NYU School of Medicine
NYU LANGONE MEDICAL CENTER

Real World Outcomes of Faricimab

Yasha Modi, MD
Associate Professor of Ophthalmology
NYU Langone Health, New York University

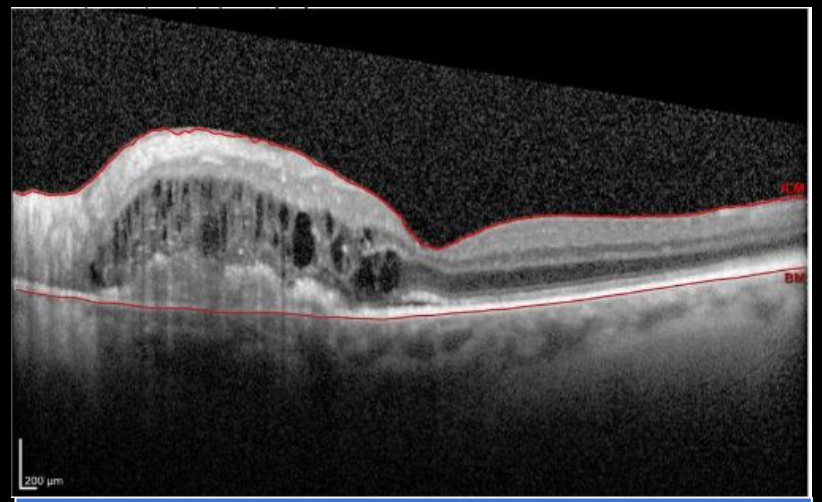
Who Do We Treat with Faricimab in the Real World?

- Who should I start?

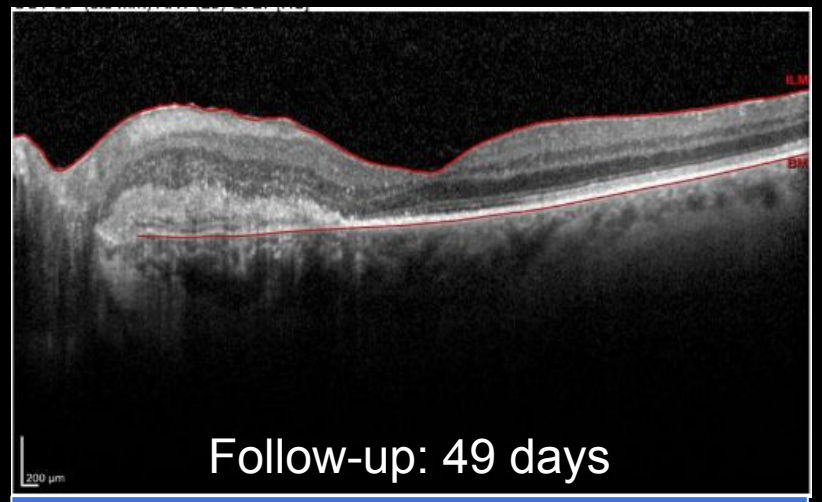
  Extrapolated experience over the last decade (switching from bevacizumab or ranibizumab to aflibercept)

- Clinical study demonstrated good outcomes for treatment-naïve patients… But what about patients with recalcitrant disease? How do those patients fare?

Case 1: Treatment-Naïve Patient



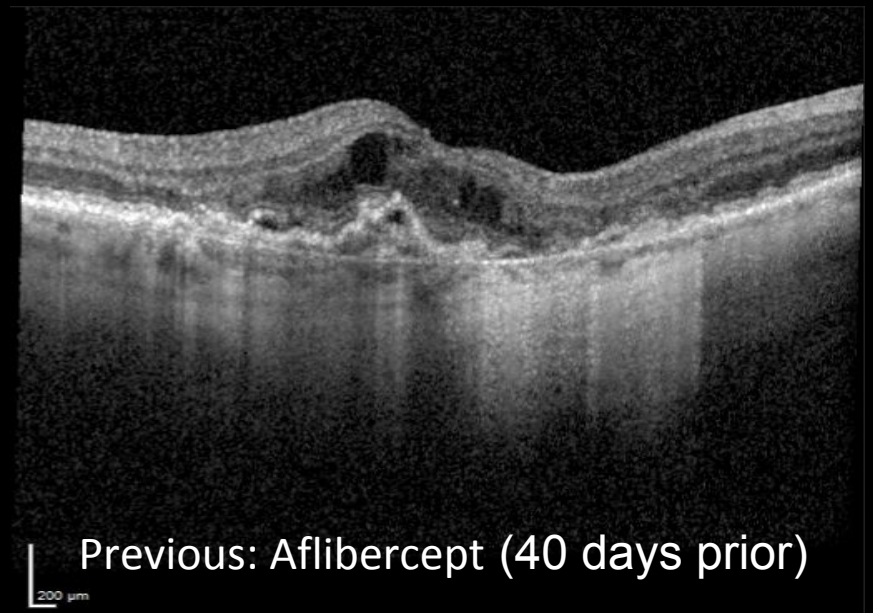
BCVA: 20/100
CST: 363 µM
Presence of IRF and hemorrhage at baseline



