NEW ORLEANS ACADEMY OF OPHTHALMOLOGY

Real World Studies on Steroids in Uveitic macular edema

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Financial Disclosures

- *Consultant:* Alimera, Allergan, ANI, Apellis, EyePoint, Genentech, Astellas, , Ocular Therapeutics, Regeneron
- *Speaker Contracted by Ineligible Company:* Allergan, ANI, Apellis, EyePoint, Genentech, Astellas, Regeneron
- *Independent Research Contractor:* Allergan, Apellis, Ashvatha ,EyePoint, Genentech, Astellas, , Kodiak, Optos, Regeneron, Rezolute, Valo
- **Individual Stocks and Stock Options (privately held):* Aviceda, Inflammasome, Nanoscope, Olives BioTherapeutics

IOP: SCS triamcinolone

Durability with suprachoroidal injection of triamcinolone acetonide injectable suspension for uveitic macular edema and use of rescue therapy in clinical practice

Michael Singer, Durga Borkar, Abhishek A. Nair, Andrew LaPrise, Kristian Garcia, Joel Fain, Teresa Brevetti, David J. Harrison

IOP: SCS triamcinolone

Introduction

IOP: SCS triamcinolone

Background:

- Triamcinolone acetonide injectable suspension for suprachoroidal use is a corticosteroid indicated for the treatment of macular edema (ME) associated with uveitis
- Suprachoroidal administration via proprietary SCS Microinjector™ is a technique in which drug is delivered to the space between the sclera and the choroid
  - The medication distributes in the suprachoroidal space and is delivered directly to the retina and choroid, sparing the anterior chamber
  - This minimizes the potential for cataract formation and/or increased intraocular pressure
- In clinical trials, the time to rescue therapy relative to subjects' first injection was assessed, however all patients were required by protocol to have a second injection or sham at week 12[1]
  - A subset of patients were followed past 6 months in the Magnolia study and 50% went as long as 6 months without rescue[2]

Objective:

- To understand durability of suprachoroidal triamcinolone acetonide injectable suspension and subsequent practice patterns for treatment of uveitic macular edema (UME) in clinical practice

1. Yeh S, Khurana RN, Shah M, et al. Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial. *Ophthalmology*. 2020;127(7):948-955. doi:10.1016/j.ophtha.2020.01.006
2. Khurana RN, Merrill P, Yeh S, et al. Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). *Br J Ophthalmol*. 2022;106(8):1139-1144. doi:10.1136/bjophthalmol-2020-317560

IOP: SCS triamcinolone

Methods

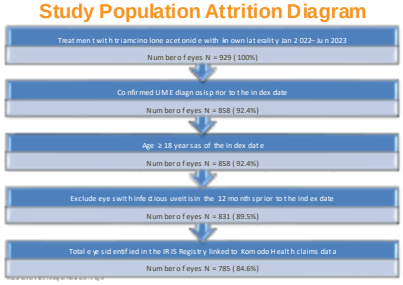
IOP: SCS triamcinolone

- Patients ≥18 with a diagnosis of non-infectious UME and a suprachoroidal injection of triamcinolone acetonide after January 2022 were identified in the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)
  - The date of the first suprachoroidal injection defined the index date
- IRIS data was linked to Komodo open-source claims data (Jan 2022 to Jun 2023) using the Datavant token to identify corticosteroid use
  - Rescue was defined as use of injectable, implanted, or topical corticosteroids after the initial triamcinolone acetonide suprachoroidal injection
- Patients were followed for 24 weeks after their injection for duration
- A sub-study was performed on IOP: patients followed for 48 weeks

IOP: SCS triamcinolone

Results

Study Population Attrition Diagram



Baseline Demographic and Clinical Characteristics

Total eyes	838 (1000%)
Age	
Mean (SD)	682 (136)
Sex	
Female	557%
Male	443%
Race	
Asian	17%
Black or African American	94%
White	858%
Other race	83%
Unknown	148%
Ethnicity	
Hispanic	48%
Non-Hispanic	647%
Unknown	304%
Insurance/payer type	
Medicare	534%
Medicare Advantage	97%
Medicaid	46%
Commercial	260%
Other/Unknown	63%

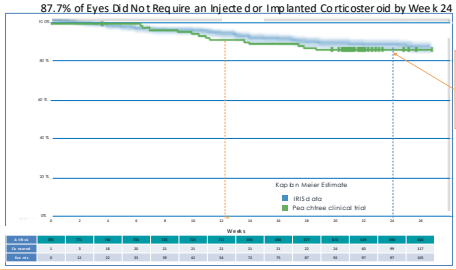
Ocular comorbidities	
Uncontrolled diabetic retinopathy	448%
Cataract	247%
nAMD	23%
DR with DME	35%
DR with out DME	43%
MH from CRVO	16%
MH from BRVO	26%
Retinal Detachment	144%
Posterior uveitis	811%
Panuveitis	146%

Treating provider subspecialty	
Retina/Vitreous Specialist	863%
Cataract /Anterior Segment Specialist	59%
Other/ Unknown	78%

Prior corticosteroid use *	
Injectable/implantable with or without topical	352%
Topical only	173%

Time to Rescue with Injectable/Implantable Corticosteroids

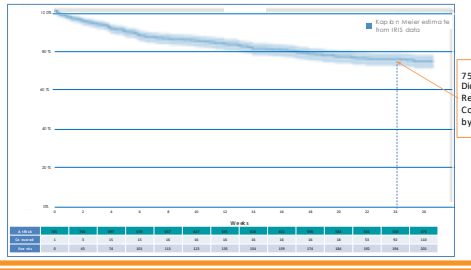
87.7% of Eyes Did Not Require an Injected or Implanted Corticosteroid by Week 24



In Peachtree 86.5% did not require rescue therapy by week 24

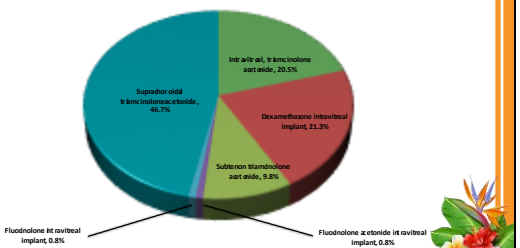
*In Peachtree, all subjects had a second injection at week 12

Time to Rescue with Any Corticosteroid



75.4% of Eyes Did Not Require Any Corticosteroid by Week 24

Types of Injected/Implanted Rescue Therapy



- Only 12% % of patients with UME required a subsequent injected or implanted corticosteroid in the 24 weeks after a single suprachoroidal injection of triamcinolone
  - Suprachoroidal triamcinolone was used in 45% of patients who had a second injectable/implantable corticosteroid
- An additional 12% of patients used only a topical corticosteroid in the same time period
- A second suprachoroidal injection 12 weeks after the first was only seen in 2.4% of patients and does not appear to be part of routine practice
  - By comparison, all subjects in the Peachtree clinical trial were required by protocol to have a second suprachoroidal injection at week 12
- These results are similar to those of the Peachtree trial in which 13.5% of subjects required rescue by week 24
- In addition, nearly half of these patients a history of ocular hypertension or glaucoma and over half had prior steroid use suggesting that there were chronic, hard to treat patients

IOP with Fluocinolone implant

CALM

CALM: 36-month safety outcomes with the 0.18 mg intravitreal fluocinolone acetonide implant for non-infectious uveitis

Michael Singer, MD[1]
ON BEHALF OF THE CALM REGISTRY STUDY INVESTIGATORS AND SUPPORTING CLINICAL SITES

[1]Medical Center Ophthalmology Associates, San Antonio, TX

IOP with Fluocinolone implant

Purpose & Methods

PURPOSE

To analyze phase 4 **real-world outcomes** among **patients with chronic NIU-PS receiving the IVT 0.18 mg fluocinolone acetonide implant (FAi)**

METHODS

Real-world data were collected for patients ≥18 years old **treated with the 0.18 mg IVT FAi** from US sites participating in the **CALM registry study**

As available, uveitis recurrence, OCT, visual acuity,* vitreous haze, IOP measurements, and other safety data including adverse events, cataract extractions, and IOP-lowering surgeries, were collected for each follow-up visit

*Snellen acuities were converted to ETDRS letter scores.
ETDRS, Early Treatment Diabetic Retinopathy Study; **FAi,** fluocinolone acetonide implant; **IOP,** intraocular pressure; **IVT,** intravitreal; **NIU-PS,** non-infectious uveitis affecting the posterior segment; **OCT,** optical coherence tomography.

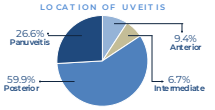
IOP with Fluocinolone implant

Results: Baseline Characteristics & Demographics

N=267 eyes from 200 patients	
Age, mean ± SD	62.8 ± 14.2
Female, n (%)	131 (65.5)
Pseudophakic, n (%)*	237 (88.8)
Race, n (%)	
White	138 (69.0)
Black	33 (16.5)
Hispanic/Latino	17 (8.5)
Other	10 (5.0)
Asian	2 (1.0)

*At baseline, 28 (10.5%) eyes were ephakic and 2 (0.7%) eyes were aphakic.
SD, standard deviation.

LOCATION OF UVEITIS

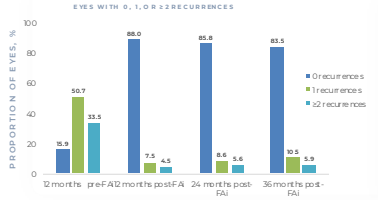


- **>85% of eyes** were diagnosed with **posterior or panuveitis**
- Most cases were **idiopathic (63.5%)**, and **sarcoidosis (6.1%) was the most common known etiology**
- Mean ± SD **duration of uveitis was 5.6 ± 5.7 years**

IOP with Fluocinolone implant

Results: Reduced Uveitis Recurrences After the 0.18 mg FAi

EYES WITH 0, 1, OR ≥2 RECURRENCES



12 months before FAi, 8.4% of eyes had ≥1 recurrence of uveitis

36 months after FAi, 16.5% of eyes had ≥1 recurrence of uveitis

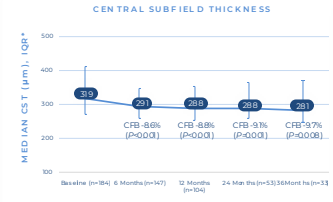
Through 36 months, 4.9% of eyes **received >1 FAi**

- 4.5% received 2
- 0.4% received 3

Recurrence of uveitis was determined by investigators/as noted in patient charts, with no prespecified clinical criteria.
Sum of percentages may not equal 100% due to rounding.
FAi, fluocinolone acetonide implant.

IOP with Fluocinolone implant

Results: Reduced Central Subfield Thickness after the 0.18 mg FAi

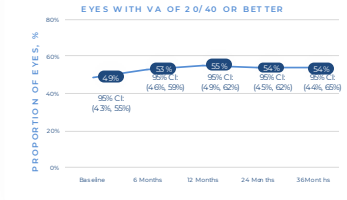


- Reduction in CST was maintained through 36 months post-FAi
- The proportion of eyes with CST ≥300 µm decreased from 56% at baseline to 40% at 36 months

n=number of eyes.
*IQR illustrated as a barat each timepoint showing upperand lower quartiles.
†CFB results are fromseparate linear mixedmodelanalyseson log-transformed data.
CFB, change frombaseline **CST,** centr al subfield thickness; **FAi,** fluocinolone acetonide implant; **IQR,** interquartile range

IOP with Fluocinolone implant

Results: Stable VA After the 0.18 mg FAi



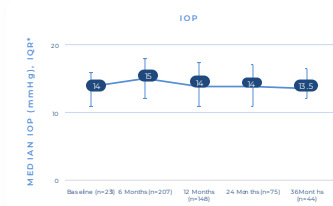
Through 36 months:

- The proportion of eyes with VA of 20/40 or better was stable post-FAi
- 19% of patients had an increase of ≥15 ETDRS letters* vs baseline (95% CI: 12%, 29%)

*mean acuities were converted to ETDRSletter scores.
Results are fromlogisticregression modelwithgeneralized estimating equations.
CI, confidence interval; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **FAi,** fluocinolone acetonide implant; **VA,** visual acuity.

IOP with Fluocinolone implant

Results: Stable IOP After the 0.18 mg FAi



Through 36 months, median **IOP remained stable**

IOP-lowering medication reported for 21.7% (58/267 eyes) at baseline and 36.5% (19/52 eyes) at 36 months

n=number of eyes.
*IQR illustrated as a barat each timepoint showing upperand lower quartiles.
FAi, fluocinolone acetonide implant; **IOP,** intraocularpressure; **IQR,** interquartile range

IOP with Fluocinolone implant

Results: IOP Event & Surgery Rates After the 0.18 mg FAi

IOP Events and Surgeries Through 36 Months	n (%) N=267	Months to event from baseline, mean ± SD
IOP increase >10 mmHg from baseline*	40 (17.3)	14.5 ± 11.0
IOP >30 mm Hg	15 (5.6)	11.0 ± 10.0
Laser trabeculoplasty	3 (1.1)	5.0 ± 3.5
MIGS	3 (1.1)	24.0 ± 3.0
Incisional IOP-lowering surgery	12 (4.5)	
Tube implantation	8 (3.0)	11.6 ± 9.7
Trabeculectomy with antimetabolites†	2 (0.8)	15.0 ± 8.5
Trabeculectomy without antimetabolites†	2 (0.8)	4.5 ± 2.1

4 (14.3%) of eyes had cataract surgery
- * n=28 eyes were phakic at baseline

*N=281 eyes with available data.
†MMC=5-FU antimetabolite.
5-FU, 5-fluorouracil; **FAi,** fluocinolone acetonide implant; **IOP,** intraocular pressure; **MIGS,** micro-invasive glaucoma surgery; **MMC,** mitomycin C; **SD,** standard deviation.

IOP with Fluocinolone implant

Limitations

- Participating sites examined and managed patients using their own protocols
- Investigators were not able to completely ensure control and consistency over data collection and input due to the retrospective nature of the study
- Pre-FAi treatment data was not collected
- Participants could be added into the registry at any time after the FAi was implanted, leading to variable rates of follow-up
- Administration details of IOP-lowering medications were not reported in the study

FAi, fluocinolone acetonide implant.

IOP with Fluocinolone implant

Conclusions

- The 0.18 mg IVT FAi is **indicated for the treatment of chronic NIU-PS**[1]
- Evidence from this **real-world registry** builds on controlled clinical studies[2-4]
- The 0.18 mg FAi **provided long-term improvements in inflammatory flares,** with no new safety signals

THREE YEARS POST-IVT FAi

- Substantial reduction in rate of uveitis flares vs pre-FAi
- Improved OCT findings and stable vision

FAi, fluocinolone acetonide implant; **IVT,** intravitreal; **NIU-PS,** non-infectious uveitis affecting the posterior segment; **OCT,** optical coherence tomography.
1. YUTIQ. Prescribing Information. Alimera Sciences, Inc; June 2022. 2. Singer MA, et al. Ophthalmol Surg Lasers Imaging Retina. 2021;52(7):387-390. 3. Parikh A, et al. JAMA Ophthalmol. 2021;139(3):308-315. 4. Jaffe GJ, Pavesio CE; Study Investigators. Ophthalmology. 2021;127(10):1318-1404.

