



## The Glaucoma Gauntlet – Managing Cases from Diagnosis to Treatment

Dr. Mitch Ibach


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Host: Dr. Stephanie Woo





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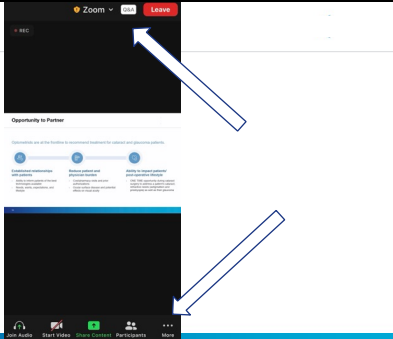
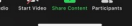


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### Speaker Bio –



Dr. Mitch Ibach is a residency trained optometrist at Vance Thompson Vision in Sioux Falls, SD. Dr. Ibach attended the Pacific University College of Optometry where he graduated summa cum laude. Mitch completed his residency training at Minnesota Eye Consultants with a concentration on cornea, refractive surgery, external disease and glaucoma. In September of 2014, he joined Vance Thompson Vision to focus on advanced anterior segment surgery care and pathology. Mitch is a fellow of the American Academy of Optometry, an Intrepid Eye Society member, a member with the American Optometric Association, Optometric Glaucoma Society (OGS), and the South Dakota Optometric Society. Mitch serves as the associate residency director at Vance Thompson Vision and is also an adjunct clinical faculty for the Illinois College of Optometry and the Pikesville College of Optometry.



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### Financial Disclosures for Dr. Ibach

|                    |                              |           |
|--------------------|------------------------------|-----------|
| Aerie              | Consultant/lecturer          | Honoraria |
| Allergan           | Consultant                   | Honoraria |
| Avellino           | Consultant                   | Honoraria |
| Bausch & Lomb      | Consultant                   | Honoraria |
| Dompe              | Consultant/lecturer          | Honoraria |
| Equinox            | Investor                     | None      |
| Glaukos            | Consultant/lecturer          | Honoraria |
| Heru               | consultant/lecturer          | Honoraria |
| Kala               | consultant                   | Honoraria |
| New World Medical  | consultant                   | Honoraria |
| Ocular Therapeutix | consultant/lecturer/research | Honoraria |
| Oyster Point       | consultant/lecturer          | Honoraria |
| Sight Sciences     | consultant/lecturer          | Honoraria |
| Sun Pharma         | Lecturer                     | Honoraria |

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## All financial relationships have been mitigated.

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### Glaucoma Gauntlet: managing cases from diagnosis to treatment

Mitch Ibach OD, FAAO  
Vance Thompson Vision  
Associate residency coordinator

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### Financial Disclosures- Ibach

**Disclosure Statement:**

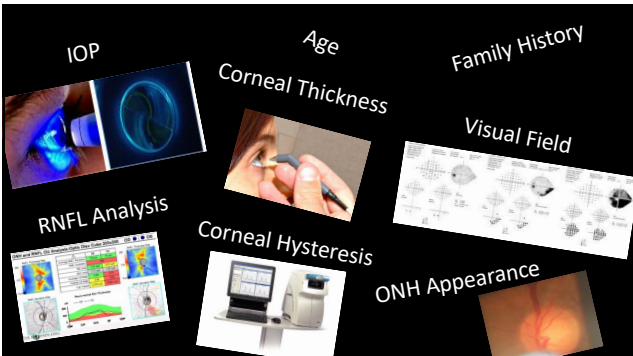
- Aerie - consultant/speaker
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- Bausch Health -- consultant
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- Glaukos - consultant/speaker
- Heru - consultant/speaker
- Kala - consultant
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IOP

Age

Family History

Corneal Thickness

Visual Field

RNFL Analysis

Corneal Hysteresis

ONH Appearance

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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      No Meds  
          20/20 OS


