

# TOPICAL IOP LOWERING MEDICATIONS

## INTERACTIVE EDITION



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SOCRATIVE.COM

STUDENT

ROOM IS: SPALDING4876

# CASE

- 61 / W / M
- CC:
  - here for DM eye eval, uses OTC for reading without complaints, happy at distance without rx, no ocular comfort problems
- OCULAR PAIN:
  - 0/10
- OTHER PAIN:
  - 0/10
- OCULAR HISTORY:
  - LEE 3 YRS by VA OPTHALMOLOGIST
    - DM Without Retinopathy OU
    - .6/.6, IOP 21/20 via NCT
    - H/O Broken orbital floor OS 35 yrs ago
- MEDICAL HISTORY:
  - +DM x 6 yrs (last a1c 11.6, 6 mos prior 7.2), +insulin, +htn (last bp 125/80), -heart +chol, -stroke, -cancer, -thyroid –migraines –MS
- MEDS:
  - Metformin, Insulin, Atorvastatin, Losartan, Sildenafil, Vit D3
- ALLERGIES:
  - NONE
- FAMILY HISTORY:
  - -dm, -glaucoma, -blind
- SOCIAL HISTORY:
  - -etoh, -tobacco

# CASE

- VISION
  - sc 20/25
  - sc 20/40+2
- PRELIMS
  - NORMAL PUPILS, NO APD
  - FTFC OD OS
  - FROM
- REFRACTION
  - +125-100x085 20/20
  - +150-175x095 20/20
  - ADD: +250 20/20 OU 12-24"
- SLIT LAMP
  - Adnexa: normal ou
  - Lids / Lashes: normal ou
  - Conj: concretions inferiorly ou
  - Cornea: normal ou
  - A/C: deep and quiet ou
  - Iris: few flat nevi ou
- IOP: 25/23@ 820a
- Pachym: 564/565
- GONIO:
  - ou open to cbb 360, no PAS, recess, nv, tr pig
- DFE:
  - LENS: trace ACC / trace NS ou
  - See photos for:
    - C/D, ONH, Macula, Post Pole, Vessels
  - Vitreous: PVD ou
  - Periphery: normal ou

# DFE



9/19/2019 9:18:46.0



9/19/2019 9:19:06.9

# RNFL

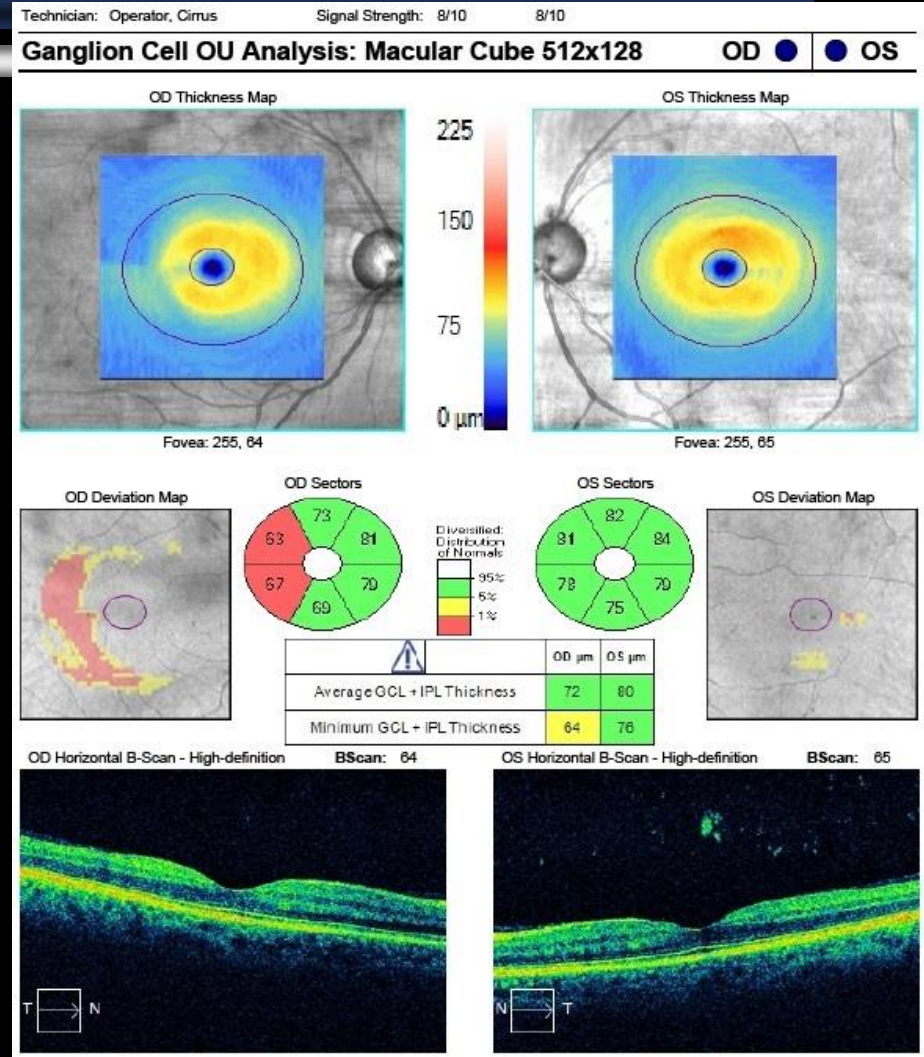
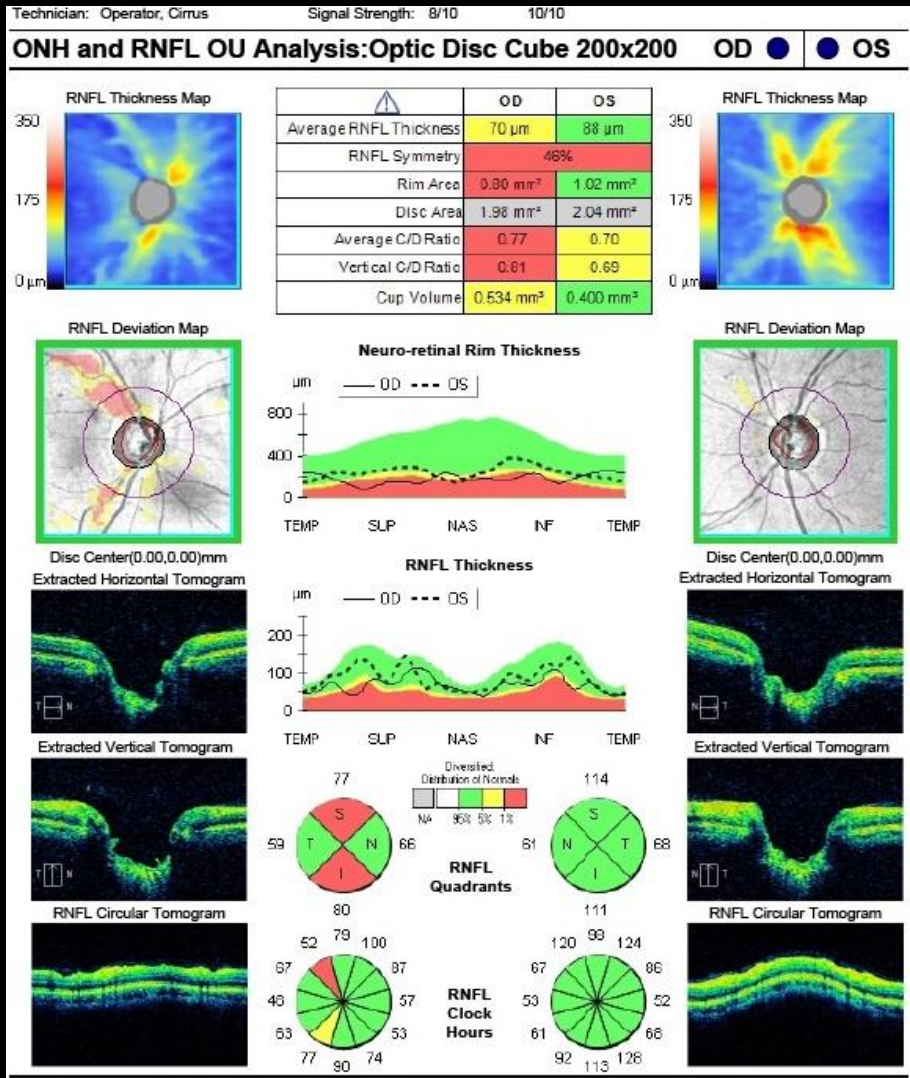


9/19/2019 9:18:46.0



9/19/2019 9:19:06.9

# OCT RNFL / GCC



# WHAT ARE YOU GOING TO DO?

- A. MONITOR THE PATIENT
- B. TREAT THE PATIENT
- C. REFER TO LOCAL OPTOMETRIST
- D. REFER TO LOCAL GENERAL OPHTHALMOLOGIST
- E. REFER TO LOCAL FELLOWSHIP TRAINED GLAUCOMA SPECIALIST



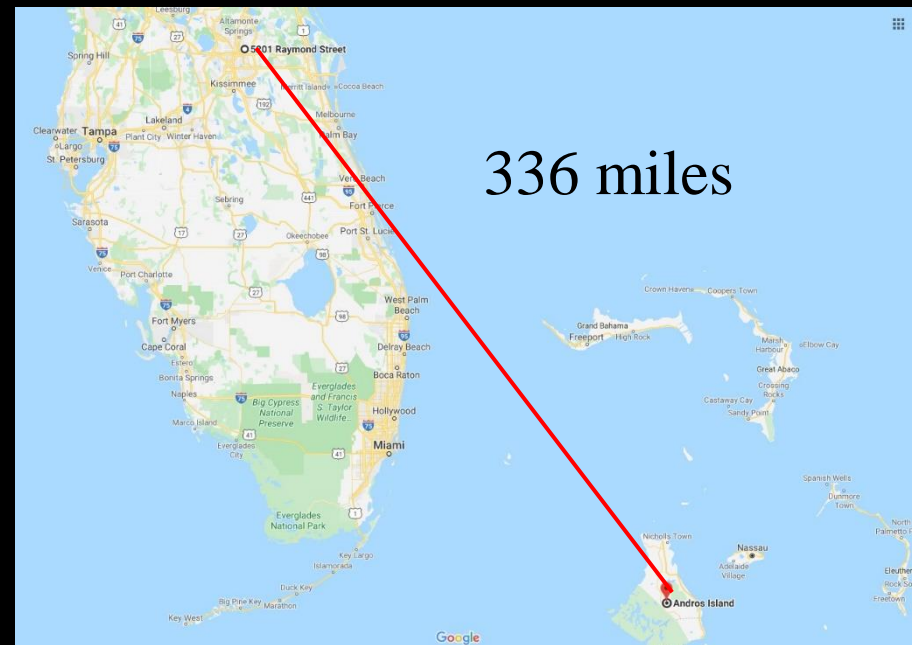
# IN A PERFECT WORLD...

- REMEMBER
  - TYPICALLY, GLAUCOMA IS A LONG, SLOW, GRADUAL PROCESS
  - IN MOST CASES, THERE'S TIME TO...
- GATHER BASELINE DATA
  - **GET AT LEAST 3 IOP READINGS**
    - PREFERABLY ON DIFFERENT DAYS
    - PREFERABLY AT DIFFERENT TIMES OF THE DAY
      - MODIFIED DIURNAL CURVE
    - GOAL IS TO DETERMINE THE HIGHEST IOP
      - HELPS TO DETERMINE TARGET IOP
      - MAY INFLUENCE DECISION ABOUT MEDICATION EFFECTIVENESS
  - **GET PACHYMETRY AND GONIOSCOPY**
  - **DOCUMENT THE ONH**
    - PHOTOS
  - **DOCUMENT THE RNFL, GCC**
    - OCT, ETC.
  - **GET VISUAL FIELD**
    - HELPS STAGE THE DISEASE
    - HELPS DETERMINE TARGET IOP

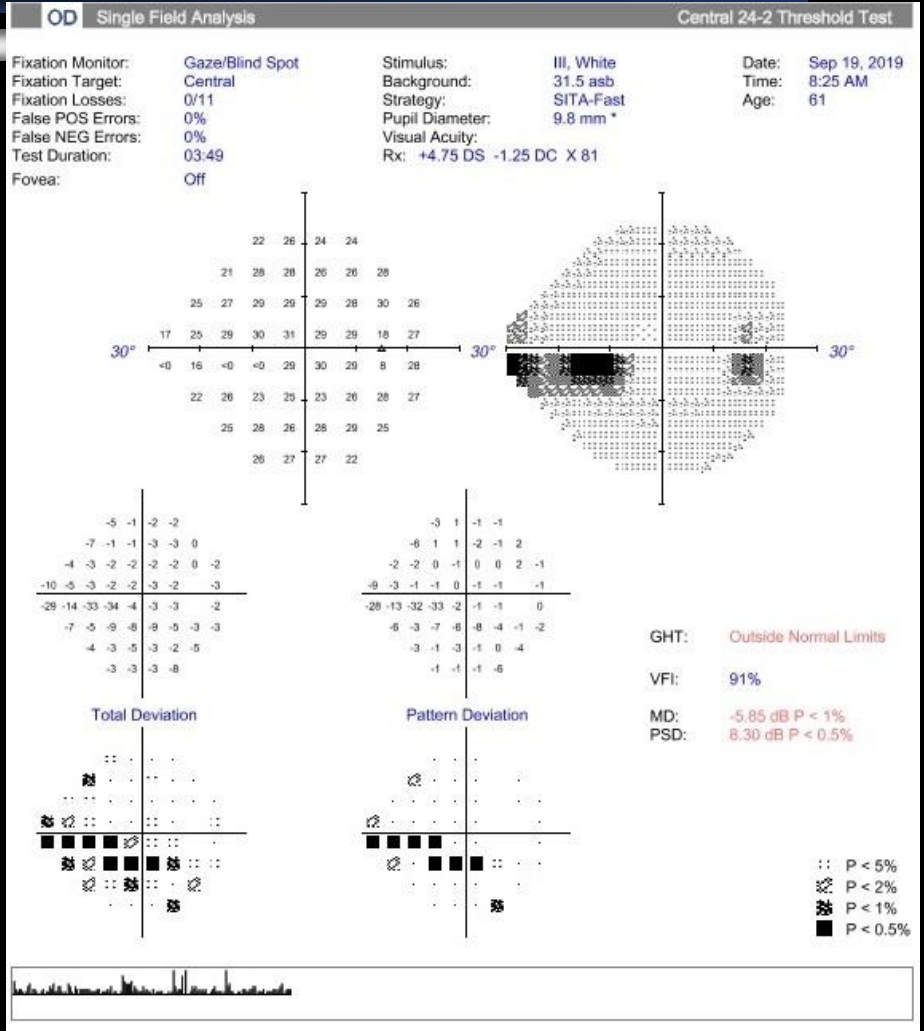
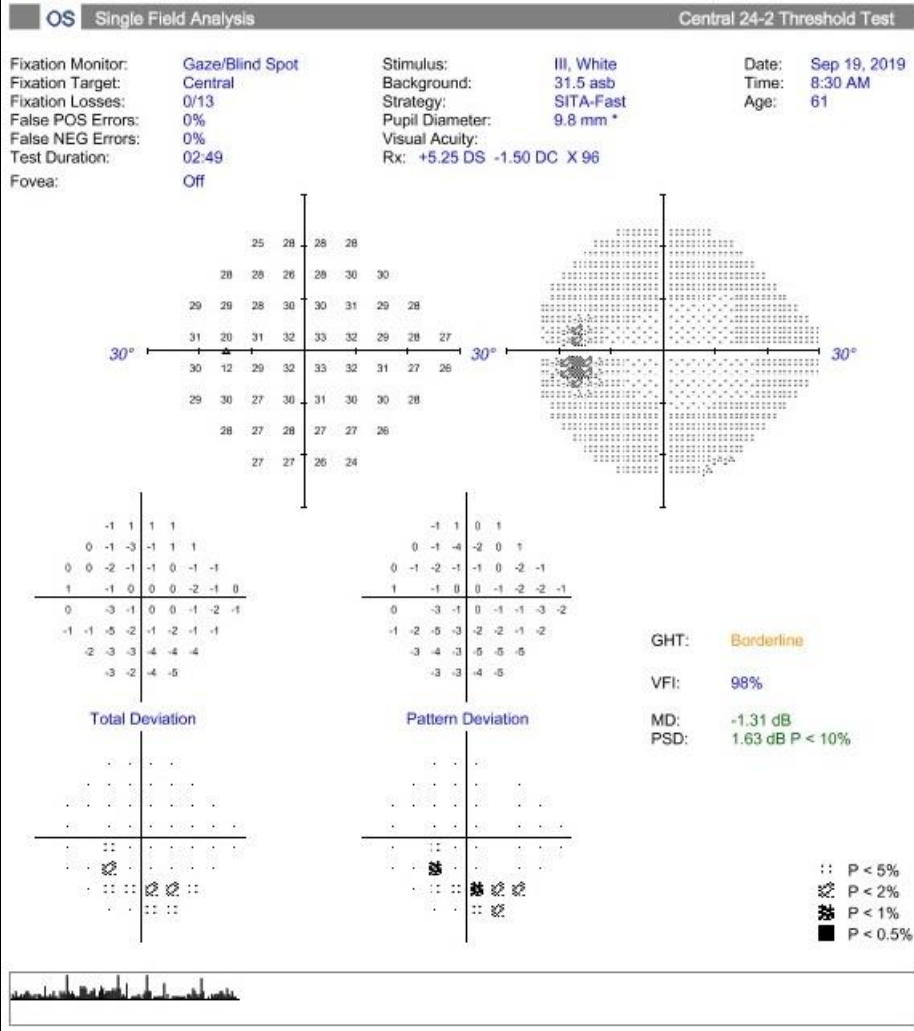


# THIS IS REALITY...

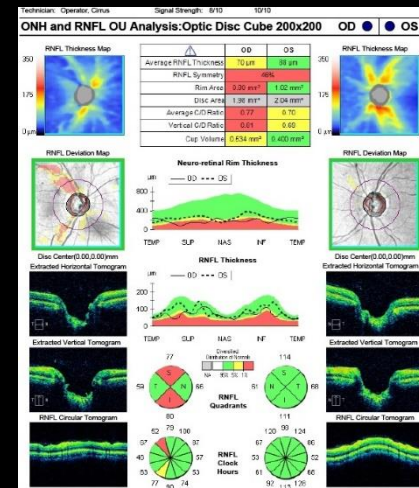
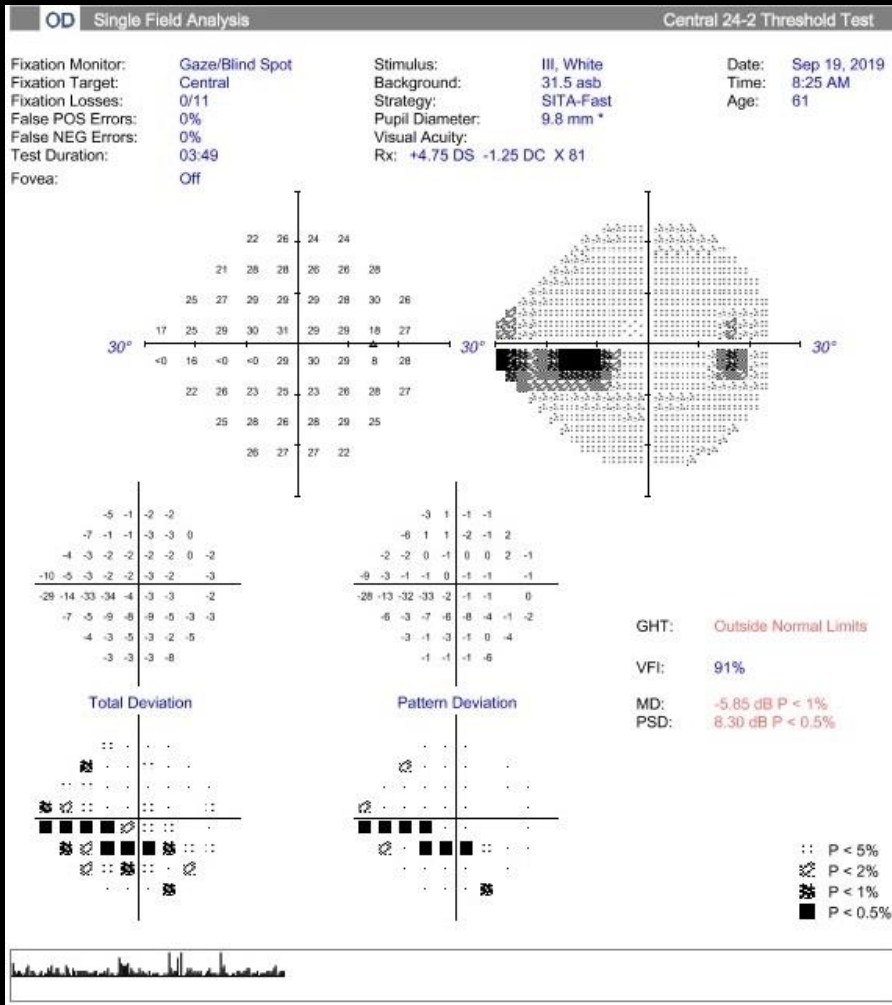
- PATIENT LIVES IN BAHAMAS
  - HE REPORTS IT IS VERY DIFFICULT AND EXPENSIVE TO GET HERE
  - HE GUARANTEES HE WILL NOT BE BACK HERE FOR AT LEAST 3 MONTHS
- SO NOW WHAT?



