

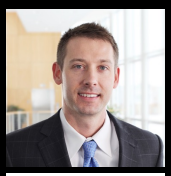
Glaucoma Gauntlet: managing cases from diagnosis to treatment

Mitch Ibach OD, FAAO
Vance Thompson Vision
Residency coordinator

1

Financial Disclosures- Ibach

Disclosure Statement:
Alcon – consultant/speaker
Allergan – consultant
Bausch Health- consultant
Dompe – consultant/speaker
Equinox LLC./Balance Ophthalmics– shareholder
Glaukos - consultant/speaker
iCare -- consultant
New World Medical – consultant
Sight Sciences – consultant/speaker
Sun – consultant
Tarsus – consultant
Viatris -- consultants
Zeiss – consultant



VANCE THOMPSON VISION

All relevant relationships have been mitigated

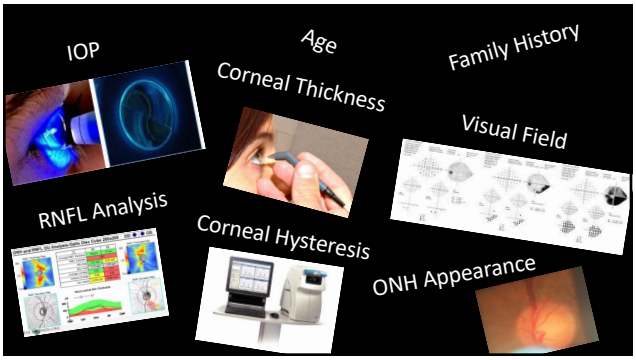
2

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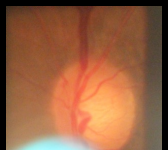
- Or to participate via mobile device without the app, text vision to 22333 to join

3



4

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

Tmax: Unknown

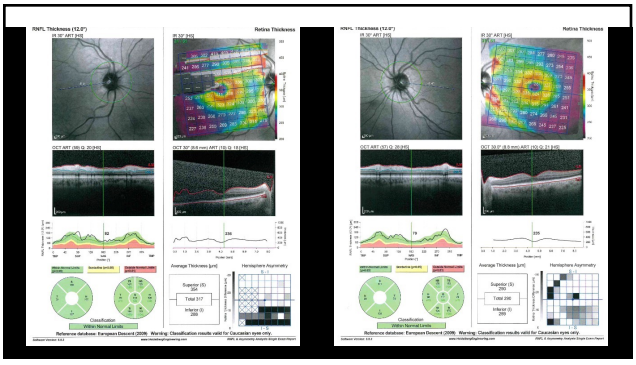
Gonio
Ciliary Body



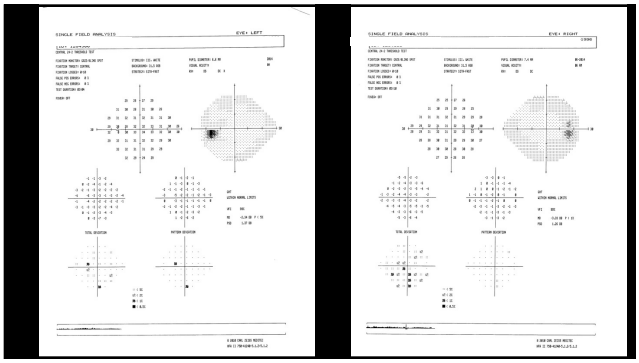
Corneal Hysteresis:
OD: 10.5 OS: 10.5

ONH Eval: 0.50/0.50 OD
0.60/0.60 OS

5



6



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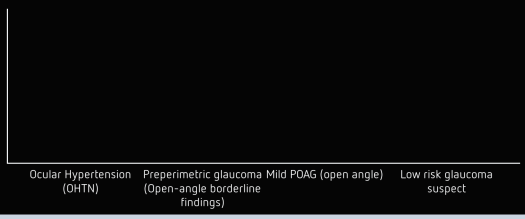
In this 65 yo Patient I would diagnose

- 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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In this 65 yo. patient I would diagnose...



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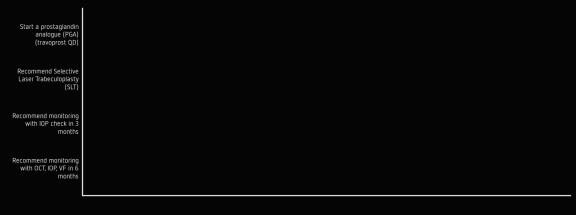
For management of LM, I would

- 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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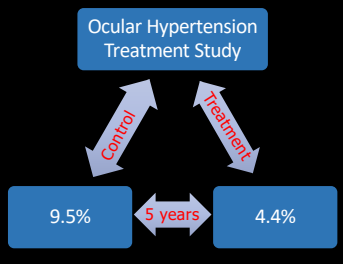
For management of LM, I would...



Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

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But Why?



Gordon, M., Beiser, J., Brandt, J., Heuer, D., Higginbotham, E., Johnson, C., & Keltner, J. (2002, June). The Ocular Hypertension Treatment Study. *Archives of Ophthalmology, 120*, 714-720.

12

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.

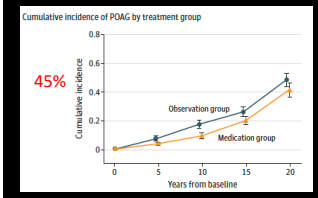
Coleman, A., Gordon, M., Kass, M., & Beiser, J. (2004, October). Baseline Risk Factors for the Development of Primary Open-Angle Glaucoma in The Ocular Hypertension Treatment Study. *American Journal of Ophthalmology, 138*(4), 684-685.

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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. Heuer, MD; Eve J. Higginbotham, MD; Richard K. Parrish, MD; Cheryl L. Khanna, MD; James D. Brandt, MD; Joorn B. Soltau, MD; Chris A. Johnson, PhD; John L. Keltner, MD; Julia B. Huecker, 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



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., Heuer, D., Higginbotham, E., Parrish, R., Khanna, C., Brandt, J., ... 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, 139*(5), 558-566.

14

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)

15

PLOS ONE

OPEN ACCESS

Citation: Kansal Y, Armstrong JJ, Pintwala R, Hutnik C (2018) Optical coherence tomography for glaucoma diagnosis: An evidence based meta-analysis. PLoS ONE 13(1): e0190621. https://doi.org/10.1371/journal.pone.0190621

Editor: Patrice E. Fort, University of Michigan, UNITED STATES

Received: June 30, 2017

Accepted: December 18, 2017

Published: January 4, 2018

RESEARCH ARTICLE

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

Vinay Kansal[1], James J. Armstrong[2], Robert Pintwala[2], Cindy Hutnik[3,4,5]

- 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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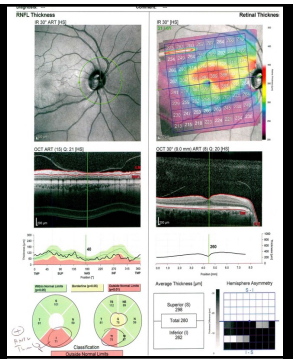
OCT

Pay attention to TSNIT curve.

Pay attention to the actual numbers in the segmentation plot

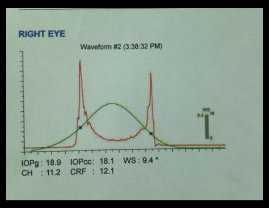
Pay attention to the numbers between eyes in the segmentation plot

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

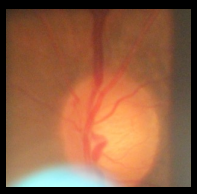
287 Eyes → 54 (19%) developed repeatable VF defects

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.

