1

HEART OF AMERICA EYE CARE CONGRESS

THE PRESENTER HAS THE FOLLOWING FINANCIAL DISCLOSURES

Myze
Azura
Scope
Iveric Bio
Ocular Therapeutix
Glaukos
Horizon
Versea

Trukera
Ivantis
Orasis
Claris Bio
Twenty/Twenty Therapeutics
Aldeyra
Dompe
RVL
Oyster Point

Allergan
Alcon
Visus
Thea
Bruder
Glaukos
Buasch & Lomb

ALL RELATIONSHIPS HAVE BEEN MITIGATED

"Our corporate sponsors are instrumental in making sure the HOAECC is a success. However, our sponsors are not directly involved in the selection, emphasis or development of our educational program."

2

GLAUCOMA PREVALENCE AND PATIENT NEED

3

PREVALENCE OF GLAUCOMA

- **70 million** affected worldwide[1]
- Leading cause of irreversible blindness worldwide[2]
- **3.3 million** in US[3]
- Glaucoma accounts for **over 10 million** visits to physicians each year[4]
- 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** annually[5]

4

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 1;122(4):451-2.
4. Center for Disease Control and Prevention/National Center for Health Statistics, 2010 & 1995
5. NEI, Report of the Glaucoma Panel, Fall 1998

4

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

5

5

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

6

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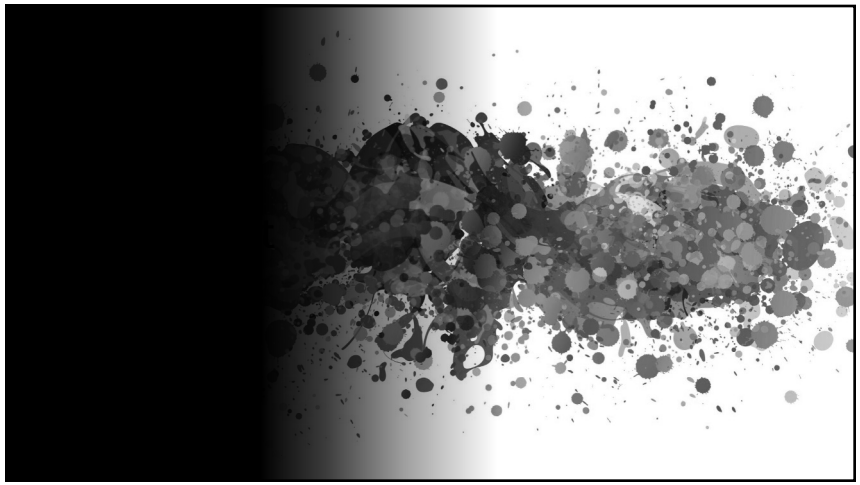


7

Good Detailed History

- Risk Factors
  - FmHx
    - Which family member
  - Age
  - Race
  - HTN
  - DM
  - Heart disease
  - Sleep apnea
  - Corticosteroid use
  - Medications
- High IOP
- Physiologically large CD
- Thinner corneas
- Optic nerve sensitivity
- Narrow angles
- Pseudoexfoliation
- Retinal surgeries
- Hx of Uveitis
- Eyeball length
- Eye trauma

8

Complete exam

- Anterior exam
  - High pressures?
  - Signs of damage or inflammation?
  - ITI defects?
  - Endothelial pigment?
  - Pseudoexfoliation?
  - Angles open? Iris insertion?
  - Anything else?
- Posterior exam
  - Cataracts? What type?
  - Signs of inflammation?
  - Signs of retinal surgery or damage?
  - ONH CD sizing
  - ONH color
  - PPA of beta zone?
  - Hemorrhage?

9

Standard of Care for Diagnosis and Management

- OCT
- Visual Field
- Pachymetry
- Gonioscopy
- Intraocular pressure

10

ADDITIONAL INFORMATION

- Corneal hysteresis
- OCT anterior segment
- Fundus photography

11

INTRAOCULAR PRESSURE UPDATES

12

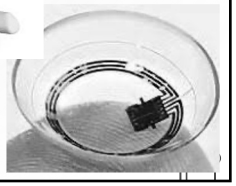
IN OFFICE IOP

- Applanation Tonometry
  - Goldman Applanation Tonometry
    - Gold standard
    - Based on average corneal thickness of 520 micr
    - Perkins is a portable version
  - New technology/design
    - CATS Tonometer Prism
    - Disposable Goldman tips
- Indentation Tonometry
  - Tono-pen
- Rebound Tonometry
  - iCare
    - IC200
- Non Contact tonometry
  - Ocular Response Analyzer