IOP with Fluocinolone implant

References

- Jaffe GJ, Pavesio CE; Study Investigators. Effect of fluocinolone acetonide insert on recurrence rates in noninfectious intermediate, posterior, or panuveitis: three-year results. *Ophthalmology*. 2020;127(10):1395-1404.
- Parekh A, et al. Risk factors associated with intraocular pressure increase in patients with uveitis treated with the fluocinolone acetonide implant. *JAMA Ophthalmol*. 2015;133(5):568-573.
- Singer MA, et al. IOP elevation in patients treated with fluocinolone acetonide insert for chronic noninfectious uveitis affecting the posterior segment. *Ophthalmic Surg Lasers Imaging Retina*. 2021;52(7):387-390.
- YUTIQ. Prescribing information. Alimera Sciences, Inc; June, 2023. https://yutiq.com.

Conclusion

- Different sustained delivery steroid medications are able to control inflammation.
- Study design and primary outcome differ by medications
- They seem to decrease the treatment burden of disease
- However one has to balance safety and efficacy as:
- They all have side effects including cataracts and increased IOP.

HEADS-UP 3D VISUALIZATION IN VITREORETINAL SURGERY

1

1

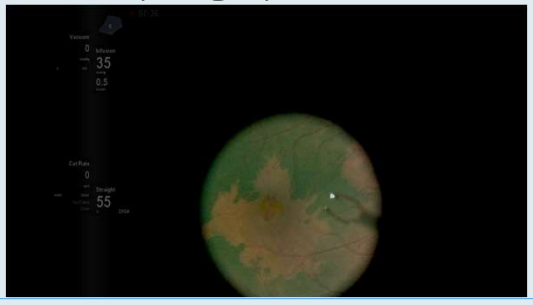
Disclosures

- Consultant: Alimera, Allergen, Alcon, Genentech, Ocuphire Pharm, Ocular Therapeutics, ANI Pharmaceuticals
- Investigator: Alimera, Genentech, Inc., Jaeb Center for Health Research, Regeneron, Novartis, Ocuphire Pharm, Parexel, Ocular Therapeutics
- Speaker: Genentech, Inc., Apellis, Astellas, Regeneron

2

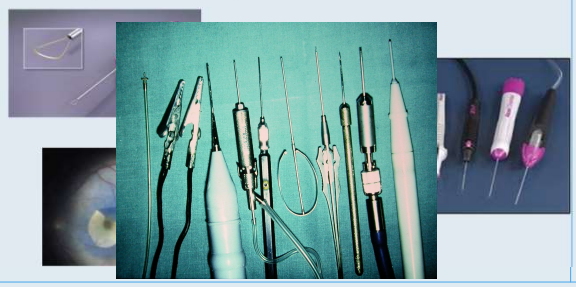
2

Vitrectomy Surgery



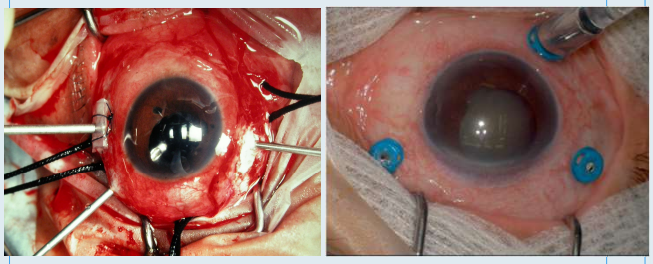
3

We have seen evolution in surgical instrumentation & techniques over the past decades



4

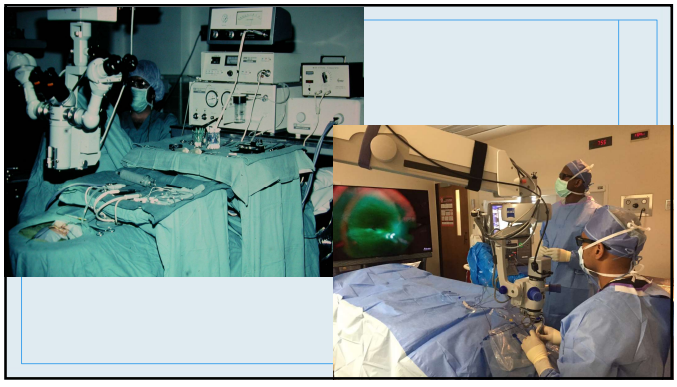
Smaller Gauge Vitrectomy



20 gauge

25 gauge

5



6

Types of "Heads-Up" Display Systems

- Ngenuity 3D (Alcon) - 2016
- Artevo 800 (Zeiss) - 2019
- Beyeonics One ophthalmic exoscope (BVI/Beyeonics vision)
  - relies exclusively on digital oculars
  - not yet available for purchase in the United States

Beyeonics.com

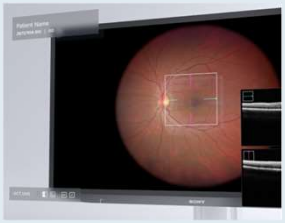
7

Ngenuity

1. 3D high dynamic range camera
2. 3D 4K OLED display
3. High speed graphics processor
4. Polarized glasses

8

Artevo 800



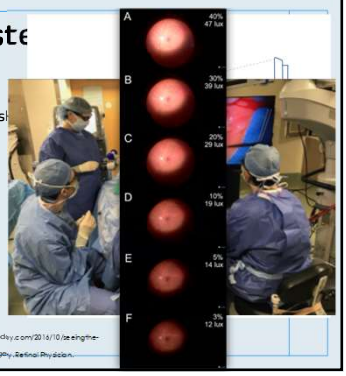
Integrates intra-operative OCT technology

Zeiss.com

9

3D visualization syste

- Lower levels of illumination- reduces ris of phototoxicity (35% Illumination vs 10% illumination)
- Enhanced depth of field (up to 3x)
- Educational benefits
- Ergonomics



Yonekawa, Y. Seeing the World Through 3-D Glasses. Retina Today. Available at: http://retinatoday.com/2016/10/seeing-the-world-through-3-d-glasses/
Franklin A, Sarangapani R, Yin L, et al. Digital vs analog surgical visualization for vitreoretinal surgery. Retinal Physician. https://www.retinalphysician.com/

10

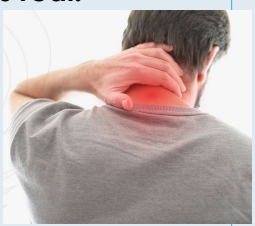
Video

11

11

Disability from musculoskeletal issues in ophthalmology is real!

- AAO survey: 51.8% ophthalmologists have neck, upper extremity or lower back MSK symptoms
- Retina specialists: 55.4% back + neck pain, 21.4% back pain, 8.3% neck pain
- Quality of Life + Financial loss due to temporary/permanent disability

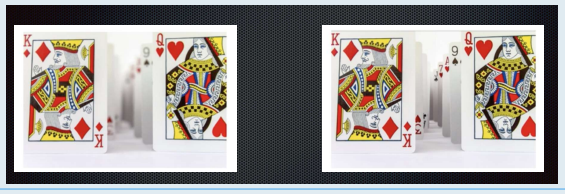


Dhimitri KC, McGwin G, McNeal SF, et al. Symptoms of musculoskeletal disorders in ophthalmologists. Am J Ophthalmol. 2005;139(1):179-181.
Marx JL, Wertz F, Dhimitri KC. Work-related musculoskeletal disorders in ophthalmologists. Techniques in Ophthalmology. 2005;3(1):54-61.
Desai URT, Abdulhak MM, Bhatti R. Occupational Back and Neck Problems in Vitreoretinal surgeons. Paper presented at: the American Society of Retina Specialists Annual Meeting; San Diego; August 2004.

12

ENHANCED Visualization

- 19% greater magnification than traditional scope
- 3x Enhanced depth of field: more profound in older surgeons
  - Presbyopia correlated with more gain in depth of field!



13

IMPROVED Visualization

- Excellent resolution not just better picture, also improved stereopsis[2,5]
- Color manipulation with filters, gain adjustment to better visualize
  - Vitreous hemorrhage
  - Fluid air exchange- decrease glare

2. Chow DR. NGENUITY: Is 3D surgery associated with increased stereopsis—myth or fact? Presented at ASRS. August 11-17, 2017. Boston.
5. Franklin A, Sarangapani R, Yin L, et al. Digital vs analog surgical visualization for vitreoretinal surgery. Retinal Physician. https://www.retinalphysician.com/issues/2017/may-2017/digital-vs-analog-surgical-visualization-for-vitre.

14

Ergonomics- One of the Biggest PROs

- Better posture all day- relax spine
- Potentially add years to your career!
- Less headaches (from accommodation)

3. Yonekawa, Y. Seeing the World Through 3-D Glasses. Retina Today. Available at: http://retinatoday.com/2016/10/seeingthe-world-through-3-d-glasses/
5. Franklin A, Sarangapani R, Yin L, et al. Digital vs analog surgical visualization for vitreoretinal surgery. Retinal Physician. https://www.retinalphysician.com/issues/2017/may-2017/digital-vs-analog-surgical-visualization-for-vitre.

15

Educationally benefits the ENTIRE team

- Immersive experience
- Assistant can anticipate next steps
- High resolution for operating, recording & feedback
- Better ergonomics for observer(s)
- Better teaching tool than side scope[6]

6. Arthur, Dhipak; Babu Kannan, Naresh; Sen, Sagnik; Ramasamy, Kim. Digitally assisted vitreoretinal surgery: A unique surgical teaching tool for beginners. Indian Journal of Ophthalmology 70(2):p 477-481, February 2022.

16

New upgrades- Color BOOST!

Video Courtesy: Dr. Steve Houston

17

THANK YOU FOR YOUR ATTENTION

18

Increased Intraocular Pressure in Steroid Studies

Michael Singer, M.D.
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Director of Clinical Research
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Comparing different steroids is similar to comparing apples, oranges, and grapefruit



They share common features: they are all fruit, they are all round, but they are definitely not the same.

(I didn't use lemons, since nobody wants their product to be a lemon!)

Steroid Therapies for Posterior Uveitis

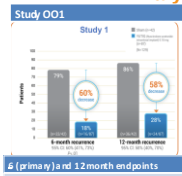
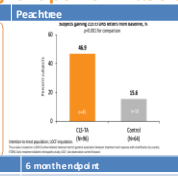
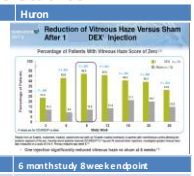


YutiQ	Xipere	Dex implant
Fluocinolone Acetonide 0.18mg	Supra-choroidal Triamcinalone 4mg/100ul	Dexamethasone 0.7mg
Intravitreal	Supra-choroidal	intravitreal
Approved 2017	Awaiting approval	Approved 2010
Label: up to 3 years	Label: every 3 months	Label: up to 6 months

Phase 3 Studies for Posterior Uveitis

- **Huron Study**: Dexamethasone implant, had a reduction of vitreous haze of 46.8% vs 11.8 % sham at eight weeks.
- **Peachtree Study**: Suprachoroidal triamcinolone , 46% of treated patients vs 15.6% of control patients obtained a 15-letter improvement at 6 months.
- In Study 001, 0.18 mg Fluocinolone acetonide 60% less patients on active medication had recurrence of uveitis vs control at 6 months, while recurrence was decreased in 58% of patients at 12 months vs control.

Primary endpoint: Phase 3 studies

Study OO1	Peachtree	Huron
		
& (primary) and 12 month endpoints	6 month endpoint	6 month study 8 week endpoint
Vitreous Haze Recurrence	Visual Acuity (15 letter gain)	Reduction of Vitreous Haze
In study 001, 0.18 mg Fluocinolone acetonide 60% less patients on active medication had recurrence of uveitis vs control at 6 months, while recurrence was decreased in 58% of patients at 12 months vs control.	Peachtree study: Suprachoroidal triamcinolone 46% of treated patients vs 15.6% of control patients obtained a 15 letter improvement.	Huron Study: Dexamethasone implant had a reduction of vitreous haze of 46.8% vs 11.8% sham at eight weeks.

What are the adverse events of concern?

- Cataracts: Surgically Curable
- Increased IOP: (what keeps you up at night!)

Cataract Incidence (as documented as adverse event)

Fluocinolone (Study 001)	CSA-TS (Peachtree)	Dexamethasone implant (Huron)
56% vs 23% control	7.3% vs sham 6.3%	15% vs 7%

Not all of these cataracts underwent surgery

Increased IOP incidence

Fluocinolone implant- Study 001 6-month Data

IOP-related Outcome, n (%)	Fluocinolone implant N=87	Sham N=42
Overall IOP >21mm Hg at any post baseline visit	**24 (27.6%)**	**7 (16.7%)**
IOP elevation ≥12 mmHg change from baseline at any post baseline visit	12 (13.8%)	2 (4.8%)
IOP elevation ≥30 mmHg absolute reading at any post baseline visit	**9 (10.3%)**	**0**
Any IOP-lowering medication	**18 (20.7%)**	**8 (19.0%)**
Any surgical intervention for an elevated IOP	**2 (2.3%)**	**0**

Dexamethasone Implant: Huron

IOP-related Outcome, n (%)	Dexamethasone implant N=76	Sham Control N=75
Highest number of patients with IOP elevation ≥10 mmHg change from baseline at any visit	8/71 (11.3%) Week 6	1 (1.5%) Week 6
IOP elevation ≥35 mmHg absolute reading at any post baseline visit	3 (4.1%) Week 12	0 (0.0 %) Week 12
On IOP-lowering medication at week 26	13 (16.9%)	7 (9.2%)
Incisional surgery for an elevated IOP Adverse Event	0	0

CLS-TA: Peachtree Elevated IOP*

IOP-related Outcome, n(%)	CLS-TA 4.0 mg N=96	Control (with local corticosteroid rescue) N=38	Control (without local corticosteroid rescue) N=18
Elevated IOP Adverse Events*	11 (11.5%)	10 (26.3%)	0 (0%)
IOP elevation ≥10 mmHg change from baseline at any visit	9 (9.4)	8 (21.1%)	0 (0%)
IOP elevation ≥30 mmHg absolute reading at any post baseline visit	5 (5.2)	4 (10.5%)	0 (0%)
Given any additional IOP-lowering medication	7 (7.3%)	6 (15.8%)	0 (0%)
Any surgical intervention for an elevated IOP Adverse Event	0	0	0

*"Elevated IOP" includes the preferred terms (a) IOP increased, (b) ocular hypertension, and (c) glaucoma

IOP in Uveitis Studies a deeper dive

IOP and Steroids: A deeper dive

- Dex implant in real life studies
- Fluocinolone Calm study and Pivotal (Study 001) looking at IOP over 30
- Iris registry of suprachoroidal triamcinolone

IOP in dex implant studies: increased IOP rate: 20-25%

- **Chrome Study Canada**: increased IOP, 120 eyes total with a total of 24 events for DME (25.0%; 6/24), RVO (27.6%; 8/29), and uveitis (10.0%; 2/20) patients
- **Safodex study**: Among 1,000 intravitreal injections, ocular hypertension was recorded for 28.5% of injected eyes over a mean follow-up period of 16.8 months (3-55)
- **Geodex study**: Amongst 294 intravitreal implants, ocular hypertension (>25 mmHg) was recorded in 0, 8 and 9.5% in White, Latino, and South Asian groups, respectively. However, IOP > 20 mmHg was recorded in 14%, 28% and 27% in White, Latino, and South Asian groups, respectively. Incidence of very high IOP (>35 mmHg) was lower in all geographical groups. It was 3% in Latino followed by 2% in South Asian group.