Susanna CN, Diniz-Filho A, Daga FB, Susanna BN, 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), doi: 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.

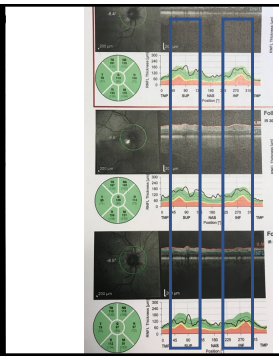
BCVA: 20/20 OD
20/20 OS

IOP: 23 OD
23 OS

ONH Eval: 0.50/0.50 OD
0.65/0.65 OS

No Meds
Tmax: 27 OU

20



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

Baseline

6 months

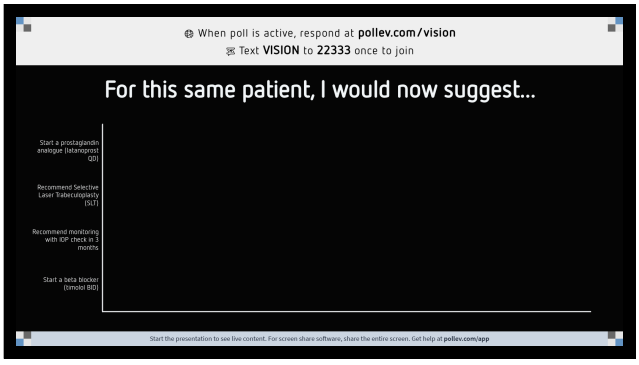
15 months

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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)

22



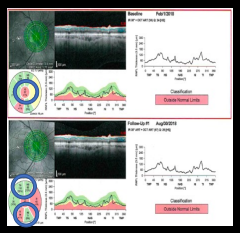
23

What Change Matters?

Average RNFL = ~ 4 microns

Superior/Inferior RNFL = ~ 7 microns

Macular GCL-IPL = ~ 4 microns



- Mwanza JC 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. 2015

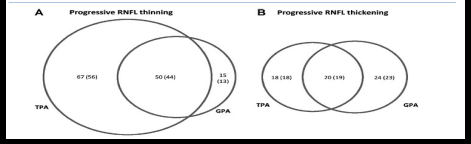
24

What We Do Know- OCT Helps!

Table 1. Comparisons of Rates of Change of Visual Field Index and Average Retinal Nerve Fiber Layer Thickness in Eyes with and without Progressive Retinal Nerve Fiber Layer Thinning Detected by Guided Progression Analysis and Trend-based Progression Analysis

	GPA			TPA		
	Eyes with RNFL Thinning (95% CI)	*Eyes without RNFL Thinning* (95% CI)	*P*	*Eyes with RNFL Thinning* (95% CI)	*Eyes without RNFL Thinning* (95% CI)	*P*
Rate of change of VFI	−0.76 %/yr (−1.07 to −0.46 %/yr)	−0.26 %/yr (−0.46 to −0.07 %/yr)	0.019	−0.59 %/yr (−0.87 to −0.32 dB/yr)	−0.19 %/yr (−0.39 to 0.02 %/yr)	0.020
Rate of change of average RNFL thickness	−0.90 μm/yr (−1.25 to −0.56 μm/yr)	−0.21 μm/yr (−0.29 to −0.14 μm/yr)	<0.001	−0.72 μm/yr (−0.92 to −0.51 μm/yr)	−0.07 μm/yr (−0.14 to 0.01 μm/yr)	<0.001

CI = confidence interval; dB = decibels; GPA = Guided Progression Analysis; RNFL = retinal nerve fiber layer; TPA = Trend-based Progression Analysis; VFI = visual field index.



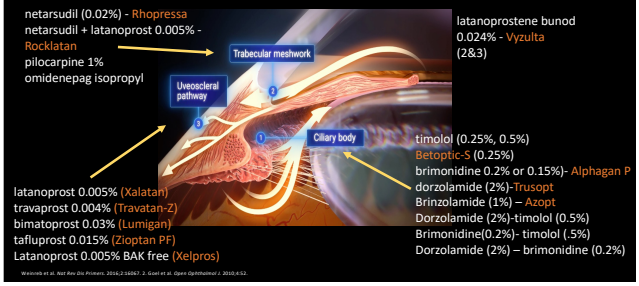
Marco, Y., Lin, C., Weinreb, R., Lai, G., Chiu, V., & Leung, C. (2016, June). Risk of Visual Field Progression in Glaucoma Patients with Progressive Retinal Nerve Fiber Layer Thinning. *Ophthalmology*, *123*(6), 1201-1210.

25

Aqueous Suppressants	Uveoscleral Outflow	Aqueous Suppressants	Uveoscleral Outflow + TM outflow	Rho-Kinase Inhibitor	Compounded Meds
-B-blockers -Alpha-2-adrenergics -CAI's	-Prostaglandins	-Combo Drops			-B-blockers -Alpha-2-adrenergics -CAI's -PGA's
Timoptic *timolol *betaxolol Alphagan P *brimonidine Azopt *brinzolamide Trusopt *dorzolamide	Lumigan *bimatoprost Travatan Z *travoprost Xalatan *latanoprost Zioptan Xelpros *latanoprost BAK free Iyuzeh *latanoprost PF	Combigan *brimonidine-timolol Cosopt *dorzolamide-timolol Simbrinza	Vyzulta	Rhopressa Rocklatan	

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Drop Mechanisms of Action



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

latanoprostene bunod 0.024% - Vyzulta (2&3)

latanoprost 0.005% (Xalatan)
travaprost 0.004% (Travatan-Z)
bimatoprost 0.03% (Lumigan)
tafluprost 0.015% (Zioptan PF)
Latanoprost 0.005% BAK free (Xelpros)

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

Weinreb et al. *Nat Rev Dis Primers*. 2016;2:16067. 2. Goel et al. *Open Ophthalmol J*. 2010;4:52.

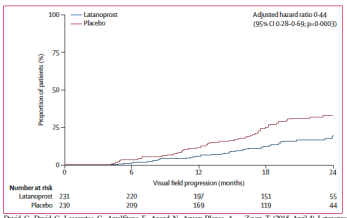
27

Why are PGAs first line?

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

Primary Open-Angle Glaucoma PPP 2020. American Academy Of Ophthalmology, 2020, p.97

25-33% ↓



David, G., David, C., Lascaratos, G., Arnalfitano, F., Anand, N., Azuara-Blanco, A., ... Zeyen, T. (2015, April 4). Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. *The Lancet*, *385*, 1295-1304

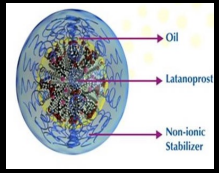
28

(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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Latanoprost 0.005% PF (IYUZEH)

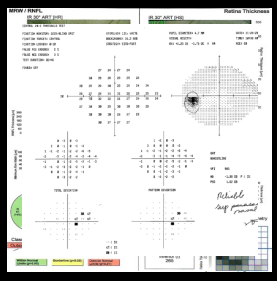
- 1st full preservative-free latanoprost
- Targets uveoscleral outflow
- IOP decrease 3-8mmHG
- QD dosing

NOW APPROVED
iyuzeh™
(latanoprost ophthalmic solution) 0.005%

Charters, L. (2022, December 15). Thea receives FDA approval for preservative-free latanoprost for IOP reduction. Ophthalmology Times.

