Glaucoma Update

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  - University of Houston College of Optometry

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Disclosures for Dr Schmidt

- Dr Schmidt is a consultant or advisor for the following:
  - Tarsus
  - Allergan
  - B&L
  - Tenpoint Pharmaceuticals
  - Topcon
  - Orasis
  - Glaukos
  - Sun Pharmaceuticals
  - Thea Pharmaceuticals
  - Sight Science
  - Alcon
  - Apellis
  - Sydnexis
  - Visus
  - Harrow Pharmaceuticals
  - Lenz Therapeutics
- All potential conflicts of interest have been mitigated

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Disclosures for Dr Marrelli

- Dr Marrelli is a consultant or advisor for the following:
  - Alcon
  - Balance
  - B&L
  - Topcon
  - Glaukos
  - Carl Zeiss Meditec
- All potential conflicts of interest have been mitigated

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Glaucoma Drugs – Tapping that Pipeline!!!

- Nothing New For A While, and then… BOOOM!
- Rhopressa
- Rocklatan
- Vyzulta
- But those are so 2019!!
- Anything else??

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But really… Is There Anything New??

Iyuzeh-
(latanoprost 0.005%)

Thea Pharmaceuticals

Let's talk about this…

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Iyuzeh (latanoprost 0.005%)

- Does that sound familiar?
- Monoprost (in Europe) – the market leader in PGA in Europe
- This actually is PRESERVATIVE FREE latanoprost!!
- Single dose container
- But does it really work??

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Iyuzeh – Phase 3 data

- Compared to Xalatan (Switch Study)
- Stable POAG pxs on Xalatan
- 8 day washout period
- 3 months on Iyuzeh

- IOP reduction was 4-8mm Hg on Xalatan
- IOP reduction was 3-8mm Hg on Iyuzeh

- Baseline IOP was 19mmHG!!

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Iyuzeh – Phase 3 data- Adverse Effects

- Xalatan group
  - Hyperemia – 31%
  - Eye Irritation – 34%

- Iyuzeh Group
  - Hyperemia – 34%
  - Eye irritation – 19%

- ZERO reports of SPK

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Subsequent Iyuzeh studies

- European data – Higher baseline IOP (24mm Hg)
  - IOP lowered to 15.5mm Hg
  - Same rate of adverse effects
- Bachrach data (2023 AGS)
  - 12 week trial comparing to Xalatan
  - Similar IOP reduction (as measured by ability to get IOP <18mm Hg)
  - 2% experienced redness or ocular irritation
  - 0% SPK

  Fewer ocular side effects (13.9% vs 22.5%)
- PASSY study
  - 97% tolerated drop
  - AT usage decreased 24%

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#What's The Big Deal??

- OSD is an epidemic in glaucoma
- Will this improve compliance?
- Will this cost $1M??
- Is it better than what we have?

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Rhopressa (netarsudil) – Aerie Pharmaceuticals

- New class of drugs – Rho-kinase inhibitor
- MOA – "Triple Action"
- - relaxes trabecular meshwork similar to pilocarpine (enhances outflow)
- - lowers episcleral venous pressure
- - blocks fibrotic response at t.m.(increases perfusion)
- QD dosing
- Looks especially effective at IOP 25 mmHg or less

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Rhopressa (netarsudil) -MOA

Works at the cellular level within the trabecular meshwork

ROCK inhibitors improve outflow by relaxing contraction and stress fibers at the t.m.

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What Do We Know About Rhopessa (netarsudil 0.02%)

- Rhopressa QD is non-inferior to timolol 0.5% BID in lowering IOP
- Expected IOP reduction 3.7 -7.0mm Hg
- Rhopressa seems to better at lowering IOP (as compared to itself) in pressures < 25mm Hg
- IOP lowering effect is maintained over 12 months
- Was given a broad label by FDA

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Rhopressa – Adverse Effects

Generally well tolerated

Conjunctival hyperemia – 53%

- Did not worsen with time
- Mild-36.8%, moderate – 10.5%, severe -0.6%
- D/C rate due to redness -~3%

Corneal verticillata – 18%

Conjunctival hemorrhage – 15%

- All are transient and considered mild

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What's to like about Rhopressa?

New MOA so… it is absolutely different

It should be additive

Definitely works better at lower IOP

What about side effects?

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Rhopressa- some thoughts

- How are you positioning it in your practice??
- What are our clinical experiences 2 years later?
- Is it a first line drug?
- What about insurance coverage?
- What color top does it have??

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Update on Rhopressa

- Relaxes Actin & Myosin fibers > Increases outflow at t.m.
- Yields 35% Improvement in tm outflow in glaucoma patients (vs 20% improvement in normal)
- Excellent response on episcleral venous pressure- netarsudil reduces EVP by 10% - no other drop achieves this
- No longer needs to be refrigerated after opening

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M.O.S.T. Study

- Real World Open Label Phase 4 Study
- ASCRS 2020
- To determine efficacy of Rhopressa as an adjunct med
- Investigator's Choice – Rhopressa + any other agent
- 24.4% African-American participants

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M.O.S.T. Results

Rhopressa + PGA - IOP 21.1> 16.9 mmHg (20% reduction)

Rhopressa + 2 meds – 20.6 > 16.6 mmHg (20% reduction)

Notice the low baseline IOP

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More M.O.S.T. Results

- % of pxs less than < 18mm Hg
  - <18mm -72.7 % (from 34.4%)
  - <17mm- 65% (from 25.2%)
  - <15mm -40.6% (from 15.9%)
  - <14mm- 30.1% (from 11.3%)

- 2/3 of all patients achieved IOP < 17mm Hg

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M.O.S.T. Tolerability rates

Hyperemia – 20.* %

D/C rate – hyperemia 3.4%

Tolerability rating

67.8-73.1% good or decent (physician response)

65-78% good or decent (Patient response)

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A Brand New Molecule to Discuss!!!

- Omlonti – omidenepag isopropyl
- MOA - EP2 Receptor
- Ocuvex/ Santen
- Approved for lowering IOP in Glaucoma and OHTN
- 1 drop QD

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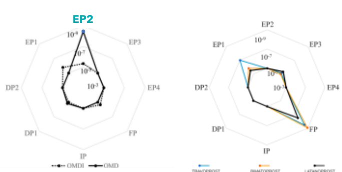
Receptor Affinity



Activity[3]

	EP1	EP2	FP
	EC_{50}, nM		
OMDI	>10,000	>10,000	>10,000
OMD (FREE ACID)	-	**8.3**	-

1. Kirihara T, Taniguchi T, Yamamura K, Iwamura R, Yoneda K, Odani-Kawabata N, Shimazaki A, Matsugi T, Shams N, Zhang JZ. Pharmacologic Characterization of Omidenepag Isopropyl, a Novel Selective EP2 Receptor Agonist, as an Ocular Hypotensive Agent. Invest Ophthalmol Vis Sci. 2018 Jan 1;59(1):145-153.
2. Matsuo M, Matsuoka Y, Tanito M. Efficacy and Patient Tolerability of Omidenepag Isopropyl in the Treatment of Glaucoma and Ocular Hypertension. Clin Ophthalmol. 2022 Apr 26;16:1261-1279.
3. Kirihara T, Taniguchi T, Yamamura K, Iwamura R, Yoneda K, Odani-Kawabata N, Shimazaki A, Matsugi T, Shams N, Zhang JZ. Pharmacologic Characterization of Omidenepag Isopropyl, a Novel Selective EP2 Receptor Agonist, as an Ocular Hypotensive Agent. Invest Ophthalmol Vis Sci. 2018 Jan 1;59(1):145-153.
4. Stjemschantz JW. From PGF(2alpha)-isopropyl ester to latanoprost: a review of the development of xalatan: the Proctor Lecture. Invest Ophthalmol Vis Sci. 2001 May;42(6):1134-45. PMID: 11328719.