IOP: SCS triamcinolone

IOP: SCS triamcinolone

Durability with suprachoroidal injection of triamcinolone acetonide injectable suspension for uveitic macular edema and use of rescue therapy in clinical practice

Michael Singer, Durga Borkar, Abhishek A. Nair, Andrew LaPrise, Kristian Garcia, Joel Fain, Teresa Brevetti, David J. Harrison

IOP: SCS triamcinolone

Introduction

IOP: SCS triamcinolone

- Patients ≥18 with a diagnosis of non-infectious UME and a suprachoroidal injection of triamcinolone acetonide after January 2022 were identified in the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)
  - The date of the first suprachoroidal injection defined the index date
- IRIS data was linked to Komodo open-source claims data (Jan 2022 to Jun 2023) using the Datavant token to identify corticosteroid use
  - Rescue was defined as use of injectable, implanted, or topical corticosteroids after the initial triamcinolone acetonide suprachoroidal injection
- Patients were followed for 24 weeks after their injection for duration
- A sub-study was performed on IOP: patients followed for 48 weeks

IOP: SCS triamcinolone

Results

Safety sub analysis

Safety sub analysis

IOP Data:

- A subset of the original data set was used to obtain IOP data for 48 weeks

Safety sub analysis

Baseline Demographic and Clinical Characteristics : IOP data

The study identified a total of 396 eyes corresponding to 357 patients in the data between Jan 2022 and Dec 2023

Total patients	357 (100.0%)
Age	
Mean (SD)	67.1 (12.6)
Sex	
Female	54.1%
Male	45.9%
Race	
Asian	1.4%
Black or African American	7.3%
White	65.0%
Other races	16.8%
Unknown	9.5%

Ocular comorbidities	
Cataract	49.6%
Glaucoma/Ocular Hypertension	43.1%
DR without DME	5.0%
Retinal Detachment	19.9%
Posterior uveitis	87.7%
Panuveitis	1.04%

Approximately 28% of the patients had a baseline intraocular pressure >22 mmHg

Safety sub analysis

Elevation in IOP after SCS traimcin alone administration over the 48-week period was low in real-world clinical practice

IOP elevation characteristics	Real-world clinical practice N = 357 (100%)	MAGNOLIA clinical trial N = 28 (100%)
Change in IOP ≥10 mmHg	51 (14.2)	4 (14.3)
Change in IOP ≥25 mmHg	4 (1.1)	2 (7.1)
Change in IOP ≥30 mmHg	0 (0.0)	1 (3.6)

IOP elevation rates were consistent with recently presented data at ASRS 2024

Mammo.. D et al., ASRS Stockholm July 2024

Safety sub analysis

Elevation in IOP after SCS triamcinolone administration over the 48-week period was low in real-world clinical practice

IOP elevation characteristics	Real-world clinical practice N = 357 (100%)
Change at 6 weeks	21 (5.8%)
Change at 12 weeks	36 (10.1%)
Change at 24 weeks	47 (13.2%)
Change at 48 weeks	51 (14.2%)

Safety sub analysis

Elevation in IOP >25 after SCS triamcinolone administration over the 48-week period was low in real-world clinical practice

IOP elevation characteristics	Real-world clinical practice N = 4 (100%)
Change at 12 weeks	2 (0.56%)
Change at 24 weeks	1 (0.28 %)
Change at 48 weeks	1 (0.28%)

Safety sub analysis

Conclusion:

- Only 12% of patients with UME required a subsequent injected or implanted corticosteroid in the 24 weeks after a single suprachoroidal injection of triamcinolone
- Only 14.2% patients experienced an elevated IOP of ≥10 mmHg at 48 weeks in real-world clinical practice despite 43.1% of patients with a history of glaucoma.
- These changes occurred at 6,12, 24,and 48 weeks
- 1.1% patients with an elevated IOP of ≥25 mmHg and these occurred at 12, 24, and 48 weeks.
- No patients with an elevated IOP ≥30 mmHg much lower than that observed in the Magnolia clinical trial
- SCS triamcinolone should be considered in patients with history of glaucoma or at risk for steroid induced ocular hypetension
- Follow up for these patients could be at month 1, 3, 6 and every 3 months subsequently to capture this increase of 10mm Hg of IOP

IOP with Fluocinolone implant

IOP with Fluocinolone implant

Fluocinolone Acetonide Intravitreal Insert for NIU-PS: Significant IOP Elevations Through 36 Months

Michael A Singer, MD
Clinical Professor of ophthalmology,
University of Texas Health Science Center,
San Antonio, TX

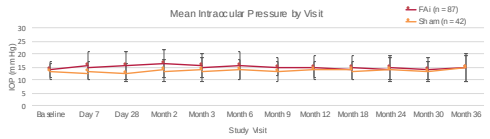
IOP with Fluocinolone implant

Objective:

- Uveitis has long been associated with elevated intraocular pressure (IOP)
- Corticosteroids, widely used to treat non-infectious uveitis affecting the posterior segment (NIU-PS), are known to decrease aqueous humor outflow and increase IOP
- This analysis was initiated to characterize the timing and severity of significant IOP elevation in eyes treated for NIU-PS using a single 0.18 mg fluocinolone acetonide intravitreal (FAi) insert for 36 months.

IOP with Fluocinolone implant

Elevated IOP



Elevated IOP	FAi	Sham
≥ 12 mmHg increase	20 (23.0%)	11 (26.2%)
IOP ≥ 30 mmHg	15 (17.2%)	5 (11.9%)

Elevated IOP Tx	FAi	Sham
IOP lowering medication s*	37 (42.5%)	14 (33.3%)
IOP lowering surgeries	5 (5.7%)	5 (11.9%)

* Minimum of 7 days treatment

IOP with Fluocinolone implant

Details of IOP ≥ 30mmhg Events

	FAi (n = 87)	
Number of Events	15 (17.2%)	
Time to Event		
Mean Time	241 days	(≈ 8 months)
Median Time	153 days	(≈ 5 months)
Minimum Time	8 days	
Maximum Time	1108 days	(≈ 3 years)
Events per Time Frame		
7 to 30 days	5 (33.3%)	
3 to 6 months	5 (33.3%)	
6 to 18 months	4 (26.7%)	
3 years	1 (6.7%)	

IOP with Fluocinolone implant: Visual field results

Change in Mean Deviation through 36 Months

Change in Visual Field Mean Deviation (dB) - Baseline to 36 Months						
	FAi Subset with IOP ≥30 mmHg		*Full Study Population*			
	Study Eye	Fellow Eye	Study Eye - FAi	Fellow Eye - FAi	Study Eye - Sham	Fellow Eye - Sham
MEAN (SD)	3 (11.483)	3.49 (9.364)	4.62 (50.337)	- 2.83 (10.152)	- 1.20 (13.555)	- 1.69 (11.207)
MEDIAN	1.95	1.55	-0.40	0.00	1.10	0.30
MIN	- 20.7	- 10.2	-43.3	- 28.4	- 51.5	- 45.4
MAX	31	26	410.1	22.3	19.8	15.4

IOP with Fluocinolone implant

Discussion:

- IOP elevation in the FAi and Sham groups were similar and primarily managed using standard topical IOP lowering medications
- Fifteen eyes (17.2%) treated with FAi had IOP elevations to ≥ 30 mmHg
  - One-third of the events (5) occurred between 7 days and 1 month
  - One-third of the events (5) occurred between 3 and 6 months
  - Delayed events happened between 6 and 18 months (4) and at 3 years (1)
- Overall, FAi had no significant impact on the progression of visual field loss in this subset of study patients through 36 months when compared to the fellow eye
- The pattern of significant IOP events suggests that evaluations within the first month, 3, and 6 months; and every 3 months thereafter, could detect the majority of severe IOP increases

IOP with Fluocinolone implant

CALM

CALM: 36-month safety outcomes with the 0.18 mg intravitreal fluocinolone acetonide implant for non-infectious uveitis

Michael Singer, MD[1]
ON BEHALF OF THE CALM REGISTRY STUDY INVESTIGATORS AND SUPPORTING CLINICAL SITES

[1]Medical Center Ophthalmology Associates, San Antonio, TX

IOP with Fluocinolone implant

CALM

CALM: 36-month safety outcomes with the 0.18 mg intravitreal fluocinolone acetonide implant for non-infectious uveitis

To be reported by Dr. Sumit Sharma

[1]Medical Center Ophthalmology Associates, San Antonio, TX

IOP with Fluocinolone implant

CALM

CALM: 36-month safety outcomes with the 0.18 mg intravitreal fluocinolone acetonide implant for non-infectious uveitis

To be discussed by Dr. Sumit Sharma

[1]Medical Center Ophthalmology Associates, San Antonio, TX

Does Increased IOP Cause Long Term Optic Nerve Damage?

RNFL Study

Background:

- 27-32% of eyes treated with Dex implant® implant have transient IOP elevations Increased IOP is a risk factor for glaucoma[1,2]
- Safety and efficacy profiles well-established for
- However, no study has been performed using OCT data to evaluate RNFL thickness in those that have IOP spikes (visual field are unreliable in RVO)

Purpose:

- To examine the effect of IOP spikes on the RNFL after treatment with the DEX implant
- So, do these temporary IOP spikes associated with Dex implant® lead to long-term damage to the RNFL?

1. Capone A,Jr., Singer MA, Dodwell DG, et al. Efficacy and safety of two commercial dexamethasone intravitreal implant injections for treatment of macular edema related to retinal vein occlusion (Shasta study). *Retina*. 2014;34:343-51.
2. Boyer DS, Yoon YH, Belfort R,Jr., et al. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. *Ophthalmology*. 2014;121:1904-14.

RNFL Study

Results:

Demographics (n= 48 patients – 96 eyes)		
Age (yrs)		72.7
Sex	Male	51%
	Female	49%
Race		
	White	57%
	Hispanic	29%
	Black	1%
	Other	13%
Diagnosis		
	BRVO	34%
	DME	25%
	CRVO	23%
Other including	Uveitis	6%
	CME	6%
	wAMD	4%

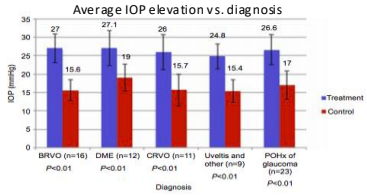
RNFL Study

Results:

- History of Glaucoma: 48%
- Mean time between initial IOP spike and OCT imaging: 1.8 months (range: 4–83 months; median: 13.5 months)
- Mean number of Dex implant before IOP spike: 2.1 (range: 1–12).
- Average IOP spike: 26.4 ± 4.3 mmHg
- Range: 22–38mmHg
- Average IOP of untreated eye at time of IOP spike: 16.5 ± 3.6 mmHg (P = 0.00)
- Mean central corneal thickness: 569µm (treated), 571µm (control); P=0.61
- ≥ 1 IOP lowering drop used: 76% (± standard deviation)

RNFL Study

Average IOP elevation vs. diagnosis

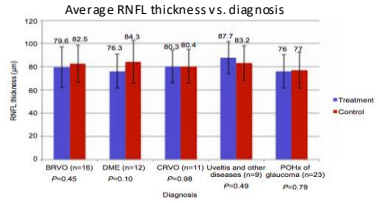


Overall, no difference in average RNFL thickness in treated vs. untreated eyes (80.4±15.5µm and 82.6±15.8µm, respectively; P=0.33) (± standard deviation)

- Error bars indicate SD.

RNFL Study

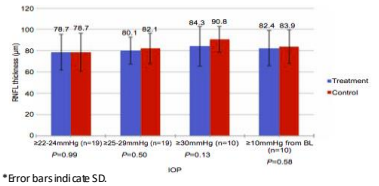
Average RNFL thickness vs. diagnosis



*Error bars indicate SD.

RNFL Study

Average RNFL thickness vs. degree of IOP elevation



*Error bars indicate SD.

RNFL Study

Conclusions

- IOP spikes ≥ 22 mmHg after Dexi implant implantation demonstrated no significant difference in the average RNFL thickness compared to control, regardless of diagnosis or history of glaucoma
- *IOP* ≥ 22 mmHg or ≥ 10 mmHg from baseline did NOT demonstrate significantly thinner RNFL compared to control, regardless of magnitude of IOP elevation
- Topical IOP-lowering drops may be adequate in the management of temporary IOP spikes to prevent RNFL damage
- Temporary elevation of IOP after Dexi implant implantation does not lead to meaningful changes in RNFL thickness, regardless of etiology or magnitude of IOP increase

Case Study

Conclusion

- Different sustained delivery steroid medications are able to control inflammation.
- Study design and primary outcome differ by medications
- However, they all have side effects including cataracts and increased IOP.
- The incidence of increased IOP varies by medication, but seems to be manageable by topical medications as the incidence of surgical intervention is very low.
- In addition, data looking at the effects of increased in intraocular pressure do not seem to be associated with retinal nerve fiber layer damage.

