Therapeutic Strategies in Clinical Eye Care

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www.eyeupdate.com

Financial Disclosure

Drs Ron Melton and Randall Thomas are consultants to, on the speakers bureau of, on the advisory committee of, or involved in research for the following companies: ICARE and B+L

02.03.2023

CDC Provides Update on Pseudomonas Aeruginosa Associated with Artificial Tears

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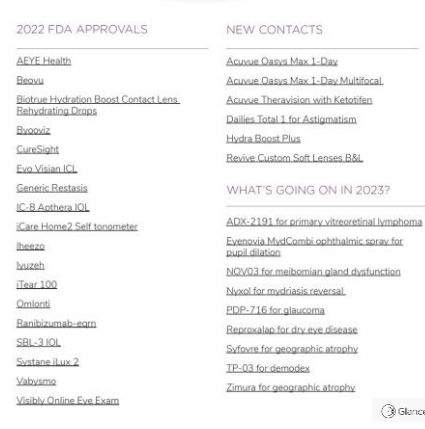
The Centers for Disease Control and Prevention (CDC) issued a Health Alert Network (HAN) Health Advisory in regards to infections of 55 people in 12 states related to the use of artificial tears.

Patients with infections reported more than 10 different brands of artificial tears, and some patients used multiple brands. The majority of patients who used artificial tears reported using EzriCare Artificial Tears, a preservative-free, over-the-counter product packaged in multidose bottles. CDC laboratory testing identified the presence of the outbreak strain in opened EzriCare bottles with different lot numbers collected from two states.

"Patients and health care providers should immediately discontinue using EzriCare artificial tears pending additional guidance from CDC and the Food and Drug Administration (FDA)," the CDC stated.



*A Study on Nanodropper Performance

- "Some patients run out of drops too soon, have trouble affording drops, or experience excessive side effects."
- The Nanodropper adaptor delivered 2.6 times the total number of drops for all medications."
- "Drop volume greater than 20 microliters provided no real additional benefit which may explain why drops almost always roll down the cheek, no matter how accurately they are placed."
- "The Nanodropper may theoretically reduce medical waste by more than 50%."

EyeNet Magazine, July 2023

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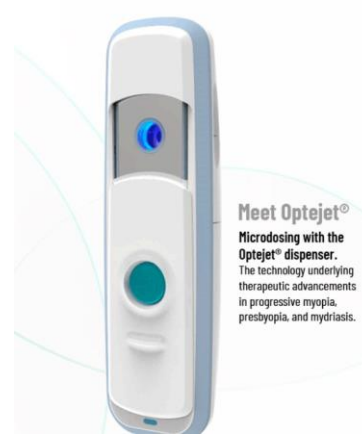


FDA APPROVES FIRST FIXED-DOSE COMBINATION FOR MYDRIASIS

Eyenovia announced that the FDA has approved its tropicamide and phenylephrine hydrochloride ophthalmic spray 1%/2.5% (Mydcombi)—the first FDA-approved fixed-dose combination of tropicamide and phenylephrine.[1] The spray is formulated for inducing mydriasis for diagnostic

Vuity (Pilocarpine 1.25%)

- First of a new wave of drugs to enhance near vision in presbyopia
- Induced miosis increases depth of focus
- About 30% of patients gained about 3 lines of near vision with slight compromise of distance vision
- Urge caution when regarding compromised night driving
- Dosage: 1 drop OU daily, PRN – onset in about 20 minutes
- Effect duration: 2 to 6 hours – can dose another drop if needed
- Side effect potential: HA, conjunctival hyperemia, retinal detachment – use with caution in patients with anterior uveitis
- Marketed by Allergan in a 5 ml bottle containing 2.5 ml of drug. It is preserved with 0.0075% BAK (Xalatan has 0.02% BAK)

The Finer Points Regarding Vuity™

- Vuity "may also include hydrochloric acid and/or sodium hydroxide for pH adjustment to between 3.5 and 5.5, if necessary."
- "Patients should be advised to exercise caution in night driving and other hazardous occupations in poor illumination. In addition, miotics may cause accommodative spasm."
- Regarding the very slight risk of retinal detachment, "Patients should be advised to seek immediate medical care with sudden onset of vision loss.
- On the good side, there could be "increased lacrimation."
- Vuity also contracts the ciliary muscles and may shift the eye to a more myopic state."

Vuity™ [package insert] Allergan 2021

*Retinal Detachment and Pilocarpine

- "Prior to prescribing pilocarpine for presbyopia, physicians should inform patients of potential adverse events and consider that patients undergo a screening dilated examination, particularly if they are myopic, to determine if they are at higher risk for retinal detachment. Findings on history and examination that could indicate an increased risk of detachment may include lattice retinal degeneration, a personal or family history of retinal detachment, higher degrees of myopia, and prior retinal tears. Before the initiation of therapy, patients should be appropriately informed regarding symptoms of retinal tears or detachment, which includes flashes, floaters, and visual field loss."

