



Earlier Co-Management of Today's Glaucoma Patient With the Latest Medical Therapies and Drug-Delivery Methods

Dr. Cecelia Koetting

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Host: Dr. Ariel Cerenzie

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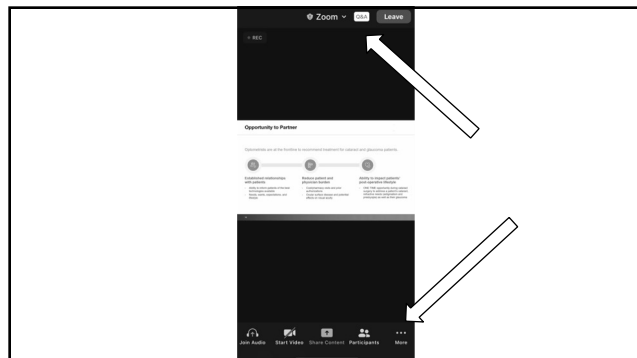
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Speaker Bio –

Dr. Koetting practices at the MD/OD practice Hines Sight in Denver, CO. Her primary focus is in anterior segment and ocular surface disease, neuro-optometry, and peri-operative care. Dr. Koetting is fellow in the American Academy of Optometry, a diplomate of the American Board of Optometry, active member of AOA and has served as both local and state officers in AOA. She was named young Optometrist of the year in 2019 by the state of Virginia, receiving the Vanguard of the Year Award. Dr. Koetting lectures locally, nationally and internationally at conferences and has written for multiple publications.



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Financial Disclosures for Dr. Koetting

Eyevance/Santen Speaker/consultant
 RVL Speaker/consultant
 Thea consultant
 Alkermes consultant
 Bruder consultant
 Allergan consultant
 Vnus consultant
 Orasis consultant
 Johnson and Johnson research
 Tarsus Consultant/research
 Claris Bio consultant
 Avallino consultant
 Alcon speaker/consultant
 Glaukos speaker/consultant
 Ocular Therapeutix Research
 Oyster Point Speaker/consultant
 Dompe Speaker/consultant
 Kala consultant yes
 SightSciences Consultant/speaker

Dr. Cecelia Koetting

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**All financial relationships
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Dr. Cecelia Koetting

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Earlier Co-Management of Today's Glaucoma Patient with the Latest Medical Therapies & Drug-Delivery Methods

Cecelia Koetting OD FAAO DipABO
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Disclosures

- Ocular Therapeutix
- Glaukos
- Horizon
- Quidel
- Eyevance
- Alcon
- Tarsus
- Thea
- Kala
- Ivantis
- Orasis
- RVL
- Oyster Point
- Dompe

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GLAUCOMA PREVALENCE AND PATIENT NEED

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Prevalence of Glaucoma

- **70 million** affected worldwide¹
- Leading cause of irreversible blindness worldwide²
- **3.3 million** in US³
- Glaucoma accounts for **over 10 million** visits to physicians each year⁴
- In terms of Social Security benefits, lost income tax revenues, and health care expenditures, the cost to the U.S. government is estimated to be **over \$2.5 billion** annually⁵



1. Center for Disease Control and Prevention/National Center for Health Statistics, 2010 & 1995
 2. NEI, Report of the Glaucoma Panel, Fall 1998
 3. Ferris FL, Tielsch JM. Archives of Ophthalmology. 2004; Apr 124(4):453-9
 4. Center for Disease Control and Prevention/National Center for Health Statistics, 2010 & 1995
 5. NEI, Report of the Glaucoma Panel, Fall 1998

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The Disease Burden

- Glaucoma is not easily detected and can thus go undiagnosed, thereby leading to an irreversible loss of vision
- Patients experience vision defects in tasks involving central and near vision (e.g. reading, mobility outside the home)
- Glaucoma is a significant predictor of depression

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NORMAL VISION



EARLY GLAUCOMA



ADVANCED GLAUCOMA

Impact of Earlier Detection

If IOP is lowered in time, patients either don't go blind, or the rate of progression is significantly slowed down