Real World Studies in AMD and DME

Michael Singer M.D.
Hannah Khan, MPH; Aamir A. Aziz, BS; Preston O'brien, BS; Arshad M. Khanani, MD, MA

Financial Disclosures

- *Consultant*: Alimera, Allergan, ANI, Apellis, EyePoint, Genentech, Astellas, , Ocular Therapeutics, Regeneron
- *Speaker Contracted by Ineligible Company*: Allergan, ANI, Apellis, EyePoint, Genentech, Astellas, Regeneron
- *Independent Research Contractor*: Allergan, Apellis, Ashvattha ,EyePoint, Genentech, Astellas, , Kodiak, Optos, Regeneron, Rezolute, Valo
- **Individual Stocks and Stock Options (privately held)*: Aviceda, Inflammasome, Nanoscope, Olives BioTherapeutics

Medications are approved due to clinical trials

- However real -life studies may under or overperform the clinical trial results
- The differences are based on:
- Study design
- Patient population
- Disease studied
- Type of medication

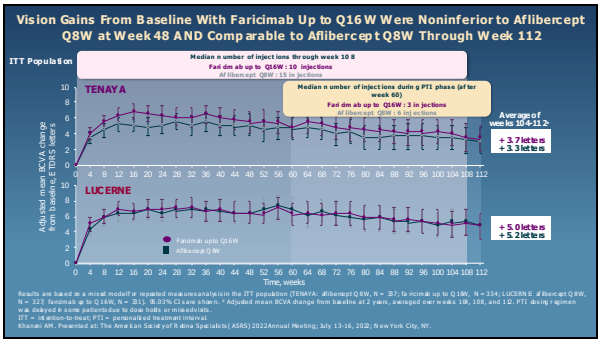
Real life studies

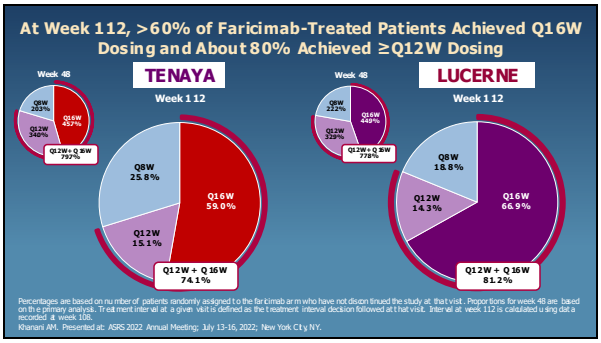
- Faricimab:
- TRUCKEE for AMD
- TAHOE for DME

- Steroids for DME
- Reinforce : Dex implant
- Paladin: Fluocinolone implant

Faricimab for AMD

- Tenaya and Lucerne





Hannah Khan, MPH; Aamir A. Aziz, BS; Preston O'brien, BS; Arshad M. Khanani, MD, MA

The Real-World Efficacy and Safety of Faricimab in Neovascular Age-Related Macular Degeneration: The TRUCKEE Study – 3 Year Results

Michael Singer, MD

Disclosures:

Consultant: Alimera, Allergan, <ANI, Apellis, Eye Point, Genentech, Astellas, , Ocular Therapeutix, Regeneron

Speaker Contracted by Ineligible Company: Allergan, ANI, Apellis, Eye Point, Genentech, Astellas, Regeneron

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*Individual Stocks and Stock Options (privately held): Avicada, Inflammasome, Nanoscope, Olives BioTherapeutics

The TRUCKEE Study is a collaborative clinician directed and organized study with no industry sponsor across multiple sites in the US.

CRO Services provided by Vial

TRUCKEE Study: Design

Evaluating efficacy and safety of faricimab in real-world patients with nAMD

Target Patient Population

- Treatment-naïve AND previously-treated patients

Ongoing Data Collection

- Demographics
- Prior treatment history
- Efficacy (vision, central subfield thickness, retinal fluid status)
- Durability
- Safety

Patient Recruitment End Date: August 2024

3609 eyes* of 2883 total patients

Total: 20,176 intravitreal injections

Three faricimab injection follow-up: 2 281 eyes

Six faricimab injections follow-up: 1 086 eyes

Nine faricimab injections follow-up: 542 eyes

*Data-Cut as of January 12th, 2025
**Follow-up defined as a completed office visit after the noted faricimab injection

TRUCKEE Results: Demographics

Population (N = 2883 patients, 3609 eyes)

Variable	Mean	Range
Age (years)	80.48	32 - 100
Variable	**Groups**	**N (%)**
Gender (patients)	Male	1048 (36.4%)
	Female	1440 (49.9%)
	Not Reported	395 (13.7%)
Last anti-VEGF injection (eyes)	**Aflibercept**	**1511 (41.9%)**
	Bevacizumab	401 (11.1%)
	Brolucizumab	134 (3.7%)
	Ranibizumab	647 (17.9%)
	Treatment Naïve	348 (9.6%)
	Not known	568 (15.8%)

Efficacy After Three Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 1828 eyes)
Previous Interval: 45.1 days
Current Interval: 52.6 days
Increase in interval post-faricimab: + 7.5 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	59.73 (0.01)	60.97 (0.01)	+1.24 letters	0.42
CST (µM)	312.71 (0.12)	283.27 (0.09)	-29.44 µM	**< 0.0001**
PED Height	263.46 (0.64)	241.83 (0.59)	-21.63 µM	**< 0.001**

*Based on Snellen to ETDRS conversion

Efficacy After Three Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 1042 eyes)
Previous Interval: 44.0 days
Current Interval: 50.6 days
Increase in interval post-faricimab: + 6.6 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	61.55 (0.02)	63.08 (0.02)	+1.53 letters	0.0943
CST (µM)	313.63 (0.18)	287.13 (0.14)	-26.50 µM	**< 0.0001**
PED Height	256.01 (0.88)	242.26 (0.97)	-13.74 µM	**0.018**

*Based on Snellen to ETDRS conversion

Efficacy After Three Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 223 eyes)
Current Interval: 47.5 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	56.50 (0.12)	59.85 (0.11)	+3.35 letters	**0.0068**
CST (µM)	383.66 (0.83)	292.84 (0.66)	-90.82 µM	**< 0.0001**
PED Height	271.37 (2.44)	226.64 (2.46)	-44.73 µM	**0.0073**

*Based on Snellen to ETDRS conversion

Resolution of Fluid After Three Injections of Faricimab

Efficacy After Six Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 863 eyes)
Previous Interval: 43.8 days
Current Interval: 57.1 days
Increase in interval post-faricimab: + 13.3 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	58.93 (0.03)	59.19 (0.03)	+0.26 letters	0.82
CST (µM)	321.30 (0.23)	284.05 (0.19)	-37.11 µM	< 0.00001
PED Height	275.16 (1.01)	226.50 (0.77)	-48.66 µM	< 0.00001

*Based on Snellen to ETDRS conversion

Efficacy After Six Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 503 eyes)
Previous Interval: 42.5 days
Current Interval: 56.5 days
Increase in interval post-faricimab: + 14.0 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	61.58 (0.04)	62.03 (0.04)	+0.45 letters	0.80
CST (µM)	323.31 (0.36)	286.88 (0.30)	-36.43 µM	< 0.0001
PED Height	281.54 (2.16)	242.12 (1.44)	-39.42 µM	0.001

*Based on Snellen to ETDRS conversion

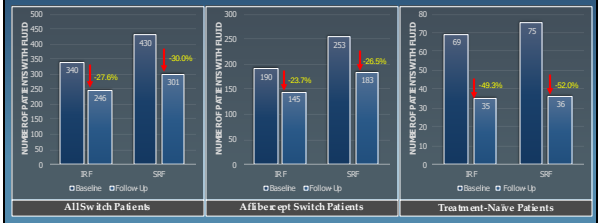
Efficacy After Six Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 124 eyes)
Current Interval: 66.1 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	55.72 (0.22)	59.64 (0.25)	+3.92 letters	0.013
CST (µM)	385.47 (1.24)	297.25 (1.02)	-88.22 µM	< 0.0001
PED Height	270.06 (2.95)	223.82 (2.28)	-46.24 µM	0.003

*Based on Snellen to ETDRS conversion

Resolution of Fluid After Six Injections of Faricimab



Efficacy After Nine Injections of Faricimab in All-Switched Patients

Population with Follow-up (N = 436 eyes)
Previous Interval: 42.1 days
Current Interval: 57.6 days
Increase in interval post-faricimab: + 15.5 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	58.74 (0.05)	58.40 (0.06)	-0.34 letters	0.0795
CST (µM)	333.68 (0.44)	285.24 (0.48)	-48.44 µM	**< 0.00001**
PED Height	285.06 (1.62)	246.12 (1.02)	-38.94 µM	**0.035**

*Based on Snellen to ETDRS conversion

Efficacy After Nine Injections of Faricimab in Aflibercept-Switched Patients

Population with Follow-up (N = 269 eyes)
Previous Interval: 40.5 days
Current Interval: 55.0 days
Increase in interval post-faricimab: + 14.5 days

Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	61.38 (0.08)	60.62 (0.09)	-0.76 letters	0.131
CST (µM)	341.08 (0.63)	292.97 (0.47)	-48.11 µM	**<0.0001**
PED Height	285.52 (2.26)	252.35 (1.86)	-33.17 µM	0.36

*Based on Snellen to ETDRS conversion

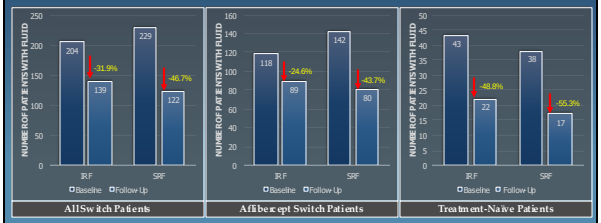
Efficacy After Nine Injections of Faricimab in Treatment-Naïve Patients

Population with Follow-up (N = 61 eyes)
Current Interval: 72.4 days

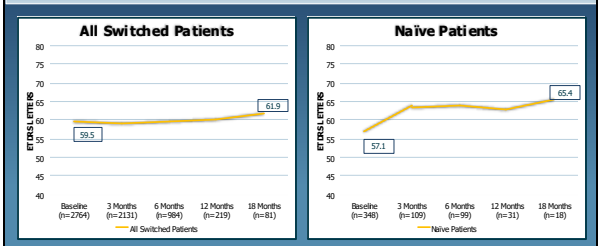
Variable	Baseline Mean (SEM)	Follow-Up Mean (SEM)	Change	P-Value Percent Change
ETDRS (letters)*	57.22 (0.40)	61.20 (0.34)	+3.98 letters	0.017
CST (µM)	397.98 (2.10)	283.54 (1.68)	-114.44 µM	<0.0001
PED Height	270.59 (4.16)	216.72 (14.36)	-52.87 µM	0.013

*Based on Snellen to ETDRS conversion

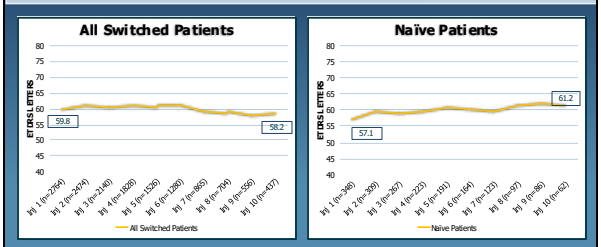
Resolution of Fluid After Nine Injections of Faricimab



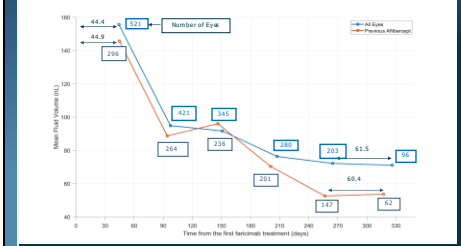
Visual Acuity Overtime at 18 Months



Visual Acuity Overtime After 10 Injections

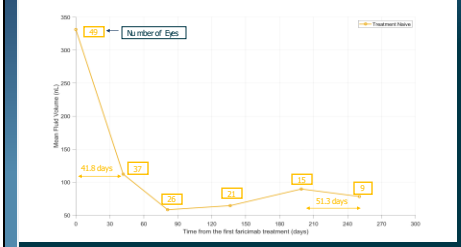


Total Fluid Reductions over Five Treatments



Total retinal fluid volume reduction in both all eyes and aflibercept-switched patients, demonstrating significant decreases in volume and increases in treatment interval after sustained treatments.

Total Fluid Reductions over Five Treatments



Total retinal fluid volume reduction in treatment-naïve patients, demonstrating rapid decrease in total fluid after first injection of faricimab.

Safety Outcomes

Number of Patients	2883
Number of Eyes	3609
Number of Injections	20,176
Intraocular Inflammation (IOI) Rate	0.08%
Endophthalmitis Rate	0.029%

Event	Number of Cases	Resolved	VA Returned to Baseline	Retreated with Faricimab
Endophthalmitis	6* *Five cases were culture positive	6/6	6/6	4/6
Anterior Chamber Cells	2* *One case had previous inflammation on brolucizumab	4/4	4/4	1/4
Uveitis	6	6/6	6/6	3/6
Iritis	2* *One case was bilateral; other eye untreated	2/2	2/2	2/2
Vitritis	3* *Two cases had previous inflammation on brolucizumab	3/3	3/3	2/3
Non-occlusive Vasculitis	2** *One patient with bilateral occurrence	2/2	2/2	0/2

Key TakeAways

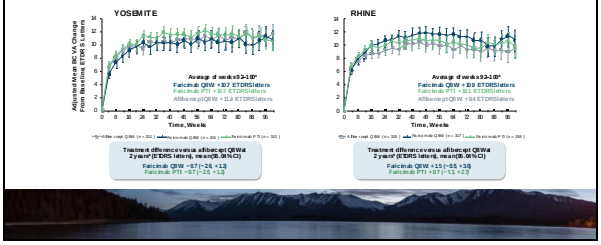
- In a real-world setting, with **20,176 injections in 3609 eyes**, faricimab continues to demonstrate **rapid improvement** in all anatomic parameters in **both treatment-naïve and previously-treated patients**.
- Treatment-naïve patients show **rapid disease control with improvement in vision** as well as **extended treatment interval**.
- Patients **switched to faricimab from aflibercept** had interval extension of **2 weeks after 6 faricimab** injections.
- Faricimab demonstrates a low rate of IOI/endophthalmitis with one report of bilateral non-occlusive vasculitis. All **events resolved and vision returned to baseline** in all cases.

THANK YOU to ALL SITES IN TRUCKEE

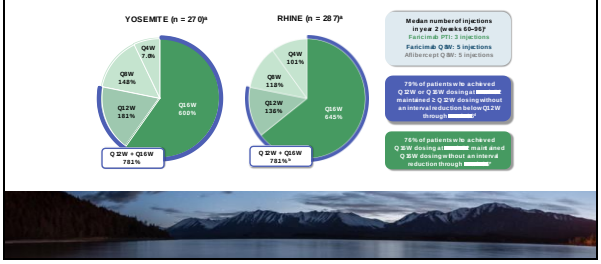
Faricimab for DME

- Yosemite and Rhine

Vision Gains With Faricimab Q8W and PTI Up to Q16W Were Noninferior to Aflibercept Q8W at 1 Year and Maintained Through Year 2



Durable Vision Gains With Faricimab Were Achieved with Q16W Dosing in ≥ 60% of the PTI Arms at Week 96



The TAHOE Study

Real World Efficacy and Safety of Faricimab in DME - 1 Year Results

Michael Singer, MD

Hannah Khan, MPH; Aamir A. Aziz, BS; Preston O'brien, BS; Arshad M. Khanani, MD, MA

Disclosures:

- Consultant: Alimera, Allergan, <ANI, Apellis, Eye Point, Genentech, Astellas, , Ocular Therapeutix, Regeneron
- Speaker Contracted by Ineligible Company: Allergan, ANI, Apellis, Eye Point, Genentech, Astellas, Regeneron
- Independent Research Contractor: Allergan, Apellis, Asthvena, Eye Point, Genentech, Astellas, , Kodiak, Optos, Regeneron, Rezolute, Valo
- *Individual Stocks and Stock Options (privately held): Aviceda, Inflammasome, Nanoscope, Olives BioTherapeutics

The TAHOE Study is a collaborative clinician directed and organized study with no industry sponsor across multiple sites in the US.

