STATE BOARD OF OPTOMETRY
2450 DEL PASO ROAD, SUITE 105, SACRAMENTO, CA 95834
P (916) 575-7170 F (916) 575-7292 www.optometry .ca.gov

Continuing Education Course Approval Checklist

Title: What's New in Glaucoma

Provider Name: UCSF c/o Dr. Jane Kuo

☑Completed Application
Open to all Optometrists? ☑Yes ☐No
Maintain Record Agreement? ☑Yes ☐No

☑Correct Application Fee

☑Detailed Course Summary

☑Detailed Course Outline

☑PowerPoint and/or other Presentation Materials

☐Advertising (optional)

☑CV for EACH Course Instructor

☑License Verification for Each Course Instructor
Disciplinary History? ☐Yes ☑No

CALIFORNIA STATE BOARD OF OPTOMETRY

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CONTINUING EDUCATION COURSE APPROVAL APPLICATION

$50 Mandatory Fee

FEES PAID

Pursuant to California Code of Regulations (CCR) § 1536, the Board will approve continuing education (CE) courses after receiving the applicable fee, the requested information below and it has been determined that the course meets criteria specified in CCR § 1536(g).

In addition to the information requested below, please attach a copy of the course schedule, a detailed course outline and presentation materials (e.g., PowerPoint presentation). Applications must be submitted 45 days prior to the course presentation date.

Please type or print clearly.

Course Title	**Course Presentation Date**
What's New in Glaucoma	02/05/2017

Course Provider Contact Information

Provider Name

Jane (First) Kuo (Last) _____ (Middle)

Provider Mailing Address

Street 10 Koret Way **City** San Francisco **State** CA **Zip** 94131

Provider Email Address jane.kuo@ucsf.edu

Will the proposed course be open to all California licensed optometrists?	☑ YES ☐ NO
Do you agree to maintain and furnish to the Board and/or attending licensee such records of course content and attendance as the Board requires, for a period of at least three years from the date of course presentation?	☑ YES ☐ NO

Course Instructor Information

Please provide the information below and attach the curriculum vitae for each instructor or lecturer involved in the course. If there are more instructors in the course, please provide the requested information on a separate sheet of paper.

Instructor Name

Jane (First) Kuo (Last) _____ (Middle)

License Number 14154 TLG	**License Type** Optometry
Phone Number (510) 3900279	**Email Address** jane.kuo@ucsf.edu

I declare under penalty of perjury under the laws of the State of California that all the information submitted on this form and on any accompanying attachments submitted is true and correct.

Signature of Course Provider 01/06/2017 *Date*

Title: What's New in Glaucoma?
Presenter: Jane Kuo, OD FAAO

Summary
Many new treatment modalities continue to develop and it is valuable and important for our fellow colleagues to be aware of the options available for the treatment and management of glaucoma patients. The course will discuss new developments in therapeutic eye drops and surgical treatments, specifically MIGS (minimally invasive glaucoma surgeries) including the iStent, CyPass, and Trabectome as well as micropulse lasers. The lecture will also review the latest clinical data and other technologies coming down the pipeline.

UCSF Optometry Course: What's New in Glaucoma?

Jane Kuo, OD FAAO

Outline

I. What's New in Glaucoma- Overview
   A. New developments in therapeutics
   B. New developments in surgical treatments

II. New glaucoma medications in pipeline
   A. Overview of current medications

   B. Rho kinase (ROCK) and Rho GTPase
      1. mechanism of action

   C. Rhopressa
      1. clinical trials: Rocket 1, Rocket 2, Rocket 3, Rocket 4
      2. side effects of medication
      3. current status

   D. Rolactan
      1. clinical trials: Mercury 1, 2, 3
      2. side effects of medication
      3. current status & NDA filing

   E. Visneo (latanoprostene bunod 0.024%)
      1. mechanism of action
      2. clinical trial: Apollo, Jupiter
      3. side effects of medication
      4. current status & FDA approval

   F. Trabodenosen
      1. mechanism of action
      2. clinical trial & MATrX-1
      3. side effects of medication
      4. current status

III. Delivery Systems
   A. Purpose: poor patient compliance

   B. Bimatoprost Insert
      1. design - preservative-free ocular ring
      2. side effects / dislodgment
      3. clinical trials

   C. Plug delivery

1. design- sustained release Travoprost
2. clinical trials

IV. New surgical treatments: Minimally Invasive Glaucoma Surgeries (MIGS)

A. Trabectome

1. FDA approval
2. purpose / procedure
3. side effects
4. clinical studies

B. Glaukos - iStent

1. iStent FDA approval
2. clinical studies
3. Second Generation iStent
    i. differences between first generation and second
    ii. current FDA status
4. iStent Supra
    i. design and purpose
    ii. clinical study
    iii. status of FDA approval

C. CyPass Microstent

1. Design & purpose
2. FDA approval
3. clinical trials- COMPASS
4. first surgery at UCSF

D. Brief overview of other MIGS procedure in pipeline

1. XEN Gel Stent
2. Hydrus
3. InnFocus
4. StarFlo
5. Kahook Dual Blade

E. Co-management

1. discussion of treatment options
2. advantages and disadvantages of MIGS

V. Cyclophotocoagulation

A. History of cyclophotocoagulation / purpose

B. Two approaches: transcleral vs endoscopic

C. Transcleral

1. procedure
2. complications and side effects
3. treatment type

D. Endoscopic
    1. procedure, use in conjunction with cataract surgery
    2. complications and side effects
    3. treatment type

E. Micropulse laser
    1. FDA approval
    2. mechanism of action / purpose
    3. clinical studies
    4. types: micropulse TCP or SLT
    5. advantages / disadvantages
    6. co-management

VI. Conclusion
    A. Overview of therapeutic and surgical options
    B. Take home messages

UCSF Optom Course

What's New in Glaucoma?!