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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

32

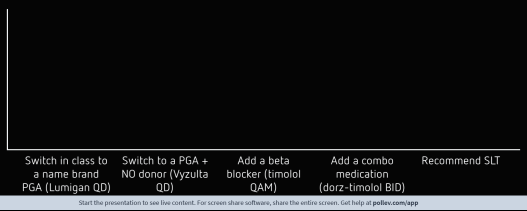
For this very same patient on a PGA , I would now suggest

- A. Switch in class to a name brand PGA (Lumigan QD)
- B. Switch to a PGA + NO donor (Vyzulta QD)
- C. Add a beta blocker (timolol QAM)
- D. Add a combination medication (dorz-timolol BID)
- E. Recommend SLT

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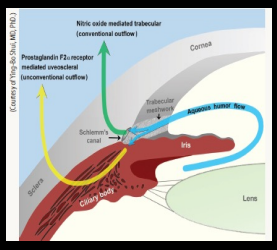
For this very same patient on a PGA , I would now suggest…

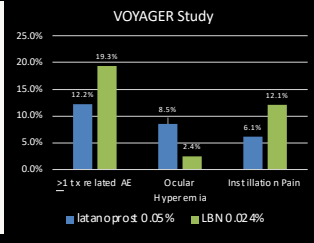


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Vyzulta (latanoprostene bunod 0.024%)





Siegfried, C. (2017, September). Nitric Oxide: A Therapeutic Target for Glaucoma. *Glaucoma Today*, 57-59.
Weinreb, R., Ong, T., Sforzolini, B., Vittitow, J., Singh, K., & Kaufman, P. (2014, December 8). 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*, 738-745.

35

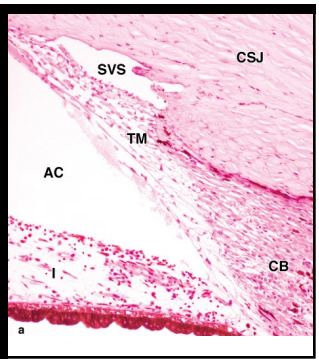
Nitric Oxide

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 synthase in human glaucoma. Invest Ophthalmol Vis Sci. 1995



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

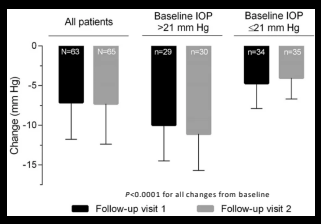
- Multicenter, noninterventional retrospective chart review
- Charts were included if patients
  - Were aged ≥ 18 years
  - had no history of medical, laser, or surgical intraocular pressure (IOP)-lowering intervention
  - Had at least two follow-up visits (spanning ≥ 2 months) following initiation of 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.

Oleke, C.O., Burstein, E.S., Trubnik, V. et al. Ophthalmol Ther 9, 1041–1053 (2020). https://doi.org/10.1007/s40123-020-00307-0

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Results: Mean (SD) IOP Change from Baseline

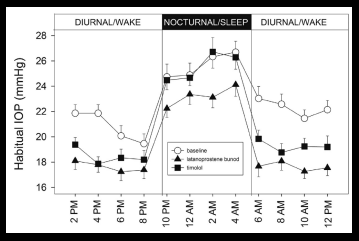
- LBN use resulted in a mean (SD) reduction from baseline of 7.1 (4.7) and 7.3 (5.1) mmHg at the first and second follow-up visits, respectively ($P < 0.0001$ for both).
  - Reductions among patients with IOP > 21 mmHg ($n = 30$) at baseline were 10.0 (4.5) and 11.1 (4.6) mm Hg at the first and second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



Okeke, C.O., Burstein, E.S., Trubnik, V. et al. Ophthalmol Ther 9, 1041–1053 (2020). https://doi.org/10.1007/s40123-020-00307-0

38

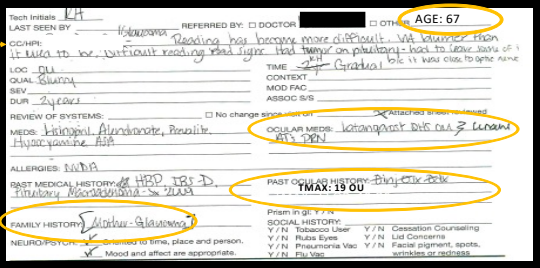
Nocturnal IOP Lowering



Liu J et al Am J Ophthalmol 2016;

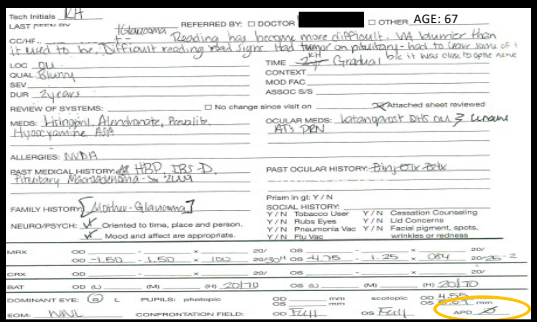
39

Glaucoma Eval – Pt. DB



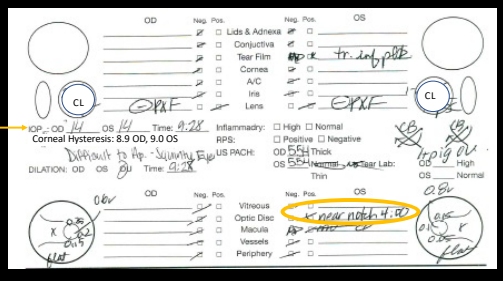
40

Glaucoma Eval - DB



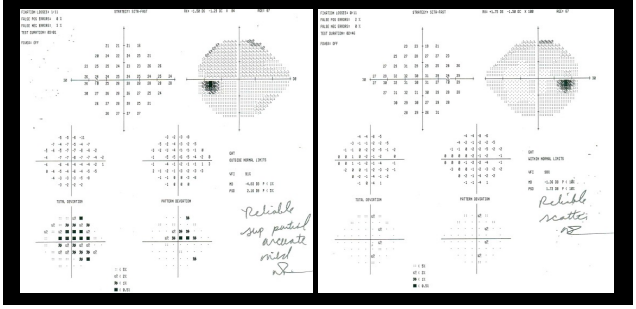
41

Glaucoma Eval - DB

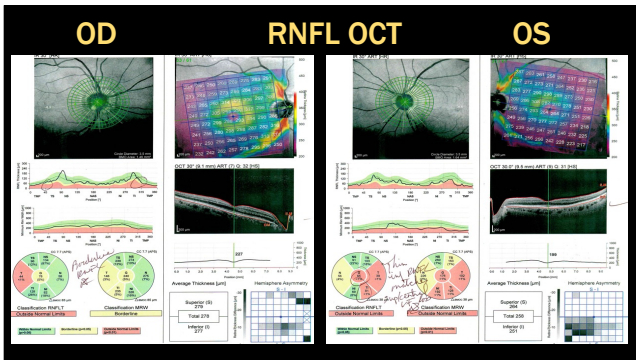


42

Visual Field



43

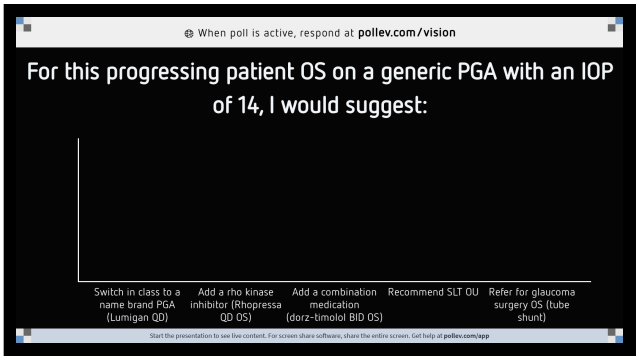


44

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 (dorz-timolol BID OS)
- D. Recommend SLT OU
- E. Refer for glaucoma surgery OS (tube shunt)

45



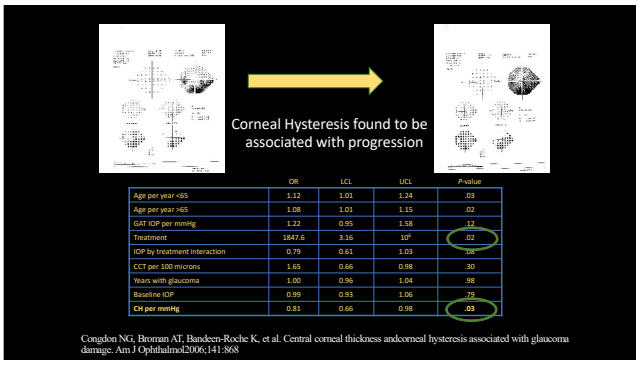
46

What does it all mean?