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Standard Treatment Options for Glaucoma

Standard Treatment Options

- Glaucoma Medications
- Laser Trabeculoplasty
- Invasive Surgery
 - Trabeculectomy / Shunt
- Micro invasive glaucoma surgery

Challenges

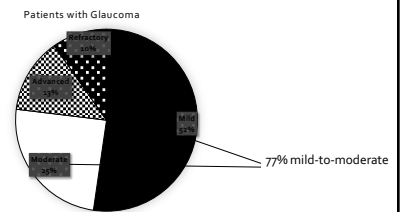
- Long-term exposure to glaucoma medication can cause corneal surface damage
- Non-compliance to medication
 - More than 90% of patients are non-adherent, and nearly 50% stop taking their medications before 6 months¹
- Less durability in laser treatments
- Risks associated with invasive surgery
- Cost burden to patients & system

1. Nordstrom BL. Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol*. 2002;144:1258-1264.

15

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Mild-to-Moderate Glaucoma Predominates



Paradigm Shift to Surgical Options Earlier

1. Data on file, Glaukos Corporation

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Compliance in Glaucoma

- Compliance with glaucoma medications is a huge issue and patients do not use the drops reliably
- For glaucoma patients, estimates of non-compliance were¹
 - 50% non-compliant
 - 16% totally non-compliant
 - 35% improper administration technique



1. Rajurkar K, et al. *Journal of current ophthalmology*. 2018 Jun 1;30(2):125-9.

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Current and Emerging Pharmacological Therapy Options

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Difficulties with Drops

- Irritation on installation and ocular surface toxicity
- Patient compliance
- Patients may have difficulty applying drops accurately, especially for older patients
- Hit or miss of renewal of costly prescriptions that run out at different times
- Ocular redness and ocular adnexa changes over time
- Add to the burden of using medicines day in and day out for a disease that they don't believe they have, cannot feel, or self-monitor

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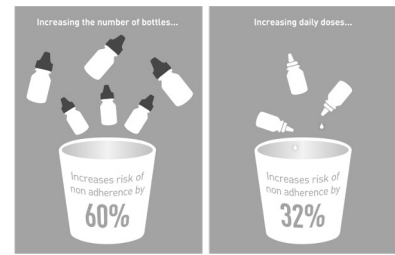
The Problem with Multiple Drops



- Increased exposure to preservatives
- Reduced efficacy with the addition of more drops

Kim CY, et al. British Journal of Ophthalmology. 2017 Jun 1;101(6):801-7.

The Problem with Multiple Drops



- Increased exposure to preservatives
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Kim CY, et al. *British Journal of Ophthalmology*. 2017 Jun 1;101(6):801-7.

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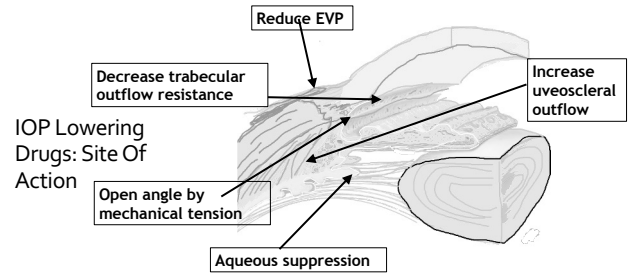
Topical Medications

Topical Medications

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IOP Lowering Drugs: Site Of Action

- Reduce EVP
- Decrease trabecular outflow resistance
- Increase uveoscleral outflow
- Open angle by mechanical tension
- Aqueous suppression

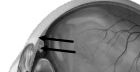


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New Classes of IOL Lowering Drugs

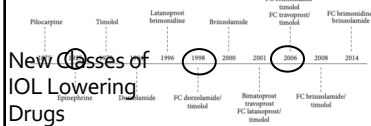
New Classes of IOL Lowering Drugs

- Nitric oxide-donating PGA
- ROCK inhibitors

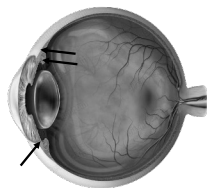


The diagram illustrates the location of the intraocular lens (IOL) within the eye. The IOL is shown as a circular structure in the anterior chamber. An arrow points to the site of drug administration, which is the anterior chamber.

