New Developments in Glaucoma

Relevant Disclosures Bacharach

Aerie  Alcon  Allergan  Eyegate  Glaukos  Heidelberg  Icon Bioscience  Injectsense  Kala  Ocular Therapeutix  Ono  Optovue  Ora  Rigel  Santen  Senju  Topcon  Ora  Optovue  Ora  Rigel  Santen  Senju  Topcon

What's New With Tonometry?

iCare Tonometer
- New design
- Enhanced Ergonomics
- Easy to use
- Accurate
- Precise

iCare Features
- Improved forehead support
- New Positioning Assistant
- Improved forehead adjustment knob
- Large OLED Color Display
- EasyNav: New Navigation Interface
- New Ergonomic AMS Measure button

Flume Trail, Tahoe, Ca
Rebound Technology

- Easy-to-use
- Quick, effective routine barely noticeable by the patient
- No topical anaesthetics or disinfection needed
- Disposable probe touches the cornea very lightly
- Suitable also for non-compliant patients and children
- Proven accurate by several independent studies
- Truly portable

Measurement Basics

- The probe touches the cornea very gently
- Measurement takes place in 0.1 seconds
- Corneal reflex after 0.2 seconds
- Measurement of motion parameters
- To be repeated 6 times in order to minimize deviation and to produce a calculated measurement value
- Whole procedure (6x both eyes) takes about one minute

Rebound Tonometry is Accurate

- Bench testing
- Repeatability (coefficient of variation): <8%

<table>
<thead>
<tr>
<th>Range of IOP</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>≤ 20 mmHg</td>
<td>± 1.2 mmHg</td>
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<tr>
<td>&gt; 20 mmHg</td>
<td>± 2.2 mmHg</td>
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Clinical Studies

REPRODUCIBILITY AND TOLERABILITY OF THE ICARE REBOUND TONOMETER IN SCHOOL CHILDREN

"Measurement of intraocular pressure (IOP) with the rebound tonometer (RBT) is a highly reproducible method in schoolchildren showing high intraobserver and interobserver correlation and it seems to be very comfortable when performing IOP measurements in schoolchildren without an anesthetic." Sahin A, Basmak H, Niyaz L, Yildirim N. J Glaucoma. 2007 Mar;16(2):185-8

AGREEMENT OF REBOUND TONOMETER IN MEASURING INTRAOCULAR PRESSURE WITH THREE TYPES OF APPLANATION TONOMETERS


iCare HOME tonometer

- Intended as an adjunct for monitoring IOP of adult patients (self-use). The HOME tonometer is designed for use at home or on the go.
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.

Positioning Light
- Red and green light signals help patients correctly position the tonometer.

Automatic Eye Recognition
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

Automatic Measurement Sequence
The tonometer can operate in two modes:
Series mode
- Pressing the measurement button for a sustained period of time (more than 2 seconds) initiates the measurement function and the tonometer takes six measurements in rapid succession
Single mode
- The measurement button must be pressed each time to initiate the measurement, i.e. six samples for the whole measurement cycle

New User Interface Panel
- Simple Indicator Lights and Audible Alerts
- Interpretation only by a health care professional
- Does not display the IOP measurement
- Mitigating concerns that the patient or caregiver might improperly use the information provided by the device

Should we adjust our GAT value based on the CCT?
Reanalysis of the baseline prediction model for the development of POAG from OHTS substituting IOP adjusted for CCT for unadjusted IOP

CONCLUSION:
The calculation of individual risk for developing POAG in ocular hypertensive individuals is simpler and equally accurate using IOP and CCT as measured, rather than applying an adjustment formula to correct IOP for CCT.


"Assuming that CCT can be used as a correction factor for GAT is a misinterpretation of the results of OHTS... that couldn’t be further from the truth. Adjusting IOP based on CCT is attempting to instill a degree of precision into a flawed measurement. You may actually correct in the wrong direction. The issues related to the most accurate tonometry need to include the material properties of the cornea.