Jane Kuo, OD FAAO
UCSF Department of Ophthalmology- Glaucoma

Overview

- New developments in therapeutics
- New developments in surgical treatments- MIGS

Glaucoma Medications

* Like to start with PGA
- if ineffective- check instillation technique or switch PGA

* B-blocker

* Combo: Cosopt, Combigan, Simbrinza

* CAI / Brimonidine

* Still high.. need for laser/surgery & oral diamox

Pipeline

Therapeutics

- Rhopressa
- Rolactan
- Latanoprostene

Inserts

- Bimatoprost Ring
- Rolactan
- Travoprost Plug

Therapeutics

Rho kinase (ROCK) and Rho GTPase

- induces reversible modification to cell morphology in TM and juxtacanalicular regions

Other properties:

- Enhance ocular blood flow
- Inhibit postoperative scarring
- Promote retinal ganglion cell survival and axon regeneration (animal models)

Rhopressa™ (Aerie Pharmaceuticals, US)

- Small-molecule inhibitor of both ROCK and norephinephrine transporter (NET)

- MOAs:
  - increase outflow through TM
  - decrease EVP
  - inhibit NET to reduce fluid production

Rocket 1

Phase III clinical trials

Rhopressa 0.02% QD vs timolol 0.5% dosed BID **failed** to demonstrate **non-inferiority** compared to timolol for patients in the study with IOPs <27mmHg

~ 20% lost efficacy at week 6 and day 90

Rocket 2

- 1:1:1 Rhopressa 0.02%QD vs Rhopressa 0.02% BID vs timolol 0.5% BID

- Primary endpoint: non-inferiority to timolol in both arms

- Mean diurnal IOP in daily arm: 21.4 mm Hg to 17.4 mm Hg at day 90

Side effects

- most common adverse event: hyperemia
  35 % of patients, 80% scored it as mild
- Rhopressa BID had higher incidence of adverse events but more efficacious than daily dose

- NDA filed but withdrawn in Oct 2016, expected submission in January 2017

- Rocket 3 is a 12-month safety-only study in Canada

- Rocket 4 is designed to provide adequate six-month safety data for regulatory filing purposes in Europe

Rhopressa 0.1% daily vs 0.02% daily vs latanoprost 0.005% daily (28 days)

Conclusions

- AR-13324 0.01% and AR-13324 0.02% produced clinically and statistically significant reductions in IOP
- AR-13324 0.02% was less effective than latanoprost by approximately 1 mm Hg in patients with unmedicated IOPs in the range of 22 – 36 mm Hg
- AR-13324 0.02% had equivalent efficacy to latanoprost (within 0.2 mm Hg) in patients with baseline IOPs of 22 – 26 mm Hg
- AR-13324 0.2% maintained similar efficacy regardless of baseline IOP, whereas latanoprost was less effective at baseline IOPs of 22 - 26 mmHg. Both latanoprost and timolol have been previously reported to show less absolute lowering of IOP in patients with lower baseline IOPs[5].
- The only drug-related adverse event of note was conjunctival hyperemia which for the majority of patients was mild to moderate and transient

Roclatan™ (Aerie Pharmaceuticals, US)

Daily drug combination of
Rhopressa + latanoprost

- Mercury 1 study (Phase III, 12 month 3-arm) comparing Roclatan vs Rhopressa vs latanoprost

- Mercury 2: 90 day efficacy trial expected in 2017

Mercury 1

Patients with open angle glaucoma (OAG) or ocular hypertension (OHT)

with IOP >20 mmHg and < 36 mmHg

N=718 subjects randomized at 58 US sites

↓

Patients randomized
1:1:1

Roclatan™
PG324
(netarsudil/latanoprost)
QD (PM)

Rhopressa™
Netarsudil
(AR-13324) 0.02%
QD (PM)

Latanoprost
0.005%
QD (PM)

Primary endpoints:

- Efficacy: Mean IOP at nine time points (08:00, 10:00, and 16:00 at Week 2, Week 6, and Month 3)
- Safety: Ocular and systemic safety during a 12-month treatment period

4

ClinicalTrials.gov Identifier: NCT02558400

Results

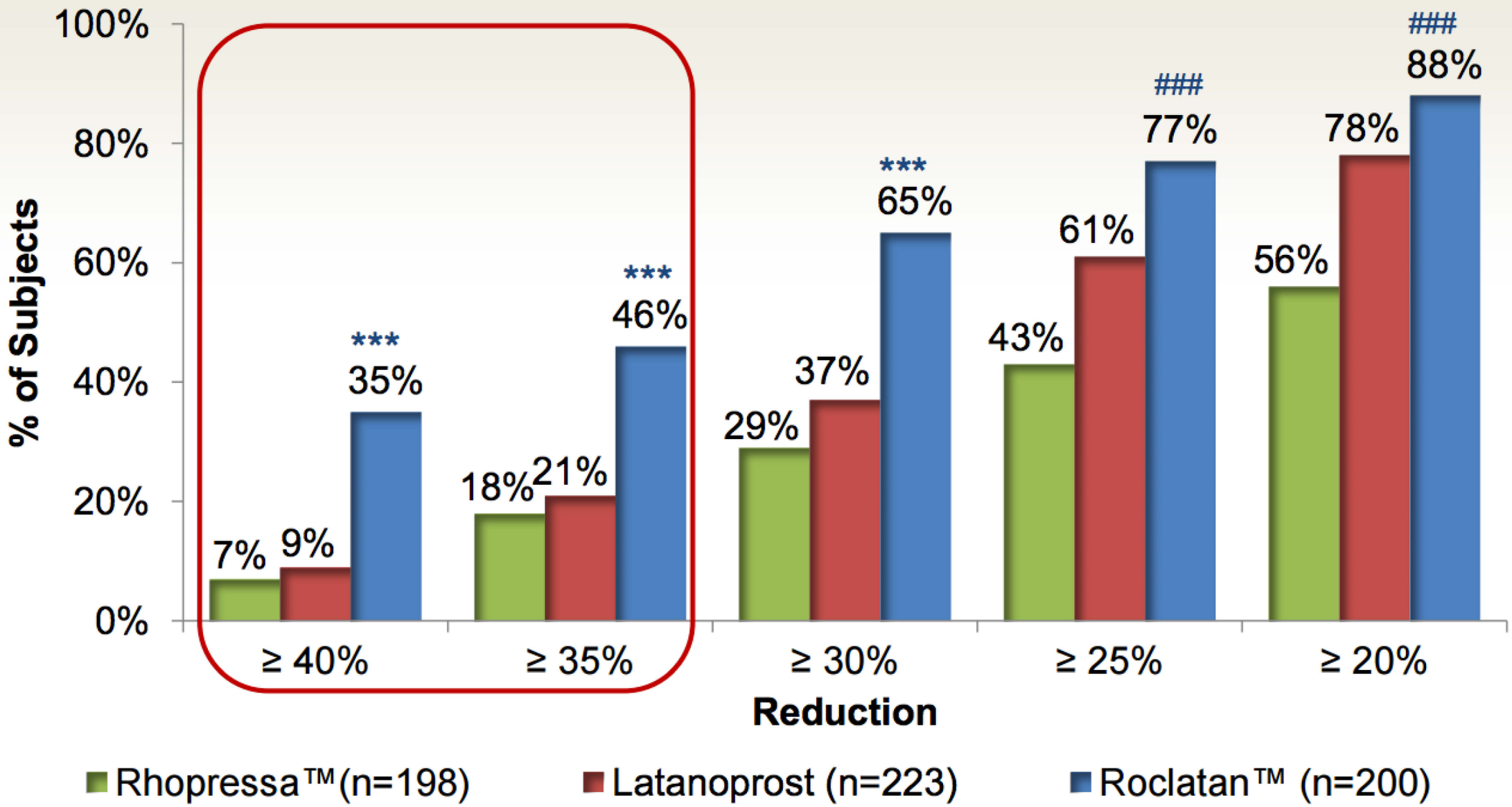
- Achieved primary efficacy endpoint, demonstrated statistical **superiority over both latanoprost and RhopressaTM**