New Classes of IOL Lowering Drugs



- Nitric oxide-donating PGA
- ROCK inhibitors



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Nitric oxide-donating PGA

The diagram illustrates the chemical structures of latanoprost acid and butanediol mononitrate. Latanoprost acid is a cyclopropane derivative with a hydroxyl group, a methyl group, and a side chain containing a double bond and a carboxylic acid group. Butanediol mononitrate is a four-carbon chain with hydroxyl groups at both ends and a nitrate group at the other end. The diagram shows the conversion of butanediol to nitric oxide (NO) and 1,4-butanediol.

latanoprost acid

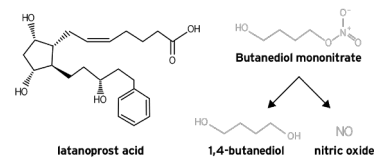
butanediol mononitrate

1,4-butanediol

nitric oxide

- Increase uveoscleral outflow
- Relaxation of Trabecular meshwork and Scleral channel

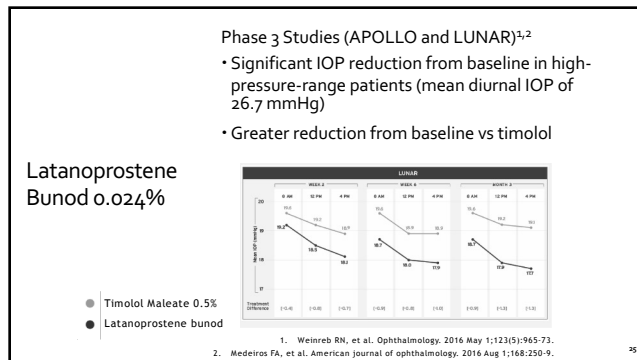
Nitric oxide-
donating PGA



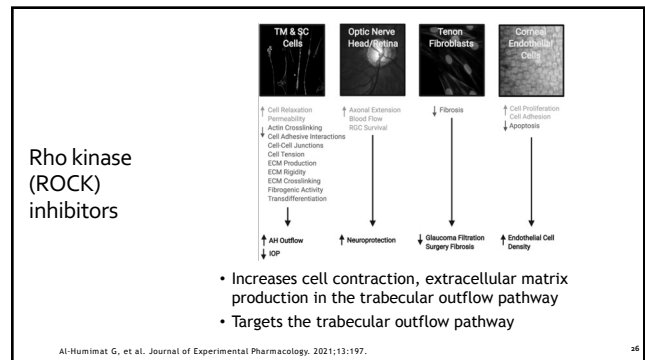
- Increase uveoscleral outflow
- Relaxation of Trabecular meshwork and Scleral channel

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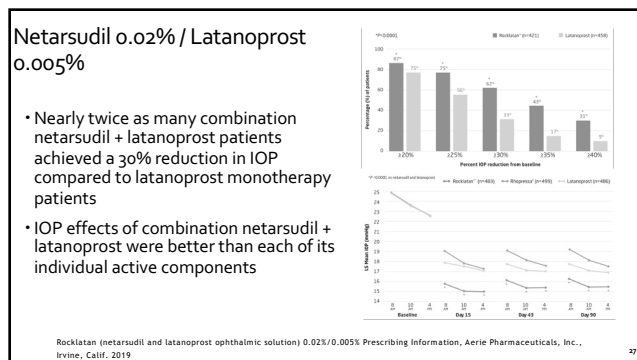
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Compounded Medications

- Preservative free formulations may decrease side effects of topical drops
- Combination therapies may change efficacy and compliance of medications

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Topical Ocular Glaucoma Medication Pipeline