13

AT HOME IOP

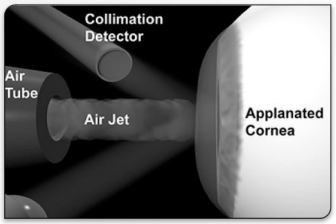
- iCare Home
  - At home device to check
- Sensimed Triggerfish contact lens
  - Continuous 24 hour monitoring



14

CORNEAL HYSTERESIS

- CH is not an inherent property of the cornea, but rather reflects how the cornea reacts to an external force.
- The average CH in normal eyes has been shown to range from 9.6 to 10.7 mmHg with strong correlation between the two eyes of the same patient, whereas mean values in POAG are lower and range from from 8 to 10 mmHg



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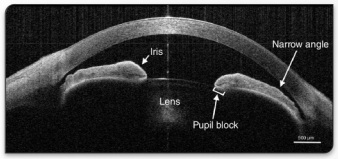
OCT ANTERIOR SEGMENT



- Angle evaluation
- Useful as an adjunct to gonioscopy as well as a substitute when gonioscopy is not feasible due to corneal pathology or lack of patient co-operation

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DIAGNOSING AND STAGING

17

VISUAL FIELD UPDATES

- Virtual helmet/goggles visual fields
  - Smaller footprint
  - Cost
  - Portable

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MEDICARE

STAGING GLAUCOMA (MEDICARE SYSTEM)

Stage	Code	Optic Nerve	RNFL	Visual Field
Early/Mild	H40.1131	Abnormalities consistent with glaucoma	Changes consistent with glaucoma	No abnormalities on standard visual field. (Abnormalities may be present on SWAP or FDT.)
Moderate	H40.1132	Abnormalities consistent with glaucoma	Changes consistent with glaucoma	Abnormalities in one hemifield, but not within 5 degrees of fixation
Advanced/ Severe	H40.1133	Abnormalities consistent with glaucoma	Changes consistent with glaucoma	Abnormalities in both hemifields, and/or loss within 5 degrees of fixation in one or both hemifields

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CASE 1ANSWER:
MODERATE STAGE OD
ADVANCED STAGE OS

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CASE 2ANSWER:
MODERATE STAGE OD
GLAUCOMA SUSPECT OS

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STANDARD TREATMENT OPTIONS FOR GLAUCOMA

Standard Treatment Options	Challenges
Glaucoma Medications	Long-term exposure to glaucoma medication can cause corneal surface damage
Laser Trabeculoplasty	Non-compliance to medication
Invasive Surgery	–More than 90% of patients are non-adherent, and nearly 50% stop taking their medications before 6 months[1]
Trabeculectomy / Shunt	Less durability in laser treatments
Micro invasive glaucoma surgery	Risks associated with invasive surgery
	Cost burden to patients & system

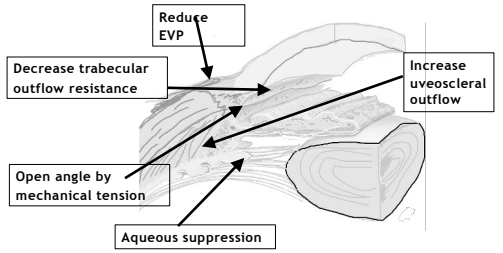
1. Nordstrom BL. Persistence and adherence with topical glaucoma therapy. Am J Ophthalmol. 2005;140:598–606.

22

TOPICAL TREATMENT UPDATES

23

IOP Lowering Drugs: Site Of Action



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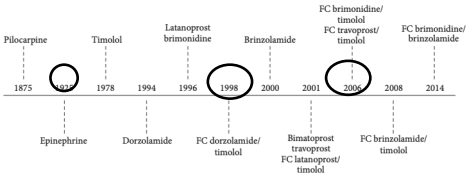
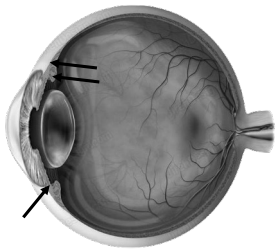
New 'ish' Classes of IOL Lowering Drugs