CRO Services provided by Vial

Study Locations

TAHOE Study: Design

Evaluating efficacy and safety of faricimab in real-world patients with DME

Target Patient Population

Treatment-naïve AND previously-treated patients with DME

Ongoing Data Collection

Demographics
Prior treatment history
Efficacy (vision, central subfield thickness, retinal fluid status)
Durability
Safety

TAHOE Study: Design

669 eyes* of 411 total patients treated with faricimab (study population)

Follow-up** after three faricimab injections available for 347 eyes

Follow-up** after six faricimab injections available for 279 eyes

Follow-up** after nine faricimab injections available for 64 eyes

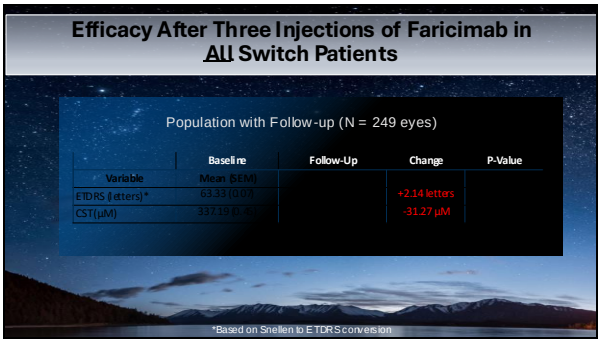
* Data-Cut as of August 2024
** Follow-up defined as a completed office visit after the noted faricimab injection

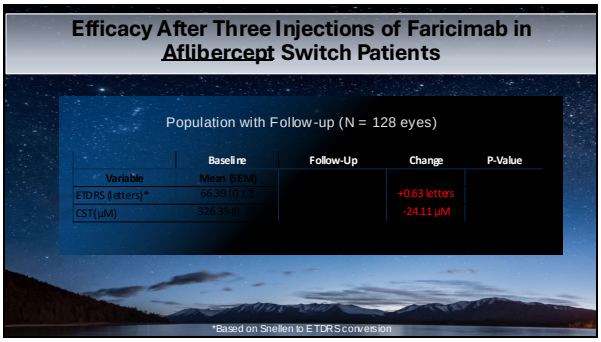
Results: Demographics

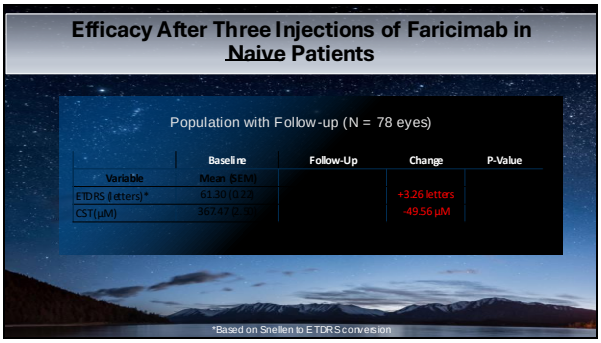
Population (N = 411 patients, 669 eyes)

Variable	Mean	Range
Age (years)	65.5	

Variable	Groups	N (%)
Gender (patients)	Male	
	Female	
Last anti-VEGF injection (eyes)	Aflibercept	


Efficacy After Three Injections of Faricimab in All Switch Patients
Population with Follow-up (N = 249 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
63.33 (0.0.7)
+2.14 letters
CST(µM)
337.19 (0.4
-31.27 µM
*Based on Snellen to ETDRS conversion


Efficacy After Three Injections of Faricimab in Aflibercept Switch Patients
Population with Follow-up (N = 128 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
66.39 (0.1.2
+0.63 letters
CST(µM)
326.39 (0.7
-24.11 µM
*Based on Snellen to ETDRS conversion


Efficacy After Three Injections of Faricimab in Naive Patients
Population with Follow-up (N = 78 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
61.30 (0.2.5
+3.26 letters
CST(µM)
367.47 (2.5
-49.56 µM
*Based on Snellen to ETDRS conversion

Efficacy After Six Injections of Faricimab in All Switch Patients

Population with Follow-up (N = 132 eyes)

Variable	Baseline Mean (SEM)	Follow-Up	Change	P-Value
ETDRS (letters)*	62.68 (0.13		+2.07 letters	
CST(µM)	340.53 (0.39		-38.69 µM	

*Based on Snellen to ETDRS conversion

Efficacy After Six Injections of Faricimab in Aflibercept Switch Patients

Population with Follow-up (N = 77 eyes)

Variable	Baseline Mean (SEM)	Follow-Up	Change	P-Value
ETDRS (letters)*	65.52 (0.20		+0.91 letters	
CST(µM)	344.86 (1.47		-43.97 µM	

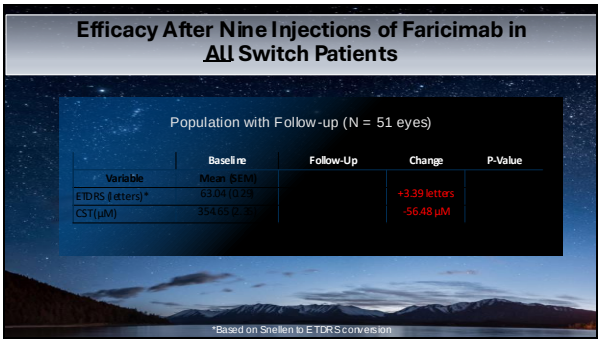
*Based on Snellen to ETDRS conversion

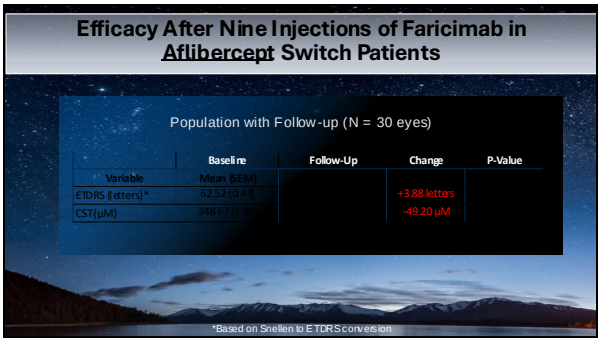
Efficacy After Six Injections of Faricimab in Naive Patients

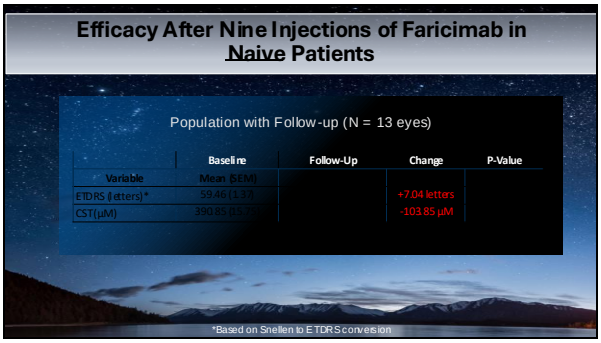
Population with Follow-up (N = 39 eyes)

Variable	Baseline Mean (SEM)	Follow-Up	Change	P-Value
ETDRS (letters)*	57.54 (0.53		+6.59 letters	
CST(µM)	370.89 (4.23		-52.36 µM	

*Based on Snellen to ETDRS conversion


Efficacy After Nine Injections of Faricimab in All Switch Patients
Population with Follow-up (N = 51 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
63.04 (0.79
+3.39 letters
CST(µM)
354.65 (2.
-56.48 µM
*Based on Snellen to ETDRS conversion


Efficacy After Nine Injections of Faricimab in Aflibercept Switch Patients
Population with Follow-up (N = 30 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
62.52 (0.43
+3.88 letters
CST(µM)
348.67 (3.82
-49.20 µM
*Based on Snellen to ETDRS conversion


Efficacy After Nine Injections of Faricimab in Naive Patients
Population with Follow-up (N = 13 eyes)
Baseline
Follow-Up
Change
P-Value
Variable
Mean (SEM)
ETDRS (letters)*
59.46 (1.33
+7.04 letters
CST(µM)
390.85 (15.
-103.85 µM
*Based on Snellen to ETDRS conversion

Safety Outcomes

Number of Patients	414
Number of Eyes	669
Number of Injections	3,104
Intraocular Inflammation (IOI) Rate	0.09%

Event	Number of Cases	Resolved	VA Returned to Baseline	Retreated with Faricimab
Anterior Uveitis*	3* *One patient, OU One patient, OS	3/3	3/3	0/3

No cases of Retinal Vasculitis, Endophthalmitis, or Retinal Artery Occlusion have been observed

Conclusions

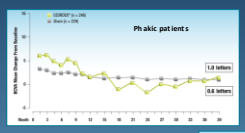
- TAHOE is an ongoing collaborative study looking at the efficacy and safety of faricimab in a real-world setting
- Faricimab demonstrates rapid improvement in anatomy and vision in treatment naive patients
- In switch patients, benefits of faricimab increase with continued treatment, with improvements in anatomy with normalization of CST (300µm) after 3 injections
- 3,104 injections were performed with 2 cases of IOI and no cases of endophthalmitis, vasculitis or artery occlusion
- More data will be collected and presented at future meetings

Corticosteroids

Dexamethasone Implant: MEAD Study

Mean Change in BCVA (ETDRS Letters)

MEAD



The occurrence of cataracts in the corticosteroid group impacted visual acuity during the study

REINFORCE: A Prospective Multicenter Study of Dexamethasone Intravitreal Implant (DEX) in Diabetic Macular Edema (DME)

Michael A. Singer, MD1; Pravin U. Dugel, MD2; Howard F. Fine, MD3; Antonio Capone, Jr., MD4; John Maltman, PhD5

Introduction

- Dexamethasone intravitreal implant (DEX) has shown efficacy in patients with diabetic macular edema (DME) in controlled trials
- Data on real-world outcomes in DME patients receiving DEX as monotherapy or adjunctive therapy are limited

Study Objective

- To assess the effectiveness, safety, and real-world use of DEX in clinical practice in patients with DME

Study Design / Methods

- Prospective, multicenter, observational registry study
- Study did not provide, nor require by protocol, any treatment beyond the initial DEX treatment required for registry inclusion
- Ocular history, treatment, and outcomes data were collected at the patient's first DEX injection and each subsequent visit up to 1 year
- Assessments and schedule of follow-up visits at the discretion of the physician
- Amount of data collected depended upon the number of follow-up visits
- Snellen visual acuity was converted to approximate ETDRS letters for analysis using the method of Gregori et al[1]

Primary Endpoints

- Mean maximum BCVA change (best improvement) from baseline following each DEX injection
- Percentage of patients with ≥15-letter improvement in BCVA
- Average improvement in BCVA (area-under-the-curve [AUC] approach)

Baseline Patient Demographics and Study Eye Characteristics

Parameter	Patient Population (N=177)	Study Eyes (N=180)[a,b]
Mean age (range), years	67.0 (38–90)	
Male, %	52.5	
White, %	84.2	
BCVA (*n = 172*) Mean (range), approximate ETDRS letters Mean (range), Snellen equivalent		54.4 (0–85) ~20/80 (CF–~20/20)
Mean CRT (range), µm (*n = 140*)		424.6 (179–920)
Mean IOP (range), mm Hg		15.2 (8–27)
Phakic, %		29.4
Pseudophakic, %		60.6

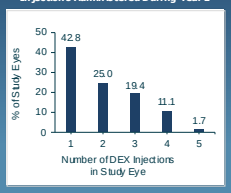
[a] Three patients had both eyes included in the study.
[b] Means calculated using observed values and percentages calculated based on total number of study eyes; some study eyes had missing data.
BCVA=best corrected visual acuity; CF=counting fingers; CRT=central retinal thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; IOP=intraocular pressure.

Baseline Diabetes Characteristics and Previous Treatment

Characteristic, n (%)	Patient Population (N=177)[a]
Diabetes duration >15 years	92 (52.0)
Type 2 diabetes	121 (68.4)
HbA1c ≤8%	30 (16.9)
HbA1c >8%	6 (3.4)
Missing HbA1c data	141 (79.7)
Nonischemic DME perfusion status	113 (63.8)
Ischemic DME perfusion status	8 (4.5)
Nonapplicable or missing DME perfusion status	56 (31.6)
DME duration ≥1 year	118 (65.6)[b]
Previous DME treatment	166 (93.8)
Previous laser	63 (35.6)

DEX Usage

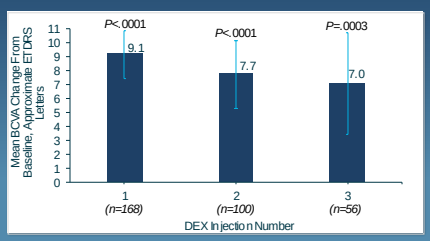
Frequency Distribution of Number of DEX Injections Administered During Year 1



- Mean DEX injection frequency was 2.0 (± 1.1, SD) injections in Year 1
- Mean time between DEX injections was 152.7 (± 64.5, SD) days
- DEX was used as monotherapy in 99 (55.0%) study eyes
- 81 study eyes (45%) received 1 or more other intravitreal injections during the study
  - Most common: aflibercept, ranibizumab, or bevacizumab

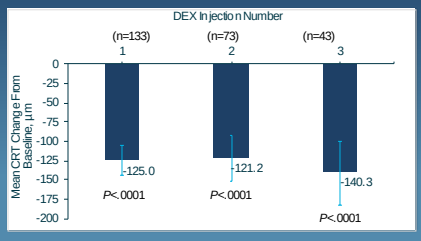
2017 Retina World Congress, Singer et al

Mean Peak Improvement in BCVA From Baseline After Each DEX Injection



Error bars indicate 95% CI.
2017 Retina World Congress, Singer et al

Mean Change in CRT From Baseline After Each DEX Injection



Error bars indicate 95% CI.
2017 Retina World Congress, Singer et al.

Other Key Efficacy Endpoints

Outcome Measure	Result	*P* Value
Percentage of study eyes with ≥15-letter improvement in BCVA from baseline during the study	36.0% (62/172)	
Mean average improvement in BCVA from baseline during the study using the AUC approach (95% CI)	3.6 letters (2.3, 5.0)	
Mean maximum change in BCVA from baseline during the study (95% CI)	11.7 letters (10.0, 13.5)	<.0001
Mean maximum change in CRT from baseline during the study (95% CI)	−137.7 µm (−158.2, −117.3)	<.0001
Percentage of study eyes achieving BCVA of 20/40 or better and CRT ≤300 µm at the same visit[a]	19.4% (19/98)	

[a] Percentage calculated among study eyes that had baseline BCVA worse than 20/40 and baseline CRT >300 µm.
AUC = area-under-the-curve; BCVA = best-corrected visual acuity; CI = confidence interval; CRT = central retinal thickness.
2017 Retina World Congress, Singer et al.