IOP: 27 OD; 27 OS

Pachymetry: 583 OD  
                  583 OS

Tmax: Unknown

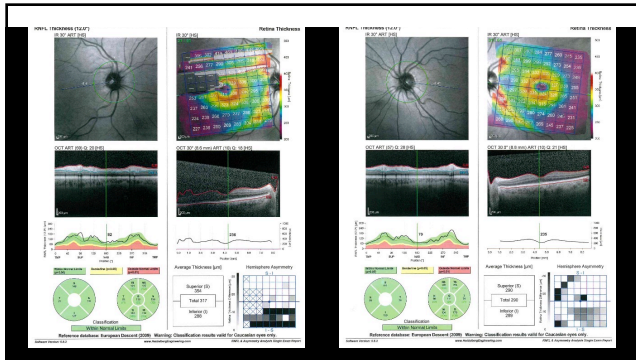
Corneal Hysteresis: OD: 10.5 OS: 10.5

Gonio Ciliary Body

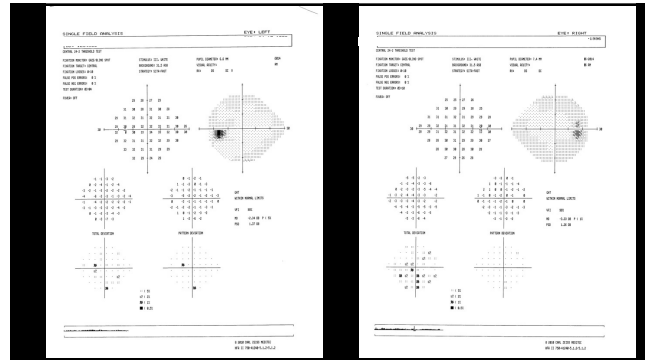


ONH Eval: 0.50/0.50 OD  
                  0.60/0.60 OS

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In this 65 yo Patient I would diagnose

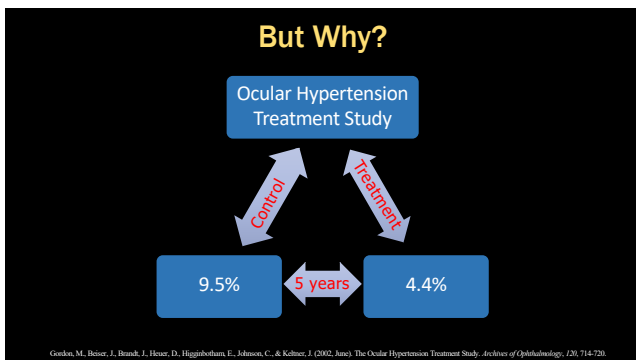
- A. Ocular Hypertension (OHTN)
- B. Preperimetric glaucoma (Open-angle borderline findings)
- C. Mild POAG (open angle)
- D. Low risk glaucoma suspect

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For management of LM, I would

- A. Start a prostaglandin analogue (PGA) (travoprost QD)
- B. Recommend Selective Laser Trabeculoplasty (SLT)
- C. Recommend monitoring with IOP check in 3 months
- D. Recommend monitoring with OCT, IOP, VF in 6 months

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**What We Do Know- OHTS**

**TABLE 1. Hazard Ratios for Baseline Factors Predictive of Primary Open-angle Glaucoma**

| Baseline Factor              | Model Including PSD, VC/D | Model Excluding PSD, VC/D |
|------------------------------|---------------------------|---------------------------|
| Age (decade)                 | 1.25 (1.04,1.49)          | 1.29 (1.09,1.53)          |
| IOP (mm Hg)                  | 1.11 (1.05,1.18)          | 1.10 (1.04,1.17)          |
| CCT (per 40 μ decrease)      | 1.82 (1.51,2.19)          | 1.92 (1.60,2.30)          |
| History of diabetes mellitus | 0.35 (0.15,0.78)          | 0.38 (0.17,0.86)          |
| PSD (per 0.2 dB)             | 1.25 (1.06,1.48)          | Excluded                  |
| VC/D (per 0.1)               | 1.32 (1.20,1.45)          | Excluded                  |

CCT = central corneal thickness; IOP = intraocular pressure; PSD = pattern standard deviation; VC/D = vertical cup-to-disk ratio.