Am J Ophthalmol. October, 2022

New Preservative-Free Latanoprost

- With epidemic prevalence of DED, it is generally virtuous to limit ocular surface exposure to potentially toxic preservatives.
- PF Latanoprost 0.005% is used exactly like the original formulation.
- No refrigeration is required
- Packaging:
  6 foil packs containing 5 individual unit doses providing a 30-day supply
- Marketed as iyuzeh™ eye drop solution by Thea Pharma, Inc. (theapharmainc.com)

*Omlonti (0.002% omidenepag)

- In the three studies, IOP reductions were observed for all treatment arms. In the Omlonti arm the reduction in IOP ranged from 5-7 mm Hg across all three studies. The corresponding reductions for the timolol and latanoprost arms were 5-7 mm Hg and 6-8 mm Hg, respectively.
- It is simply another prostaglandin
- Preserved with 0.005% BAK

Omlonti® Package insert. Santen Inc. 2022

Omlonti® Equals Timolol – Consider Cost

- In the 15 ed studies, IOP reductions were observed for all treatment arms. In the Omlonti arm the reduction in IOP ranged from 5-7 mm Hg across all three studies. The corresponding reductions for the timolol and latanoprost arms were 5-7 mm Hg and 6-8 mm Hg, respectively.

Omlonti® Package insert. Santen Inc. 2022

Timolol Eyedrops to Treat Migrane Headache

- Oral timolol or propranolol are effective in helping prevent migraine HAs, but are ineffective for treating acute HA.
- Oral beta blockers must be metabolized in the liver which is why they are not effective for acute treatment.
- However, "the use of eyedrops has the advantage of attaining peak plasma levels quickly at levels high enough to abort the acute migraine attacks effectively."
- Instill 1-2 drops at the onset of the attack; 80% were significantly helped in 20 min.

JAMA Ophthalmol. Nov 2020

Topical Ophthalmic Timolol in Dermatology

- Timolol is used to treat congenital capillary hemangiomas, and to stop early onset migraine HA.
- Now it has been found to cure a rare, post traumatic vasculodermatopathy.
- Reactive angioendotheliomatosis is a benign vasculoproliferation disease often occurring at the site of traumatic scars.
- Treatment was 0.5% timolol eye drops (two drops three times a day for six weeks)
- It appears that beta adrenergic receptor blockade has a role in some forms of vascular lesions.

JAMA Dermatology, July 2021

Durysta (bimatoprost implant) 10 mcg

- First FDA-approved biodegradable, intracameral implant
- Indicated to reduce IOP in patients with open angle glaucoma or ocular hypertension via a sustained-release drug delivery system
- Reduces IOP approximately 5-8 mmHg
- Most common adverse reaction was conjunctival hyperemia (27%); nonocular was headache (5%)
- Physician's office purchases Durysta and is responsible for entering the procedure code (66030) and special medication code (J-code)

MIGS in Perspective

- "Some MIGS may afford patients with glaucoma greater drop-free disease control than cataract surgery alone."
- "Study data associate the Hydrus® with greater drop-free glaucoma control and IOP lowering than the iStent®; however, these effect sizes were small.

JAMA Ophthalmology. September 2021

The Impact of MIGS in Reducing IOP

- "There is some evidence to support the role of MIGS devices in the current treatment armamentarium for glaucoma with a goal of modest IOP and topical medication reduction."
- "Many previous articles included studies which suffered from limitations including bias, conflicts of interest, industry sponsorship, and a lack of standardized reporting."
- "Hydrus was superior to iStent in terms of both IOP and topical medication reductions postoperatively."
- Further trials are necessary to elucidate the role of MIGS in the glaucoma treatment paradigm.

Survey Ophthalmol, Sept-Oct 2021

Thoughts on MIGS

- "Although MIGS is promising for mild to moderate glaucoma and ideally has a medication-sparing effect, more large clinical trials and longer follow-up are needed. Additionally, more comparative evidence between MIGS and topical medications is needed to determine their place in treatment algorithms,"

Ophthalmology Times, Oct, 2022

Expert Perspective on Rebound Tonometry

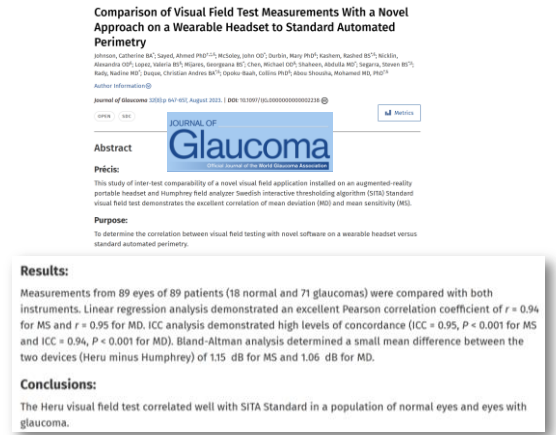
- "The iCare rebound tonometer demonstrated significantly lower test-retest variability than Goldman tonometry with good inter-operator and inter-device reproducibility, supporting it's value in monitoring IOP changes over time aiding clinicians in assessing the effectiveness of glaucoma therapy and consistency of IOP control."
- "Rebound tonometry can characterize IOP changes over time more robustly than Goldman tonometry."