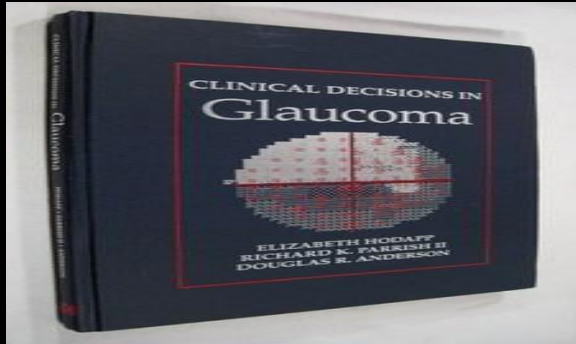
# DILATED VF 24-2 SITA FAST



# VF LOSS CORRESPONDS TO ONH NOTCH AND RNFL LOSS



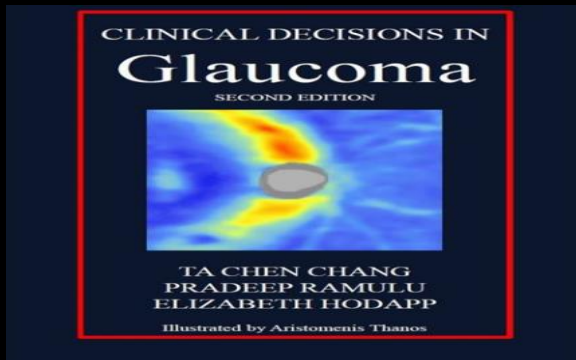
# YOUR PATIENT HAS GLAUCOMA...NOW WHAT?



Drs. Hodapp, Parrish and Anderson  
Clinical Decision in Glaucoma 1993

and again in

Drs. Chang, Ramulu and Hodapp  
Clinical Decisions in Glaucoma 2<sup>nd</sup> Edition, 2016



There are five basic steps to follow in managing a patient with glaucoma:

1. Establish a good baseline.
2. Set a reasonable target for intraocular pressure (IOP).
3. Lower the pressure.
4. Follow up with the patient to see if the target pressure is maintained and if the glaucomatous damage progresses.
5. Modify the target pressure and treatment as indicated by the patient's course.

# LOWER THE IOP

- IOP LOWERING IS THE ONLY PROVEN METHOD TO TREAT GLAUCOMA



Study	Average Baseline IOP	Baseline	Percent of Patients Who Progressed Despite Treatment
EMGT <sup>2</sup>	20.6	25%	45%
CIGTS <sup>3</sup>	27	38%	15% (15% actually showed improvement)
AGIS <sup>4</sup>	23.7-24.8	40%	0% (no progression with mean IOP 12.3 mmHg)

Early Manifest Glaucoma Trial = EMGT; Collaborative Initial Glaucoma Treatment Study = CIGTS; Advanced Glaucoma Intervention Study = AGIS

SUMMARY TABLE FROM

Lifferth A. Optometric Management, Volume: 55, Issue: July 2020, page(s): 46

## Glaucoma Clinical Trials: IOP Lowering and Progression

Study	IOP Reduction	% Progression Tx / no Tx
OHTS <sup>1</sup>	20% target	4.4% / 9.5% (over 5 yrs)
EMGT <sup>2</sup>	25% (average)	45% / 62% (over 6 yrs)
CNTGS <sup>3</sup>	30% target	12% / 35% (over 7 yrs)
CIGTS <sup>4</sup> (med)	~35% (average)	Mean progression near 0
CIGTS <sup>4</sup> (surg)	~48% (average)	Mean progression near 0
AGIS <sup>5</sup>	< 18 at all visits	Mean progression near 0

\*10% reduction in risk with every 1 mm Hg of additional IOP lowering

1. Kass MA, et al. *Arch Ophthalmol*. 2002;120:701.
2. Heijl A, et al. *Arch Ophthalmol*. 2002;120:1269.
3. CNTG Study Group. *Am J Ophthalmol*. 1998;126:498.
4. Lichter PR, et al. *Ophthalmology*. 2001;108:1943.
5. AGIS Investigators. 7. *Am J Ophthalmol*. 2000;130:429.

# HOW TO LOWER THE IOP

- MEDICATION

- MECHANISM

- INCREASE OUTFLOW
- DECREASE PRODUCTION

- OPTIONS

- TOPICAL, ORAL, A/C INSERT

- LASER

- MECHANISM

- INCREASE OUTFLOW

- OPTIONS

- ALT / SLT / MLT

- SURGERY

- MECHANISM

- INCREASE OUTFLOW

- MIGS

- TRABECTOME, ISTENT, CYPASS, XEN
- HYDRUS, KAHOOK DUAL BLADE
- ETC.

- TRABECULECTOMY

- WITH OR WITHOUT MMC

- TUBE / SHUNT / GDD

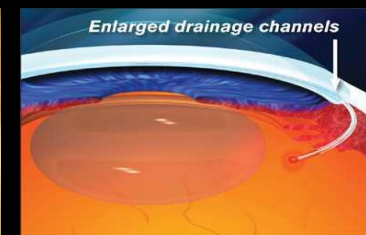
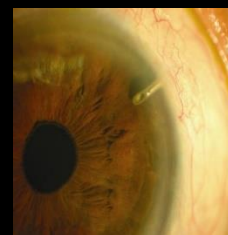
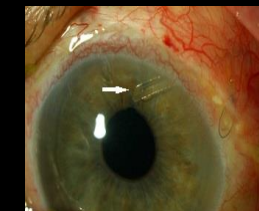
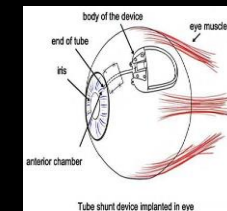
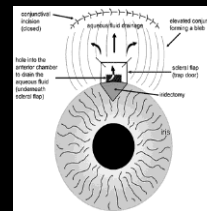
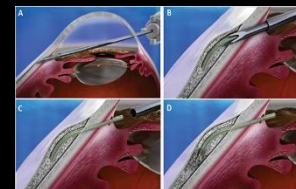
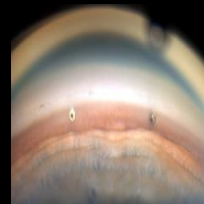
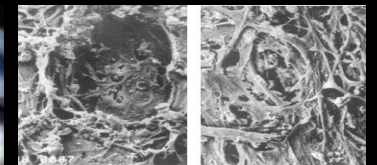
- VALVED, NONVALVED

- OTHER

- EXPRESS SHUNT, CANALOPLASTY
- ETC.

- DECREASE PRODUCTION

- ECP, MICROPULSE, CYCLODESTRUCTION
- ETC.



# WHICH METHOD IS BEST?

- EACH PATIENT IS DIFFERENT
  - NOT EVERYONE CAN / SHOULD OR WANTS TO USE DROPS
- MEDICINE, LASER, SURGERY
  - ALL LOWER IOP
  - ALL REDUCE RISK OF OPTIC NERVE DAMAGE, VF LOSS, BLINDNESS
- SAFETY
  - EACH HAS POTENTIAL SIDE EFFECTS
  - SOME ARE CONTRAINDICATED IN CERTAIN PATIENTS
- THINGS TO CONSIDER
  - PATIENT PREFERENCES
  - DISEASE STATE
  - TARGET IOP
  - MEDICAL COMORBIDITIES

**Annals of Internal Medicine** | REVIEW

## Comparative Effectiveness of Treatments for Open-Angle Glaucoma: A Systematic Review for the U.S. Preventive Services Task Force

Michael V. Boland, MD, PhD; Ann-Margret Ervin, PhD, MPH; David S. Friedman, MD, MPH, PhD; Henry D. Jampel, MD; Barbara S. Hawkins, PhD; Daniela Vollenwelder, MD; Yohalakashmi Chelladurai, MBBS, MPH; Darcy Ward, BA; Catalina Suarez-Cuervo, MD; and Karen A. Robinson, PhD

**Background:** Glaucoma is an acquired degeneration of the optic nerve and a leading cause of blindness worldwide. Medical and surgical treatments that decrease intraocular pressure may prevent visual impairment and blindness.

**Purpose:** To compare the effectiveness of medical, laser, and surgical treatments in adults with open-angle glaucoma with regard to decreasing intraocular pressure and preventing optic nerve damage, vision loss, and visual impairment.

**Data Sources:** MEDLINE, CENTRAL, and an existing database for systematic reviews (through 2 March 2011); MEDLINE, EMBASE, LILACS, and CENTRAL for primary studies (through 30 July 2012).

**Study Selection:** English-language systematic reviews; randomized, controlled trials; and quasi-randomized, controlled trials for most outcomes and observational studies for quality of life and harms.

**Data Extraction:** Two investigators abstracted or checked information about study design, participants, and outcomes and assessed risk of bias and strength of evidence.

**Data Synthesis:** High-level evidence suggests that medical, laser, and surgical treatments decrease intraocular pressure and that medical treatment and trabeculectomy reduce the risk for optic nerve damage and visual field loss compared with no treatment. The direct effect of treatments on visual impairment and the comparative efficacy of different treatments are not clear. Harms of medical treatment are primarily local (ocular redness, irritation); surgical treatment carries a small risk for more serious complications.

**Limitation:** Heterogeneous outcome definitions and measurements among the included studies; exclusion of many treatment studies that did not stratify results by glaucoma type.

**Conclusion:** Medical and surgical treatments for open-angle glaucoma lower intraocular pressure and reduce the risk for optic nerve damage over the short to medium term. Which treatments best prevent visual disability and improve patient-reported outcomes is unclear.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

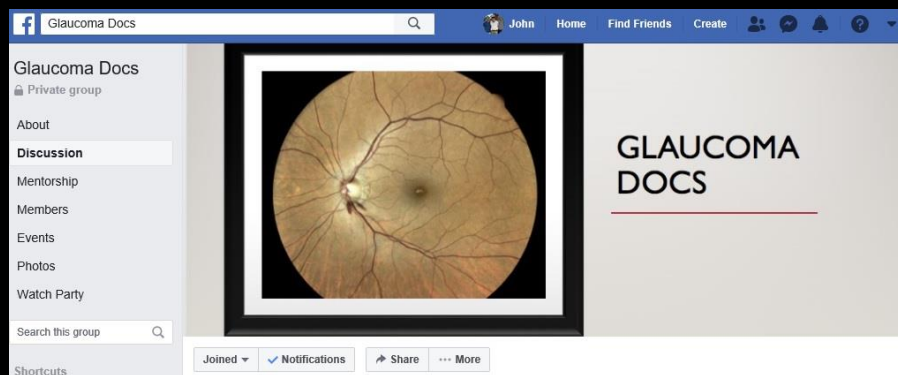
*Ann Intern Med.* 2013;158:271-279.  
For author affiliations, see end of text.


www.annals.org

BOLAND MV, ERVIN AM, FRIEDMAN DS, ET AL. Comparative effectiveness of treatments for open-angle glaucoma: a systematic review for the US Preventive Services Task Force. *Ann Intern Med.* 2013; 158(4):271-279.

# WHAT ARE PEOPLE DOING?

## FEBRUARY 2020 FACEBOOK POLL



 **Rahul Minkeyfromaladdin Gupta** created a poll. February 2

Let us hypothetically ignore ancillary case-specific factors (age, trabecular pigmentation, highest known eye-pressure, typical eye-pressure, patient-dexterity or other traits, local cost, et cetera):

Which is your typical favor for initial treatment of primary open-angle glaucoma?

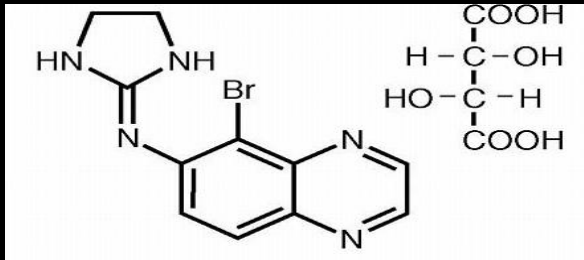
Thank you.

- Eye drop
- About fifty–fifty eye-drop versus laser (here, case-dependent)
- Selective- or argon-laser trabeculoplasty (S.L.T. or A.L.T.)
- Other (please specify in comments)

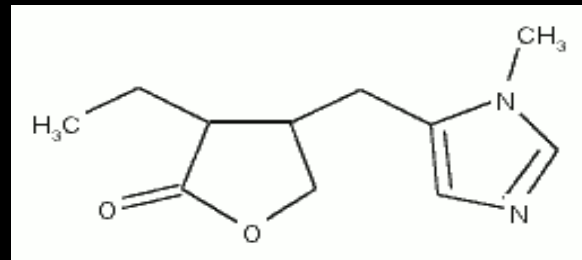
Reaction icons: 31 likes, 4 comments, 1 share.



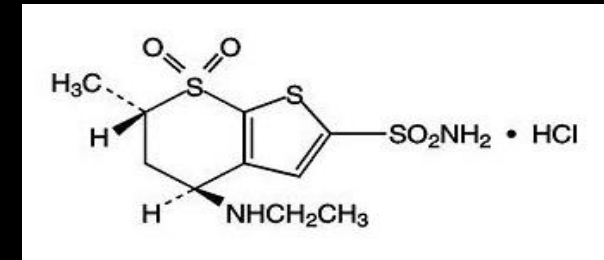
# PHARMACOLOGY REVIEW



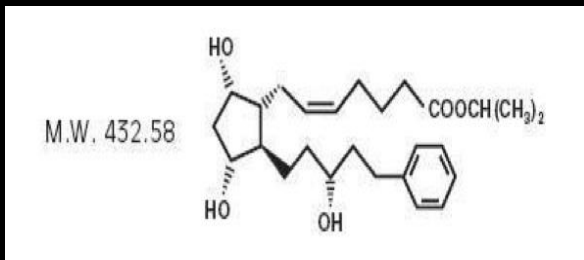
Brimonidine



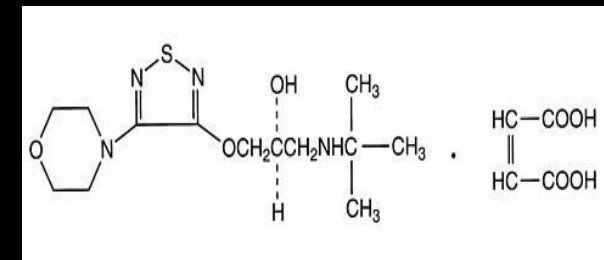
Pilocarpine



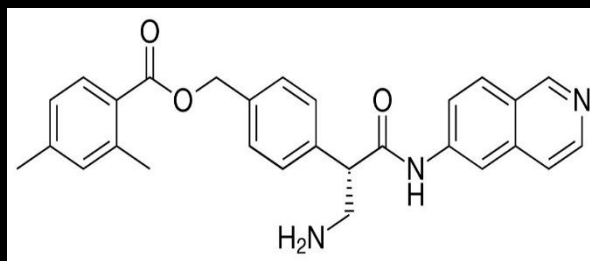
Dorzolamide



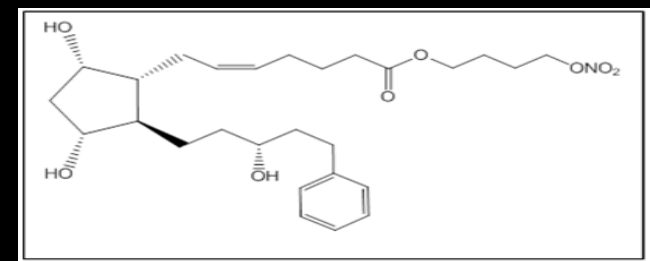
Latanoprost



Timolol



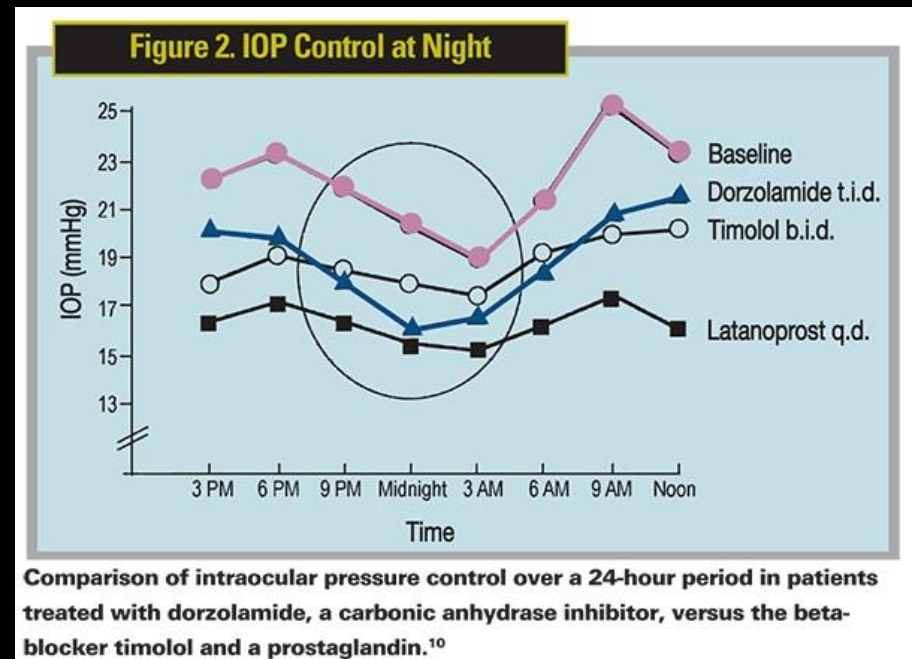
Netarsudil



Latanoprostene Bunod + Nitric Oxide

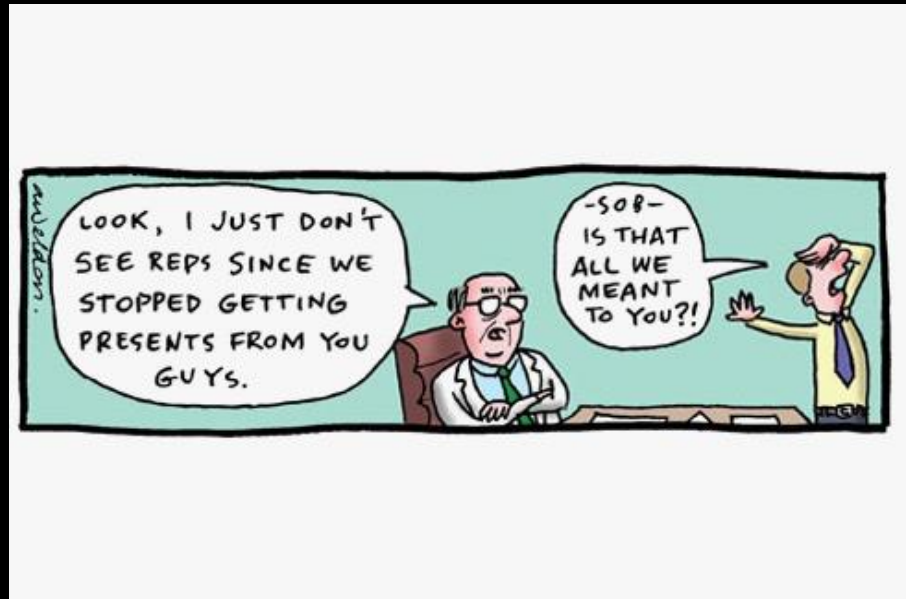
# THINGS TO CONSIDER PRIOR TO CHOOSING THE MEDICATION

- THE PATIENT
  - EVERYONE IS DIFFERENT
- EFFICACY
  - MAGNITUDE OF IOP LOWERING
  - ABILITY TO FLATTEN THE DIURNAL CURVE
- SIDE EFFECTS / TOLERABILITY
- DOSING FREQUENCY / CONVENIENCE
- COST



# WHAT'S NOT MENTIONED?

- THE PHARMACEUTICAL SALES REP



# SHOULD YOUR PATIENT NEED LOWER IOP, WHAT DO YOU DO?

- A. START PROSTAGLANDIN
- B. START CHOLINERGIC
- C. START BETA-BLOCKER
- D. START ALPHA-AGONIST
- E. START CARBONIC  
ANYHDRASE INHIBITOR
- F. START COMBINATION
- G. START RHO-KINASE  
INHIBITOR
- H. SEND FOR ALT / SLT
- I. SEND FOR MIGS
- J. SEND FOR TRAB / TUBE



# IOP LOWERING EFFICACY



Ophthalmology  
Volume 112, Issue 7, July 2005, Pages 1177-1185

Original Article

## Intraocular Pressure–Lowering Effects of All Commonly Used Glaucoma Drugs: A Meta-analysis of Randomized Clinical Trials

## IOP-Lowering Efficacy: Prostaglandin Analogues vs Other Antiglaucoma Treatments

Treatment	Mean Change From Baseline as % Change in IOP	
	Peak	Trough
Bimatoprost	33	28
Travoprost	31	29
Latanoprost	31	28
Timolol	27	26
Brimonidine	25	18
Betaxolol	23	20
Dorzolamide	22	17
Brinzolamide	17	17

IOP = intraocular pressure  
Adapted with permission from van der Valk R et al. *Ophthalmology*. 2005;112:1177–1185.

van der Valk, Rikkert et al. “Intraocular pressure-lowering effects of all commonly used glaucoma drugs: a meta-analysis of randomized clinical trials.” *Ophthalmology* vol. 112,7 (2005): 1177-85.

