Minimally Invasive Glaucoma Surgery

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Disclosure

- Speakers Bureau for Aerie, Alcon, Allergan, Biotissue, Centervue, Glaukos, Oculus, Optovue, Reichert, Synemed, Telscreen, Valeant

Trabeculectomy

- Long-standing primary glaucoma surgical procedure
- Medical adjuncts
  - 5-FU
  - Mitomycin C
- Suture lysis
- Generally effective
- Risks
- Predictability

Carol Thin Leaking Bleb

Hypotony

MCE due to elevated IOP
5-FU-Induced Keratopathy

Mark One Week Postop
- PO Day 1 IOP 14
- PO Day 4 Eye soft, quiet
- PO Day 7 IOP 43

Is there a better way?

MIGS

Alcon Express Drainage Device
NOT a MIGS Procedure
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

**Concomitant Cataract & Glaucoma Patients – US**

Significant Treatment Opportunity
One in Five Eyes with Cataract on OHT Medication
3.5M US Cataract Procedures

- 20.5%
- Minimum of 1 OHT Med
- 79.5%
- Cataract Only
- 718K


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

**Kahook Dual Blade**

- Unroof trabecular meshwork and inner wall of Schlemm’s canal
Cypass Shunt

Approved for use in conjunction with cataract surgery

**XEN® Gel Stent**

**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**
- 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

**Ab–Interno Bleb Low–lying diffuse**

**RESHAPING GLAUCOMA MANAGEMENT**

XEN® is the first procedure that creates a low-lying, ab-interno bleb in refractory glaucoma

- Low-lying and diffuse
- Example of elevated, cystic bleb
CLINICAL TRIAL CRITERIA

Established in a phase 3, prospective, multicenter, single-arm, open-label, 13-month, US clinical trial.

Study population:
- 65 patients with refractory glaucoma
- Mean age 70.3 years
- Prior cataract surgery: 45 (69.2%)
- Prior inclusion glaucoma procedure: 41 (63.1%)
- Mean visual field mean deviation (MD) score: -15 dB
- Mean IOP at baseline: 25.1 (± 4.2) mm Hg
- Mean decrease in IOP from baseline to 12 months: 15.9 (± 8.7) mm Hg

Primary effectiveness measures:
- Proportion of subjects at 12 months achieving ≥ 20% 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
- 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</th>
<th>n/N (Di) (SN CI)*</th>
<th>Mean ± SE (95% CI)**</th>
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<tbody>
<tr>
<td>with Same or Fewer Medications (N=65)*</td>
<td>76.3% (60.5%, 88.8%)</td>
<td>-6.4 ± 1.1 mmHg (−8.7, −4.2)</td>
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Primary effectiveness analysis using observed data and failure for subjects with glaucoma-related secondary surgical intervention and multiple imputations for missing data.

DEMESTRATED SAFETY

In the Pivotal Clinical Trial

- 0 of 65 subjects experienced intraoperative complications
- 0% surgical complications
- 0% hyphema
- 0% conjunctival perforation
- 0% iris/lens damage
- 0 of 65 subjects experienced persistent hypotony (IOP < 6 mm Hg at 2 visits > 30 days apart)*
- Hypotony (IOP < 6 mm Hg at any time): 24.6% (16/65)*

*No clinically significant consequences were associated with hypotony, such as choroidal effusions, suprachoroidal hemorrhage, or hypotony maculopathy. IOP < 6 mm Hg was defined as an adverse event, regardless of whether there were any associated complications or sequelae related to the low pressure. Thirteen cases occurred at the 1-day visit; there were no cases of persistent hypotony, and no surgical intervention was required for any case of hypotony.

