

**ELARA**

**Safety and Efficacy of Aflibercept 8 mg  
in Patients with nAMD or DME:  
Primary Results from the Phase 3b ELARA Trial**

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# Disclosures



- David Brown has served as scientific advisor for Regeneron/Bayer and Genentech/Roche and as a member of the Regeneron Combination Products Steering Committee
- The ELARA trial was sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA). The sponsor participated in the design and conduct of this trial, data interpretation, and preparation of this presentation
- This trial includes research conducted on human patients. Institutional Review Board approval was obtained prior to initiation of the trial
- Medical writing support was provided by Stephanie Agbu, PhD, of Regeneron Pharmaceuticals, Inc.

# Background



- Aflibercept 8 mg at extended dosing intervals demonstrated BCVA gains and CRT reductions comparable to aflibercept 2q8 over 2 years in pivotal trials in nAMD (PULSAR) and DME (PHOTON)<sup>1-4</sup>
  - In both trials, the majority of aflibercept 8 mg-treated patients achieved  $\geq 16$ -week dosing intervals<sup>1-4</sup>
- However, the efficacy and safety of aflibercept 8 mg every 4 weeks, and whether aflibercept 8 mg can improve outcomes in patients who have received previous anti-VEGF treatment for nAMD or DME, have not been extensively evaluated

**The ELARA trial evaluates the safety and efficacy of monthly dosing with aflibercept 8 mg in previously treated patients with nAMD or DME**

2q8, aflibercept 2 mg every 8 weeks; BCVA, best-corrected visual acuity; CRT, central retinal thickness; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

1. Lanzetta P et al. *Lancet*. 2024;403(10432):1141-1152. 2. Brown DM et al. *Lancet*. 2024;403(10432):1153-1163. 3. Korobelnik JF et al. *Ophthalmology*. 2025;133(1):39-50. 4. Do DV et al. *Ophthalmology*. 2025;133:S0161-6420(25)00707-9.

# ELARA Study Design



1110 patients enrolled across 53 US sites

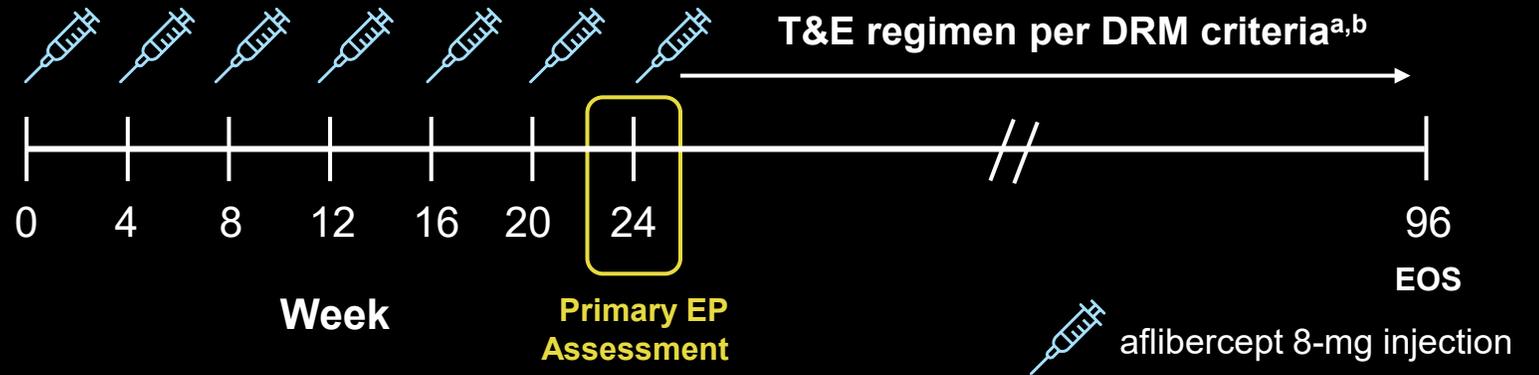
Study eyes (N=1110) **previously treated** with  $\geq 3$  anti-VEGF injections within 5 months prior to study start in:

**nAMD (n=622)**

Patients aged  $\geq 50$  years with CNV lesions due to nAMD

**DME (n=488)**

Patients aged  $\geq 18$  years with center-involved DME



## <sup>a</sup>DRM-E: Interval Extension

- **nAMD**
  - No retinal fluid in central subfield **AND**
  - No new onset foveal neovascularization or foveal hemorrhage **AND**
  - No interval shortening within the prior 12 weeks
- **DME**
  - CST  $< 300 \mu\text{m}$  (or  $< 320 \mu\text{m}$  on Spectralis) **AND**
  - $\leq 10\text{-}\mu\text{m}$  increase from lowest previous CST value
- Intervals are extended in **2-week increments** in patients whose dosing intervals were never shortened and in **1-week increments** in patients whose dosing intervals were shortened previously
- The maximum interval is Q24

## <sup>b</sup>DRM-S: Interval Shortening

- **nAMD**
  - Any new retinal fluid in central subfield **OR**
  - New onset foveal neovascularization or foveal hemorrhage **OR**
  - $> 5$ -letter loss in BCVA from best previous BCVA value that is attributable to recurrent or persistent disease
- **DME**
  - $> 25\text{-}\mu\text{m}$  increase in CST from lowest previous CST value **OR**
  - $> 10$ -letter loss in BCVA from best previous BCVA value that is attributable to recurrent or persistent disease
- Intervals are shortened in **1-week increments**, and the minimum interval is Q4

# Patient Disposition at Week 24



	nAMD	DME	Total
<b>Enrolled</b>	622	488	1110
<b>Completed Week 24, n (%)</b>	595 (95.7)	471 (96.5)	1066 (96.0)
<b>Reason for discontinuation, n</b>			
Withdrawal of consent	20	10	30
Adverse event	4	3	7
Death	2	2	4
Lost to follow-up	1	2	3

# Baseline Demographics



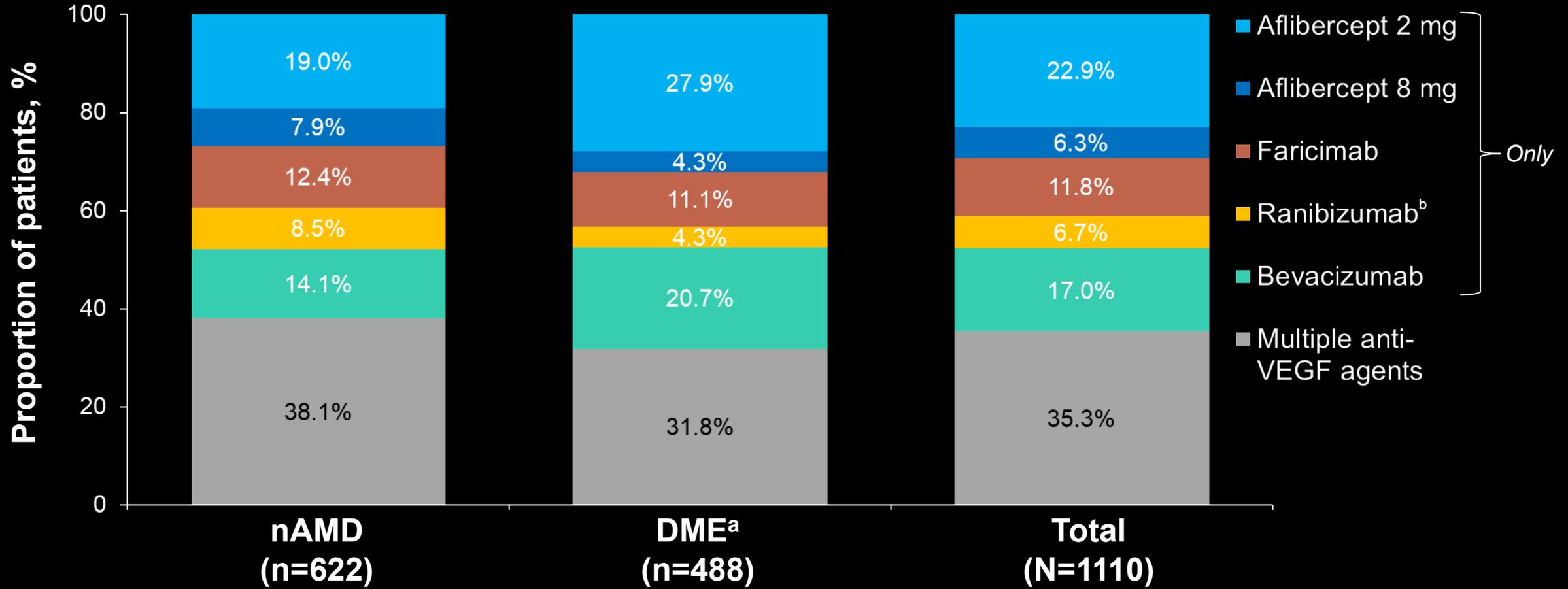
	nAMD (n=622)	DME (n=488)	Total (N=1110)
<b>Age, mean (SD), years</b>	77.1 (8.5)	62.8 (9.8)	70.8 (11.5)
<b>Female, n (%)</b>	360 (57.9)	203 (41.6)	563 (50.7)
<b>Hispanic or Latino, n (%)</b>	43 (6.9)	114 (23.4)	157 (14.1)
<b>Race, n (%)</b>			
White	589 (94.7)	387 (79.3)	976 (87.9)
Black or African American	8 (1.3)	51 (10.5)	59 (5.3)
Asian	21 (3.4)	38 (7.8)	59 (5.3)
Other <sup>a</sup>	2 (0.3)	3 (0.6)	5 (0.5)
Not reported	2 (0.3)	9 (1.8)	11 (1.0)
<b>History of hypertension, n (%)</b>	459 (73.8)	397 (81.4)	856 (77.1)

