

COURSE SYLLABUS

20/100

T

H E

20/70

S U N

20/50

C O A S T

20/40

S E M I N A R

20/25

F O R O P T O M E T R Y

20/20

A P R I L 2 5 - 2 6 , 2 0 2 6



Saturday April 25

- 7:45 am - 8:15 am** **Registration**
Exhibit Hall Open
Continental breakfast - sponsored by *St. Luke's Cataract and Laser Institute*
- 8:15 am - 9:55 am** **Advances in Cornea, Cataract, Refractive and Glaucoma Surgery (2, TQ, COPE: 103831-GO)**
Neel R. Desai, M.D. and Priti Panchal, O.D.
- 9:55 am - 10:40 am** **Break**
Exhibit Hall Open
- 10:40 am - 12:20 pm** **Amblyopia Management for Primary Care O.D.s (1, COPE: 103274-FV)**
Acquired Brain Injury: What the O.D. Needs to Know (1, COPE: 103273-FV)
Richard Sorkin, O.D.
- 12:20 pm - 1:10 pm** **Lunch** - sponsored by *Retina Vitreous Associates of Florida*
Exhibit Hall Open
- 1:10 pm - 1:20 pm** **Lighthouse of Pinellas Update**
- 1:20 pm - 1:30 pm** **FOA Update**
- 1:30 pm - 3:10 pm** **Pharmaceutical Update - Innovations and Insights for Eye Care (2, TQ, COPE: 103324-PH)**
Greg Caldwell, O.D.
- 3:10 pm - 3:30 pm** **Break**
- 3:30 pm - 5:10 pm** **Latest Advances in Eye Care Technology - Innovations in Early Detection and Management (2, TQ, COPE:103700-GO)**
Greg Caldwell, O.D.

Sunday April 26

- 7:30 am - 8:00 am** **Registration**
Continental breakfast - sponsored by *the POA*
- 8:00 am - 9:40 am** **Grand Rounds - Improving Eye Care and Outcomes for Patients (2, TQ, COPE: 103866-TD)**
Greg Caldwell, O.D.
- 9:40 am - 10:00 am** **Break**
- 10:00 am - 11:40 am** **Prevention of Medical Errors (2, COPE: 102834-EJ)**
Alice Sterling, O.D.
- 11:40 am - 12:00 pm** **Lunch** - sponsored by *LENZ Therapeutics*
- 12:00 pm - 1:40 pm** **Florida Jurisprudence (2, COPE: 101024-EJ)**
Alice Sterling, O.D.



Pharmaceutical Update
Innovations and Insights for Eye Care


Greg Caldwell, OD, FAAO
The Suncoast Seminar
April 25-26, 2026



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Disclosures- Greg Caldwell, OD, FAAO
All relevant relationships have been mitigated.

- Lectured for: Alcon, B&L, Dompé, Lenz
Disclosure: Receive speaker honorariums
- Advisory Board: Dompé, Tarsus, Envision
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 Pharnanex
- 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

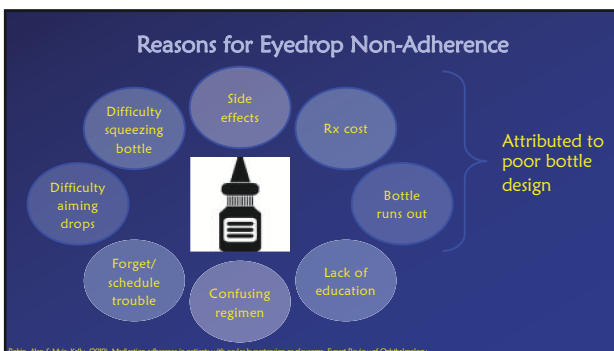
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Pharmaceutical Resource Matrix

- Commercial/Sales
 - Representatives
 - On label, educational lunches, samples, discount cards, coupon
 - Organize the promotional dinner
- 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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Reasons for Eyedrop Non-Adherence