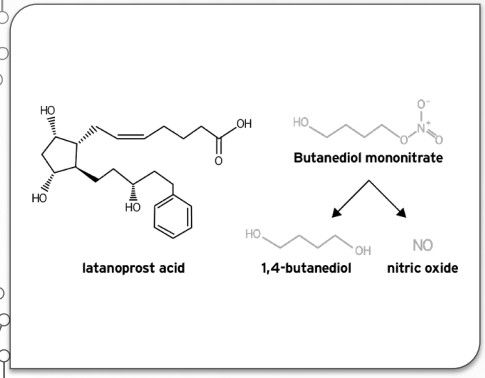




- Nitric oxide-donating PGA
- ROCK inhibitors

25

25



NITRIC OXIDE-DONATING PGA

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

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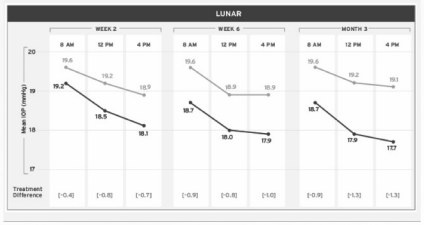
LATANOPROSTENE BUNOD 0.024%

Phase 3 Studies (APOLLO and LUNAR)[1,2]

- Significant IOP reduction from baseline in high-pressure-range patients (mean diurnal IOP of 26.7 mmHg)
- Greater reduction from baseline vs timolol



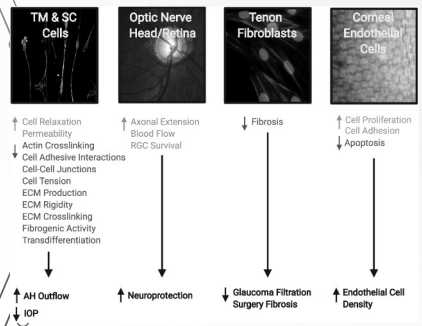
Timolol Maleate 0.5%
Latanoprostene bunod

27

1. Weinreb RN, et al. Ophthalmology. 2016 May 1;123(5):965-73.
2. Medeiros FA, et al. American journal of ophthalmology. 2016 Aug 1;168:250-9.

27

RHO KINASE (ROCK) INHIBITORS

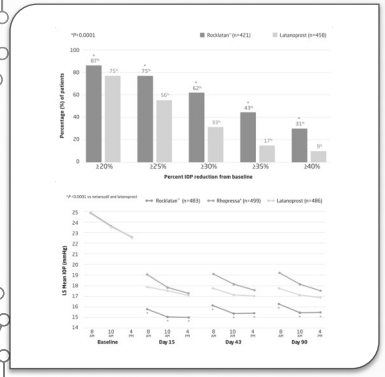


- Increases cell contraction, extracellular matrix production in the trabecular outflow pathway
- Targets the trabecular outflow pathway

28

Al-Humimat G, et al. Journal of Experimental Pharmacology. 2021;13:197.

28

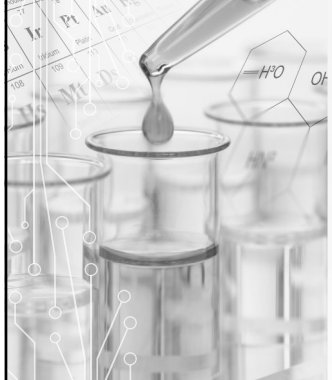


NETARSUDIL 0.02% / LATANOPROST 0.005%

- Nearly twice as many combination netarsudil + latanoprost patients achieved a 30% reduction in IOP compared to latanoprost monotherapy patients
- IOP effects of combination netarsudil + latanoprost were better than each of its individual active components

Rocklatan (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% Prescribing Information, Aerie Pharmaceuticals, Inc., Irvine, Calif. 2019

29



PRESERVATIVE FREE TOPICAL GLAUCOMA TREATMENT OPTIONS

- Iyuzeh
  - Preservative free Latanoprost

30

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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NEW DRUG-DELIVERY OPTIONS

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NEED FOR SUSTAINED IOP REDUCTION

Intraocular Pressure Fluctuation

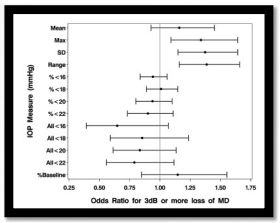
A Risk Factor for Visual Field Progression at Low Intraocular Pressures in the Advanced Glaucoma Intervention Study

Joseph Caprioli, 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] Brenda W. Gillespie, PhD,[3] Leslie M. Niziol, MS,[1] Paul R. Lichter, MD,[1] Rohit Varma, MD, MPH,[4] for the CIGTS Study Group*



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ADVANTAGES OF SUSTAINED RELEASE MEDICATIONS

- Improved adherence
- Improved tolerability and corneal sparing
- Sustained IOP control
- Higher concentration delivery to target MOA