Follow-up: 49 days

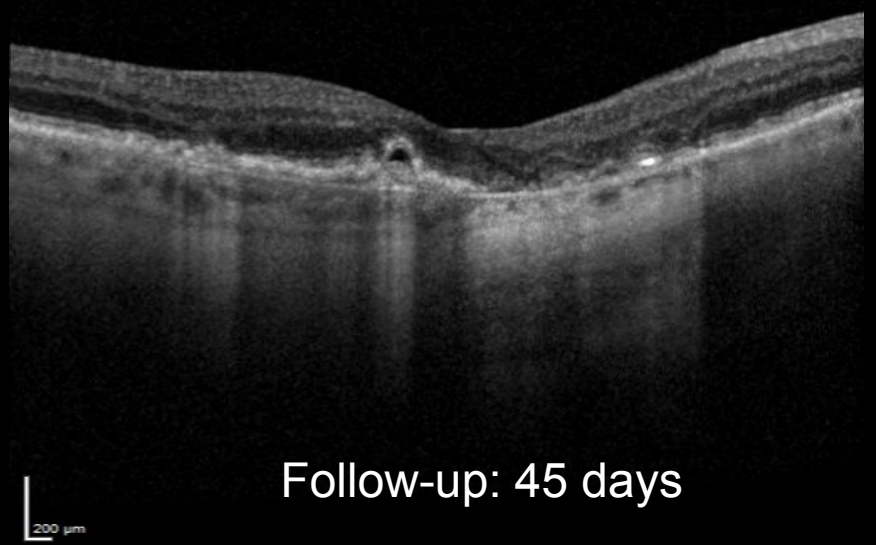
BCVA: 20/40
CST: 240 µM
Fluid resolution with improved visual acuity

Case 2: Exudative AMD receiving aflibercept



Previous: Aflibercept (40 days prior)

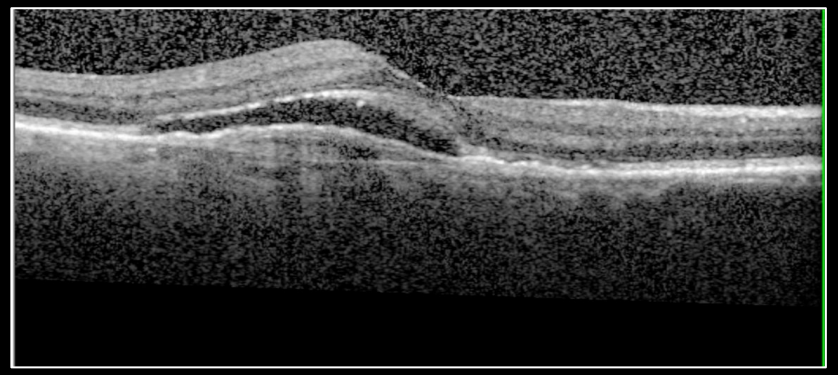
BCVA: 20/50
CST: 399 µM



Follow-up: 45 days

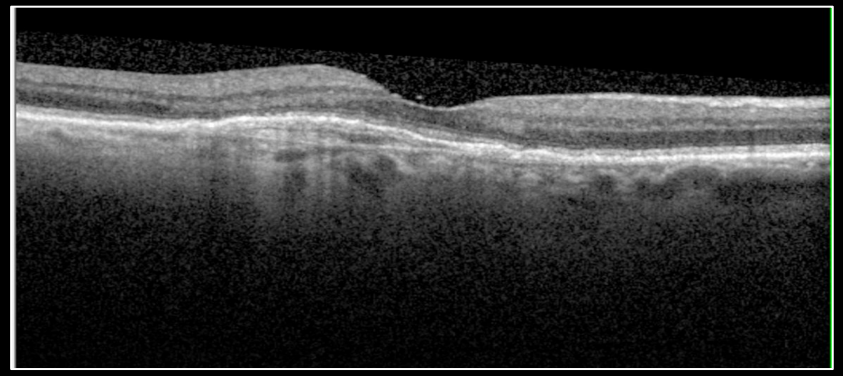
BCVA: 20/40
CST: 210 µM

The Problem with Case Studies...

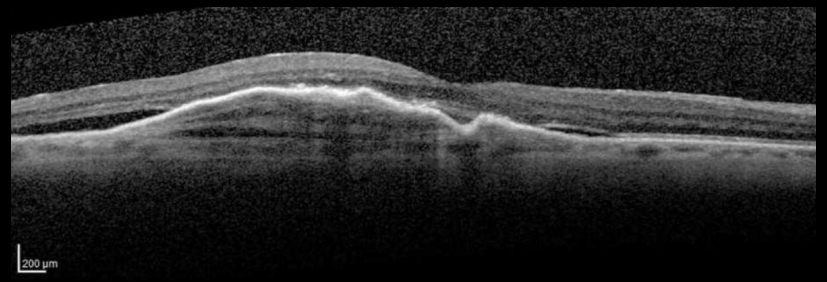


BCVA: 20/40
CST: 385 µM
Aflibercept give 31 days prior

Switched to Faricimab

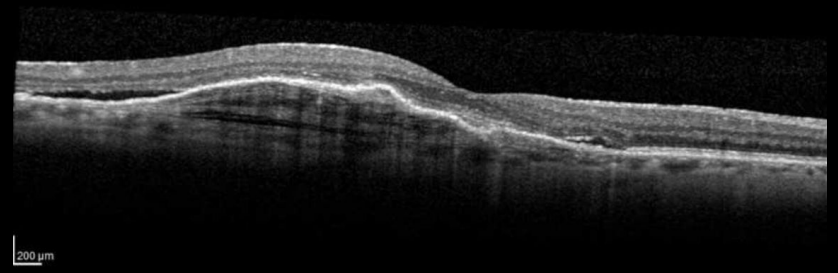


BCVA: 20/30
CST: 280 µM



BCVA: 20/30-2
Aflibercept given 28 days prior

Switched to Faricimab



BCVA: 20/40

Invites Cognitive Bias (Selection Bias)

SINCE THE LAUNCH OF VABYSMO IN JANUARY 2022, REAL-WORLD EVIDENCE for >13,000 PATIENTS HAS BEEN REPORTED

RWE IN nAMD	• Wolfe JD, Khan H, Aziz AA, et al. The TRUCKEE Study: Real-World Efficacy and Safety of Faricimab in Neovascular AMD. Presented at the Retina Society 55th Annual Scientific Meeting; November 2-5, 2022. RS Oral Presentation • Rush RB and Rush SW. Intravitreal Faricimab for Aflibercept-Resistant Neovascular Age-Related Macular Degeneration. *Clinical Ophthal.* 2022;16:4041-4046. • Ali F, Tabano D, Garmo V, et al. Real-World Use of Faricimab: From the IRIS® Registry. Presented at the Hawaiian Eye and Retina Meeting; January 17, 2023.
RWE IN DME	• Rush RB and Rush SW. Faricimab for treatment-resistant diabetic macular edema. *Clinical Ophthal.* 2022;16:2797-2801. • Ali F, Tabano D, Garmo V, et al. Real-World Use of Faricimab: From the IRIS® Registry. Presented at the Hawaiian Eye and Retina Meeting; January 17, 2023.