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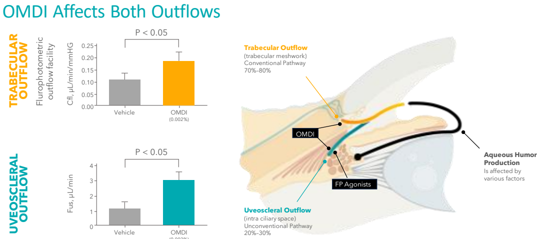
OMDI Affects Both Outflows



1. Matsuo M, Matsuoka Y, Tanito M. Efficacy and Patient Tolerability of Omidenepag Isopropyl in the Treatment of Glaucoma and Ocular Hypertension. *Clin Ophthalmol*. 2022 Apr 26;16:1261-1279.

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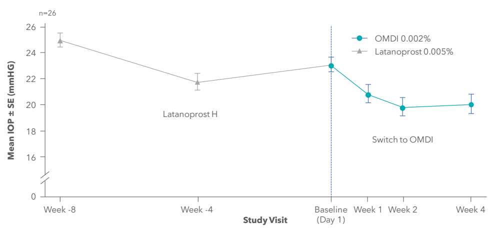
In Latanoprost Non-Responders



1. Aihara M, Ropo A, Lu F, Kawata H, Iwata A, Odani-Kawabata N, Shams N. Intraocular pressure-lowering effect of omidenepag isopropyl in latanoprost non-/low-responder patients with primary open-angle glaucoma or ocular hypertension: the FUJI study. Jpn J Ophthalmol. 2020 Jul;64(4):398-406. .

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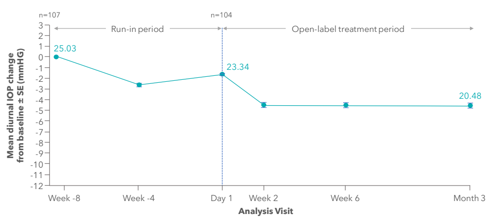
Repeatable Results



1. Panarelli JF, Bowden EC, Tepedino ME, Odani-Kawabata N, Pei Z, McLaurin EB, Ropo A. Omidenepag Isopropyl in Latanoprost Low/Nonresponders With Primary Open Angle Glaucoma or Ocular Hypertension: A Phase 3, Nonrandomized, Two-Phase, Open-Label Study. *J Glaucoma*. 2023 Dec 1;32(12):999-1005.

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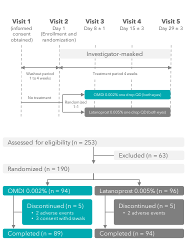
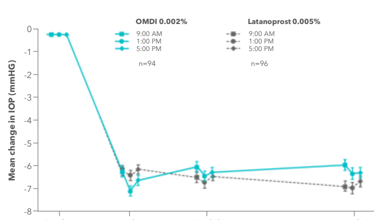
Non-Inferiority — Latanoprost





1. Aihara M, Lu F, Kawata H, et al. Omidenepag isopropyl versus latanoprost in primary open-angle glaucoma and ocular hypertension: the Phase 3 AYAME study. Am *J Ophthalmol*. 2020;220:53-63..

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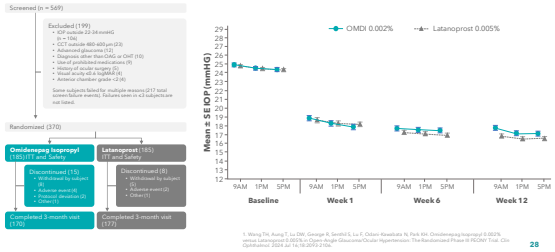
Non-Inferiority – 12 Weeks



1. Wang TH, Aung T, Lu DW, George R, Senthil S, Lu F, Odani-Kawabata N, Park KH. Omidenepag Isopropyl 0.002% versus Latanoprost 0.005% in Open-Angle Glaucoma/Ocular Hypertension: The Randomized Phase III PRIORY Trial. Clin Ophthalmol. 2024 Jul 16;18:2079-2106.

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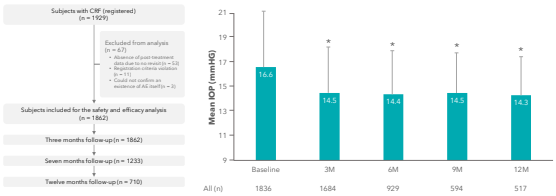
Long-Term Benefit



1. Nakazawa T, Takahashi K, Kuwayama Y, Nomura A, Shimada F. Interim Results of Post-Marketing Observational Study of Omidenepag Isopropyl for Glaucoma and Ocular Hypertension in Japan. Adv Ther. 2022 Mar;39(3):1359-1374. doi: 10.1007/s12325-021-02035-8. Epub 2022 Jan 20.

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EP2 Agonist PAP | Side-effect profile

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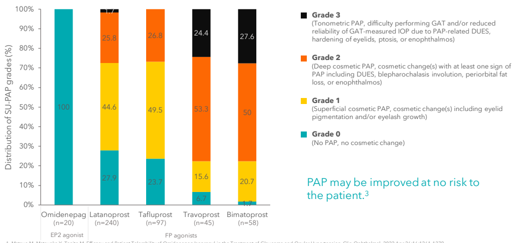
Prostaglandin-Associated Periorbitopathy



PAP may be improved at no risk to the patient.[3]

1. Matsuo M, Matsuoka Y, Tanito M. Efficacy and Patient Tolerability of Omidenepag Isopropyl in the Treatment of Glaucoma and Ocular Hypertension. Clin Ophthalmol. 2022 Apr 26;16:1261-1279.
2. Tanito M, Ishida A, Ichioka S, et al. Proposal of a simple grading system integrating cosmetic and tonometric aspects of prostaglandin-associated periorbitopathy. Medicine. 2021;100(34):e26874.
3. Nakakura S, Terao E, Fujisawa Y, Tabuchi H, Kiuchi Y. Changes in Prostaglandin-associated Periorbital Syndrome After Switch from Conventional Prostaglandin F2α Treatment to Omidenepag Isopropyl in 11 Consecutive Patients. J Glaucoma. 2020 Apr;29(4):326-328.

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A Predictable, Well-Tolerated Safety Profile

Appearance-altering AEs:
2.0% for OMLONTI (n = 4/204)[1]

Hyperemia:
Most hyperemia events were <u>mild</u> in the trials.

Only **2%** discontinuation from Pivotal Phase 3 (n = 4/185)

Most common AEs
Pooled across all clinical trials.

Adverse Event	Rate % (n = 600)
Conjunctival hyperemia	9%
Photophobia	5%
Blurred vision	4%
Dry eye	3%
Instillation site pain	3%
Eye pain	2%
Ocular hyperemia	2%
Punctate keratitis	2%
Headache	2%
Eye irritation	1%
Visual impairment	1%

1. OMLONTI [package insert]. Emeryville, CA: Santen Inc.; 2022.
2. Wirta DL, Lu F, Odani-Kawabata N, Chabi A, Bacharach J. Omidenepag isopropyl 0.002% QD vs timolol maleate BID for open-angle glaucoma/ocular hypertension: the SPECTRUM 4 Trial. Paper presented at: Annual Meeting of American Academy of Ophthalmology; November 12-15, 2021; New Orleans, LA.PO215.