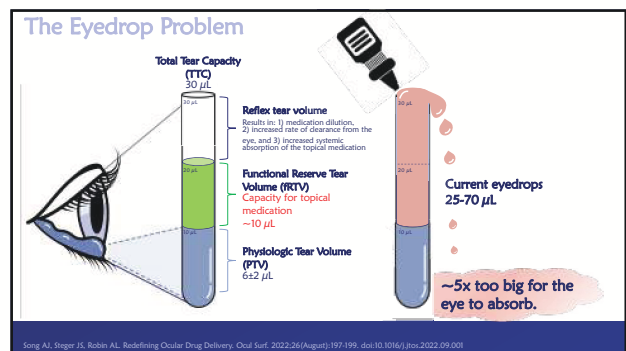


Attributed to poor bottle design

Robb, Alan C.M.D., Fello., 2009. Medication adherence in patients with ocular hypertension or glaucoma. Expert Review of Ophthalmology.

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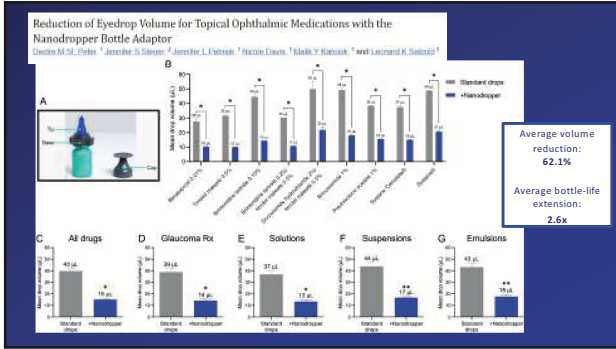
The Eyedrop Problem



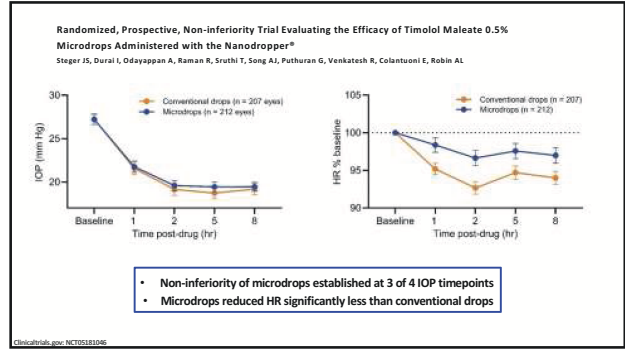
~5x too big for the eye to absorb.

Song AJ, Steger JS, Robb AL. Redefining Ocular Drug Delivery. Ocul Surf. 2022;26(August):197-199. doi:10.1016/j.jaos.2022.09.001

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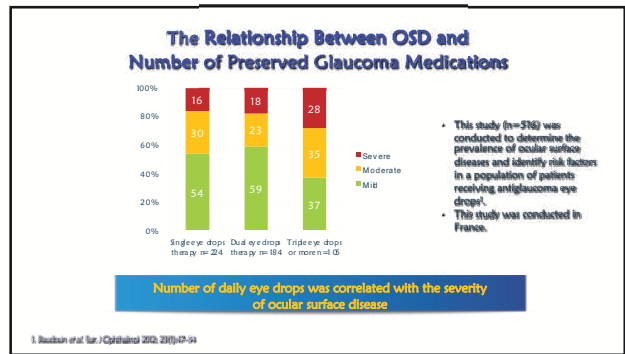
8

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

Follicular Conjunctivitis

Superficial Punctate Keratitis (SPK)