Incidence of Adverse Events

All Adverse Events Reported in 3 or More Patients

Adverse Event, n (%)	Patient Population (N=177)
Any adverse event	69 (39.0)
IOP increased	11 (6.2)
Conjunctival hemorrhage	8 (4.5)
Vitreous floaters	7 (4.0)
Dry eye	6 (3.4)
Ocular hypertension	6 (3.4)
Posterior capsule opacification	6 (3.4)
Glaucoma	5 (2.8)
Macular fibrosis	4 (2.3)
Vision blurred	4 (2.3)
Cataract	3 (1.7)
Eye pain	3 (1.7)
Photopsia	3 (1.7)
Vitreous detachment	3 (1.7)
Vitreous hemorrhage	3 (1.7)

IOP = intraocular pressure.

IOP Parameters

Parameter, n (%)	Study Eyes (N=180)[a]
At any time during the study	
• IOP ≥25 mm Hg	22 (12.2)
• IOP ≥35 mm Hg	5 (2.8)
• IOP increase of ≥10 mm Hg from baseline	23 (12.8)

- 41 (22.8%) patients used IOP-lowering medication during the study
- No glaucoma surgeries were reported

[a]Percentages calculated based on the total number of study eyes; 9 study eyes had missing baseline and/or follow-up IOP data.
IOP = intraocular pressure.
2017 Retina World Congress, Singer et al

Incidence of Adverse Events

Adverse Event, n (%)	Patient Population (N =177)
Any adverse event	69 (39.0)
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Cataract	3 (1.7)
Eye pain	3 (1.7)
Photopsia	3 (1.7)
Vitreous detachment	3 (1.7)
Vitreous hemorrhage	3 (1.7)

IOP = intraocular pressure.
2017 Retina World Congress, Singer et al

Conclusions

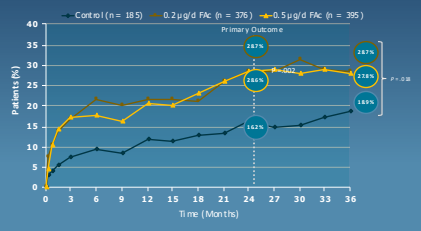
- In real-world clinical practice, DEX monotherapy and adjunctive therapy improved BCVA and CRT in patients with DME
- No new safety concerns were identified

2017 Retina World Congress, Singer et al

Flucinolone FAME Study

Patients Gaining ≥15 ETDRS Letters
(Primary Endpoint)

FAME



Campochiaro PA, et al. Ophthalmology. 2012;119:2125-32.

Three Year Outcomes from the PALADIN Phase IV Study

0.19 mg Fluocinolone Acetonide Implant for DME

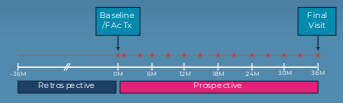
Michael Singer, MD
Medical Center Ophthalmology Associates
San Antonio, TX

On Behalf of the PALADIN Study Group

PALADIN Phase IV Trial in DME

Prospective, open-label observational study designed to evaluate the safety and efficacy of the 0.19-mg FAc intravitreal implant over 36 months for DME

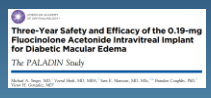
202 eyes received the 0.19 mg FAc implant **on-label** to determine the incidence of **IOP lowering procedures** and **IOP related signals**.



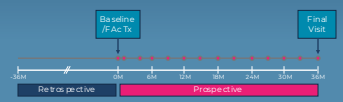
PALADIN Phase IV Trial in DME

Prospective, open-label observational study designed to evaluate the safety and efficacy of the 0.19-mg FAc intravitreal implant over 36 months for DME

202 eyes received the 0.19 mg FAc implant **on-label** to determine the incidence of **IOP lowering procedures** and **IOP related signals**.


Three-Year Safety and Efficacy of the 0.19-mg Fluocinolone Acetonide Intravitreal Implant for Diabetic Macular Edema

The PALADIN Study



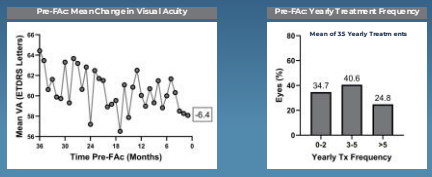
PALADIN Phase IV Trial in DME

Prospective, open-label observational study designed to evaluate the safety and efficacy of the 0.19-mg FAc intravitreal implant over 36 months for DME

Baseline Characteristics	All Eyes (n = 202)
Age, Mean ± SD, (y)	67.00 ± 9.13
Male, n (%)	98 (48.5)
Lens Status, n(%) Pseudophakic Phakic	17 3 (85.60) 29 (14.40)
Follow Up Time Post-ILUVIEN (months), Mean ± SD	27.56 ± 10.99
Baseline IOP, Mean ± SD, mmHg	14.86 ± 3.76
Baseline BCVA, Mean ± SD, Letters	61.50 ± 16.67
Baseline BCVA 20/40 or better, n (%)	65 (32.18)
Baseline CST, Mean ± SD, µm	375.60 ± 126.70
Baseline CST ≤ 300 µm, n (%)	65 (32.18)

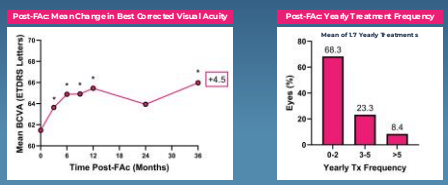
Pre-FAc: Vision Loss with Undertreatment

In the 36 months pre-FAc, eyes lost vision with less than optimal treatment frequency



Post-FAc: Vision Gain with Less Treatment

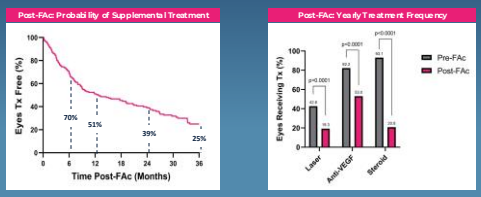
In the 36 months post-FAc, eyes gained a significant amount of vision while needing less frequent therapy for DME



* Denotes significance from baseline with p<005

Better Disease Control with Less Treatment

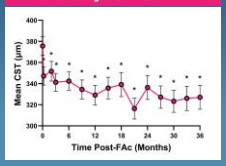
Eyes that received the FAc implant had a 25% chance of remaining treatment free over 3 years and saw significant reductions in DME therapies needed.



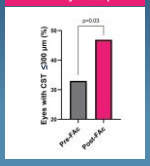
Better Disease Control with Less Treatment

Eyes that received the FAc implant were 1.4 times more likely to see CST values less than 300 µm at 36 months compared to baseline

Post-FAc Mean Change in Center Subfield Thickness



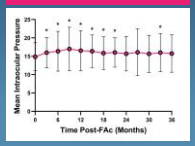
Percent Eyes ≤ 300 µm



Steroid Challenge Mitigates IOP Events

On-label, IOP events were similar to real world use in the USER study and less frequent than the Phase III FAME study (prior to inclusion of steroid challenge)

Mean Intraocular Pressure



IOP Related Event	All Eyes (n=202), n (%)
IOP Increase > 10 mmHg	44 (21.78)
IOP Elevation > 25 mmHg	48 (23.76)
IOP Elevation > 30 mmHg	22 (10.89)
Trabeculoplasty	4 (1.98)
Incisional IOP-Lowering Surgery Neovascular Glaucoma	8 (3.96) 3 (1.49)
Any IOP-Lowering Medication	41 (20.30)

* Denotes significance from baseline with p<0.05
Mean Follow-up Post-FAc was 27.52 Months – All Eyes

Steroid Challenge Predicts FAc Response

Predictive value (PV) determines the percentage of eyes that will remain at or below 25 mmHg post-FAc if a similar response was seen with steroid challenge

	Any PV (n)	Last PV (n)
All Eyes (n=202)	77.95% (155)	96.92% (196)

PALADIN: FAc Remains Safe and Consistent over 36 Months

- Over 36 Months, the 0.19 mg FAc Implant Provided Improved Disease Control over Standard of Care
  - Significant Increase in Visual Acuity
  - Significant Reduction in DME Therapies
  - Significant Reduction in Macular Edema
- Additionally, the FAc Implant Remains Safe with a High Predictability of IOP Response from a Single Steroid Challenge
- The 0.19mg FAc implant provides a durable treatment option that reduces the burden of care for patients with DME

Conclusion

- Medicines are approved based on clinical trial data
- However clinical trials are a laboratory and may not be indicative of real life
- Real World studies give a perspective on what results a doctor can expect when using the medicines in clinical practice
- Sometimes the medicines under perform sometimes the medicines over perform

Vasculitis after Intravitreal Injections

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Financial Disclosures

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- *Speaker Contracted by Ineligible Company:* Allergan, ANI, Apellis, EyePoint, Genentech, Astellas, Regeneron
- *Independent Research Contractor:* Allergan, Apellis, Ashvattha ,EyePoint, Genentech, Astellas, , Kodiak, Optos, Regeneron, Rezolute, Valo
- **Individual Stocks and Stock Options (privately held)* Aviceda, Inflammasome, Nanoscope, Olives BioTherapeutics

Objectives

- Understand the hypersensitivity mechanisms relevant to retinal therapies.
- Review intravitreal injection-associated vasculitides, including: vancomycin, brolucizumab, pegcetacoplan, aflibercept 8mg, ocular ischemic inflammation, and faricimab.
- Discuss diagnostic tools and management strategies.

Hypersensitivity Reactions

Type	Mechanism	Examples in Ophthalmology
Type I	Immediate, IgE-mediated (e.g., peanut allergy)	Anaphylaxis, angioedema
Type II	Cytotoxic, antibody-mediated	Blood transfusion reactions
Type III	Immune complex-mediated, complement activation	Brolucizumab-associated vasculitis, HORV (Vancomycin-associated), Faricimab/aflibercept-associated vasculitis
Type IV	Delayed, T-cell-mediated	Pegcetacoplan-associated vasculopathy and choroiditis, 8mg Aflibercept-associated vasculitis

Hemorrhagic Occlusive Retinal Vasculitis (HORV)

Cause: Likely a Type III Hypersensitivity Reaction (immune complex deposition).

- Inciting Agent: Prophylactic intracameral vancomycin during cataract surgery.

Timing:

- Onset 1–14 days post-surgery.
- Delay suggests an immune-mediated rather than direct toxic reaction.

Mechanism:

- Deposition of vancomycin-antibody immune complexes in retinal vessels.
- Results in small-vessel vasculitis primarily affecting retinal venules.
- Associated with severe retinal ischemia and hemorrhage.
- Choroidal involvement as well

Reference: Wilden AJ, et al. Ophthalmology. 2015. DOI: 10.1016/j.ophtha.2015.03.036

HORV Clinical Findings

Presentation:

- Painless vision loss (central or peripheral).
- Onset: 1–14 days after cataract surgery.

Signs:

- Mild anterior chamber inflammation (1+ to 3+ cells).
- Diffuse retinal hemorrhages and vascular occlusion.
- Venous predilection for occlusive vasculitis.
- Widefield FA: Severe peripheral non-perfusion and venous staining.

Complications:

- Neovascular glaucoma in ~64% of eyes.
- Severe vision loss despite aggressive treatment.

Reference: Wilden AJ, et al. Ophthalmology. 2015. DOI: 10.1016/j.ophtha.2015.03.036

HORV Management

Aggressive Corticosteroid Therapy

- Systemic and topical steroids.

Anti-VEGF Therapy

- Intravitreal bevacizumab for retinal ischemia and neovascularization.

Panretinal Photocoagulation (PRP)

- Prevention of neovascular glaucoma due to severe ischemia.

Vitrectomy

- In cases of vitreous hemorrhage or severe inflammation.

Avoid Re-challenge with Vancomycin

- If HORV is suspected, avoid intraocular vancomycin in future procedures.

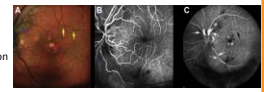
Brolucizumab-Associated Vasculitis

Delayed-onset retinal vasculitis following intravitreal brolucizumab injection.

Mechanisms:

Immune Response:

- Type III Hypersensitivity: Immune complexes form and deposit in retinal vessels.
- Activation of complement cascade leads to inflammation and vasculitis.



Antidrug Antibodies (ADAs):

- 53%–67% of patients develop antibodies to brolucizumab.
- Associated with higher risk of inflammation and vasculitis.

Clinical Significance:

- Involves occlusive retinal vasculitis.
- Associated with potential for severe vision loss.
- Usually not a first injection phenomenon.
- It is a delayed hypersensitivity response

References
Monés, J., et al. *Ophthalmology*, 2021. DOI: 10.1016/j.ophtha.2020.12.015 Witkin, A. J., et al. *Ophthalmology*, 2020. DOI: 10.1016/j.ophtha.2020.03.023

Brolucizumab-Associated Vasculitis Clinical Findings

Delayed presentation

Average onset 25 days (range 3–63 days) post-injection.

Symptoms:

- Blurry vision (62%)
- Floaters (46%)
- Pain (31%)
- Redness (19%)

Imaging:

- Fluorescein Angiography (FA): Filling defects, leakage, staining.
- Color Fundus Photography: Arterial sheathing, boxcarring, retinal whitening.
- Predominantly affects arteries (91%) vs. veins (79%).

References
Monés, J., et al. *Ophthalmology*, 2021. DOI: 10.1016/j.ophtha.2020.12.015 Witkin, A. J., et al. *Ophthalmology*, 2020. DOI: 10.1016/j.ophtha.2020.03.023

Brolucizumab-Associated Vasculitis Management

Discontinue Brolucizumab

- Immediately stop further brolucizumab injections.

Anti-Inflammatory Treatment

- Initiate high-dose systemic corticosteroids (e.g., oral prednisone 60 mg/day).
- Consider intravitreal corticosteroids for severe intraocular inflammation.

Address Occlusive Vasculitis

- Antiplatelet Therapy: To reduce the risk of thrombosis (consultation with a vascular specialist if needed).
- Vasodilators: May be considered to improve retinal perfusion.

Adjunctive Therapies:

- Immunomodulatory Agents for refractory cases (e.g., methotrexate, mycophenolate mofetil).

Close Monitoring

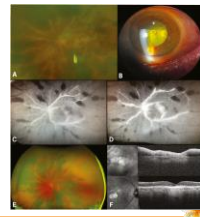
- Frequent follow-up with widefield fluorescein angiography (FA) to assess for progression or resolution of vasculitis.
- Monitor for complications: retinal ischemia, neovascularization, or macular edema.