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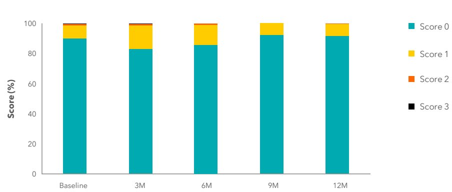
Percentage of Patients for Each Hyperemia Score



1. Nakazawa T, Takahashi K, Kuwayama Y, Nomura A, Shimada F. Interim Results of Post-Marketing Observational Study of Omidenepag Isopropyl for Glaucoma and Ocular Hypertension in Japan. *Adv Ther.* 2022 Mar;39(3):1359-1374. doi: 10.1007/s12325-021-02035-8. Epub 2022 Jan 20.

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So, a patient on latanoprost needs 4 more mm of IOP reduction- do you…

- Add Rhopressa?
- Switch to Rocklatan??
- Add a combo drop??
- Switch to a combo drop??
- Switch to another PGA?
- SLT??

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Elasil, Wang et al , (AJO, May 2014)

- Conclusion – "In POAG substantial RNFL thinning or structural loss appears to be necessary before functional visual field defects become detectable."
- Study showed that there are tipping points on RNFL thickness after which VF defects appear
  - AVG mean RNFL thickness 89 microns BUT>>>
  - Superior RNFL tipping point was 100 microns
  - Inferior RNFL tipping point was 73 microns

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How Does This Affect My Decision Making?

- Interpret OCTs differently
- Get more OCTs

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Speaking of Structure vs Function..

- Banegas SA, et al. – J Glaucoma May 2015
- Compared VF, OCT and Stereo Photographs for their ability to pick up progression
- 68% of progressive cases identified by OCT were initially classified as G suspects
- 61% of progressive cases identified by VF were initially classified as POAG

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Conclusion

- "Progressing Eyes detected by OCT had a higher mean RNFL thickness (>83 microns) and higher mean VFI than progressing eyes detected by VF or stereo photos."
- Soooo….
  - OCT is more likely to detect progression in pre-perimetric disease
  - VF and Photos better at detecting progression in more advanced stages of the disease

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Clinically Important???

What is the significance of this data?

Does this give greater import for 1 test over another?

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- This gives further credence that ALL 3 of the tests have value INDEPENDENT of each other!!

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Visual Fields and Glaucoma

- Are they still cool?
- Are they considered the standard of care?
- How often?
- Can they still be relied upon?
- Do they better measure early detection or progression?

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Visual Fields Are Still Really Cool, But What's the Problem With Them?

- Hard tests to take
- Subjective nature can cause poor reliability
- Poor reproducibility
- Fluctuation between tests
- Takes multiple tests to establish baseline and to show progression
- Patients don't seem to like them!!

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How To Improve VF Test Results

1. Shorten the test time
2. Change the Testing Strategy
3. Increase Spot Size
4. Improve the Testing Environment
5. Increase Frequency of Testing

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SITA Faster

- 2/3 of the test time of SITA Fast
- ½ the test time of SITA Standard
- The test time reductions are greatest in eyes with more severe VF loss
- The average 24-2 test time w/ SITA Faster is ~2 minutes

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SITA Faster - What's The Big Deal?

- Reduces test time by reducing time between presentation of test spots
- Does not dumb down the test!
- Gets rid of redundancies that have been discovered over past 20 years

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SITA Faster – So Again I Say, What's The Big Deal?

- Current recommendations are for more frequent Visual Field testing on each px (EGS, OGS)
- Faster test should allow the patients to be more accepting of the test and better test takers
- Faster tests should see Drs more willing to order tests more frequently
- More frequent VF testing should:
  - Facilitate earlier detection of glaucoma
  - Allow for earlier detection of progression
  - Better determine the rate of progression
- All of which allow us to better clinical decisions for our patients

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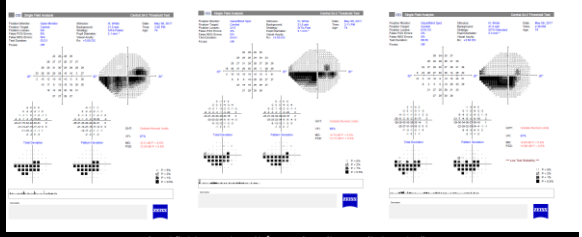

Visual fields courtesy Skåne University Hospital, Malmö, Sweden

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SITA Faster vs SITA Fast

- SITA Faster produces similar results to SITA Fast
- No loss of reproducibility
- Improved reliability
- SITA Faster results integrate into the existing Guided Progression Analysis (GPA) of that individual patient

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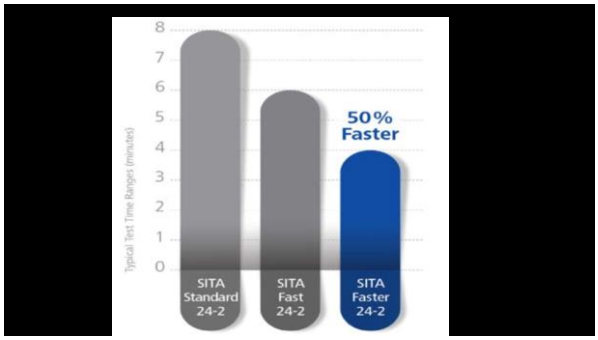

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To Improve Visual Field Analysis Remember The ”5 Rs”

Right Test Strategy

Reliability

Repeatability

Reproducibility

Right Software

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Not your mother’s visual field analyzer anymore!..!..!

Welcome to A Brave New World

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ORIGINAL STUDY

Perimetric Comparison Between the IMOvifa and Humphrey Field Analyzer

Takashi Nishida, MD, PhD; Mark Edani, MD; Robert N. Weinreb, MD; Jose Arias, MD; Cristiana Fiorile, MD, MAE; Fahd Mohammadzadeh, MD; and Yasser Moghimi, MD

J Glaucoma • Volume 32, Number 2, February 2023

- IMOvifa (TEMPO) reduced measurement time by 39%
- MD, PSD, and VFI values for IMOvifa showed good agreement with HFA SITA-Fast strategy.
- Reduced fatigue for both patient and examiner

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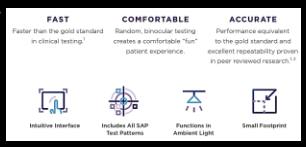
What Makes Tempo Faster?

- Designated dark room not required, **less patient movement** from room to room
- **No eye patching**, no stopping to occlude second eye – one continual, uninterrupted test
- **Stimuli presented to right and left eye randomly** – patient unaware of eye being tested at each point



1. M Edani, T Nishida, S Moghimi, JM Arias, C Vasile, V Mohammadzadeh, RN Weinreb; Comparison Between a New Perimetry Device (IMOvifaTM) and Humphrey Field Analyzer; ARVO Annual Meeting Abstract, IOVS June 2022, Vol.63, 1272 - A0442. 2. M Tafreshi, J Mercau MA, D Kazanoff OD, M Durbin PhD, N El-Nimri OD PhD, and K Cieslinski; Repeatability of Visual Fields Taken With the IMOvifa (Tempo) Binocular Perimeter, ARVO 2023, Poster Number 5925.

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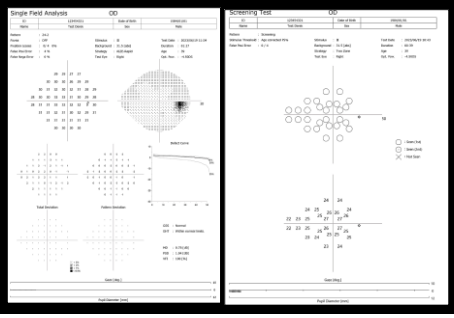
Threshold & Screening Reports



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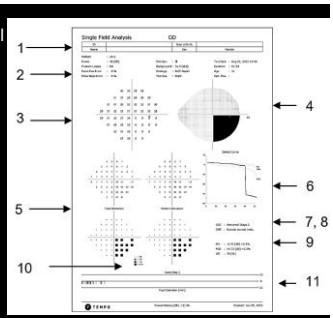
Single Field Analysis (SF) in Detail

1. **Patient data**
2. **Information on the test and reliability indices**.
3. **Threshold values** (dB) are the measured sensitivity thresholds.
4. **Grayscale** is a graphical map of the threshold values.
5. **Deviation plots**
6. **Defect curve** – a graphical representation that provides a summary of the visual field and distinguishes between local and diffuse defects.