# Baseline Characteristics of Study Eye



	nAMD (n=622)	DME (n=488)	Total (N=1110)
<b>BCVA, mean (SD), ETDRS letters</b>	68.0 (15.3)	69.8 (13.4)	68.8 (14.5)
Snellen equivalent	20/40	20/40	20/40
Patients with BCVA >73 ETDRS letters, n (%)	276 (44.4)	232 (47.5)	508 (45.8)
<b>CST, mean (SD), <math>\mu\text{m}</math></b>	254.3 (66.0)	328.1 (104.0)	287.1 (92.5)

# Previous Anti-VEGF Treatment Within Prior 6 Months



SAF.

<sup>a</sup>Data for 1 patient in the DME cohort were missing.

<sup>b</sup>Ranibizumab or ranibizumab biosimilar (ranibizumab-eqrn or ranibizumab-nuna).

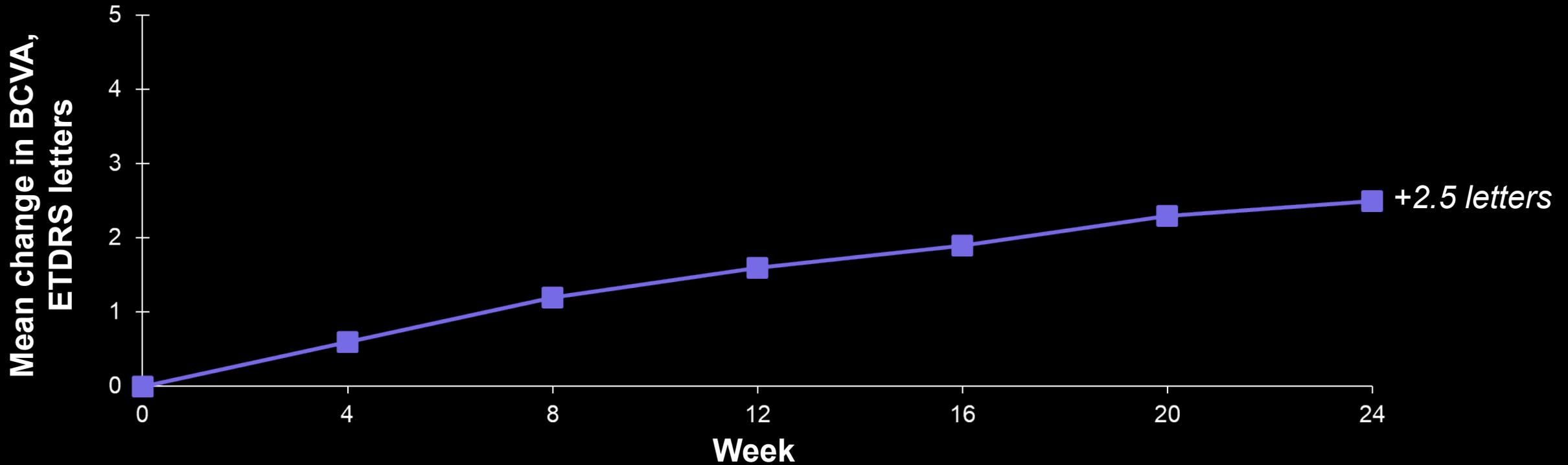
# Number of Previous Anti-VEGF Injections in Study Eye 6 Months Prior to Study Start