Coleman, A., Gordon, M., Kass, M., & Boies, J. (2004, October). Baseline Risk Factors for the Development of Primary Open-Angle Glaucoma in the Ocular Hypertension Treatment Study. American Journal of Ophthalmology, 138(A), 644-655.

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**JAMA Ophthalmology | Original Investigation**

### Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-up

Michael A. Kass, MD; Dale K. Heuser, MD; Eve J. Higginbotham, MD; Richard K. Parrish, MD; Cheryl L. Khanna, MD; James D. Brantley, MD; Joseph D. Soltau, MD; Chris A. Johnson, PhD; John L. Kolker, MD; Julia B. Hauckler, MS; Bradley S. Wilson, MA; Lei Liu, PhD; J. Phillip Miller, AB; Harry A. Quigley, MD; Mae O. Gordon, PhD; for the Ocular Hypertension Study Group

**45%**

1. African American patients showed a significantly higher conversation rate.

2. Combining both cohorts, the cumulative rate of Visual Field loss was 25.2%

Kass, M., Heuser, D., Higginbotham, E., Parrish, R., Khanna, C., Brantley, J., et al. Ocular Hypertension Study Group. (2021, April 15). Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-Up. *JAMA Ophthalmology*, 7(9), 558-566.

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### Do I Need OCT?

- Optical Coherence Tomography (OCT) is non-invasive cross-sectional imaging tool
  - Light waves (IR) scattered by ocular structures are measured by interferometry
- Use in glaucoma
  - Peripapillary retinal nerve fiber layer (RNFL)
  - Macular nerve fiber layers (mNFL)
  - Ganglion cell layer with inner plexiform layer (GCIPL)
  - Ganglion cell complex (mNFL + GCIPL)

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**PLOS ONE**

RESEARCH ARTICLE

### Optical coherence tomography for glaucoma diagnosis: An evidence based meta-analysis

Vinay Kansal<sup>1</sup>, James J. Armstrong<sup>2</sup>, Robert Pinthuis<sup>3</sup>, Cindy Hutnik<sup>4,5\*</sup>

- Meta-analysis of 150 studies (16,104 glaucomatous eyes)
- Studied the accuracy (AUC) for imaging devices used and area of tissue imaged
  - All devices performed similarly
  - Of the RNFL areas, it's most accurate to look at **average** (0.897), **superior** (0.855) and **inferior** (0.895)
  - In general, macular thickness values have similar accuracy to RNFL
    - Exception is total macular thickness, which is not as useful!

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### OCT

- Pay attention to TSNIT curve.
- Pay attention to the actual numbers in the segmentation plot
- Pay attention to the numbers between eyes in the segmentation plot
- Beware of the artifact!

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### What We Do Know- Hysteresis Matters

(Low) CH has been consistently shown to be independently and strongly associated with or predictive of glaucoma progression

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### Corneal Hysteresis and Glaucoma in Suspects

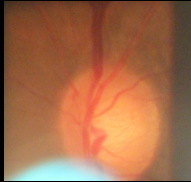
287 Eyes → 54 (19%) developed repeatable VF defects

**Glaucoma vs No Glaucoma**  
 9.5 +/- 1.5 vs 10.2 +/- 2.0 mmHg

Conclusion: Baseline lower CH measurements were significantly associated with increased risk of developing glaucomatous visual field defects over time. The prospective longitudinal design of this study supports a role of CH as a risk factor for developing glaucoma.

Suzanna CH, Disha Fikra A, Daga FB, Susanna BM, Zhu F, Ogata NG, Medeiros FA. A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor Predicting Development of Glaucoma. *American Journal of Ophthalmology*. 2018; 190: 10.1016/j.ajo.2017.12.018

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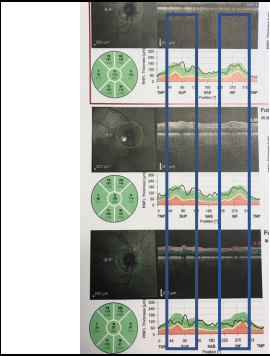
VF – normal OU  
OCT – see next slide

Patient LM returns for scheduled F/U approximately 15 months after initial presentation. She reports no changes in vision.