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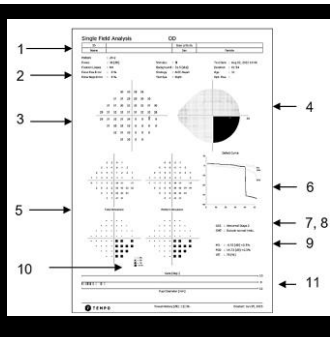
Single Field Analysis (SF) in Detail

7. **GSS (Glaucoma Staging System)** classifies the field based on a plot of Mean Deviation (MD) and Pattern Standard Deviation (PSD).
8. **GHT (Glaucoma Hemifield Test)** analyses the asymmetry between the inferior and superior fields and gives a categorical value such as within normal limits after.
9. **Global Indices**
   - **MD (Mean Deviation)** is the average difference between the patient's overall visual field sensitivity compared to normal vision in the same age group.
   - **PSD (Pattern Standard Deviation)** is a measure of the threshold variability and indicates how the shape of the measured field differs from that of an age-matched normal eye.
   - **VFI (Visual Field Index)** gives a percentage for overall vision. A VFI of 100% indicates no visual field loss whereas 0% means the patient is perimetrically blind.
10. **Probability symbols**
11. **Gaze tracking/pupil diameter**



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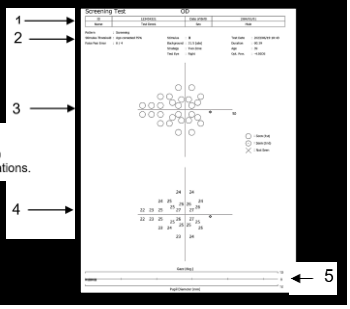
Screening Report in Detail



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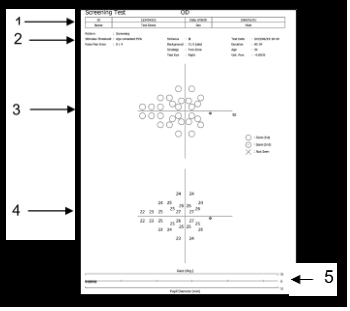
Screening Report in Detail

1. **Patient data**
2. **Information on the test and reliability indices.**
3. **Plot of patient's response to a Goldman size III stimulus** presented at an intensity that an average subject of that age would see with 95% or 99% of the time depending on the option chosen.
4. **Plot of intensity of stimulus** (dB)
5. **Gaze tracking/pupil diameter**



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What are your thoughts on Tempo?

- Advantages?
- Disadvantages?
- Is this a screening device or diagnostic/progression device?
- What strategy do we order?
- How do we incorporate this into our busy day?

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THE RISE OF VR-BASED VISUAL FIELD TESTING

- Compact, portable systems reduce the clinic or store footprint
- Allow more clinic space for speciality eye care or retail optical activiti
- Shorter test durations with improved patient comfort
- Suitable for remote and in-clinic use
- Opens doors to tele-eyecare
- Improved ADA compliance
- Improves doctor and technician productivity
- Improves the quality of patient care
- But not all VR systems are created equal…

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Preliminary Report on a Novel Virtual Reality Perimeter Compared with Standard Automated Perimetry - Journal of glaucoma 9/15/20

- "The global mean sensitivity of the Visu*ALL* and the HFA correlated significantly in both normal (r=0.5, *P*=0.001) and glaucoma (r=0.8, *P*<0.001) groups. The mean sensitivity of all quadrants also correlated significantly in both groups. The Visu*ALL* mean sensitivity had a greater (0.98) Receiving Operating Characteristic (ROC) curve than HFA (0.93) mean sensitivity (*P*=0.06) in discriminating normal versus glaucoma.
- There was an excellent correlation between the VisuALL and the SAP in normal and glaucoma patients and VisuALL showing a high diagnostic performance."

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INDEPENDENT VALIDATION OF HERU

- Johnson et al. (2023) – JOG
- Participants: 71 glaucoma patients, 18 healthy controls
- Results:
  - MD: r = 0.94, ICC = 0.97
  - MS: r = 0.95, ICC = 0.97
  - PSD: r = 0.89, ICC = 0.93


Comparison of Visual Field Test Measurements With a Novel Approach on a Wearable Headset to Standard Automated Perimetry

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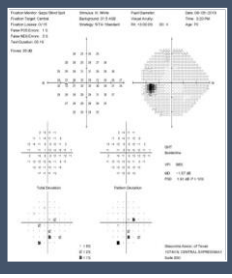
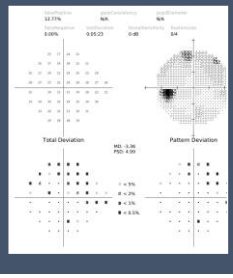
Visuall vs HFA printout





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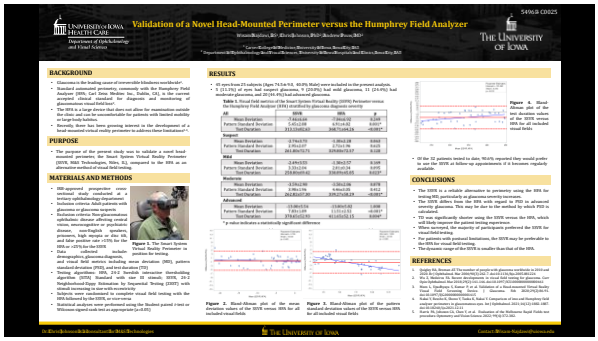


66

PERFORMANCE COMPARISON

Feature	Heru	Olleyes VisuALL	Radius XR	PatmScan VF2000	Virtusi Field
Validation Strength	ICC: 0.97 (MD, MS) 0.93 (PSD)	ICC: 0.95 (MD), 0.84 (PSD)	Slope: 0.48 A slope of 0.48 means Radius XR only detects about half the magnitude of visual field loss compared to HFA.	Kappa: 0.63 overall	ICC: 0.86 (MD), 0.82 (PSD), 0.47 (Pointwise)
Correlation in Normal Eyes	r = 0.94 (combined)	r = 0.5	Not reported	Not reported	Not reported
Correlation in Glaucoma Eyes	r = 0.94 (combined)	r = 0.8	Unable to Differentiate between 1-15 db Poor Correlation 16-23 db Only Correlation 24-40 r = 0.94	Kappa: 0.76 (mild), 0.70 (severe), 0.37 (moderate)	r = 0.87 (MD), 0.94 (PSD)
Test Duration (Glaucoma Group)	~4 min Per Published Study	9.28 min Per Published Study	~5 min	~5.5 min	~Not Reported
Test Duration (Normal Group)	~4 min Per Published Study	6.13 min Per Published Study	~5 min	~5.5 min	~Not Reported
Eye Tracking	Yes	Yes	No	No	VF3: No, VF3 Pro: Yes
Gaze-Based Input	Yes	No	No	No	No
FDA Cleared	Yes	Yes	Yes	Yes	Yes
Spectacle Compatibility	Yes	Yes	No	Yes	Yes
Algorithm Type	SITA-like AI Driven	Full Threshold	Custom	Custom	Custom
Pediatric Validation	Pending	r = 0.39 to 0.11	Not tested	Not tested	Not tested
Dynamic Range	Wide	Moderate	Restricted (15-40 dB)	Moderate	Moderate (low pointwise ICC)
Published Peer-Reviewed Study	Yes (IOG 2023)	Yes (IOG 2021, TVST 2024)	Yes (TVST 2024)	Yes (IOG 2024, IOVR 2022)	Yes (OPO 2024)

67

CONCLUSIONS

- Several VR-based perimetry devices show clinically acceptable validity
  - Performance often varies by disease severity, with better performance in moderate to severe glaucoma
- FDA clearance alone does <u>not</u> guarantee equivalence to gold standard HFA
- The heterogeneity of published studies limits the depth of comparable validity assessments
- Future research is needed to:
  - Standardize testing protocols
  - Validate devices in broader patient populations
  - Evaluate detection of progression over time

68

Are Virtual Reality Visual fields the way of the future?