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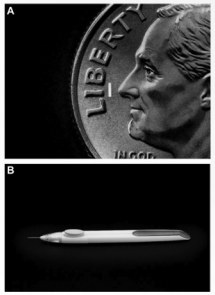
BIMATOPROST IMPLANT (DURYSTA-ALLERGAN)



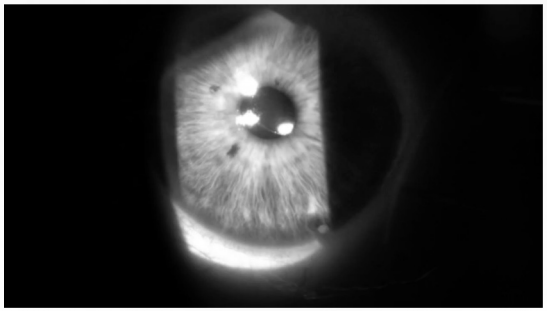
- Currently the only FDA-approved glaucoma drug delivery device
- 1 mm in length, biodegradable, preservative-free, placed into anterior chamber using sterile applicator with preloaded implant and 28-gauge needle
- Delivers drug intracamerally for up to 4 months
- Phase 3 (ARTEMIS) clinical trial: 5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

35

Medeiros FA, et al. Ophthalmology. 2020 Dec 1;127(12):1627-41.

35

SULCUS DURYSTA



Video courtesy of Dr. Nathan Radcliffe

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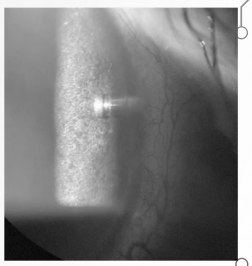
TRAVOPROST INTRAOCULAR IMPLANT (IDOSE TR - GLAUKOS)

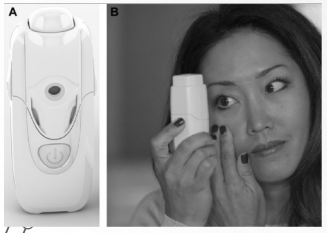


- 1.8 x 0.5 mm biocompatible titanium implant releases a proprietary formulation of travoprost
- Implanted into the trabecular meshwork using an ab interno approach in an operating room
- Phase 2 clinical trial: IOP reduction of 8.3 mm Hg IOP from baseline to 36 months (compared to 8.5 mm Hg in the slow-release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

https://www.healio.com/news/ophthalmology/20220112/idose-tr-shows-continued-iop-reduction-safety-at-36-months. Accessed May 23, 2022.

37

MICRODOSE LATANOPROST (EYENOVIA)



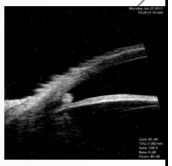
- Patients self-administer micro-dose of latanoprost using 75% less drug and preservative while maintaining efficacy
- Phase 2 clinical trial:
  - Patients were successful 88% of the time (compared to <50% of the time with standard drops)
  - 29% drop in IOP from baseline (consistent with the average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

38

Pasquale LR, et al. Clin Ophthalmol. 2018 Nov 28;12:2451-2457.

38

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

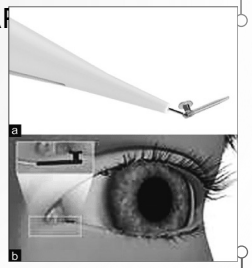
39

Srilatha V, et al. Invest. Ophthalmol. Vis. Sci. 2020;61(7):3488.
Image courtesy of Dr. Paul Singh

39

PUNCTAL PLUG WITH LATANOPROST AND TRAVOPROST (EVOLUTE - MATI THERAP

- 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



40

Blum-Shouchane K, Geffen, N, Zahavi, A.Sustained drug delivery platforms-A new era for glaucoma treatment. Clinical and Experimental Vision and Eye Research. 2019;2:22-29.

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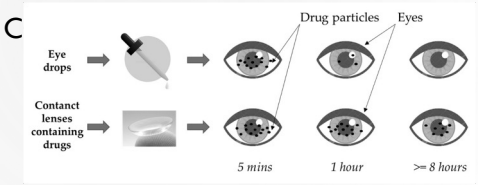
DRUG-ELUTING C

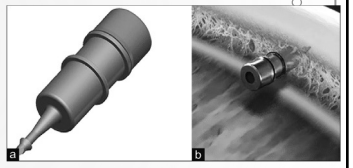


- Potential advantages: Large residence time on the eye and upward of 50% bioavailability in comparison with eye drop formulations
- Challenges: Patient compliance, prescription in the lenses, ocular surface disease issues, and replacement schedules.