- Roclatan IOP lowering exceeded
  *latanoprost in a range of 1.3 to 2.5 mmHg
  *Rhopressa in a range of 1.8 to 3.0 mmHg

- RoclatanTM reduced mean diurnal IOPs to 16 mmHg or lower in 61 percent of patients

Roclatan™ Phase 3 Responder Analysis

Day 90: % of Patients with IOP Reductions of ≥ 20%

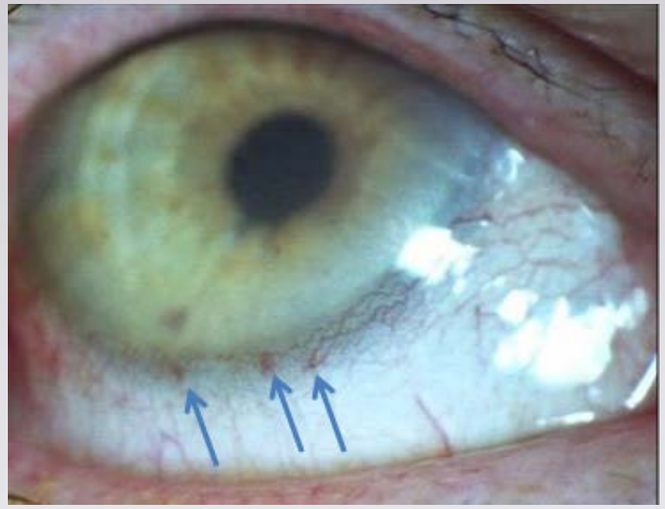


***p<0.0001 vs Latanoprost and Rhopressa™
###p<0.0001 vs Rhopressa™, p<0.05 vs Latanoprost

Side Effects

- The most common adverse event was hyperemia and conjunctival hemorrhage

Adverse Events (≥5.0% in any group)	Roclatan™ n=238	Rhopressa™ n=244	Latanoprost n=236
Eye Disorders			
Conjunctival Hyperemia	126 (52.9%)	99 (40.6%)	33 (14.0%)
Conjunctival Hemorrhage	25 (10.5%)	34 (13.9%)	1 (0.4%)
Eye Pruritus	18 (7.6%)	17 (7.0%)	3 (1.3%)
Lacrimation Increased	14 (5.9%)	15 (6.1%)	1 (0.4%)
Cornea Verticillata	12 (5.0%)	9 (3.7%)	0 (0.0%)
Administration Site Conditions			
Instillation site pain	45 (18.9%)	51 (20.9%)	15 (6.4%)



What's Next?

- Mercury 2: 90 day efficacy trial – 2017
- Mercury 3 (Europe): Efficacy study, comparing to a leading combo product
- Roclatan NDA filing expected near year-end 2017

Visneo (Latanoprostene bunod 0.024%)

(Nicox & Baush + Lomb, US)

Novel nitric oxide (NO) donating prostanoid FP receptor agonist

latanoprost acid

↑ aqueous outflow
uveoscleral outflow

butanediol mononitrate

relax TM/Schlemms
↑ aqueous outflow

Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension

The APOLLO Study

Robert N. Weinreb, MD,[1] Baldo Scassellati Sforzolini, PhD,[2] Jason Vittitow, PhD,[2] Jeffrey Liebmann, MD[3]

End Points:

- Primary: IOP at each of the 9 assessment time point
- Secondary:
  - proportion of subjects with IOP <18mmHg
  - proportion of subjects with IOP reduction ≥ 25%

Other Studies

- Jupiter: 52- Week Safety Study
  * mean baseline IOP 19.6
    - proportion of subjects with IOP <18mmHg
    - proportion of subjects with IOP reduction ≥ 25%

- CONSTELLATION: 24-hour IOP lowering study
  * demonstrated better 24-hour IOP control vs timolol

Expecting FDA approval by 2017

Trabodenoson
(Inotek Pharmaceuticals, US)

- mimetic drug targets the A1 receptor subtype causing ↑ in metabolic activity that leads to digestion and removal of proteins that can block the healthy outflow of aqueous humor

- Recall: 3 adenosine receptors (A1, A2A, A3) in TM lower IOP when activated

Studies

(+) Phase II results
N=144; drug decreased IOP by 7mmHg after 28days compared to placebo
No systemic ADE and less hyperemia than PGAs

Phase II: fixed-dose combo with latanoprost (no results currently)

Phase III: MATrX-1 safety and efficacy study vs timolol, expected 2016/2017

Acucela and Otsuka Pharmaceuticals:
A2A agonist, OPA-6566
*conducted a phase 1/2 clinical trial in 2012