James Brandt, MD
Director, Glaucoma Services
UC Davis

"Correction nomograms that adjust GAT IOP based solely on CCT are neither valid nor useful in individual patients" - Pg 18. Robert N. Weinreb, James D. Brandt, David Garway-Heath and Felipe Medeiros. World Glaucoma Association on Intraocular Pressure; Consensus Series 4; May 5, 2007

"We should not assume that corneal thickness is the parameter of greatest interest in monitoring glaucoma or in determining what features of the eye are important in optic nerve damage. Physiology is more important than anatomy." - Harry Quigley, Director of Glaucoma Service, Wilmer Eye Institute

The Cornea and IOP Measurement

The corneal thickness-based IOP adjustment

The problem with CCT-based IOP adjustment

Thickness is NOT resistance

Ocular Response Analyzer Technology

The instrument

2002: Clinical research with ORA commences
2005: The 1st generation ORA was made commercially available
2012: Generation II ORA was launched
3rd Generation "ORA G3" introduced September 2015

Measures:
- Corneal Hysteresis (CH)
- Goldmann–correlated IOP (IOPg)
- Corneal compensated IOP (IOPc)

Ocular Response Analyzer Technology

How does it work?
Define & Describe IOPcc
Corneal-Compensated Intraocular Pressure

- An Intraocular Pressure measurement that is less affected by corneal properties than other methods of tonometry, such as Goldmann (GAT). IOPcc has essentially zero correlation with CCT in normal eyes and stays relatively constant post-LASIK.

- \[ \text{IOPcc} = P_2 - (0.43 \times P_1) \]

ORA vs GAT: Biomechanical Properties of the cornea

- 153 eyes of 78 subjects (Normals, no OAG)
- Measured
  - Goldmann tonometry
  - IOPcc using Ocular Response Analyer
  - CCT
  - Corneal curvature
  - Axial Length

Results

- GAT IOP measurements were significantly associated with CCT (\(P=0.001\))
  - Each 100 um increase in CCT resulted in 2.7mm Hg increase in GAT IOP (\(P=0.001\))
- and corneal curvature (\(P<0.001\))
  - Each 1.0-um increase in the radius of corneal curvature resulted in 3.3mm Hg decrease in GAT IOP (\(P<0.001\))
- Axial length was not associated with GAT
- ORA IOPcc measurements were not associated with any of the ocular variables

Results/Conclusion

- The difference between GAT and IOPcc measurements was significantly influenced by CCT
  - Thicker corneas have higher GAT IOP measurements compared with IOPCC
  - In thin corneas, GAT IOP measurements tended to be lower than IOPCC.
- ORA IOPcc measurements seem to provide an estimate of IOP that is less influenced by corneal properties than those provided by GAT
Corneal Hysteresis as a Risk Factor for Development of Glaucoma

- Prospective observational study
  - 287 eyes of 199 patients suspected of having glaucoma followed for an average of 3.9 ± 1.8 yrs
  - VF normal at baseline
  - Progression = 3 consecutive abnormal VFs
  - 54/287 (19%) showed progression
  - CH lower in those showing progression
    - 9.5 +/- 1.5 mmHg in progressing
    - 10.2 +/- 2.0 mmHg in non-progressing (P=0.012)
    - Each 1 mm lower CH means 22% greater risk progr.
  - Still predictive in multivariate analysis
    - After adjusting for age, IOP, CCT, PSD


Corneal Hysteresis and Progressive RNFL Loss in Glaucoma

- 186 eyes of 133 patients with OAG followed for an average of 3.8 ± 0.8 years
  - Investigate the relationship between baseline CH, CCT, average IOP and rates of RNFL loss during follow up
  - Each 1 mmHg lower CH was associated with a 0.13 um per year faster rate of RNFL loss. (P=0.015)
  - GAT IOP was also associated with a faster rate of RNFL loss (P=0.010)
  - CCT, older age and AA ancestry were not associated with faster rate of RNFL loss