# WHAT'S THE NAME OF THE NEWEST PROSTAGLANDIN?

- A. VOLTAREN
- B. VIGAMOX
- C. VIAGRA
- D. VYZULTA
- E. VOLDEMORT
- F. VALTREX
- G. VALSARTAN
- H. VICODIN
- I. VERAPAMIL
- J. VADER

What's My  
Name?

# PROSTAGLANDINS

## • OPTIONS

- XALATAN (1996)
  - GENERIC 0.005% (2011)
  - XELPROS (NO BAK, 2018)
- RESCULA (2000)
  - D/C THEN REINSTATED 2013
- LUMIGAN
  - 0.3% (2001) – NOW D/C
  - .01% (2010)
- TRAVATAN (2001)
  - TRAVATAN Z (NO BAK, 2006)
- ZIOPTAN (2012)
- VYZULTA (2017)



+

# PROSTAGLANDINS

- MECHANISM

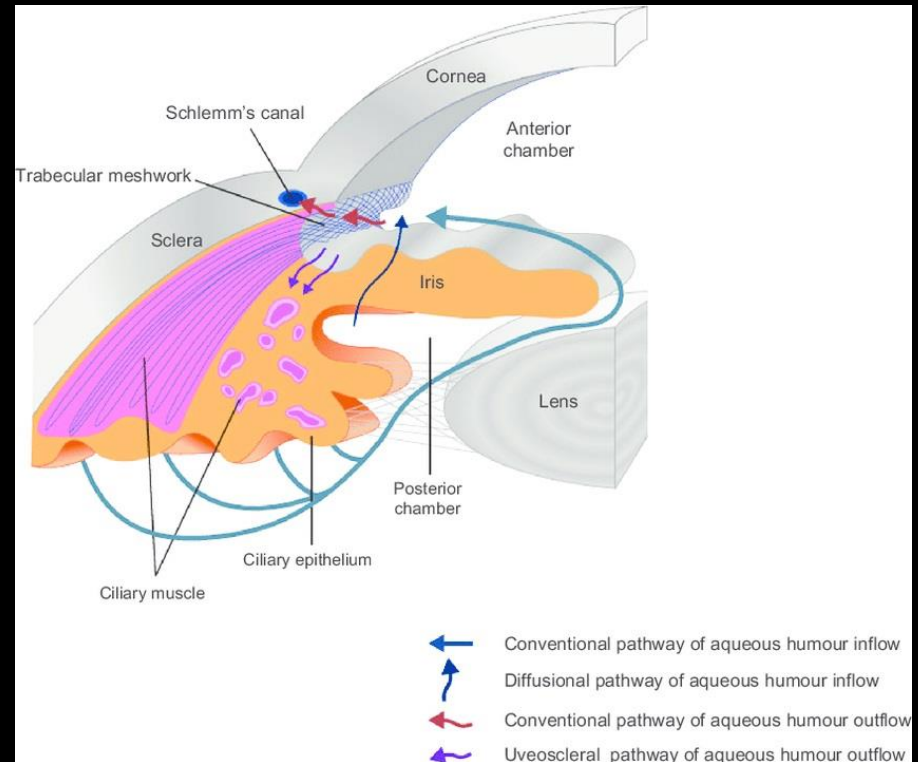
- ALL ENHANCE UVEOSCLERAL OUTFLOW
  - LUMIGAN MAY AID CONVENTIONAL TM OUTFLOW

- EFFICACY

- 25-35% REDUCTION OF IOP
- IOP REDUCTION STARTS 3-4 HRS
- MAXIMUM IOP EFFECT 8-12 HRS
- 24-36 HOUR DURATION OF EFFECT AND MAYBE EVEN LONGER
  - DON'T TELL YOUR PATIENTS!

- DOSING

- ONCE A DAY (PREFER AT NIGHT)





# IS THERE A DIFFERENCE?

## IOP

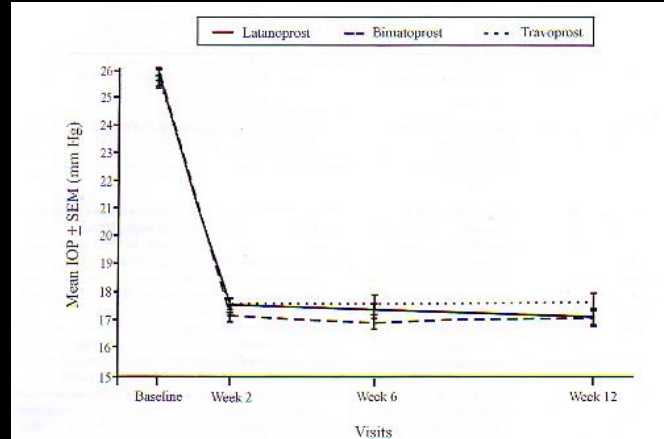


FIGURE 5. Unadjusted 8:00 AM mean intraocular pressure (IOP) levels by treatment and visit (intent-to-treat population).

## HYPEREMIA

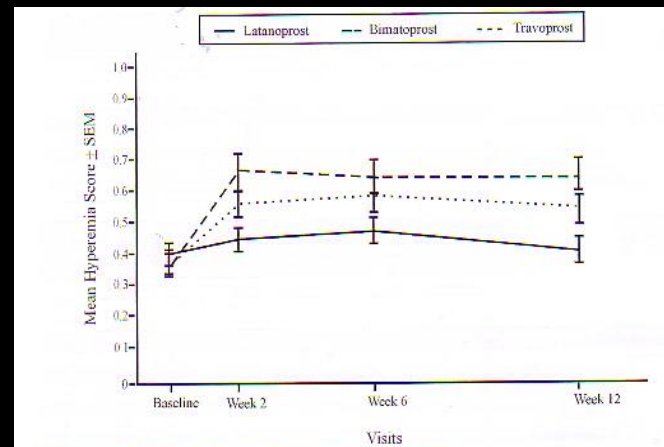


FIGURE 9. Mean hyperemia (investigators' assessments) score by treatment and visit.



# PROSTAGLANDINS (LATANOPROST)

## • OCULAR SIDE EFFECTS

### • >10%

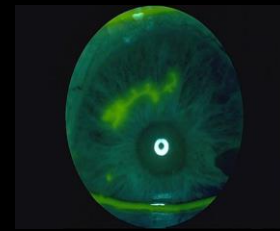
- FOREIGN BODY SENSATION
- EYE PAIN, STINGING, HYPEREMIA
- DISCHARGE
- INCREASED EYELASH LENGTH

### • 1-10%

- PUNCTATE KERATITIS, BLURRED VISION
- INCREASED EYELASH THICKNESS, BURNING
- EYELID PAIN, TEARING, CRUSTING, PHOTOPHOBIA
- IRIS HYPERPIGMENTATION (MELANIN)

### • <1%

- PERIORBITAL / LID CHANGES (SULCUS DEEPENING)
- **HYPERPIGMENTATION OF EYELIDS**
- HSK, MACULAR EDEMA, TRICHIASIS
- UVEITIS



# PROSTAGLANDIN ASSOCIATED PERIORBITOPATHY

- **SIGNS**

- DEEPENING OF SUPERIOR LID SULCUS
- PTOSIS
- ENOPHTHALMOS
- INVOLUTION OF DERMATOCHALASIS

- **MECHANISM**

- NOT COMPLETELY UNDERSTOOD
- THEORY
  - SMOOTH MUSCLE CONTRACTION
  - PERIORBITAL FAT CELL ATROPHY

- **COSMESIS**

- - MAYBE AVOID PROSTAGLANDINS IF UNILATERAL
- + BLEPHAROPLASTY IN A BOTTLE
  - PERIORBITAL FAT ATROPHY PHOTO AFTER 1 MONTH



# PROSTAGLANDINS

## (LATANOPROST)

- **SYSTEMIC SIDE EFFECTS**

- 1-10%
  - INFLUENZA, ARTHRALGIA, BACK PAIN, MYALGIA, SKIN RASH
  - NASOPHARYNGITIS, UPPER RESPIRATORY TRACT INFECTION
- <1%
  - ANGINA, ASTHMA, DIZZINESS, DYSPNEA, HEADACHE, PALPITATIONS

- **CONTRAINDICATIONS / WARNINGS / PRECAUTIONS**

- IRIS PIGMENTATION CHANGES MAY BE PERMANENT
- PERIOcular SKIN / LASH CHANGES MAY REVERSE AFTER STOPPING
- AVOID IN THOSE WITH
  - PRIOR / ACTIVE INFLAMMATION AND / OR HSK
- USE WITH CAUTION
  - APHAKES, TORN POSTERIOR LENS CAPSULE, THOSE AT RISK OF MAC EDEMA

- **OTHER**

- TOPICAL NSAIDS MAY DIMINISH THE IOP LOWERING OF PROSTAGLANDIN

# WHEN TO USE PROSTAGLANDINS

- Y - 1<sup>ST</sup> LINE PRIMARY OPEN ANGLE GLAUCOMA
- Y - 1<sup>ST</sup> LINE OC HTN / GLAUCOMA SUSPECT
- Y - 1<sup>ST</sup> LINE PSEUDOPHAKIA WITH GLAUCOMA
- Y - PIGMENTARY GLAUCOMA
- Y - PSEUDOEXFOLIATIVE GLAUCOMA
- Y - TRAUMATIC / ANGLE RECESSSION GLAUCOMA
- Y - NORMAL TENSION GLAUCOMA
- Y - CHRONIC NARROW ANGLE GLAUCOMA
  
- N - ACUTE ANGLE CLOSURE GLAUCOMA
- N - UVEITIC GLAUCOMA
- N - NEOVASCULAR GLAUCOMA

TIME FOR  
SOMETHING  
NEW!

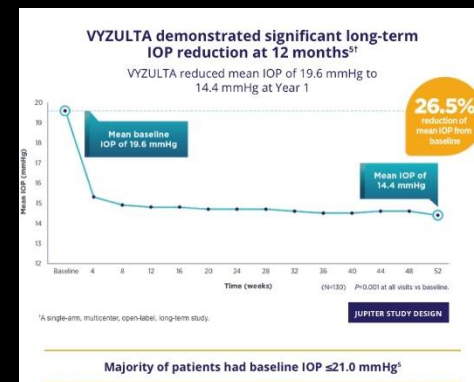
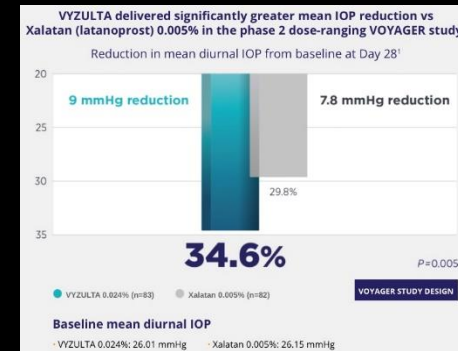
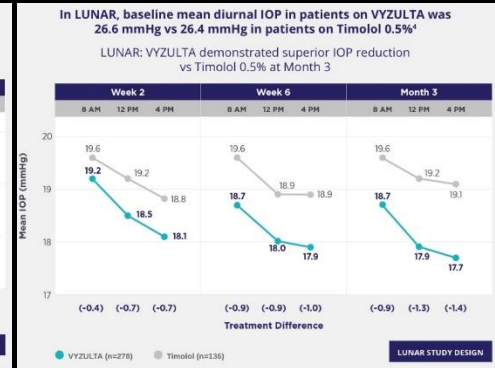
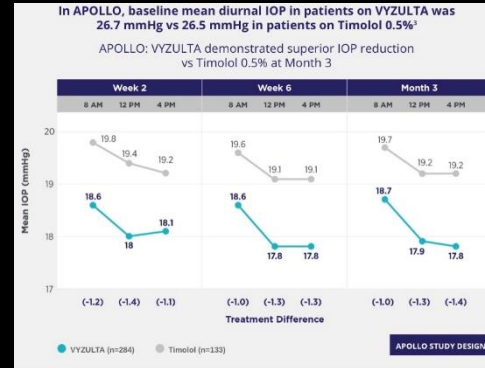
# VYZULTA

- LATANOPROSTENE BUNOD 0.24%
  - BAUSCH AND LOMB
  - FDA APPROVED 2017
- MECHANISM
  - METABOLIZED INTO LATANOPROST AND NITRIC OXIDE
  - LOWERS IOP
    - LATANOPROST
      - UVEOSCLERAL (NONCONVENTIONAL)
    - NITRIC OXIDE
      - RELAXATION OF TM AND SCHLEMM'S CANAL (CONVENTIONAL)
  - VASCULAR EFFECT
    - NITRIC OXIDE MAY ALSO INCREASE OPTIC NERVE BLOOD FLOW
- DOSING
  - QHS
  - ONSET 1-3 HOURS
  - PEAK EFFECT 11-13 HOURS



# VYZULTA EFFICACY

- STUDIES ON EFFICACY
  - APOLLO AND LUNAR
    - COMPARED TO TIMOLOL
  - VOYAGER
    - COMPARED TO XALATAN
  - MERCURY
    - NTG PATIENTS





# VYZULTA

- OCULAR SIDE EFFECTS
  - SAME AS OTHER PROSTAGLANDINS
  - 1-10%
    - LOCAL APPLICATION SITE PAIN
    - CONJUNCTIVAL HYPEREMIA, EYE IRRITATION, EYE PAIN
- SYSTEMIC SIDE EFFECTS
  - SAME AS OTHER PROSTAGLANDINS
- CONTRAINDICATIONS / WARNINGS / PRECAUTIONS
  - SAME AS OTHER PROSTAGLANDINS

**In APOLLO and LUNAR: 6 out of 811 patients treated with VYZULTA discontinued treatment due to ocular adverse events<sup>3,4,6</sup>**

Less than 1% discontinued due to ocular adverse reactions<sup>5</sup>

• 0.6% of patients discontinued therapy due to ocular adverse events, including hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis, and foreign body sensation

Most common adverse reactions<sup>3,7†</sup>

Adverse Reactions	VYZULTA (n=811)	Timolol 0.5% (n=271)
Conjunctival Hyperemia	5.9%	1.1%
Eye Irritation	4.6%	2.6%
Eye Pain	3.6%	2.2%
Ocular Hyperemia	2.0%	0.7%
Instillation Site Pain	2.0%	1.8%

†Pooled results from the APOLLO and LUNAR studies: ocular adverse reactions occurring in ≥2% of study eyes.<sup>3,7</sup>



# QUESTION

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HOW DO YOU DETERMINE HOW LOW THE IOP SHOULD BE?

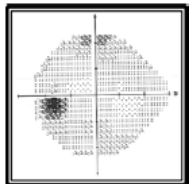
# TARGET IOP

- STUDIES HAVE SHOWN
  - NOT ENOUGH CLINICAL NOTES INCLUDE AN IOP TARGET
- SET TARGET BASED ON VISUAL FIELD
  - OC HTN / G SUSPECT 20-30%
  - MILD 30%
    - ONH AND / OR OCT ABNORMAL, VF CLEAN
  - MODERATE 40%
  - SEVERE 50%
- ADJUST LOWER IF PROGRESSION

## Mild or Early Stage Glaucoma

ICD-9 365.71; ICD-10 7th digit "1"

- Optic Nerve abnormalities consistent with glaucoma
- but NO visual field abnormalities on any visual field test
- OR abnormalities present only on short-wave-length automated perimetry or frequency doubling perimetry

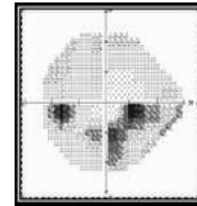


30%

## Moderate Stage Glaucoma

ICD-9 365.72; ICD-10 7th digit "2"

- Optic nerve abnormalities consistent with glaucoma
- AND glaucomatous visual field abnormalities in ONE hemifield and
- NOT within 5 degrees of fixation (note: 5 degrees = involvement of spots nearest fixation)

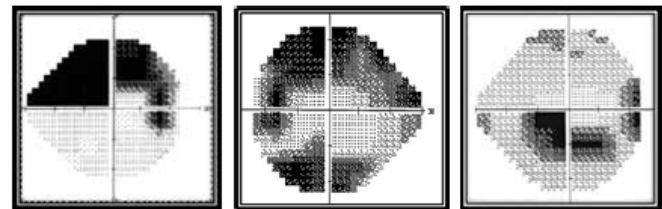


40%

## Advanced, Late, Severe Stage

ICD-9 365.73; ICD-10 7th digit "3"

- Optic nerve abnormalities consistent with glaucoma
- AND glaucomatous visual field abnormalities in BOTH hemifields
- AND/OR loss within 5 degrees of fixation in at least one hemifield.



50%

# WHAT'S IT GOING TO TAKE TO REACH YOUR TARGET?

- 20-30% REDUCTION (OC HTN / NTG / MILD)
  - 1-2 TOPICAL MEDICATIONS
  - **POSSIBLY**
    - LASER OR MIGS
- 30-40% REDUCTION (MILD-MODERATE)
  - 2-3 TOPICAL MEDICATIONS
  - **POSSIBLY**
    - LASER, MIGS
- 40-50% REDUCTION (MODERATE-SEVERE)
  - 3-4 TOPICAL MEDICATIONS
  - **POSSIBLY**
    - LASER, ORAL CAI
    - INCISIONAL SURGERY (TRABECULECTOMY OR TUBE)
    - CYCLODESTRUCTIVE PROCEDURE

# WHAT IF NOT AT TARGET?

- DON'T PANIC
  - THAT IS NOT UNCOMMON
- TWO IOP MEDICATIONS NEEDED
  - OHTS (39%) TO ACHIEVE 20% REDUCTION
  - CIGTS (50%) TO ACHIEVE TARGET IOP
- OPTIONS
  - CHANGE WITHIN CLASS
  - CHANGE TO A DIFFERENT CLASS
    - CAI, BB, ALPHA-AGONIST, RHO-KINASE INHIBITOR
  - ADD A MEDICATION
    - SINGLE
    - COMBINATION
  - REFER FOR LASER
  - REFER FOR SURGERY
- STILL HAVE TO CONSIDER
  - THE PATIENT
    - EVERYONE IS DIFFERENT
  - EFFICACY
    - MAGNITUDE OF IOP LOWERING
    - ABILITY TO FLATTEN THE DIURNAL CURVE
  - SIDE EFFECTS / TOLERABILITY
  - DOSING FREQUENCY / CONVENIENCE
  - COST

# SHOULD YOUR PATIENT NEED LOWER IOP, WHAT DO YOU DO NEXT?

- A. CHANGE PROSTAGLANDIN
- B. SWITCH TO DIFFERENT CLASS
- C. ADD CHOLINERGIC
- D. ADD BETA-BLOCKER
- E. ADD ALPHA-AGONIST
- F. ADD CARBONIC ANHYDRASE INHIBITOR
- G. ADD COMBINATION
- H. ADD RHO-KINASE INHIBITOR
- I. SEND FOR ALT / SLT
- J. SEND FOR MIGS
- K. SEND FOR TRAB / TUBE



# PEOPLE WANT TO KNOW

SURVEY OF OPHTHALMOLOGY VOLUME 53 • SUPPLEMENT 1 • NOVEMBER 2008



## A Review of Additivity to Prostaglandin Analogs: Fixed and Unfixed Combinations

Rania Tabet, MD,<sup>1</sup> William C. Stewart, MD,<sup>2,3</sup> Robert Feldman, MD,<sup>1</sup> and Anastasios G.P. Konstas, MD, PhD<sup>4</sup>

Volume 53 Supplement 1 November 2008

ASCRS FOR SURGEONS. FOR YOU.

# EYE WORLD

CURRENT ISSUE | PAST ISSUES | EW WEEKLY | EW ON SITE | OPHTHALMOLOGY DU SINE S

EyeWorld - GLAUCOMA - After a prostaglandin, what's next?

**EW Weekly**

1. Use protection for mouth, nose, and eyes when treating potential coronavirus cases
2. Ocuphire enters agreement to license oral, small-molecule drug candidate for DR, DME
3. First single-cell analysis of uveal melanoma announced
4. DEXYOU to be developed, commercialized in mainland China and other countries

[View EW Weekly Archives](#)

**I choose TECNIS' Personalized Vision for outstanding visual acuities.**  
— Eric D. Donnenfeld, MD #EyeChooseTECNIS

**FEBRUARY 2014**

**GLAUCOMA** After a prostaglandin, what's next?  
**by Tony Realini, MD, MPH**

*What is the best adjunct when prostaglandin monotherapy isn't enough?*

Weight loss provides independent risk for dry conditions described in the Directions for Use that could increase complications or impact patient outcomes. Intraocular O<sub>2</sub> reserves may be insufficient in patients where central visual field reduction may not be tolerated, such as macular degeneration, retinal pigment epithelium changes, and other conditions. The lens should not be moved in the

2014

REVIEW



## Medical therapy for glaucoma: what to add after a prostaglandin analogs?

Angelo P. Tanna and Albert B. Lin

Volume 26 Number 2 March 2015

# REVIEW of Ophthalmology

HOME | CME | TOPICS | EVENTS | NEWSLETTER | JOBS

**Sanjay Asrani, MD, Durham, N.C.**

PUBLISHED 5 APRIL 2016

## When a Prostaglandin Drop Isn't Enough

Many patients need more than a prostaglandin in order to reach your target IOP. Here are the pros and cons of each option.