	nAMD (n=622)	DME <sup>a</sup> (n=488)	Total (N=1110)
<b>Previous anti-VEGF injections in the study eye in prior 6 months, n (%)</b>			
3 injections	181 (29.1)	195 (40.0)	376 (33.9)
4 injections	212 (34.1)	175 (35.9)	387 (34.9)
5 injections	168 (27.0)	97 (19.9)	265 (23.9)
6 injections	48 (7.7)	11 (2.3)	59 (5.3)
≥7 injections	8 (1.3)	1 (0.2)	9 (0.8)

SAF.  
<sup>a</sup>Data for 1 patient in the DME cohort were missing.

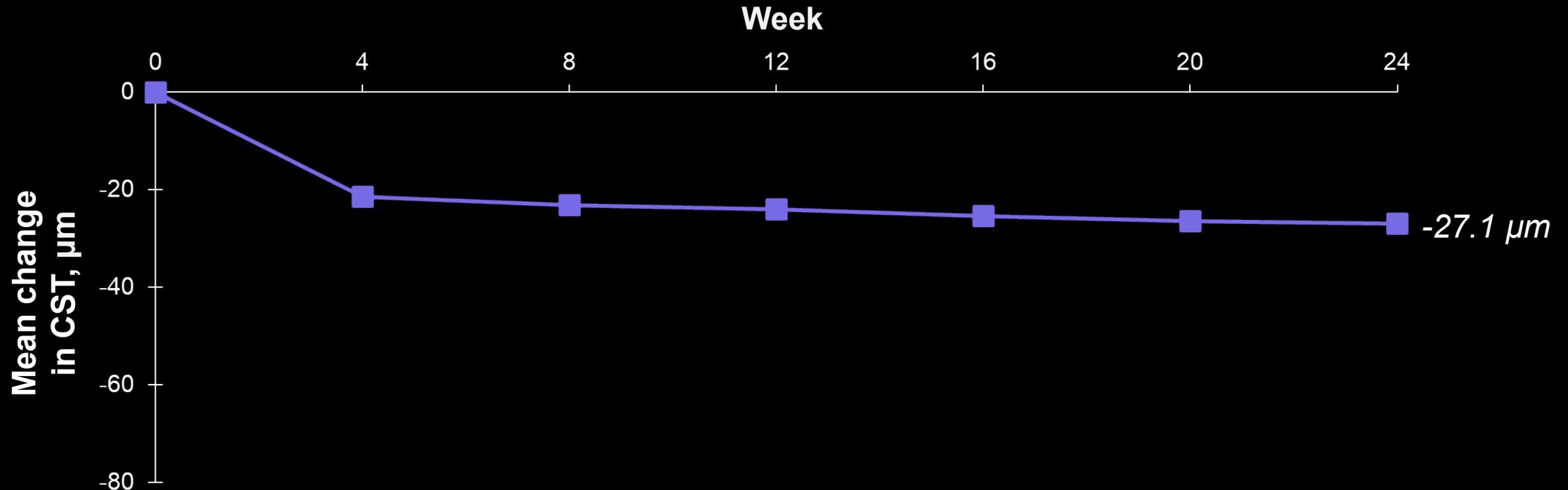
# Mean Change in BCVA Through Week 24 in Patients with nAMD



	Mean BCVA at BL	Mean change in BCVA at Week 24	Proportion of patients with ≥5-letter gain at Week 24	Mean number of injections through Week 24
<b>nAMD (n=622)</b>	68.0 letters	+2.5 letters	32.9%	6.0

