Managing Your Patients’ Glaucoma: Classic Cases and Conundrums

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• Aerie – C/L
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• Bausch + Lomb – C/L
• Ocular Therapeutix - C
• EyePoint - C
• Sight Sciences – C
• Dompe - C
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Case 1

Patient LM 65 year old female
CC: “I was told I am at risk for glaucoma”

BCVA: 20/20 OD 20/20 OS No Meds

IOP: 27 OD; 27 OS

Pachymetry: 583 OD 583 OS

ONH Eval: 0.50/0.50 OD 0.55/0.55 OS

Tmax: Unknown

Corneal Hysteresis: OD: 10.5 OS: 10.5

Gonio Ciliary Body
Ocular Hypertension Treatment Study

Baseline Factors that Predict POAG
- Higher IOP
- Thinner CCT
- Older age
- Greater PSD on HVF
- Larger vertical or horizontal C/D ratio

9.5% 4.4%


CCT AS A RISK FACTOR

WHAT IOP DO I START THERAPY?
Assess risk
- Age
- IOP
- CCT
- C/D ratio
- PSD

Consider other factors (race, family history, myopia, CH)
Use your best clinical judgement
Corneal Hysteresis (CH)

Corneal Hysteresis reflects the ability of the corneal tissue to dissipate energy.

Function of viscoelastic damping.

Provides insight into ocular properties that were not previously understood or conceived of.


CH as a Predictor of Progression/Risk
Case 2

- 71-year-old African-American male
- Medical History: HTN
- Family History: HTN, DM
- BCVA: 20/20 +1 OU

- IOP: 29 mm Hg OD; 26 mm Hg OS
- C/D: 0.80/0.80 OD; 0.65/0.65 OS
- Pachymetry: 510 OD; 514 OS
- Corneal Hysteresis: 8.0 OD; 8.9 OS
- Gonioscopy: Open to CB OU w/ trace pigment in TM
- VF’s – See next slide
- OCT’s – See next slide
Prostaglandins

- latanoprost 0.005% (Xalatan)
- travoprost 0.004% (Travatan-Z)
- bimatoprost 0.03% (Lumigan)
- tafluprost 0.015% (Zioptan PF)

latanoprostene bunod 0.024% (Vyzulta)
Nitric Oxide

Endogenous in the human body

Causes alterations in the cytoskeletal network

Reduced NO in TM, Schlemm’s canal, and ciliary muscle


VOYAGER Study
latanoprostene bunod 0.004% (Vyzulta)

JUPITER Study
latanoprostene bunod 0.024% (Vyzulta)

latanoprost ophthalmic emulsion 0.005% (Xelpros)

BAK-free latanoprost ophthalmic emulsion

Swollen Micelle Microemulsion (SMM) Technology

Reduces IOP up to a mean of 6 mmHg to 8 mmHg in randomized clinical trials
**Single Agent Adjunctive Agents**

**Beta Blockers**
- Timoptic (timolol 0.25, 0.5%; Merck)

**Timolol Alternative Formulations**
- Timolol XE-timolol maleate 0.25%, 0.5% in Gel-rite
- Timoptic in Ocudose 0.25%, 0.5%
- Icilol – Qd dosing
- Betoptic-S

**Alpha-adrenergic Agonists**
- (brimonidine 0.2%, 0.15%, 0.1%)

**Carbonic Anhydrase Inhibitors**
- Trusopt (dorzolamide HCL solution 2%)
- Azopt (brinzolamide 1% suspension)

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**netarsudil 0.02% (Rhopressa)**

MOAs

- **trabecular outflow**
- **episcleral venous pressure**

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**netarsudil 0.02% (Rhopressa)**

*Studied BICO*:

- **Up to 5 mmHg IOP reduction seen with Rhopressa**

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**netarsudil 0.02% (Rhopressa)**

*Up to 5 mmHg IOP reduction*
10/27/20

Rhopressa (netarsudil 0.02%)

~ 15-20% Hyperemia at baseline
20% Corneal Verticillata
17% Conjunctival Heme


Combination Therapy

CoSopt Ophthalmic Suspension
Timolol 0.5%
Dorzolamide 0.2%

Simbrinza
Brinzolamide 1%
Brimonidine 0.2%

Combigan Ophthalmic Solution
Brimonidine 0.2%
Timolol 0.5%

netarsudil 0.02% + latanoprost 0.005% (Rocklatan)

- RHO protein kinase (destabilizes actin in TM)
- Rock inhibitor (lowers EVP)
- Latanoprost (uveoscleral outflow)

Mean IOP reduction at 3 months

PATIENTS, %

IOP REDUCTION FROM BASELINE, %

Pooled Mercury 1 and Mercury 2 Data
Mean IOP Reduction at 3 months
Selective Laser Trabeculoplasty