Li, CC, Chauhan, A. Ind Eng Chem Res 2006; 45: 3718–3734.
Peng, C-C, et al. Biomaterials 2010; 31: 4032–4047.

41

IDOSE TR GLAUKOS



- Travoprost continuous release
  - Slow release or fast release
- Phase 3 data
  - Non inferiority to timolol 0.5% BID
  - 81% slow release were free of other IOP lowering meds @ 12 months

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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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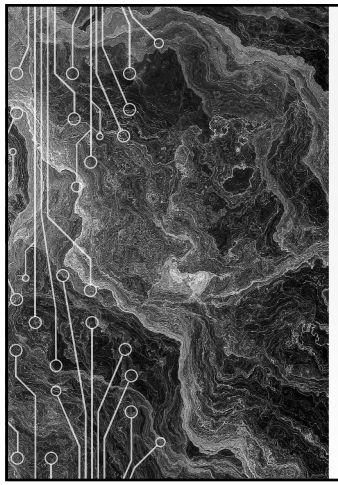

SURGICAL GLAUCOMA TREATMENT UPDATES: MIGS

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DEFINING MIGS

MIGS ARE:

IOP-lowering surgery with the following characteristics:

- Minimally traumatic
- Conjunctiva-sparing
- High safety profile
- Rapid recovery
- Can be combined with cataract extraction or standalone
- 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

- 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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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 + 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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MIG 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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MIG MOA: TRABECULAR MESHWORK BYPASS

- iStent (2012)
- iStent inject (2018)
- iStent inject (W) (2021)
- iStent Infinite (2022)
- Hydrus (2018)

55

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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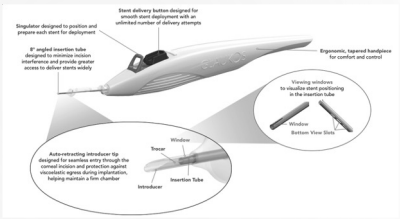
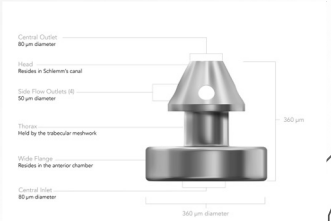
ISTENT INFINITE

- iStent infinite® gives you the versatility to treat a variety of patients who have failed prior medical and surgical intervention,
- Can be combined with cataract surgery or in a standalone surgical setting.





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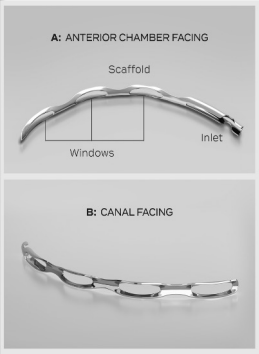
HYDRUS MICROSTENT



- 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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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)

IM-0095-1 Rev A

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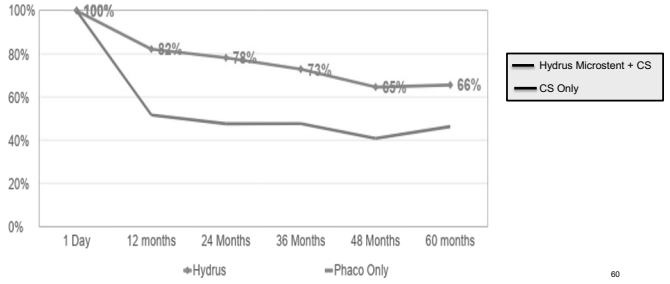
HORIZON: Medication Free[1]

MEDICATION FREE 0-60 MONTHS

Durable effect through 5 Years



20-30% margin over 5 years follow up

p < 0.001

IM-0095-1 Rev A 1. Data on file – Ivantis, Inc.