The pending VOYAGER study will include an additional 5,000 patients receiving Vabysmo in a real world setting

Abbreviation: RWE=Real-World Evidence.

The TRUCKEE Study
Real World Efficacy and Safety of Faricimab in Neovascular AMD

Ramanath Bhandari MD, Hannah Khan, MPH; Aamir A. Aziz, BS; Ashwin Gupta, BA; Aigerim Saulebayeva, MD; Ashkan M. Abbey, MD; David R.P Almeida, MD, PhD, MBA; Robert L. Avery, MD; Himanshu K. Banda, MD; Mark R. Barakat, MD; Emmanuel Y. Chang, MD, PhD; Carl J. Danzig, MD; Sara J. Haug, MD, PhD; Nikolas J.S. London, MD; Michael A. Singer, MD; Veeral S. Sheth, MD, MBA, FASRS, FACS; Jeremy M. Wolfe, MD; Arshad M. Khanani, MD, MA, FASRS

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, pigment epithelial detachments)
- Durability
- Safety

TRUCKEE Study Design

491 total patients treated with faricimab (study population)

A total of 1,231 intravitreal injections administered

One month follow up was available for 335 patients (37 naive patients and 298 previously-treated patients)

89% were previously treated

Results: Demographics

(N = 335 patients, 376 eyes with follow-up)

Variable	Mean	Range
Age (years)	79.8	44-100

Variable	Groups	N (%)
Gender	Male	149 (44.5%)
	Female	185 (55.5%)
Last anti-VEGF injection	**Aflibercept**	**237 (63.0%)**
	Ranibizumab	58 (15.4%)
	Brolucizumab	26 (6.9%)
	Bevacizumab	16 (4.3%)
	Treatment Naïve	39 (10.4%)

* Follow-up defined as a completed office visit after the first faricimab injection

What Happens After 1 Faricimab Injection?

- In the absence of a control arm, it's difficult to demonstrate benefit of any treatment.

- Temporal association after first faricimab exposure highlights the potential biologic activity of the drug.

- Avoids "regression to the mean" problem with repeat injections of same medication

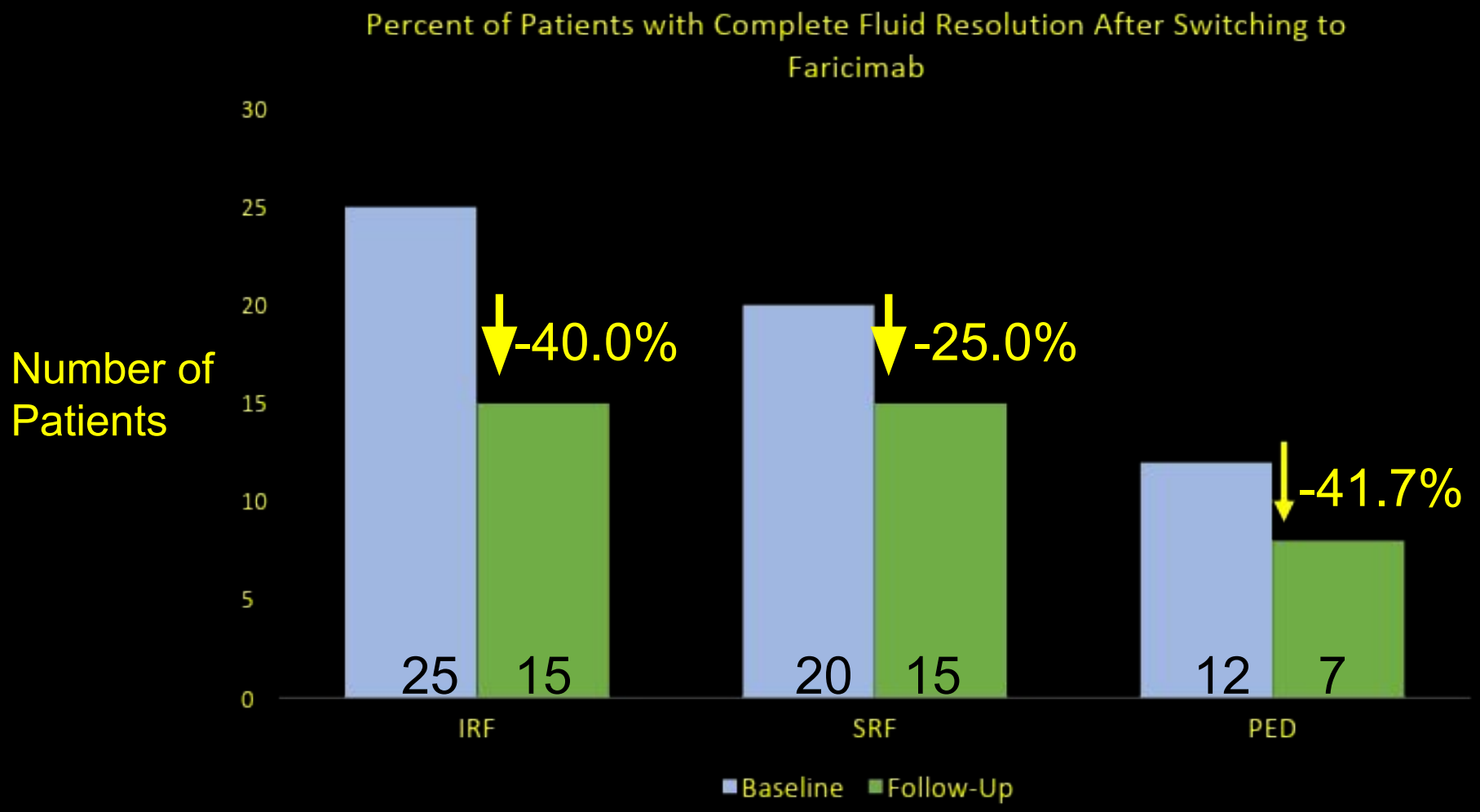
Efficacy After One Injection of Faricimab in Treatment Naive Patients