- Selectively targets and laser burns pigmented TM cells

SLT Studies

- SLT Med Study (2012)
- Dr. Katz @ Wills Eye in Philadelphia
- J Glaucoma 2012;21:460-468

- SLT (100 applications over 360 degrees of TMJ) vs. prostaglandin analog
- Primary outcome -> IOP
- Secondary outcome -> # of treatment steps
SLT Med Study Treatment Arms

![Diagram of SLT Med Study Treatment Arms]

SLT vs. Prostaglandins

- SLT Med Study (2012)
  - Results:
    1. IOP reduction:
      - SLT – 25.7% IOP reduction
        - IOP reduced from 24.5 to 18.2 (6.3 mmHg reduction)
      - Prostaglandin – 28.3% IOP reduction
        - IOP reduced from 24.7 to 17.7 (7.0 mmHg reduction)
    2. # of treatment steps:
      - SLT group - 11% of eyes required additional SLT
      - Prostaglandin group - 27% of eyes required additional medication

Primary Outcome - Quality of Life at 3 years
Secondary Outcome – Cost, cost-effectiveness, clinical effectiveness, and safety

Conclusions:
- No significant difference in QOL
- 87% probability of SLT vs 1st treatment being more cost-effective
- SLT at target IOP 93% of visits vs 91.3% at target for meds
Results at 3 years

• Rates of disease deterioration
  • SLT - 3.8% (23 eyes)
  • Meds - 5.8% (36 eyes)

• Glaucoma surgeries
  • SLT – 0
  • Meds – 11

Steroid After Laser Trabecloplasty (SALT)

<table>
<thead>
<tr>
<th>Steroid</th>
<th>NSAID</th>
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<tbody>
<tr>
<td>IOP Pre-Op: 23.3 mm Hg</td>
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<tr>
<td>12 week IOP check</td>
<td>12 week IOP check</td>
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<tr>
<td>IOP lowering of 5.2±2.7 mmHg</td>
<td>IOP lowering of 6.2±3.1 mmHg</td>
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Steady state IOP ~ 6 weeks (new baseline)

Future options/Emerging Therapies

• Do we need anything else?

• Glaucoma Drug Delivery
Patients Attitudes Towards Drug Delivery

- Triple Combination Eye Drop – 85%
- Microdose Eye Spray – 54%
- Drug-eluting Contact Lens – 31%
- Drug-eluting Periocular Ring Insert – 43%
- Injectable Subconjunctival Drug Insert – 32%
- Injectable Anterior Chamber Implant – 30%


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Bimatoprost SR (Allergan)
(10-microgram bimatoprost sustained-release implant)

- Biodegradable bimatoprost sustained-release implant
- FDA-approved and indicated to reduce IOP in patients with open angle glaucoma or OHT
- Single intracameral administration
- Phase I/II/III Studies
Bimatoprost SR (Allergan)
(10-microgram bimatoprost sustained-release implant)

**24 Month Phase I/II Clinical Trial**

- **75 subjects**
- bimatoprost pellet (6, 10, 15, or 20 micrograms)
- topical bimatoprost 0.03%

**24 months – IOP reduction**
- 7.5, 7.3, 7.3, 8.9 mm Hg

**Rescued/Retreatment**
- 68% - 6 mos.
- 40% - 12 mos.
- 28% - 24 mos.
2 x 20 Month Phase III (ARTEMIS)

- The device as implanted intracamerally at 4-month intervals for 1 year (Office-based procedure)
- 1,112 subjects
- Durysta vs 2 x topical timolol
- 30% IOP reduction from baseline over 12-week primary efficacy period

Conclusion: Noninferior to timolol administered as an eye drop twice a day.

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Phase III (ARTEMIS 3)

- The device as implanted intracamerally at 4-month intervals for 1 year (Office-based procedure)
- 742 subjects
- Durysta vs 2 x topical timolol
- Baseline IOP 24 mm Hg
- At 1 Year IOP maintained at 16-17 mm Hg

*80% - additional 12 months without retreatment

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Phase III (ARTEMIS)

- 27% - conjunctival hyperemia
- 10% - post administration 2 days
- 5.4% - endothelial cell loss over 20 months
- 5% - iritis
Case 3:

65-year-old, Caucasian female referred for a cataract evaluation and opinion on her glaucoma. She states her night-time VA is terrible, and she has started to struggle during the day as well.