J Glaucoma, August, 2021

Expert Perspective on Self-Tonometry

- "Currently iCare Home is the best option for self-tonometry because it does not require anesthesia and has a system that allows the patient to know when the device is aligned and will get the best possible values."
- "The iCare Home can be used for self-measurement by most trained individuals and IOP measurements obtained using iCare Home tonometry by self- and third-party assessment showed a slight underestimation compared to GAT."

Survey Ophthalmol. Sept-Oct, 2022



Comparison of Visual Field Test Measurements With a Novel Approach on a Wearable Headset to Standard Automated Perimetry

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JOURNAL OF Glaucoma

Official Journal of the World Glaucoma Association

Abstract

Précis:

This study of inter-test comparability of a novel visual field application installed on an augmented-reality portable headset and Humphrey field analyzer Swedish interactive thresholding algorithm (SITA) Standard visual field test demonstrates the excellent correlation of mean deviation (MD) and mean sensitivity (MS).

Purpose:

To determine the correlation between visual field testing with novel software on a wearable headset versus standard automated perimetry.

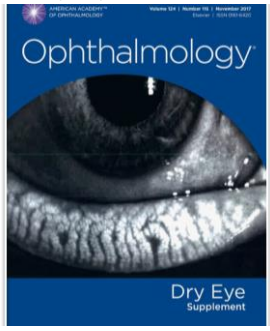
Results:

Measurements from 89 eyes of 89 patients (18 normal and 71 glaucomas) were compared with both instruments. Linear regression analysis demonstrated an excellent Pearson correlation coefficient of $r = 0.94$ for MS and $r = 0.95$ for MD. ICC analysis demonstrated high levels of concordance (ICC = 0.95, $P < 0.001$ for MS and ICC = 0.94, $P < 0.001$ for MD). Bland-Altman analysis determined a small mean difference between the two devices (Heru minus Humphrey) of 1.15 dB for MS and 1.06 dB for MD.

Conclusions:

The Heru visual field test correlated well with SITA Standard in a population of normal eyes and eyes with glaucoma.

Dry Eye Disease

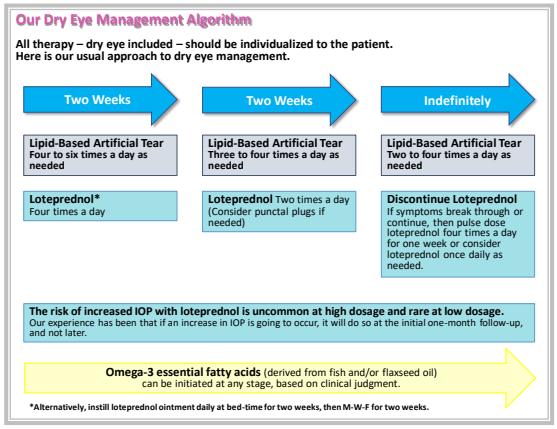


- "Dry eye disease is a heterogeneous disorder of the ocular surface in which the common denominator is inflammation."
- "Topical corticosteroids also play an important role in breaking the inflammatory cycle." "Repeated short-term pulse therapy has produced a disease-free state for more than 1 year in a study of patients with Sjögren's syndrome."
- **"Inflammation is one of the major targets in treating DED, and breaking the cycle of inflammation is crucial in improving symptoms. All patients DED deserve a trial of anti-inflammatory therapy at some point during their treatment." "Corticosteroids are one of the most effective and rapid therapies available for suppressing inflammation on the ocular surface."**
- "Treatment of DED is based on minimizing inflammation and optimizing various components of the tear film."

*Steroids for DED

- "Treat any inflammation on the ocular surface, of course. Start with a topical steroid in "pulse" mode, attempting to quell both the visible inflammation and symptoms quickly without ongoing prescription therapy."