BCVA: 20/20 OD    IOP: 23 OD  
          20/20 OS           23 OS

ONH Eval: 0.50/0.50 OD    No Meds  
              0.65/0.65 OS       Tmax: 27 OU

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Serial OCT shows progressive RNFL loss OD but still "in the green".

Baseline  
6 months  
15 months

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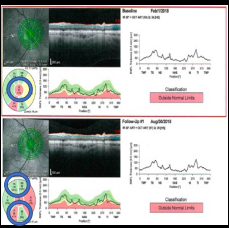
For this same patient, I would now suggest

- A. Start a prostaglandin analogue (latanoprost QD)
- B. Recommend Selective Laser Trabeculoplasty (SLT)
- C. Recommend monitoring with IOP check in 3 months
- D. Start a beta blocker (timolol BID)

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### What Change Matters?

Average RNFL = ~ 4 microns  
Superior/Inferior RNFL = ~ 7 microns  
Macular GCL-IPL = ~ 4 microns



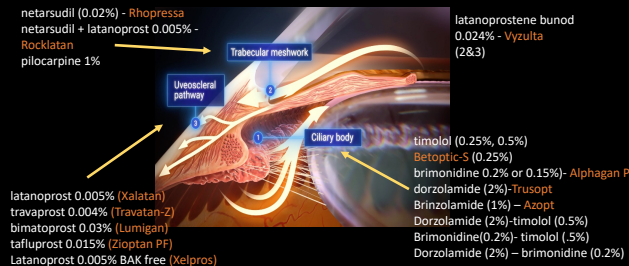
• Misra IC et al. Ability of cirrus HD-OCT optic nerve head parameters to discriminate normal from glaucomatous eyes. Ophthalmology 2011  
• Kim KE. Long-term reproducibility of macular ganglion cell analysis in clinically stable glaucoma patients. Invest Ophthalmol Vis Sci 2013

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| Aqueous Suppressants                          | Uveoscleral Outflow   | Aqueous Suppressants  | Uveoscleral Outflow + TM outflow | Rho-Kinase Inhibitor   | Compounded Meds   |
|---|---|---|----------------------------------|------------------------|---|
| -B-blockers<br>-Alpha-2-adrenergics<br>-CAI's | -Prostaglandins   | -Combo Drops  |                                  |                        | -B-blockers<br>-Alpha-2-adrenergics<br>-CAI's<br>-PGA's |
| Timoptic<br>*timolol<br>*betaxolol            | Lumigan<br>*bimatoprost<br>Travatan Z<br>*travoprost<br>Xalatan<br>*latanoprost<br>Zioptan<br>Xelpros | Combigan<br>*brimonidine-timolol<br>Cosopt<br>*dorzolamide-timolol<br>Simbrinza | Vyzulta                          | Rhopressa<br>Rocklatan |   |

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### Drop Mechanisms of Action



netarsudil (0.02%) - Rhopressa  
netarsudil + latanoprost 0.005% - Rocklatan  
pilocarpine 1%

latanoprostene bunod 0.024% - Vyzulta (2&3)

timolol (0.25%, 0.5%)  
Betoptic-S (0.25%)  
brimonidine 0.2% or 0.15%- Alphagan P  
dorzolamide (2%)-Trusopt  
Brimonidine (1%) - Azopt  
Dorzolamide (2%)-timolol (0.5%)  
Brimonidine(0.2%)- timolol (.5%)  
Dorzolamide (2%) – brimonidine (0.2%)

Worthing et al. Nat Rev Clin Oncol. 2016;12(10):577-588. doi:10.1038/nrco.2016.102

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### Why are PGAs first line?