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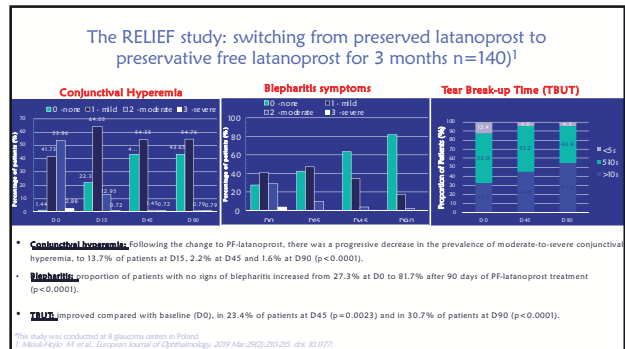
Preservatives in IOP Lowering Medications

BRAND NAME	ACTIVE INGREDIENT	PRESERVATIVE	CONCENTRATION
EYE DROPS WITH BENZALKONIUM CHLORIDE (BAK)			
Heptin	Brimonidine 0.2%	BAK 0.01%	
Beyo 3	Brimonidine 1.0%	BAK 0.01%	
Beyo 3	Brimonidine 1.5%	BAK 0.01%	
Lunigan	Brimonidine 0.2%	BAK 0.02%	
Lunigan	Brimonidine 0.3%	BAK 0.02%	
Lunigan	Brimonidine 0.5%	BAK 0.02%	
Lunigan	Brimonidine 0.7%	BAK 0.02%	
Lunigan	Brimonidine 1%	BAK 0.02%	
Lunigan	Brimonidine 1.5%	BAK 0.02%	
Lunigan	Brimonidine 2%	BAK 0.02%	
Lunigan	Brimonidine 2.5%	BAK 0.02%	
Lunigan	Brimonidine 3%	BAK 0.02%	
Lunigan	Brimonidine 4%	BAK 0.02%	
Lunigan	Brimonidine 5%	BAK 0.02%	
Lunigan	Brimonidine 6%	BAK 0.02%	
Lunigan	Brimonidine 7%	BAK 0.02%	
Lunigan	Brimonidine 8%	BAK 0.02%	
Lunigan	Brimonidine 9%	BAK 0.02%	
Lunigan	Brimonidine 10%	BAK 0.02%	
Lunigan	Brimonidine 11%	BAK 0.02%	
Lunigan	Brimonidine 12%	BAK 0.02%	
Lunigan	Brimonidine 13%	BAK 0.02%	
Lunigan	Brimonidine 14%	BAK 0.02%	
Lunigan	Brimonidine 15%	BAK 0.02%	
Lunigan	Brimonidine 16%	BAK 0.02%	
Lunigan	Brimonidine 17%	BAK 0.02%	
Lunigan	Brimonidine 18%	BAK 0.02%	
Lunigan	Brimonidine 19%	BAK 0.02%	
Lunigan	Brimonidine 20%	BAK 0.02%	
EYE DROPS CONTAINING ALTERNATIVE PRESERVATIVES			
Alphagan P	Brimonidine 0.1%, 0.15%	Phenol (stabilized acrylate complex) 0.025%	
Alphagan	Latanoprost 0.005%	Potassium sulfate	
Timoptic	Timolol 0.25%, 0.5%	Benzodachium bromide 0.02%	
Traslet Z	Timolol 0.004%	soGlu [®]	
PRESERVATIVE-FREE EYE DROPS			
Cocept PF	Dorzolamide 2% / timolol 0.2%	Preservative-free	
PF Latanoprost	Latanoprost 0.005%	Preservative-free	
Ziphan	Timolol 0.015%	Preservative-free	
Timoptic in Quilista	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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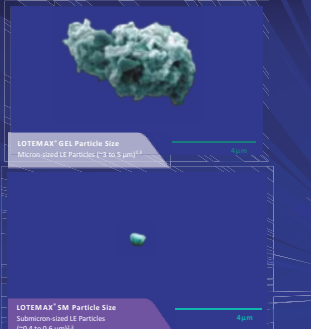
MOA versus MOD

Mechanism of Action – MOA

- * Rhopressa
- * Mibebo
- * Xdemvy
- * Tryptyr
- * Vizz

Mechanism of Delivery – MOD

- * Various Ioteprednol products
- o Lotemax SM 0.38% and TID
- * Various Cyclosporin products



