

Innovations in Eye Care

A Rapid-Fire Presentation


What's Here, What's Coming, and What You Need to Know

February 2, 20/20

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A Rapid-Fire Presentation
What's Here, What's Coming, and What You Need to Know

Greg Caldwell OD, FAAO
Delaware Optometric Association
Winter Thaw Seminar
February 2, 20/20


Disclosure Statement
(next slide)



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Disclosures- Greg Caldwell, OD, FAAO

- Will mention many products, instruments and companies during our discussion
- I don't have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association - President 2010
 - POA Board of Directors 2006-2011
- American Optometric Association, Trustee 2013-2016
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Aerie, Alcon, Allergan, BioTissue, OptoVue
- Advisory Board: Allergan, Sight Sciences, Sun, Takeda
- Involve: PA Medical Director, Credential Committee
- Optometric Education Consultants- Scottsdale, St. Paul, Quebec City, Nashville, and Orlando/Disney OCT Users meeting; Owner



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Financial Obligations



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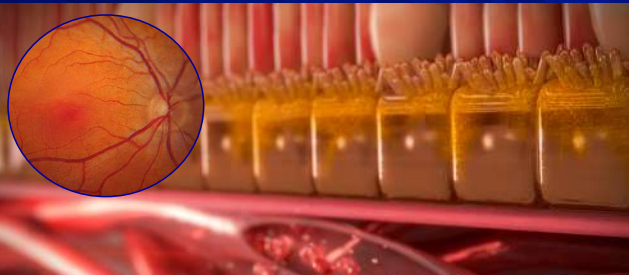
Course Description and Learning Objectives

This course will reveal, feature, and spotlight innovations in primary eye care that will impact every optometrist. Technologies, pharmaceuticals, products, services, and processes that advance eye care will be discussed in a rapid-fire presentation. This course will keep you "in the know" for delivering advanced patient care.

- Introduce the innovation to the clinician in each of the topic areas
- Discuss how the innovation will impact the diagnosis and treatment in eye care
- Reveal the benefit of embracing the innovation
- Demonstrate how it will impact patient care
- Demonstrate how to integrate the innovation into the clinician's practice
- Enhance the clinician's knowledge of selected innovations that impact eye care

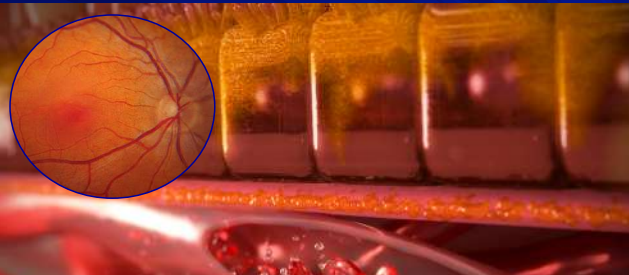
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Healthy Choriocapillaris, Bruch's, RPE, and Photoreceptors

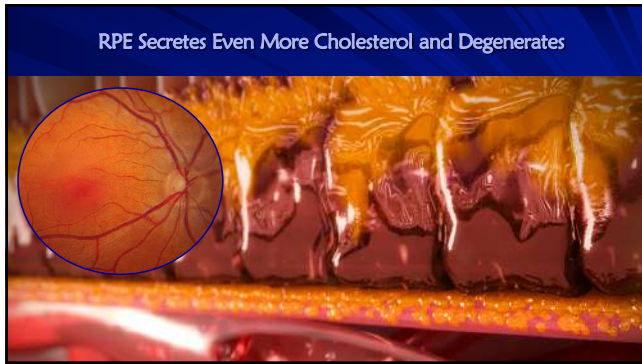


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Cholesterol Barrier Deposited Along Bruch's and RPE



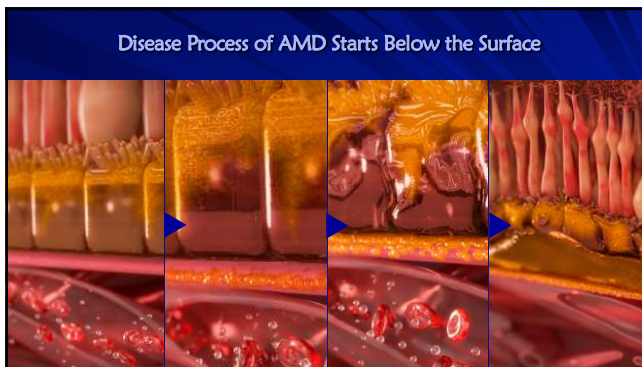
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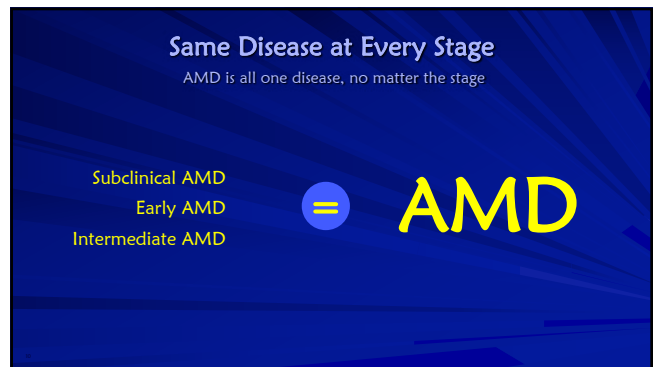
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Impaired Dark Adaptation is Earliest Biomarker of AMD

RESEARCH SHOWS:
 Impaired dark adaptation identifies subclinical AMD **at least three years before** it can be seen with imaging, OCT or clinical exam.