- Most efficacious
- Once daily dosing
- Minimal systemic SE's
- Uveoscleral outflow slows @night

25-33% ↓

Adjusted hazard ratio 0.44 (95% CI 0.28-0.69, p<0.0003)

| Visual field progression (months) | Latanoprost | Placebo |
|-----------------------------------|-------------|---------|
| 0                                 | 235         | 235     |
| 6                                 | 200         | 209     |
| 12                                | 197         | 169     |
| 18                                | 183         | 139     |
| 24                                | 55          | 44      |

David G, David C, Laganas G, Amalfitano F, Anand N, Anwar-Hayat A, Zeyen T. 2015, April 4. Latanoprost for open-angle glaucoma (XGT3) compared with placebo. *Cochrane Database of Systematic Reviews*. 2015;4:CD010306.

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### What PGA should I Use?

- 60 Previously untreated patients with POAG
- Baseline IOP 25-26mmHG at 8:00am
- 1\* endpoint IOP at 3 months after starting medication

Monotherapy in POAG

| Medication     | IOP decrease mmHG |
|----------------|-------------------|
| latanoprost QD | 6.5               |
| bimatoprost QD | 7.5               |

Nair N, Ali Z, Latif E, Nair L, Abi Z. Comparison of efficacy of latanoprost 0.005% with bimatoprost 0.01% in patients with open angle glaucoma. *Med Forum*. 2019;90(7):17-21.

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### (Xelpros) latanoprost emulsion 0.005%

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

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### 1 Year Later

BCVA: 20/20 OD  
20/20 OS Med: PGA QD

IOP: 18 OD; 18 OS

Pachymetry: 583 OD  
583 OS

ONH Eval: 0.65/0.65 OD  
0.70/0.70 OS

Tmax: 27 OU

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### For this very same patient on a PGA, I would now suggest

- Switch to a PGA + NO donor (Vyuzulta QD)
- Add a beta blocker (timolol QAM)
- Add a combination medication (dorzi-timolol BID)
- Recommend SLT

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### Vyuzulta (latanoprostene bunod 0.024%)

VOYAGER Study

| Endpoint          | latanoprost 0.05% | LBN 0.024% |
|-------------------|-------------------|------------|
| ≥1 tx related A/E | 12.2%             | 19.3%      |
| Ocular Hyperemia  | 8.5%              | 2.4%       |
| Instillation Pain | 6.1%              | 12.1%      |

Siegfried C. (2017, September). Nitric Oxide: A Therapeutic Target for Glaucoma. *Glaucoma Today*, 37-59.  
Wangshu P, Cheng T, Shirokawa H, Vitman J, Singh R, & Kaufman J. (2018, December). A randomized, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open-angle glaucoma: the VOYAGER study. *Br J Ophthalmol*. 733-743.

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### Nitric Oxide

Endogenous in the human body

Causes alterations in the cytoskeletal network

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

Nathanson JA et al. Alterations of ocular nitric oxide synthesis in human glaucoma. Invest Ophthalmol Vis Sci. 1995

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### Retrospective Chart Review on Real-World Use of Latanoprostene Bunod 0.024% in Treatment-Naïve Patients with Open-Angle Glaucoma

- Multicenter, noninterventional retrospective chart review
- Charts were included if patients
  - Were aged ≥ 18 years
  - had no history of medical, laser, or surgical intraocular pressure (IOP)-lowering intervention
  - Had at least two follow-up visits (spanning ≥ 2 months) following initiation of LBN treatment.
- Data extracted from the charts included age, sex, race, cup-to-disk ratio, central corneal thickness, IOP, visual acuity (VA), concomitant medications, and adverse events.
- Reduction in IOP was determined for the overall dataset and in patients with IOP ≤ 21 mm Hg and > 21 mm Hg
  - In patients treated bilaterally, the eye with the higher baseline IOP was the study eye.

