New Minimally Invasive Glaucoma Surgery Options
Leon W. Herndon Jr., MD

What Is MIGS?

- Smart weapons, targeting the enemy, with minimal to no collateral damage
- Ab interno
- Must have minimal alteration of the tissue
  - No conjunctival incision
- Must be safe
- At least modestly efficacious
- Rapid recovery

Bleb Complications

Glaucoma Surgery: The New Frontier

- MIGS is preeminent in the minds of doctors, patients, industry, and the ophthalmology media
- With so much churning in the ophthalmic field, how can we find clarity and establish practice patterns?
- Can we practice evidence-based medicine?
- How do we pick the right procedure for any given patient?
- Can we individualize the treatment of glaucoma?
- How many different treatment modalities can one surgeon handle?
MIGS—A New Philosophy

- Glaucoma surgery was reserved for patients losing vision despite maximum medical therapy
- Reserving it as a last resort was appropriate because of the high associated risks
- The hallmark of MIGS, however, is safety


Patient Profiles: New Procedures

**MIGS-Type Procedures**
Ab Interno Schlemm’s/Suprachoroidal
- Mild-moderate disease
- Open-angle
- Modest IOP target (ie, 15-16 mm Hg)
- Able to tolerate some meds


**Trabeculectomy-Type Procedures**
- Moderate-advanced disease
- Progressing normal pressure glaucoma
- Open or narrow angle
- Low IOP target (ie, < 13 mm Hg)
- Intolerant to most meds
Implant Placement

1. Trabecular Micro-Bypass/Schlemm’s Canal

2. Suprachoroidal Space

3. External Bypass/Subconjunctival Space

Overview of the MIGS Landscape

<table>
<thead>
<tr>
<th>FDA PMA</th>
<th>MIGS CLASS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaukos iStent</td>
<td>2012</td>
</tr>
<tr>
<td>Glaukos iStent Inject</td>
<td>2018</td>
</tr>
<tr>
<td>Ivantis Hydrus</td>
<td>2018</td>
</tr>
<tr>
<td>Alcon CyPass</td>
<td>2016</td>
</tr>
<tr>
<td>Allergan Xen</td>
<td>2016</td>
</tr>
</tbody>
</table>
Overview of the MIGS Landscape

<table>
<thead>
<tr>
<th>CLASS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellex ABiC</td>
<td>Canal/Trabecular Dilation</td>
</tr>
<tr>
<td>Sight Sciences</td>
<td>Canal/Trabecular Dilation</td>
</tr>
<tr>
<td>Visco360; Omni</td>
<td></td>
</tr>
<tr>
<td>New World Medical</td>
<td>Trabecular Meshwork Removal</td>
</tr>
<tr>
<td>Kahook Dual Blade (KDB)</td>
<td></td>
</tr>
<tr>
<td>Sight Sciences</td>
<td></td>
</tr>
<tr>
<td>Trab360; Omni</td>
<td></td>
</tr>
<tr>
<td>NeoMedix</td>
<td>Trabecular Meshwork Removal</td>
</tr>
<tr>
<td>Trabectome</td>
<td></td>
</tr>
</tbody>
</table>

Putting MIGS Into Perspective
MIGS Approaches: Trabecular Micro-Bypass

Second-Generation Trabecular Micro-Bypass Injector

- Heparin-coated titanium
- Dimensions: 360 x 230 μm with radial symmetry
- Injected through the trabecular meshwork into Schlemm's canal
- Treatment consists of implantation of two stents

Second-Generation Trabecular Micro-Bypass Procedure

- Step 1. Approach perpendicular to the tissue
- Step 2. Penetrate the tissue with trocar
- Step 3. Lightly press on the TM (or dimple), hold steady, then deploy stent

One, Two, or Three Trabecular Bypass Stents Standalone Dose-Response Study

Dose Response Seen With 4- to 7-mm Hg IOP Reductions From Screening and 90+% Medication Reductions

<table>
<thead>
<tr>
<th></th>
<th>One stent</th>
<th>Two stents</th>
<th>Three stents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>24.9</td>
<td>25.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Baseline</td>
<td>11.8</td>
<td>12.3</td>
<td>12.3</td>
</tr>
<tr>
<td>Day 1</td>
<td>11.5</td>
<td>12.3</td>
<td>12.3</td>
</tr>
<tr>
<td>Week 1</td>
<td>11.5</td>
<td>12.3</td>
<td>12.3</td>
</tr>
<tr>
<td>Month 1</td>
<td>12.0</td>
<td>12.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Month 3</td>
<td>12.0</td>
<td>12.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Month 6</td>
<td>12.0</td>
<td>12.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Month 12</td>
<td>12.0</td>
<td>12.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Month 18</td>
<td>12.0</td>
<td>12.8</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Note: final numbers in manuscript different than this graph.
Trabecular Bypass Stent Standalone or + Phaco in Naïve or Prior Glaucoma Surgery Patients
Case Series—IOP Through 18M