(N = 37 patients, 39 eyes)

	Baseline	Follow-Up	Change	P-Value
Variable	**Mean [SEM]**	**Mean [SEM]**		
ETDRS (letters)*	55.8 letters [0.59]	60.7 letters [0.51]	+4.9 letters	0.076
CST (µM)	380.4 µM [2.86]	295.9 µM [2.26]	-84.5 µM	**<0.001**
PED Height** (µM)	199.3 µM [10.4]	105.5 µM [12.6]	-93.8 µM	**0.001**

*Based on Snellen to ETDRS conversion
**If applicable

IRF, SRF & PED Outcomes in Treatment Naive Patients after One Injection of Faricimab



Efficacy After One Injection of Faricimab in All Patients Switched from Any Anti-VEGF

(N = 298 patients, 337 eyes with follow-up)

	Baseline	Follow-Up	Change	P-Value
Variable	**Mean [SEM]**	**Mean [SEM]**		
ETDRS (letters)*	60.0 letters [0.06]	60.7 letters [0.06]	+0.7 letters	0.196
CST (µM)	328.0 µM [0.35]	302.7 µM [0.35]	-25.3 µM	**<0.001**
PED Height** (µM)	244.5 µM [1.55]	185.6 µM [1.60]	-58.9 µM	**<0.001**

Previous Interval: 44.2 days **Follow-up Interval: 43.5 days**

*Based on Snellen to ETDRS conversion
**If applicable

But what about switching from aflibercept to faricimab?

Efficacy After One Injection of Faricimab in All Patients Switched From Aflibercept

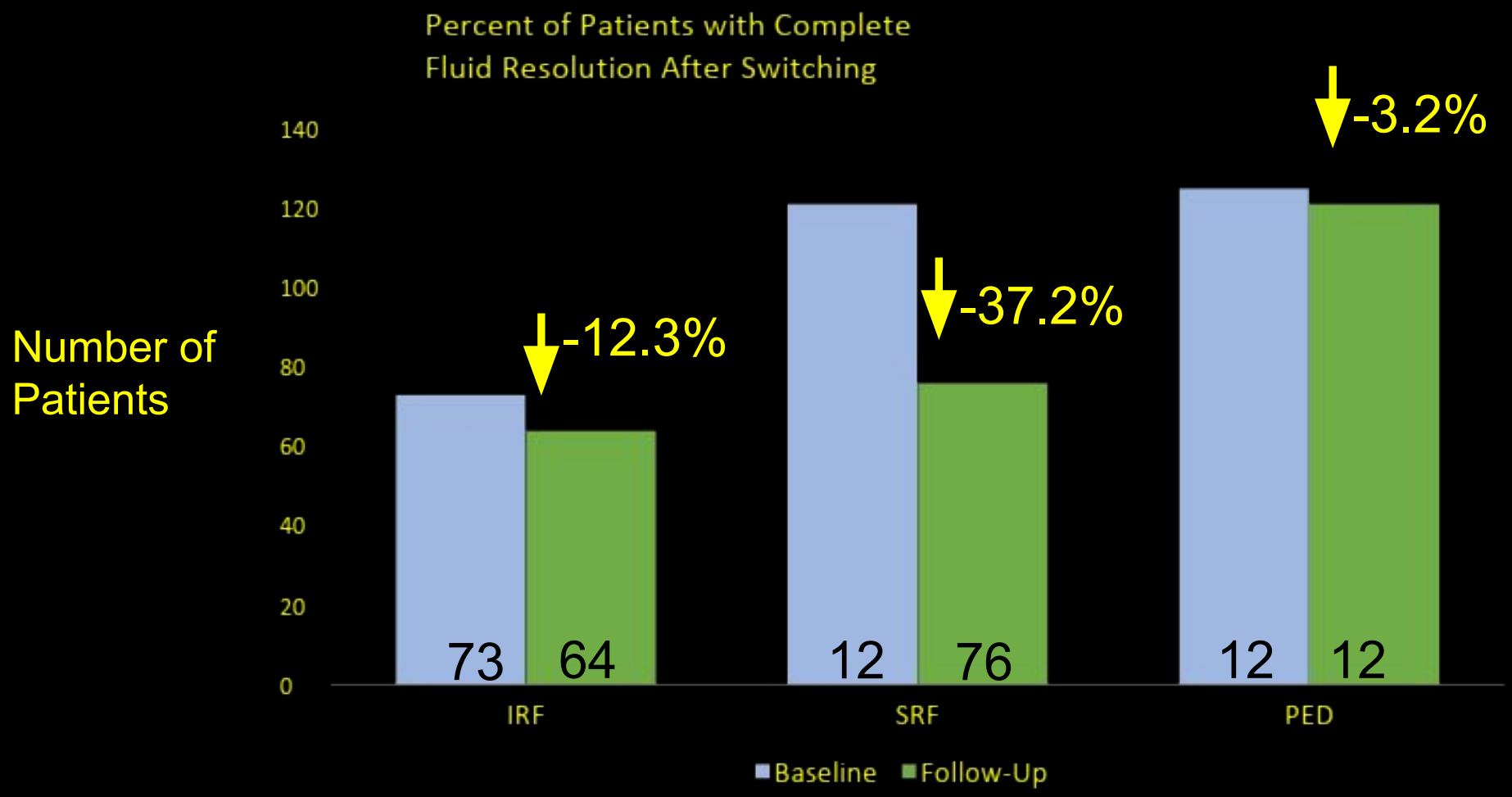
Population with Follow-up (N = 209 patients, 237 eyes)