- NCX 470 (Nicox SA)
 - PGA formed from nitric oxide donating compound
 - In phase III
- Cromakalim prodrug 1 (CKLP1) and QLS-101 (Qlaris Bio)
 - New MOA reduction of episcleral venous pressure
 - Animal studies only CKLP-1
 - QLS-101 phase II
- Omidenepag isopropyl (Omdj, Santen)
 - Used in Japan and Asia since 2018
 - Non prostaglandin prostanoid EP2 receptor agonist
 - In FDA review since Feb 2021

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New Drug-Delivery Options

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Need for Sustained IOP Reduction

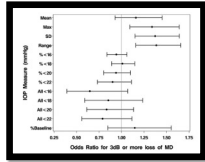
Intraocular Pressure Fluctuation A Risk Factor for Visual Field Progression at Low Intraocular Pressures in the Advanced Glaucoma Intervention Study

Joseph Caporali, MD, Anne L. Coleman, MD, PhD

- IOP fluctuation stronger predictor of progression than average IOP
- Especially in eyes with low average IOP

Intraocular Pressure Control and Long-term Visual Field Loss in the Collaborative Initial Glaucoma Treatment Study

David C. Musch, PhD, MPH^{1,2}, Timothy W. Gillette, PhD³, Louis M. Nishik, MD⁴, Paul R. Lachar, MD⁵, Robin Turner, MD, MPH⁶, Jay M. Cioffi, MD⁷, David H. Kesseler, MD⁸



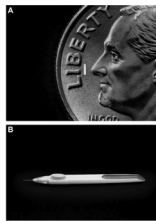
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Potential advantages of sustained release medications

- Improved adherence
- Improved tolerability
- Sustained IOP control
- Higher concentration of target tissue

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Bimatoprost Implant (Durstal-Allergan)



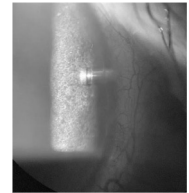
- Currently the only FDA-approved glaucoma drug delivery device
- 1 mm in length, biodegradable, preservative-free, placed into anterior chamber using sterile applicator with preloaded implant and 28-gauge needle
- Delivers drug intracamerally for up to 4 months
- Phase 3 (ARTEMIS) clinical trial: 5 to 8 mm Hg reduction from baseline over 15 weeks

Medeiros FA, et al. Ophthalmology. 2020 Dec 1;127(12):1827-31.

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Travoprost Intraocular Implant (iDose TR - Glaukos)

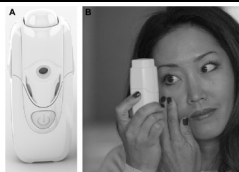
- 1.8 x 0.5 mm biocompatible titanium implant releases a proprietary formulation of travoprost
- Implanted into the trabecular meshwork using an ab interno approach in an operating room
- Phase 2 clinical trial: IOP reduction of 8.3 mm Hg from baseline to 36 months (compared to 8.5 mm Hg in the slow-release arm and 8.2 mm Hg in the timolol arm)



<https://www.moxio.com/news/ophthalmology/20220112/iDose-TR-shows-continued-IOP-reduction-safety-at-36-months>. Accessed May 23, 2022.

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Microdose Latanoprost (EyeNovia)

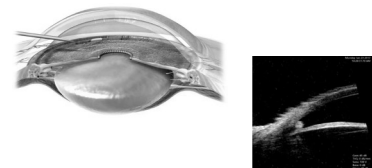


- Patients self-administer micro-dose of latanoprost using 75% less drug and preservative while maintaining efficacy
- Phase 2 clinical trial:
 - Patients were successful 88% of the time (compared to <50% of the time with standard drops)
 - 29% drop in IOP from baseline (consistent with the average 26% decrease of conventional latanoprost eye drops)

Papadimitrakou FA, et al. Clin Ophthalmol. 2018 Nov 28;12:2011-2017.