Okada, C.O., Barone, E.S., Trabak, V. et al. Ophthalmol Ther 9, 1041–1051 (2020). https://doi.org/10.1007/s00123-020-00307-0

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### Results: Mean (SD) IOP Change from Baseline

- LBN use resulted in a mean (SD) reduction from baseline of 7.1 (4.7) and 7.3 (5.1) mmHg at the first and second follow-up visits, respectively ( $P < 0.0001$  for both).
  - Reductions among patients with IOP > 21 mmHg ( $n = 30$ ) at baseline were 10.0 (4.5) and 11.1 (4.6) mm Hg at the first and second follow-up visits ( $P < 0.0001$  for both).
- Mean % IOP lowering was 31% in all patients ( $N=65$ ), 22% in patients with IOP ≤ 21 mm Hg ( $n=35$ ), and 41% in patients with IOP > 21 mm Hg ( $n=30$ ) at the 2<sup>nd</sup> follow-up visit.

Okada, C.O., Barone, E.S., Trabak, V. et al. Ophthalmol Ther 9, 1041–1051 (2020). https://doi.org/10.1007/s00123-020-00307-0

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### Glaucoma Eval – Pt. DB

Handwritten notes include: "Reading has become more difficult... it used to be difficult reading that sign... Had tumor on primary - had to take care of it...".

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### Glaucoma Eval - DB

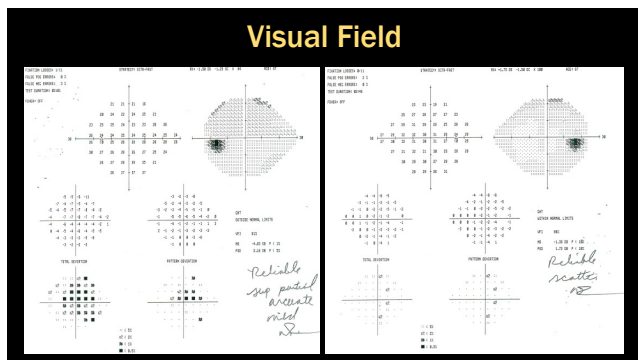
Handwritten notes include: "Reading has become more difficult... it used to be difficult reading that sign... Had tumor on primary - had to take care of it...".

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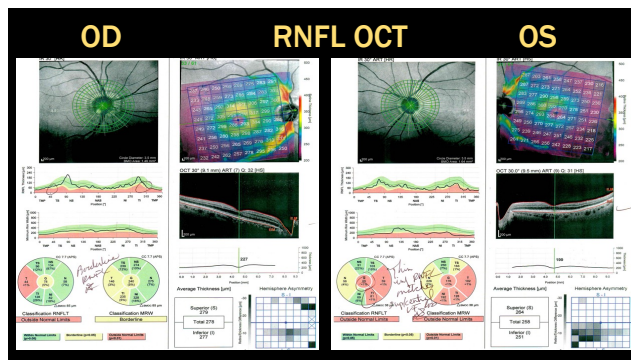
### Glaucoma Eval - DB

Handwritten notes include: "Reading has become more difficult... it used to be difficult reading that sign... Had tumor on primary - had to take care of it...".

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For this progressing patient OS on a generic PGA with an IOP of 14, I would suggest

- A. Switch in class to a name brand PGA (Lumigan QD)
- B. Add a rho kinase inhibitor (Rhopressa QD OS)
- C. Add a combination medication (dorzi-timolol BID OS)
- D. Recommend SLT OU
- E. Refer for glaucoma surgery OS (tube shunt)

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Corneal Hysteresis found to be associated with progression

|                              | OR     | LCL  | UCL             | P-value |
|------------------------------|--------|------|-----------------|---------|
| Age per year <65             | 1.12   | 1.01 | 1.24            | .03     |
| Age per year ≥65             | 1.08   | 1.01 | 1.15            | .02     |
| GAT IOP per mmHg             | 1.22   | 0.95 | 1.58            | .17     |
| Treatment                    | 1847.6 | 3.16 | 10 <sup>6</sup> | .02     |
| IOP by treatment interaction | 0.79   | 0.61 | 1.03            | .08     |
| CCT per 100 microns          | 1.65   | 0.66 | 0.98            | .30     |
| Years with glaucoma          | 1.00   | 0.96 | 1.04            | .98     |
| Baseline IOP                 | 0.99   | 0.93 | 1.06            | .79     |
| CI per mmHg                  | 0.81   | 0.66 | 0.98            | .03     |

Congdon NG, Bruman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. Am J Ophthalmol 2006;141:868

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Rhopressa (netarsudil 0.02%)

RhCK, rho kinase.  
1. Kazaniet al. J Ocul Pharmacol Ther. 2016;34:380-2. Weisheit et al. Nat Rev Dis Primers. 2016;2:16067. 3. Geel et al. Open Ophthalmol J. 2010;4:52.