UAB ALSTAR Study
Prospective Study of Subclinical AMD

- Sample consisted of 325 adult's w/o clinically detectable AMD
- At baseline, 24% of the subjects exhibited impaired dark adaptation
- AMD status determined at 3-year follow-up visit

sources: Owsley, C et al. Ophthalmology, 2016;123(2):344-351.


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This Leads to a More Comprehensive AMD Classification System: Structure + Function

PROGRESSION	No AMD		No drusen or small drusen ≤ 63 μm No AMD pigmentary abnormalities
	Subclinical AMD		No drusen or small drusen ≤ 63 μm No AMD pigmentary abnormalities <i>Impaired dark adaptation</i>
	Early AMD		Medium drusen > 63 μm and ≤ 125 μm No AMD pigmentary abnormalities <i>Impaired dark adaptation</i>
	Intermediate AMD		1 large druse > 125 μm and/or Any AMD pigmentary abnormalities <i>Impaired dark adaptation</i>
	Advanced AMD		2 forms: Geographic Atrophy and Neovascular AMD

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Dark Adaptometry Validated in Multi-Site Study




- High Sensitivity**
Correctly identified 90.6% of confirmed AMD cases
- High Specificity**
Correctly identified 90.5% of confirmed normal cases
- High Accuracy**
90.6% overall

sources: Juckoon GR, et al. Invest Ophthalmol Vis Sci. 2014;55(3):1427-1431.

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Dark Adaptation in AMD Function Test

- AdaptDx was First Automated Dark Adaptometer Available for Clinical Use
- Measures how long to recover from bright light to darkness
 - Rod intercept line (RI) time
- Functional test that can help overcome the challenges in diagnosing AMD
- Alabama Study on Early Age-Related Degeneration (ALSTAR)
 - Able to detect subclinical 3 years before clinically visible
 - 325 adults without clinically detectable AMD
- Rod deterioration happens in earliest stages of AMD
 - Earlier detection before visual acuity
- AdaptDx 92284
 - Sensitivity 90.6%
 - Specificity 90.5%



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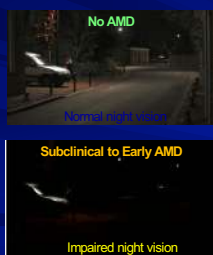
AdaptDx Pro Now Available for Clinical Use



- Handheld Controller with Rechargeable Battery and USB-C Cable
- AdaptDx Pro
- Diopter Adjustments
- LCD Display

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This Means We Now Have an *Early* Symptom We Can Use to Help Diagnose AMD



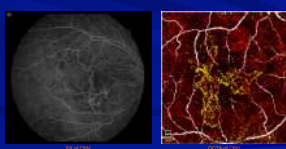
- Night vision impacted in early AMD: 30+ studies
- AMD patients often give up driving at night
- Night vision is impaired before day vision
- Typically ECP's chalk this complaint up to cataracts

Ask Every Patient Over 50 About Their Night Vision

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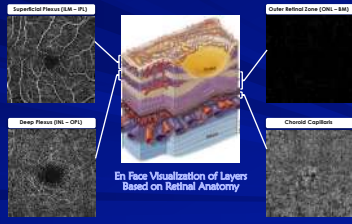
OCT Angiography A New Approach to Protecting Vision

- Non-invasive visualization of individual layers of retinal vasculature
- Pathology not obscured by fluorescein staining or pooling
- Image acquisition requires less time than a dye-based procedure
- Reduced patient burden allows more frequent imaging to better follow disease progression and treatment response



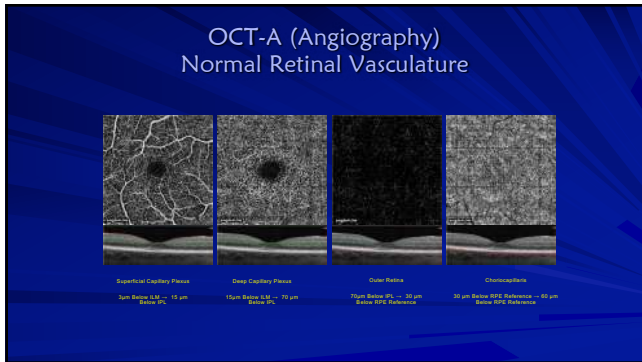
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Enface OCT-A Slabs Based on Retinal Anatomy