60

60

MIG MOA: DILATION

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

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MOA: SUBCONJUNCTIVAL SPACE

- Xen (2016)
- Preserflo Ab-Externo Microshunt (pending)

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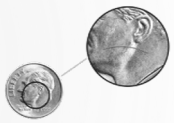
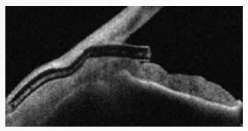
THE XEN GEL STENT



- A glaucoma implant designed to reduce intraocular pressure in eyes suffering from refractory glaucoma
- 6-mm length, 45-micron inner diameter- about the length of an eyelash
- Composed of gelatin, cross-linked with glutaraldehyde
- Aqueous is filtered through stent to subconjunctival space, mimicking traditional filter surgery
- Can be stand alone or combined with phaco



1. XEN® Directions for Use; 2. Vogt et al. In: Blume-Peytavi et al, eds. *Hair Growth and Disorders*. 2008.

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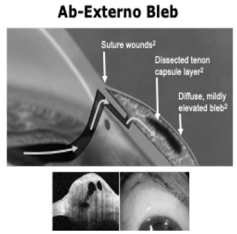
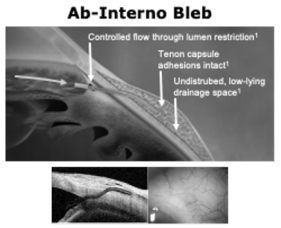
The XEN Procedure Creates a Low Lying, Ab-interno Bleb in Refractory Glaucoma



Example of elevated, cystic bleb



- Low-lying and diffuse[1]

1. Dapena and Ros. *Revista Española de Glaucoma e Hipertensión Ocular*. 2015; 2. Errico et al. *Clin Ophthalmol*. 2011.

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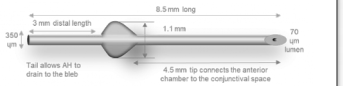
PRESERFLO MICROSHUNT



- designed to reduce IOP
- minimizing the risk of postoperative hypotony and vision-threatening hypotony-related complications
- Published efficacy and safety outcomes with the device are encouraging and suggest that higher concentrations of intraoperative MMC may be associated with higher rates of surgical success

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PRESERFLO MICROSHUNT CLINICAL OUTCOMES

14.3 mmHg Mean post-op IOP on 0.6 mean medications at month 12[1]

74% Lower rate of hypotony requiring intervention vs. trabeculectomy through month 12[1]

72% Of patients were medication-free at month 12[1]

39% Lower rate of interventions vs. trabeculectomy through month 12[1]

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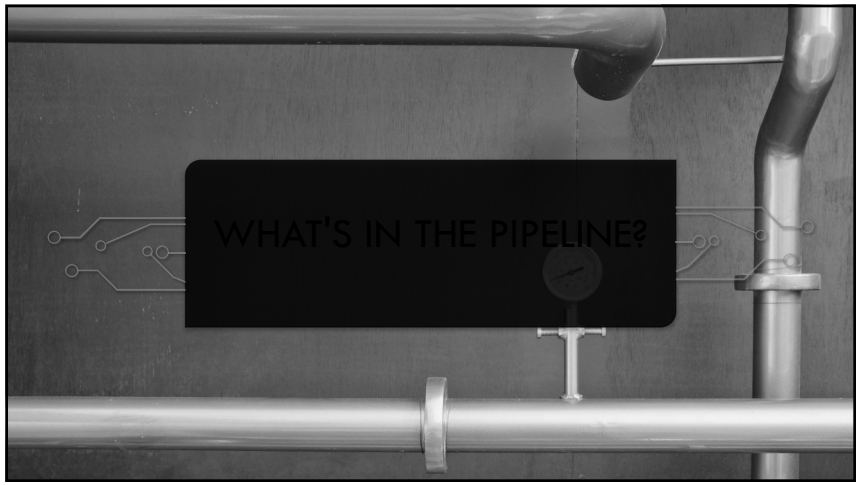

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TOPICAL OCULAR GLAUCOMA PIPELINE

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 (Omdi, Santen)
- Used in Japan and Asia since 2018
- Non prostaglandin prostanoid EP2 receptor agonist
- In FDA review since Feb 2021

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a. **DRAINAGE TO OCULAR SURFACE**
   i. **Sollevio** *(Alevio)* **INVESTIGATIONAL**
   ii. **Beacon Aqueous Microshunt** *(MicroOptx)*
b. **AQUEOUS OUTFLOW AT MESHWORK**
   i. **Therapeutic Ultrasound for Glaucoma** *(TUG, EyeSonix)*
c. *Schlemm canal*
   i. **iStent Infinite** *(Glaukos)*
   ii. **iPrime Viscodelivery System** *(Glaukos)*
d. *Supraciliary Drainage*
   a. *iStent Supra*
   b. *MINject*
e. *MIG Bleb Surgeries*
   a. *PreserFlo MicroShunt (Santen)*
   b. *Minimally Invasive Micro Sclerostomy (MIMS, Sanoculis)*

MIGS
PIPELINE

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