New Horizons in Glaucoma Devices

Steven Vold MD
Vold Vision
February 4, 2017
# Financial Disclosures

<table>
<thead>
<tr>
<th>Company</th>
<th>Nature of Affiliation</th>
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</thead>
<tbody>
<tr>
<td>• Vold Vision, P.L.L.C</td>
<td>• Founder and Chief Executive Office</td>
</tr>
<tr>
<td>• BK Ventures Group</td>
<td>• Principal and Director</td>
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<tr>
<td>• Aeon, Allergan, Arie Pharmaceuticals, Calhoun Vision, SOLX, Ocular</td>
<td>• Grants/Research Support</td>
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<tr>
<td>Therapeutix, Forsight Labs, InnFocus, AqueSys, Ivantis, Glaukos, Alcon</td>
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<td>Allergan, Transcend Medical, Bausch &amp; Lomb</td>
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<td>Iridex, Carl Zeiss Meditec, Glaukos, Alcon,</td>
<td>Consultant</td>
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<td>Lumenis, Transcend Medical, Volk Optical,</td>
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<td>Wavetec Vision</td>
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<tr>
<td>Alphaeon, TrueVision Systems, Ocunetics</td>
<td>Stock/Shareholder</td>
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<tr>
<td>Neomedix, Allergan</td>
<td>Speakers’ Bureau</td>
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Case 1. Clinical History

72 y.o. man presents for regular yearly examination complaining of ocular redness, ocular FB sensation and difficulty reading fine print
Past Ocular History: POAG OU
Past Medical History: Coronary artery disease
Family History: Multiple family members with POAG
Medications: Timolol 0.5% OU QAM; Latanoprost OU QHS
Clinical Examination

Best-corrected Visual Acuity: 20/30 OU, but does glare to 20/50 OU
Manifest Refraction: -1.50 sphere OU
Visual fields: Early arcuate defects OU
Corneal Pachymetry: 540 um OD; 546 um OS
Goldmann Tonometry: 23 mm Hg OU
OHS: 0.7 OU with disc heme inferiorly
How do you recommend that we manage this patient?

1) Alter glaucoma medication regimen
2) Laser trabeculoplasty
3) Filtration surgery alone
4) Combined cataract and filtration surgery
5) Combined cataract and iStent surgery
Current Standard Treatments and Limitations

51% of glaucoma patients are on 2 or more medications.

Addition of 3rd and 4th med, no benefit.

* Neelakantan MD, A, J Glaucoma 2004 Apr;13(2):130-6, “Is addition of a Third or Fourth antiglaucoma medication effective?”
# Current Standard Treatments and Limitations

<table>
<thead>
<tr>
<th>Complications</th>
<th>Trab (%)</th>
<th>External Shunts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications: Intra Op</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>Post Op (1 Yr):</td>
<td>57%</td>
<td>34%</td>
</tr>
<tr>
<td>Choroidal Effusion</td>
<td>19%</td>
<td>16%</td>
</tr>
<tr>
<td>Choroidal Hemorrhage</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Shallow / Flat AC</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>Hyphema</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Vision Loss (≥2 lines)</td>
<td>28%</td>
<td>17%</td>
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</tbody>
</table>

1. ASO Gedde et al 2007, Vol 143: 9-22 TVT Study
MIGS is transforming the way we treat combined cataract and glaucoma

% Patients with Concurrent Glaucoma and Cataracts Receiving Combined Phaco-Glaucoma Surgery

- MIGS
- Trabs/Tubes

MIGS Introduction

Market Scope, 2012
The Evolution of Trabecular Bypass Procedures in Adults
Nylon Filament Trabeculotomy. Comparison with the results of conventional drainage operations in glaucoma simplex

Redmond Smith (London) 1969
Transactions of the Ophthalmological Society of New Zealand

Fig. 1 (a)—Diagram to show the technique of nylon filament trabeculotomy.
Retrospective review of 149 eyes
Ab externo trabeculotomies
Mean +/- SD follow up time: 9.5 +/- 7.1 years
Mean +/- SD IOP at last follow up: 15.6 +/- 5.0
Success rate of nearly 90%
Problems with Trabeculotomy Ab Externo

Length of time (30-60+ minutes)
Numerous Conjunctival and Scleral sutures required
Violate the superior conjunctiva
May preclude or diminish success rates for a subsequent trabeculectomy
Relatively invasive
ABiC (Ab Interno Canaloplasty) vs GATT (Gonioscopy Assisted Transluminal Trabeculotomy)
CYCLO G6™ Glaucoma Laser System
MicroPulse® P3 – Cyclophotocoagulation with MicroPulse Technology

• Excellent Safety Profile
• Efficient & Straightforward for physician and patient
• Can be performed in the Office & OR
• Predictability
Next-Generation Glaucoma Microstents and Implants: Right Around the Corner