2016

# TRADITIONAL OPTIONS





# AT A MINIMUM, WHAT DO YOU CHECK PRIOR TO STARTING A BETA-BLOCKER?

- A. INSURANCE
- B. SPONTANEOUS VENOUS PULSE
- C. RESTING PULSE
- D. ANY BREATHING PROBLEMS
- E. C and D
- F. ALL OF THE ABOVE
- G. NONE OF THE ABOVE



# AT A MINIMUM, WHAT DO YOU CHECK PRIOR TO STARTING A CAI?

- A. PEANUT ALLERGY
- B. SULFA ALLERGY
- C. LATEX ALLERGY
- D. POULTRY ALLERGY
- E. ALL OF THE ABOVE
- F. NONE OF THE ABOVE



# WHAT IS THE MOST COMMON PATIENT COMPLAINT WITH BRIMONIDINE?

- A. EYES GET RED
- B. EYES ITCH
- C. IRIS COLOR CHANGE
- D. LASH LENGTHENING
- E. DARK CIRCLES AROUND EYES
- F. A + B
- G. ALL OF THE ABOVE
- H. NONE OF THE ABOVE



# TRADITIONAL OPTION “HIGHLIGHTS”



- MECHANISM
  - REDUCES AQUEOUS PRODUCTION
- EFFICACY
  - 19-29% IOP REDUCTION
- DOSING
  - QD OR Q12H
- OCULAR SIDE EFFECTS
  - >10% BURNING, STINGING
- SYSTEMIC SIDE EFFECTS
  - **BRADYCARDIA, SHORTNESS OF BREATH**, DROWSINESS, DECREASED LIBIDO
- CONTRAINDICATIONS
  - ASTHMA, COPD, BRADYCARDIA, CHF, HIGH CHOLESTEROL



- MECHANISM
  - REDUCES AQUEOUS PRODUCTION
- EFFICACY
  - UP TO 24% IOP REDUCTION AFTER 2 HOURS
- DOSING
  - Q12H OR Q8H
- OCULAR SIDE EFFECTS
  - >10% **BURNING**, SPK DISCOMFORT, STINGING
- SYSTEMIC SIDE EFFECTS
  - SKIN RASH, BITTER TASTE, FATIGUE
- CONTRAINDICATIONS
  - **SULFA ALLERGIES**



- MECHANISM
  - REDUCES AQUEOUS PRODUCTION
  - MAY INCREASE UVEOSCLERAL OUTFLOW
  - REDUCES EVP
- EFFICACY
  - 20-25% IOP REDUCTION AFTER 2 HOURS
- DOSING
  - Q12H OR Q8H
- OCULAR SIDE EFFECTS
  - >10% **ALLERGIC CONJUNCTIVITIS**, HYPEREMIA
- SYSTEMIC SIDE EFFECTS
  - >10% DROWSINESS
- CONTRAINDICATIONS
  - MAO INHIBITORS

# PROSTAGLANDIN + ?

SURVEY OF OPHTHALMOLOGY VOLUME 53 • SUPPLEMENT 1 • NOVEMBER 2008



## A Review of Additivity to Prostaglandin Analogs: Fixed and Unfixed Combinations

Rania Tabet, MD,<sup>1</sup> William C. Stewart, MD,<sup>2,3</sup> Robert Feldman, MD,<sup>1</sup> and Anastasios G.P. Konstas, MD, PhD<sup>4</sup>

TABLE 1

*PG Adjunctive Therapies Comparative Studies: Alpha-adrenergic Agonists versus Other Agents*

Reference	Comparing Agent	Comparing Agent B	Result
O'Connor [2002]	brimonidine +latanoprost	dorzolamide + latanoprost	A < B
Erdogan et al [2003]	brimonidine tartrate + latanoprost	latanoprost + placebo	A > B
Stewart et al [2004]	brimonidine tartrate + latanoprost	latanoprost/timolol (morning dose)-FC	equal efficacy
Konstas et al [2005]	brimonidine purite + latanoprost	dorzolamide + latanoprost	equal efficacy
Reis et al [2006]	brimonidine tartrate + travoprost	brinzolamide + travoprost	A < B
Reis et al [2006]	brimonidine tartrate + travoprost	timolol + travoprost	A < B
Feldman et al [2007]	brimonidine purite + travoprost	timolol + travoprost	A < B

PG = prostaglandins; FC = fixed combination. Eye-drops concentrations: latanoprost 0.005%, timolol 0.5%, dorzolamide 2%, brinzolamide 0.1%, brimonidine 0.2%, travoprost 0.004%, bimatoprost 0.03%.

TABLE 2

*PG Adjunctive Therapies Comparative Studies: Topical Carbonic Anhydrase Inhibitors versus Other Agents*

Reference	Comparing Agent A	Comparing Agent B	Result
O'Connor et al [2002]	dorzolamide + latanoprost	timolol + latanoprost	A > B (small retrospective clinical trial)
Tamer et al [2007]	dorzolamide + latanoprost	timolol + latanoprost	A > B
Konstas et al [2005]	dorzolamide + latanoprost	brimonidine purite + latanoprost	equal efficacy
Maruyama et al [2006]	dorzolamide + latanoprost	carteolol + latanoprost	equal efficacy
Reis et al [2006]	brinzolamide + travoprost	brimonidine tartrate + travoprost	A > B
Hollo et al [2006]	brinzolamide + travoprost	timolol + travoprost	equal efficacy
Tsukamoto et al [2005]	dorzolamide + (latanoprost + timolol)-FC	brinzolamide + (latanoprost + timolol)-FC	equal efficacy

PG = prostaglandins; FC = fixed combination; BB = beta-blocker. Eye-drops concentrations: latanoprost 0.005%, timolol 0.5%, dorzolamide 2%, brinzolamide 0.1%, brimonidine 0.2%, travoprost 0.004%, bimatoprost 0.03%.

# PGA + TRADITIONAL OPTIONS

## IOP AND SIDE EFFECT COMPARISON



### SYSTEMATIC REVIEWS / META-ANALYSIS OF

### PROSTAGLANDIN + **BB** or **CAI** or **AA**

- **IOP**

- SIMILAR IOP REDUCTION
- ~ 15% or 2.3-3 mmHg

- **SIDE EFFECTS**

- EYE PAIN / BURNING
  - **AA > BB, CAI > BB**
- FATIGUE / WEAKNESS
  - **AA > CAI, BB > CAI**
- TASTE DISTURBANCE
  - **CAI > AA, CAI > BB**
- DRY MOUTH
  - **AA > CAI, AA > BB**

# SO...WHAT TO DO 2<sup>ND</sup>?

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# I SUGGEST...

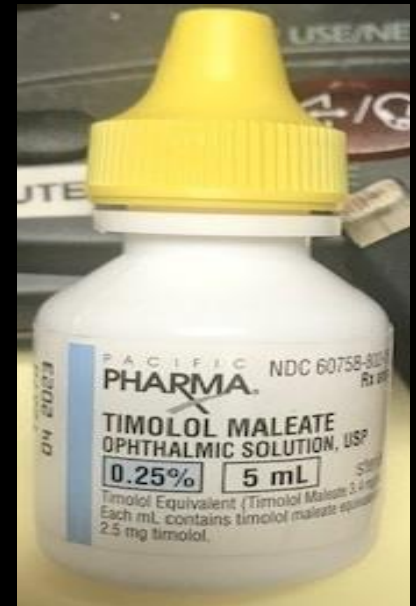
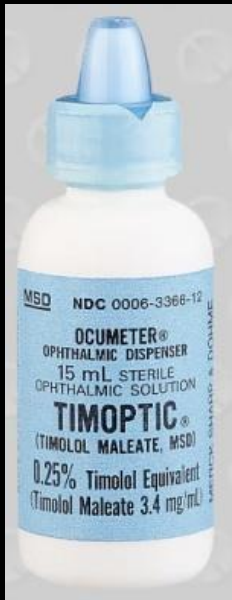
## PROSTAGLANDIN + BETA-BLOCKER

- IF NO CONTRAINDICATIONS
  - NO COPD
  - NO BRADYCARDIA (WANT PULSE > 60 BPM)
  - DEBATABLE BENEFIT IF ALREADY ON A SYSTEMIC BB
- WHY?
  - CONVENIENT DOSING
    - PROSTAGLANDIN AT NIGHT
    - TIMOLOL 0.25 or 0.5 QAM OU
  - CAUTION IF NORMAL TENSION GLAUCOMA
    - THERE IS A VASCULAR COMPONENT TO GLAUCOMA
      - BETA-BLOCKERS MAY REDUCE OPTIC NERVE PERFUSION



# QUESTIONS

SHOULD YOU USE IT ONCE A DAY OR TWICE?  
IS THERE A DIFFERENCE BETWEEN SOLUTION  
AND THE GEL OF XE?



# QD vs Q12H / Soln vs Gel

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- **SOME THINK IT DEPENDS ON THE IRIS COLOR**
  - NO REAL PROOF OF THAT
- **SOLUTION VS GEL**
  - SIMILAR EFFECT
  - GEL IS MUCH MORE EXPENSIVE
- **BETA-BLOCKERS**
  - NOT AS EFFECTIVE AT NIGHT, REDUCE ONH PERFUSION
  - PROBABLY BEST TO
    - USE QAM UNLESS IN COMBINATION
    - AVOID IN NORMAL TENSION GLAUCOMA PATIENTS

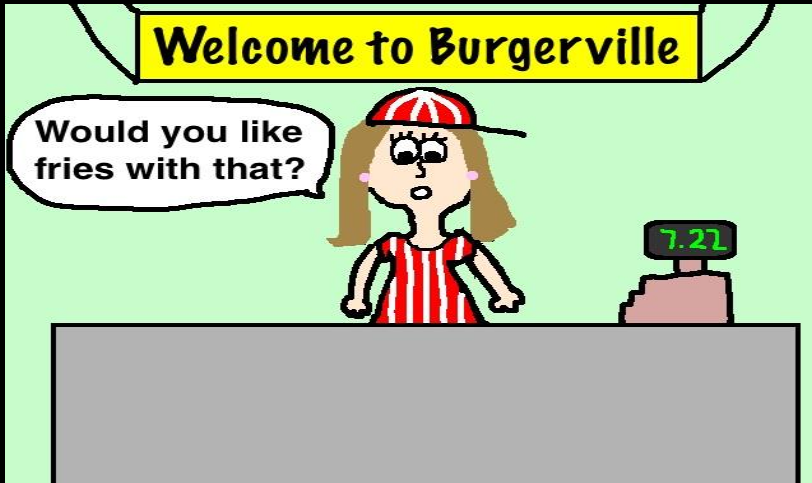
# QUESTION

**YOUR PATIENT IS STILL NOT AT TARGET.**

**YOU HAVE THE PATIENT ON 2 MEDS  
(2 BOTTLES) WHAT DO YOU DO NEXT?**

- A. ADD ANOTHER MEDICATION (3<sup>RD</sup> BOTTLE)
- B. CHANGE ONE MED TO A COMBINATION (2 BOTTLES)
- C. SEND FOR ALT / SLT
- D. SEND FOR MIGS
- E. SEND FOR TRAB / TUBE

# CONSIDER COMBOS



**Ranker** vote on >> entertainment // music // nerdy //

list ordered by all voters rerankers: 31 men women age region

- 1 Tom & Jerry
- 2 Batman & Robin
- 3 Bert & Ernie
- ADVERTISEMENT
- 4 ColinBoddy added Scooby Doo & Shaggy
- 5 pigeonthewing added Han Solo & Chewbacca

**Ranker** vote on >> entertainment // music // nerdy //

- 6 Paperboy added Mario and Luigi
- 7 Peanut Butter & Jelly
- 8 Hamburgers & Fries
- 9 Le Sheppard added Lennon and McCartney
- 10 pigeonthewing added Spongebob & Patrick

# DEPENDENDING ON WHAT YOU ADDED 2<sup>ND</sup> ...

## TRADITIONAL COMBINATION OPTIONS



- **DORZOLAMIDE / TIMOLOL**
- BOTH REDUCE AQUEOUS PRODUCTION
- GENERIC AVAILABLE
- DOSING
  - q12h

- **BRIMONIDINE / TIMOLOL**
- BOTH REDUCED AQUEOUS BRIM MAY HELP WITH UVEOSCLERAL OUTFLOW
- DOSING
  - q12h

- **BRINZOLAMIDE / BRIMONIDINE**
- BOTH REDUCE AQUEOUS PRODUCTION, BRIM MAY HELP WITH UVEOSCLERAL OUTFLOW
- SUSPENSION
  - **SHAKE WELL**
- DOSING
  - q12h or q8h

# COMBINATION PROS and CONS

- PROS

- 1 BOTTLE, 2 MEDS
- MAY IMPROVE ADHERENCE
- MAY DECREASE OCULAR SURFACE DISEASE

- CONS

- COST

- QUESTION

- COULD YOU SKIP THE INDIVIDUAL INGREDIENTS AND GO RIGHT TO A COMBO AS 2<sup>ND</sup> LINE?

- ANSWER

- MAYBE
- HOWEVER
  - WHICH INGREDIENT IS WORKING?
  - WHICH INGREDIENT CAUSED SIDE EFFECT?

# IF NO OR MINIMAL RESPONSE TO TRADITIONAL COMBINATION...

- MAKE SURE PATIENT IS ADHERENT
  - IF GOOD ADHERENCE, IT IS NOT EFFECTIVE
    - SWAP FOR ANOTHER TRADITIONAL COMBINATION OR
    - SWAP YOUR CHOSEN PROSTAGLANDIN FOR NEWER OPTION
      - VYZULTA
      - OR
      - ROCKLATAN (COMBINATION)
- IF FOLLOWING ALONG...
  - PT IS STILL ONLY USING 2 BOTTLES

**NEW  
CLASS  
ALERT!**



# RHO-KINASE INHIBITORS

- OPTION
  - RHOPRESSA (AERIE)
- MECHANISM
  - EXACT MECHANISM UNKNOWN
- DOSING
  - QHS

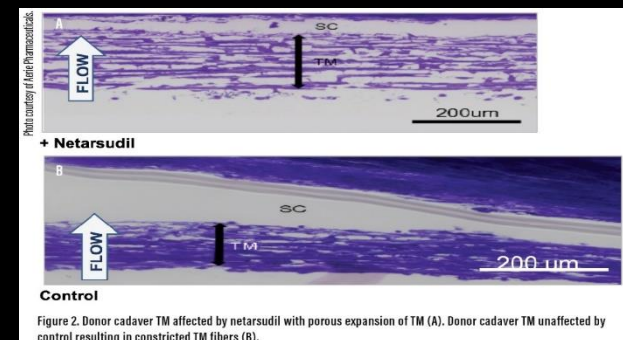
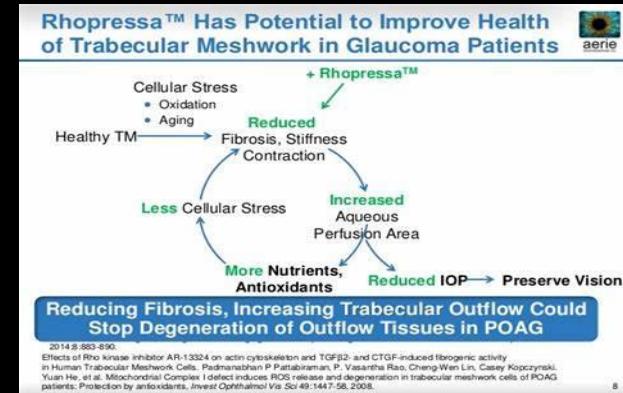
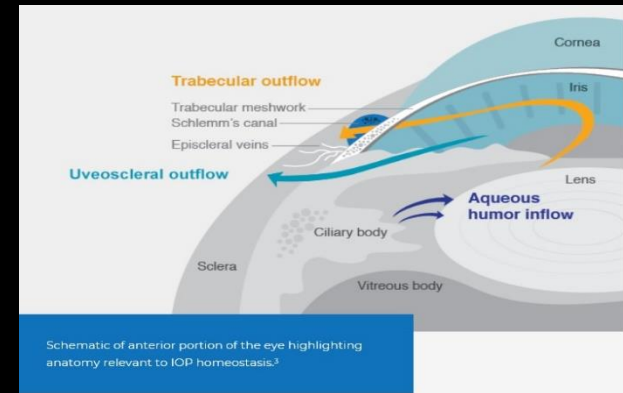


# RHO-KINASE INHIBITORS

- MECHANISM

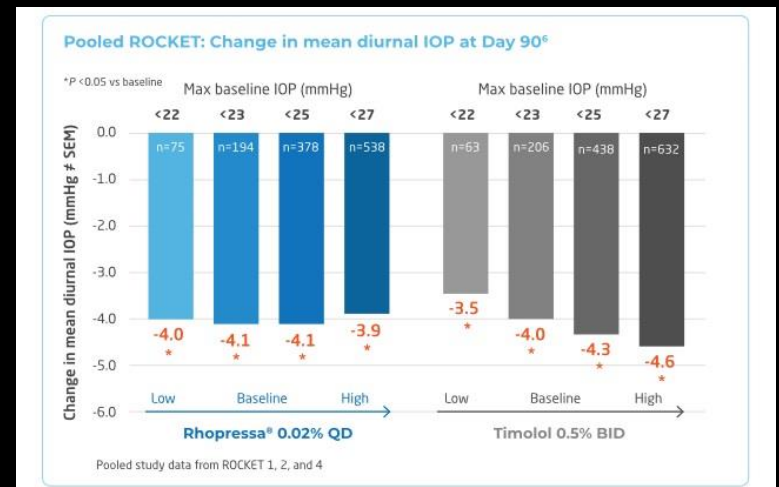
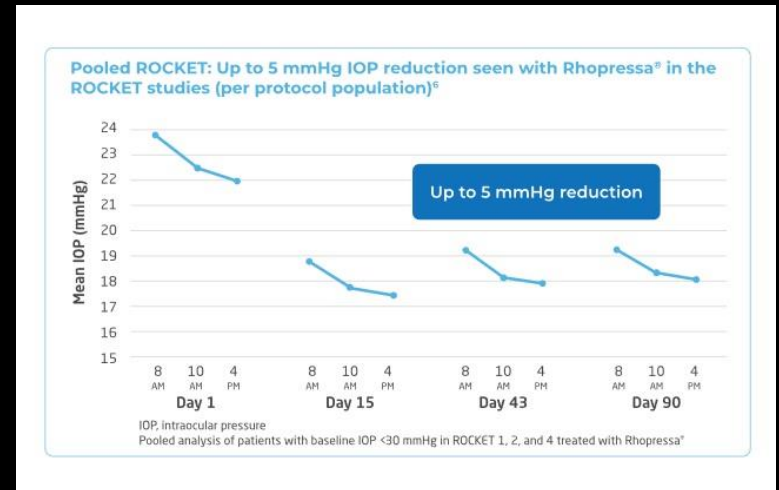
- THEORIES

- MODULATES CONVENTIONAL AQUEOUS OUTFLOW ROUTE THROUGH THE TRABECULAR MESHWORK
  - INHIBITS ROCK SIGNALLING PATHWAY THAT PROMOTES CELL CONTRACTILITY AND ADHESION OF FIBROBLAST CELLS
  - INDUCES RELAXATION AND REDUCED FOCAL ADHESIONS
- MAY REDUCE AQUEOUS PRODUCTION
- MAY DECREASE EPISCLERAL VENOUS PRESSURE



# RHOPRESSA

- EFFICACY
  - 15-22% REDUCTION OF IOP
  - MULTIPLE STUDIES DONE
    - 5 mmHg IOP REDUCTION
    - SIMILAR TO **TIMOLOL** WHEN BASELINE IOP < 25 mmHg
    - **NOT AS EFFECTIVE WITH IOP > 27 mmHg** (TIMOLOL WAS BETTER)



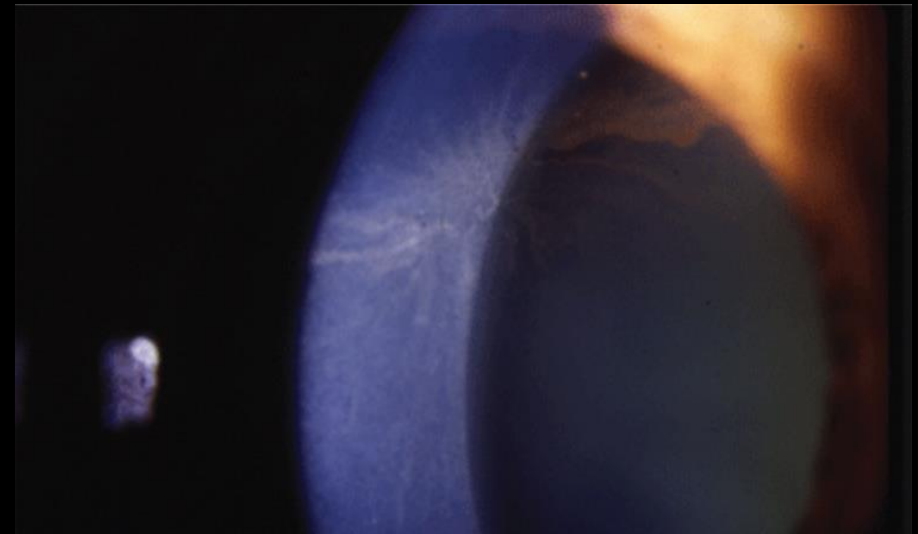
# WHAT OCULAR SIDE EFFECT MAY YOU SEE FROM RHO-KINASE INHIBITORS?