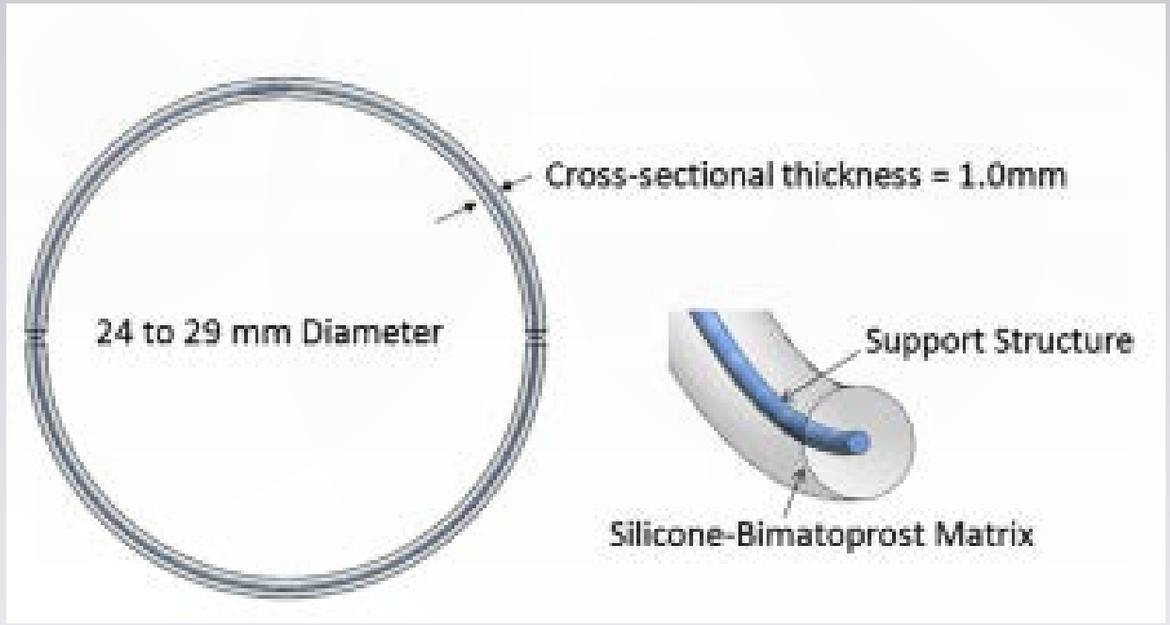
Santen Pharmaceuticals: **A2A agonist, ATL313**
*significantly decreased IOP in vivo, no recent updates or developments

Delivery Systems

- Bimatoprost Insert
- Ocular Therapeutic's Sustained Release-Travoprost

Bimatoprost Insert (ForSight VISION5, US)

- PF ocular ring containing 13mg bimatoprost
- Mixed into silicone matrix placed over polypropylene support structure



Bimatoprost Insert
(ForSight VISION5, US)

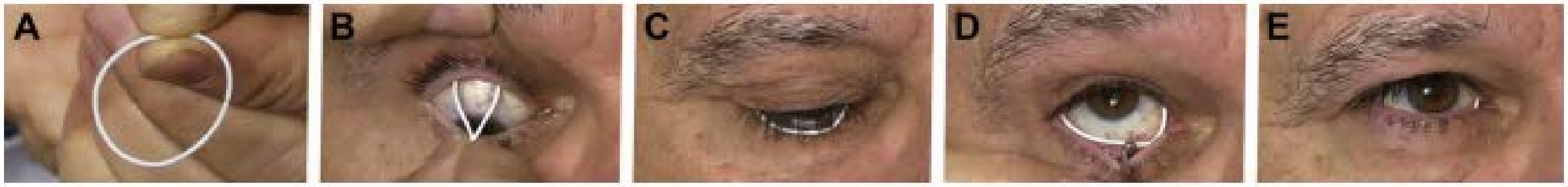


Figure 2. Photographs showing the method of placement of a bimatoprost ocular insert. **A**, The upper lid is retracted manually and the insert is placed in upper fornix by the physician. After **(B)** placement of the top half of the insert in the upper fornix, **(C)** the lower lid margin is retracted gently either manually or with a scleral depressor **(D)** to seat the bottom half of insert into the lower fornix. **E**, Insert in situ with a small portion of the insert visible in the medial canthus.

Six-Month Intraocular Pressure Reduction with a Topical Bimatoprost Ocular Insert

Results of a Phase II Randomized Controlled Study

James D. Brandt, MD,[1] Kenneth Sall, MD,[2] Harvey DuBiner, MD,[3] Robert Benza, MD,[4] Yair Alster, MD,[5] Gary Walker, PhD,[5] Charles P. Semba, MD[5]

Randomized 1:1 bimatoprost insert plus artificial tears twice daily or a placebo insert plus timolol (0.5% solution) twice daily for 6 months

Primary endpoint: non-inferiority to timolol
N= 130 OAG or OHT patients

Results

- **Met end point**; mean reduction from baseline IOP
  - bimatoprost group: 3.2 to 6.4 mmHg
  - timolol group: 4.2 to 6.4 mmHg

- Adverse events were consistent with bimatoprost or timolol exposure; no unexpected ocular AEs were observed

- Primary retention rate of the insert was 88.5% of patients at 6 months (total of 10 patients withdrew from study)

- Total of 28 dislodgements in 15 patients

OTX-TP Ocular Therapeutix's (US)

- proprietary polyethylene glycol hydrogel technology to release the preservative free travoprost drug in punctual plug form for 90 days

Product Profile:
- Sustained release depot
- Designed to replace daily therapy
- Preservative-free
- Product can be monitored by patient