Ocular Surgery News, July 25, 2023



Loteprednol Approved for Dry Eye

- October, 2020 marks the first FDA-approved steroid treatment for DED
- A 0.25% ophthalmic suspension formulation, however, only 2 or 3 shakes is necessary
- Unique "Mucus Penetrating" nanoparticle formulation enhances tear film residency time
- Approved for up to 2 weeks of QID therapy
- Can be "re-pulsed" as needed over time
- "Adverse events and IOP increases were comparable to those seen with vehicle."
- Marketed by Alcon as Eysuvis Ophthalmic Suspension

Literature Perspective on Steroids and Elevated IOP

- "IOP elevation was much more common with older steroids such as dexamethasone, prednisolone and fluorometholone, compared to newer steroids such as loteprednol, difluprednate or rimexolone."
- A note about difluprednate: "Though the occurrence of increased IOP is about 3%, the IOP elevation may be significantly higher compared to the other newer steroids." Only about 2% of patients experience "a clinically significant IOP increase" with loteprednol.
- "Post-operatively, loteprednol did not induce a significant IOP elevation and when used as a replacement for older steroids led to a significant IOP reduction in known steroid responders."

Survey Ophthalmol. March/April 2020

*Vevye™ (Cyclosporine Solution 0.1%)

- Cyclosporine is insoluble in water, however this newer formulation is soluble in water-free, preservative-free "inactive" perfluorobutylpentane (PFBP)
- PFBP by itself is beneficial in treating DED
- Since no water, there is no pH or osmolarity
- "Medical treatment for dry eye has become extraordinarily expensive for patients. Water-free cyclosporine, 0.1% may represent a marginal improvement over Restasis emulsion."
- M+T: We just don't see another cyclosporine bringing anything new to the table.

JAMA Ophthalmol. May, 2023

*The Effect of Topical Cyclosporine

- MOA: "Increases tear production in patients where it's presumed to be suppressed due to ocular inflammation associated with DED."
- What is the predominant cause of most cases of DED? It's not lack of tear production, but increased evaporation secondary to MGD!
- Better plan: Address inflammation with a month long course of loteprednol along with warm soaks and MG expression. Continue control with a PF lipid based artificial tear and punctal plugs.

Rev Optom, March 15th 2023

A Nose for Dry Eye

- Tyrvaya™ (varenicline 0.03%) nasal spray (Varenicline is the same drug as Chantix)
- A cholinergic agonist (parasympathomimetic)
- Used bid, with effectiveness in 4-6 weeks
- Main side effect: sneezing (over 80%)
- Do not shake the bottle
- Store at room temperature
- Two bottles; each good for 15 days 60 sprays/ bottle
- Consult tyrvaya.com for more information
- Marketed as Tyrvaya nasal spray by Oyster Point Pharma

Regener-Eyes for DED

- First in class eye drop
- Contains numerous anti-inflammatory cytokines and growth factors from placental-derived tissue
- Hyaluronic acid for lubrication
- Enhances the lipid layer
- Helps the body to regenerate itself
- Available as Regener-Eyes and Regener-Eyes Lite in a 3 ml sterile bottle
- See regenereyes.com

*Perfluorohexyloctane = Meibo

- A new and unique treatment for DED
- Specifically designed to target MGs
- "Meibo demonstrated statistically and clinically meaningful improvements in the signs and symptoms of DED associated with MGD."
- "Meibo is thought to spread over the ocular surface to form a long-lasting anti-evaporative barrier."
- Dosage is QID for at least 8 weeks
- Meibo contains no water or preservative

Ophthalmology, May, 2023

Neuropathic (DED) Eye Pain

- The best article we have found on this topic is available from:

https://www.ncbi.nlm.nih.gov/books/NBK542282/

Moshirfar M, Benstead EE, Sorrentino PM, et al. Ocular Neuropathic Pain. [Updated 2023 Feb 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.

Oxervate (cenegermin) 0.002% solution for Neurotrophic Keratitis

- FDA-approved in August 2018
- Eye drop delivery of human nerve growth factor
- Dosage: 6 x D (2 hour intervals) for 8 weeks
- Do Not Shake – Very complex administration protocol
- 70% "complete healing" in 8 weeks
- "Orphan Drug" – marketed by Dompe U.S., Boston

Demodex Blepharitis

- Caused by an infestation of the eyelashes and eyelash follicles by Demodex mites, the most common ectoparasite found in humans
- Reasonably common, accounting for 45% of blepharitis cases overall, and 84% in people aged 60 and older
- Symptoms: eyelid margin inflammation, redness, and ocular irritation
- Commonly occurs with rosacea or conditions such as diabetes

Lotilaner Ophthalmic Solution 0.25%

- FDA-approved July 25, 2023
- Lotilaner 0.25% is an anti-parasitic ophthalmic solution to treat demodex blepharitis
- Mechanism of action: inhibits the gamma-aminobutyrid acid (GABA)-gated chloride channels in the Demodex mites to cause paralysis in the mite and its death
- Administered BID for 6 weeks
- Side Effects: instillation site stinging and burning (10%); chalazions and punctate keratitis (<2%)
- Marketed as Xdemvy by Tarsus Pharmaceuticals

Regarding Pupillary Abnormalities

- **If there is:**
  - **No ptosis** -
  No EOM dysfunction

Then it's nothing "bad" and a scan is not indicated

Consider:

Adies, pharmacologic causation, or "discovered" physiologic anisocoria as probabilities

Management of 3rd Nerve Palsy

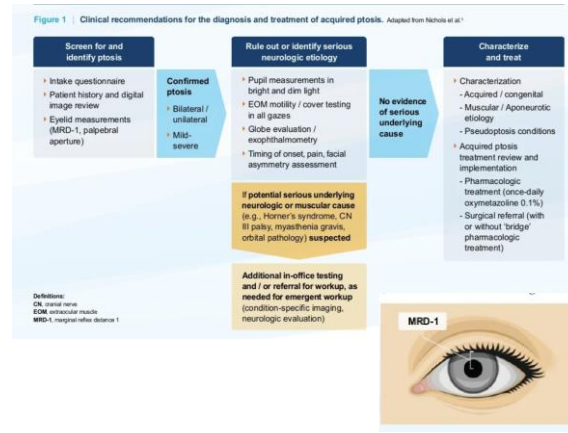
- Pain vs no pain, pupil involvement, or not
  - Does not matter!
- All patients need emergent CTA or MRA
- Send straight to ED; not to an ophthalmologist
- However, about 95% of 3rd N. palsies are simply "microvascular," and not aneurysmal in nature

Foster PJ, et al. JAMA Ophthalmol 2017;135(3):203-4.

Oxymetazoline 0.1% and Ptosis

- Afrin nasal spray = 0.05% oxymetazoline
- To help with acquired ptosis
- Alpha agonist to stimulate muller muscle
- Used once daily as needed
- Provides about .5mm - .7mm of lid rise
- Approved down to age 13
- Duration of effect is not yet known
- Marked as Upneeq (single use vial) by RVL Pharmaceuticals
- Only available via RVL Pharmacy (Upneeq.com)

JAMA Ophthalmol. Nov 2020



*Impact of Blepharodermatologic Microblading

- In this semi-permanent technique, tattoo pigment is deposited into the epidermis via cuts shaped to mimic eyebrow hair to give a more natural appearance.
- The effects of microblading fade as the epidermis sheds and regenerates.
- Tattoo ink can cause delayed hypersensitivity reactions in the eyelid tissue.

Survey Ophthalmol. Nov/Dec, 2022

*Overview of Thyroid Eye Disease (TED)

- Inflammatory autoimmune condition most often presenting with Graves disease
- TED begins with orbital and periocular inflammation
- Patients often suffer from psychosocial distress such as anxiety and depression
- There can be substantial quality of life burden confronting patient with TED, and this newer study finds such QOL impact "is probably a lot poorer than we might have thought."

JAMA Ophthalmol. Feb, 2023

Thyroid Eye Disease and Graves' Disease

- General Observations:
  - Women predominately express orbital involvement
  - Men predominately express late optic nerve compression
  - Diplopia often results from EOM enlargement and fibrosis
  - The "active phase" lasts 12-18 months, then spontaneous remission may occur
  - TED can occur at any time along the Graves' disease continuum
  - Vision compromise is rare, and can occur from exposure keratopathy or optic neuropathy
  - EOM "belly" enlargement mainly involves the inferior and medial recti

Treatment for Thyroid-related Proptosis

- New breakthrough drug to reduce proptosis
- Tepezza™ (teprotumumab) Horizon Therapeutics
- 75% achieved ~2.5mm reduction in proptosis
- I.V. infusion every 3 weeks for 8 sessions
- Mild to moderate side effects:
  - » **Muscle spasm** » **Nausea**
  - » **Alopecia** » **Diarrhea**
  - » **Fatigue** » **Hyperglycemia**
  - » **Hearing loss** » **Dry skin**
  - » **Dysgeusia** » **Headache**
- Cost is about $800,000.00 for 6 month treatment

NEJM January 23, 2020

Update on Teprotumumab (Tepezza®)

- Thyroid eye disease (TED) is a secondary expression of Graves' disease
- Many patients with TED will improve without treatment
- Cost varies: 500K per 150 lb. patient; 800K for obese patients
- Relapse rate after cessation is 40% at 72 weeks
- Main side effects: muscle spasms and nausea in 20%
- In 2020, 463 reports of side effects; 78 were serious
- Other optional approaches: thyroidectomy, a course of IV methylprednisolone for 12 weeks, or radiotherapy