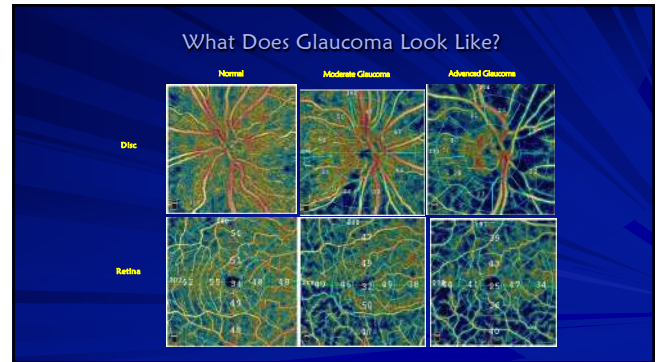


En Face Visualization of Layers Based on Retinal Anatomy

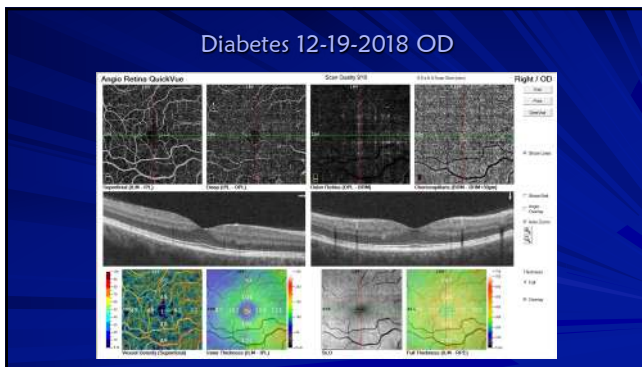
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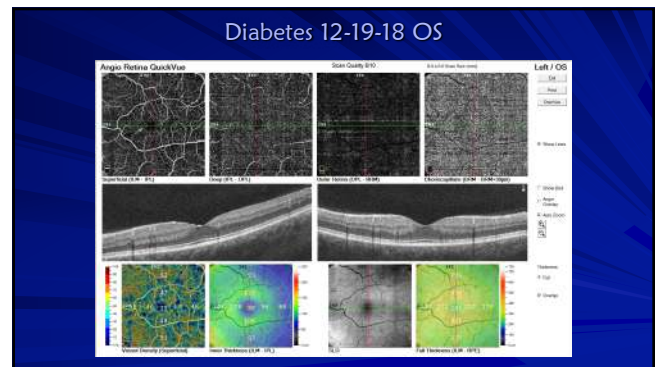
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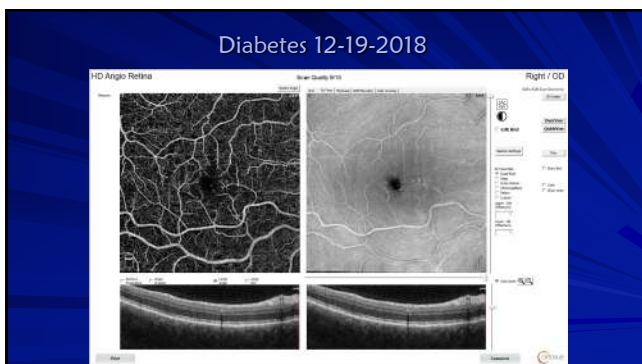
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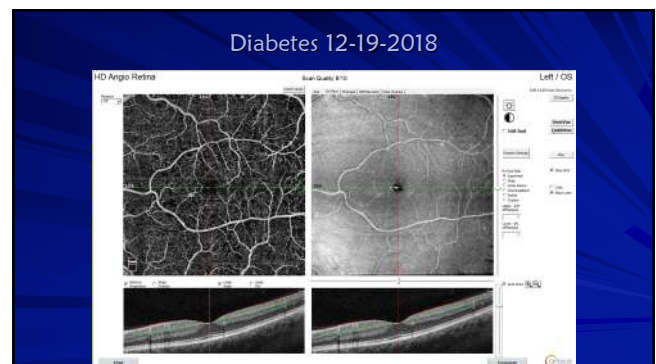
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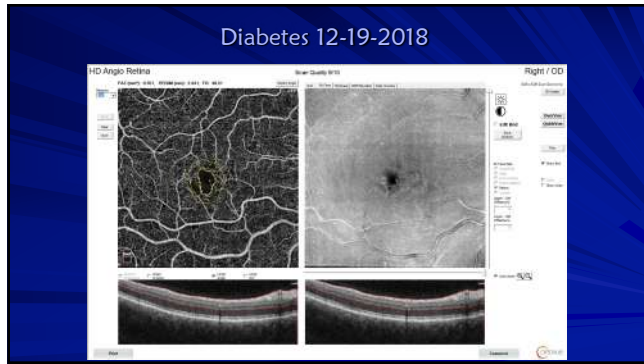
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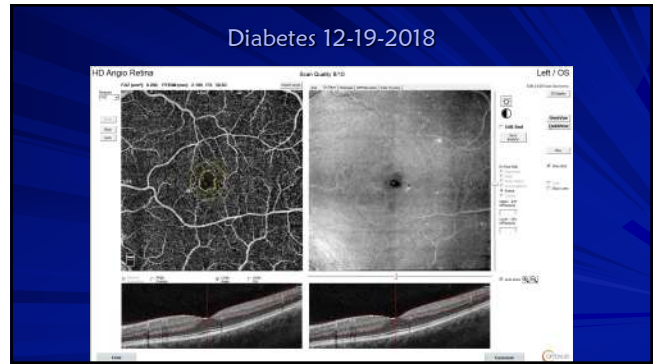
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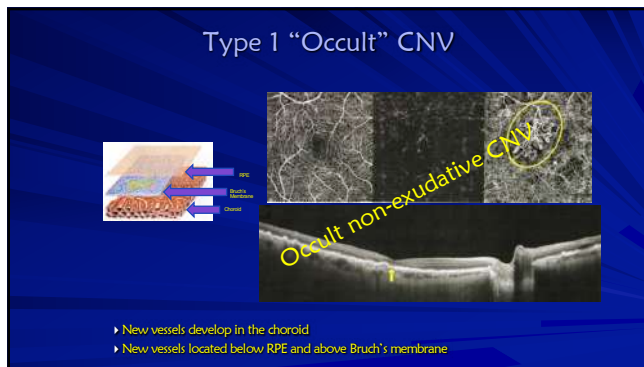
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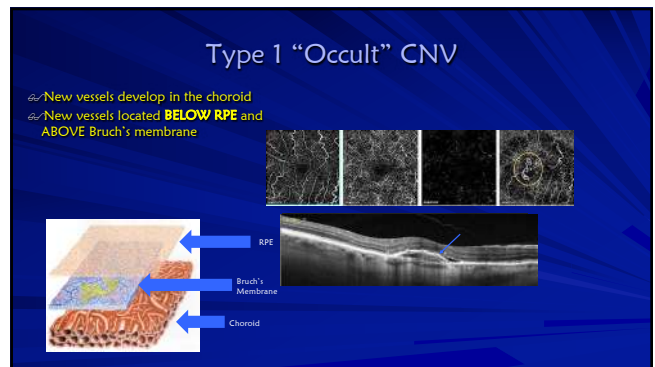
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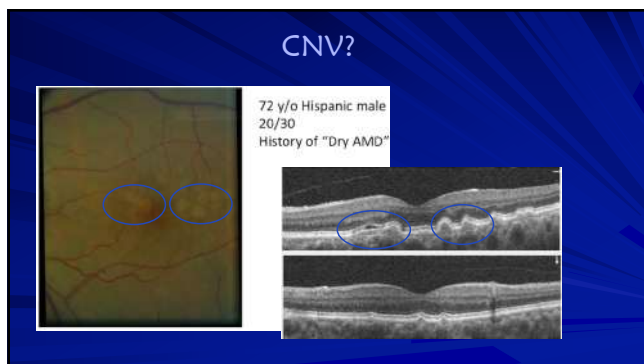
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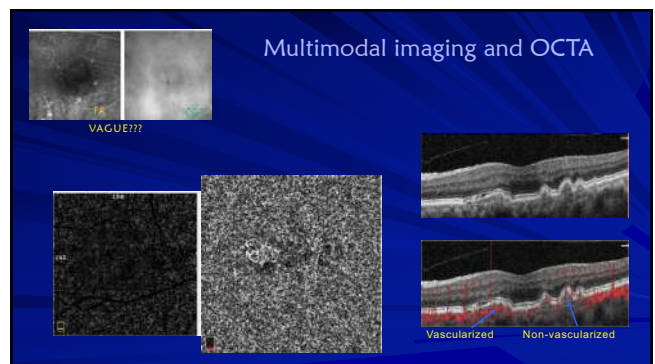