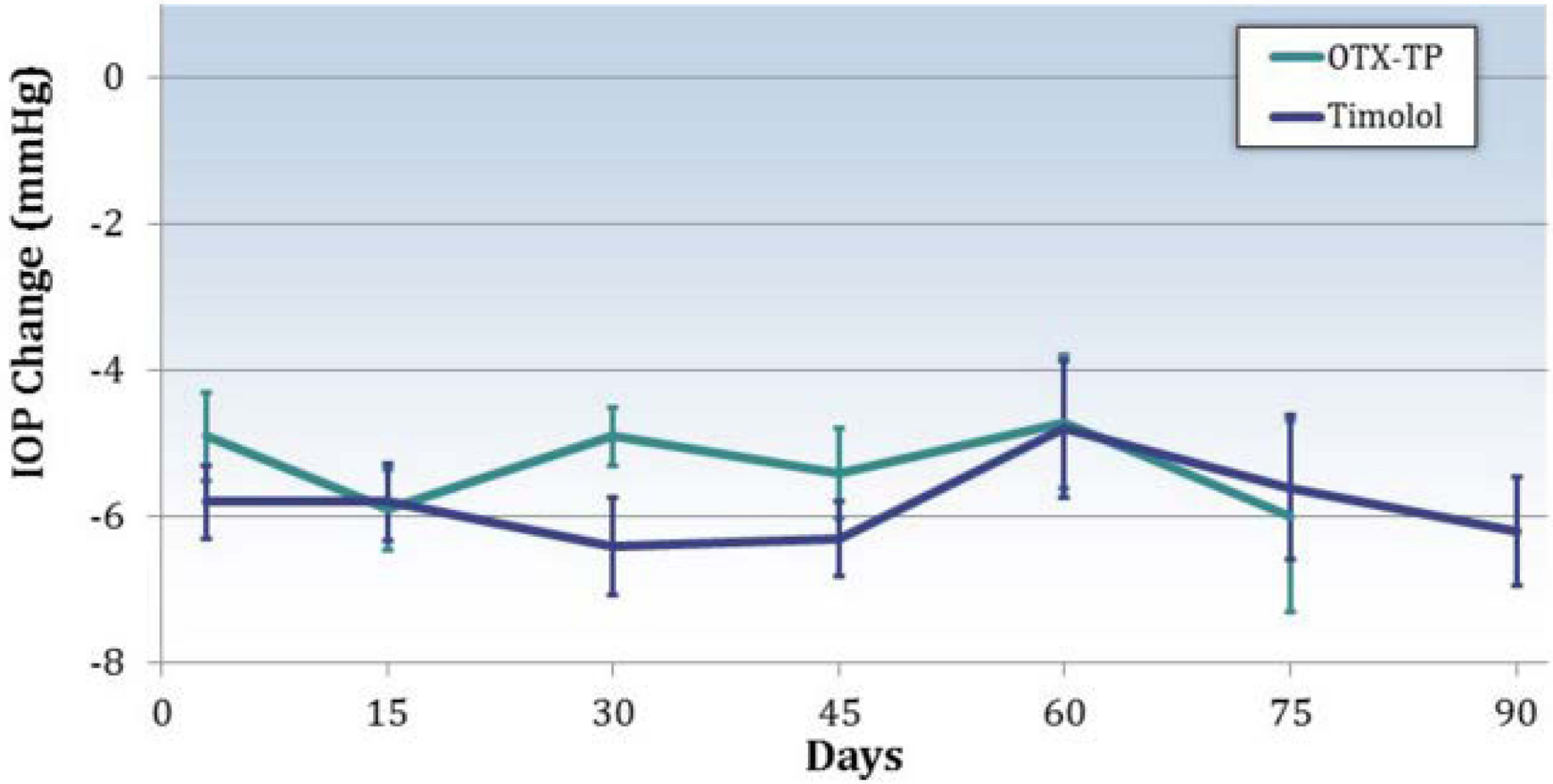
Initial Planned Indication:
- Intraocular pressure reduction for glaucoma and ocular hypertension

Delivery Method:
- Non-invasive
- Physician-administered: inserted into canaliculus
- Provides sustained delivery for up to 90 days

Sustained Release Travoprost Phase 2a Study Results

OTX-TP Comparison to Timolol and Placebo Plug

Mean 8:00 AM Reduction from Baseline



Average IOP reduction over three months with travoprost depot consistent with reduction observed with topical travoprost

- Plans for 2- Phase III clinical trials

- First phase III: ~500 subjects
  - no timolol comparison arm but instead non-drug eluting hydrogel-based intracanalicular insert

- Expect first Phase III results in early 2018, and start of second phase III in early 2017

Glaucoma Surgeries

Surgical Options

Lasers

- SLT
- LPI

MIGS

- Trabectome
- iStent
- CyPass

Surgeries

- Trabeculectomy
- ExPress
- Tubes shunt

- TCP/ECP
- Micropulse TCP

MIGS

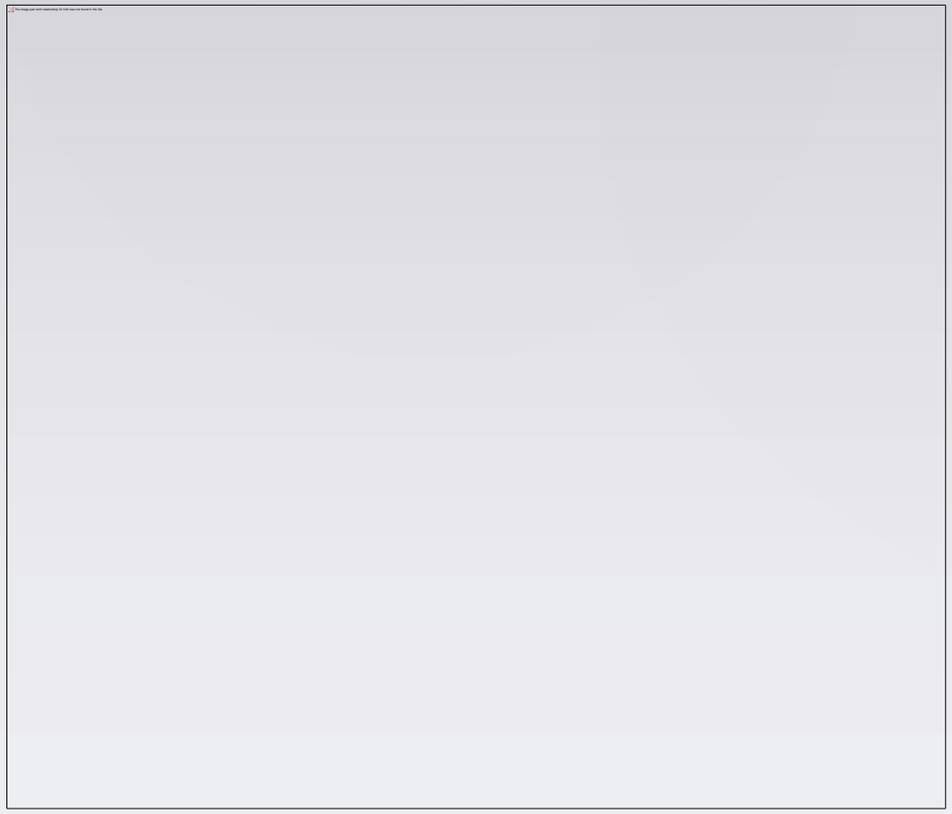
- For mild & moderate glaucoma
- Gained preference among patients & surgeons due to favorable safety profiles, ease of combination with cataract surgeries, and shorter surgical/recovery time
- Eye pressure in majority of clinical trials are typically in mid-teens
- FDA approved: Trabectome, iStent, CyPass Micro-Stent (July 2016)