- A. HYPEREMIA
- B. LASH LENGTHENING
- C. CORNEAL VERTICILLATA
- D. CME
- E. PSC
- F. A and C
- G. ALL OF THE ABOVE
- H. NONE OF THE ABOVE



# RHOPRESSA

- OCULAR SIDE EFFECTS
  - >10%
    - CONJUNCTIVAL **HYPEREMIA** (53%)
    - SITE PAIN (20%)
    - CONJ HEMORRHAGE (20%)
    - **CORNEAL DEPOSITS / VERTICILLATA** (20%)
      - SHOWED UP AT 4 WEEKS, NO IMPACT ON VISION, RESOLVED UPON DISCONTINUATION
  - 1-10%
    - ERYTHEMA OF EYELID
    - BLURRED VISION, CORNEAL STAINING, DECREASED VISUAL ACUITY, LACRIMATION
- SYSTEMIC SIDE EFFECTS
  - NONE
- CONTRAINDICATIONS
  - NONE



<https://reviewofcontactlenses.com/article/rock-and-whorl>

# WHICH OF THE FOLLOWING IS A FDA APPROVED PROSTAGLANDIN COMBINATION?

- A. GANFORT
- B. DUOTRAV
- C. XALCOM
- D. EXTRAVAN
- E. ROCKLATAN
- F. ALL OF THE ABOVE
- G. NONE OF THE ABOVE

# RHO KINASE INHIBITOR + PROSTAGLANDIN

- OPTIONS

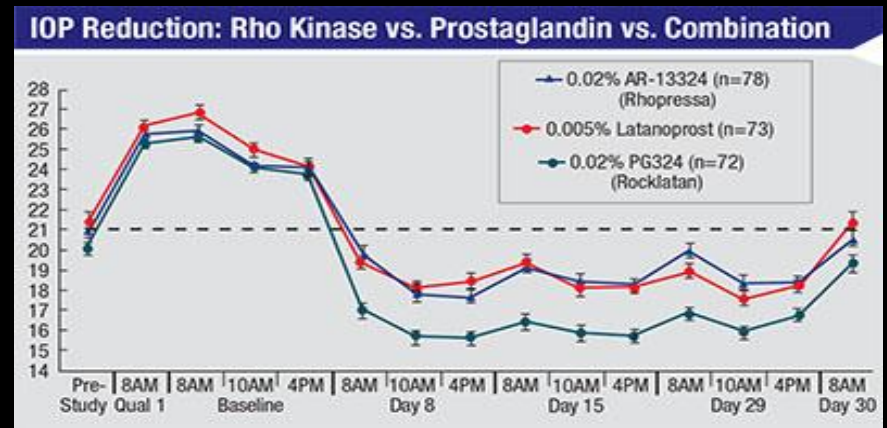
- ROCKLATAN (3/13/19)

- NETARSUDIL 0.02% AND LATANOPROST 0.005%
- AERIE PHARMACEUTICALS



# RHO KINASE INHIBITOR + PROSTAGLANDIN

- MECHANISM
  - SAME AS COMPONENTS
- EFFICACY
  - MERCURY 1 AND 2 TRIALS
    - COMPARED TO LATANOPROST
    - COMPARED TO RHOPRESSA
- DOSING
  - QHS
- OCULAR SIDE EFFECTS
  - SAME AS COMPONENTS
- SYSTEMIC SIDE EFFECTS
  - SAME AS COMPONENTS
- CONTRAINDICATIONS
  - SAME AS COMPONENTS



REVIEW OF OPHTHALMOLOGY ONLINE 06/05/16



In the MERCURY-1 trial, conducted to support the approval of Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%, Rhopressa® further demonstrated mean **IOP reduction up to 6.1 mmHg<sup>6</sup>**

- Phase 3 studies, MERCURY-1 and MERCURY-2 both included a wide range of baseline IOPs (>17 to <36 mmHg) vs ROCKET trials<sup>9,10</sup>



# MY PROBLEM WITH THE “NEW” OPTIONS (CURRENTLY)

- COST IS AN ISSUE (AS OF 1/21/21)
  - VYZULTA \$219.35
  - RHOPRESSA \$286.82
  - ROCKLATAN \$303.02
- FYI
  - AT THE VA WE HAVE TO TRY ALL CLASSES OF MEDS PRIOR TO USING ANY OF THE “NEW” OPTIONS
  - HOWEVER, THEY WILL BE CONSIDERED/APPROVED IF
    - DOCUMENTED SIDE EFFECTS
    - FAILURE TO ACHIEVE TARGET IOP
    - PATIENT STILL PROGRESSING

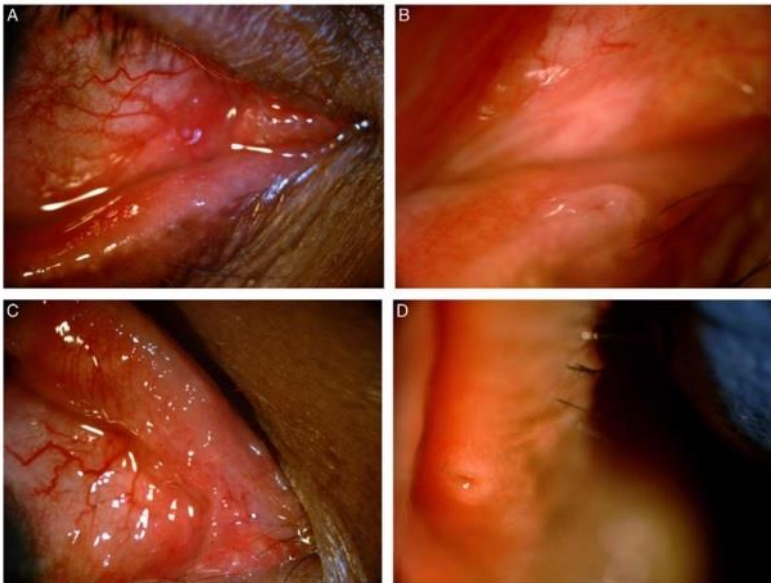
# RHOPRESSA

- POTENTIAL OCULAR SIDE EFFECT
  - PUNCTAL STENOSIS
    - MAY RESULT IN TEARING
    - REVERSAL AFTER DISCONTINUING
- TWO REPORTS IN 2022

## Punctal Stenosis Associated with Topical Netarsudil Use

Thomas M. Meirick, MD, Raghu C. Mudumbai, MD, Matthew M. Zhang, MD, Philip P. Chen, MD

Ophthalmology 2022;129:765-770



**FIGURE 3.** Slit-lamp photos of the right eye from 1 patient showing: (A) complete closure of the right lower punctum 171 days after initiation on topical netarsudil, (B) reopening of the right lower punctum 83 days after stopping topical netarsudil, (C) complete closure of the left lower punctum 171 days after initiation of topical netarsudil and (D) reopening of the left lower punctum 83 days after stopping topical netarsudil. Figure 3 can be viewed in color online at [www.glaucomajournal.com](http://www.glaucomajournal.com).

## Partial Stenosis and Complete Punctal Closure Following Topical Netarsudil Use for Glaucoma

Ramy Rashad, MD, MBA, Catherine Zhu, MD, Anna C. Kupcha, MD,  
Alberto G. Distefano, MD, Haben Kefella, MD, and Manishi A. Desai, MD

J Glaucoma 2022;31:920–925

# MY PROBLEM WITH THE “NEW” OPTIONS (CURRENTLY)

- COST IS AN ISSUE (AS OF 1/21/21)
  - VYZULTA \$219.35
  - RHOPRESSA \$286.82
  - ROCKLATAN \$303.02
- FYI
  - AT THE VA WE HAVE TO TRY ALL CLASSES OF MEDS PRIOR TO USING ANY OF THE “NEW” OPTIONS
  - HOWEVER, THEY WILL BE CONSIDERED/APPROVED IF
    - DOCUMENTED SIDE EFFECTS
    - FAILURE TO ACHIEVE TARGET IOP
    - PATIENT STILL PROGRESSING

# RAMPING UP TOPICAL TREATMENT (at the VA)

- MAXIMUM MEDICAL THERAPY
  - 1<sup>ST</sup> LINE (1 BOTTLE)
    - PROSTAGLANDIN
  - 2<sup>ND</sup> LINE (2 BOTTLES)
    - ADD GENERIC TIMOLOL OR DORZOLAMIDE OR BRIMONIDINE
  - 3<sup>RD</sup> LINE (2 BOTTLES)
    - CHANGE TO COMBINATION
      - GENERIC COSOPT OR SIMBRINZA OR COMBIGAN
  - 4<sup>TH</sup> LINE (2 BOTTLES)
    - CHANGE PROSTAGLANDIN TO
      - VYZULTA OR ROCKLATAN

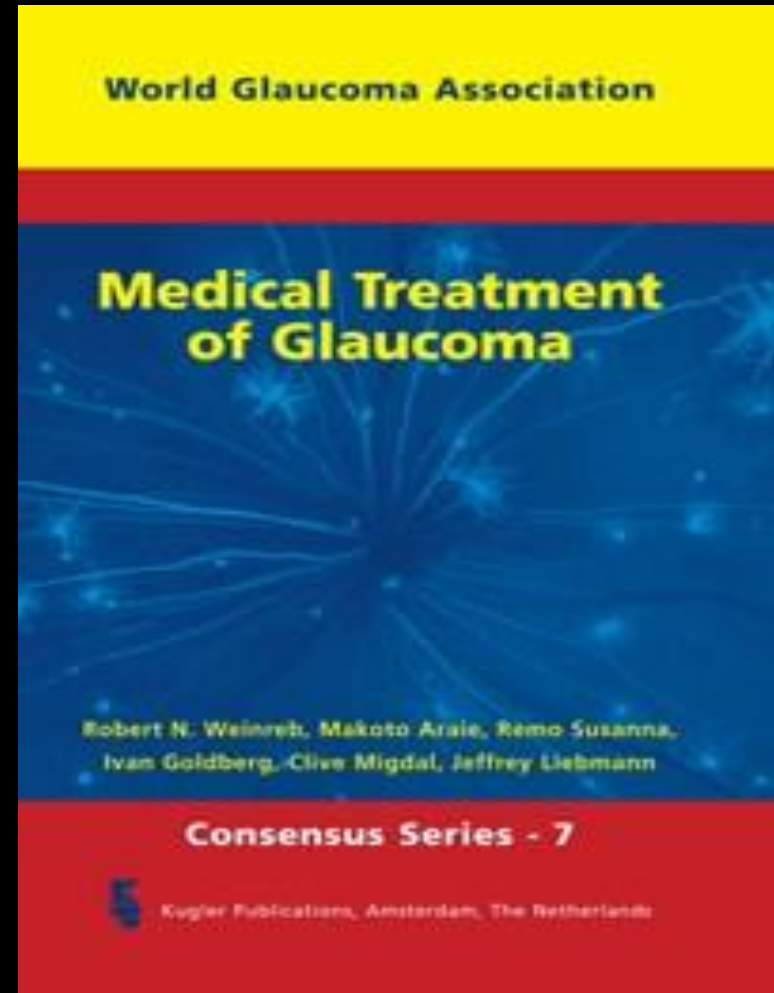


# WHEN SHOULD AN OPTOMETRIST REFER

- MULTIPLE MEDICATIONS HAVE BEEN TRIED AND...
  - IF PATIENT IS ADHERENT
    - TARGET IOP HAS NOT BEEN REACHED
    - PATIENT IS PROGRESSING
  - IF PATIENT IS NONADHERENT
- THE PATIENT WOULD LIKE ANOTHER OPINION
- WHEN THE OPTOMETRIST IS NO LONGER COMFORTABLE

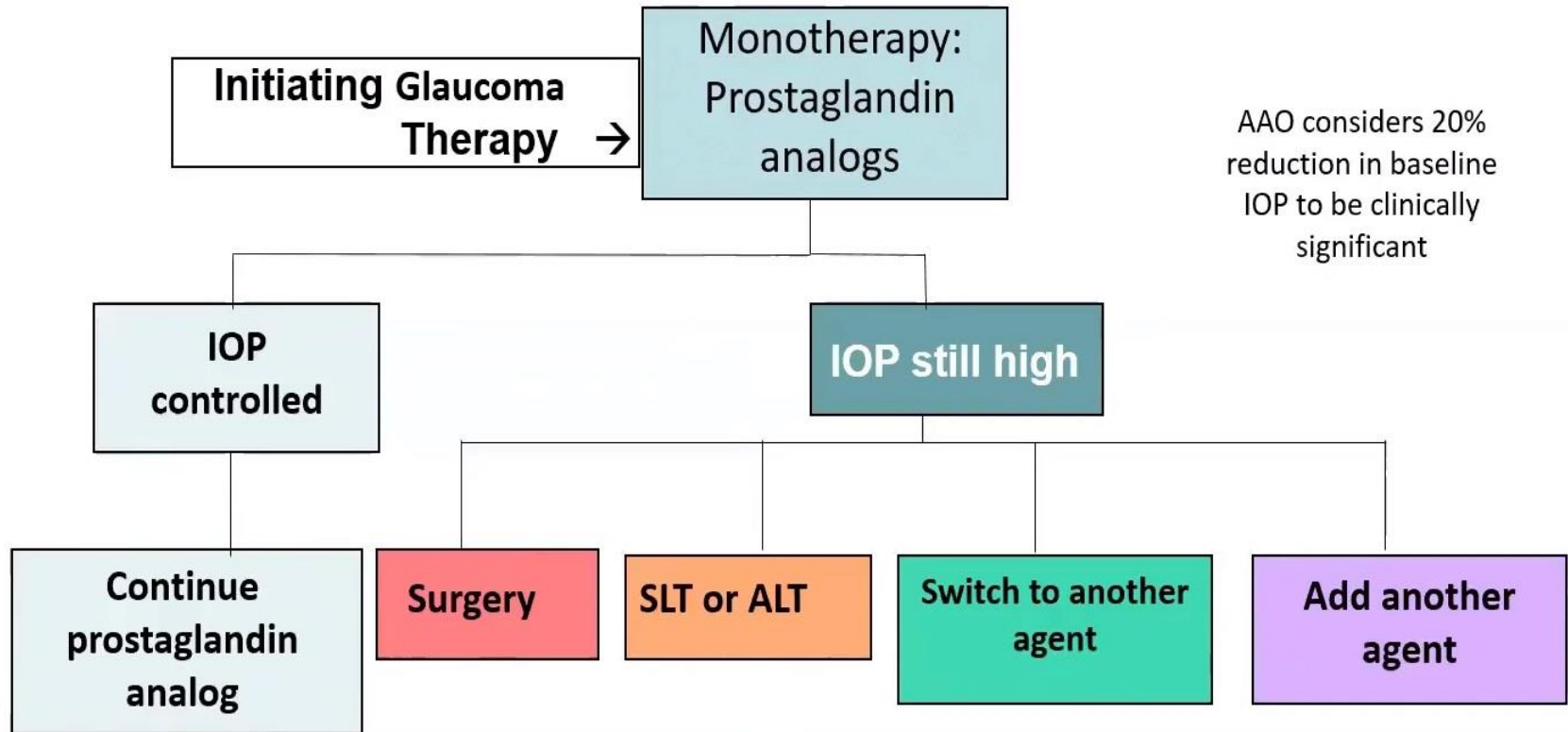
# WGA CONSENSUS STATEMENTS

- INITIAL RESPONSE SHOULD BE AT LEAST 20% BELOW BASELINE
  - SWITCHING WITHIN CLASS IS OPTION
    - 2 DRUGS IN SAME CLASS NOT RECOMMENDED
- 2<sup>ND</sup> DRUG OR **LASER**
  - WHEN NOT AT TARGET
  - 2<sup>ND</sup> DRUG EFFICACY NOT AS GOOD
    - 2 DRUGS IN SAME CLASS NOT RECOMMENDED
- COMBINATIONS
  - AS EFFICACIOUS AS INDEPENDENT AGENTS USED TOGETHER
    - CONVENIENT
    - LESS PRESERVATIVES
    - POSSIBLE BETTER ADHERENCE
- **SURGERY**
  - USED WHEN MEDICINE OR LASER
    - FAILS TO REACH TARGET
    - ALLERGY
    - INTOLERANCE
    - POOR ADHERENCE
    - LACK OF AVAILABILITY
    - PATIENT STILL PROGRESSING



MAY 1, 2010

# TREATMENT ALGORITHM



**EUGENE AND MARILYN GLICK  
EYE INSTITUTE**

INDIANA UNIVERSITY

**LOU CANTOR, MD**  
CYBERSIGHT WEBINAR

<https://cybersight.org/portfolio/lecture-glaucoma-surgery-an-evolving-art-and-science/>

# QUESTION

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WHICH PATIENTS SHOULD I WORRY ABOUT?



# PATIENTS IN TROUBLE

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- PATIENT PRESENTING WITH SEVERE DAMAGE
  - BASED ON OPTIC NERVE, NERVE FIBER LAYER, VISUAL FIELD
- PATIENT WHO IS YOUNG
- PATIENT WHO IS AFRICAN AMERICAN
- PATIENT WHO IS AN IOP SPIKER
- PATIENT WITH A THINNER CORNEA
- PATIENT WITH A FAMILY MEMBER (SIBLING) WHO IS BLIND FROM GLAUCOMA
- PATIENT BLIND IN ONE EYE FROM GLAUCOMA
- PATIENT WHO IS NON-COMPLIANT
- PATIENT WHO SHOWS PROGRESSION DESPITE TREATMENT

# OTHER THINGS TO CONSIDER



# MEDICATION SIDE EFFECTS

## • CIGTS

- MEDICINE VS SURGERY
- 607 PATIENTS, 29-75 YRS, 55% MALE, 38% BLACK
- **QOL TEST(S):** VAQ, SIP
  - > 25% REPORTED
    - IRRITATION
    - BURNING
    - PAIN
    - REDNESS

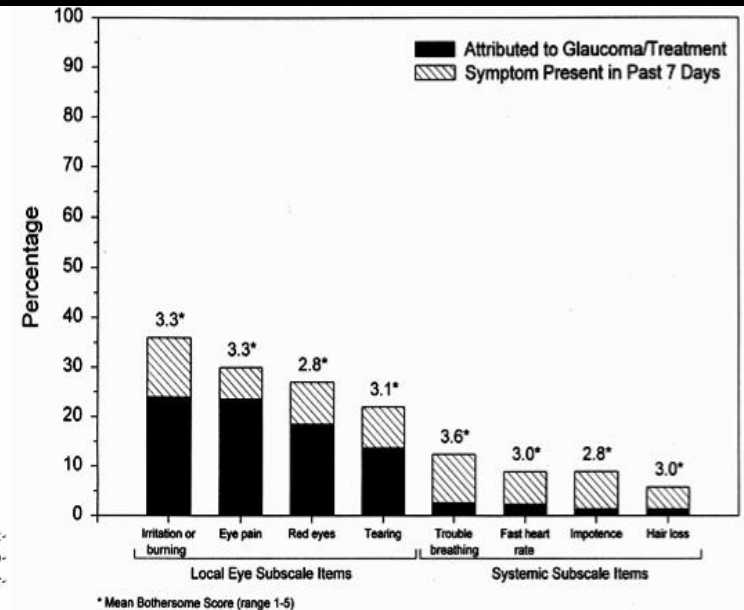
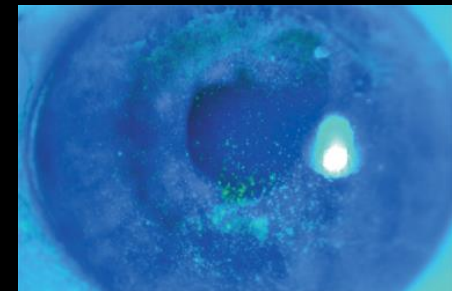
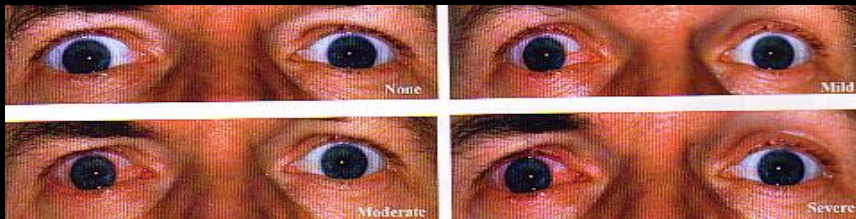


Figure 3. Percentage of patients reporting selected local eye and systemic symptoms, with the associated mean bothersome score.