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Receptors

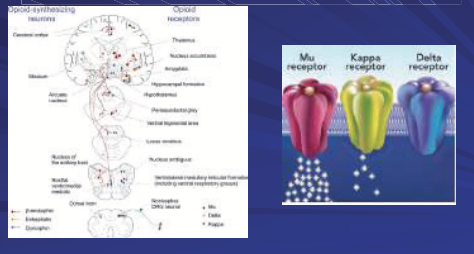
- Opioids relieve pain and induce pain relief by binding to the opioid receptors (mu, kappa, delta) in the brain and spinal cord:
- Mu, kappa, delta** receptors in other places of the body = ADRs
- * Mu: analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction
- * Kappa: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

Opioid Receptor Class	Effects
Mu	Euphoria, respiratory analgesia, constiction, flatulence, miosis, loss of reflexes (pupils)
Mu ₂	Respiratory depression, cardiovascular and gastrointestinal effects, nausea, sensory blockade
Delta	Skeletal analgesia, cardiovascular depression, decreased brain and myocardial oxygen demand
Kappa	Skeletal analgesia, diuresis, psychotomimetic effects, loss of back inhibition of sympathetic system

Adapted from references 2 and 3.

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Mu, Delta, and Kappa Receptors



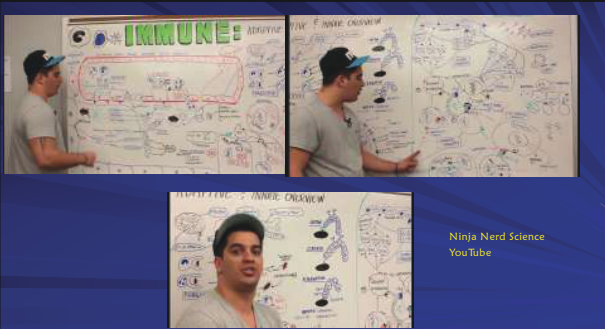
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Receptors

OPIOIDS IN THE BODY

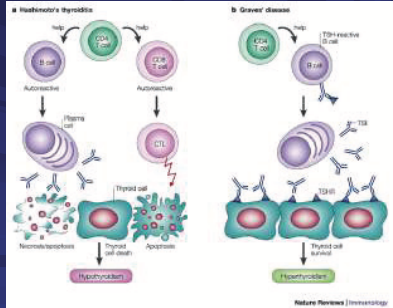


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Ninja Nerd Science
YouTube

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Hashimoto's thyroiditis


Graves' disease

Hashimoto's thyroiditis: Autoimmune thyroid disease: new models of cell death in autoimmunity

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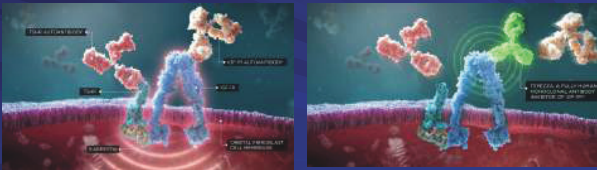
Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics - HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
 - Chinese Hamster Ovary
 - Infusion, 8 total, every 3 weeks
- Thyroid eye disease
 - IGF-1 (Insulin like growth factor-1) and TSH receptors are over expressed
 - IGF-1 receptor inhibitor monoclonal antibody
 - On the orbital fibroblasts
 - Initiating downstream inflammatory cascade
 - Cytokines, hyaline, heparanase
 - Differentiation into adipocytes and myofibroblasts
- Phase 2 and published in New England Journal of Medicine
- Phase 3 completed
 - Published: New England Journal of Medicine
 - PDUFA - March 2020, was approved early in 2020



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Teprotumumab-trbw (Tepezza)