Ophthalmology, August 2021

Clinical Guidance on HCQ Use

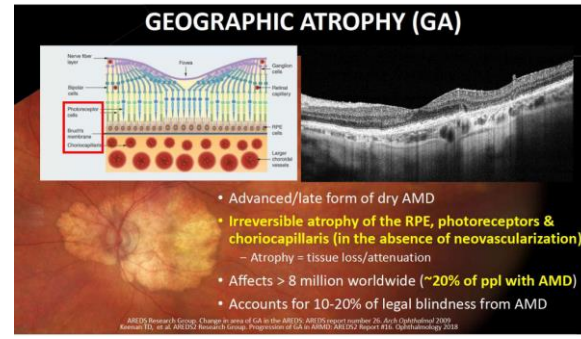
- Recommended dosage 5mg/kg/day
- Excessive dosing is now based on a dose greater than 300mg/day; a significant reduction from the historic use of 400 mg/day.
- High daily dosage relative to body weight and cumulative dose are the primary risk factors for retinopathy
- "Asians represent a vulnerable population because of the combination of possibly increased excessive dosing and an atypical disease pattern.
- Kidney disease and concurrent use of tamoxifen risk factors
- 1 in 4 patients currently overdosed, especially by dermatologists
- Low actual body weight is uniformly a major risk factor
- Never stop HCQ without consultation with the prescriber
- Effective communication within the patient care team is critical
- Proper dosing key to avoiding retinopathy

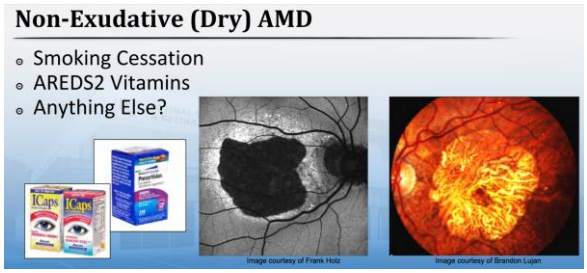
Ophthalmology, July, 2021

Pentosan Polysulfate Sodium (Elmiron) Maculopathy

- Only FDA-approved drug to treat interstitial cystitis (painful inflammation of the bladder)
- FDA-approved in 1996 (same as Xalatan) 100 mg TID
- Like Plaquenil, extended use (about 4 years) can cause a toxic (geographic) maculopathy in approximately 20% of patients.
- Like Plaquenil, visual acuity is initially preserved even with visible maculopathy
- Evaluate annually with OCT and fundus photographs
- Bottom line: in patients taking Pentosan, educate the patient and communicate with their urologist.

Ophthalmology June 2020





*Iveric Bio Receives U.S. FDA Approval for IZERVAY™ (avacincaptad pegol intravitreal solution), a New Treatment for Geographic Atrophy

August 5, 2023

– IZERVAY is the only approved GA treatment with a statistically significant reduction in the rate of GA progression at the 12-month primary endpoint across two Phase 3 clinical trials –

– IZERVAY slowed loss of photoreceptors and disease progression as early as six months –

– GA impacts an estimated 1.5 million people in the U.S. and can cause irreversible vision loss –

The FDA approval was based on the GATHER1 and GATHER2 Phase 3 clinical trials, which evaluated the safety and efficacy of monthly 2 mg intravitreal administration of IZERVAY in patients with GA secondary to AMD. The rate of GA growth was evaluated at baseline, 6 months, and 12 months. In each registrational trial, over a 12-month period, the primary analysis showed a statistically significant reduction in the rate of GA growth in patients treated with IZERVAY compared to sham. Slowing of disease progression was observed as early as 6 months with up to a 35% reduction in the first year of treatment.

"Geographic atrophy has a devastating impact on patients' lives and can lead to irreversible vision loss. As a C5 inhibitor, IZERVAY has shown to slow GA progression by targeting the source of retinal cell death and may preserve the upstream benefits of the complement system. The FDA approval of IZERVAY is great news for the retina community and our patients suffering from GA."

GA impacts an estimated 1.5 million people in the U.S.[1] However, approximately 75% of people living with GA in the U.S. are believed to be undiagnosed.[2] Without timely treatment, an estimated 66% of people with GA may become blind or severely visually impaired.[3]

Across the GATHER clinical trial program, the most common adverse reactions (≥ 5%) reported at 12 months in patients who received IZERVAY 2 mg were conjunctival hemorrhage (bleeding beneath the clear lining of the eye: 13%), intraocular pressure (increased fluid pressure of the eye: 9%) and blurred vision (8%).

IZERVAY met its primary endpoint in the GATHER1 (NCT02686658) clinical trial and the GATHER2 (NCT04435366) clinical trial, both of which were randomized, double-masked, sham-controlled, multicenter Phase 3 clinical trials. These trials evaluated the safety and efficacy of monthly 2 mg intravitreal administration of IZERVAY in patients with GA secondary to AMD. For the first 12 months in both trials, patients were randomized to receive either IZERVAY 2 mg or sham monthly. There were 286 participants enrolled in GATHER1 and 448 participants enrolled in GATHER2. The primary efficacy endpoints in both pivotal studies were based on GA area measured by fundus autofluorescence at three time points: baseline, month 6, and month 12. Safety was evaluated in over 700 patients with GA across the two trials.