- PROVE IT TO ME!!!
- Normative data bases
- What about progression analyses??
- Consistent reliability
- Data I can depend upon
- DO THEY ACTUALLY WORK???

69

If Virtual Reality VFs are so good…

Why aren't Glaucoma Specialists Using Them?

Why aren't they universally accepted?

70

Billing and Coding concerns

- Is this a screening or ordered test? (That will determine the fee)
- 92083 – again diagnosis must correlate with procedure code used
- Test must be ordered and interpreted
- What do you do if screening shows an abnormal result?

71

The Structure vs Function Dilemna

- Structural damage leads to functional damage
- Do they always correlate though?
- If they don't why???

72

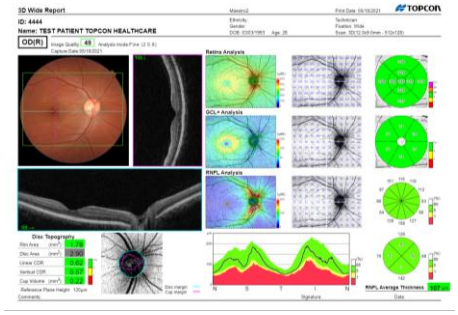
THIS ISN'T YOUR FATHER'S OCT REPORTS ANYMORE!.!.!.

Welcome To The Brave new world!!

73

3D WIDE STANDARD REPORT

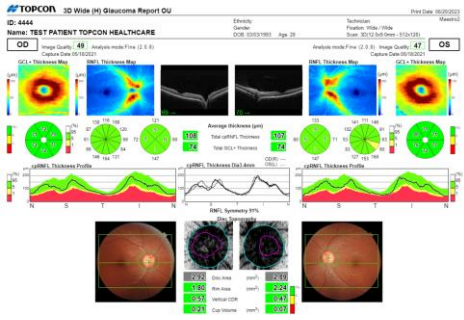
Your new standard. One scan blanketing the posterior pole generating RNFL, ONH, GCL and ETDRS data of nerve and macula.



74

3D WIDE GLAUCOMA REPORT OU

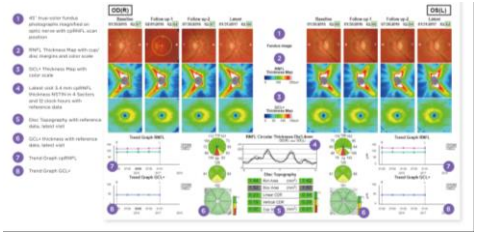
One scan per eye presents exhaustive data for the Glaucoma suspect and known Glaucoma patients alike.



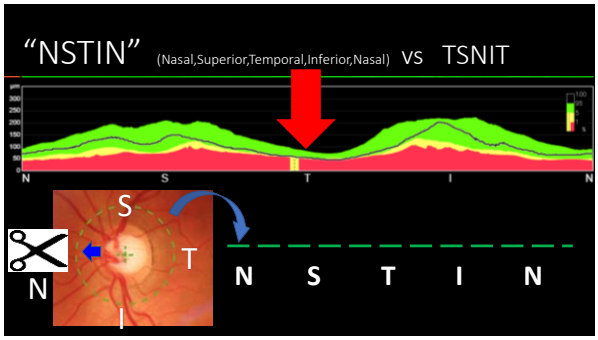
75

3D WIDE TREND REPORT OU

3 Key Metrics presented over time from just one scan per eye.



76

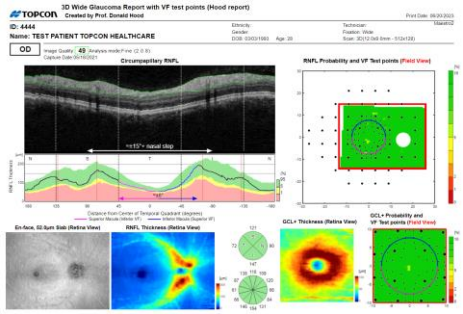


77

HOOD REPORT FOR GLAUCOMA

Generated from one **3D Wide Scan**

RNFL and GCL Probability Maps



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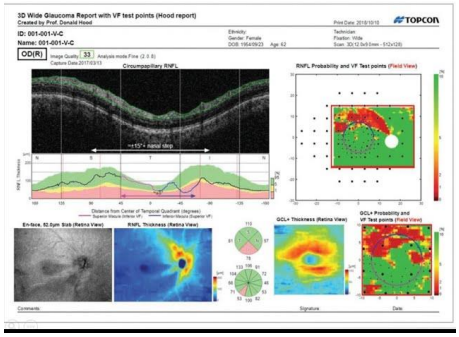
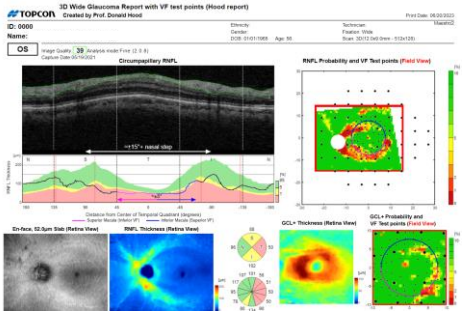


79

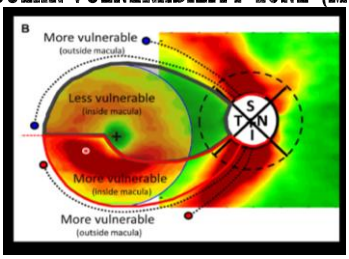
HOOD REPORT FOR GLAUCOMA

Reference STRUCTURAL RNFL and GCL deficiencies with FUNCTIONAL vulnerability.



80

MACULAR VULNERABILITY ZONE (MVZ)



81

DID YOU SEE THE DISC HEMORRHAGE?

82

Detection and Prognostic Significance of Optic Disc Hemorrhages during the Ocular Hypertension Treatment Study

Donald L. Budenz, MD, MPH,[1] Douglas R. Anderson, MD,[1] William J. Feuer, MS,[1] Julia A. Beiser, MS,[2] Joyce Schiffman, MS,[2] Richard K. Parrish II, MD,[1] Judy R. Piltz-Seymour, MD,[2] Mae O. Gordon, PhD,[2] Michael A. Kass, MD,[2] Ocular Hypertension Treatment Study Group

Main Outcome Measures: Incidence of optic disc hemorrhages and POAG end points.
Results: Median follow-up was 96.3 months. Stereophotography-confirmed glaucomatous optic disc hemorrhages were detected in 128 eyes of 123 participants before the POAG end point. Twenty-one cases (16%) were detected by both clinical examination and review of photographs, and 107 cases (84%) were detected only by review of photographs ($P<0.0001$). Baseline factors associated with disc hemorrhages were older age, thinner corneas, larger vertical cup-to-disc ratio, larger pattern standard deviation index on perimetry, family history of glaucoma, and smoking status. The occurrence of a disc hemorrhage increased the risk of developing POAG 6-fold in a univariate analysis ($P<0.001$; 95% confidence interval, 3.6–10.1) and 3.7-fold in a multivariate analysis