<https://www.tepezza.com/hc/tepezza-moa/>

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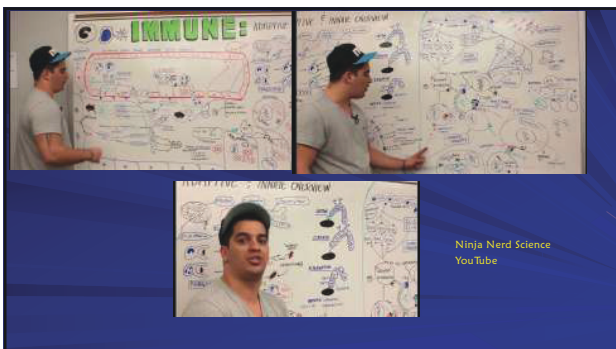
"If I started seeing changes, I'd carry my car to the eye doctor's office. That's how on top of your vision you have to be."
- Henry Winkler

GA Won't Wait™

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Ninja Nerd Science
YouTube

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Complement factor H in AMD: Driv[ing] genetic associations and pathobiology

Chowdhury R, Sengco J, et al. *Genes* 2019;10:1138

Show Details

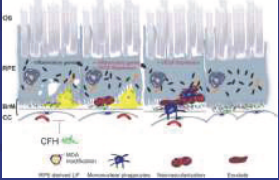
Full-text article: [https://doi.org/10.3390/genes10081138](#)

Abstract

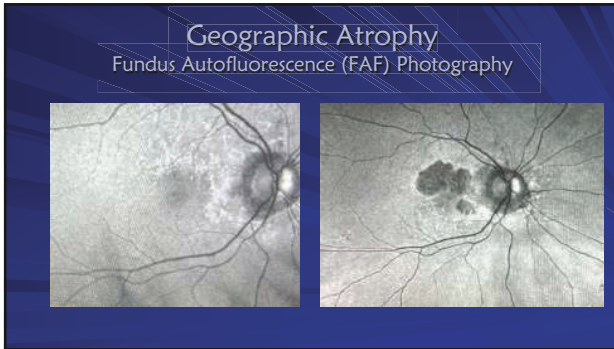
Age Related Macular Degeneration (AMD) is a complex multifactorial disease characterized by early signs of RPE/photoreceptor atrophy in Bruch's Membrane (BM) and late stage of the AMD pigment epithelial (RPE) cell layer (RPE). Genetic studies have strongly implicated & highlighted the importance of complement & in particular the common HFE variant in Complement Factor H (CFH) in development of early (intermediate) stages of AMD. The CFH H1282Y polymorphism increases risk for AMD.

Complement Cascade Effects in AMD

CFH	C3a	C5a
Competition with lipoproteins resulting in late AMD deposit formation	Disrupts RPE/photoreceptor attachment	Disrupts RPE/photoreceptor attachment
Alters inflammatory effects of C3a and C5a	Induces VEGF production and choroidal angiogenesis	Induces VEGF production, choroidal angiogenesis and oxidative stress




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Syfovre (pegcetacoplan injection)


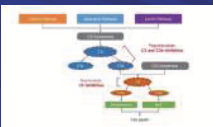
- Apellis Pharmaceuticals
- February 2023 – approved
- Indication: Treatment of geographic atrophy (GA) secondary to dry age-related macular degeneration (AMD)
- Mechanism of action: targeted C3 inhibition therapy
 - Regulating excessive activation of the complement cascade, which could lead to the onset and progression of diseases
- Administered: Intravitreal injection
- Macular degeneration is associated with overaction of the complement system
- C3 activation – inflammation, phagocytosis, cell membrane disruption
- C3 inhibitor is mechanism of action (MOA)
 - Synthetic, peptide-based inhibitor of C3
 - Prevents overactivation



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Izervay (avacincaptad pegol intravitreal solution)

- Iveric Bio – Now Astellas
- August 2023 – approved
- Indication: treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)
- PEGylated RNA aptamer
- Mechanism of action – complement C5 inhibitor formulated to slow GA progression
- Macular degeneration is associated with overaction of the complement system