- 50% of all POAG patients have a positive family history
  - Their 1st degree relatives have 9-fold increased risk of developing glaucoma
- 22% lifetime risk for 1st degree relatives vs 2.3% in normal controls
  - 10.4% in siblings with glaucoma vs 0.7% in siblings of normal

1.Awadalla M.S., Fingert J.H., Roos B.E. Copy number variations of TBK1 in Australian patients with primary open-angle glaucoma. Am J Ophthalmol. 2015;159:124–130
2.Wolfs R.G.C., Klaver C.C.W., Ramrattan R.S., Van Duijn C.M., Hofman A., de Jong P. T.V.M. Genetic risk of primary open-angle glaucoma. Arch Ophthalmol. 1998;116:1640–1645

47

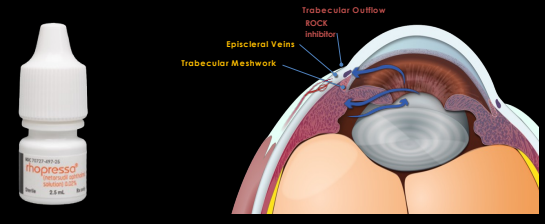


	OR	LCL	UCL	P-value
Age per year <65	1.12	1.01	1.24	.03
Age per year >65	1.08	1.01	1.15	.02
GAT IOP per mmHg	1.22	0.95	1.58	.12
Treatment	1847.6	3.16	10^8	.02
IOP by treatment interaction	0.79	0.61	1.03	.08
CCT per 100 microns	1.65	0.66	0.98	.30
Years with glaucoma	1.00	0.96	1.04	.98
Baseline IOP	0.99	0.93	1.06	.79
CH per mmHg	0.81	0.66	0.98	.03

Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness andcorneal hysteresis associated with glaucoma damage. Am J Ophthalmol2006;141:868

48

Rhopressa (netarsudil 0.02%)



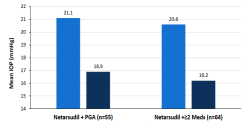
ROCK, rho kinase.
1. Kazemi et al. J Ocul Pharmacol Ther. 2018;34:380. 2. Weinreb et al. Nat Rev Dis Primers. 2016;2:16067. 3. Goel et al. Open Ophthalmol J. 2010;4:52.

49

M.O.S.T Study of Netarsudil

4-4.5mmHG

Netarsudil as Adjunctive Therapy



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)

Zaman F, Geser SC, 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;37(6):1011-1020

50

M.O.S.T Study of Netarsudil

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

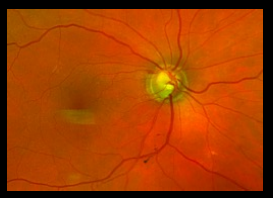
Adverse Events	All M.O.S.T. Patients N=260	Adjunctive Therapy group N=161
Adverse Events (≥ 5%)		
Conjunctival hyperemia	54 (20.8%)	32 (19.9%)
Vision blurred	19 (7.3%)	10 (6.2%)
Conjunctival hemorrhage	14 (5.4%)	8 (5.0%)
Instillation site pain	14 (5.4%)	8 (5.0%)

Zaman F, Geser SC, 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;37(6):1011-1020

51

Patient MW- Demographics & Entrance Testing

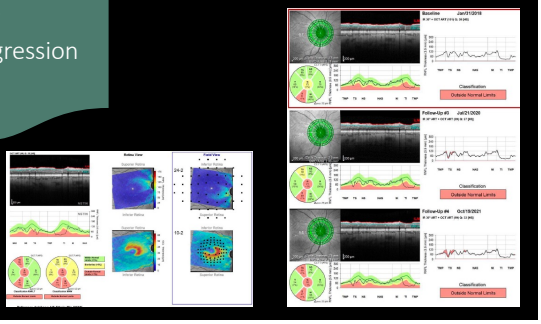
- LTG follow-up. OD worsening?
- GAT → 13, (6mo ago 14) Tmax 15; 9, (6 mo ago 13, Tmax 17
- Meds: dorz./tim. BID OU, Lumigan QD OU
- PACH → 530; 520
- CH → 8.1; 9.3
- Gonio: open to SS OU, mild pigment



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

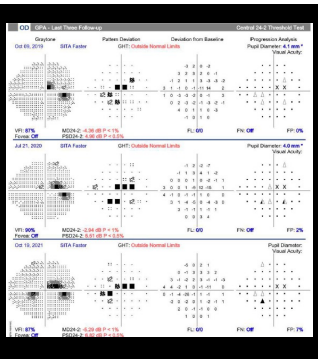
52

OCT Progression



53

HFA Visual Field



PSD 4.96

PSD 5.51

PSD 6.82

54

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

55

When poll is active, respond at **pollev.com/vision**
Text **VISION** to **22333** once to join

What is your treatment goal for low tension glaucoma?

Reduction of IOP is irrelevant in LTG
25% reduction from baseline IOP
30% reduction from baseline IOP
40% reduction from baseline IOP

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

56

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 = 79)	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.

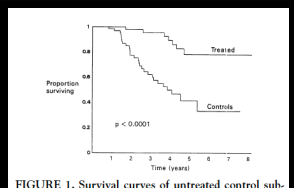


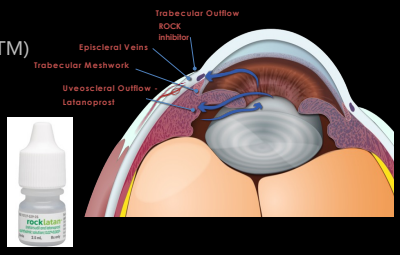
FIGURE 1. Survival curves of untreated control subjects and treated patients from randomization using protocol-defined end points.

Collaborative Normal-Tension Glaucoma Study Group. . (1998, October). Comparison of Glaucomatous Progression Between Untreated Patients with Normal-Tension Glaucoma and Patients with Therapeutically Reduced Intraocular Pressures. *Ophthalmology, 126*(4), 487-497.

57

Rocklatan (netarsudil 0.02% and latanoprost0.005%)

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



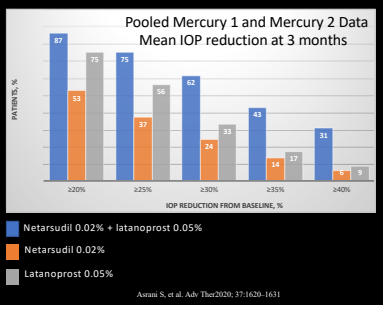
ROCK, rho kinase.
1. Kazemi et al. J Ocul Pharmacol Ther. 2018;34:380. 2. Weinreb et al. Nat Rev Dis Primers. 2016;2:16067. 3. Goel et al. Open Ophthalmol J. 2010;4:52.