Mean ±SD IOP, mm Hg

- Naïve to surgery (n = 33)
- Prior glaucoma surgery (n = 32)

Naïve Eyes: 12.5-mm Hg IOP decrease (47% reduction)
Eyes With Prior Sx: 12.2-mm Hg IOP decrease (45% reduction)

Postoperative Adverse Events

<table>
<thead>
<tr>
<th>Postoperative Events</th>
<th>Cataract Surgery With Trabecular Bypass Stent</th>
<th>Cataract Surgery Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular surface disease</td>
<td>62 (16.1%)</td>
<td>20 (16.8%)</td>
</tr>
<tr>
<td>Stent obstruction, partial or complete, regardless of how long the obstruction is present</td>
<td>24 (6.2%)</td>
<td>NA</td>
</tr>
<tr>
<td>Any intraocular inflammation (non-preexisting) remaining or arising after the protocol’s specified medication regimen is complete</td>
<td>22 (5.7%)</td>
<td>5 (4.2%)</td>
</tr>
<tr>
<td>Secondary surgical intervention</td>
<td>21 (5.4%)</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>Ocular allergies</td>
<td>11 (2.8%)</td>
<td>4 (3.4%)</td>
</tr>
<tr>
<td>Loss of BSCVA of 2 lines or more (10 letters or more on ETDRS chart) at or after 3 months postoperative</td>
<td>10 (2.6%)</td>
<td>5 (4.2%)</td>
</tr>
<tr>
<td>Posterior vitreous detachment</td>
<td>10 (2.6%)</td>
<td>5 (4.2%)</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>9 (2.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Blurred vision/visual disturbance</td>
<td>9 (2.3%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Extraocular inflammation</td>
<td>9 (2.3%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Epiretinal membrane</td>
<td>9 (2.3%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>IOP increase ≥ 10 mm Hg vs baseline IOP occurring at ≥ month 1</td>
<td>8 (2.1%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Perioperative ocular pain within 14 days of surgery</td>
<td>8 (2.1%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Vitreous floats</td>
<td>9 (2.1%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Corneal abrasion</td>
<td>8 (2.1%)</td>
<td>4 (3.4%)</td>
</tr>
</tbody>
</table>

Package insert.
Schlemm’s Canal Microstent Overview

Evolution of Canal Stenting

- **ISTENT (2012)**: BYPASS
- **ISTENT INJECT (2018)**: BYPASS + ADDED COVERAGE
- **HYDRUS MICROSTENT (2018)**: BYPASS + 90° SPAN + SCAFFOLD
Schlemm’s Canal Microstent: Ab Interno Canal-Based MIGS

Schlemm’s Canal Microstent
- Flexible, biocompatible, 8 mm–long 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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Real-Time Confirmation of Accurate Delivery

Video courtesy of I. Paul Singh, MD.

Visual Confirmation of Proper Placement—No Need for Targeting

Reliable & Efficient Access to Multiple Collector Channels

Dye Test Verifies Outflow in Stented Quadrant

Video courtesy of Ike Ahmed, MD
HORIZON Clinical Trial

Overview

HORIZON: Largest Ever MIGS Pivotal Trial

Enrolled US Pivotal Trials (MIGS + Phaco vs Phaco Alone)

<table>
<thead>
<tr>
<th>Stent Manufacturer</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>iStent GLAUKOS¹</td>
<td>239</td>
</tr>
<tr>
<td>CyPass ALCON²</td>
<td>505 (US ONLY)</td>
</tr>
<tr>
<td>iStent Inject GLAUKOS³</td>
<td>505</td>
</tr>
<tr>
<td>Hydrus Microstent IVANTIS⁴</td>
<td>556</td>
</tr>
</tbody>
</table>

HORIZON Trial: Study Design

**Eligibility**
- **Inclusion:** Mild/moderate POAG (VF MD ≥ 12 dB), cataract, 1-4 medications, no prior glaucoma surgery, ± prior SLT
- **Wash-Out & DIOP**
  - After 4-week wash-out: mean DIOP 22-34 mm Hg
- **Cataract Surgery**
  - N = 556
  - 2:1 randomization
- **Primary endpoint:** 20% reduction in washed-out DIOP at 24 months
- **Secondary endpoint:** Change in mean washed-out DIOP at 24 months
- **Medications:** mean and counts at each visit
- **Statistics:** > 90% power for primary endpoint; ITT analysis