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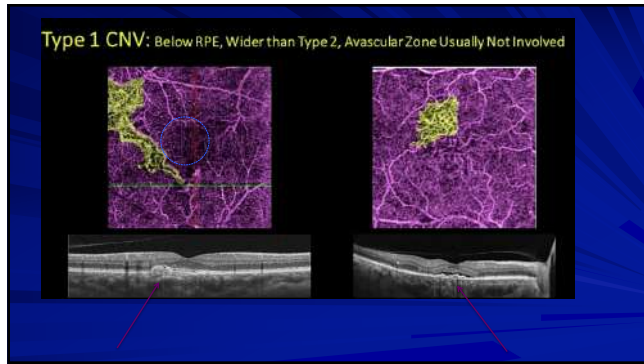
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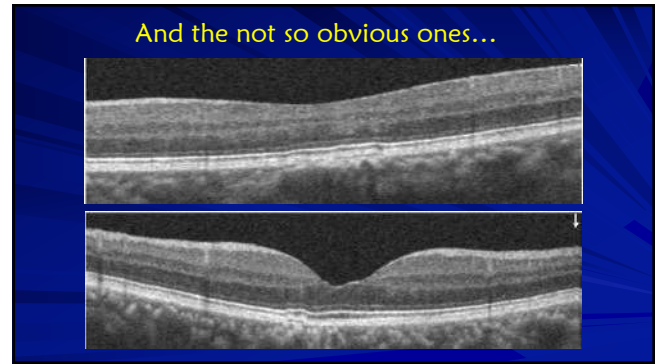
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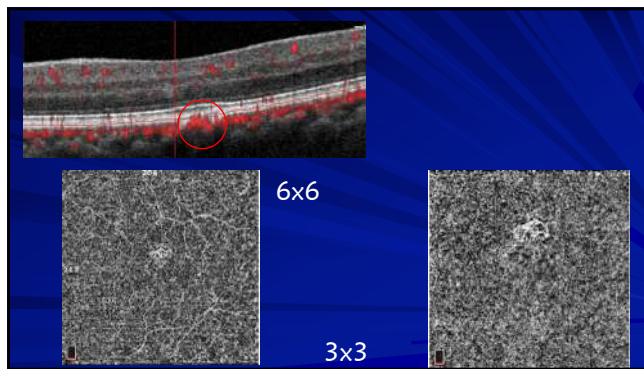
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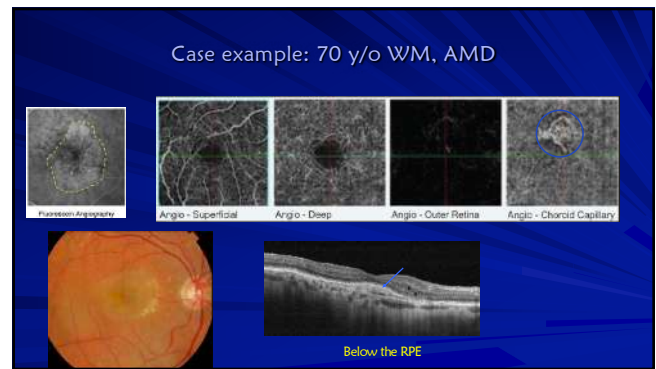
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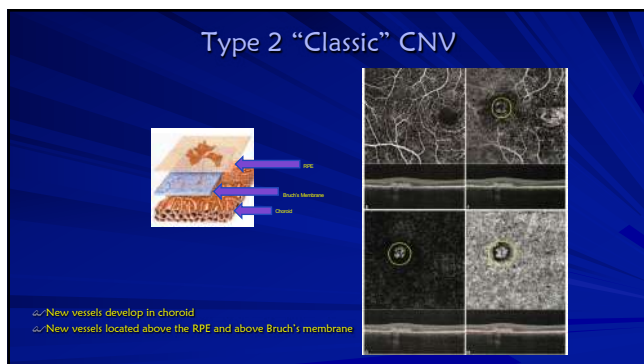
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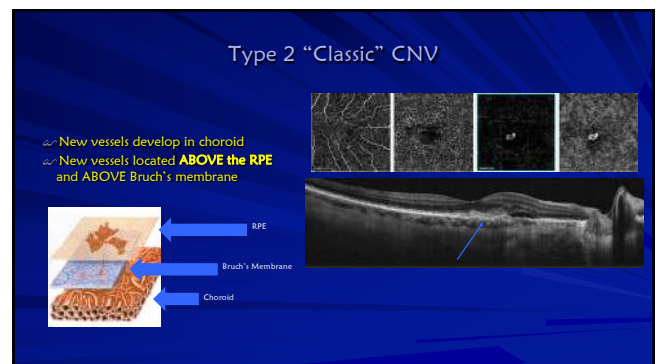
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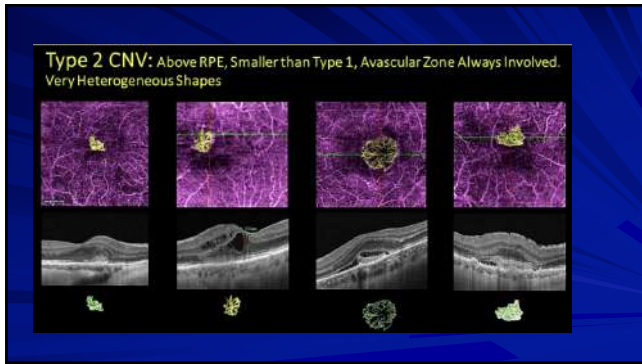
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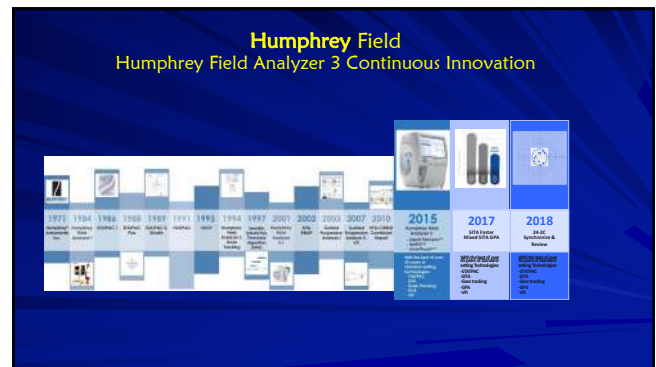
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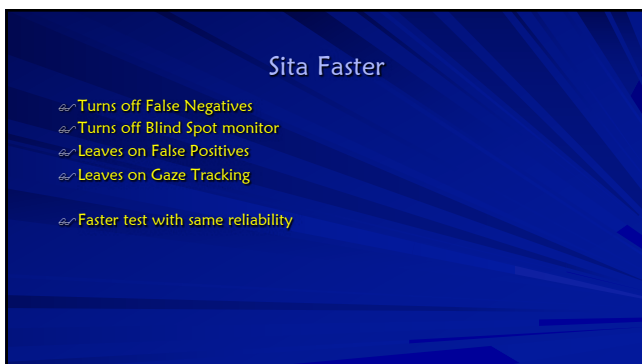
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Sita Faster