Ocular History
• POHx: Primary Open Angle Glaucoma OS>OD
• FHX:
  • Mother – glaucoma, age-related macular degeneration
• Previous Treatment Regimen: None
• Current Treatment Regimen:
  • Bimatoprost 0.01% qd OU

Medical History
• PMHx: Hyperlipidemia
• All Medications: Fluoxetine, Atorvastatin
• Allergies: Penicillin

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Best corrected visual acuity (UCVA): 20/40 OD, 20/40 OS; BAT: 20/400 OU

External exam: Normal appearance, symmetrical

Pupil exam: Equal, round, reactive to light and (-) APD

Slit-lamp exam
- Lids/Lashes: Clear, no debris, no signs of MGD OU
- Conjunctiva: Clear, no injection OU
- Cornea: Clear, no corneal staining OU, no pigment present OU
- Anterior Chamber: Clear, no cells, no flare OU
- Iris: Clear, no exfoliative material present, no transillumination defects OU
- Lens: See Image/Slide

Goldmann Applanation Tonometry: 16 mm Hg OD, 17 mm Hg OS

Central corneal thickness (CCT): 499 OD, 504 OS

Gonioscopy: Open to CB in all quadrants, no pigment in the TM, and normal iris approach

Corneal Hysteresis: 9.4 mm Hg OD, 9.3 mm Hg OS

OS
- Cup-to-Disc: 0.50/0.50, Flat, Distinct
- AV Ratio: Normal, no tortuosity
- Macula: Flat
- No PPA
- No disc hemorrhage

OD
- Cup-to-Disc: 0.70/0.70, Deep cup, Distinct
- AV Ratio: Normal, no tortuosity
- Macula: Flat
- No PPA
- No disc hemorrhage
Minimally or Micro Invasive Glaucoma Surgery (MIGS)

Procedures that have an ab-interno approach, are minimally traumatic, with at least modest efficacy, extremely high safety and rapid recovery.

HORIZON Trial – 4 Year Update

Stent + Cataract (n=369) Cataract Only (n=187)

Baseline IOP (mm Hg) after washout

- 48 months mean IOP (mm Hg)
  - preoperative medication: 25.5 (+/- 3.0) 25.4 (+/- 2.9)
  - 2 to 4 preoperative medication: 16.9 (+/- 3.3) 17.3 (+/- 3.4)

- 48 months medication free: 52.6% 47.4%

- 54% 46%

- 48 months median IOP (mm Hg) unmedicated
  - 16.7 (+/- 3.1) 17.2 (+/- 3.2)

Trabecular Microbypass Stent (iStent Inject)

Mean Unmedicated DIOP Reduction

- Change in Unmedicated DIOP
  - 5.4 mmHg
  - Phacoalone: 7.0 mmHg
  - iStent Inject Preop M24: 24.8 mmHg
  - 17.1 mmHg

Results

OMNI alone IOP

- 23.36
- 14.46
- 38.10%
- 15.57
- 33.35%
- 14.42
- 38.27%
- 13.29
- 43.11%
- 14.65
- 37.29%
- 14.00
- 40.07%

drugs

- 3.00
- 0.14
- 95.33%
- 0.29
- 90.33%
- 0.50
- 83.33%
- 0.92
- 69.33%
- 1.70
- 43.33%
- 2.00
- 33.33%

Faco OMNI IOP

- 18.70
- 12.70
- 32.09%
- 14.20
- 24.06%
- 13.50
- 27.81%
- 14.75
- 21.12%
- 12.71
- 32.03%
- 11.40
- 39.04%

drugs

- 2.80
- 0
- 100%
- 0
- 100%
- 0.30
- 89.29%
- 0.75
- 73.21%
- 1.14
- 59.29%
- 1.40
- 50%

Ab-interno Trabeculotomy + Viscoanalostomy (OMNI)

- Treats all 3 points of resistance
- Stand alone or combined with CE
- Titratable
- 7.3 mmHg mean IOP reduction from 23.7 mmHg mean medicated baseline
- Mean 12-month IOP of 15.7 mmHg.

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Subconjunctival Stent (Xen)

**Xen 45 Gel Stent: US Pivotal Clinical Trial**

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<tr>
<th></th>
<th>Baseline</th>
<th>12 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicated IOP</td>
<td>25.1 (3.7)</td>
<td>15.9 (5.2)</td>
</tr>
<tr>
<td>Glaucoma Meds</td>
<td>3.5 (1.0)</td>
<td>1.7 (1.5)</td>
</tr>
</tbody>
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**Postoperative Adverse Events**

- Hypotony: 16 (24.6%)
  - IOP < 6 mmHg at any time
- Bleb Needling: 21 (32.3%)

In Conclusion...

- **Glaucoma** is both a **medical** and **surgical** disease
  - Key to success is collaboration
- Trends in treatment aim to **balance** effectiveness and safety
- MIGS procedures allow for **interventional glaucoma**