First-Generation Devices Paving the Way

Next-Generation Trabecular Microstents

Next-Generation Uveoscleral Microstents

Next-Generation Subconjunctival Implants
Next-Generation Trabecular Microstents
Increasing access to Schlemm’s canal to drive more flow

**iStent Inject**
- CE Mark in 2009
- US IDE trial in progress
- Allow for 2 access points through the trabecular meshwork, expanding potential outflow through Schlemm’s canal
  - Multiple iStents have been shown to have improved IOP-lowering effect

**Hydrus Microstent**
- CE Mark in 2011
- US IDE trial in progress
- Creates entry point through trabecular meshwork and stents open several clock hours to enhance outflow through Schlemm’s canal

1. Belovay, JCRS 2012
Hydrus Surgical Video
Next-Generation Uveoscleral Microstents
Unlocking the eye’s natural potential through a new mechanism of action

**CyPass Micro-Stent**
- CE Mark in 2009
- US IDE trial completed
- Leverage uveoscleral outflow, bypassing potentially diseased trabecular outflow pathway
- 6.35 mm length, with lumen of 0.3 mm
- Currently undergoing FDA review, estimated approval end of 2016

**iStent Supra**
- CE Mark in 2011
- US IDE trial in progress
- Leverages uveoscleral outflow, bypassing potentially diseased trabecular outflow pathway
- 4 mm length, with lumen of 0.16 mm
Next-Generation Subconjunctival Implants
Accessing a well-worn path in new ways

**XEN Gel Stent**
- CE Mark in 2012
- US IDE trial in progress
- Placed ab interno with outflow into subconjunctival space
- Used in conjunction with Mitomycin-C

**InnFocus Microshunt**
- CE Mark in 2012
- US IDE trial in progress
- Only trial randomized vs trabeculectomy
- Place ab externo into conjunctival pocket
- Used in conjunction with Mitomycin-C
## Estimated FDA approval for MIGS implants

<table>
<thead>
<tr>
<th>MIGS – Ab-interno implants</th>
<th>Estimated FDA approval</th>
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<tbody>
<tr>
<td>Glaukos iStent (PMA)</td>
<td>Q3 – 2012</td>
</tr>
<tr>
<td>Transcend Medical CyPass Micro-Stent (PMA)</td>
<td>Q3 – 2016</td>
</tr>
<tr>
<td>Glaukos iStent Inject (PMA)</td>
<td>Q1 – 2018</td>
</tr>
<tr>
<td>Ivantis Hydrus (PMA)</td>
<td>Q4 – 2018</td>
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<tr>
<td>Glaukos iStent Supra (PMA)</td>
<td>Q1 – 2020</td>
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*Market Scope 2015 Analyst reports*
CyPass Micro-Stent

- Recently approved by FDA
- Novel aqueous outflow enhancement: non-trabecular
- Suprachiliary vs trabecular stenting
- *Ab interno*, non-perforating, no bleb, no MMC
Tapping into the Uveoscleral Outflow Pathway

• Uveoscleral outflow: considered pressure independent and contributes **up to 57% of natural aqueous outflow**

• Aqueous percolates through the ciliary body and **exits into the suprachoroidal space**, primarily through the sclera and choroidal blood vessels

• Bypasses Schlemm’s canal and collector channels, which may be **atrophic in glaucoma patients**

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Fellman. Episcleral venous fluid wave correlates with the type and extent of canal-based surgery. AGS 2014 abstract.
CyPass Clinical Outcomes
Mild –Moderate Glaucoma

Combined with Phaco
CyCle Study

Mean IOP (mmHg)
Baseline 25.5
M6 16.9
M12 16.6
M24 15.8
Reduction: -35%

CyPass Implantation Only
DUETTE Study

Mean IOP (mmHg)
BL (n=65) 24.5
M6 (n=52) 17.7
M12 (n=48) 16.8
Reduction: -32%

Hoeh, Klin Monbl Augenheil 2014
Garcia-Feijoo, AJO 2015.
COMPASS Study of the CyPass Micro-Stent
Largest randomized controlled trial of a glaucoma implant to date

- Terminal wash out at 12 and 24 months
- Strict criteria for re-introduction of meds
- Rigorous analysis of endothelial cell density
- Strong primary endpoint outcome: 2-year diurnal un-medicated IOP change

N = 255  EMGT trial
N = 276  ABC trial
N = 212  TVT trial
N = 240  iStent trial
N = 505  COMPASS trial
The Future of Uveoscleral Microstents

- Presence of aqueous lake posterior to and around the micro-stent was imaged and identified using OCT and UBM
- Some patients had a greater degree of subscleral aqueous lake
- This increased lake correlated with improved IOP outcomes

<table>
<thead>
<tr>
<th>Fluid Behind and Around</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
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<tbody>
<tr>
<td></td>
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<table>
<thead>
<tr>
<th>Tenting</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
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<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
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CyPass Vx
Enabling CyPass Micro-Stent with Visco-Expansion