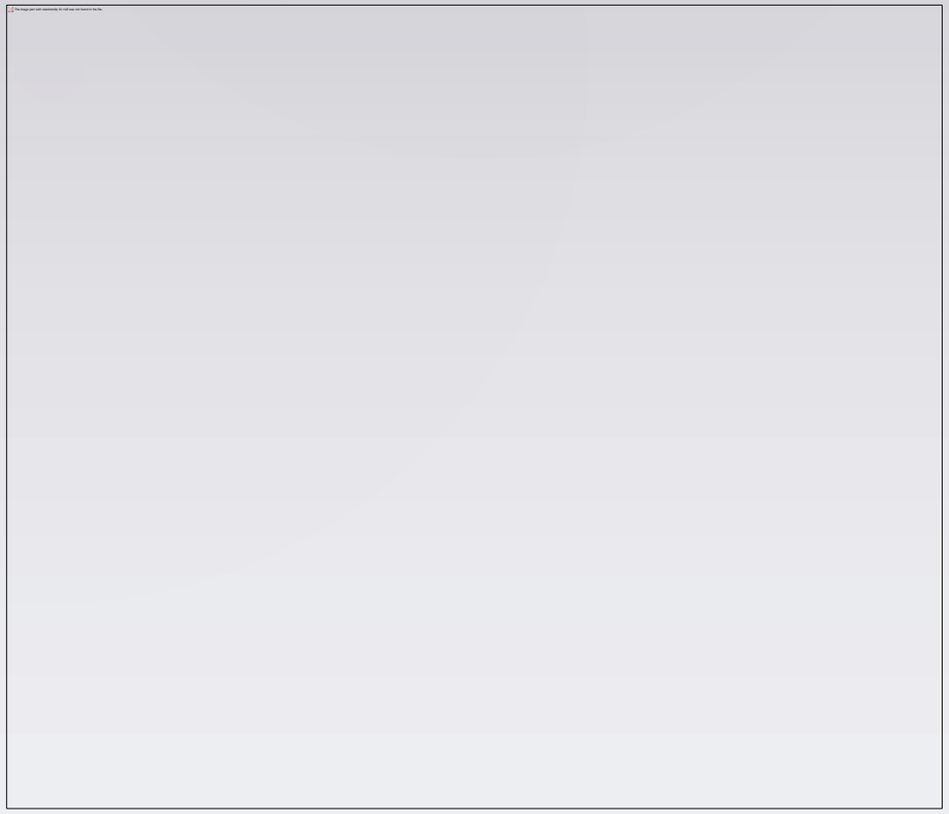
Trabectome (NeoMedix)

Remove 60-120 deg of TM and inner wall of Schlemm's canal with electrocautery

iStent (Glaukos)

- Device creates a patent bypass through the TM to Schlemm's canal to improve aqueous outflow *in conjunction* with phacoemulsification/IOL





Ophthalmology. 2011 Mar;118(3):459-67. doi: 10.1016/j.ophtha.2010.07.007. Epub 2010 Sep 15.

Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract.

Samuelson TW[1], Katz LJ, Wells JM, Duh YJ, Giamporcaro JE; US iStent Study Group.

Compared iStent +CE/IOL vs CE/IOL alone

- 18% more iStent eyes had IOP ≤ 21
- 17% more iStent had ≥20% reduction IOP
- less iStent patients on drops

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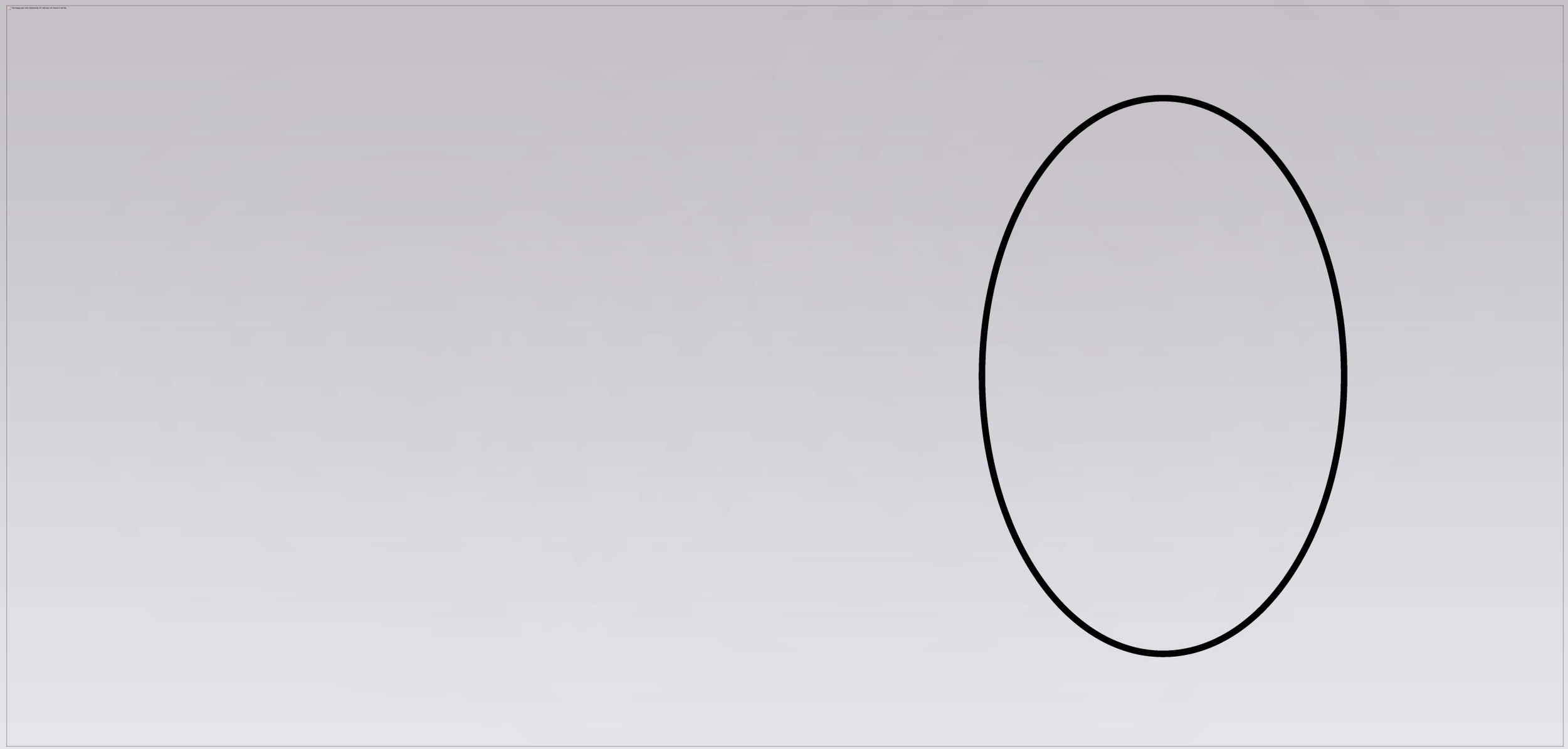


iStent Inject®

Shape of iStent

Delivery: “Nail Gun”