Implementing ORA in Your Practice

- CPT code 92145 - code published January 1, 2015
  - 92145: Corneal hysteresis determination, by air impulse stimulation, unilateral or bilateral with interpretation and report
  - According to An Insider’s View published by the AMA: “this test achieved Category I status because the clinical utility has been established and usage has grown since 2007 when the Category III code was implemented”
  - Reichert is working with consultants, regional champion MDs, and MAC directors in strategic fashion to ensure positive payment policies (LCDs)
  - Bilateral reimbursement approximately $16.00

Payments for 92145, Medicare Administrative Contracts: Jan 2016

<table>
<thead>
<tr>
<th>MAC</th>
<th>Negative LCD</th>
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<tbody>
<tr>
<td>NH</td>
<td>$14.00-$15.80</td>
</tr>
<tr>
<td>NC</td>
<td>$14.60-$15.10</td>
</tr>
<tr>
<td>WI</td>
<td>$14.00-$15.20</td>
</tr>
<tr>
<td>SC</td>
<td>$14.50-$18.90</td>
</tr>
<tr>
<td>AR</td>
<td>$14.00-$17.20</td>
</tr>
<tr>
<td>CA</td>
<td>$14.20-$15.20</td>
</tr>
<tr>
<td>LA</td>
<td>$15.50-$17.80</td>
</tr>
</tbody>
</table>


Wooldridge Conclusions

- Do use Goldmann
  - But recognize its limitations!
  - 60 year-old technology
  - ORA Probably better, truer IOP measurements
  - Currently using both instruments
  - Frequently vary in IOP measurements

What’s New in Perimetry
Should we do 10–2 Visual fields?

Prevalence and Nature of Early Glaucomatous VF Defects on 10–2

- 100 glaucomatous eyes with 24–2 MD < 6dB
  - Tested with 10–2
  - As many abnormal 10–2 hemifields (53%) as abnormal 24–2 hemifields (59%).
  - Of the eyes with normal 24–2 hemifields, 16% were classified as abnormal with the 10–2 test
  - Of the abnormal 10–2 hemifields, 68%, 8%, and 25% were arcuatelike, widespread, and other, respectively
  - Superior VF defects were deeper and closer to fixation than those in the inferior VF


Conclusion

- The 10–2 VF was abnormal in nearly as many hemifields as was the 24–2 VF, including some with normal 24–2 VF, suggesting that the 24–2 test is not optimal for detecting early damage of the macula.
- The pattern of the defects was in agreement with a recent model of macular damage.

10–2 vs. 24–2 VF Progression Analysis in Glaucoma

- Compare the efficacy of 10–2 vs. 24–2 VFs in detecting progression of initial parafoveal scotoma (IPFS) in glaucomatous eye
- 50 eyes followed for 5.7 years
- Ave. of 7.7 VF’s obtained

Results

- Mean global progression rate was significantly greater in 10–2 analysis (~0.40±0.51 dB/yr) than in 24–2 analysis (~0.23 ± 0.28 dB/yr) (P=0.01).
- Within the central 10 degrees of VF, 10–2 analysis detected significantly more progressing eyes than 24–2 analysis (24 vs. 7 eyes; P<0.001).
- Within the central 10 degrees, mean localized progression rate (~1.3 vs. ~0.4 dB/yr) and mean number of progressing points (2.5 vs. 0.5) were significantly greater in 10–2 than in 24–2 analyses (10–2 vs. 24–2; all P<0.001).

Conclusion

- In glaucoma patients with an IPFS, the 10–2 VF detects more progressing eyes than the 24–2 VF, suggesting that closer surveillance of the central VF using 10–2 VF is warranted in these eyes.