	Baseline	Follow-Up	Change	P-Value
Variable	**Mean [SEM]**	**Mean [SEM]**		
ETDRS (letters)*	61.5 letters [0.08]	61.7 letters [0.08]	+0.2 letters	0.782
CST (µM)	329.8 µM [0.48]	303.5 µM [0.45]	-26.3 µM	**<0.001**
PED Height** (µM)	231.6 µM [1.87]	180.1 µM [1.91]	-51.5 µM	**<0.001**

Previous Interval: **43.0 days** Follow-up Interval: **43.8 days**

*Based on Snellen to ETDRS conversion
**If applicable

Outcomes of IRF, SRF & PED in Aflibercept Switch Patients After One Injection of Faricimab



THE TRUCKEE STUDY: Safety RESULTS

Safety Outcomes

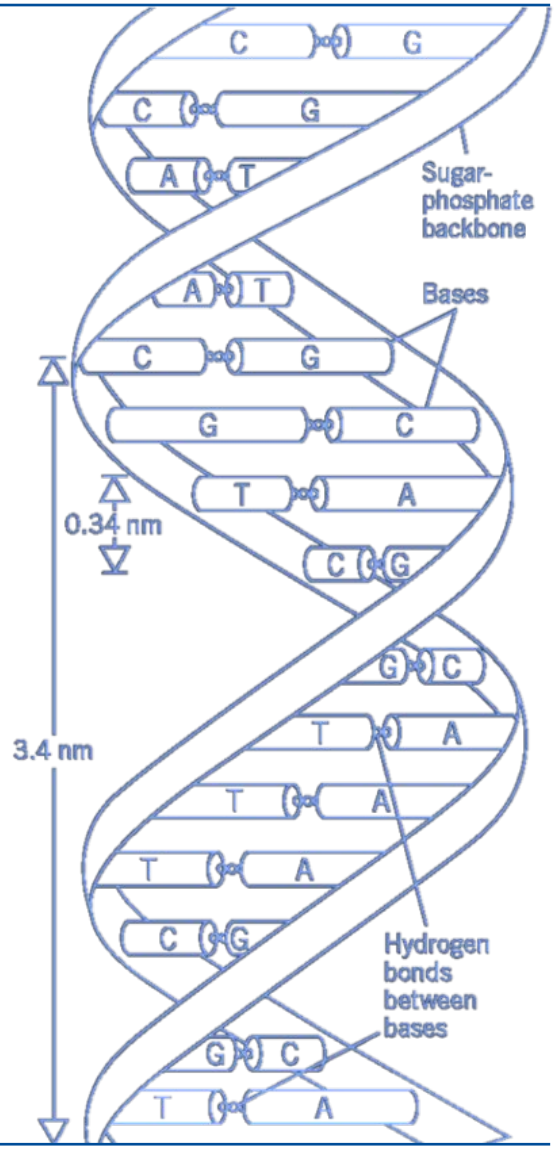
Number of patients	491
Number of eyes	550
Number of injections	1,231
Cases of infectious endophthalmitis	1*
Cases of intraocular inflammation	1†
Cases of retinal vasculitis	0
Cases of retinal artery occlusion	0

Notes: *culture positive endophthalmitis. †widefield fluorescein angiography confirms absence of occlusive vasculitis/retinitis

Thoughts? Does the vision and CST mirror the Latvian population?