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Biologic Aptamer versus Antibody

Aptamer	Antibody	Aptamer
More stable		Easy to synthesize
Easy to synthesize		Low risk of immunogenicity
Small size		

Syfovre (pegcetacoplan)
Izervay (avacincaptad pegol)

Bevacizumab (Avastin)
Ranibizumab (Lucentis)
Aflibercept (Eylea)
Pegfilgrastim (Neupogen)
Vabysmo (faricimab-voea)

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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 closest manufacturing process of a biologic drug

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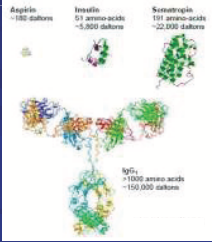
Size and Complexity of Biologic Drugs

- 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

Size & Complexity – Small Molecule Drugs & Proteins

	Small Molecule Drug	Large Molecule Drug	Large Biologic
Size	Aspirin ~1 atom	hGH ~3000 atoms	IgG Antibody ~25,000 atoms
Complexity	Bike ~20 lbs	Car 3000 lbs	Business Jet ~30,000 lbs (without fuel)

<http://www.arbio.org/im/all-molecules-true-biologics-and-the-bio-similar-debate>

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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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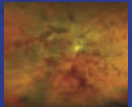
Past Treatments for Choroidal Neovascularization (CNV)

- 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-dbil (Beovu)
 - Humanized single-chain antibody fragment - 10-9-2019
 - 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 18, 2023 at 6:05 PM EDT

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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Pavblu (aflibercept-ayyh)

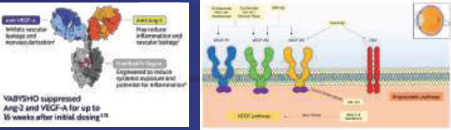
- First Aflibercept biosimilar
 - Amgen
 - Eylea is a registered trademark of Regeneron Pharmaceuticals
- 2 mg injection
- Indicated for the treatment of
 - Neovascular Age-Related Macular Degeneration (AMD)
 - Macular Edema following Retinal Vein Occlusion (RVO)
 - Diabetic Macular Edema (DME)
 - Diabetic Retinopathy (DR)



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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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Is AMD an Acute or Chronic Condition?

Strategy

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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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An Evening with Dr. Paul Bernstein

Historical Context I

- 18th century: *macula lutea* first noted by anatomists
- 1940s: Initial identification as a xanthophyll by Wald

Macular Pigment

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Macular Pigment

Imaging lutein and zeaxanthin in the human retina with confocal resonance Raman microscopy

Shiomi Y^{1,2}, Patel M, George C, Gregory T, Rogers C, Ayres-Schneppell J, Anantharam Rangaswami M, Yu Yao Chang¹, Li Jie Gu¹, Jessica M. Fackler¹, and Paul S. Bernstein^{1,2*}

¹Department of Ophthalmology and Visual Sciences, Johns Hopkins University, Baltimore, MD, USA; ²Johns Hopkins All Children's Hospital, Allentown, PA, USA

Fig. 4. Distribution of total carotenoids in a human retinal section. (Top) A

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Search Bar: ARED2 FAQ NEI

Will taking the ARED2 or ARED22 supplements prevent AMD?

Yes. In a randomized controlled trial, the ARED2 supplement significantly reduced the annual progression of intermediate to advanced AMD and may help to slow down your vision loss. The ARED22 supplement has been shown to have similar benefits for more than 30 years. Use the benefits of the ARED2 formulation from the start of your life.

Can I take a daily multivitamin if I am taking one of the ARED2/ARED22 formulas?

Yes. The ARED2 and ARED22 formulas are not designed for medical claims. In ARED2, we use 100% of the study participants that took multivitamins along with the ARED2 formulas. In ARED22, we used 100% of our participants that took multivitamins.