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M.O.S.T Study of Netarsudil

4-4.5mmHG

Netarsudil as Adjunctive Therapy

\*\*\* Population. Note: Details patients whose a prior medication was switched to netarsudil.

In the group studied, netarsudil provided consistent IOP reductions whether added to prior PGA monotherapy (4.3 mmHg) or prior combination therapy (4.5 mmHg).

Zeman F, Georj SC, Schwartz GF, Stuenkel JM. A multicenter, open-label study of netarsudil for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension in a real-world setting. Curr Med Res Opin. 2021 Jun;37(6):1011-1020.

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# M.O.S.T Study of Netarsudil

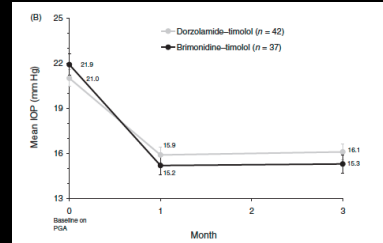
## Adverse Events in the M.O.S.T. Safety Population

| Adverse Events               | All M.O.S.T. Patients<br>N=260 | Adjunctive Therapy group<br>N=161 |
|------------------------------|--------------------------------|-----------------------------------|
| <b>Adverse Events (≥ 5%)</b> |                                |                                   |
| Conjunctival hyperemia       | 54 (20.8%)                     | 32 (19.9%)                        |
| Vision blurred               | 19 (7.3%)                      | 10 (6.2%)                         |
| Conjunctival hemorrhage      | 14 (5.4%)                      | 8 (5.0%)                          |
| Instillation site pain       | 14 (5.4%)                      | 8 (5.0%)                          |

Zaman F, Geor S, Schwartz GF, Swan C, Williams JM. A multicenter, open-label study of netarsudil for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension in a real-world setting. *Curr Med Res Opin.* 2021 Jun;17(6):1011-1020.

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## Which Combination Do You Add?



Nixon D, Yan D, Chartrand J, Pennefather R, Simons S, & Hollander D (2009). Three-month randomized parallel-group comparison of brimonidine-timolol versus dorzolamide-timolol fixed-combination therapy. *Current Medical Research and Opinion*, 26(7), 1642-1653.

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## Patient MW- Demographics & Entrance Testing

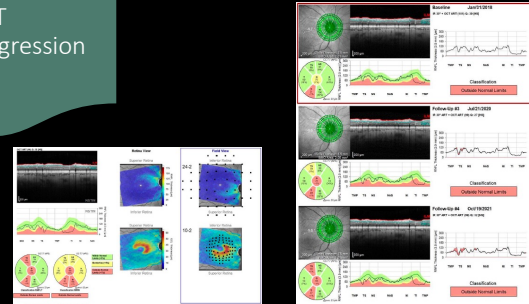
- LTG follow-up. OD worsening?
- GAT → 13, (6mo ago 14) Tmax 15  
→ 9, (6 mo ago 13, Tmax 17)
- Meds: dorz./tim. BID OU, Lumigan QD OU
- PACH → 530  
→ 520
- CH → 8.1  
→ 9.3
- Gonio: open to SS OU, mild pigment



C/D: 0.8v w/DH at 10:00

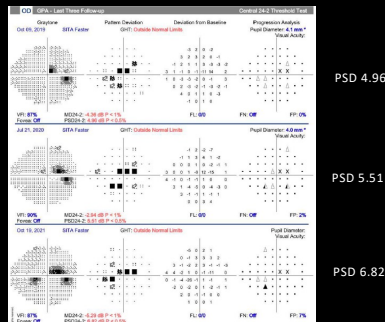
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## OCT Progression



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## HFA Visual Field



PSD 4.96

PSD 5.51

PSD 6.82

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## What is your treatment goal for low tension glaucoma?