Yungtai Kung, Sung Chul Park; Joseph Simonson; Daniel Su; Carlos Gustavo V. De Moraes; Xian Zhang; Donald C. Hood; Jeffrey M. Liebmann; Robert Ritch
Comparing Glaucoma Progression on 24–2 and 10–2 Visual Field’s

- Compared mean deviation change on 10–2 and 24–2 VF’s
- 167 eyes with glaucoma
- Mean of 9 VF’s obtained over 9 years FU
- Compared the rates of MD change in eyes with different severities of VF loss (early [MD better than –6 dB], moderate [-6 dB to –12 dB], advanced [-12 to –20 dB] and severe [MD worse than –20 dB]) at baseline (based on the MD on 24–2 VF)
- Median rate of MD change was comparable in mild (–0.45 dB/year vs. –0.40 dB/year, \( P = 0.42 \)) and moderate (–0.32 dB/year vs. –0.40 dB/year, \( P = 0.26 \)) VF loss categories
- Significantly greater on 10–2 VFs in advanced (–0.28 dB/year vs. –0.21 dB/year, \( P = 0.04 \)) and severe (–0.18 dB/year vs. –0.06 dB/year, \( P <0.001 \)) VF loss categories

Rao HL, Begum VU et al. PLOS ONE DOI:10.1371/journal.pone.0127233 May 15, 2015

Annette

- 69yoWF referred with large cups
- IOP
  - R 16, 11, 14 mmHg
  - L 18, 13, 16 mmHg
  - (three separate exams)
- ORA IOP R 15.3 L 17.5 CH R 9.8 L 9.9
- CCT R 599 L 603
Macular Ganglion cell density

- 50% of ganglion cells located in central 4.5mm
- Peak ganglion cell density is 15,000 cells/mm² in macula (white region)
- GCC map covers central 6mm area

Nerve Head Map (NHM4) with Database comparisons

Patient Information
- RNFL Thickness Map
- RNFL Sector Analysis
- Optic Disc Analysis
- Parameter Tables
- TSNIT graph
- Asymmetry Analysis

Retinal Ganglion Cells extend through three retinal layers

GCC is:
- Nerve Fiber Layer – Ganglion cell axons
- Ganglion cell layer – Cell bodies
- Inner Plexiform Layer - Dendrites
Rao et al. found GCC had similar accuracy levels as FD RNFL (AROC = 0.81 for GCC vs 0.88 for RNFL).

Seong et al. found similar results (AROC = 0.95 for GCC and 0.97 for RNFL).

Kim et al. found AROC values were higher for RNFL vs GCC in a group of advanced glaucoma patients (AROC = 0.92 for GCC vs 0.96 for RNFL), but GCC values were higher than RNFL in a group of early glaucoma patients (AROC = 0.83 for GCC vs 0.78 for RNFL).

Huang et al. compared the diagnostic accuracy for GCC, optic disc, and RNFL from the RTVue.

AROC for RNFL was highest (AROC = 0.92), with GCC second (AROC = 0.86), and vertical C/D ratio a close third (AROC = 0.854).

They found the accuracy improved when they combined all three structures in an LDF (AROC = 0.97).

Huang JY, Pekmezci M, Mesiwala N, Kao A, Lin S. J of Glaucoma. 2010;113 patients with different stages of glaucoma; 30 normals

Imaged NFL and GCC with Optovue RTVue-100

Conclusions:GCC and NFL thickness measurements performed by FD–OCT showed high diagnostic ability in detecting glaucoma. Mean thickness values can be determined for each glaucoma stage.

Studied longitudinal (4 years) and cross sectional age and IOP effects on 192 normals (40–75yo)

NFL thickness decreased 0.14 +/− 0.07 um per year (P = 0.04)

NFL was 0.21 +/− 0.06 um thinner (P < 0.001).

GCC thickness decreased 0.25 +/− 0.05 um per year (P < 0.001)

GCC thickness was 0.17 +/− 0.05 um thinner per year of baseline age (P < 0.001)

Equivalent to 0.2% per year

IOP had no effect on rate of thinning

Angle Measurements

Normal
Narrow

OCT Angle

Pre-LPI Post-LPI

PDS with Iris Concavity

OD OS

CORNEA
- Full 6x6mm Pachymetry Mapping
- Minimum Thickness Marker
- Change & Symmetry Analysis
VYZULTA is metabolized into 2 moieties1,4,7
- Latanoprost acid, a prostaglandin analog, works primarily within the uveoscleral pathway2,8
- Butanediol mononitrate releases nitric oxide, which is thought to relax the trabecular meshwork9-12