HFA3 SITA FASTER RESULTS ARE EQUIVALENT TO SITA FAST AND SITA STANDARD

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Opportunities for Improvement in Central 10 Degrees

Glaucomatous damage of the macula
Doc Siml-Fun Rev. 2014 Jan; 3(2): 1-21
 Donald C. Hood^{1,2,3}, Ali S. Elzay^{4,5}, Carlos Gustavo V. de Moraes^{6,7}, Jeffrey M. Liebmann^{8,9,10} and Robert Ritch¹¹

- Glaucomatous damage of the macula is common and can occur early in the disease
- Can be missed or underestimated or both, with standard 24-2 VF tests that use a 6° grid

The Prevalence and Nature of Early Glaucomatous Defects in the Central 10° of the Visual Field
Invest Ophthalmol Vis Sci. 2014; 55(10): 3333-3341
 Wang, Y., et al. | Donald C. Hood, M.D.,^{1,2,3} Ali S. Elzay, M.A.,⁴ Jeffrey M. Liebmann, M.D.,^{5,6,7} Robert Ritch, M.D.,^{8,9,10,11} Hood, D.C.,¹²

24-2 and 10-2 VF Examples
 Blue cross region on the 24-2 VF = central 10-2 VF
 (A) Both are abnormal.
 (B) 24-2 VF normal; 10-2 VF abnormal
 (C) 24-2 VF abnormal; 10-2 VF normal

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Highest Importance Locations Chosen from 10-2 Pattern

Selecting additional test locations to enhance the 24-2 pattern using a scoring system

- The expert group selected specific 10-2 test point locations
- Prevalence and depth of glaucomatous macular defects were systematically evaluated to select optimum test points
- Pattern covers areas known to be susceptible to glaucomatous defects both from structural and functional studies

Selected test locations are shown in red boxes

The expert group: Donald C. Hood, Stuart K. Gardiner, Allison M. McKendrick and William H. Swanson.