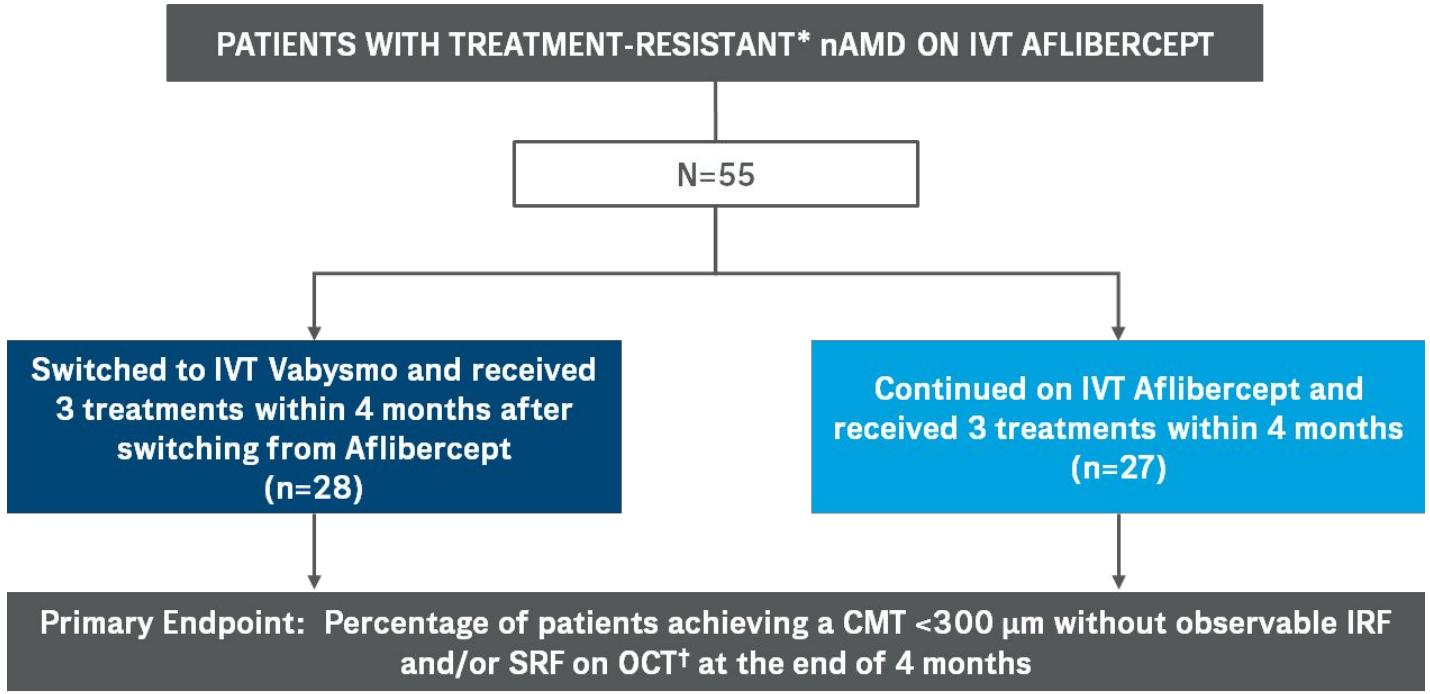
INTRAVITREAL FARICIMAB FOR AFLIBERCEPT-RESISTANT nAMD

Rush RB and Rush SW. Intravitreal Faricimab for Aflibercept-Resistant Neovascular Age-Related Macular Degeneration. *Clinical Ophthal.* 2022;16:4041-4046.



Abbreviation: nAMD=neovascular age-related macular degeneration.

Retrospective CASE-CONTROLLED STUDY IN TREATMENT-RESISTANT nAMD PATIENTS



INCLUSION CRITERIA

- Actively receiving IVT aflibercept for nAMD prior to February 2022 study start
- Managed by a T&E protocol primarily based on the presence/absence of IRF and/or SRF
- Received ≥6 IVT aflibercept treatments during the previous 12 months (370 days)
- Undergone ≥4 IVT aflibercept treatments during the previous 6 months (180 days), and
- CMT of ≥300 µm with observable IRF and/or SRF at the beginning of the study period

EXCLUSION CRITERIA

- Baseline Snellen BCVA worse than 20/200
- An ocular treatment other than anti-VEGF therapy performed within 6 months (180 days) of the initiation of the study interval (i.e., cataract surgery, pars plana vitrectomy, intravitreal steroid injection), and
- A condition considered by the examiner to be responsible for a loss ≥2 Snellen lines of visual acuity unrelated to the diagnosis of nAMD (i.e., cataract, epiretinal membrane, glaucoma, stroke-related vision loss, etc.)

Notes: *Patients were considered recalcitrant to treatment if a fluid-free macula on OCT could not be achieved despite ≥6 anti-VEGF injections over a 12-month period. †OCT was performed using the Heidelberg Spectralis system. Baseline and final OCT images were evaluated for the presence/absence of IRF and SRF by 2 masked fellowship-trained vitreoretinal specialists. If disagreement between the two specialists occurred, a third masked specialist made the final determination.

Abbreviations: CMT=central macular thickness; IRF=intraretinal fluid; IVT=intravitreal; nAMD=neovascular age-related macular degeneration; OCT=optical coherence tomography; SRF=subretinal fluid; T&E=treat-and-extend; VEGF=vascular endothelial growth factor.

Reference: Rush and Rush. Clinical Ophthal. 2022:16;4041-4046.

BASELINE DEMOGRAPHICS

		IVT Vabysmo (n=28)	IVT Aflibercept (n=27)	P Value
Age, years (range)		76.4 (73.4-79.4)	75 (71.9-78)	0.5
Gender, n (%)	Female	14 (50)	12 (44.4)	0.68
	Male	14 (50)	15 (55.6)	
Lens status, n (%)	Pseudophakic	23 (82.1)	22 (81.5)	0.95
	Phakic	5 (17.9)	5 (18.5)	
# IVT anti-VEGF injections prior to the study interval, n (range)		16.8 (13.8-19.7)	17.7 (14.7-20.7)	0.64
CMT on OCT (µm)		393.3 (376.5-410.1)	399.9 (382.8-417)	0.58
BCVA, logMAR (range)		0.75 (0.68-0.82)	0.7 (0.63-0.77)	0.25

Abbreviations: BCVA=best-corrected visual acuity; CMT=central macular thickness; IVT=intravitreal; logMAR=logarithm of the minimum angle of resolution; OCT=optical coherence tomography; VEGF=vascular endothelial growth factor.