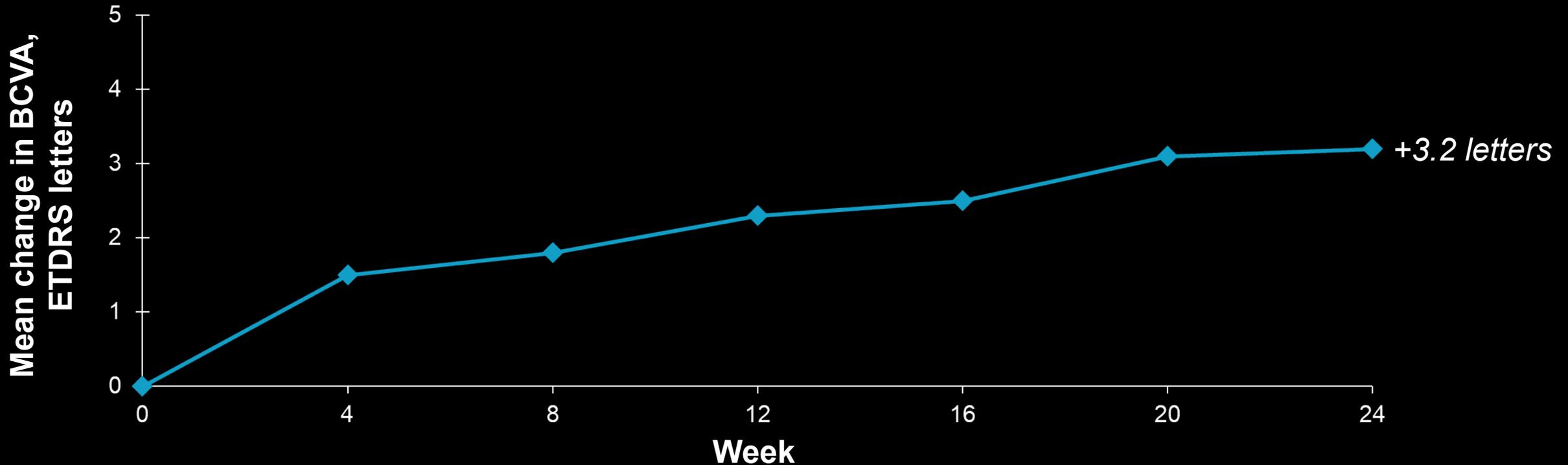
SAF, observed cases.  
BL, baseline.

# Mean Change in CST Through Week 24 in Patients with nAMD



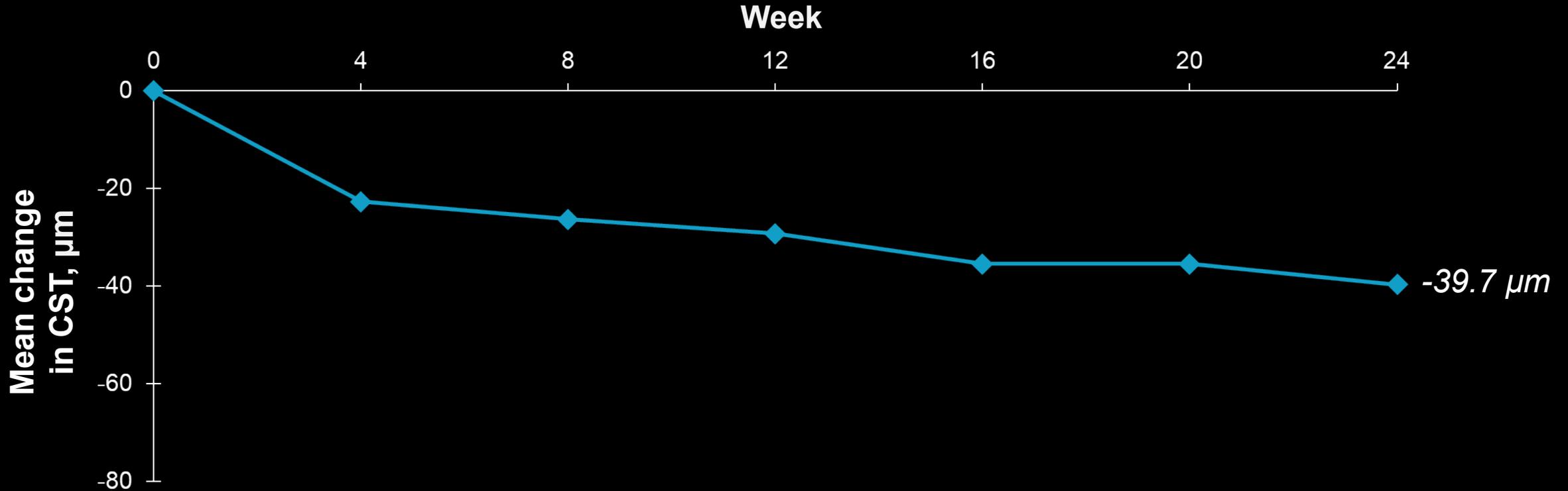
	Mean CST at BL	Mean change in CST at Week 24	Mean number of injections through Week 24
nAMD (n=622)	254.3 μm	-27.1 μm	6.0