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Resulting SITA Faster 24-2C Pattern on HFA3

The 24-2C test pattern combines all 24-2 points + ten selected 10-2 points (shown in OD orientation)

Large Gray	24-2 pattern
Large Orange	Ten additional 24-2C points
Small Gray	10-2 pattern

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SITA Faster 24-2C showed enhanced sensitivity to detect visual field loss in Central 10 degrees

Evaluation of the SITA Faster 24-2C visual field test

Parameter	NA	Mean (SD)	95% CI	95% CI	95% CI	Parameter	NA	Mean (SD)	95% CI	95% CI	95% CI
Any 10-2	20	0.44(0.52)	0.14(0.40)	0.30(0.50)	0.52(0.42)	Any 24-2	20	0.28(0.45)	0.04(0.33)	0.33(0.43)	0.44(0.42)
Any 10-2 Flag	25	0.36(0.52)	0.12(0.32)	0.24(0.41)	0.45(0.40)	Any 24-2 Flag	20	0.40(0.42)	0.19(0.32)	0.32(0.41)	0.45(0.41)
Any 10-2 Flag	20	0.56(0.50)	0.34(0.40)	0.30(0.41)	0.58(0.41)	Any 24-2 Flag	20	0.32(0.41)	0.21(0.31)	0.30(0.34)	0.40(0.40)
Any 10-2 Flag	20	0.34(0.50)	0.12(0.32)	0.20(0.32)	0.50(0.41)	Any 24-2 Flag	20	0.40(0.42)	0.21(0.32)	0.32(0.41)	0.40(0.40)

- SITA Faster 24-2C showed an enhanced sensitivity to detect visual field loss in the central 10 degrees over the SITA Fast 24-2 pattern
- Increased total and pattern deviation flagging of the ten additional SITA Faster 24-2C points corresponded to the flagging of the same points tested on the SITA Fast 10-2 test

Zeiss ARVO Poster 2018

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Minimize Time and Maximize Information with HFA3

SITA Faster 24-2

- Test in 2 minutes or less
- ~50% faster than SITA Standard: ~30% faster than SITA Fast

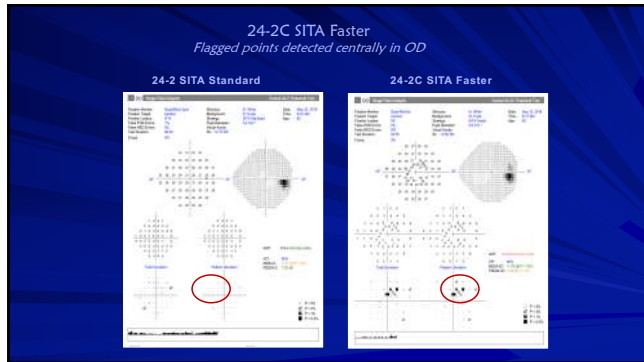
SITA Faster 24-2C

- More information in the central field
- ~20% faster than SITA Fast 24-2

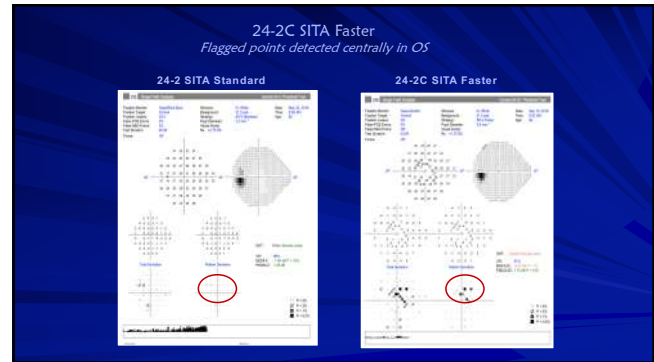
Mixed SITA GPA

- Clinical equivalence of tests allows intermixing SITA Faster, Fast, Standard, 24-2, 30-2, and 24-2C in progression analysis
- Add new tests to patient progression
- Helps immediately adopt SITA Faster

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What is it?

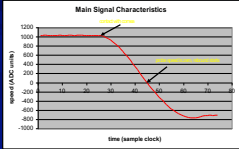
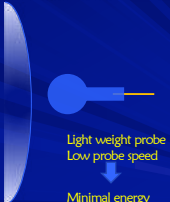
- The Icare® HOME tonometer
 - *Handheld
 - *Battery operated device
 - *Without the need for topical anesthetic
- Intended as an adjunct for monitoring IOP of adult patients (self-use)
- Caregivers in cases where the patient is not able to obtain their own measurements



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Technology

Light weight (26.5 mg) probe touches the cornea with low speed (0.25-0.30 m/s)





Light weight probe
 Low probe speed
 Minimal energy

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Icare® HOME tonometer

- IOP, date, time, eye recognition (right/left) and measurement quality are all stored in the internal memory.
- Data is transferred to a PC for further analysis by the prescribing physician.
- New features: positioning light, automatic eye recognition system, series or single measurements, new user interface panel.




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Icare EyeSmart: Automatic Eye Recognition

The tonometer includes an automatic eye recognition system that identifies which eye is being measured.