- A. Reduction of IOP is irrelevant in LTG
- B. 25% reduction from baseline IOP
- C. 30% reduction from baseline IOP
- D. 40% reduction from baseline IOP

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**Collaborative Normal-Tension Glaucoma Study**

**Glaucoma Progression**  
Treated: 12%  
Untreated: 35%

| TABLE 2. Comparison of Follow-up Results Between the Treated and Untreated Control Groups* |                        |                        |         |
|--|------------------------|------------------------|---------|
|  | Control Group (n = 78) | Treated Group (n = 61) | P value |
| MD at stabilization  | -7.54 ± 4.31           | -9.42 ± 4.82           | .02     |
| IOP during follow-up (mm Hg)   | 16.0 ± 2.1             | 10.6 ± 2.7             | <.0001  |
| MD during follow-up  | -8.08 ± 4.28           | -9.62 ± 4.53           | .05     |
| MD slope during follow-up (dB per year)  | -0.4018 ± 3.65         | -0.4992 ± 1.97         | .85     |

MD = mean defect; IOP = Intraocular pressure.  
\*Values are mean ± SD unless otherwise indicated.

**FIGURE 1.** Survival curves of untreated control subjects and treated patients from randomization using protocol-defined end points.

Collaborative Normal-Tension Glaucoma Study Group. (1998, October). Comparison of Glaucoma Progression Between Untreated Patients with Normal-Tension Glaucoma and Patients with Therapeutically Reduced Intraocular Pressures. *Ophthalmology*, 105(10), 487-497.

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**Rocklatan (netarsudil 0.02% and latanoprost 0.005%)**

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

ROCK, the kinase.  
F. Kozou et al. J Ocul Pharmacol Ther. 2016;34:300-2. Wazir et al. Nat Rev Dis Primers. 2016;2:16007. J. Coel et al. Open Ophthalmol J. 2010;4:42.

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**netarsudil 0.02% + latanoprost 0.005% (Rocklatan)**

**Episcleral Venous Pressure**

- EVP is the back-pressure in conventional outflow
- 8-11mmHG is normal
- netarsudil has been shown to lower EVP

**IOP = production/outflow + EVP**

Six A, et al. Presented at the Association of Research in Vision and Ophthalmology 2023 Annual Meeting (ARVO 2023), April 29-May 3, 2023, Vancouver, BC, Canada.

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**The Role of the Medically Minded OD in Glaucoma**

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**THANK YOU & PEACE**

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**Thank you! Please join us for our next COPE events**

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**CAROTENOIDS: PRESCRIBING FOR OCULAR HEALTH & VISUAL PERFORMANCE**

Date: October 20, 2022  
Time: 5:30PM - 6:30PM PST  
COPE Accredited CE Credit

Speaker  
*Dr. Jennifer Stewart*

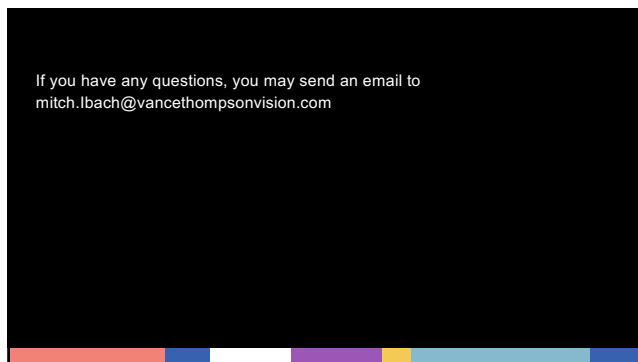
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**HOW TO DETECT SUB CLINICAL AMD**

Speaker  
**DR. BARRY EIDEN**

WEDNESDAY, NOVEMBER 2, 2022  
TIME: 5:30 PM - 6:30 PM PST  
COPE accredited CE credit

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