83

Detection and Prognostic Significance of Optic Disc Hemorrhages during the Ocular Hypertension Treatment Study

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- Disc hemorrhages detected in 128 eyes of 123 participants
- 21 cases detected by both doctor and photos
- **107 cases (84%) were detected only by a review of photography**

84

DISK HEMORRHAGES AND RATE OF PROGRESSION (MEDEIROS ET AL)

- Cohort of the DIGS
- Pxs followed for 8 years for VF progression (using the VFI)
- 20% had disk hemorrhage
- Eyes with disk heme had more than double the rate of VF loss
- Eyes w/ more than 1 disk heme showed an even higher rate of VF progression
- Persons with disk heme in general had a more severe glaucoma

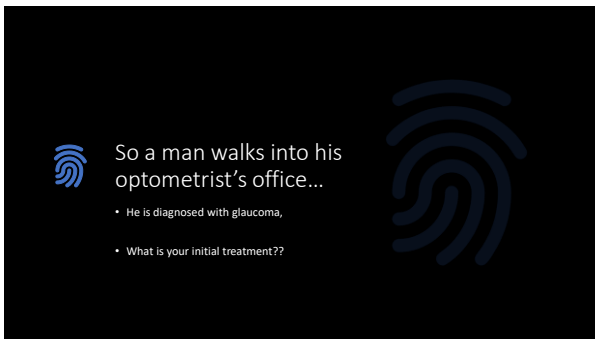
85

SPEAKING OF OPTIC DISK HEMORRHAGES

- BUDENZ ET AL, (OHTS GROUP) – AJO 2/17
- 13 YEAR DATA

- ODH ARE AN INDEPENDENT PREDICTOR FOR POAG
- ODH ARE PREDICTIVE OF PROGRESSION
- PREDICTIVE FACTORS FOR ODH ARE SIMILAR TO THOSE FOR POAG (IN OHT PXS)
  - Thin corneas
  - Thinner rims
  - Higher IOP
  - Older age

86



87

LiGHT Study

- SLT versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicenter randomized controlled trial

Gus Gazzard, Eugenias Konstantakopoulos, David Garway-Heath et al

www. thelancet.com Vol 393 April 13, 2019

- Pxs had to have mild or moderate glaucoma based on VF criteria
- Target IOP reduction 20-30% (depending on severity)
- Standard SLT energy protocols
- Medicine group – 1st line PGA, 2nd Line Beta blocker, 3rd line CAI or Alpha agonist
- Both groups followed for 36mths

88

LiGHT study outcomes

Both groups showed similar efficacy in lowering IOP

- 16.3mm Hg Drop group, 16.6 mm Hg SLT Group
- 78.2% SLT group required no drops, 12% required 1 drop
- 64.6% drop group controlled on 1 drop, 18.5% required 2 drops
- 0% SLT Group required trab, 3.3% Drop group required trab
- 93% SLT group at target IOP, 95% Drop group

SLT Group spent 202 pounds less on care

So what does this mean for us , our clinics and our patients??

89

Does The LiGHT Study…

1) Change your impression of the efficacy of SLT?

2) Change your impression of when you would recommend SLT for your patients?

3) Change your impression on who may be good candidates for SLT?

90

Automated Direct SLT (Belkin)

91

Belkin DSLT

- Rapid, non-contact Direct SLT
- Delivers similar energy as traditional SLT
- Automated delivery of energy through limbus (transconjunctival)
- Without Gonioscopy
- Will be approved in US within months!!

92

DSLT Data

Baseline IOP 26.7-

- Patients were washed out of all meds
- Some pxs were treatment naïve

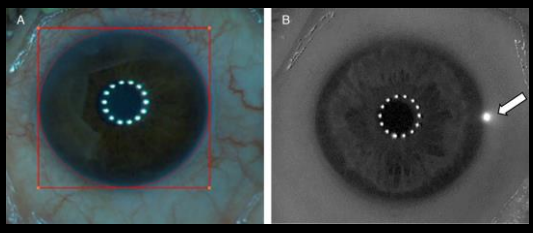
After tx IOP

- 1 mth – 21.7mm Hg (18.1% reduction)
- 3 mth- 20.8mm HG (21.4%)
- 6 mth 21.5mm Hg (18.8% reduction)

At 6 mths medication need reduced from 1.6 to 0.4

93

Automated Direct SLT



94

#This Is A BFD!!

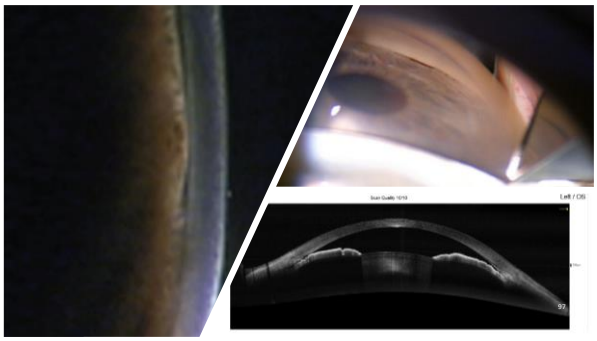
Are we ready???

95

So, a patient on latanoprost needs 4 more mm of Iop reduction- do you…

- Add Rhopressa?
- Switch to Rocklatan??
- Add a combo drop??
- Switch to a combo drop??
- Switch to another PGA?
- SLT??

96

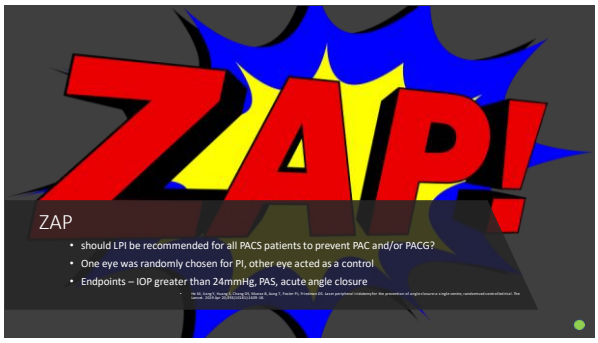


97

Critical Questions

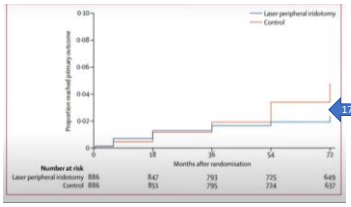
- Should we dilate?
- Should we perform gonioscopy?
- Should we perform or recommend LPI?
- Should we recommend cataract extraction?

98



99

ZAP



- End of 3 years – not much going on, continue study another 3 years
- showed a statistically significant but clinically small decrease in the risk of PAC conversion and **recommend against the widespread use of prophylactic LPIs in their study population**
- 44 PACS patients needed treatment to prevent one new PAC case over six year
- 126 needed to prevent one case of PACG

100

ZAP – 14 year data!!!

- 69% reduced risk of PAC with LPI
- NNT to prevent 1 case of PAC at 14 years is 12.35
- "prophylactic LPI should be recommended preferentially to those at the highest risk because the annual incidence of PAC was low"

Yuan Y, Wang W, Xiong R, Zhang J, Li C, Yang S, Friedman DS, Foster PJ, He M. 14-Year Outcome of Angle-Closure Prevention with Laser Iridotomy in the Zhongshan Angle Closure Prevention Study: Extended Follow-Up of a Randomized Controlled Trial. Ophthalmology. 2023 Apr 4.

101

What about dilation?