# TOXICITY OF TOPICALS

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- OCULAR SURFACE DISEASE
  - REDNESS, TEARING, IRRITATION, BURNING, FOREIGN BODY SENSATION, LIGHT SENSITIVITY, INTERMITTENT BLURRED VISION
  - MECHANISM IS UNKNOWN
    - CONJUNCTIVAL HYPEREMIA
    - CELLULAR APOPTOSIS
    - INFLAMMATORY CELL INFILTRATION OF CONJUNCTIVA
- 15% OF ELDERLY PATIENTS
- UP TO 60% OF GLAUCOMA PATIENTS
- IMPACT
  - QUALITY OF LIFE
  - MAY REDUCE FUTURE SUCCESS OF GLAUCOMA SURGERY

# PRESERVATIVE FREE

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- OPTIONS

- TIMOLOL
- ZIOPTAN
- COSOPT
- LATANOPROST
  - XELPROS (FDA APPROVED 9/18)
  - NO BAK, 2.5 ML BOTTLE

- PROS

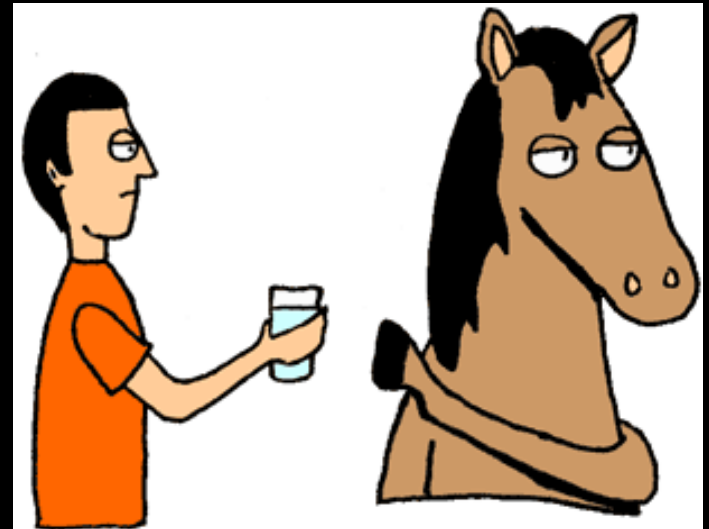
- LESS IRRITATION, LESS DISCOMFORT
- HEALTHIER OCULAR SURFACE
- MAY PRESERVE THE CONJUNCTIVA FOR TRAB / TUBE SUCCESS

- CONS

- COST

# NONCOMPLIANCE

**You Can  
Lead a  
Horse to  
Water...**



- DEFINITION

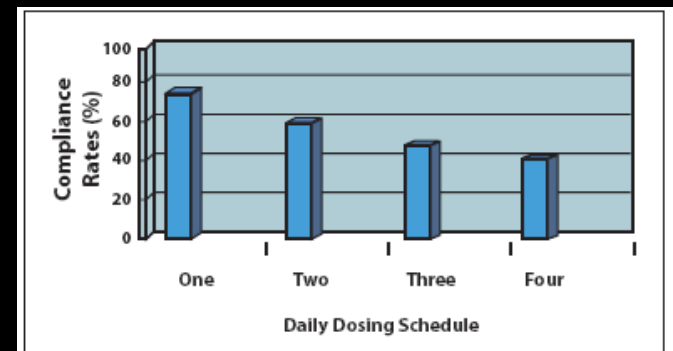
- THE INTENTIONAL OR ACCIDENTAL FAILURE TO COMPLY WITH A PHYSICIAN'S EXPRESSED OR IMPLIED DIRECTIONS WITH REGARD TO TAKING MEDICATIONS OR FUTURE APPOINTMENTS

- ONLY 27-59% OF PATIENTS FOLLOW INSTRUCTIONS

- 10% OF GLAUCOMA RELATED BLINDNESS HAS BEEN ATTRIBUTED TO PATIENT NONCOMPLIANCE

# REASONS FOR POOR ADHERENCE

- FORGETFULNESS
- INCONVENIENCE
- DOSING FREQUENCY
- DIFFICULTY GETTING APPT
- NOT CONSIDERED SERIOUS
- WAITING TIME IN CLINIC
- INABILITY TO INSTILL DROPS
- SIDE EFFECTS OF MEDICATION
- CONFUSING INSTRUCTIONS
- COST OF THERAPY
- NO IMPROVEMENT OF SYMPTOMS
- LACK OF TRANSPORTATION
- RAN OUT OF MEDICATIONS
- FEAR
- LACK OF INSURANCE
- TOO MANY MEDICATIONS



# IMPROVING ADHERENCE

- USE FEWEST DROPS NECESSARY
- REVIEW INSTILLATION
- TIMING SHOULD BE CONVENIENT FOR THE PATIENT
  - TIE THE DRUG TO A DAILY TASK
- COMMUNICATION
  - DISCUSS FINDINGS, RISK FACTORS, REASON FOR TREATMENT
  - DISCUSS SIDE-EFFECTS
  - REMIND OF IMPORTANCE OF COMING TO APPTS AND TAKING MEDICATION EVEN THOUGH NO CHANGE IN VISION OR HOW EYES FEEL
  - WILL BE LONG TERM, NOT ONE AND DONE BUT MANAGED / MONITORED FOR LIFE
- RECOMMEND MAIL ORDER
- SET ALARMS ON CELL PHONE, ETC.







Department of Veterans Affairs

**DRUG SCHEDULE** date \_\_\_\_\_

LEFT EYE	BREAKFAST	RIGHT EYE
	LUNCH	
	SUPPER	
	BEDTIME	
PRECAUTIONS/COMMENTS		

• Remember to mail in your refill slips to the pharmacy early  
 • Do not **EVER** run out of any medication  
 • You should always have an appointment scheduled  
 • Any problems, concerns, side-effects, please **CALL**  
 • If you are taking more than one eye medication, wait 5 minutes between instillation of drops.

Patient Name / Nombre: \_\_\_\_\_ Date / Fecha: \_\_\_\_\_

	Latanoprost 0.005% (blue-green top / tapa azul verde)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every Night / Cada Noche
	Timolol 0.5% (yellow top / tapa amarillo)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every Morning / Cada Manana <input type="checkbox"/> Every 12 Hours / Cada Doce Horas
	Brimonidine 0.2% (purple top / tapa purpura)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every 8 Hours / Cada Ocho Horas <input type="checkbox"/> Every 12 Hours / Cada Doce Horas
	Dorzolamide 2% (orange top / tapa anaranjada)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every 8 Hours / Cada Ocho Horas <input type="checkbox"/> Every 12 Hours / Cada Doce Horas
	Dorzolamide 2% & Timolol 0.5% (dark blue top / tapa azul oscuro)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every 12 Hours / Cada Doce Horas
	Brimonidine 1% & Brimonidine 0.2% (light green top / tapa verde claro)	<input type="checkbox"/> Right Eye / Ojo Derecho <input type="checkbox"/> Left Eye / Ojo Izquierdo <input type="checkbox"/> Both Eyes / Ambos Ojos <input type="checkbox"/> Every 8 Hours / Cada Ocho Horas <input type="checkbox"/> Every 12 Hours / Cada Doce Horas

Shake Well / Agitar Bien

Should you have any questions about your eye medications, call telephone triage at 407-596-1404 or 1-800-846-8866.

**OrlandoVAMC**  
PHCC APPROVED

Si usted tiene alguna pregunta acerca de sus medicamentos para los ojos, llame triage telefonico al 407-596-1404 or 1-800-846-8866.



# QUESTION

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SHOULD I WORRY ABOUT COST?

# COST

- VIA GOODRX.COM AS OF 5/16/23
  - GENERIC LATANOPROST (\$11.45-17.42)
  - GENERIC TRAVATAN Z (\$40.81-53.27)
  - GENERIC BIMATOPROST (\$27.85-53.08)
  - GENERIC BRIMONIDINE 0.2% (\$4.14-11.80)
  - GENERIC DORZOLAMIDE (\$3.99-16.27)
  - GENERIC TIMOLOL (\$1.75-10.91)
  - GENERIC TIMOPTIC XE (\$58.75-189.99)
  - BETOPTIC-S (\$345.80-377.56)
  - GENERIC DORZOLAMIDE/TIMOLOL (\$3.38-26.05)
  - GENERIC COMBIGAN (\$66.80-140.47)
  - SIMBRINZA (\$185.71-219.26)
  - RHOPRESSA (\$307.24-336.43)
  - ROCKLATAN (\$324.69-355.59)
  - VYZULTA (\$238.89-263.38)
  - PF TIMOLOL
  - PF ZIOPTAN
  - PF COSOPT PF
  - PF XELPROS
- TARGET / WALMART
  - (\$4 / 30d, \$10 / 90d)
    - TIMOLOL 0.25 OR 0.5%
    - LEVOBUNOLOL 0.5%
    - PILO 1 OR 2%

# QUESTION



ARE GENERICS JUST AS GOOD?

# GENERICS

**TABLE 1. OPHTHALMIC DRUGS AVAILABLE  
IN GENERIC FORM**

- Beta-blockers (timolol, levobunolol, carteolol, betaxolol)
- Alpha-adrenergic agonist (brimonidine 0.15%, 0.2%)
- Topical carbonic anhydrase inhibitor (dorzolamide)
- Parasympathomimetic (pilocarpine)
- Fixed combination (dorzolamide/timolol)
- Oral carbonic anhydrase inhibitor (acetazolamide, methazolamide)
- Prostaglandin analogue (available outside the United States)

- TO GET FDA APPROVAL
  - SAME ACTIVE INGREDIENT
  - IDENTICAL STRENGTH, DOSAGE FORM, ROUTE
  - SAME INDICATION FOR USAGE
  - BE BIOEQUIVALENT
  - SAME BATCH REQUIREMENTS
    - IDENTITY, STRENGTH, PURITY, QUALITY
  - SIMILAR SHELF LIFE
  - SAME MANUFACTURING PROCESS REGULATIONS

# GENERICS

- **HOWEVER**
  - NOT REQUIRED TO BE THERAPEUTICALLY EQUAL UPON RELEASE
- **TIMOPTIC XE VS GENERIC**
  - **STATISTICALLY DIFFERENT IN IOP LOWERING AT 16 HRS**
  - **NAME BRAND HAD BETTER EFFICACY AND TOLERABILITY**



# GENERIC LATANOPROST

- 2007 STUDY IN INDIA
  - 30 PATIENTS
  - XALATAN HAD LOWER IOP THAN GENERIC LATANOPROST
  - SIMILAR SIDE EFFECTS
  - HIGHER pH AND PARTICULATE MATTER
    - MAY AFFECT STABILITY, RELEASE OF ACTIVE DRUG
- NOW AVAILABLE IN THE U.S.
  - MANUFACTURERS
    - APOTEX, MYLAN, B&L, FALCON (VA)
    - GREENSTONE
      - SAME FACILITY AS PFIZER'S XALATAN
- PROS
  - CHEAPER
    - COST = \$12.08-29 / 2.5 ml @ GOODRX.COM
- CONS
  - ? AS EFFECTIVE



Summary of intraocular pressure (in mm Hg) of study eye(s) at week 12

Week	Xalatan® followed by generic latanoprost (Latanoprost) (Group A) Mean (SD)	Generic latanoprost (Latanoprost) followed by Xalatan® (Group B) Mean (SD)	P-value
Baseline	23.64 (3.13)	22.74 (2.47)	0.3988
Week 12	14.29 (1.61)	16.98 (2.49)	0.0036
Week 24	15.36 (1.71)	16.09 (1.49)	0.236

# GENERICS

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- PROBLEMS

- DROP SIZES DIFFER, BOTTLE HARDER TO HANDLE, TOUGHER TO TELL WHEN NEED REFILLS, CLOGGED DROPPER, ETC.
- DROPS JUST RUN OUT WITHOUT SQUEEZE, ETC
- ALL OF THE ABOVE
  - MAY LEAD TO NONCOMPLIANCE

- RECOMMENDATION

- BE CAREFUL
  - TRIAL AND ERROR TO SEE HOW PATIENT DOES
- IF NOT AS EFFECTIVE
  - CONSIDER WRITING “DISPENSE AS WRITTEN” ON RX

# CASE

- 61 / W / M
- CC:
  - here for DM eye eval, uses OTC for reading without complaints, happy at distance without rx, no ocular comfort problems
- OCULAR PAIN:
  - 0/10
- OTHER PAIN:
  - 0/10
- OCULAR HISTORY:
  - LEE 3 YRS by VA OPTHALMOLOGIST
    - DM Without Retinopathy OU
    - .6/.6, IOP 21/20 via NCT
    - H/O Broken orbital floor OS 35 yrs ago
- MEDICAL HISTORY:
  - +DM x 6 yrs (last a1c 11.6, 6 mos prior 7.2), +insulin, +htn (last bp 125/80), -heart +chol, -stroke, -cancer, -thyroid –migraines –MS
- MEDS:
  - Metformin, Insulin, Atorvastatin, Losartan, Sildenafil, Vit D3
- ALLERGIES:
  - NONE
- FAMILY HISTORY:
  - -dm, -glaucoma, -blind
- SOCIAL HISTORY:
  - -etoh, -tobacco



# CASE

- VISION
  - sc 20/25
  - sc 20/40+2
- PRELIMS
  - NORMAL PUPILS, NO APD
  - FTFC OD OS
  - FROM
- REFRACTION
  - +125-100x085 20/20
  - +150-175x095 20/20
  - ADD: +250 20/20 OU 12-24"
- SLIT LAMP
  - Adnexa: normal ou
  - Lids / Lashes: normal ou
  - Conj: concretions inferiorly ou
  - Cornea: normal ou
  - A/C: deep and quiet ou
  - Iris: few flat nevi ou
- IOP: 25/23@ 820a
- Pachym: 564/565
- GONIO:
  - ou open to cbb 360, no PAS, recess, nv, tr pig
- DFE:
  - LENS: trace ACC / trace NS ou
  - See photos for:
    - C/D, ONH, Macula, Post Pole, Vessels
  - Vitreous: PVD ou
  - Periphery: normal ou

# DFE



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9/19/2019 9:19:06.9

# RNFL

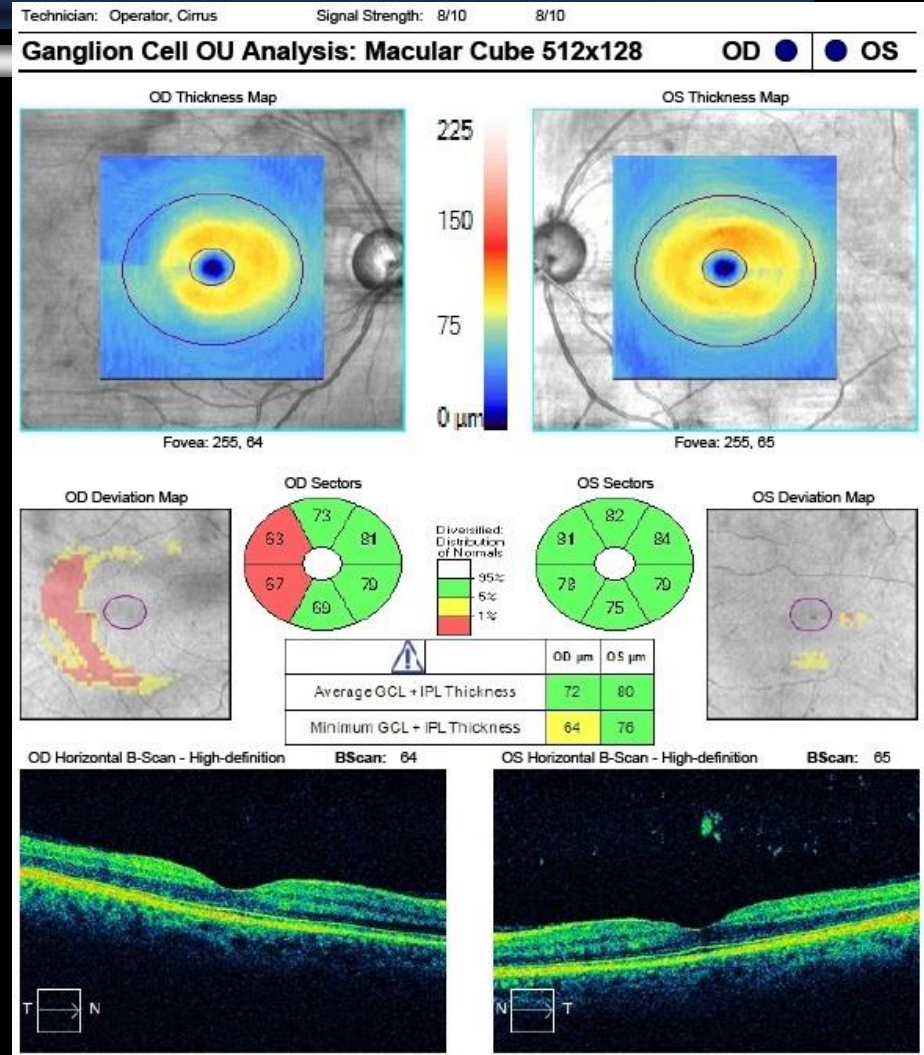
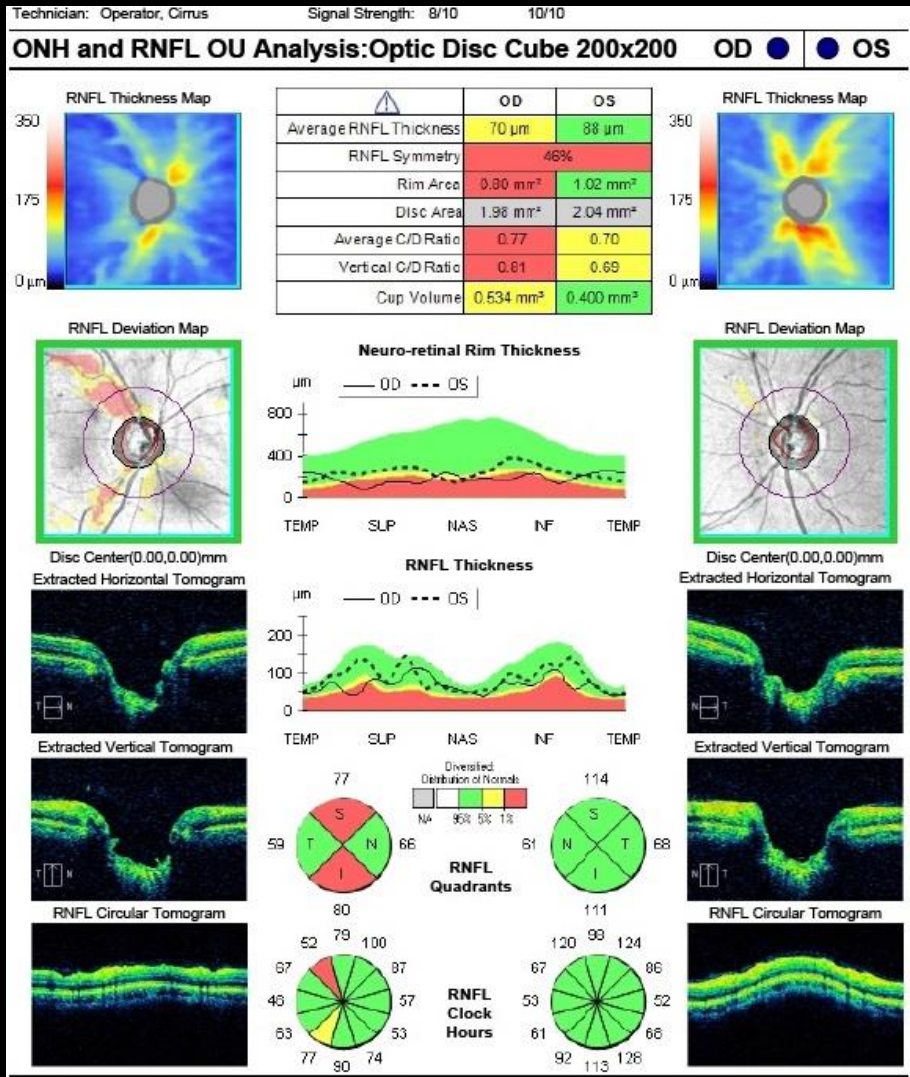


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# OCT RNFL / GCC



# WHAT ARE YOU GOING TO DO?

- A. GATHER DATA, MONITOR ONLY
- B. GATHER DATA, THEN TREAT
- C. GATHER DATA, TREAT THE PATIENT TODAY
- D. REFER TO LOCAL OPTOMETRIST
- E. REFER TO LOCAL OPHTHALMOLOGIST

