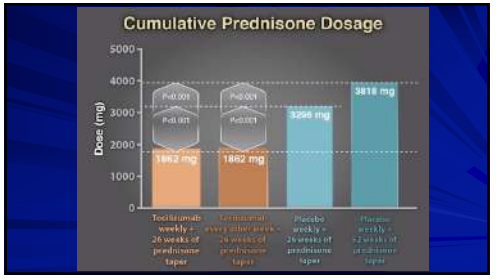

203

Actemra™ (tocilizumab)

- Tocilizumab does not directly treat GCA
  - Reduces steroid load after disease has been adequately treated by steroids and enhances disease remission
- Steroids are main therapy
- Studies are ongoing to see:
  - What is the lowest steroid tapering dose that can be used with tocilizumab
  - Future studies may show tocilizumab as steroid replacement

204

Tocilizumab (Actemra)

WARNING: RISK OF SERIOUS INFECTIONS

See full prescribing information for complete boxed warning.

- **Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving ACTEMRA. (5.1)**
- **If a serious infection develops, interrupt ACTEMRA until the infection is controlled. (5.1)**
- **Perform test for latent TB; if positive, start treatment for TB prior to starting ACTEMRA. (5.1)**
- **Monitor all patients for active TB during treatment, even if initial latent TB test is negative. (5.1)**

205

Olumiant™ (baricitinib) and Rinvoq™ (upadacitinib)

- Janus Kinase inhibitors
  - Indicated for the treatment of adult patients with moderate/severe active rheumatoid arthritis
    - Must have failed 1 or more TNF-alpha inhibitors (e.g. Remicade, Humira)
- THE HUB-BUB? It is an orally administered medication, as opposed to MOST of the others that are injectables!
  - Known as "un-jections"

206

Family Medicine

- Aimovig™ (erenumab-aooe)
- Ajovy ™ (fremanezumab-vfrm)
  - Approved 2018
  - Indicated for the PREVENTIVE treatment of migraine in adult patients
  - Calcitonin gene-related receptor antagonist
    - SQ injection
    - Once per month for either product
    - Once every three months for Ajovy™
- ADRs: constipation, injection site reactions

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Erenumab (Aimovig)

5.2 Constipation with Serious Complications

Constipation with serious complications has been reported following the use of AIMOVIG in the postmarketing setting. There were cases that required hospitalization, including cases where surgery was necessary. In a majority of these cases, the onset of constipation was reported after the first dose of AIMOVIG; however, patients have also presented with constipation later on in treatment. AIMOVIG was discontinued in most reported cases of constipation with serious complications. Constipation was one of the most common (up to 3%) adverse reactions reported in clinical studies *[see Adverse Reactions (6.1)]*.

Monitor patients treated with AIMOVIG for severe constipation and manage as clinically appropriate *[see Patient Counseling Information (17)]*. The concurrent use of medications associated with decreased gastrointestinal motility may increase the risk for more severe constipation and the potential for constipation-related complications.

5.3 Hypertension

Development of hypertension and worsening of pre-existing hypertension have been reported following the use of AIMOVIG in the postmarketing setting. Many of the patients had pre-existing hypertension or risk factors for hypertension. There were cases requiring pharmacological treatment and, in some cases, hospitalization. Hypertension may occur at any time during treatment but was most frequently reported within seven days of dose administration. In the majority of the cases, the onset or worsening of hypertension was reported after the first dose. AIMOVIG was discontinued in many of the reported cases.

Monitor patients treated with AIMOVIG for new-onset hypertension, or worsening of pre-existing hypertension, and consider whether discontinuation of AIMOVIG is warranted if evaluation fails to establish an alternative etiology.