Pre-loaded with 2 iStents

Trying to get FDA approval as stand alone device

iStent Supra®

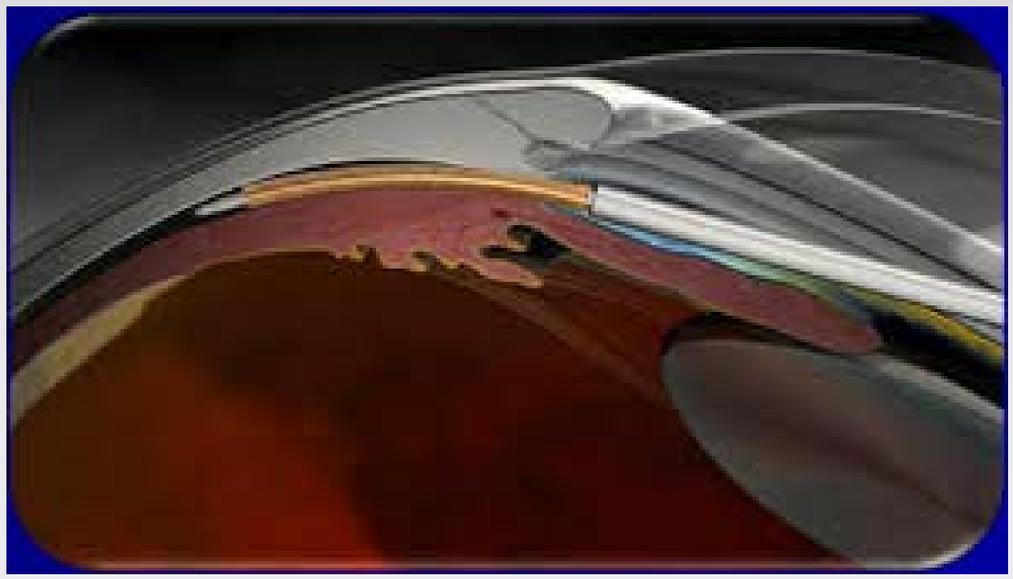
- 4mm tube of polyethersulfone (PES) and titanium
- Accesses the suprachoroidal space
- Anticipating FDA approval in 2018

tiny tube-like stent

6.35mm length, 300um lumen biocompatible polyimide

FDA approved July 2016 as stand alone de

CyPass Micro-Stent (Alcon)



Other MIGS:

XEN Gel Stent

Hydrus

InnFocus

Gold Micro Shunt

StarFlo

*all show promising preliminary data

MIGS Co-management

Discussion of tx options especially if patient also needs CE

View angle with gonioscopic lens
- note clock hours of TM removed in trabectome
- note positioning of stent & patency

Disadvantages of MIGS:
- cost
- not as effective in lowering IOP
* phaco alone have shown to decrease IOP between 2-4mmHg

Hyphema is generally limited and self-resolving but can cause vision to fluctuate

Cyclophotocoagulation

ablates the ciliary processes subsequently
lowering the production of aqueous humor
typically for refractory glaucoma in eyes with
poor visual potential or blind/painful eyes

Cyclophotocoagulation

TCP: transscleral, diode laser applied superficially at the peri-limbal site

ECP: endolaser probe is applied intraoperatively through limbal or pars plana

TCP

non-penetrating but unable to visualize tissue, titrate“popping” sound

typically treat 270deg- 360 deg

complications: +pain, +inflammation, CME, sympathetic ophthalmia, can easily over treat leading to hypotony & phthisis