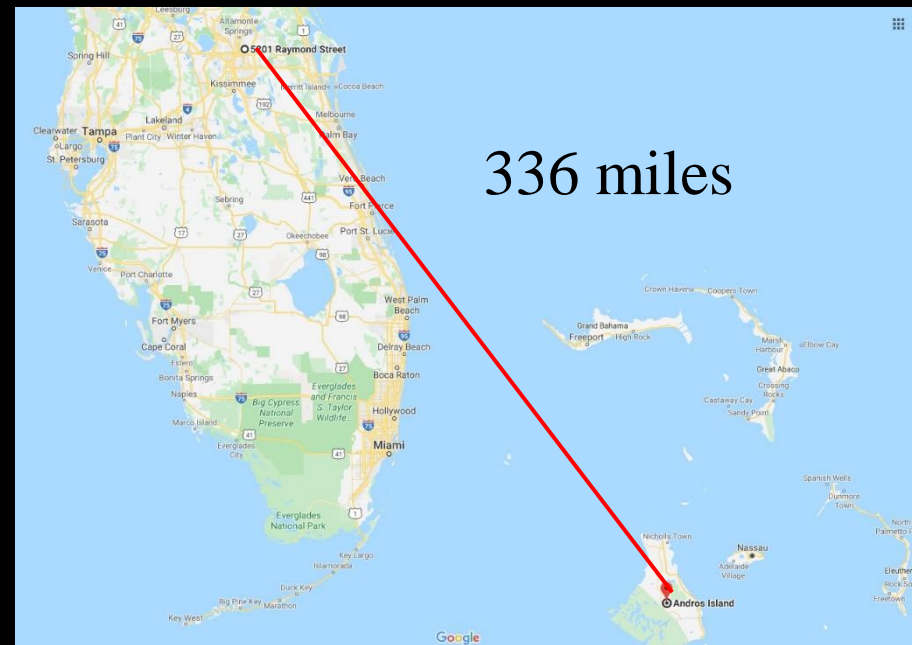


# IN A PERFECT WORLD...

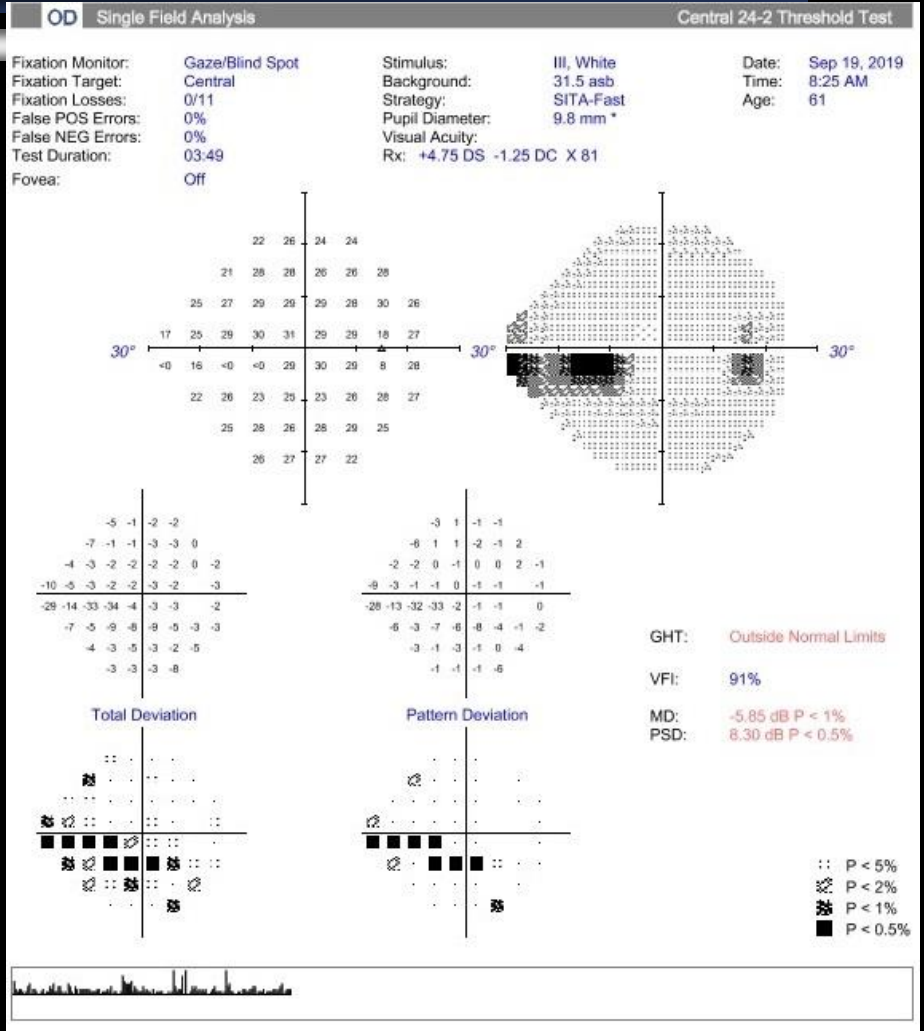
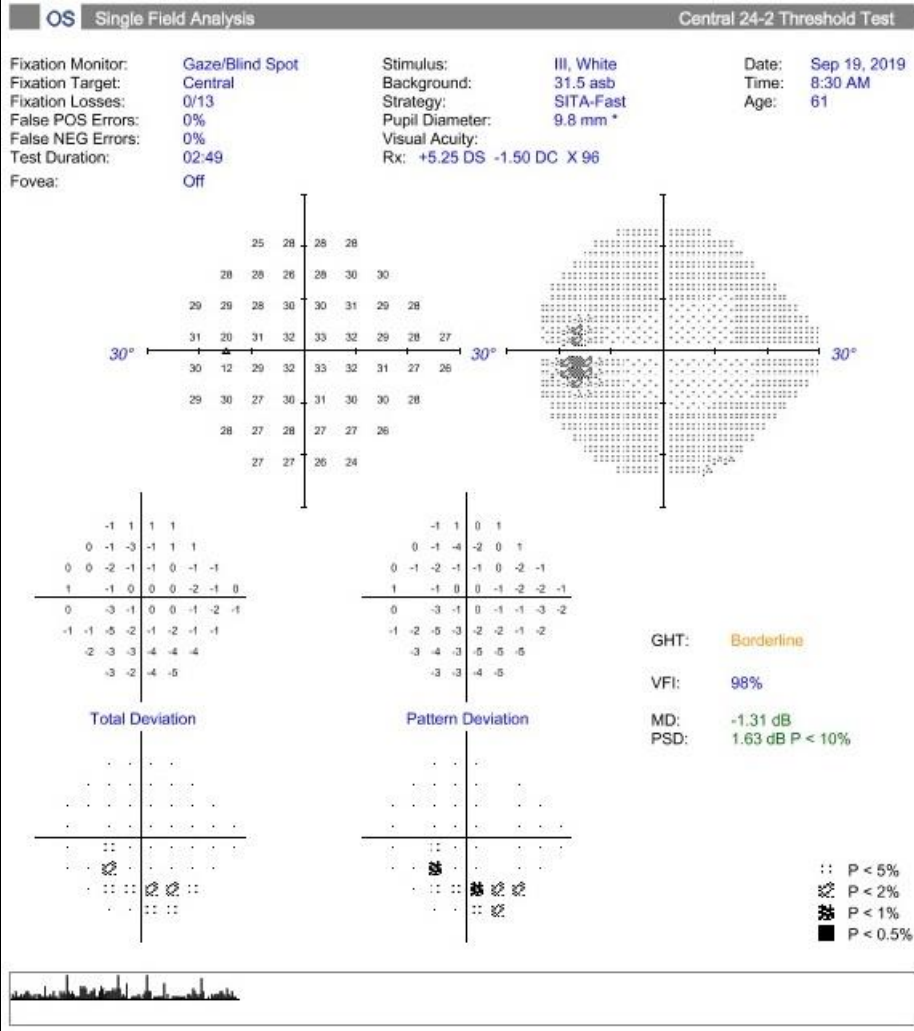
- REMEMBER
  - TYPICALLY, GLAUCOMA IS A LONG, SLOW, GRADUAL PROCESS
  - IN MOST CASES, THERE'S TIME TO...
- GATHER BASELINE DATA
  - **GET AT LEAST 3 IOP READINGS**
    - PREFERABLY ON DIFFERENT DAYS
    - PREFERABLY AT DIFFERENT TIMES OF THE DAY
      - MODIFIED DIURNAL CURVE
    - GOAL IS TO DETERMINE THE HIGHEST IOP
      - HELPS TO DETERMINE TARGET IOP
      - MAY INFLUENCE DECISION ABOUT MEDICATION EFFECTIVENESS
  - **GET PACHYMETRY AND GONIOSCOPY**
  - **DOCUMENT THE ONH**
    - PHOTOS
  - **DOCUMENT THE RNFL, GCC**
    - OCT, ETC.
  - **GET VISUAL FIELD**
    - HELPS STAGE THE DISEASE
    - HELPS DETERMINE TARGET IOP

# THIS IS REALITY...

- PATIENT LIVES IN BAHAMAS
  - HE REPORTS IT IS VERY DIFFICULT AND EXPENSIVE TO GET HERE
  - HE GUARANTEES FHE WILL NOT BE BACK HERE FOR AT LEAST 3 MONTHS
- SO NOW WHAT?

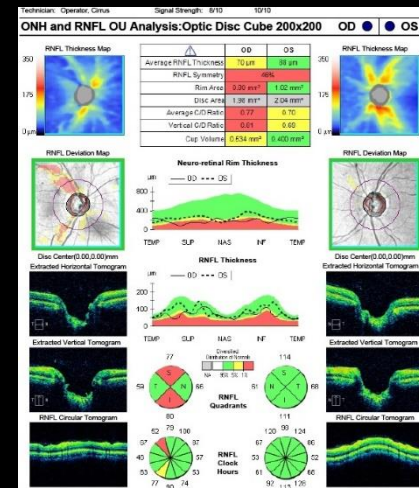
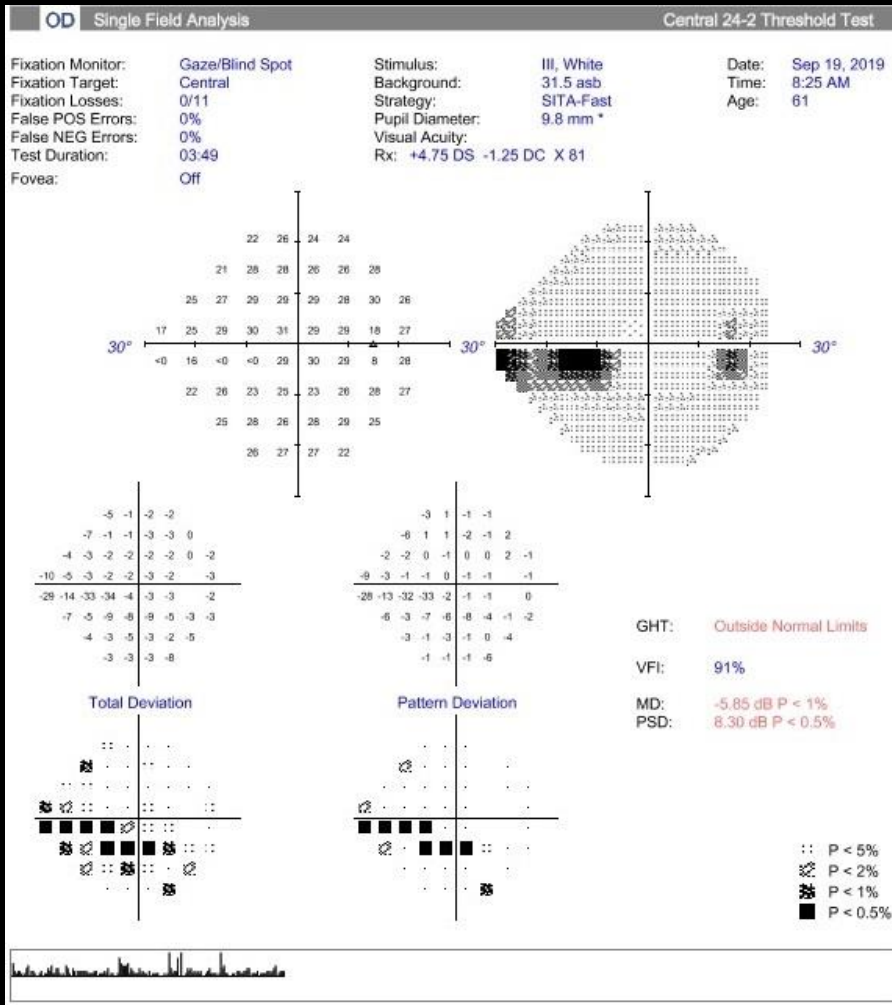


# DILATED VF 24-2 SITA FAST

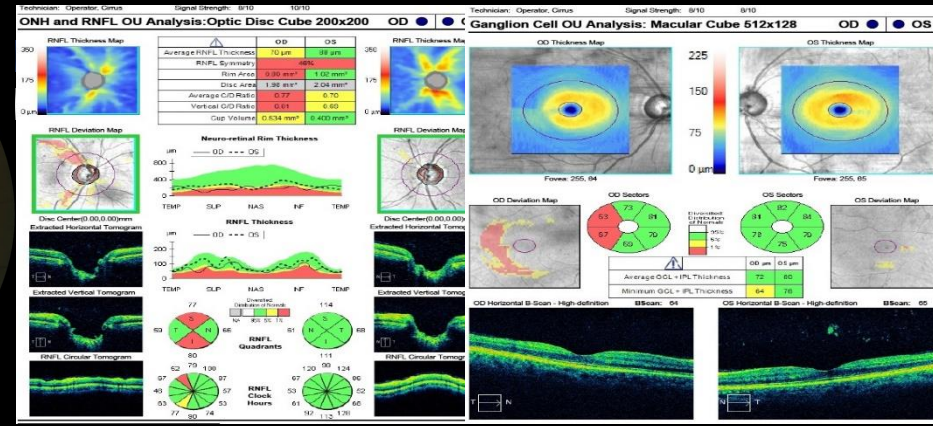




# VF LOSS CORRESPONDS TO ONH NOTCH AND RNFL LOSS



# CASE

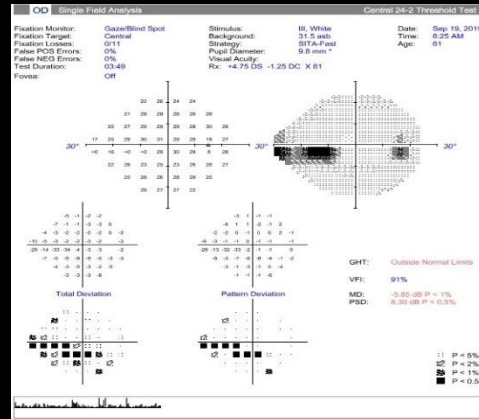
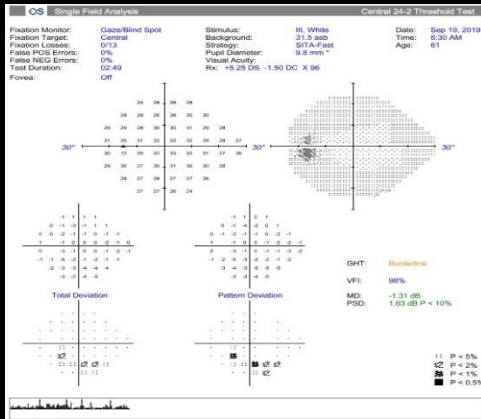


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## PLAN:

- REVIEWED GLAUCOMA
- RECOMMEND LOWER IOP
- NEED FOR LONGTERM TREATMENT / MONITORING EVEN WITHOUT SYMPTOMS TO POSSIBLY PREVENT ONH DAMAGE / VF LOSS / BLINDNESS
- RX START **LATANOPROST** QHS OU
  - EDUCATED HOW/WHY TO USE AND NEED TO REPORT ANY SIDE EFFECTS
- REMINDED NEED FOR 100% COMPLIANCE WITH MEDS/APPTS

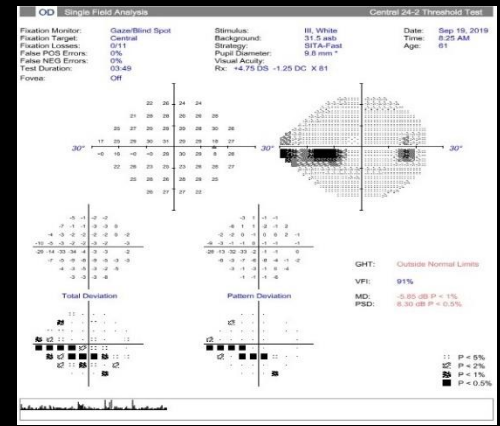
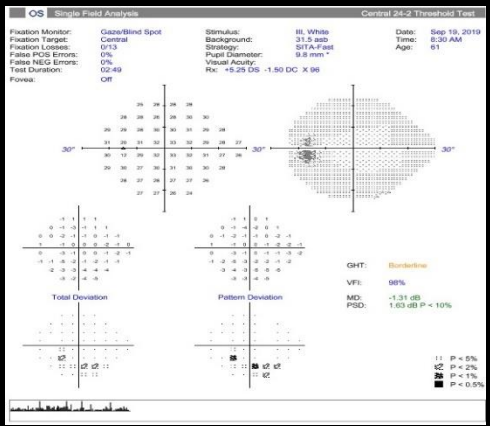
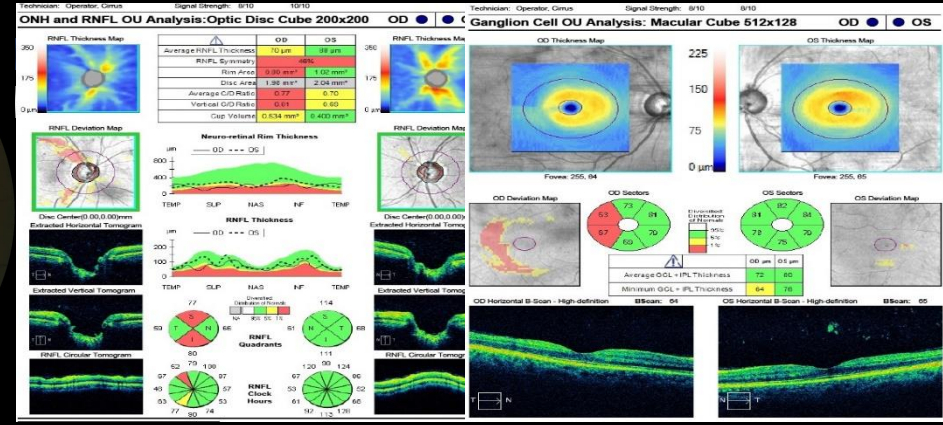


## WHAT'S NEXT?

- RTC 3 MOS (NORMALLY 4-6 WEEKS)
- PER PT REQUEST DUE TO LIVING IN BAHAMAS

# CASE FOLLOW-UP

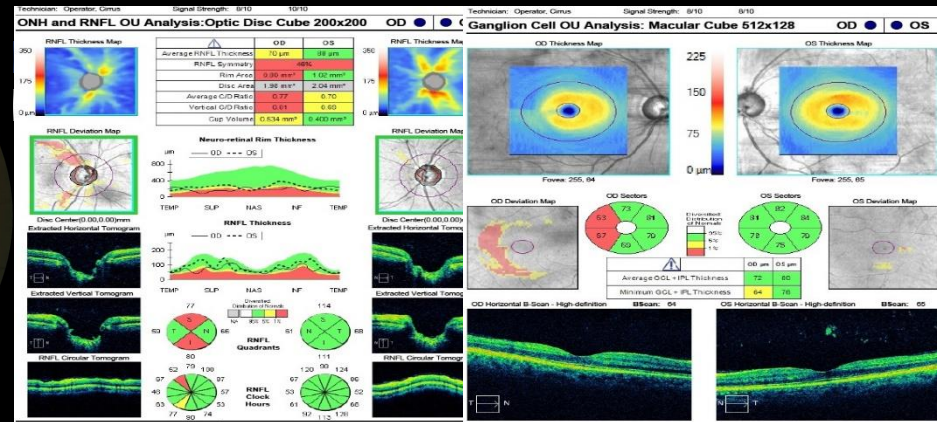
## 3 mos LATER



IOP: 20/19 latanoprost qhs ou (25/23 pre-tx)  
TARGET IOP <15 (40%) / <16 (30%)

WHAT'S NEXT?