VYZULTA (latanoprostene bunod ophthalmic solution), 0.024%

- Indicated for the reduction of intraocular pressure (IOP) in patients with OAG or OHTN
- Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent
- Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation
- Use with caution in patients with a history of intraocular inflammation (iris, uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation
- Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema
- There have been reports of bacterial keratitis associated with the use of multidose containers of topical ophthalmic products that were inadvertently contaminated by patients
- Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration
- Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%)
Discussion

Low OPP has been proposed as a risk factor for glaucomatous damages. Alteration of OPP pressure can occur by changes in BP and/or IOP. Although the mean arterial blood pressure did not change significantly under either test agent of latanoprostene bunod or timolol over the 24-hour period, the latanoprostene treatment increased the diurnal OPP over the baseline owing to a significant IOP reduction during the diurnal period. Treatment with timolol showed no significant effect on diurnal OPP, probably because of a relatively smaller IOP reduction. Results also showed a greater nocturnal OPP under the latanoprostene treatment compared to the timolol treatment, reflecting the smaller effect of timolol on IOP lowering combined with some reduction in MABP. The latanoprostene treatment is expected to be more beneficial than the timolol treatment if one considers the difference in ocular perfusion pressure during the day and night.

Summary

Treatment with latanoprostene bunod 0.024% once daily resulted in IOP lowering during the diurnal/wake period as well as during the nocturnal/sleep period. Treatment with latanoprostene bunod showed a greater nocturnal IOP-lowering effect compared to treatment with timolol 0.5% solution twice daily. Latanoprostene bunod treatment significantly increased diurnal ocular perfusion pressure from the baseline. Ocular perfusion pressure during the nocturnal period was higher under latanoprostene bunod treatment than under timolol treatment.

Vyzulta References

Roclatan (netarsudil ophthalmic solution) 0.02% and latanoprost

- May be first glaucoma product to lower IOP through all 4 mechanisms:
  - increasing aqueous outflow through both the trabecular meshwork and the uveoscleral pathway,
  - reducing aqueous production in the eye
  - reducing episcleral venous pressure.
- Superior to its two components netarsudil and latanoprost used separately.

Rhopressa Latanoprost Roclatan

**Mercury 2 Roclatan Responder Analysis**

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

<table>
<thead>
<tr>
<th>Reduction</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roclatan™ (n=121)</td>
<td><strong>59%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latanoprost (n=235)</td>
<td><strong>44%</strong></td>
<td><strong>41</strong></td>
<td><strong>21</strong></td>
<td><strong>13</strong></td>
<td><strong>10</strong></td>
</tr>
<tr>
<td>Rhopressa™ (n=235)</td>
<td><strong>27</strong></td>
<td><strong>22</strong></td>
<td><strong>13</strong></td>
<td><strong>10</strong></td>
<td><strong>10</strong></td>
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**Mercury 2 Results Consistent with Mercury 1 90-day Efficacy Results**

- Roclatan™ met the criteria for demonstrating superiority (p<0.0001) over both latanoprost and Rhopressa™ for the primary efficacy analysis
- IOP-lowering effect of Roclatan™ was greater (1-3 mmHg) than monotherapy with either latanoprost or Rhopressa™ throughout the duration of the study (i.e., Week 2, Week 6, Month 3)
- Roclatan™ reduced mean diurnal IOPs to 16 mmHg or lower in 56% of patients, a significantly higher percentage than observed in the comparator arms (25% Rhopressa™, 36% latanoprost)
- The most common adverse event for Roclatan™ was conjunctival hyperemia, which was reported in nearly 55% of patients and was scored as mild for ~70% of these patients
- There were no drug-related serious or systemic adverse events

Recent Trends in Glaucoma Surgery

- Bypass trabecular meshwork or use suprachoroidal approach
- Usually performed in conjunction with cataract surgery
- More effective in lowering IOP than Phaco alone
- Easier for surgeon and patient than trabeculectomy though less effective
- May reduce or eliminate dependence on meds

Minimally Invasive Glaucoma Surgery (MIGS)