# Mean Change in BCVA Through Week 24 in Patients with DME



	Mean BCVA at BL	Mean change in BCVA at Week 24	Proportion of patients with $\geq 5$ -letter gain at Week 24	Mean number of injections through Week 24
<b>DME (n=488)</b>	69.8 letters	+3.2 letters	36.8%	5.8

# Mean Change in CST Through Week 24 in Patients with DME



	Mean CST at BL	Mean change in CST at Week 24	Mean number of injections through Week 24
<b>DME (n=488)</b>	328.1 µm	-39.7 µm	5.8

# Ocular Safety in the Study Eye Through Week 24



	nAMD (n=622)	DME (n=488)	Total (N=1110)
<b>Patients with ≥1 ocular TEAE, n (%)</b>	106 (17.0)	109 (22.3)	215 (19.4)
<b>Ocular TEAEs occurring in &gt;15 patients overall, n (%)</b>			
Conjunctival hemorrhage	21 (3.4)	18 (3.7)	39 (3.5)
Cataract	7 (1.1)	13 (2.7)	20 (1.8)
Vitreous floaters	9 (1.4)	8 (1.6)	17 (1.5)
Dry eye	9 (1.4)	7 (1.4)	16 (1.4)
<b>Patients with ≥1 serious ocular TEAE, n (%)</b>	1 (0.2)	4 (0.8)	5 (0.5)
Endophthalmitis	0	3 (0.6)	3 (0.3)
Retinal detachment	1 (0.2)	0	1 (<0.1)
Vasculitis	0	1 (0.2)	1 (<0.1)

# Intraocular Inflammation in the Study Eye Through Week 24



	nAMD (n=622)	DME (n=488)	Total (N=1110)
<b>Patients with <math>\geq 1</math> IOI TEAE, n (%)</b>	6 (1.0)	5 (1.0)	11 (1.0)
Endophthalmitis	1 (0.2)	3 (0.6)	4 (0.4)
Eye inflammation	2 (0.3)	0	2 (0.2)
Iritis	1 (0.2)	1 (0.2)	2 (0.2)
Eye infection	1 (0.2)	0	1 (<0.1)
Iridocyclitis	1 (0.2)	0	1 (<0.1)
Uveitis	0	1 (0.2)	1 (<0.1)