208

Antibodies of Thyroid Dysfunction

- TSH Receptor Antibodies
  - Stimulating TSH receptor antibody
    - Thyroid Stimulating Immunoglobulin (TSI)
  - Thyroid blocking antibody (TBAb)
- Thyroid Peroxidase Antibodies (TPOAb)
  - TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
  - TPOAb contributes to thyroid cellular destruction
- Most autoimmune thyroid dysfunctions have a combination of thyroid antibodies, however depending on which AB is more abundant results in the outcome of the disease

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Similar receptors are found in the skin, fat and muscle of the orbit

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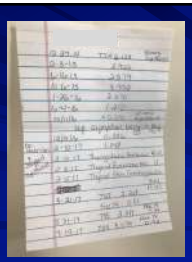

You're in the Know

Normal Values
Thyroglobulin 20 IU/ml
Peroidase <35 IU/ml
TSI 1.75 IU/ml

It does work!

211

Immunosuppression?

- Biologics
  - ✱ Immunosuppression biologics – suppress the immune system to get the effe3ct
    - Remicade – "1st generation"
      - Chimeric molecule - mouse and human protein, a lot of sensitivity
    - Humira
      - Anti-TNF (RA and Crohn's Disease
      - Fully human protein, less sensitivity
    - Rituxan
      - CD 20 suppressor (B cell suppression)
    - Actively suppress the immune system
  - ✱ Immunomodulary
    - Tepezza
      - IGF-1R inhibitor
      - Full humanized monoclonal antibody
        - All the proteins are human – less to no sensitivity – more focused effect
      - Obital fibroblasts to myofibroblast or adipocytes
      - Hyaluronic acid, glycosaminoglycan

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Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
  - Chinee Hamster Ovary
  - Infusion, 8 total, every 3 weeks
- Thyroid eye disease
  - IGR-1 (Insulin like growth factor 1) and TSH receptors are over expressed
- IGF-1 receptor inhibitor monoclonal antibody
  - On the orbital fibroblasts
    - Inhibiting downstream inflammatory cascade
      - Cytokines, hyaluran, leukotriene
      - Differentiation into adipocytes and myofibroblasts
- Phase 2 and published in New England Journal of Medicine
- Phase 3 completed
  - Not published
- PDUFA- March 2020, was approved early in 2020

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Teprotumumab-trbw (Tepezza)




https://www.tepezza.com/hcp/tepezza-moa/

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Teprotumumab-trbw (Tepezza)

- Clinical Activity Score
  - Spontaneous pain, gaze evoked pain, eyelid erythema, chemosis, inflammation
  - Scale of 7, needed 4 to be in the study
    - 78% improved to 0 or 1, 7% improved 0 or 1 with placebo
- Proptosis
  - Improvement of 2 mm or better
    - 83% had 2 mm or better, 10% with placebo
    - Average was 3.2 mm at week 24
- Diplopia
  - Scale of 0, 1, 2, or 3
    - 68% improved 1 point, 29% with placebo
- Grave's Ophthalmopathy -Quality of Life Score
  - Scale 0-100
    - 17.28 point improved, 1.80 with placebo

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Teprotumumab-trbw (Tepezza)

- **Infusion Reactions (mild/moderate):** approximately 4% of patients
  - transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain - will occur within 1.5 hours of an infusion
  - For those who have had a previous reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, or corticosteroid and/or administering at a slower infusion rate.
- **Preexisting Inflammatory Bowel Disease**: may cause an exacerbation of preexisting inflammatory bowel disease ("IBD")
  - Monitor patients for flare; may require discontinuation of Teprotumumab (Tepezza)
- **Hyperglycemia:** Increased blood glucose or hyperglycemia
  - In clinical trials, 10% of patients experienced hyperglycemia
  - Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with teprotumumab
  - Patients with preexisting diabetes should be euglycemic before beginning treatment

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Teprotumumab-trbw (Tepezza)

- Infusion center
  - ✱Go to Horizon website
  - ✱Contact Us
  - ✱Type in your question
    - Looking for infusion center

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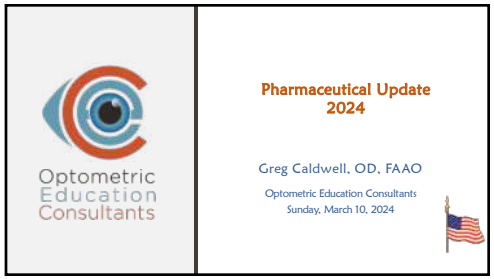
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Optometric Education Consultants
Sunday, March 10, 2024

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