References:
Khan, J. et al. Ophthalmology, 2021. DOI: 10.1016/j.ophtha.2020.12.05
Khan, A. J. et al. Ophthalmology, 2021. DOI: 10.1016/j.ophtha.2020.03.02

Pegcetacoplan Associated Vasculitis

Mechanism:

- Drug-induced, immune-mediated, retinal vasculopathy and choroiditis (DIRVAC)
- Likely a mixed-type, delayed hypersensitivity reaction involving:
  - T-cells, macrophages, and eosinophils



Clinical Features:

- **Almost always** a first injection phenomenon
- **Delayed Onset**: ~9-12 days post-injection
- **Symptoms:**
  - Vision loss
  - Retinal hemorrhages
  - Vessel sheathing
  - Vascular non-perfusion

References: Nehar, A., et al. Ophthalmology Retina, 2024. DOI: 10.1016/j.oret.2024.10.009

Pegcetacoplan Clinical Data

Histopathologic Findings:

- **Vascular Thrombosis** and **Retinal Necrosis**
- **Dense Inflammatory Infiltrate:**
  - Uvea, optic nerve, and episclera
  - Predominantly T-cells, macrophages, and eosinophils

Complications:

- Severe vision loss despite corticosteroid treatment
- Enucleation may be required for pain control

Management:

- High-dose corticosteroids (systemic and intravitreal)
- Monitoring for ischemia and neovascular complications

DIRVAC and COVID-19 Vaccination

Potential Mechanism:

- **PEGylation** (**Polyethylene Glycol**) in pegcetacoplan and COVID-19 vaccines
  - May induce **anti-PEG antibodies**
  - Possible cross-reactivity leading to delayed hypersensitivity

References: Nehar, A., et al. *Ophthalmology Retina*. 2021. DOI: 10.1016/j.oret.2021.10.005.

Pegcetacoplan Associated Vasculitis Management

Immediate Cessation of Pegcetacoplan:

- Stop **Pegcetacoplan** injections at the first signs of intraocular inflammation or vasculitis.

Corticosteroid Therapy:

- Initiate topical or systemic corticosteroids based on severity:
  - **Mild cases:** Topical steroids (e.g., prednisolone acetate 1%).
  - **Moderate to severe cases:** Systemic steroids (e.g., oral prednisone, 0.5–1 mg/kg/day).

Vasculitis-Specific Considerations:

- Assess for potential choroidal and retinal vascular occlusion using fluorescein angiography (FA) or optical coherence tomography angiography (OCTA).

Immunomodulators:

- Consider the use of immunomodulatory therapy (e.g., methotrexate, mycophenolate mofetil) in refractory or recurrent cases.

Avoid Anti-VEGF During Active Vasculitis:

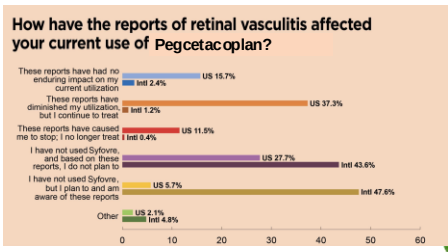
- Once inflammation resolves, cautiously reintroduce therapy under strict observation.

Long-Term Monitoring:

- Regular follow-up for recurrent inflammation, retinal structural integrity, and visual function.
- Document changes using OCT, OCTA, and FA imaging to guide further treatment.

References:
Khan M, et al. "Systemic-associated intraocular inflammation: Safety and outcomes." *Retina*. 2021.
Pegcetacoplan Product/Safety Information. Apellis Pharmaceuticals, 2023.

2024 PAT Survey



Faricimab-Associated Vasculitis

Overview:
- Faricimab: A bispecific antibody targeting VEGF-A and Angiopoietin-2.
- Approved for **neovascular AMD** and **diabetic macular edema**.

Vasculitis Incidence:
- Rare adverse event, rate approximately **0.06 per 10,000 injections**.
- Cases reported in clinical practice post-approval.

Mechanism:
- Hypothesized delayed hypersensitivity reaction with immune complex deposition.

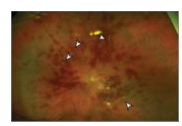
References
Coral M, et al. "Faricimab-associated retinal vasculitis: A case report." Ophthalmology Retina. 2023.
Gherasim M, et al. "Immune-mediated adverse events following Faricimab administration." Retina Cases and Brief Reports 2023.

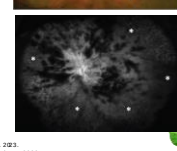
Faricimab-Associated Vasculitis – Clinical Findings

Presenting Symptoms:
- Sudden visual loss, floaters, or scotomas.
- Often occurs 3–5 weeks post-injection.

Ophthalmic Examination:
- Retinal vascular occlusion (arterial and/or venous).
- Hemorrhages and ischemic signs (e.g., paracentral acute middle maculopathy).
- Significant leakage on fluorescein angiography.

Differential Features:
- Resembles Brolucizumab-associated vasculitis but potentially less frequent.





References
Lee K, et al. "Clinical spectrum of Faricimab-associated vasculitis." American Journal of Ophthalmology Case Reports 2023.
Reichel E, et al. "Vasculitis in patients treated with Faricimab: A clinical study." Investigative Ophthalmology & Visual Science 2023.

Faricimab-Associated Vasculitis – Management

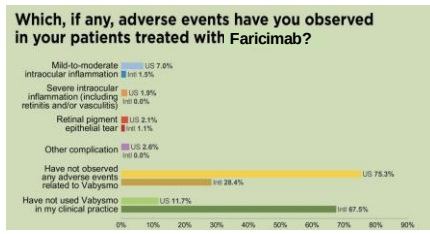
Immediate Actions:
- **Discontinue Faricimab** upon suspicion.
- Rule out infectious causes with imaging and sterile cultures.

Treatment Protocol:
- **Systemic Corticosteroids:**
  - Prednisolone (1 mg/kg/day) with gradual taper.
- **Intravitreal Corticosteroids:**
  - Dexamethasone implant in severe cases.
- **Adjunctive Measures:**
  - Manage secondary complications like ischemia and neovascularization with PRP or cautious anti-VEGF use post-resolution.

Prognosis:
- Variable outcomes: Visual stabilization possible but recovery often limited.

References
Lee K, et al. "Clinical spectrum of Faricimab-associated vasculitis." American Journal of Ophthalmology Case Reports 2023.
Reichel E, et al. "Vasculitis in patients treated with Faricimab: A clinical study." Investigative Ophthalmology & Visual Science 2023.

2023 PAT Survey



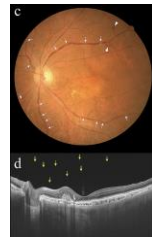
Aflibercept 8mg Associated Vasculitis

Overview:
- Aflibercept 8 mg is a higher-dose anti-VEGF agent, approved for neovascular AMD and diabetic macular edema. It offers extended durability and reduced injection frequency compared to 2 mg Aflibercept.

Emerging Concern:
- Retinal vasculitis associated with mild intraocular inflammation (IOI) has been reported post-approval.

Potential Mechanism:
- Hypothesized immune response to the higher protein concentration in 8 mg Aflibercept.
- Type 3 hypersensitivity reaction
- Induction of inflammatory cytokine cascades similar to other anti-VEGF agents.

Significance:
- Vasculitis cases highlight the need for cautious clinical monitoring despite minimal incidence in pivotal trials (e.g., QUASAR, PULSAR).



References:
Matsumoto, M., et al. "Aflibercept 8 mg: Safety and Emerging Insights from Real-World Cases." *Journal of Retina and Vitreous Diseases*, 2023.
QUASAR Study Data. Eyeka HCP adage Insert, 2023.

Aflibercept 8mg Associated Vasculitis: Clinical Findings

Incidence: Vasculitis associated with 8mg aflibercept remains very rare much less than .001 percent.

Time to Onset: Observed predominantly within 1–3 months of treatment initiation.
- **First Injection Phenomenon:** Frequently noted after the initial dose but possible in subsequent doses.
- Can be seen in patients with inflammation after second generation medications (brolucizumab and faricimab

Signs and Symptoms:
- Retinal venous narrowing and mild intraretinal hemorrhage.
- Leakage seen on fluorescein angiography.
- Mild vitritis evident on OCT imaging.

Severity: Most cases resolve without significant vision loss when managed appropriately.

References:
Matsumoto, M., et al. "Aflibercept 8 mg: Safety and Emerging Insights from Real-World Cases." *Journal of Retina and Vitreous Diseases*, 2023.
QUASAR Study Data. Eyeka HCP adage Insert, 2023.

Aflibercept 8mg Associated Vasculitis: Management

Immediate Steps: Suspend Aflibercept 8 mg injections.

Medications:
- Posterior subtenon triamcinolone acetonide.
- Adjunctive topical betamethasone or prednisolone eye drops.

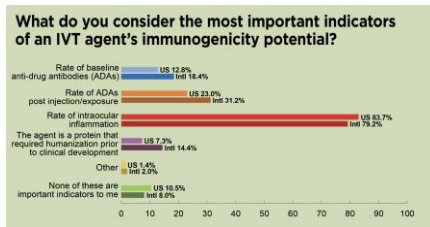
Avoid additional anti-VEGF injections until inflammation resolves.

Precautions:
- Monitor closely during the first few injections for signs of inflammation.
- Consider switching to a different anti-VEGF agent in patients with severe inflammatory history.

Prognosis: Favorable outcomes with early recognition and steroid treatment.

References:
Matsumoto, M., et al. "Aflibercept 8 mg: Safety and Emerging Insights from Real-World Cases." *Journal of Retina and Vitreous Diseases*, 2023.
QUASAR Study Data. Eylea HDP advancement, 2023.

2024 PAT Survey



Ocular Ischemic Inflammatory Syndrome (OIIS)

A syndrome characterized by retinal ischemia and inflammation often associated with diabetes mellitus (DM).

Mechanism:
- Chronic ischemia due to carotid artery stenosis and diabetic microvascular damage.
- Inflammatory response triggered by ischemic hypoxia.
- Elevated levels of VEGF and pro-inflammatory cytokines.

Role of Diabetes Mellitus:
- Hyperglycemia-induced damage to retinal capillaries.
- Systemic vascular disease increasing susceptibility to ischemic changes.

Presentation: Ischemia out of proportion to diabetic retinopathy severity.

Ocular Ischemic Inflammatory Syndrome (OIIS)

Anterior Segment Findings

- Rubeosis
- Hyphema

Posterior Segment Findings:

- Mild diabetic retinopathy despite ischemic complications.
- Retinal hemorrhages and vascular leakage.

Diagnostic Workup:

- Carotid workup
- Fluorescein Angiography (FA):
  - Significant vascular leakage resembling vasculitis.
  - Delayed retinal perfusion and capillary non-perfusion.

Risk of Anti-VEGF Therapy in OIIS

Mechanisms:

VEGF suppression leads to:

- Reduced compensatory neovascularization.
- Exacerbation of ischemia.
- Potential vascular occlusion due to vasoconstriction and endothelial damage.

Consequences:

- Worsening ischemia and retinal vascular occlusion.
- Potential for vision loss or exacerbation of inflammatory changes.

High-Risk Factors:

- History of rubeosis iridis or hyphema.
- Significant ischemia on FA.

Case 1: OIIS treated with bevacizumab

64-year-old male with DM presents with 20/80 vision

- 2+ Rubeosis moderate NPDR

Patient given intravitreal bevacizumab

3 days later returns with pain.

- Vision 20/100.

2 weeks later returns with decreased vision: CF

- FA shows gross non perfusion and box carring
- Patient given dex implant and PRP.

Workup demonstrated extreme bilateral carotid disease

- Rubeosis resolved
- **Vision remains CF**

Before anti-VEGF 2 weeks after anti-VEGF

Case 2: OIIS Treated with Dexamethasone Implant

64-year-old male with DM presents with vision loss OD

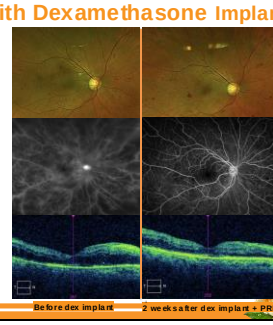
- VA OD dropped from 20/50 to 20/200 in 1 week
- New rubeosis

Treated with dexamethasone implant initially

Followed up with bevacizumab and PRP 2 weeks later.

Workup similarly demonstrated extensive carotid disease

- **VA result was 20/20**



Before dex implant

2 weeks after dex implant + PRP

Management Strategy for OIIS

Control Inflammation First:

- Dexamethasone Implant to reduce inflammation and vascular leakage.

Address Ischemia:

- Panretinal Photocoagulation (PRP) to reduce VEGF production.

Anti-VEGF Therapy (If Needed):

- Administer only after vasculitis and inflammation resolve.

Rationale:

- Prevent worsening ischemia and vascular occlusion by stabilizing inflammation before VEGF suppression.

Management Summary

Condition	Trigger	Management Strategy
HDRV	Vancomycin	**Immediate corticosteroids** (systemic, topical, intravitreal) **Anti-VEGF therapy** for neovascularization **Panretinal photocoagulation (PRP)** to prevent neovascular glaucoma
Brolucizumab-Associated Vasculitis	Brolucizumab	**Discontinue brolucizumab** immediately **Aggressive corticosteroids** (systemic, topical, intravitreal) **Anti-VEGF rechallenge** only after full resolution of inflammation (using alternative agents) **Imaging**: FA, ICGA to monitor for recurrence
Pegaptanib-Associated Vasculopathy (DIRVAC)	Pegaptanib	**High-dose corticosteroids** (systemic and intravitreal) **Pain control** measures; consider **enucleation** for severe cases **Monitor closely** for signs of ischemia and neovascular complications **Screen for recent IDVID-19 vaccination** due to potential **PEG hypersensitivity**
Faricimab-Associated Vasculitis	Faricimab	**Discontinue Faricimab immediately** **Aggressive corticosteroid therapy** **Imaging**: FA, OCT for monitoring occlusive events Consider alternative anti-VEGF agents cautiously
Bmg Aflibercept-Associated Vasculitis	Aflibercept Bmg	**Stop treatment** upon detection of vasculitis **Administer corticosteroids** (systemic/intravitreal) Imaging (FA, ICGA) to evaluate inflammation Monitor for reintroduction of treatment post-resolution
Ocular Ischemic Inflammatory Syndrome (OIIS)	Diabetes Mellitus, Carotid Disease	**Dexamethasone implant** for initial treatment **PRP** and/or **anti-VEGF** (after resolving vasculitis) **Avoid immediate anti-VEGF** due to risk of vascular occlusion **Carotid disease management** (e.g., endarterectomy if indicated)

Conclusion

Early recognition and intervention of vasculitis is critical for patient safety.