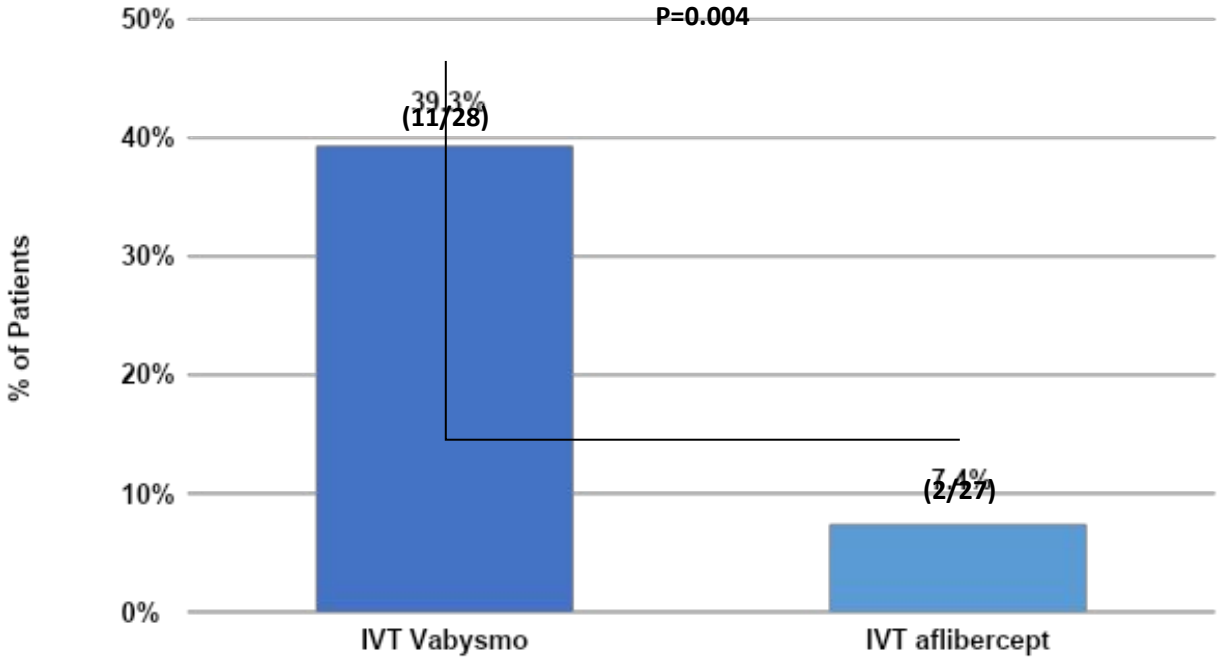
- **N=55**
- **There were no significant differences between cohorts at baseline**

Reference: Rush and Rush. Clinical Ophthal. 2022:16;4041-4046.

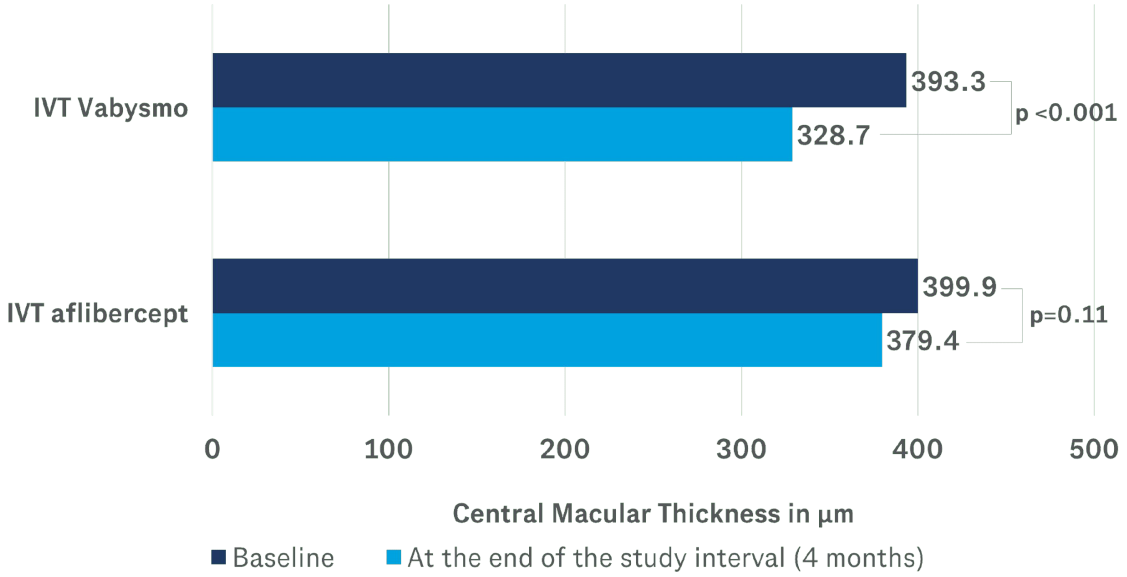
RESULTS AT 4 MONTHS

Central macular thickness

Primary Endpoint: Percentage of patients attaining CMT <300 µm without IRF or SRF on OCT at 4 months