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Intracanalicular Travoprost Implant (OTX-TP - Ocular Therapeutix)



- Resorbable, preservative free, intracanalicular
- Delivers travoprost to the ocular surface for 90 days
- Phase 3 clinical trial: IOP reduction between 3.27 mm Hg and 5.27 mm Hg

Schlotterbeck V, et al. Invest. Ophthalmol. Vis. Sci. 2020;61(17):3488. Image courtesy of Dr. Paul Singh

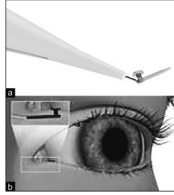
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Punctal Plug with Latanoprost and Travoprost (Evolute - Mati Therapeutics)

- A L-shaped punctal plug utilizing both a latanoprost and travoprost core
- Designed to create a unidirectional flow into the tear film to reduce systemic absorption of the drug
- Phase 2 clinical trial: 20% reduction in IOP at 3 months with 92% retention

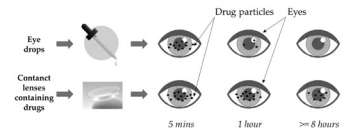


Blum, Shoshana, K. Garbus, N. Zilman, A. Sustained drug delivery platform: A new era for glaucoma treatment. Clinical and Experimental Vision and Eye Research. 2018;2:22-28.

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Drug-Eluting Contact Lenses



- Potential advantages: Large residence time on the eye and upward of 50% bioavailability in comparison with eye drop formulations
- Challenges: Patient compliance, prescription in the lenses, ocular surface disease issues, and replacement schedules.

Li, C.C., Choudhury, A. and Eng, Chem Res 2000, 35: 1718-1724.
Peng, C. C. et al. Biomaterials 2010, 31: 6812-6817.

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IENV515 Aerie

39

iDose Glaukos

40

Evolute Mati
punctal plug

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Bimatoprost
ocular ring
Allergan

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Potential Benefits of Sustained Release Medications

- OSD improvement
- Increased compliance
- Decreased monthly co-pays
- 24 hour treatment

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Challenges of sustained release medications

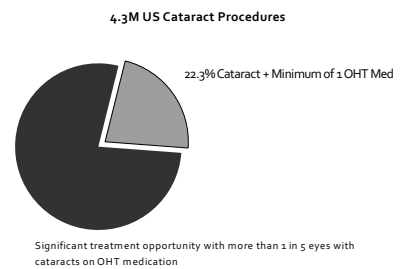
- Risks associated with intraocular procedure
- Optimal dosing frequency still to be determined
- Yet to determine which patients will most benefit
- Unclear if they will be cost effective

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MIGS

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Concomitant Cataract & Glaucoma Patients – US



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Defining MIGS

MIGS ARE:

IOP-lowering surgery with the following characteristics:

1. Minimally traumatic
2. Conjunctiva-sparing
3. High safety profile
4. Rapid recovery
5. Can be combined with cataract extraction or standalone
6. Provides more modest IOP lowering than trabeculectomy

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Defining MIGS

MIGS ARE NOT:

- Necessarily (include or require) a stent
- Only limited to the time of cataract surgery
 - Can be performed as a stand-alone procedure
- Only reserved for moderate or severe disease
 - May be beneficial for those appropriate patients with milder disease

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Why MIGS?

To effectively lower IOP with a minimally-invasive procedure

Advantages:

- Micro-incisional
- Minimal tissue manipulation
- Higher safety profile
- Rapid visual recovery
- Efficacious
- Patient compliance
- Less IOP fluctuation
- Cost to patient
- Ocular Surface

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When should we refer patients for glaucoma related surgery?

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Benefits of Optometric Co-Management

- Familiar with patient's history
- Building rapport with patient and family
- Building rapport with surgeons
 - Allows for best surgical outcome
- Opportunity for growth
- Learn proper management of pre-operative and post-operative care
- Allows you to be better educated about new advancements/technologies

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Indications for Referral for Surgery- When Should You Refer?