58

netarsudil 0.02% + latanoprost 0.005% (Rocklatan)

Pooled data Mercury 1&2

- Comparing Rocklatan to it's individual parts
- 708 subjects randomized 1:1:1
- Baseline IOP 24mmHG, mean IOP reduction Rocklatan ~8.5mmhg



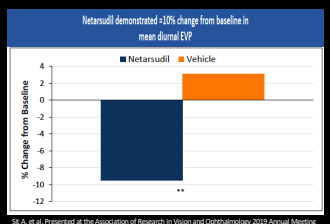
Asrani S, et al. Adv Ther2020; 37:1620–1631

59

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



Sit A, et al. Presented at the Association of Research in Vision and Ophthalmology 2019 Annual Meeting (ARVO 2019); April 29-May2, 2019; Vancouver, BC, Canada.

IOP = production/outflow + EVP

60

Add Another Drop?

- Rates for persistence are generally below 50% at 1 year
- Patients with adjunctive therapy commonly reported more problems with medication use than those on monotherapy.
- A study of adjunctive therapy suggested that patients prescribed a second ocular hypotensive medication refilled their first-prescribed medication less regularly
- Busche and Gramer also reported decreased adherence when multiple medications were used



Gail F. Schwartz, Harry A. Quigley, Adherence and Persistence with Glaucoma Therapy, Survey of Ophthalmology, Volume 53, Issue 6, Supplement, 2008,Pages S57-S68
A.L. Robin, D. CovertDoes adjunctive glaucoma therapy affect adherence to the initial primary therapy? Ophthalmology, 112 (2005), pp. 863-868
S. Busche, E. Gramer[Improved eyedrop administration and compliance in glaucoma patients. A clinical study] Klin Monatsbl Augenheilkd, 211 (1997), pp. 257-262

61

Simple Drops – Imprimis Pharmaceuticals

- Preservative free combination drops
- One way valve system for sterility
- Potentially lower cost to patients
- Goal to increase compliance



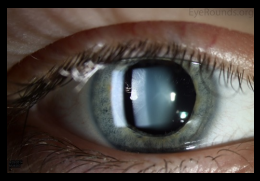
- LAT, LAT-DS, TIM-LAT, BRIM-DOR, TIM-BRIM-DOR, TIM-DOR-LAT, TIM-BRIM-DOR-LAT

http://eyewiretoday.com/2017/05/04/imprimis-pharmaceuticals-to-launch-its-simple-drops-combination-glaucoma-drops-ascrs

62

Patient EH- Demographics & Entrance Testing

- GL Eval: 63-year-old female w/ FHx: mom, sister
- GAT → 21, TMAX 24; 22, TMAX 23
- PACH → 526; 519
- CH → 10.4; 10.4
- C/D → 0.35v; 0.50v

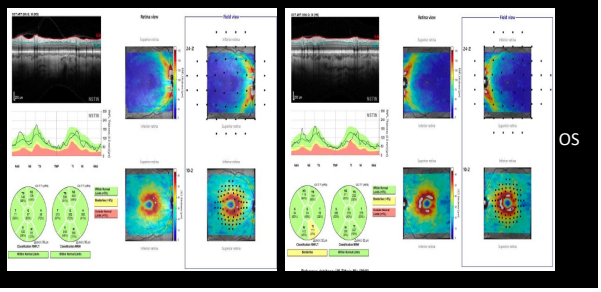


Gonio: open to CB OU, mild pigment

63

OCT (RNFL)

OD

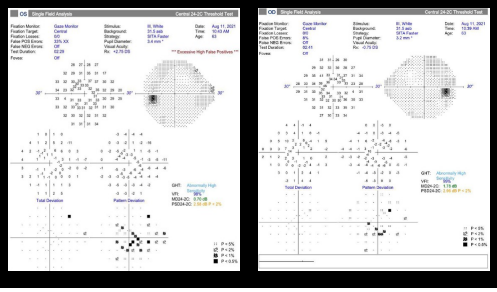


OS

64

HFA Visual Field

OS

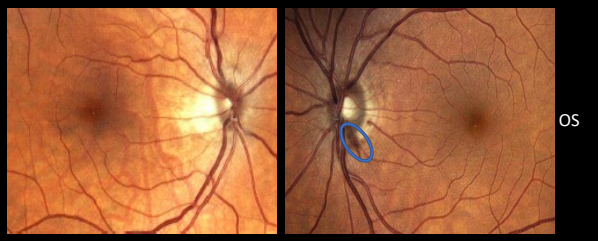


OD

65

Disc Photos with a Drance Heme OS

OD



OS

66

Disc Hemorrhage Prevalence and Significance

Glaucoma Screening Study

2,161 eyes had disc photos

Table 1.—Prevalence of Optic Nerve Head Hemorrhage (per Eye)*

Study	Normal Eyes	Glaucoma Suspect Eyes	Eyes With Glaucoma
Prospective studies			
Present study			
First examination	0/661 (0)	6/1377 (0.44)	3/123 (2.44)
Second examination	0/279 (0)	7/1027 (0.68)	0/107 (0)
Kitazawa et al[11]	2/946 (0.21)	1/408 (0.25)	8/363 (2.20)
Bengtsson et al[12]	5/3000 (0.17)	...	7/18 (38.9)

Table 6.—Progression of Nerve Fiber Layer Atrophy 1 Year After Disc Hemorrhage (DH)*

	DH	Non-DH	P
Glaucoma suspect eyes	3/7 (42)	2/56 (3)	.007
Eyes with glaucoma	1/2 (50)	2/15 (13)	NS†

Diehl, C., Quigley, H., Miller, N., Sommer, A., & Burney, E. (1990, April). Prevalence and Significance of Optic Disc Hemorrhage in a Longitudinal Study of Glaucoma. *Archives of Ophthalmology, 108.*

67

What does a Disc Hemorrhage mean?

Evidence-based understanding of disc hemorrhage in glaucoma

*Eun Jung Lee, MD, Hyun Joo Kee, MD, Jong Chul Han, MD, Changwon Kee, MD**

Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

1. Classically considered a "Risk factor" for glaucoma.
2. Mechanism not fully understood→ ischemic theories and mechanical theories
3. Emerging evidence to use DH's as an "indicator of progression"
4. Early manifest glaucoma trial (EMGT)--> DH predicted progression w/hazard ratio of 1.02%

Jung Lee, E., Joo Kee, H., Chul Han, J., & Kee, C. (2021). Evidence-based understanding of disc hemorrhages in glaucoma. *Survey of Ophthalmology, 66*, 412-422.

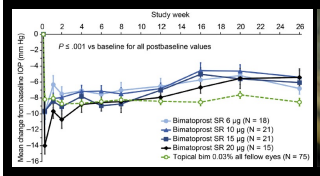
68

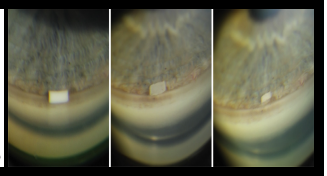
Bimatoprost SR (Durysta)

(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





Lewis, R., Christie, W., Day, D., Craven, R., Walters, T., Bejanian, M., ... Robinson, M. (2017, March). Bimatoprost Sustained-Release Implants for Glaucoma Therapy: 6-Month Results From a Phase I/II Clinical Trial. *Ophthalmology, 175*, 137-147.