- Two infrared LED transmitters below probe (1)
- One infrared LED sensor above probe (2)
- The infrared light is reflected from nose back to the sensor
- The sensor knows from which transmitter the reflected infrared light came from and thus which eye, right or left, was measured
- The resulting eye indication is stored into the memory of the tonometer



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Rebound Tonometry is Safe

- ~ No significant safety issues reported for the Icare® ic100 & TA01i tonometers with a large number sold worldwide (40,000) and in the United States (9,000)
 - * In use by health care personnel with varying degrees of tonometer experience and some of which have little or no ophthalmic training.
- ~ No significant safety issues reported for the Icare® HOME tonometer or its predecessor, Icare ONE; over 2,000 tonometers in use worldwide
 - * Majority in Europe after Icare ONE received CE mark in late 2009 and was introduced in 2010.

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Why 24 Hr Monitoring?

24 hour IOP monitoring can reveal higher peaks and wider fluctuations of IOP than those found during routine office visits. Research reports a steady daily increase in IOP in some patients being treated for glaucoma.

- ✓ Barkana Y, Anis S, Liebmann J, et al. Arch Ophthalmol. 2006;124:793-797.

Studies have shown IOP rises when a patient is supine; IOP peaks were measured upon awakening and declined within 30 minutes.


- ✓ Barkana Y, Anis S, Liebmann J, et al. Arch Ophthalmol. 2006;124:793-797.

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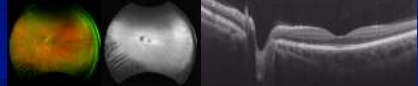
Innovations

Instruments
Wide Field

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The only ultra-widefield retinal imaging device with integrated OCT enabling eye care professionals enhance their clinical exams and improve practice economics

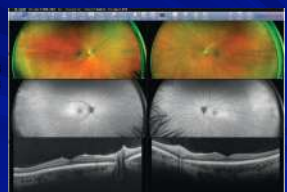



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Monaco...
provides more information faster

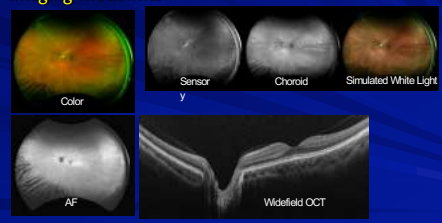
Monaco can capture color and **optomap af** images along with posterior pole OCT scans **of both eyes** in as little as 90 seconds.

This quick, comprehensive look inside the eye has been shown to enhance pathology detection and significantly improve clinic flow.



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Monaco...
imaging modalities



Color, Sensor, Choroid, Simulated White Light, AF, Widefield OCT

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Xelpros™
 (latanoprost ophthalmic solution 0.005%)

- ~ Sun Pharmaceuticals
- ~ Approved September 2018
- ~ Dosage: QD
- ~ Reduce IOP in open-angle glaucoma and ocular hypertension
- ~ Xelpros is the first latanoprost product not formulated with the preservative benzalkonium chloride
 - * Potassium sorbate 0.47% - preservative
- ~ Mechanism of delivery with castor oil
- ~ Reduces IOP in patients with open-angle glaucoma and ocular hypertension
 - * Up to a mean of 6 mm Hg to 8 mm Hg in randomized clinical trials

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Xelpros™
 (latanoprost ophthalmic solution 0.005%)

- ~ Not available in pharmacies
- ~ A direct pay between patient and partnering pharmacies
 - * Capstan Pharmacy
 - * Transition Pharmacy
- ~ Xelpros Xpress offers:
 - * No prior authorizations
 - * No coupon activation
 - * No callbacks
 - * Prompt fulfillment and refills
 - * \$55 for 30 days, \$110 for 90 days



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Rhopressa™ 0.02%
 (netarsudil ophthalmic solution)

- ~ Aerie Pharmaceuticals
 - * Approved December 2017
 - * Treatment of glaucoma or ocular hypertension
 - * Rho kinase inhibitor
 - ROCK-NET inhibitor
 - * Once daily in the evening
 - Twice a day dosing is not well tolerated and is not recommended
 - * Side Effects
 - Conjunctival hyperemia
 - Corneal verticillata
 - Conjunctival hemorrhage

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Rhopressa (ROCK-NET Inhibitor) Triple-Action

3 Identified IOP-Lowering Mechanisms

- ROCK inhibition relaxes TM¹, increases outflow^{1,2}
- NET inhibition reduces fluid production²
- ROCK inhibition lowers Episcleral Venous Pressure (EVP)³

1. Wang SK, Chang RT. An emerging treatment option for glaucoma: Rho kinase inhibitors. *Clin Ophthalmol* 2014;8:883-890.
2. Wang JF, Villalobos JE, Kocopoulos C, Bello JL. Effect of U0124, AR-13324, a ROCK, and norepinephrine transporter inhibitor, on aqueous humor dynamics in rhesus monkey eyes. *J Glaucoma* 2015; 24(1):51-54.
3. Kell AM, Kocopoulos C. Effect of AR-13324 on episcleral venous pressure (EVP) in Dutch Belled rabbits. *ARVO* 2014. Abstract 2000

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Rhopressa™ 0.02% (netarsudil)

Causes Expansion of TM in Donor Eyes
 Increases TM Outflow Facility in Clinic

Trebacular Meshwork (Donor Eyes)

TM Outflow Facility (Healthy Volunteers)

Change (%)

vs. Baseline vs. Placebo

1. Kim R et al. Invest Ophthalmol Vis Sci. 2016;57(14):4997-5009. 2. Su AJ et al. Presented at AOS 2017.

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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	Baseline IOP <25 to <25 mmHg		Baseline IOP ≥25 to <30 mmHg	
	Netarsudil QD	Timolol BID	Netarsudil QD	Timolol BID
Median	-4.2	-4.3	-4.0	-5.3
Mean	-4.1	-4.3	-3.7	-5.3
Max	-10.7	-10.8	-12.3	-12.0