- Visually significant cataract
- Maximum medical therapy
- Uncontrolled glaucoma
- Ocular surface disease
- Allergies
- Independence from glasses
- Difficulty with drops
 - Dexterity, insurance/price, dependence on caregiver/family member

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Combined Cataract and Glaucoma Procedures vs. Stand Alone

- Convenience for patient and surgeon
- Increased risk for complications with multiple surgeries
- Only few MIGS procedures can be stand alone
 - OMNI
 - Trabectome
 - ABiC
 - XEN Gel Stent
- Procedures may advance cataract and still can affect vision during postoperative period

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Preparing Patient for Glaucoma Surgery

- Patient education
 - Visual potential
 - MIGS options
 - Drops before and after surgery
- Obtain baseline testing prior to surgery
 - OCT and HVF
 - Need for documentation to determine severity of glaucoma
 - Gonioscopy!
- Communication with surgeon
 - Stage of glaucoma
 - IOP history, surgical history, drop history
 - Patient goals

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Preparing Patients for Ophthalmic Surgery

- Educational pamphlet/information
 - From surgeon's office
 - Brochure provided by your office
- Prepare patients for what to expect during surgery
- Discuss options with patients
 - IOL options
 - Glaucoma procedures
- Discussing both pre- and post-operative care
 - Visual potential
 - Drops
 - Restrictions

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MOA: Gonioscopy

- Gonioscopy-assisted transluminal trabeculectomy (GATT) w/ iTrack (2014)
- Kahook Dual Blade (2015)
- Trabectome (2004)
- TrabEx (2018)

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TrabEx TrabEx+

- Surgical removal of a strip of trabecular meshwork
- TrabEx- has laser-cut sharp blades for TM excision
- TrabEx+ incorporates irrigation-aspiration (I/A)
 - AC pressurization
 - Management of bleeding
 - Maintenance of a good angle view while performing



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MOA: Trabecular Meshwork Bypass

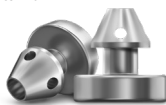
- iStent (2012)
- iStent inject (2018)
- iStent inject (W) (2021)
- Hydrus (2018)

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The iStent inject W Trabecular Micro-bypass

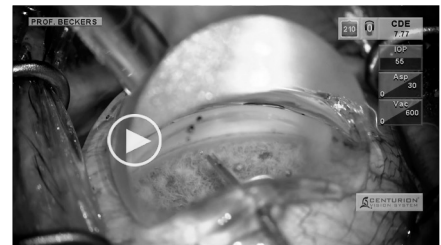
For patients with cataracts and glaucoma, iStent inject W is:

- FDA approved therapy for the treatment of elevated IOP in adult patients with mild-to-moderate primary open-angle glaucoma in conjunction with cataract surgery
- An *ab interno*, micro-bypass system designed to restore natural physiological outflow through two openings through the trabecular meshwork
- Placed during cataract surgery

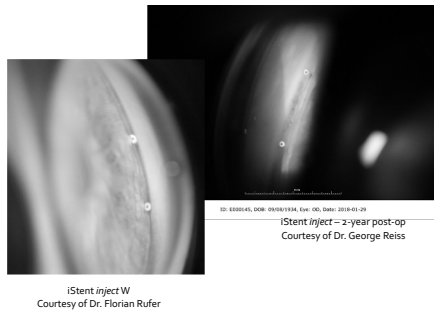


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iStent inject W Surgical Procedure



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Post-Op
Images

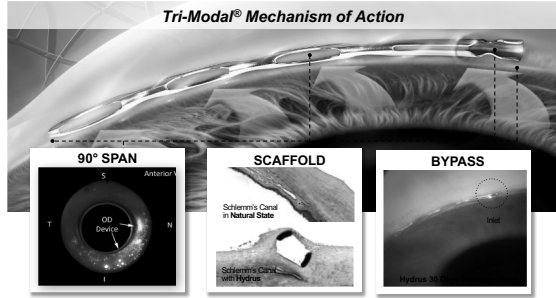
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Hydrus
Microstent

- Flexible, biocompatible 8 mm length microstent
- Made out of nitinol (highly biocompatible material used in cardiovascular stents)
- Contoured to match canal curvature
- Three open windows face anterior chamber
- The canal-facing surface is completely open for unobstructed collector channel access