69

Phase III (ARTEMIS 1/2)



- The device as implanted intracamerally at 4-month intervals for 1 year
- (Office-based procedure)
- 742 subjects
- Durysta (10ug/15ug) vs. timolol BID
- Baseline IOP 24 mm Hg
- At 1 Year IOP maintained at 16-17 mm Hg



*60% - additional 12 months without retreatment

Medeiros, F., Walters, T., Kolko, M., Coote, M., Bejanian, M., Goodkin, M., ... Weinreb, R. (2020, December). Phase 3, Randomized, 20-Month Study of Bimatoprost Implant in Open-Angle Glaucoma and Ocular Hypertension (Artemis 1). *Ophthalmology, 127*(12), 1627-1641

70

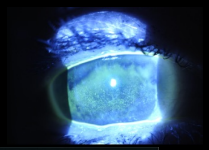
In Office Implantation



71

Patient GM- Demographics & Entrance Testing

- New Glaucoma eval
- GAT → 17, Tmax 20 / 21, Tmax 22
- Meds: Artificial tears, struggles with drops
- PACH → 550 / 560
- C/D → 0.75v / 0.80v
- Gonio: open to CB OU, mild pigment

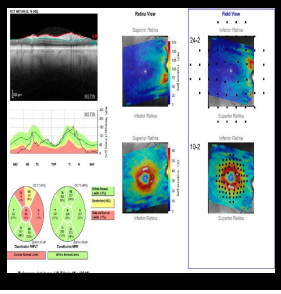




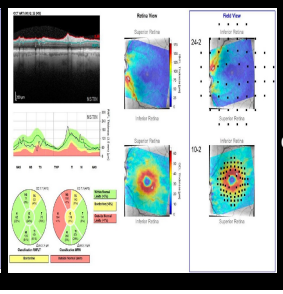
72

OCT (RNFL/GCC)

OD



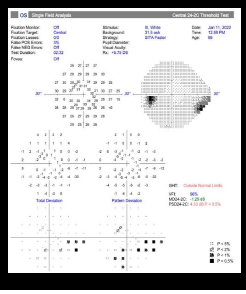
OS

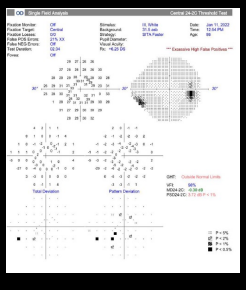


73

HFA Visual Field

OS

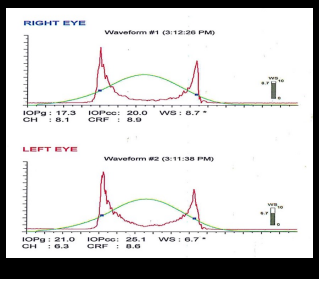


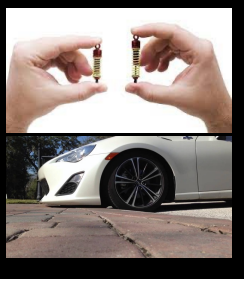


OD

74

Corneal Hysteresis

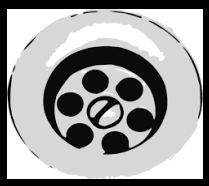




75

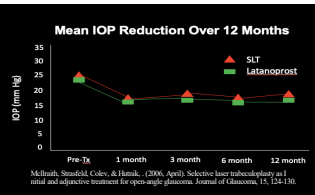
SLT

- Selective Laser Trabeculoplasty
  - Selectively targets and laser burns pigmented TM cells
  - Activates inflammation to ↓ IOP
  - Macrophage uptick
    - Secondary glaucomas have a high number of pigmented TM cells
    - ?? More effective.

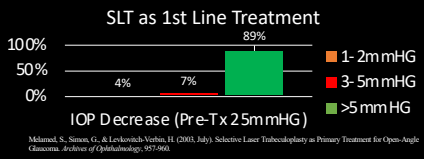


76

SLT Efficacy



Melloth, Stoodilel, Coley, & Hutnik, (2006, April). Selective laser trabeculoplasty as i nitial and adjunctive treatment for open-angle glaucoma. Journal of Glaucoma, 15, 124-130.



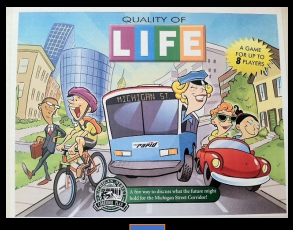
Melamed, S., Simon, G., & Levkovitch-Verbin, H. (2003, July). Selective Laser Trabeculoplasty as Primary Treatment for Open-Angle Glaucoma. *Archives of Ophthalmology*, 957-960.

77

Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial

SLT: 95% @target, 78% med free
Drops: 93.1% @target, 65% 1 med



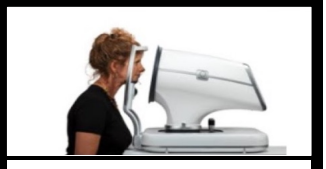


Gazzard G, Konstantopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicenter randomized controlled trial. Lancet. 2019;393(10180):1505-1516.

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What's New in SLT

- FDA Approves Belkin's EAGLE DSLT December 2023. (Alcon)
- Direct selective laser trabeculoplasty (DSLT)
- Noncontact SLT, 120 automated shots to limbal area
  - DSLT vs. SLT (30 subjects)
  - 1-year IOP reduction
    - DSLT: 21%
    - SLT: 33%



Direct selective laser trabeculoplasty in open angle glaucoma study design: a multicentre, randomised, controlled, investigator-masked trial (GLAUrious)

Nathan Congdon,[1,2] Augusto Azuara-Blanco,[3] Yoram Solberg,[3] Carlo E Traverso,[4] Michele Iester,[4] Carlo Alberto Cutolo,[4] Alessandro Biagini,[4] Tin Aung,[5] Scott J Fudemberg,[6] Richard Lindstrom,[7,8] Thomas Samuelson,[7] Kuldev Singh,[9] Evtan Z Blumenthal,[10,11] Gus Gazzard,[12,13] and GLAUrious study group

Geffen N et al. *Journal of Glaucoma*. 2017;26(3):201-207.

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GLAUrious Trial: SLT vs. DSLT

Purpose
- Compare DSLT outcomes to manual SLT (non-inferiority)
- Demonstrate safety and efficacy of DSLT

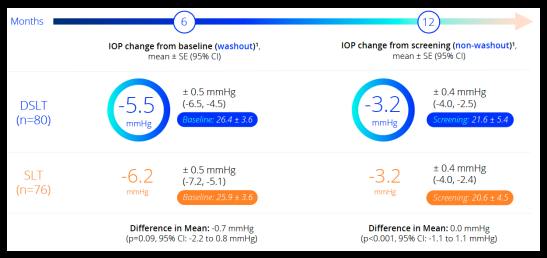
Effectiveness Endpoints
- Primary: Difference in mean IOP reduction from baseline (washout) at 6 months
- Secondary:
  1. Proportion with >20% IOP reduction at 6 months without SSI
  2. Change in # of medications at 6 months

Patient Parameters[1]	DSLT	SLT
N	80	76
Age (avg)	66.0	66.0
Male (%)	60.0%	56.6%
OAG (%)	66.3%	71.1%
OHT (%)	20.0%	10.5%
PXF + PG (%)	13.8%	18.4%
Treated Eye OD (%)	45.0%	59.2%
Screening IOP mmHg (avg ± SD)	21.6 ± 5.4	20.6 ± 4.5
Baseline Washout IOP mmHg (avg ± SD)	26.4 ± 3.6	25.9 ± 3.6
Hypotensive Med Count	1.2 ± 1.0	1.1 ± 1.0

1. GLAUrious Study - Clinical Study Report (CSR), CA-RP-01-006, Rev. 01; 2022

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GLAUrious Trial: SLT vs. DSLT



1. GLAUrious Study - Clinical Study Report (CSR), CA-RP-01-006, Rev. 01; 2022

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Durability and Repeatability

How long does SLT maintain efficacy in your patients?