Change in CMT from baseline at 4 months



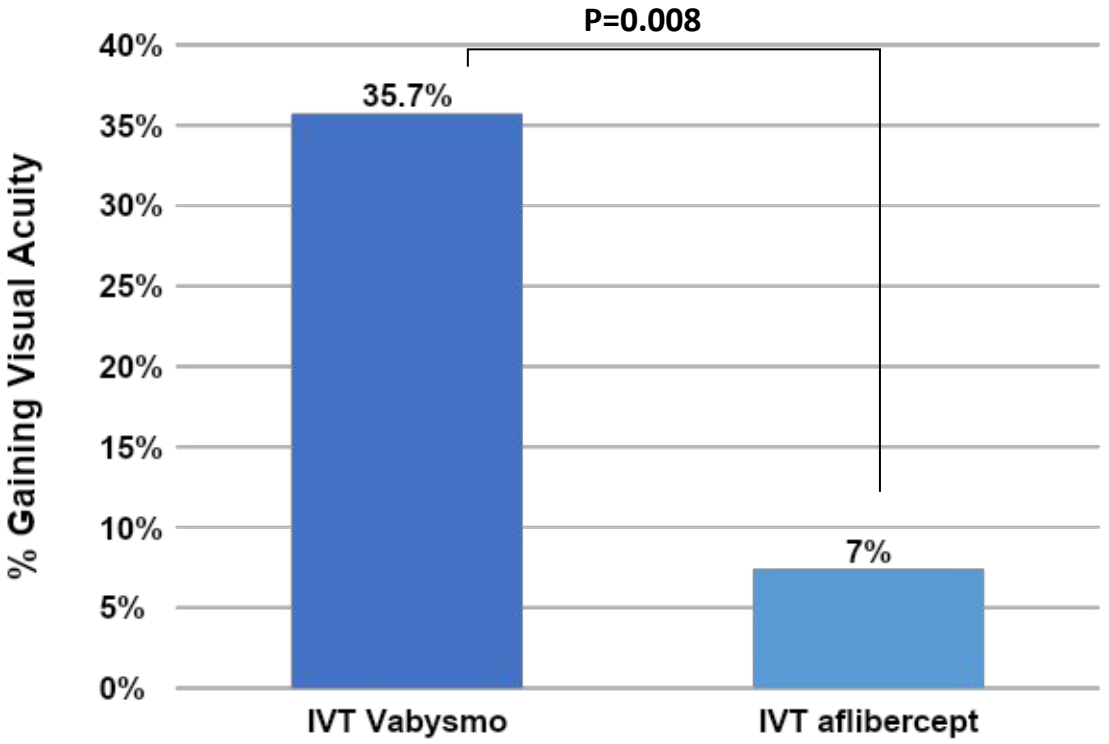
Abbreviations: BCVA=best-corrected visual acuity; CMT=central macular thickness; IVT=intravitreal; OCT=optical coherence tomography.

Reference: Rush and Rush. Clinical Ophthal. 2022:16;4041-4046.

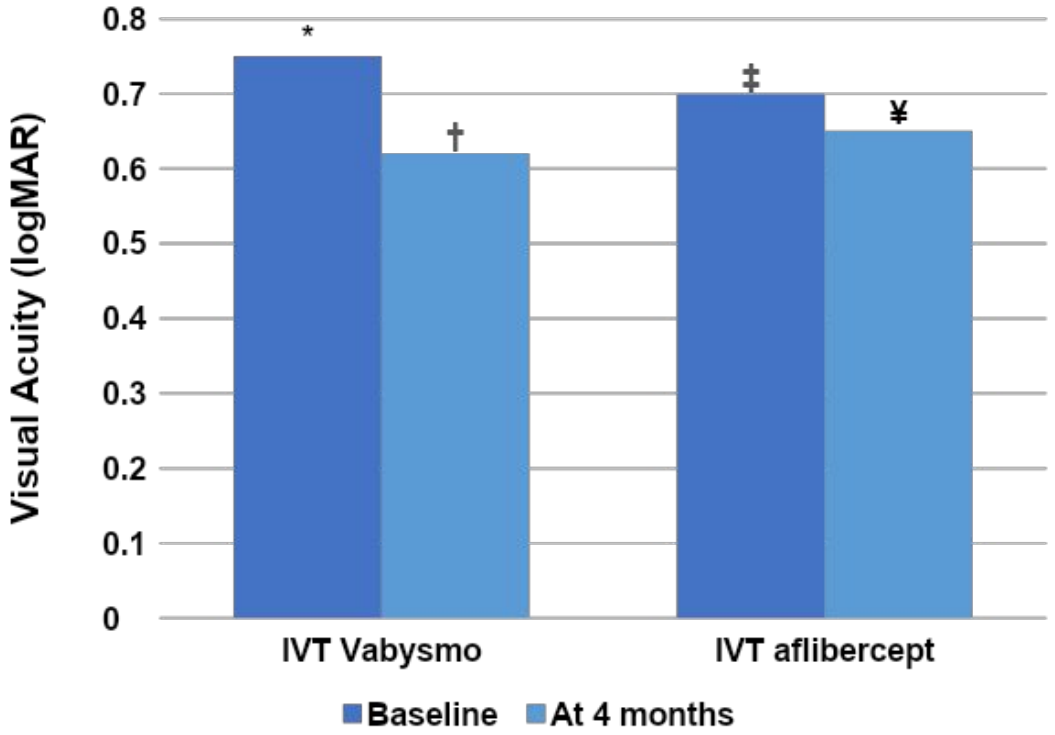
RESULTS AT 4 MONTHS

Visual Acuity

Percentage of patients who gained ≥2 lines of visual acuity at 4 months compared to baseline



Change in visual acuity over the study period



Notes: *logMAR range 0.68-0.83, Snellen 20/114; †LogMAR range 0.55-0.69, Snellen 20/83; ‡LogMAR range 0.63-0.77, Snellen 20/100; ¥LogMar range 0.58-0.72, Snellen 20/89.

Abbreviations: IVT=intravitreal; logMAR=logarithm of the minimum angle of resolution.

Reference: Rush and Rush. Clinical Ophthal. 2022:16;4041-4046.

AUTHOR IDENTIFIED STRENGTHS AND WEAKNESSES

STUDY STRENGTHS

- Case-control design with well-matched Study and Control Groups
- Moderately large number of cases involved, and
- Real-world setting employing a typical treat-and-extend regimen used by most specialists, thereby allowing for a practical application to others treating this patient population.

STUDY WEAKNESSES

- Retrospective design
- Utilization of logMAR visual acuity as opposed to ETDRS letter scoring, and
- Relatively short follow up period

Abbreviations: ETDRS=Early Treatment Diabetic Retinopathy Study; logMAR=logarithm of the minimum angle of resolution.

Reference: Rush and Rush. Clinical Ophthal. 2022:16;4041-4046

My Take Home Messages…

- Faricimab demonstrates efficacy in the real world.

- There is likely an incremental benefit when switching aflibercept patients to faricimab *on average*.

- Durability of faricimab in the real world not evaluated just yet (recent study enrollment).