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Tri-Modal® Mechanism of Action

Source: Gong H, Johnson W, et al. Poster #115
American Glaucoma Society, New York 2013Source: Hays CL, Tello CB, et al. Invest
Ophthalmol Vis Sci. 2014;55:1930-1935

Courtesy of the Ahmed, MD

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HORIZON 3- 5
YEAR
FOLLOW-UP

- HORIZON is unique: only MIGS pivotal study with 5-year continuous follow-up
 - 80% study follow-up of patients at 5 years
- Primary endpoint assessment was based on washed out IOP at 24 months... medication wash out was discontinued after for practical reasons
- Long term effectiveness based on:
 - Medication free
 - Failure rates (progression to surgery)
 - Safety findings (vision, ECD, and adverse events)

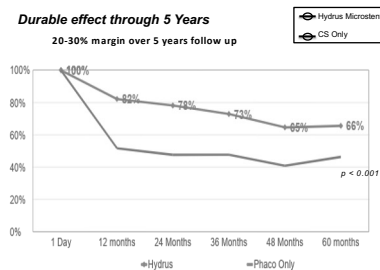
80-0000-1 Rev. A

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HORIZON:
Medication
Free¹

MEDICATION FREE 0-60 MONTHS

Durable effect through 5 Years
20-30% margin over 5 years follow up



80-0000-1 Rev. A 1. Data on file - iSonic, Inc.

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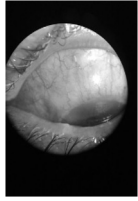
MOA: Dilation

- ABIC w/iTrack (2015)
- Visco 360 (2015)
- iPrime
- Omni (combo)
- Streamline (2022)

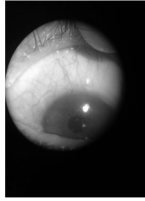
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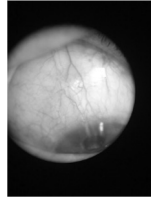
XEN Ab-Interno Bleb Examples



Post-op day 1



Post-op month 12



Post-op month 18

Images courtesy of Francisco Miller, MD, and Vanessa Vora, MD

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MOA: Cyclophotocoagulation

- Endocyclophotocoagulation (ECP)
- Micropulse Diode laser transscleral Cyclophotocoagulation (MP3)

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MOA: Subrachoroidal Space

- Cypass**
- No longer in production

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MIGS Pipeline


- DRAINAGE TO OCULAR SURFACE**
 - Sellacke (Alvisi)
 - Beaumont Aqueous Microshunt (MicroClyx)
- AQUEOUS OUTFLOW AT MESHWORK**
 - Therapeutic Ultrasound for Glaucoma (TUG, EyeSonic)
- Sclerum canal**
 - Istent Inflixite (Glaukos)
 - Prime ViscoDelivery System (Glaukos)
- Suprachoroidal Drainage**
 - Istent Supra
 - MINject
- MIG Bleb Surgeries**
 - PreserFlo MicroShunt (Santner)
 - Minimally Invasive Micro Sclerostomy (MIMS, Sanoculis)

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Thank You!

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CAROTENOIDS:
PRESCRIBING FOR
OCULAR HEALTH & VISUAL
PERFORMANCE



Date: October 20, 2022
Time: 5:30pm - 6:30PM PST
Speaker
Dr. Jennifer Stewart
COPE Accredited CE Credit

Date: October 20, 2022
Time: 5:30 pm PST
Speaker: Dr. Jennifer Stewart
Topic: Carotenoids- Prescribing for Ocular Health and Visual Performance
COPE: 1 hour virtual CE

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If you have any questions, you may send an email to
Dr.CeceliaKoetting@gmail.com

Dr.CeceliaKoetting@gmail.com

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COPE Course# 80467-GL
Course Title: *Earlier Co-Management of Today's Glaucoma Patient With the Latest Medical Therapies and Drug-Delivery Methods*

Dr.CeceliaKoetting@gmail.com

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