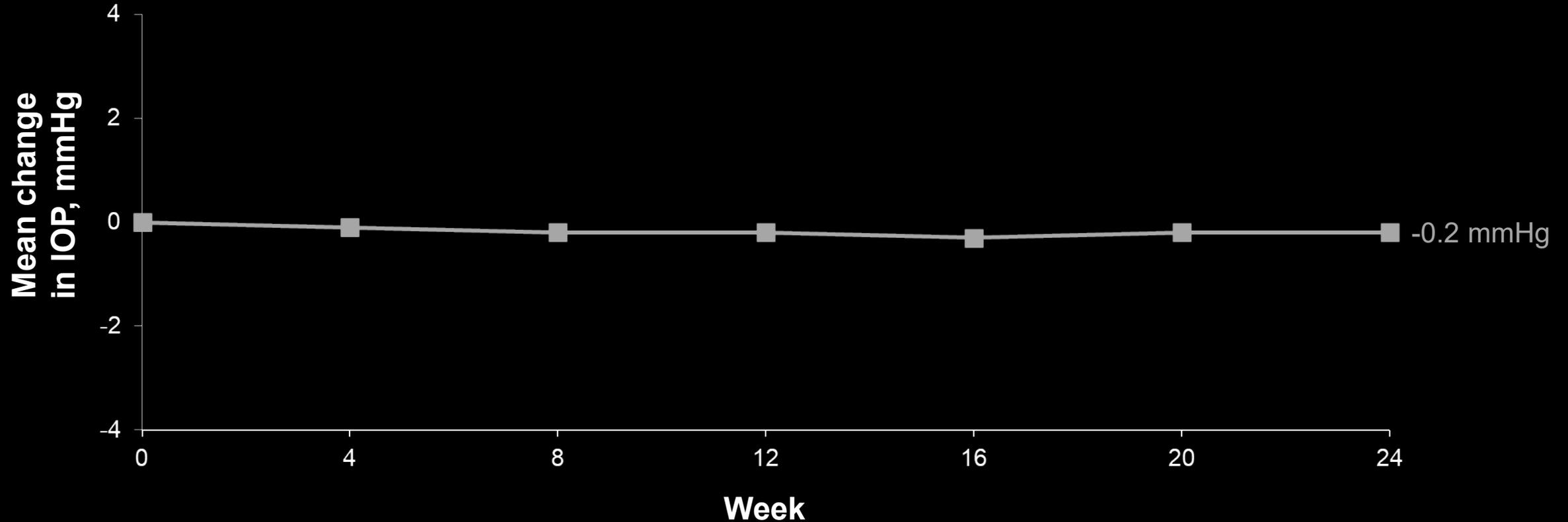
# Intraocular Pressure in the Study Eye Through Week 24



	nAMD (n=622)	DME (n=488)	Total (N=1110)
Patients with $\geq 10$ mmHg increase in pre-dose IOP from baseline <sup>a</sup>	16/616 (2.6%)	15/486 (3.1%)	31/1102 (2.8%)
Patients with pre-dose IOP $\geq 25$ mmHg <sup>a</sup>	10/622 (1.6%)	13/488 (2.7%)	23/1110 (2.1%)
Patients with pre- or post-dose IOP $\geq 35$ mmHg <sup>a</sup>	1/622 (0.2%)	4/488 (0.8%)	5/1110 (0.5%)

SAF.  
IOP, intraocular pressure.  
<sup>a</sup>At any visit.

# Mean Change in Pre-dose IOP in All Patients Through Week 24



# Non-ocular Safety Through Week 24



	nAMD (n=622)	DME (n=488)	Total (N=1110)
<b>Patients with ≥1 serious non-ocular TEAE, n (%)</b>	31 (5.0)	35 (7.2)	66 (5.9)
<b>Serious non-ocular TEAEs occurring in ≥3 patients overall, n (%)</b>			
Cerebrovascular accident	1 (0.2)	3 (0.6)	4 (0.4)
Myocardial infarction	2 (0.3)	2 (0.4)	4 (0.4)
Anemia	0	3 (0.6)	3 (0.3)
Pneumonia	2 (0.3)	1 (0.2)	3 (0.3)
<b>Patients with ≥1 hypertension-related TEAE, n (%)</b>	22 (3.5)	14 (2.9)	36 (3.2)
<b>Death, n (%)<sup>a</sup></b>	2 (0.3)	4 (0.8)	6 (0.5)

# ELARA Summary of Week 24 Results



- Aflibercept 8 mg every 4 weeks achieved meaningful functional and anatomic improvements at Week 24 in patients previously treated with anti-VEGF agents for nAMD or DME
- The safety profile of monthly dosing with aflibercept 8 mg through Week 24 was consistent with the established safety profile of both aflibercept 2 mg and 8 mg
  - No clinically relevant change was observed in pre-dose IOP with aflibercept 8 mg every 4 weeks
  - Incidence of hypertension events and death was low and consistent with that of prior aflibercept trials

Mean Change in BCVA Through Week 24