A. 6-12 months
B. 2-3 years
C. >5 years
D. >10 years
E. One and done-- forever

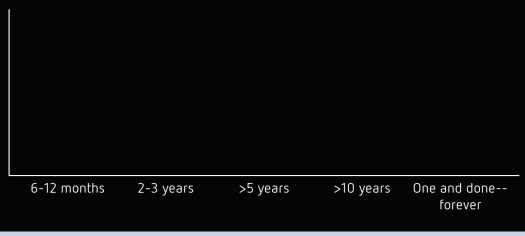


Weinand F, Althen F. Long-term clinical results of selective laser trabeculoplasty in the treatment of primary open angle glaucoma. Eur J Ophthalmol. 2006;16(1):100-104.

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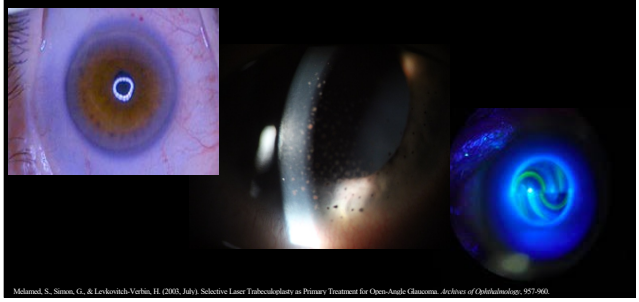
How long does SLT maintain efficacy in your patients?



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83

Adverse Events with SLT/DSLT



Melamed, S., Simon, G., & Levkovitch-Verbin, H. (2003, July). Selective Laser Trabeculoplasty as Primary Treatment for Open-Angle Glaucoma. *Archives of Ophthalmology*, 957-960.

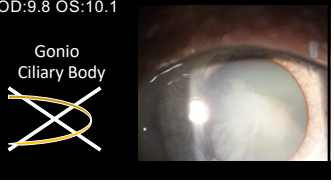
84

Patient MC- Demographics & Entrance Testing

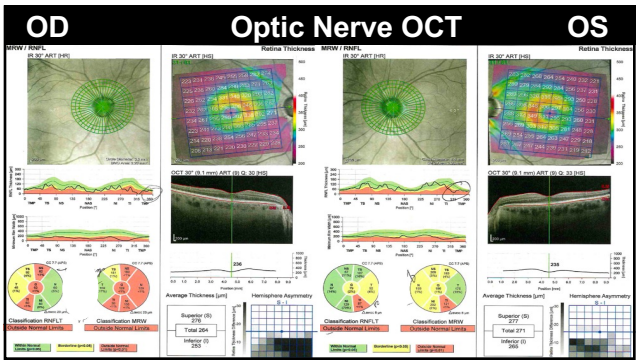
- 60 year old female
- CC: Elevated IOP w/headaches, Fhx glaucoma, glare
- BCVA: 20/20- (BAT 20/60); 20/20- (BAT 20/70)
- GAT: 16, TMAX 28; 18, TMAX 28
  Cosopt BID OU, Trav. Z QD OU
- PACH: 593, 595
  ONH: 0.85V, 0.85V

Corneal Hysteresis
OD:9.8 OS:10.1

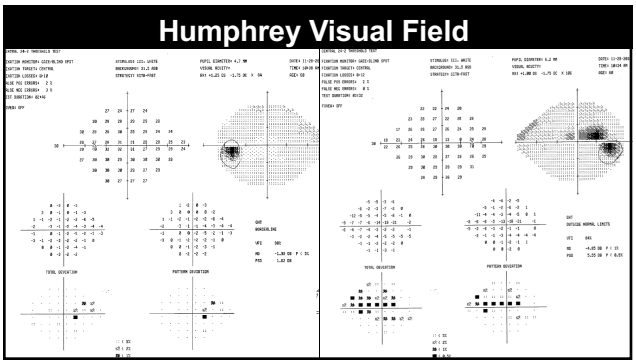
Gonio
Ciliary Body



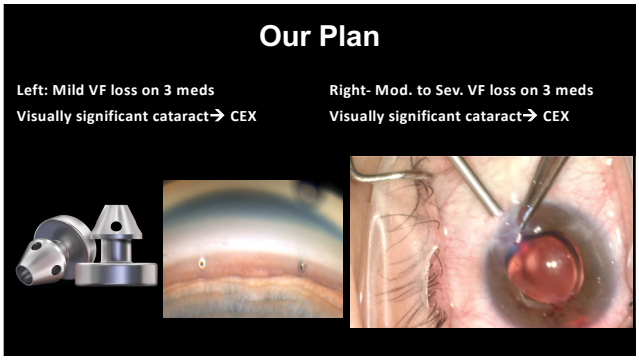
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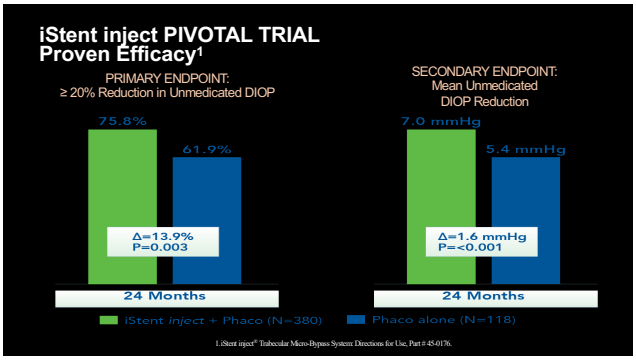
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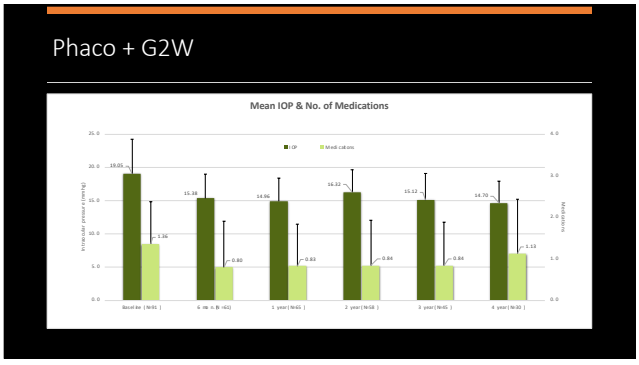
87



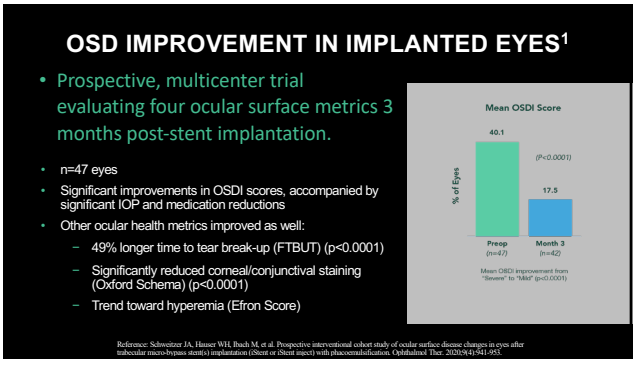
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MIGs Collaborative Care