*National Eclipse Map

Solar and Laser Retinopathy

- Similar pathophysiology: DDx- good Hx
- Central scotoma with mild to moderate reduction in BVA
- Small, focal yellowish macular lesion
- OCT: Compromise to RPE and outer layers
  - Inner layer involvement in severe damage
- Light energy is absorbed by RPE resulting in heat damage to the tissue
- Some recovery of vision may occur over several months

Antibacterial Medications

- Sulfa Preparations
- Erythromycin
- Bacitracin
- Bacitracin / Polymyxin B
- Bacitracin / Polymyxin B / Neomycin
- Chloramphenicol
- Gentamicin
- Tobramycin
- Trimethoprim / Polymyxin B

MIC_{90} Comparisons for ARMOR Surveillance Study Isolates

2020 ARMOR SURVEILLANCE DATA: MIC_{90} COMPARISONS FOR STUDY ISOLATES

	S. aureus		MRSA		CoNS		MRCoNS	
	2015 (n=100)	2020 (n=286)	2015 (n=48)	2020 (n=163)	2015 (n=98)	2020 (n=156)	2015 (n=48)	2020 (n=87)
Besifloxacin	0.25	1	2	2	0.25	2	4	4
Vancomycin	1	1	1	1	2	2	2	2
Trimethoprim	2	4	2	2	32	>128	>128	>256
Moxifloxacin	1	4	1	16	1	16	32	32
Gatifloxacin	2	4	16	16	2	16	32	32
Ofloxacin	8	>8	>8	16	8	>8	>8	32
Ciprofloxacin	8	128	256	256	8	64	64	64
Tobramycin	1	128	>265	256	4	16	16	32
Azithromycin	>512	>512	>512	>512	>512	>512	>512	>512

As a reminder, the lower the MIC_{90}, the more potent the anticipated efficacy.
*CoNS = coagulase-negative *Staph.* species, of which the majority are *Staph. epidermidis*.
Source: Asbell PA, et al. *JAMA Ophthalmol*. 2015;133(12):1445-1454.
Asbell PA, et al. *JAMA Ophthalmol*. Published Online April 9, 2020.

Differential Diagnosis of Corneal Ulcers vs. Infiltrates

Ulcer (Infection)	***Infiltrate (Inflammation)***
Rare	**Common**
Usually painful	**Mild pain**
Tend to be central	**Tend to be peripheral**
1 to 1 staining defect to lesion ratio	**Staining defect size relatively small**
Cells in anterior chamber	**Rare cells in anterior chamber**
Generalized conjunctival injection	**Sector skewed injection pattern**
Usually solitary lesion	**Can be multiple lesions**
Possible tear lake debris	**Clear tear lake**

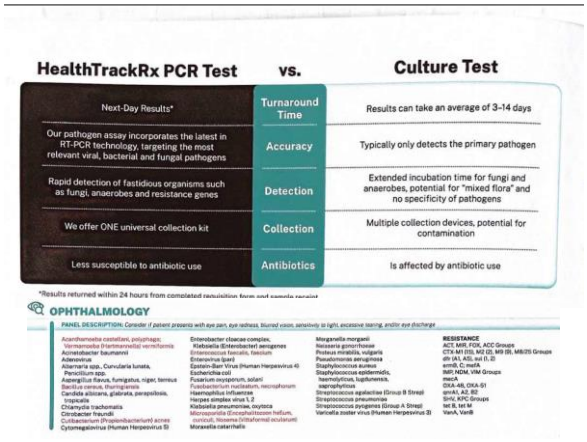
*New Combination for Corneal Ulcers

- Dual therapy for bacterial corneal ulcers has been the standard for decades.
- Tobramycin for gram negative coverage
- Vancomycin for gram positive coverage
- New combination is pre-fortified!
- Tobramycin is 1.5% (standard is 0.3%)
- Vancomycin is 5% (there is no standard)
- Marketed as Fortisite™ ophthalmic solution by ImprimisRx (owned by Harrow Health)
- Must be ordered directly (503A) via Imprimisrx.com or 844-446-6979

*An Updated Perspective on Treating Pseudomal Infection

- "Multiple studies have shown high minimal inhibitory concentrations for moxifloxacin in *P. aeruginosa* as well as a sharp increase in the percentage of *P. aeruginosa* isolates that are resistant to moxifloxacin."
- It seems likely that Fortisite is superior to moxifloxacin but no comparative studies have been done.