- Bypass trabecular meshwork or use suprachoroidal approach
- Usually performed in conjunction with cataract surgery
- More effective in lowering IOP than Phaco alone
- Easier for surgeon and patient than trabeculectomy though less effective
- May reduce or eliminate dependence on meds
MIGS: Micro–Invasive Glaucoma Surgery
- Ab–interno approach
  - Clear corneal micro–incision (<2.0mm)
  - Conjunctival sparing
- Minimally traumatic
  - Negligible disruption of normal anatomy/physiology
- Reduce the need for more aggressive surgical options while preserving that option
  - Reduce medication burden

Significant Treatment Opportunity
One in Five Eyes with Cataract on OHT Medication
3.5M US Cataract Procedures
20.5K Cataract + Minimum of 1 OHT Med
79.5% Cataract Only
718K


Trabectome

Kahook Dual Blade
- Unroof trabecular meshwork and inner wall of Schlemm’s canal

iStent Indication For Use
The iStent Trabecular Micro-Bypass Stent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication
Specifications

iStent is the smallest medical device known to be implanted in the human body and weighs just 60 µg.

- Dimensions are customized for a natural fit within the 270 µm canal space.

Therapeutic Objectives

Designed to be used in conjunction with cataract surgery to safely and effectively reduce IOP while facilitating the eye’s natural outflow in mild to moderate OAG patients:

- Lowers IOP while helping to reduce medication burden
- Decrease risk of IOP fluctuations associated with non-adherence to prescription medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Spare the conjunctiva and safely preserve future treatment options
- Minimizes risks of hypotony and bleb related complications

ab interno trabecular micro-bypass stent for the treatment of glaucoma:

- Placed in inferonasal locations with high presence of collector channel congregations
- Designed to improve continuous, physiological outflow in the lower nasal quadrants

Injector System

Single Use Disposable Pre-loaded

Snorkel in TM
Surgical Procedure

- Rails are seated against scleral wall of Schlemm’s canal
- Snorkel sits parallel to the iris plane

Lasting Outcomes Through 3 Years (T. Neuhan)

- Single iStent + Cataract Surgery Achieves IOP < 15 mm Hg Through 3 Years
- Postoperative care
  - Use normal postoperative medications
  - Antibiotic, steroid, NSAID of choice
  - Continue current glaucoma medications
  - Watch for IOP rise related to steroid response
  - Evaluate IOP in context of target IOP
  - Degree of damage, patient age, likelihood of progression
  - If indicated, decrease medical treatment in stepwise fashion
  - Perform gonioscopy to confirm iStent position

Long-Term Data Through 5 Years

- Prospective, non-comparative, uncontrolled, non-randomized, interventional case series
- 19 patients with uncontrolled mild to moderate OAG using 1 or more topical glaucoma medications
- Results after mean follow-up of 54 months
- 42% of patients were medication free, with mean IOP reduction to 14.9 mm Hg
- Mean IOP declined to 14.9 mm Hg versus preoperative medicated IOP of 19.4 mm Hg
- Number of topical medications used declined from 1.9 to 0.3 or 86%

Which is better? 1 or 2? Or 3?

- 1, 2 or 3 iStents in OAG subjects on drops
- 1 stent: 38; 2 stents 41; 3 stents 40
- 12 month IOP reduction unmedicated IOP < = 15 mmHg
  - 1 stent: 64.9%
  - 2 stents: 85.4%
  - 3 stents: 92.1%
- 18 months, mean unmedicated IOP
  - 1 stent: 15.9±0.9 mmHg
  - 2 stents: 14.1±1.0 mmHg
  - 3 stents: 12.2±1.1 mmHg
- Month 18 IOP reduction was significantly greater (P<0.001) with implantation of each additional stent, with mean of 1.84 mmHg for three-stent vs two-stent groups and 1.73 mmHg for two-stent vs one-stent groups.

Katz LJ Clinical Oph 11 December 2015
**iStent in injector**

Approved for use in conjunction with cataract surgery.