My comprehensive Anti-Oxidant Replacement and Anti-Autoimmune approach

- * Total anti-oxidant replacement (LifePak)
- * Fish oil
- * LOW dose zinc ARED22

More comprehensive than:

- * ARED22
- * Lutein and Zeaxanthin
- * Amsler grid

DIFFERENCE DEMONSTRATED

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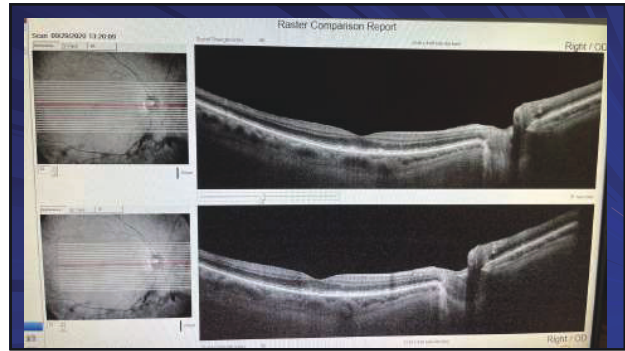
April 27, 2021 – January 26, 2022 (9 months)

Raster Comparison Report

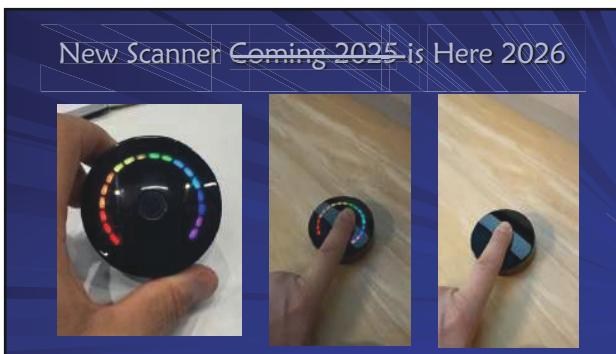
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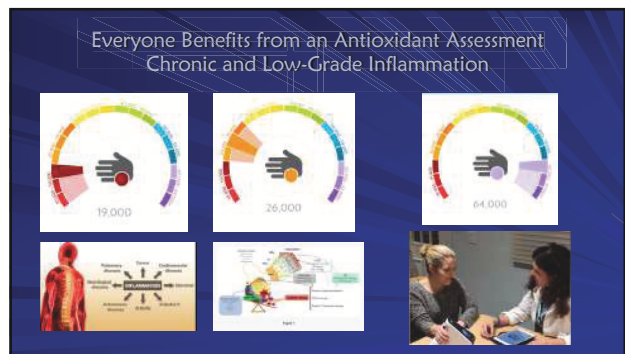
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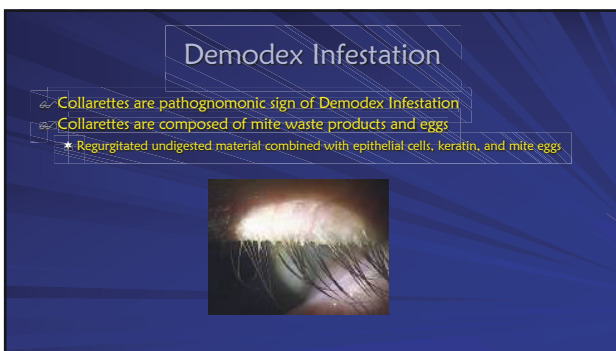
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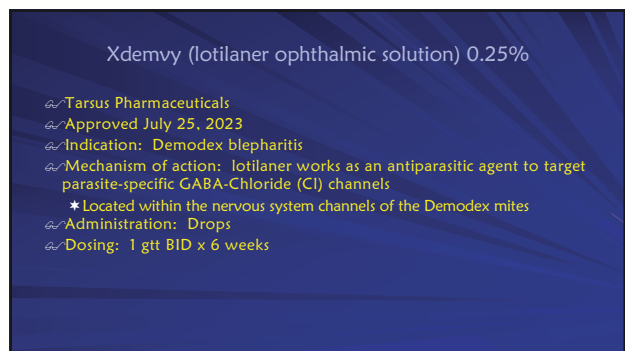
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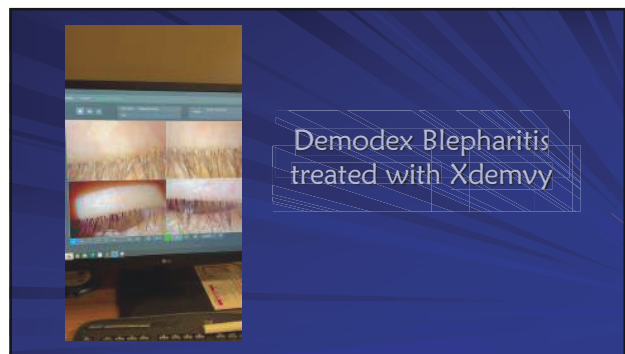
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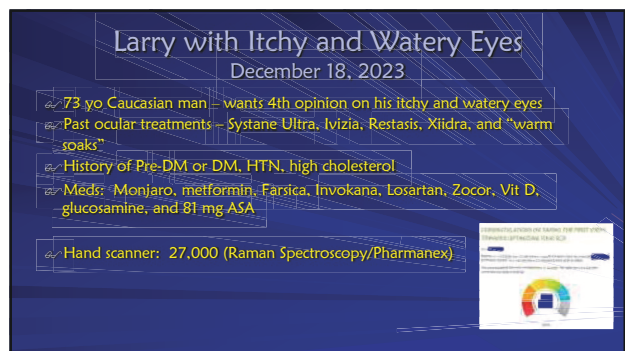