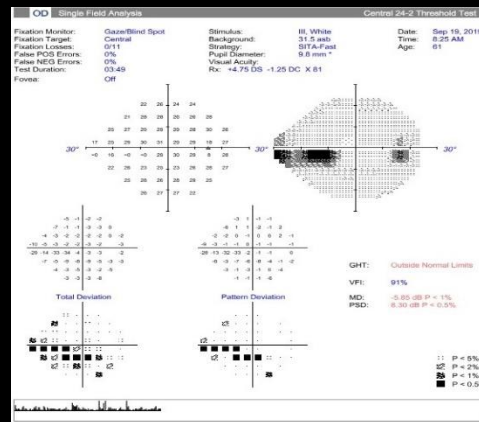
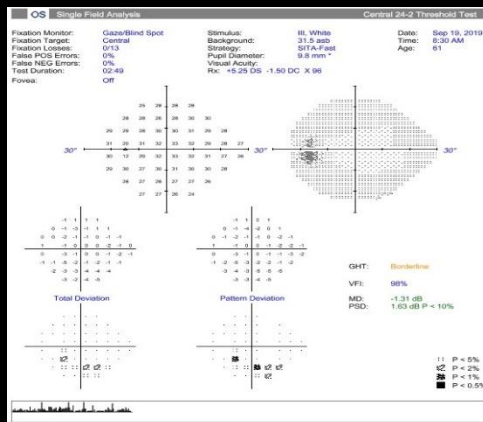
# FOLLOW-UP 3 MOS LATER



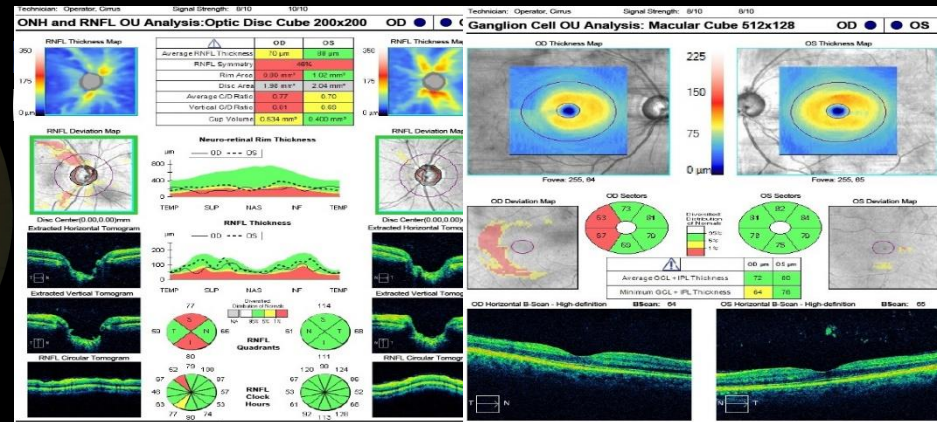
- IOP: 20/19 latanoprost qhs ou (25/23 pre-tx)
  - TARGET IOP <15 (40%) / <16 (30%)

## WHAT'S NEXT?

- Is that IOP good enough?
- Options:
  - Monitor vs change vs add another drop vs refer for laser / surgery?
- RTC when?
  - 4 mos
  - Consider WPB / Miami VA
  - Find local eye doctor in Bahamas



# FOLLOW-UP 3 MOS LATER



- IOP: 20/19 latanoprost qhs ou (25/23 pre-tx)
  - TARGET IOP <15 (40%) / <16 (30%)

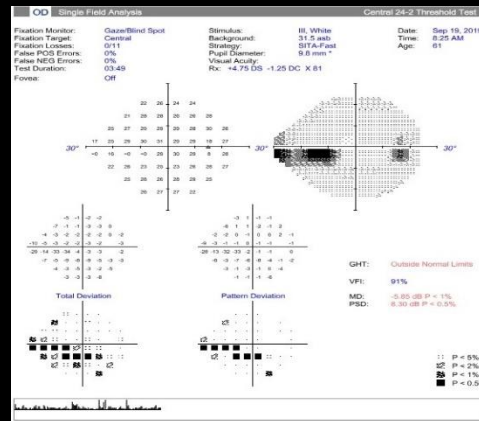
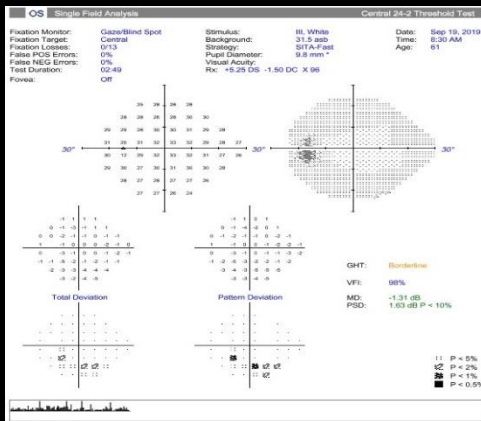
## WHAT DID WE DO?

- Rx: started **Simbrinza** q12h ou

## WHAT'S NEXT?

- RTC when?
  - 4 mos
  - Consider WPB / Miami VA
  - Find local eye doctor in Bahamas
- Consider
  - Add Med vs Referral for ALT/SLT / MIGS / Trab / Tube

## SO HOW DID HE DO?



# CURRENT STATUS...



Medical & Science

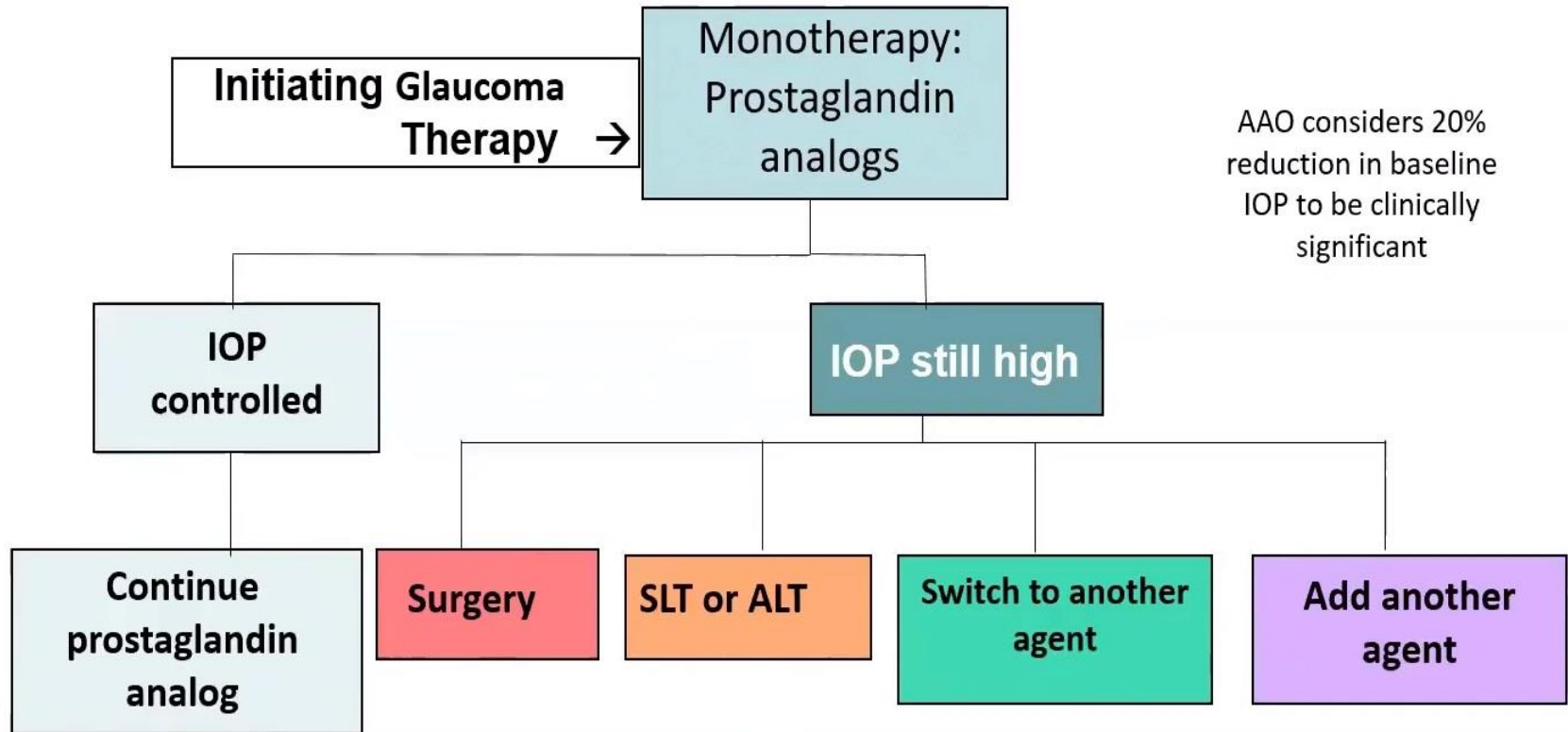
**LTFU**

means

lost to follow-up

by [acronymsandslang.com](https://www.acronymsandslang.com)

# TREATMENT ALGORITHM



**EUGENE AND MARILYN GLICK  
EYE INSTITUTE**

INDIANA UNIVERSITY

**LOU CANTOR, MD**  
CYBERSIGHT WEBINAR

<https://cybersight.org/portfolio/lecture-glaucoma-surgery-an-evolving-art-and-science/>

# BOTTLE CAP COLOR

Color Codes For Topical Ocular Medications
Anti-infectives
Anti-inflammatories/steroids
Mydriatics and cycloplegics
Non-steroidal anti-inflammatories
Miotics
Beta-blockers
Beta-blocker combinations
Adrenergic agonists
Carbonic anhydrase inhibitors
Prostaglandin analogs



# IOP LOWERING DROP OPTIONS SUMMARIZED

<b>TOPICAL GLAUCOMA DRUGS</b>				
<b>BRAND NAME</b>	<b>GENERIC NAME</b>	<b>MANUFACTURER</b>	<b>CONCENTRATION</b>	<b>BOTTLE SIZE</b>
<b>Beta Blockers</b>				
Betagan	levobunolol hydrochloride	Allergan and generic	0.25% 0.5%	5ml, 10ml 5ml, 10ml, 15ml
Betimol	timolol hemihydrate	Akorn	0.25% 0.5%	5ml 5ml, 10ml, 15ml
Betoptic-S	betaxolol hydrochloride	Novartis	0.25%	5ml, 10ml, 15ml
Istalol	timolol maleate	Bausch + Lomb	0.5%	2.5ml, 5ml
Timoptic	timolol maleate	Bausch Health and generic	0.25% 0.5%	5ml, 10ml, 15ml 5ml, 10ml, 15ml
Timoptic (preservative-free)	timolol maleate	Bausch Health	0.25%	unit-dose
Timoptic-XE	timolol maleate	Bausch Health	0.25%	unit-dose 2.5ml, 5ml
<b>Prostaglandin Analogs</b>				
Bimatoprost	bimatoprost	generic	0.03%	2.5ml, 5ml, 7.5ml
Lumigan	bimatoprost	Allergan	0.01%	2.5ml, 5ml, 7.5ml
Travatan Z	travoprost	Novartis	0.004%	2.5ml, 5ml
Travoprost	travoprost	generic	0.004%	2.5ml, 5ml
Vyzulta	latanoprostene bunod	Bausch + Lomb	0.024%	2.5ml, 5ml
Xalatan	latanoprost	Pfizer, + generic	0.005%	2.5ml
Xelpros	latanoprost ophthalmic emulsion	Sun Ophthalmics	0.005%	5ml
Zioptan	tafluprost	Akorn	0.0015%	unit-dose
<b>Alpha Agonists</b>				
Alphagan P	brimonidine	Allergan	0.1%, 0.15%	5ml, 10ml, 15ml
Brimonidine	brimonidine	generic	0.15%, 0.2%	5ml, 10ml, 15ml
<b>Carbonic Anhydrase Inhibitors</b>				
Azopt	brinzolamide suspension	Novartis	1%	5ml, 10ml, 15ml
Trusopt	dorzolamide	Merck and generic	2%	5ml, 10ml
<b>Rho Kinase Inhibitors</b>				
Rhopressa	netarsudil	Aerie Pharmaceuticals	0.02%	2.5ml
<b>Combination Glaucoma Medications</b>				
Combigan	brimonidine/timolol	Allergan	0.2%/0.5%	5ml, 10ml
Cosopt	dorzolamide/timolol	Akorn and generic	2%/0.5%	5ml, 10ml
Cosopt PF	dorzolamide/timolol	Akorn	2%/0.5%	unit-dose
Rocklatan	netarsudil and latanoprost	Aerie Pharmaceuticals	0.02%, 0.005%	2.5ml
Simbrinza	brinzolamide/brimonidine suspension	Novartis	1%/0.2%	8ml

# IOP LOWERING DROP OPTIONS SUMMARIZED

Primary Open-Angle Glaucoma PPP

TABLE 4 GLAUCOMA MEDICATIONS

Drug Classification	Agents	Methods of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Prostaglandin analogs‡	Bimatoprost Latanoprost Latanoprostene bunod Tafuprost Travoprost	Increase uveoscleral and/or trabecular outflow	25%–33%	<ul style="list-style-type: none"> <li>Increased and misdirected eyelash growth</li> <li>Periocular hyperpigmentation</li> <li>Conjunctival injection</li> <li>Allergic conjunctivitis/contact dermatitis</li> <li>Keratitis</li> <li>Possible herpes virus activation</li> <li>Increased iris pigmentation</li> <li>Uveitis</li> <li>Cystoid macular edema</li> <li>Periorbitopathy</li> <li>Migraine-like headache</li> <li>Flu-like symptoms</li> </ul>	<ul style="list-style-type: none"> <li>Macular edema</li> <li>History of herpetic keratitis</li> <li>Active uveitis</li> </ul>	C
Beta-adrenergic antagonists (beta-blockers)	<u>Nonselective</u> Carteolol Levobunolol Metipranolol Timolol <u>Selective</u> Betaxolol	Decrease aqueous production	20%–25%	<ul style="list-style-type: none"> <li>Allergic conjunctivitis/contact dermatitis</li> <li>Keratitis</li> <li>Bronchospasm</li> <li>Bradycardia</li> <li>Hypotension</li> <li>CHF</li> <li>Reduced exercise tolerance</li> <li>Depression</li> <li>Impotence</li> </ul>	<ul style="list-style-type: none"> <li>Chronic obstructive pulmonary disease</li> <li>Asthma</li> <li>CHF</li> <li>Bradycardia</li> <li>Hypotension</li> <li>Greater than first-degree heart block</li> </ul>	C
Alpha-adrenergic agonists	<u>Agracolonidine</u> Brimonidine	Decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow	20%–25%	<ul style="list-style-type: none"> <li>Allergic conjunctivitis/contact dermatitis</li> <li>Follicular conjunctivitis</li> <li>Dry mouth and nose</li> <li>Hypotension</li> <li>Headache</li> <li>Fatigue</li> <li>Somnolence</li> </ul>	<ul style="list-style-type: none"> <li>Monoamine oxidase inhibitor therapy</li> <li>Infants and children (for brimonidine)</li> </ul>	B
Parasympathomimetic agents	<u>Cholinergic agonist</u> Pilocarpine <u>Anticholinesterase agent</u> Echothiophate	Increase trabecular outflow	20%–25%	<ul style="list-style-type: none"> <li>Increased myopia</li> <li>Decreased vision</li> <li>Cataract</li> <li>Periocular contact dermatitis</li> <li>Allergic conjunctivitis/contact dermatitis</li> <li>Conjunctival scarring</li> <li>Conjunctival shrinkage</li> <li>Keratitis</li> <li>Paradoxical angle closure</li> <li>Retinal tears/detachment</li> <li>Eye or brow ache/pain</li> <li>Increased salivation</li> <li>Abdominal cramps</li> </ul>	<ul style="list-style-type: none"> <li>Areas of peripheral retina that predispose to breaks</li> <li>The need to regularly assess the fundus</li> <li>Neovascular, uveitic, or malignant glaucoma</li> </ul>	C

Primary Open-Angle Glaucoma PPP

TABLE 4 GLAUCOMA MEDICATIONS (CONTINUED)

Drug Classification	Agents	Methods of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Rho kinase inhibitors	Netarsudil	Increase trabecular outflow Decrease episcleral venous pressure Decrease aqueous production	10%–20%	<ul style="list-style-type: none"> <li>Conjunctival hyperemia</li> <li>Corneal verticillata</li> <li>Instillation site pain</li> <li>Conjunctival hemorrhage</li> <li>Keratitis</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>	... <sup>§</sup>
Topical carbonic anhydrase inhibitors	Brimonidamide Dorzolamide	Decrease aqueous production	15%–20%	<ul style="list-style-type: none"> <li>Allergic dermatitis/conjunctivitis</li> <li>Corneal edema</li> <li>Keratitis</li> <li>Metallic taste</li> </ul>	<ul style="list-style-type: none"> <li>Sulfonamide allergy</li> <li>Sickle cell disease with hyphema</li> </ul>	C
Oral carbonic anhydrase inhibitors	Acetazolamide Methazolamide	Decrease aqueous production	20%–30%	<ul style="list-style-type: none"> <li>Stevens-Johnson syndrome</li> <li>Malaise, anorexia, depression</li> <li>Serum electrolyte imbalance</li> <li>Renal calculi</li> <li>Blood dyscrasias (aplastic anemia, thrombocytopenia)</li> <li>Metallic taste</li> <li>Enuresis</li> <li>Parosmia</li> <li>Diarhea</li> <li>Abdominal cramps</li> </ul>	<ul style="list-style-type: none"> <li>Sulfonamide allergy</li> <li>Kidney stones</li> <li>Aplastic anemia</li> <li>Thrombocytopenia</li> <li>Sickle cell disease</li> </ul>	C
Hyperosmotic agents	Glycerol Mannitol	Dehydration of vitreous	No data	<ul style="list-style-type: none"> <li>Headache</li> <li>CHF</li> <li>Nausea, vomiting</li> <li>Diarhea</li> <li>Renal failure</li> <li>Diabetic complications</li> <li>Mental confusion</li> </ul>	<ul style="list-style-type: none"> <li>Renal failure</li> <li>CHF</li> <li>Potential CNS pathology</li> </ul>	C

CHF = congestive heart failure; CNS = central nervous system; FDA = Food and Drug Administration; IOP = intraocular pressure

\* Data from the Heijl A, Traverso CE, eds. Terminology and Guidelines for Glaucoma. European Glaucoma Society. 4th ed. Savona, Italy: PublComm; 2014:146-51. Available at: [http://www.iooph.org/dynamico/attachments/resources/legs\\_guidelines\\_4\\_english.pdf](http://www.iooph.org/dynamico/attachments/resources/legs_guidelines_4_english.pdf). Accessed October 16, 2020.

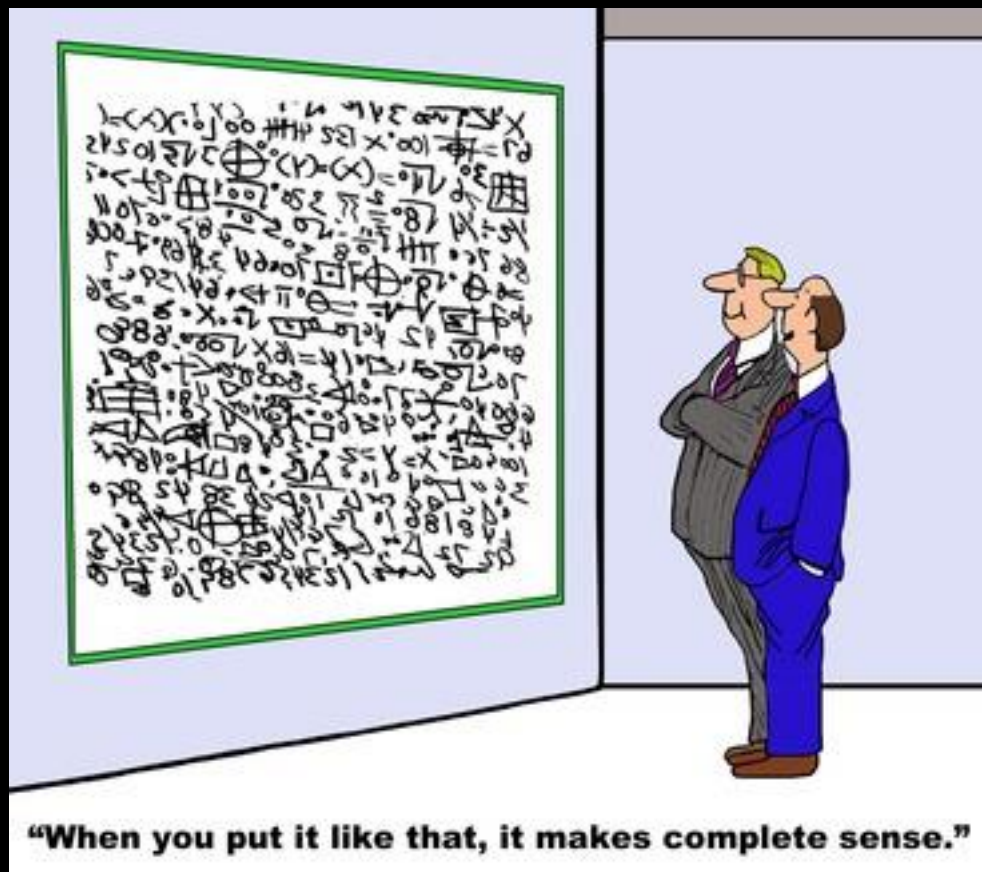
† FDA Pregnancy Category B = Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies on pregnant women. FDA Pregnancy Category C = Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

‡ Latanoprostene bunod is a new IOP-lowering agent that is rapidly metabolized to latanoprost (a prostaglandin analog) and buprenorphine (a mu-opioid receptor agonist). It enhances aqueous humor outflow through both the uveoscleral and trabecular meshwork pathways.<sup>33-34</sup>

§ The FDA replaced the ABCDX drug pregnancy categories with descriptive information regarding medication risks to the developing fetus, breastfed infant, and individual of reproductive potential under the Pregnancy and Lactation Labeling Rule in 2015. Rho-kinase inhibitors are therefore not assigned a pregnancy category. No data exist on the use of netarsudil in pregnant women. Animal studies did not demonstrate adverse effects on the developing fetus with clinically relevant intravenous exposures.<sup>34</sup>

To determine the effectiveness of topical therapy, it is necessary to distinguish between the therapeutic impact of an agent on IOP and ordinary background spontaneous fluctuations of IOP. Though monocular trials have been recommended in the past to determine whether a topical ocular hypotensive agent is effective, studies have shown that such trials are not good predictors of long-term efficacy.<sup>343, 344</sup> A monocular trial is defined as the initiation of

# ANY QUESTIONS?



# OTHER GLAUCOMA TREATMENT OPTIONS

- NEXT WEEK
  - ALTERNATIVE THERAPIES
  - MIGS
- HAVE DONE / WILL REVISIT JULY
  - LASER
  - INCISIONAL SURGERY