- **Gel stent design**
  - 6-mm length, 45-micron lumen diameter — about the length of an eyelash.
  - Gelatin, cross-linked with glutaraldehyde.
  - Hydrates and minimally swells, softens, and becomes flexible after implantation.
  - Preloaded, disposable injector with a 27-gauge, double-beveled needle.

**Cypass in position**

- Cypass in the Supra-ciliary Space.

**Cypass Aqueous Flow**

- Cypass in position.
- Aqueous Flow.

**Xen Gel Stent**

- Minimally invasive inserted using the XEN injector via an ab-interno approach, through a small corneal incision.

- In the clinical investigation, standard ophthalmic surgery techniques, viscoelastic, and mitomycin C (0.2 mg/mL) were used before injection.

- Innovative approach:
  - Requires a small corneal incision.
  - The first ab-interno approach to create a new pathway for aqueous flow from the anterior chamber to the subconjunctival space in refractory glaucoma patients.
  - XEN® is the first procedure that creates a low-lying, ab-interno bleb in refractory glaucoma.

- Gel stent design:
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  - Gelatin, cross-linked with glutaraldehyde.
  - Hydrates and minimally swells, softens, and becomes flexible after implantation.
  - Preloaded, disposable injector with a 27-gauge, double-beveled needle.
CLINICAL TRIAL CRITERIA

Established in a phase 3, prospective, multicenter, single-arm, open-label, 12-month, US clinical trial

Study population
- 65 patients with refractory glaucoma
- Mean age: 70.0 years
- Prior cataract surgery: 45 (69.2%)
- Prior incisional glaucoma procedure: 41 (63.1%)
- Nebrolidexotomy, tube shunt, trabeculotomy, trabeculoplasty (all alone or in combination): 13 (20.0%)
- No prior glaucoma procedure and unresponsive to maximally tolerated medical therapy: 10 (15.4%)
- Mean cup-to-disc ratio: 0.8

Primary effectiveness measures
- Propportion of subjects at 12 months achieving a ≥20% IOP reduction from baseline on the same or fewer number of medications than at baseline
- Mean decrease in IOP from baseline to 12 months

Primary safety measures
- Procedure-related complications
- Biomicroscopic slit lamp and optical coherence tomography
- Ocular adverse events

Established Effectiveness

Primary Effectiveness Analyses

<table>
<thead>
<tr>
<th>Proportion of Subjects with 12-Month Mean Diurnal IOP Reduction of ≥ 20% from Baseline on Same or Fewer Medications (N=65)</th>
<th>n/N (%)</th>
<th>Mean ± SE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>76.3% (65.8%, 86.8%)</td>
<td>-6.4 ± 1.1 mmHg (-8.7, -4.2)</td>
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</table>

**Study Notes:**
- Study was evaluating glaucoma-related secondary surgical intervention and multiple imputations for missing data.
- Seven subjects in the study underwent needling procedures with mitomycin C. Of these subjects, the iStent was removed in six cases and explanted in one case.
- Procedure-related complications were defined as an adverse event, regardless of whether there were any associated sequelae related to the procedure. A total of three cases were reported.
- Multiple imputations for missing data.

**Follow-up:**
- 12-month visit; there were no cases of persistent hypotony, and no surgical intervention was required for any case of hypotony.

Proportion of subjects at 12 months achieving a ≥20% IOP reduction from baseline on the same or fewer number of medications than at baseline

Mean decrease in IOP from baseline to 12 months

Mean IOP reduced to 15.9 mm Hg (N=52) from 25.1 mm Hg at medicated baseline

Reduced mean IOP by ≥25% in 15.4% (n=10/65) of patients who had no prior glaucoma procedures.

Preoperative Considerations

- **iStent Candidate**
  - Mild to moderate open angle glaucoma (no more severe than a mean deviation of -12dB)
  - Visually significant cataract is present on examination
  - Patient desires to reduce dependence on glaucoma medications

Any patient with cataracts being treated for mild to moderate open angle glaucoma with medications may be a potential candidate for an iStent

**In the Pivotal Clinical Trial**

- 0 of 65 subjects experienced intraoperative complications
  - 0% surgical complications
  - 0% hyphema
  - 0% conjunctival perforation
  - 0% iris/lens damage

**Mean IOP lowering medications reduced to 1.7 (N=52) from 3.5 at medicated baseline**

Reduced mean IOP by ≥25% in 80.8% of eyes.