A. I haven't referred patients for MIGs

B. I refer patients for MIGs surgeries, but don't do perioperative care

C. I refer patients for MIGs and actively do perioperative care

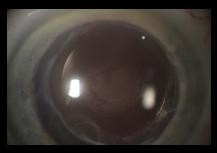
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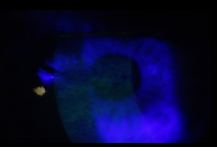


98

81 year old Glaucoma Eval

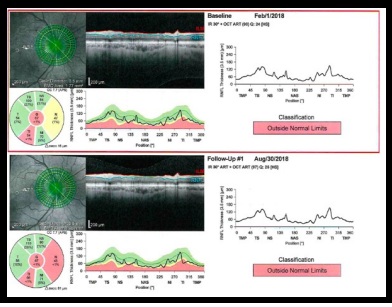
- "Primary doctor said my right visual field is worse"
- "Eye drops sting"
- Ocular Meds : Lumigan QD OU, Combigan BID OU (sensitivity to dorzolamide)
- BCVA → 20/20-1, 20/25
- Slit Lamp → PCIOL, 1+ PEE; PCIOL, 1+ PEE
- IOP → 26mmHG, 22mmHG; Pach → 491, 492
- Gonio: open to CB OU all quadrants





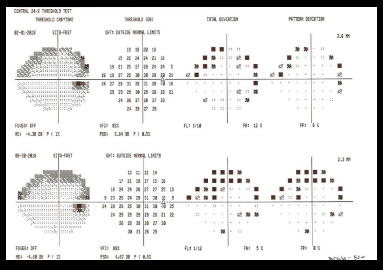
99

Focusing in on OD



100

Focusing in on OD



101

What Level of Glaucoma is this Based on VF?

- A. Glaucoma suspect
- B. Mild
- C. Moderate
- D. Severe

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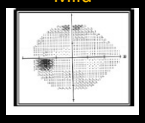
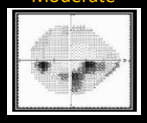
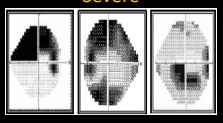
What Level of Glaucoma is this OD Based on VF?

Glaucoma suspect | Mild | Moderate | Severe

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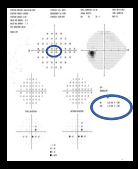
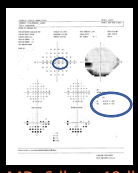
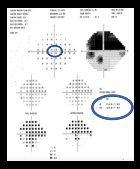
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American Glaucoma Society /AAOphthalmology PP Guidelines

Mild	Moderate	Severe
		
• ONH abnormalities & • No VF loss • Screening VF loss Ok	• ONH abnormalities & • GL VF loss 1 hemifield • No VF loss within 5* fixation	• ONH abnormalities & • GL VF both hemifields &/or • VF loss within 5* fixation

104

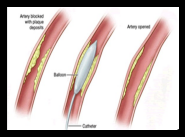
Hoddap – Parrish - Anderson

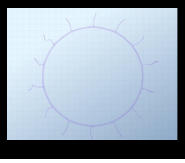
Mild	Moderate	Severe
		
1. MD <-6db 2. <25% depressed below 5% & <10 pts depressed below 1% PSD 3. Central 4 pts. all > 15db	1. MD -6db to -12db 2. <50% depressed below 5% & <20 pts depressed below 1% PSD 3. 1 Central pt. < 15db	1. MD > -12db 2. >50% depressed below 5% or >20 pts depressed below 1% PSD 3. Both hemifields 1 pt < 15db

105

Canaloplasty+Trabeculotomy (OMNI)







106

Following MIGS Further

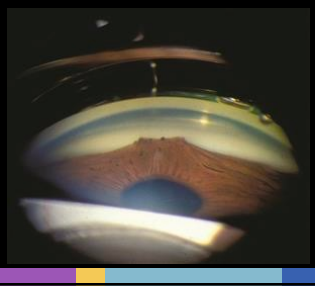
- Continue monitoring
  - IOP
    - Immediate IOP spike, add med +/- burp para
    - Fluctuates early, +/- steroid effect
  - Slit lamp exam
    - Normal inflammation, hyphema?
  - Gonioscopy
    - 1 time in global period
  - OCT and HVF
    - 3-6 months post-operatively set new baselines.

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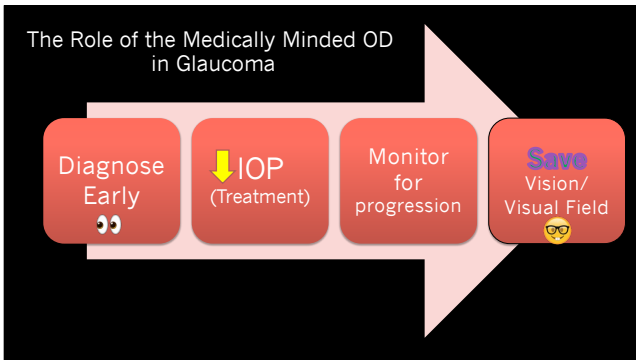
Minimally Invasive

Safety First

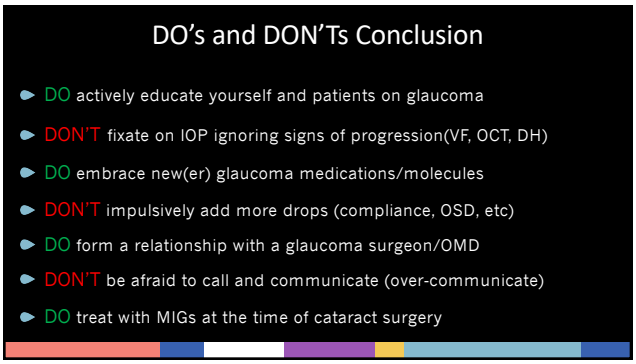
1. IOP Spikes
2. Microhyphema
3. Hypotony- Can it happen?
4. Endothelial Cell Loss
5. Peripheral Anterior Synechiae



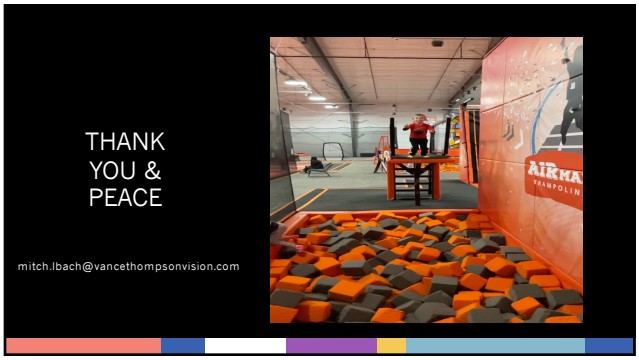
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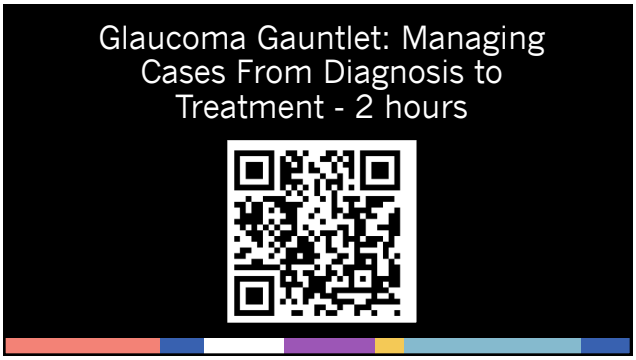
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112



113



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