Kuldev Singh, MD, MPH, Medical Monitor

Demographics and Preoperative Status

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>MS n = 369</th>
<th>No Stent n = 187</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>71.1 ± 7.9</td>
<td>71.2 ± 7.6</td>
</tr>
<tr>
<td>OD study eye, %</td>
<td>48.2%</td>
<td>49.2%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>5.7%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Black or African</td>
<td>12.2%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>78.9%</td>
<td>81.8%</td>
</tr>
<tr>
<td>Other</td>
<td>3.3%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Glaucoma medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>52.6%</td>
<td>54.0%</td>
</tr>
<tr>
<td>2</td>
<td>27.1%</td>
<td>25.7%</td>
</tr>
<tr>
<td>3</td>
<td>17.6%</td>
<td>15.0%</td>
</tr>
<tr>
<td>4</td>
<td>2.7%</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ocular and Glaucoma Status</th>
<th>MS n = 369</th>
<th>No Stent n = 187</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA, mean</td>
<td>20/40</td>
<td>20/40</td>
</tr>
<tr>
<td>VF, MD</td>
<td>-3.6 ± 2.5</td>
<td>-3.6 ± 2.6</td>
</tr>
<tr>
<td>Corneal thickness, μ</td>
<td>548 ± 32</td>
<td>549 ± 35</td>
</tr>
<tr>
<td>Prior SLT</td>
<td>15.7%</td>
<td>15.0%</td>
</tr>
<tr>
<td>Medicated IOP, mm Hg</td>
<td>17.9 ± 3.1</td>
<td>18.1 ± 3.1</td>
</tr>
<tr>
<td>(mean medications)</td>
<td>(1.7)</td>
<td>(1.7)</td>
</tr>
<tr>
<td>Washed-out DIOP, mm Hg</td>
<td>25.5 ± 3.0</td>
<td>25.4 ± 2.9</td>
</tr>
</tbody>
</table>

HORIZON: Primary Endpoint
20% Reduction in Washed-Out DIOP

Increasing Treatment Effect Through 24 Months

<table>
<thead>
<tr>
<th></th>
<th>Microstent (HM)</th>
<th>No stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Months</td>
<td>85.9%</td>
<td>70.1%</td>
</tr>
<tr>
<td>24 Months</td>
<td>77.2%</td>
<td>57.8%</td>
</tr>
</tbody>
</table>

Δ = 15.9%  P < .001
Δ = 19.5%  P < .001

ITT analysis
I-bars represent 95% confidence intervals


HORIZON: Secondary Endpoint
Change in Washed-Out DIOP

Largest IOP Reduction of All MIGS Pivotal Trials to Date

<table>
<thead>
<tr>
<th></th>
<th>Microstent (HM)</th>
<th>No stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Months</td>
<td>-8.5</td>
<td>-6.3</td>
</tr>
<tr>
<td>24 Months</td>
<td>-7.6</td>
<td>-5.3</td>
</tr>
</tbody>
</table>

Δ = -2.1 mm Hg  P < .001
Δ = -2.3 mm Hg  P < .001

ITT analysis
I-bars represent 95% confidence intervals


DukeHealth
HORIZON: Medication-Free
Medication-Free 0-24 Months

Largest Treatment Effect of All MIGS Pivotal Trials to Date

% Unmedicated at Visit

- Microstent (HM)
- No stent

24 Months
Δ = 30%
P < .001

n = 187 phaco

Cumulative Adverse Events
Through 24 Months

<table>
<thead>
<tr>
<th>Intraoperative Events</th>
<th>MS n = 369</th>
<th>No Stent n = 187</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device malposition</td>
<td>1.6%</td>
<td>0</td>
</tr>
<tr>
<td>Hyphema</td>
<td>1.1%</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postoperative events</th>
<th>MS n = 369</th>
<th>No Stent n = 187</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP-related events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trabeculectomy/GDD</td>
<td>0.8%*</td>
<td>5.8%</td>
</tr>
<tr>
<td>IOP spike (&gt; 10 mm Hg over baseline &gt; 30 days)</td>
<td>0</td>
<td>2.1%</td>
</tr>
<tr>
<td>Paracentesis &gt; 7 days</td>
<td>0.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Hypotony ≤ 6 mm Hg ≥ 1 day</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Uveitis/iritis requiring steroids</td>
<td>5.6%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Layered hyphema, &gt; 2 mm &gt; 1 day</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Laser synechialysis</td>
<td>0.8%</td>
<td>0</td>
</tr>
<tr>
<td>Tissue obstruction/obstructive PAS</td>
<td>3.8%</td>
<td>0</td>
</tr>
</tbody>
</table>

*P < .05 vs control.

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Unless otherwise indicated, photographed subjects who appear within the content of this activity or on artwork associated with this activity are models; they are not actual patients or doctors.
MIGS: Abbreviations and Acronyms

BSCVA = best spectacle-corrected visual acuity
DIOP = diurnal intraocular pressure
ETDRS = Early Treatment Diabetic Retinopathy Study
GDD = glaucoma drainage device
HM = Hydrus microstent
IOP = intraocular pressure
ITT = intention-to-treat
MD = mean deviation
MIGS = minimally invasive glaucoma surgery
MS = microstent
OD = oculus dexter (right eye)
OR = operating room
PAS = peripheral anterior synechiae
PC IOL = posterior chamber intraocular lens
PMA = premarket approval
POAG = primary open-angle glaucoma
SD = standard deviation
SLT = selective laser trabeculoplasty
TM = trabecular meshwork
VF = visual field