- Delivers viscoelastic to the supraciliary and suprachoroidal spaces
- Creates and maintains space for enhanced aqueous outflow
- Can achieve volumetric expansion 50X current CyPass Micro-Stent
IOP Reduction 12M vs Baseline

Mean IOP Change 12M

- IOP Difference
  - CyPass only (n=21): -7.0 mm ± 4.2
  - CyPass + 30 uL (n=21): -8.7 mm ± 7.8
  - CyPass + 60 uL (n=21): -9.9 mm ± 5.8

IOP reduction

Dose response trend identified with increasing volume of viscoinjection

Calvo. AAO 2015 abstract
Future Therapeutic Platform Technology in the Suprachoroidal Space

Drug-infused visco

Sustained release

Retinal disease / Neovascular glaucoma
Effective Subconjunctival Drainage Made Simple
- Delivers significant and sustained reduction of IOP through the sub-conjunctival outflow pathway
- Bypasses all potential aqueous outflow obstruction through an ab interno approach
- Spares ocular tissue, leaving all other treatment options available
- Minimizes implant related complications because of its soft, gelatin material (non-inflammatory, non-migrating)

Preloaded Injector Provides Convenience
- Pre-loaded, disposable, “IOL-like” injector comes loaded with the XEN Gel Stent.
- Can be done as a primary procedure or in combination with cataract surgery
Portfolio Progression for Hypotony Control

XEN 140
6mm/140 micron inner lumen
Minimal hypotony protection
3 year IOP= 13.6 mmHg
-38% IOP & -79% Meds
N=100

XEN 63
6mm/63 micron inner lumen
Medium hypotony protection
3 Year IOP= 12.4mmHg
-44% IOP & -76% Meds
N=150

XEN 45
6mm/45 micron inner lumen
Strong hypotony protection
1 Year IOP= 13.2mmHg
-40% IOP & -85% Meds
N=700

Progression: Same Strong Efficacy + Strong Safety/Minimal Post-Op “Fire and Forget”
Feasibility Data:
Shows Long Term Efficacy

N=674 All 3 Models

Mean IOP Over Time and Mean % Change in IOP from Best Medicated

Complete # (%) | 674 | 610 (90.5%) | 533 (79%) | 461 (74%) | 399 (63%) | 268 (42%) | 194 (29%) | 179 (26.5%) | 82 (12%) | 68 (10.5%) | 45 (7%) | 26 (4%)

Additional Surgery (Cumulative) | - | 0/ 674 (0%) | 0/ 674 (0%) | 2/ 674 (0.5%) | 8/ 674 (1%) | 14/ 674 (2%) | 23/ 674 (3%) | 26/ 674 (4%) | 27/ 674 (4%) | 30/ 674 (4%) | 30/ 674 (4%) | 32/ 674 (5%)

Missed Visit | - | 14 (2%) | 18 (2.5%) | 30 (5%) | 16 (3%) | 11 (2%) | 9 (1%) | 0 (0%) | 9 (1%) | 2 (0.5%) | 3 (0.5%) | 0 (0%)

Study Closed/ LTFU | - | 2 (0.5%) | 2 (0.5%) | 4 (0.5%) | 9 (1%) | 13 (2%) | 16 (3%) | 17 (2.5%) | 19 (3%) | 21 (3%) | 23 (3.5%) | 24 (4%)

Pre-Window | - | 48 (7%) | 121 (18%) | 128 (20%) | 206 (32%) | 333 (52%) | 432 (64%) | 452 (67%) | 537 (80%) | 553 (82%) | 573 (85%) | 592 (87%)
**XEN Bleb**

**Ab Externo Bleb** vs. **XEN Ab Interno Bleb**

After Trabeculectomy/Express After XEN

- **Suture wounds**
- **Dissected Tenon layer**
- **Chance for raised bleb with liquid pocket underneath**
- **Controlled flow through lumen restriction**
- **No trauma to conjunctiva**
- **Tenon adhesions intact**
- **Undisturbed, low lying drainage space**

**Effective IOP lowering**
- Elevated and focal due to dissection
- Thin Walled
- Higher risk of infection

**Effective IOP lowering**
- Low lying and diffuse
- Deep in the intra tenon’s tissue
- Low risk of infection
XEN: The Procedure

AqueSys @24M: Low, diffuse, posterior drainage
Glaucoma Devices: The Shape of Things to Come

• The development of patient-specific imaging and diagnostics for optimal therapy selection

• Consider trabecular bypass procedures early on

• Suprachoroidal microstents offer excellent MIGS alternative in mild-moderate open-angle glaucoma patients

• Subconjunctival microshunts appear to be promising option in the treatment of moderate to more advanced glaucomas

• The combination of aqueous outflow implants with drug delivery to achieve ideal long-term results
Thank You