XEN® reduced mean IOP by ≥ 20% in 80.8% of eyes.


demonstrated safety

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iStent® (Glaukos)

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

- Bypass Stent
  - Diameter: 1 mm
  - Length: 1 mm
  - Height: 0.3 mm
  - Surgical grade, nonferromagnetic stainless steel
  - Hyaluronic coated to promote self-centering
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

iStent® is 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 currently on hypotensive medication

- Lowers IOP and may reduce or eliminate medication burden1
- 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

Primary Source of Resistance: Diseased Trabecular Meshwork

- Abnormality of the trabecular meshwork (TM) is the primary source of elevated intraocular pressure (IOP) in open-angle glaucoma
- 50–75% of total resistance to aqueous humor outflow is found in the juxtacanalicular tissue of the TM
- Bypassing the TM allows access to Schlemm’s canal and the distal system in order to improve aqueous outflow through the conventional outflow pathways

Mechanism of Action: Anatomic Placement & Rationale

iStent® is an 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

Microstenting Schlemm’s Canal: SAFETY

- Enhancement of natural physiological outflow
- Physiologic floor minimizes risk of hypotony
  - Natural episcleral back pressure typically 8–11 mm Hg
  - Lack of bleb or conjunctival manipulation
  - Lack of blood vessels & least tissue reaction
- Minimal disruption of angle anatomy
  - Minimize risk related to cell damage, inflammation, fibrosis, PAS
- Rapid recovery, VA
- Does not preclude further glaucoma surgery if needed
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. Neuhann)

Single iStent + Cataract Surgery Achieves IOP < 15 mm Hg Through 3 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 16.1 mm Hg
  - Mean IOP declined to 16.1 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%

Long-Term Data Through 5 Years

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Pre-operative 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.

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

iStent Post-operative 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

Carl 10-3-12

- 72yo WM treated for COAG Travatan–Z OU
- Ran out of Travatan while on vacation in June
- Never refilled Rx
- IOP R 23 L 18
- S/P ½ SLT OS
- VA R 20/20 L 20/50
- Contrast Sensitivity/Glare 20/100 OU
9 Days post phaco/IOL/iStent OS
VA sc L 20/25
IOP L 18
Still on Travatan-Z OU

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
2 iStents in position

More to come

Post-op Complications
Is the iStent in correct position?

Hyphema due to iStent

iDose Travaprost Implant

Prostaglandin analogs are most common first-line medication for management of IOP

iDose Clinical Goals
- To achieve non-inferior IOP reduction compared to existing topical glaucoma therapies
- To reduce or maintain therapeutic period of IOP control (minimum of 6 months)
- To minimize side effects and achieve outcomes

Medical Needs
- Address high rates of patient non-adherence with topical glaucoma regimens
- Provide sufficient duration of effect with favorable risk profiles

iDose Next Steps
- Finalize US IND Phase III trial protocol and commence trial
- Begin process to seek regulatory approval in European markets and in Japan

iDose Travaprost

iDose Travaprost: First-of-a-Kind Intracocular Drug Delivery Device

Average IOP Reductions

iDose Travaprost US Phase II: Preliminary Efficacy Results

Average IOP reductions through Month 12 ranging from 7.9 to 8.5 mmHg in the implant arms

Represents 32-33% reduction in the implant arms
Therapeutic Objective

Travaprost Implant is designed to:

- Reduce IOP while reducing or eliminating medication use
- Spare the conjunctiva
- Decrease the risk for large IOP fluctuations that are associated with non-adherence to prescription medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Eliminate risks of bleb formation
- Safely preserve patient candidacy for all future treatment options

Clinical Study Design

- Phase III starting in first half of 2018: 1000 randomized subjects in US and international locations
- Include Ocular Hypertensive or Open-angle glaucoma
- Subjects randomized to either iDose or sham procedure; all arms are treated
- Follow-up through 3 years postoperative
- Subjects seen for a total of 19 visits: Screening, Baseline, Surgery, Day 1–2, Day 10, Week 4, Week 6, Month 3, Month 6, Month 9, Month 12, Month 15, Month 18, Month 21, Month 24, Month 27, Month 30, Month 33, and Month 36

Opportunities

- Provide your patient with the chance to obtain new technology not commercially available and to benefit medical science through participation in a clinical study
- Potentially reduce your patient’s need for ocular hypotensive medications
- Study patients are reimbursed for their time and travel
- All study visits are provided at no cost