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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

1. RHO-PRESSA® (netarsudil ophthalmic solution) 0.02%. Prescribing Information. 3. 9/2017. Association for Research in Vision and Ophthalmology and International 2017 (E-abstract 081)

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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

Conjunctival hemorrhage

Images were taken from netarsudil subjects
 Source: Courtesy of study investigators AR-13324-C5301, C5302

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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)

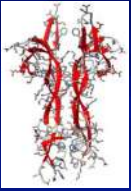
Cornea verticillata

AR-13324-C5302 netarsudil QD subject
 AR-13324-C5302 netarsudil BID subject

Images were taken from netarsudil subjects
 Source: Courtesy of study investigators AR-13324-C5302

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Active ingredient structurally identical to human nerve growth factor produced in ocular tissues



- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons¹
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s¹
- Cenegermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is **STRUCTURALLY IDENTICAL** to the NGF protein²

1. Lippman A, Nemer F, Berez E, Cappelletti G, Alessi F. Topical treatment with human growth factor for corneal neurotrophic status. *Acta Otolaryngol* 1998;118(3):214-20. 2. Lippman A, Nemer F, Berez E, Cappelletti G, Alessi F. Topical treatment with human growth factor for corneal neurotrophic status. *Acta Otolaryngol* 1998;118(3):214-20.


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OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% Weekly Device Kit

- OXERVATE™ is supplied in a weekly carton containing 7 multiple-dose vials*
- A separate weekly Delivery System Kit contains the supplies needed to administer treatment

The Delivery System Kit Contains:

- 7 vial adapters
- 42 pipettes
- 42 sterile disinfectant wipes
- 1 dose recording card
- 1 extra adapter, 3 extra pipettes, 3 extra wipes are included as spares




*Extra drug is available in each vial to take into consideration for loss or spillage during treatment administration

OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/ml) [U.S. package insert]. Boston, MA: Cornea US, Inc.; 2018.

80

OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002%
 Dosing and Administration



OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/ml) [U.S. package insert]. Boston, MA: Cornea US, Inc.; 2018.

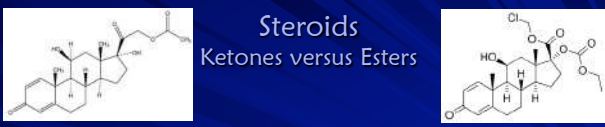
81

Innovation

loteprednol etabonate
 Lotemax

82

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


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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%
- KPI-121 loteprednol etabonate suspension 0.25%

84

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

85

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%

86

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

87

Inveltys™ - loteprednol etabonate suspension 1.0%

- ~ Kala (ka-la) Pharmaceuticals
- ~ August 2018
- ~ Now in distribution centers and pharmacies
- ~ Nanoparticle-based Mucus Penetrating Particles (MPP)
 - * "Amplified Technology"
 - * MOD
 - * Allows drug to penetrate through tear mucins
 - Increased penetration into tissues, 3-fold to other loteprednol
- ~ 1.0% post-operative inflammation and pain after ocular surgery
 - * Dosage BID
 - First ocular corticosteroid to be BID

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KPI-121 loteprednol etabonate suspension 0.25%

Stay Tuned

- ~ Kala (ka-la) Pharmaceuticals
- ~ First product indicated for the temporary relief of signs and symptoms of dry eye disease
- ~ Phase 2 and Phase 3 efficacy and safety trials
 - * STRIDE - Short Term Relief in Dry Eye
 - Over 2000 patients with dry eye disease
- ~ PDUFA date: August 15, 2019
 - * Recruiting more people
 - * Strict inclusion and exclusion criteria

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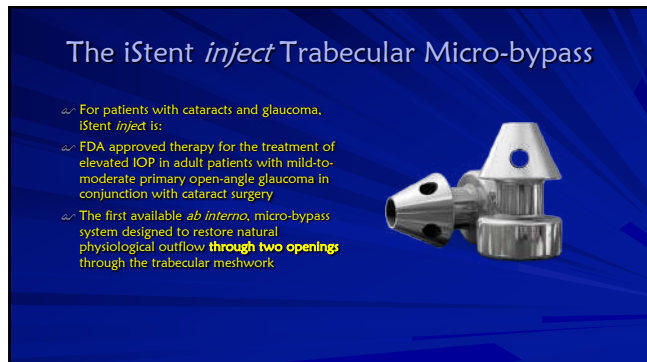
Innovations

Glaucoma

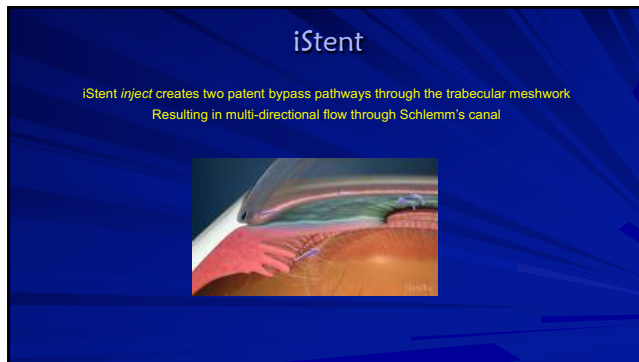
Minimally Invasive Glaucoma Surgery

MIGS

90



91



92



93



94