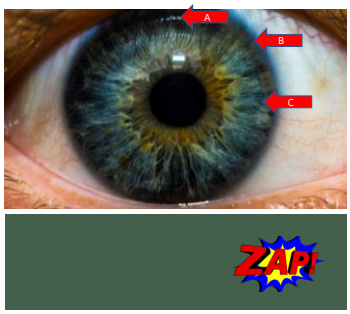
- Dilated 6 or 7 times
- 2.5% and 1%
- Everyone received 250 mg diamox
- If 8mmHg increase, drop of pilo and brimonidine

102

Highest Risk of Closure

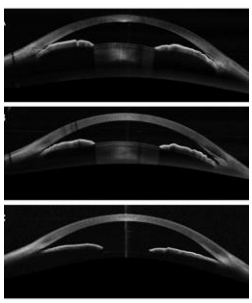
- Closed in all 4 quadrants
- Average refractive error of +4.00

103

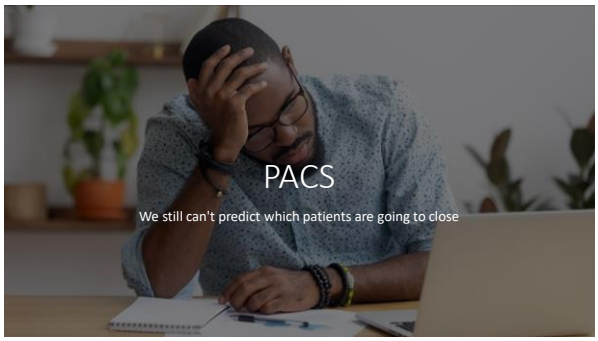


- Untreated eyes narrowed by 20%
- A is most efficacious
  - Xu BY, Friedman DS, Foster PJ, Jiang Y, Pardeshi AA, Jiang Y, Munoz B, Aung T, He M. Anatomic Changes and Predictors of Angle Widening after Laser Peripheral Iridotomy: The Zhongshan Angle Closure Prevention Trial. Ophthalmology. 2021 Jan 23

104



105



106

What do we do with PACS?

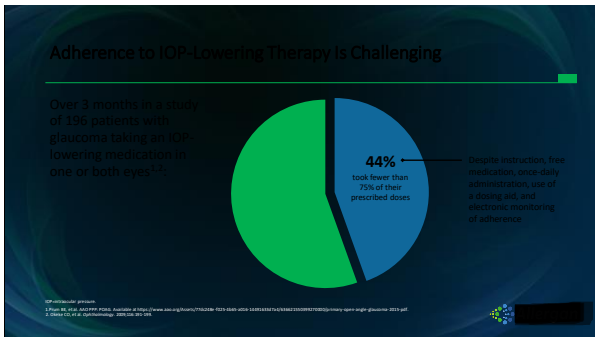
- In our clinic, we typically follow most asymptomatic PACS patients every six to 12 months. We monitor for changes in the angle, optic nerve and visual field.
- While we approach each patient individually, we generally perform LPI, clear lens exchange or cataract extraction if:
  - the patient mentions symptoms suggestive of closure
  - has a family history of angle-closure
  - if they show progression of angle narrowing or progression to PACG
  - they need frequent dilation
  - they are unusually hyperopic

107

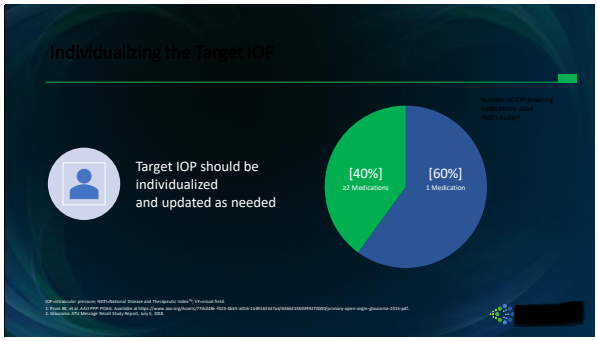
And Now It's Time To Talk About Compliance!!!!!

This is so not Cool…

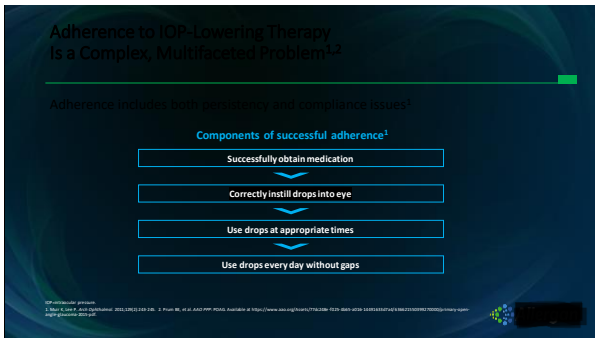
108


Adherence to IOP-Lowering Therapy Is Challenging
Over 3 months in a study of 196 patients with glaucoma taking an IOP-lowering medication in one or both eyes[1,2]:
44%
took fewer than 75% of their prescribed doses
Despite instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence

109


Individualizing the Target IOP
Target IOP should be individualized and updated as needed
[40%]
≥2 Medications
[60%]
1 Medication

110


Adherence to IOP-Lowering Therapy Is a Complex, Multifaceted Problem[1,2]
Components of successful adherence[1]
Successfully obtain medication
Correctly instill drops into eye
Use drops at appropriate times
Use drops every day without gaps

111

Compliance really is a hot topic

- Dr David Friedman – OGF Educators Meeting 9/19
- Looked at compliance studies in glaucoma- found that 70% compliance with medications was average
- But is that good enough to preserve VF?
- Friedman also showed that those who said they missed their drops some of the time… actually used their drops ~50% of the time.
- That was much worse than those who say they never miss their drops

112

Predictors of Poor Adherence – Friedman 2019

- Gaps In Visits
- Patients Don't Understand Severity Of Disease
- Cost of Drops (25%)
- Those who Travel A Lot
- Younger Pxs and Very Old Pxs
- African-Americans
- Those In Poor Health
  - These drop adherence to <60%

113

Compliance, adherence and side effects of therapy

- Compliance decreases the more bottles Rx'd
- Robin – Each extra bottle used decreased compliance by 1/3
- The more topical meds used the more ocular side effects occur
- OSD in G pxs (way) higher than initially thought
- 60% of G pxs use ocular lubricants

114

What are the biggest barriers to proper compliance?

1. Forgetfulness
2. Ability to put drops in
3. Unaware of the importance of the drops

Cost was not in the top 5!!!

115

Ways To Improve Compliance

- See Pxs more frequently… especially early in treatment
- Improve tracking system – better identify no shows
- Call/email appointment reminders
- Reminders to pxs to take their drops
- Change Dr/Patient intervention

- G pxs ask 3.2 questions at visit whereas in other chronic diseases pxs ask ~ 6 questions/visit

116

THE PROBLEM OF 24 HOUR IOP

- Both measuring and Controlling it

117

HOW IOP IS USUALLY MEASURED

- Typically a **single observation**
- During **office hours**
- A moment in time or representative of the entire day?
- Are we missing spikes, peak, or elevated IOPs at other times of day?

118

118

WHEN IS THE PEAK IOP?

- 3,025 IOP readings on 1,072 eyes
- NTG, POAG, Pre-perimetric G, OHT
- Results:
  - Peak IOP – 7AM – 20.4%
  - Noon – 17.8%
  - 5PM - 13.9%
  - 9PM – 26.7%
    - Jonas, Budde, et al. AJO, June 2005;139:136-137

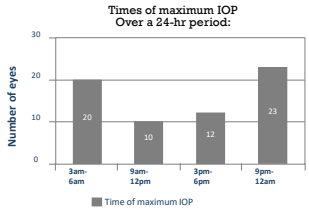
119

JONAS STUDY CONCLUSION

- "Any single IOP measurement taken between 7AM and 9PM has a higher than 75% chance to miss the highest point of the diurnal curve."
- Stresses the need for serial tonometry.