**Increased Diurnal IOP Reduction of ≥20% from Baseline on Same or Fewer Medications (N=65)**

**Mean IOP reduced to 15.9 mm Hg (N=52) from 25.1 mm Hg at medicated baseline**

**Established Effectiveness**

Reduced mean IOP by ≥25% in 80.8% of eyes.

**Demonstrated Safety**

- 0 of 65 subjects experienced intraoperative complications
- 0% surgical complications
- 0% hyphema
- 0% conjunctival perforation
- 0% iris/lens damage

**No clinically significant consequences were associated with hypotony, such as choroidal effusions, suprachoroidal hemorrhage, or hyphoconus maculopathy.**

**Mean Diurnal IOP Reduction of ≥20% from Baseline on Same or Fewer Medications (N=65)**

**Proportion of Subjects with 12-Month Mean Diurnal IOP Reduction of ≥ 20% from Baseline on Same or Fewer Medications (N=65)**

- 76.3% (65.8%, 86.8%)

**Mean Diurnal IOP Reduction from Baseline at the 12-Month Visit (N=65)**

- -6.4 ± 1.1 mmHg (-8.7, -4.2)

**Primary Effectiveness Analyses**

- Study was evaluating glaucoma-related secondary surgical intervention and multiple imputations for missing data.
- Seven subjects in the study underwent needling procedures with mitomycin C. Of these subjects, the iStent was removed in six cases and explanted in one case.
- Procedure-related complications were defined as an adverse event, regardless of whether there were any associated sequelae related to the procedure. A total of three cases were reported.
- Multiple imputations for missing data.

**Follow-up:**
- 12-month visit; there were no cases of persistent hypotony, and no surgical intervention was required for any case of hypotony.

**Study population**
- 65 patients with refractory glaucoma
- Mean age: 70.0 years
- Prior cataract surgery: 45 (69.2%)
- Prior incisional glaucoma procedure: 41 (63.1%)
- Nebrolidexotomy, tube shunt, trabeculotomy, trabeculoplasty (all alone or in combination): 13 (20.0%)
- No prior glaucoma procedure and unresponsive to maximally tolerated medical therapy: 10 (15.4%)
- Mean cup-to-disc ratio: 0.8

**Primary effectiveness measures**
- Proportion of subjects at 12 months achieving a ≥20% IOP reduction from baseline on the same or fewer number of medications than at baseline
- Mean decrease in IOP from baseline to 12 months

**Primary safety measures**
- Procedure-related complications
- Biomicroscopic slit lamp and optical coherence tomography
- Ocular adverse events

**Established Effectiveness**

- 76.3% (65.8%, 86.8%)

**Mean Diurnal IOP Reduction from Baseline at the 12-Month Visit (N=65)**

- -6.4 ± 1.1 mmHg (-8.7, -4.2)

**Primary Effectiveness Analyses**

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- 12-month visit; there were no cases of persistent hypotony, and no surgical intervention was required for any case of hypotony.

**Proportion of Subjects with 12-Month Mean Diurnal IOP Reduction of ≥ 20% from Baseline on Same or Fewer Medications (N=65)**

- 76.3% (65.8%, 86.8%)

**Mean Diurnal IOP Reduction from Baseline at the 12-Month Visit (N=65)**

- -6.4 ± 1.1 mmHg (-8.7, -4.2)
iStent Pre-op Care

- Review risks and benefits of possible medical and surgical treatment options
- Do NOT promise that the patient will be able to stop some or all of their glaucoma medications
- Continue current glaucoma medications through day of surgery
- Confirm patient’s VF, ONP and OCT are up to date
- Gonioscopy – evaluating for synechia, iris processes, narrow anatomical angles, angle recession or any other abnormalities of the angle structure that may interfere with placement of the iStent

Post-op Complications

Is the iStent in correct position?
Hyphema due to iStent