mainly reserved for refractory cases

ECP

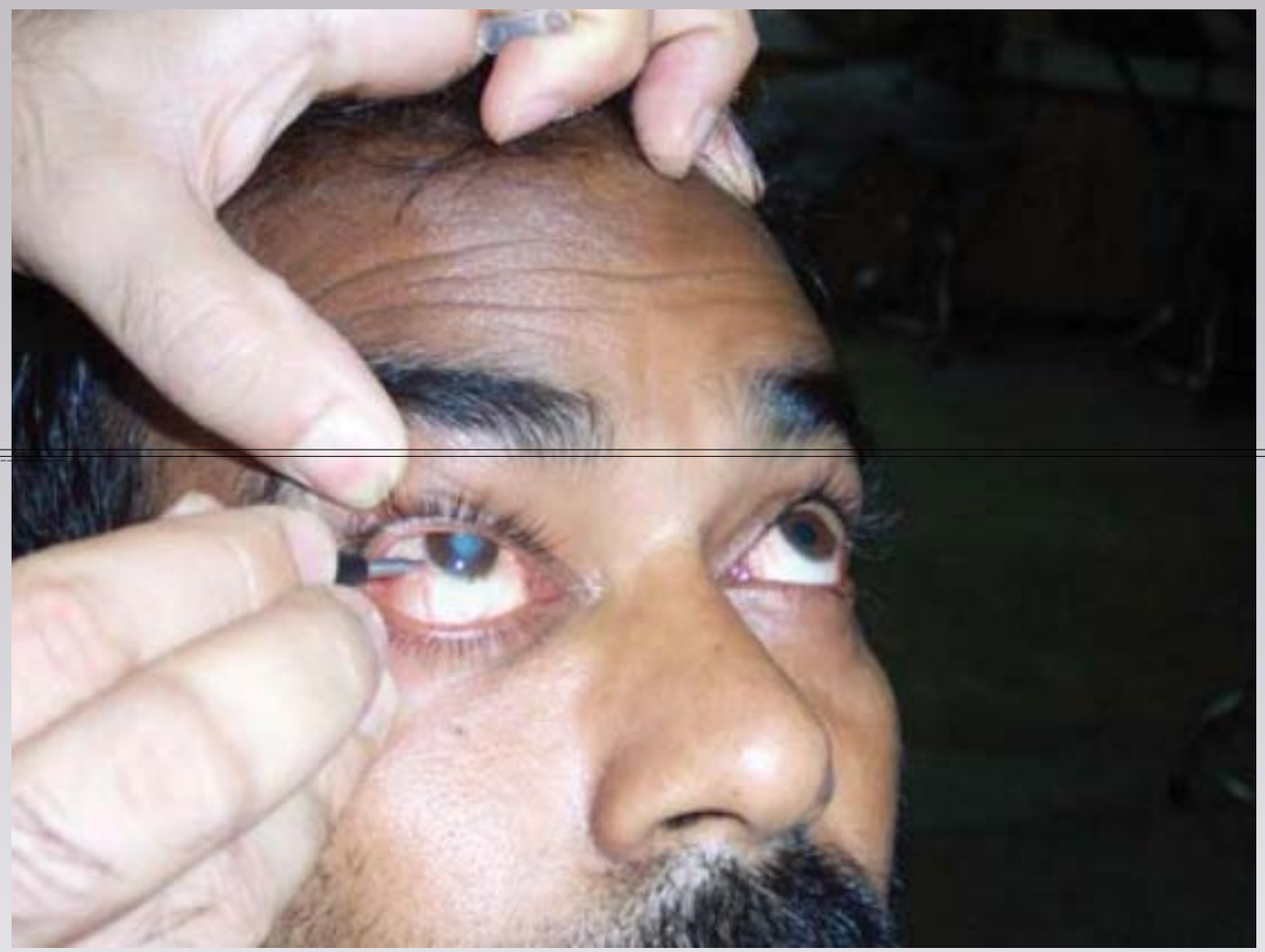
gained popularity recently

used in conjunction with cataract surgery
(can be first line of treatment)

ciliary processes are visualized, looking for ciliary processes to “whiten and shrink”

both ciliary processes and spaces between can be treated for better IOP effect

Complications: Hyphema, hypotony, fibrin exudates, cystoid macular edema, and decreased visual acuity



MicroPulse TCP

Cyclo G6 Glaucoma Laser System (Iridex Corp)

FDA approval 2015 for multiple stages of glaucoma

laser on 30% of the time and off 70% of the time

pulse creates just enough laser energy to be absorbed by pigmented ciliary epithelium that are being targeted = prevents collateral damage

retrobulbar anesthesia followed by two 80 second treatments over the superior and inferior hemispheres

MicroPulse P3 Device

NUHS Prospective Clinical Study

- 33% IOP reduction at 18 months, N = 38 patients

- Average meds reduced from 2.1 to 1.3

- 73% success rate with 1.3 sessions

Radcliffe et al. (poster @ AGS 2015)

- ~30% IOP reduction @ 3 months, N = 48 eyes

- no cases of visually significant hypotony, macular edema, or phthisis bulbi were observed

JANE KUO, O.D., F.A.A.O.

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400 Melrose Avenue
San Francisco, CA 94127
510-390-0279
jane.kuo@ucsf.edu

EDUCATION

October 2012 **FAAO, Fellow of the American Academy of Optometry**

July 2011-2012 **Veterans Affair Palo Alto & Western Blind Rehabilitation Center**, Palo Alto, CA
Optometric Resident

2007-2011 **Southern California College of Optometry**, Fullerton CA
Doctor of Optometry, May 2011
Graduating Honors: *Magna Cum Laude*

2002-2006 **University of California, Berkeley**, Berkeley, CA
Bachelor of Arts: Major in Molecular and Cell Biology
Minor in Asian American Studies

LICENSES & CERTIFICATION

Jan 2016	**American Board of Certification in Medical Optometry (ABCMO)**
June 2012	NBEO- Advanced Competence in Medical Optometry (ACMO)-passed
June 2011	California State Optometry License: 14154 TLG, TPA (expiration 01/2016)
June 2012	DEA License: MK2633938 (expiration 12/2017)
June 2008	Genentech, Inc. Visual Acuity Examiner Certification for research studies
June 2008	Novartis Visual Acuity Examiner Certification for clinical trials

EMPLOYMENT HISTORY

April 2013- present	Optometrist, University of California San Francisco - Glaucoma Services, SF, CA
Mar 2015- present	Mentor- Glaucoma Grand Rounds, UC Berkeley School of Optometry
Aug 2012- Apr 2013	Fee Basis, Veterans Affair Palo Alto, Palo Alto, CA
July 2012-Feb 2013	Associate, Los Gatos Vision Care, Los Gatos, CA
July 11-2012	Resident, Veterans Affair Palo Alto & Western Blind Rehab Center, PA, CA
Dec 2006-Aug 2007; June-August 2008	Ophthalmic Medical Technician, East Bay Retinal Consultants, Oakland, CA

PUBLICATIONS

Anticipated 2016: Glaucoma Update. COA Magazine
Anticipated 2016: Newer Surgical Options for Glaucoma. Current Ophthalmology Reports

Glaucoma and Eye Injury. California Optometry Association (COA) Magazine: Article. 2016 Aug. <http://coamagazine.org/2016/07/13/glaucoma-and-eye-injury/>

Amoozgar B, Lin SC, Han Y, Kuo J. A role for antimetabolites in glaucoma tube surgery: current evidence and future directions. Curr Opin Ophthalmol. 2016 Mar; 27(2):164-9.

Shunt, Tubes, Blebs, Oh My! [TPG]. California Optometric Association (COA) Magazine: CE Article. 2015 June. < http://www.coavision.org/i4a/pages/index.cfm?pageID=4069>

RESEARCH

Co-Primary Investigator, IRB: Myopia vs. Glaucoma

Co-Investigator, Allergan Safety and Efficacy of Bimatoprost Sustained-Release (SR) in Patients With Open-Angle Glaucoma or Ocular Hypertension

Recruiter, Correlation between NTG and Alzheimer's, PI: Yvonne Ou, MD

ACADEMIC LECTURES/PRESENTATIONS

Nov 2015	UCSF Grand Rounds Presentation: "Rathke's Cyst"
Oct 2015	SCCOS- 2 hour CE approved Lecture "Co-managing glaucoma", Santa Clara, CA
April 2015	UCSF Grand Rounds Presentation: "Disc Hemorrhages"

PROFESSIONAL DEVELOPMENT

Dec- Feb 2015	Entrepreneur in Residence/EyeCapture Course completion in Digital Health at UCSF Lean Launchpad for Healthcare

AFFILIATIONS & LEADERSHIP

2010-present	Member, American Academy of Optometry (AAO)