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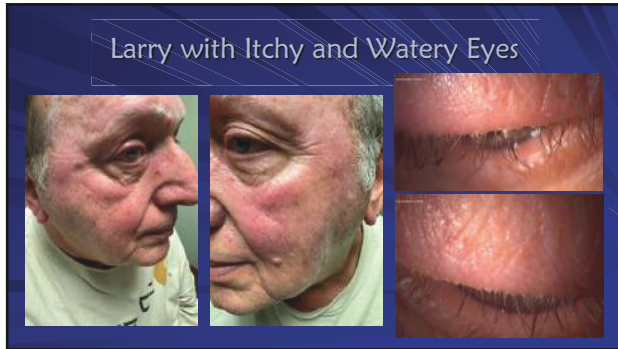
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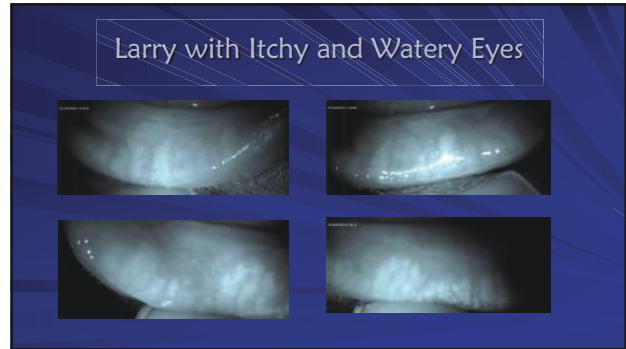
59



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Treatment: (Strategy)

- ★ Lengthy discussion on his complex ocular surface issue
 - Systemic association
 - Environment involvement
 - Lid microbiome dysfunction/dysbiosis
 - Nutritional association
- ★ Rx Xdemvy
- ★ Rx LifePak and Marine Omega
- ★ Continue Ivizta
- ★ Schedule for IPL

Includes three tables: Medication, Supplement, and Replacement Parts.

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December 18, 2023
 Xdemvy Rx written
 Importance of looking down

January 22, 2024
 12 days S/P ILP
 3 weeks Xdemvy treatment
 4 weeks on LP and MO
 Hand scan: 32,000

Includes four close-up photos of Larry's eyes showing improvement in redness and discharge.

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