JAMA Ophthalmol, June, 2023



Antibiotics - Systemic

- Penicillins
- Cephalosporins
- Tetracyclines
- Macrolides
- Fluoroquinolones

*Statement by the American College of Physicians: Key Recommendations

- For non-purulent cellulitis (skin infections)
- "Recommended antimicrobials: Cephalosporin (e.g. Cephalexin)"
- "Recommended duration: 5 days"

Journal Watch-General Medicine May, 2021

*Oral Azithromycin vs Oral Doxycycline in Treating MGD

- Doxycycline 100 mg twice a day for 6 weeks or oral azithromycin 1g once a week for 3 weeks
- With equivalent efficacy, fewer frequent side effects and a less frequent dosing regimen, azithromycin could be an attractive alternative to doxycycline in patients with MGD. "However, long-term follow-up in each group would be needed to determine if these outcomes persist for this chronic condition."

OSN, July 23, 2023

July 25, 2023

Identifying Children Likely to Benefit From Antibiotics for Acute Sinusitis

A Randomized Clinical Trial

Nader Shaikh, MD, MPH[1]; Alejandro Hoberman, MD[1]; Timothy R. Shope, MD[1]; et al

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Editorial Comment

Key Points

Question In children aged 2 to 11 years with acute sinusitis, does the efficacy of antibiotic treatment differ based on nasopharyngeal colonization with a bacterial pathogen or by the color of the nasal discharge?

Findings Children without nasopharyngeal bacterial colonization (28% of all enrolled) benefited significantly less from antibiotic treatment than children colonized with pathogens. The effect of antibiotics did not differ based on the color of the nasal discharge.

Meaning In children with acute sinusitis, antibiotic treatment had minimal benefit for those without nasopharyngeal bacterial pathogens. The antibiotic effect did not depend on the color of nasal discharge.

Anti-Viral Medicines

Topical

Trifluridine	Viroptic
Ganciclovir	Zirgan

Oral

Acyclovir	Zovirax
Valacyclovir	Valtrex
Famciclovir	Famvir

- These are anti-herpetic drugs and are ineffective against the various adenoviral serotypes -

Topical Antiviral Options

Trifluridine

- Old drug
- Indiscriminate expression
- Potentially toxic
- More frequent dosing
- Refrigerate until opened
- Thimerisol preserved
- Solution (7.5 ml bottle)
- Viroptic and generic

Ganciclovir

- New drug
- Infected cell-specific
- Minimally toxic
- Less frequent dosing
- No refrigeration needed
- BAK preserved
- Gel (5 gram tube)
- Zirgan by B+L

	Acylovir	Valacyclovir	Famciclovir
Zoster Dosage	800 mg 5x a day for 7-10 days	1000 mg TID for 7-10 days	500 mg TID for 7-10 days
Simplex Dosage	400 mg 5x a day for 7-10 days	500 mg TID for 7-10 days	250 mg TID for 7-10 days

Herpes Simplex Keratitis

- 90% of adults harbor the Herpes virus
- Strain-specific expression of the disease
- Unilateral red eye with serous discharge
- Affected cornea has decreased sensitivity
- Males more commonly affected; recur more often
- 40% chance of recurrence within 5 years
- Fellow eye not at risk of involvement (1' and 2')
- Cause of recurrence: trauma, stress, adrenergic and prostaglandin eyedrops, fever, menstruation, climate, UV light
- Treatment: topical or systemic anti-viral

Valacyclovir vs. Acyclovir for Recurrent HSV

"One-year suppression therapy with oral valacyclovir (500-mg tablet daily) was shown to be as effective and as well-tolerated as acyclovir (400-mg tablet twice daily) in reducing the rate of recurrent ocular HSV disease."

Herpes Zoster Vaccination (Shingrix)

- Shingrix is the 2nd vaccine to be FDA approved to help prevent shingles.
- Approved for people aged 50 and older
- A non-live vaccine (Zostavax is live, attenuated)
- Administered in 2 - I.M. doses (initially then 2-6 months later)
- About 90% effective and maintained over four years
- If the last Zostavax vaccine was at least 5 years ago, can have Shingrix
- Marketed by GlaxoSmithKline

Facts on Shingles

- Incidence is on the rise, and at increasing earlier ages
- Mean age of event: 52
- Patients who have had HZO should be examined "within several weeks before and after vaccination against herpes zoster" because they may be at risk for recurrent eye disease.
- We should "recommend strongly" that patients over 50 get Shingrix.
- Our advocacy could "play an important role in increasing vaccination rates."
- About 10% of people have a reaction to Shingrix, more after the second dose

Reference: Ophthalmology, Nov 2018

Herpes Zoster Ophthalmicus

- Acute vesicular eruption of ophthalmic division of 5th cranial nerve
- Etiology: varicella-zoster virus; more common after 50 or in the immuno-compromised
- Symptoms: skin pain most common
- Ocular involvement in 50%
  - more common - zoster epithelial lesions, anterior uveitis, stromal keratitis, episcleritis
  - Tx: valacyclovir 1000mg tid for 1 wk; famciclovir 500 mg tid for 1 wk; acyclovir 800mg 5x d for 1 wk
  - If ocular involvement, treat with topical steroids