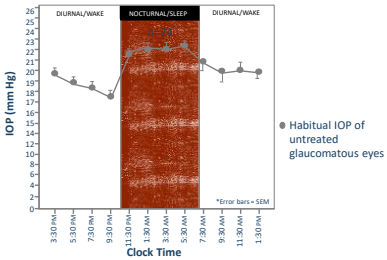
120

PEAK IOP OUTSIDE OFFICE HOURS FOR 2/3 OF EYES



121

IOP IS HIGHER AT NIGHT



122

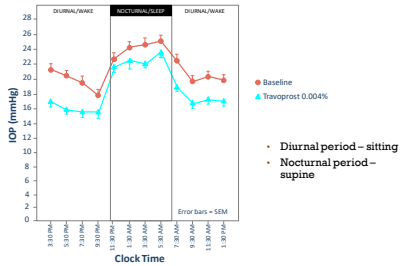
OBSERVATIONS

- Reducing IOP reduces risk of progression[1-5]
- Peak IOPs often occur outside normal office hours[6-9]
- IOP during office hours does not provide a complete picture of diurnal and nocturnal IOP[6-9]
- What does this mean about your choice of medical therapy?

1. Heijl A, et al. *Arch Ophthalmol.* 2002; 120(10): 1268-1279.
2. Kass MA, et al. *Arch Ophthalmol.* 2002; 120(10): 701-713.
3. AGIS Investigators. *Am J Ophthalmol.* 2000; 130(4): 429-440.
4. Lichter PR et al. *Ophthalmology* 2001; 108: 1943-1953.
5. CNTGS. *Am J Ophthalmol.* 1998; 126(4): 487-497.
6. Nakakura S, et al. *J Glaucoma* 2007; 16(2): 201-204.
7. Mosaed S, et al. *Am J Ophthalmol.* 2005; 139: 320-324.
8. Hughes E, et al. *J of Glaucoma* 2003; 12: 232-236.
9. Liu JH et al. *Invest Ophthalmol Vis Sci.* 2003; 44: 1586-1590.

123

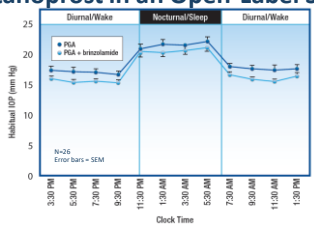
EFFECT OF TRAVOPROST ON DIURNAL AND NOCTURNAL IOP (CONT'D)



- Diurnal period – sitting
- Nocturnal period – supine

124

Brinzolamide: Adjunct to Latanoprost in an Open-Label Study



125

SO HOW DO WE BEST MEASURE 24 HOUR IOP

- Multiple iop readings
- At home monitoring
  - Triggerfish
  - Icare "home" tonometer

126

WHAT CAN WE DO TO BETTER CONTROL IOP OVER A 24 HOUR PERIOD?

- Pick the right drop(s)
- Choose the right procedure
- Identify the Problem
- Get the necessary data

127

In home tonometry

128

Icare home tonometer

- Rebound tonometer
- No anesthesia
- Px is seated
- Automatic od/os recognition
- r/g lights guide alignment
- Push button "switch"
- Can take 1 reading or 6 consecutive
- Data stored in instrument
- Download data in doctor's office

129

Icare home tonometry

- Readings are not printed out or displayed to patient
- Readings are in mm hg
- No cpt code
- Not reimbursible – because it is administered by the px
- Px rents machine from dr
  - Rental rate is set by dr
  - Abn (waiver of benefits) must be signed by px

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Icare home tonometer is it feasible?

- Pronin, brown, et al – jama ophthalmol (online) 8/31/17
- Report on reproducibility and acceptability of iop as measured by patients

- All pxs had oht or poag
- Gat and icare home tonometry performed by dr in office
- Icare home tonometry performed by px in office

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Pronin et al - results

- 73/100 pxs showed measurements w/in 5mm of doctor
- Icare home readings were consistently lower than iop/gat
- This was more pronounced in lower ranges of iop

- Self tonometry was judged “easy and comfortable” by most patients
- 92% of pxs reported: “ they would be happy to perform self-tonometry in future”

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Tagaki et al
Jglaucoma 26(7): 613-618, july 2017

- Compared iop measurements of goldmann tonometry with icare home tonometry both by patient and by doctor
- Mean iop ranges
  - Gat: 7- 20 mm Hg
  - Icare (px): 6-24mm hg
  - Icare (dr): 6-25mm hg
- Was found to be "feasible"
- Icare home showed a tendency to record higher iop readings as compared to gat

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So…

- More iop readings give us more data points from which to make decisions
- It is reproducible
- It is feasible
- But…

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I have some questions

1. Is a 5mm difference between patient and doctor acceptable?
2. Do elevated iop readings on icare home lead to vf defects
3. Is this true 24 hr data?
4. Will this become standard of care?
5. Will this data lead to a change in treatment for the px?

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Triggerfish cls

- Wearable cl sensor
  - Single use cl (8.4, 8.7, 9.1 bc), 14.1 mm diameter, 585 microns thick
- Also incorporates:
  - 2 strain gauges
  - Microprocessor
  - Periorbital adhesive (holds receiver antenna)
  - Recorder sleeve

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Triggerfish cls

- Worn for 24 straight hours
- Telemetric sensor
- Takes 30 seconds of readings at 5 min intervals for 24 hrs

- It is not tonometry
- It doesn't measure iop
- Measures strain differences

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Triggerfish cls pros

- Continual 24 hr data
- No px involvement
- Gathers data while sleeping, standing, sitting, during physical activity
- It is felt that iop changes with those activities as well

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Triggerfish Cons

- Uncomfortable
- Ugly
- Expensive
- May cause corneal issues
- Not available in U.S.

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Neuroprotection

- What Is It?
- How Is It Measured?
- Does It Actually Exist?
- Can We Even Say The Word?

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Neuroprotection with an EP2 Agonist

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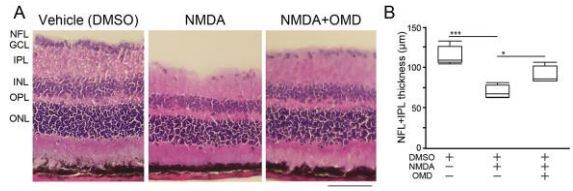
Omidenepag prevents retinal thinning



1. Nakamura N, Honjo M, Yamagishi-Kimura R, Sakata R, Watanabe S, Aihara M. Neuroprotective effect of omidenepag on excitotoxic retinal ganglion cell death regulating COX-2-EP2-cAMP-PKA/Epac pathway via Neuron-Glia interaction. Neuroscience. 2024 Aug 16;553:145-159.

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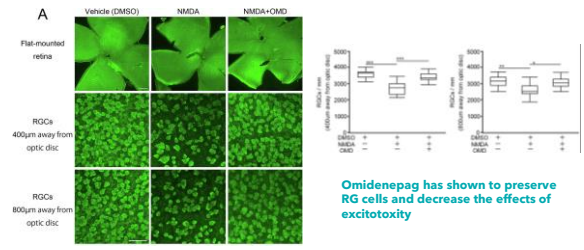
Omidenepag prevents RG cell loss



Omidenepag has shown to preserve RG cells and decrease the effects of excitotoxity

1. Nakamura N, Honjo M, Yamagishi-Kimura R, Sakata R, Watanabe S, Aihara M. Neuroprotective effect of omidenepag on excitotoxic retinal ganglion cell death regulating COX-2-EP2-cAMP-PKA/Epac pathway via Neuron-Glia interaction. Neuroscience. 2024 Aug 16;553:145-159.

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What Does Neuroprotection Mean Clinically?

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