- **HORV**: Delayed-type (Type III) immune complex-mediated reaction triggered by vancomycin.
- **Brolucizumab-Associated Vasculitis**: Delayed-type (Type III) immune complex-mediated reaction leading to occlusive vasculitis; requires discontinuation and aggressive corticosteroid treatment.
- **Pegcetacoplan-Associated Vasculitis**: Delayed hypersensitivity reaction; characterized by cell-mediated immune response, managed with high-dose corticosteroids and careful monitoring.
- **Faricimab-Associated Vasculitis:** Inflammatory and immune-mediated vasculitis. May occur at various stages of treatment. Corticosteroids are the primary management strategy..
- **8mg Aflibercept-Associated Vasculitis:** First-injection phenomenon observed; corticosteroids are essential for inflammation resolution, with close monitoring.
- **OIIS (Ocular Ischemic Inflammatory Syndrome):** Inflammatory vasculitis linked to diabetes and rubeosis; corticosteroids are the primary treatment, while anti-VEGF therapy carries a risk of worsening vascular occlusion

Collaboration, vigilance, and appropriate management strategies are essential to mitigate risks and ensure optimal outcomes.

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Management of Retinal Detachments

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New Orleans Academy of Ophthalmology
February 2025

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Disclosures

- Consultant: Alimera, Allergen, Alcon, Genentech, Ocuphire Pharm, Ocular Therapeutics, ANI Pharmaceuticals
- Investigator: Alimera, Genentech, Inc., Jaeb Center for Health Research, Regeneron, Novartis, Ocuphire Pharm, Parexel, Ocular Therapeutics
- Speaker: Genentech, Inc., Apellis, Astellas, Regeneron

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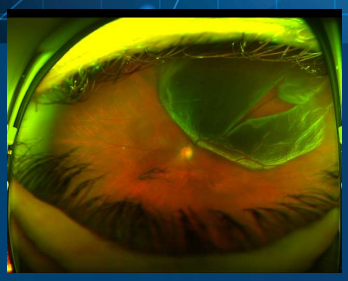
Types of Retinal Detachments

- Rhegmatogenous
- Tractional
- Exudative

4

Rhegmatogenous Retinal Detachment



Symptoms

- Flashes or "sparkles"
- Floaters or "cobwebs"
- Vision loss
- Asymptomatic

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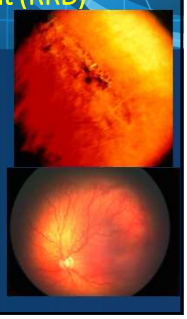
Rhegmatogenous Retinal Detachment (RRD)

- 1 in 10,000
- Age range usually 55-70 years old
- Post-surgical incidence of RD is 0.2%-3.6%
- Cataract surgery and myopia are the greatest risk factors
  - Vitreous loss
  - Myopes ~40-45% of phakic RDs
  - Consider referral to retina for evaluation post-complex cataract surgeries or for evaluation of patients with high myopia
- 3.5-5.8% risk of fellow eye RRD within 1 year and 9-10% within 4 years



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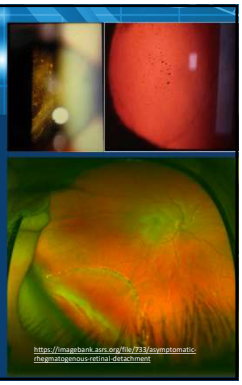
Considerations in urgency of treatment

- Timing of surgery
  - Duration of symptoms/chronicity
  - Macular status
    - based on fluid line (exam +/- OCT), vision
    - Mac on: generally within 24-48 hours
    - Mac off: within 5-7 days, but optimally sooner
  - Location of detachment
    - inferior versus superior
  - Patient anxiety

7

Exam pearls to identify RD

- Low IOP (unless chronic- could have a/c inflammation from RPE fragments)
- +APD
- Slit lamp exam
  - Anterior pigmented cell (Shafer's sign or tobacco dust)- focus behind the lens with narrow beam
  - Vitreous hemorrhage
  - Posterior vitreous detachment
- Indirect exam
  - Dynamic scleral depression



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PROLIFERATIVE VITREORETINOPATHY

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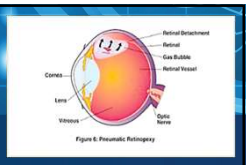
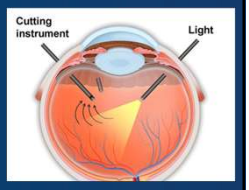
Management of RRD

- Laser for localized RD
- Pneumatic retinopexy
  - In-office procedure
  - Phakic patients with superior RD
- Scleral buckle
- Pars plana vitrectomy +/- scleral buckle





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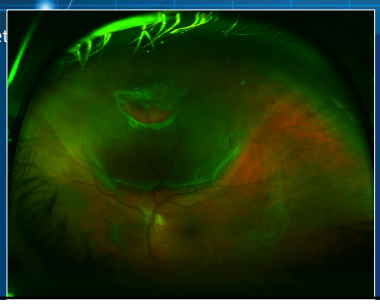
Pneumatic retinopexy - Preop

- Florida Ret



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Pneumatic retinopexy - Post-op

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Scleral buckle - Pre-op

- Florida Ret

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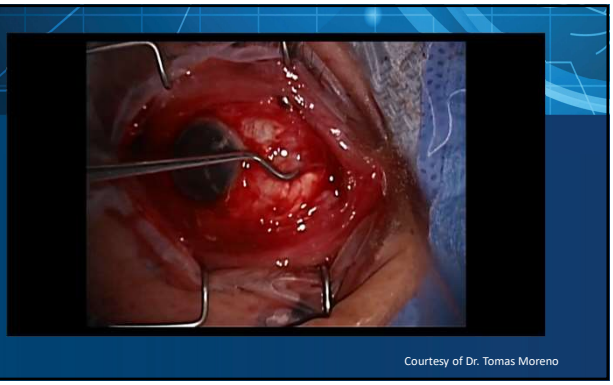

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Scleral buckle-Postop

- Florida

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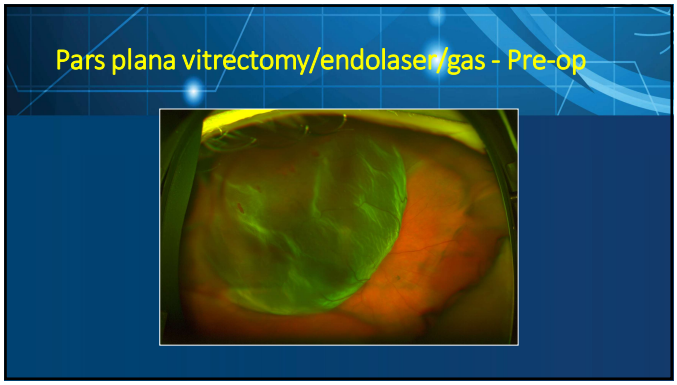
Pars plana vitrectomy/endolaser/gas - Pre-op

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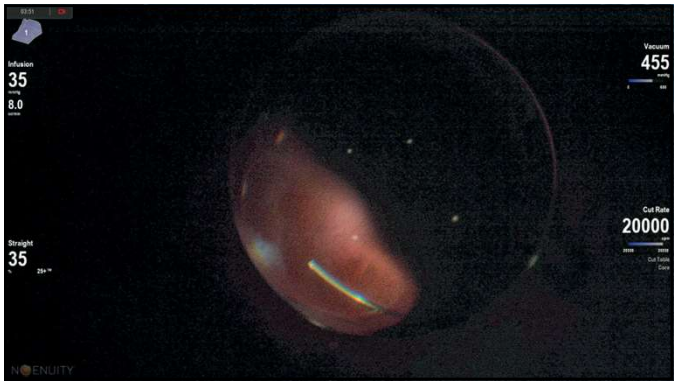
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Straight
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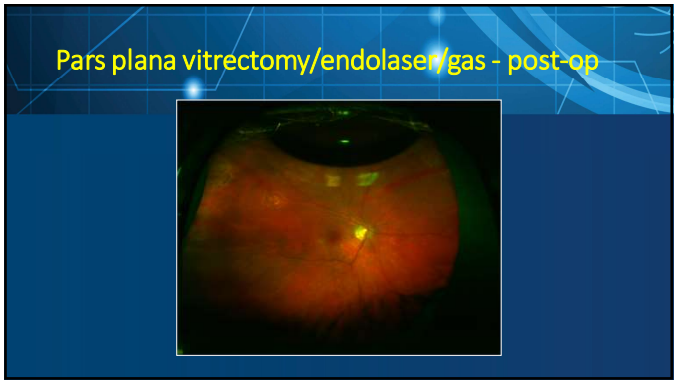
Pars plana vitrectomy/endolaser/gas - post-op

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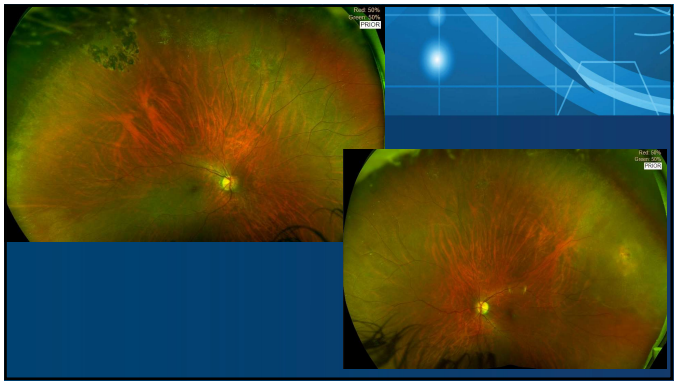

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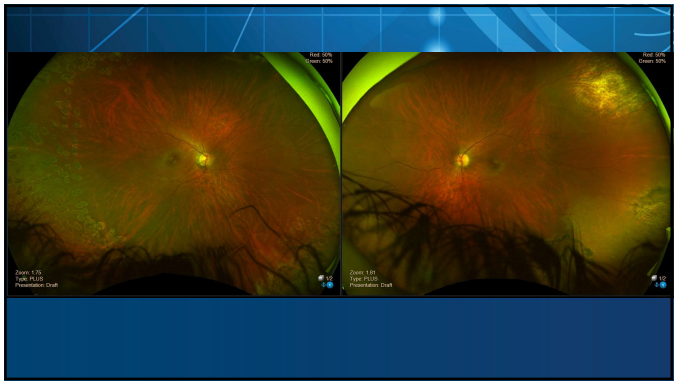

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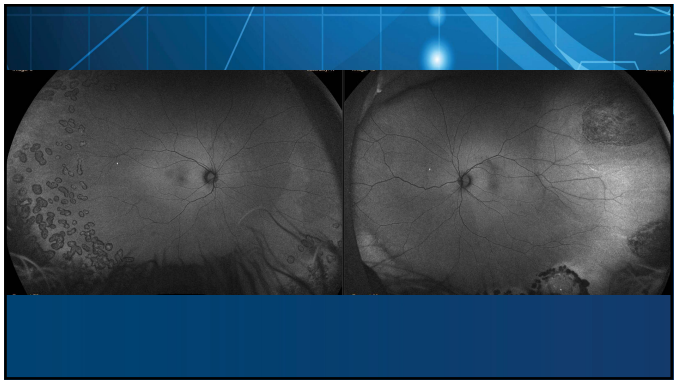
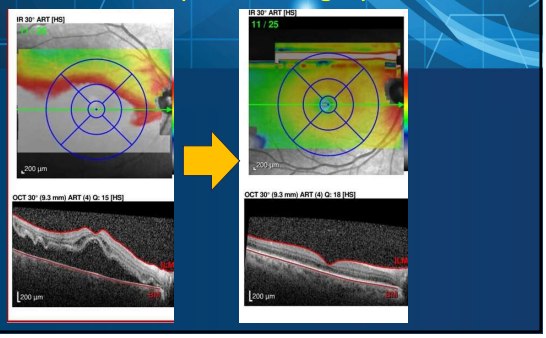


21

Pre and post RD surgery



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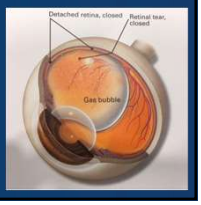
Post op considerations

- Lens Feathering from vitrectomy and tamponade
- Restrictions: ok to read and use the eye
- Intraocular gas
  - **Restrictions on travel/elevation due to risk of bubble expansion**
  - Positioning
  - Watch IOP



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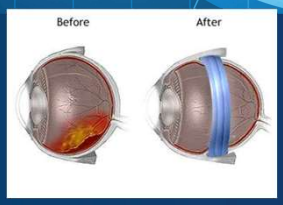
Post op considerations

- Silicone oil- Refractive changes
  - Aphakic eyes→ decreases hyperopia (convex surface to K, acts as plus lens)
  - Phakic eyes → increases hyperopia (concave surface behind lens, acts as minus lens)
  - Pseudophakic eye → myopic shift

24

Scleral Buckle

- 2-4D of myopic shift
- Silicone band supports vitreous base
- Loop intraocular muscles, pass underneath
- Buckle/vitrectomy or buckle/cryotherapy with or without tamponade
- Diplopia

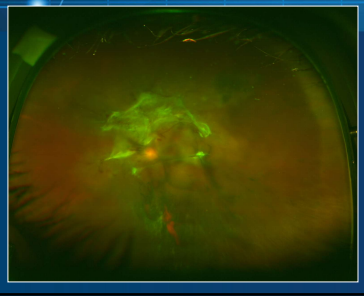


25

Traction Retinal Detachment

26

Tractional retinal detachment pre op



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VIDEO
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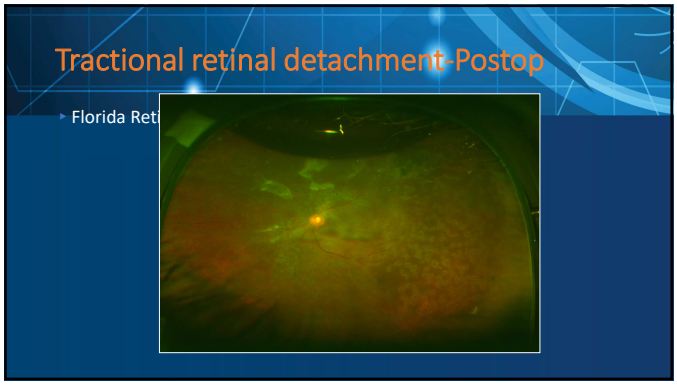
Traction Retinal Detachment
Matthew Cunningham, MD

28


Tractional retinal detachment-Postop
Florida Reti

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Exudative retinal detachment with choroidal

30

Conclusion

- There are multiple ways to repair retinal detachments
- The success rate for retinal detachment repair is 90% with a single surgery
- Considerations for the urgency of surgery is multi-factorial

31

Thanks for your attention

Top Left to Bottom Right: Kyle S. Fallgatter, MD; S.K. Steven Houston III, MD, FASRS; Jonathan A. Staman, MD; Abdallah M. Jeroudi, MD; Raul J. Moreno, MD; Jaya B. Kumar, MD, FASRS; Benjamin J. Thomas, MD; Luis G. León-Alvarado, MD; Nisarg P. Joshi, MD; Matthew A. Cunningham, MD, FASRS; James A. Staman, MD; Elias C. Mavrofrides, MD; Tomas A. Moreno, MD; and Thomas A. Barnard, MD. Thalmon R. Campagnoli, MD, joining in Fall of 2024.

32