Intravitreal Aflibercept 8 mg for Diabetic Macular Edema: Week 48 Efficacy Outcomes by Baseline Demographics in the Phase 2/3 PHOTON Trial

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Disclosures

- Dr Emanuelli is an investigator for Novartis, Novartis Institute of Biomedical Research, Regeneron Pharmaceuticals, Inc., Roche/Genentech, Adverum Biotechnologies, Kodiak Sciences, Ophthea, Nanoscope Therapeutics, and RegenxBio.
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- This trial includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
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Background

- Aflibercept 8 mg, a novel intravitreal formulation with a 4-times higher molar dose than aflibercept 2 mg, is hypothesized to provide a longer effective vitreal concentration and enable a more sustained effect on VEGF signaling
- The ongoing phase 2/3 PHOTON trial evaluates the efficacy and safety of aflibercept 8 mg versus 2 mg in patients with DME
- However, the treatment effects of aflibercept 8 mg are yet to be evaluated by baseline patient characteristics

This analysis evaluated the treatment effects of aflibercept 8 mg versus 2 mg at Week 48 by baseline patient demographics

DME, diabetic macular degeneration; VEGF, vascular endothelial growth factor.

PHOTON Study Design

Multi-center, randomized, double-masked study in patients with DME*
Randomized 1 (2q8) : 2 (8q12) : 1 (8q16)
Note: 2 mg arm received 5 initial monthly injections versus 8 mg arms, which received only 3 initial monthly injections

2q8
Aflibercept 2 mg every 8 weeks after 5 initial monthly injections
n=167

8q12
8 mg every 12 weeks after 3 initial monthly injections
n=328

8q16
8 mg every 16 weeks after 3 initial monthly injections
n=163

Primary endpoint at Week 48
Mean change in BCVA (non-inferiority)

Key secondary endpoint:
Proportion of patients with ≥2-step improvement in DRSS at Week 48

↓

End of study at Week 96
with optional 1-year extension through Week 156

*Treatment naïve and previously treated.
BCVA, best-corrected visual acuity.

PHOTON: Dose Regimen Modifications in Year 1

Primary Endpoint

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16	X	X	X	o	o	o	X	o	o	o	X	o	o

Note: 2 mg arm received 5 initial monthly injections versus 8 mg arms, which received only 3 initial monthly injections

DRM Criteria for Shortening Dosing Interval[a]

- **>10-letter loss in BCVA due to persistent or worsening DME**

AND

- **>50-micron increase in CRT**

DRM in Year 1

Intervals can only be shortened

Multiple opportunities to shorten interval

Minimum interval for all patients was Q8

- **Week 16 and 20:** Patients on 8q12 and 8q16 meeting DRM criteria shortened to Q8
- **Week 24:** Patients on 8q16 meeting DRM criteria shortened to Q12
- **Week 32 and 44 for 8q12 and Week 36[b] and 40 for 8q16:** Treatment interval shortened by 4 weeks for patients meeting DRM criteria

Stippled boxes = initial treatment phase; X = active injection; o = sham injections. Note: Figure does not reflect all dosing options once a patient is shortened.
[a]All assessments compared to Week 12.
[b]At Week 36, patients on 8q16 who were previously shortened to Q12 could have been shortened to Q8.
CRT, central retinal thickness; DRM, dose regimen modification.

Baseline Demographics

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
Age (years)	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female (%)	44.9%	36.0%	39.3%	39.1%
Race (%)				
White	67.1%	70.4%	78.5%	71.6%
Black or African American	10.8%	10.7%	5.5%	9.4%
Asian	18.0%	14.6%	14.1%	15.3%
Other	2.4%	3.0%	0.6%	2.4%
Not reported	1.8%	1.2%	1.2%	1.4%
Hispanic or Latino (%)	18.6%	16.5%	20.9%	18.1%
Duration of diabetes (years)	15.9 (10.0)	15.1 (10.0)	15.7 (10.7)	15.5 (10.2)
Hemoglobin A1c (%)	8.1 (1.5)	7.9 (1.5)	7.8 (1.5)	8.0 (1.5)
Hypertension (%)	77.8%	77.4%	79.8%	78.1%
BMI (kg/m^2)	29.9 (6.5)	30.4 (6.2)	31.0 (6.1)	30.5 (6.2)

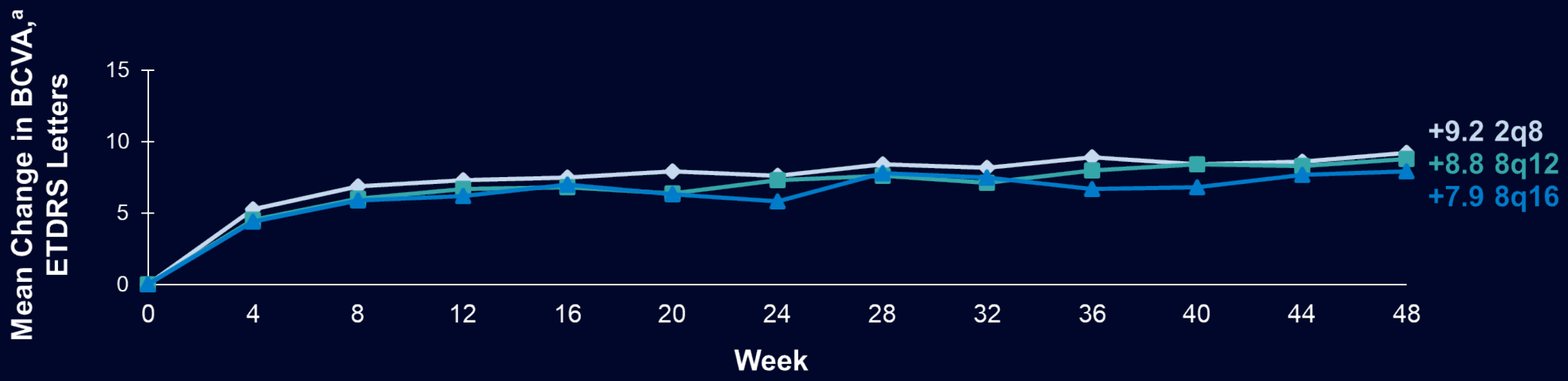
Data are mean (SD) unless otherwise indicated.
BMI, body mass index; FAS, full analysis set SAF, safety analysis set; SD, standard deviation.

Baseline Characteristics of the Study Eye

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
BCVA (ETDRS letters)	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
Snellen equivalent	20/63	20/50	20/63	20/63
20/32 (>73 to 78 letters)	12.0%	18.0%	14.1%	15.5%
20/40 or worse (≤73 letters)	88.0%	82.0%	85.9%	84.5%
CRT (μm)	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)
Prior treatment for DME (%)	44.3%	43.6%	43.6%	43.8%

Data are mean (SD) unless otherwise indicated.
ETDRS, Early Treatment of Diabetic Retinopathy Study.

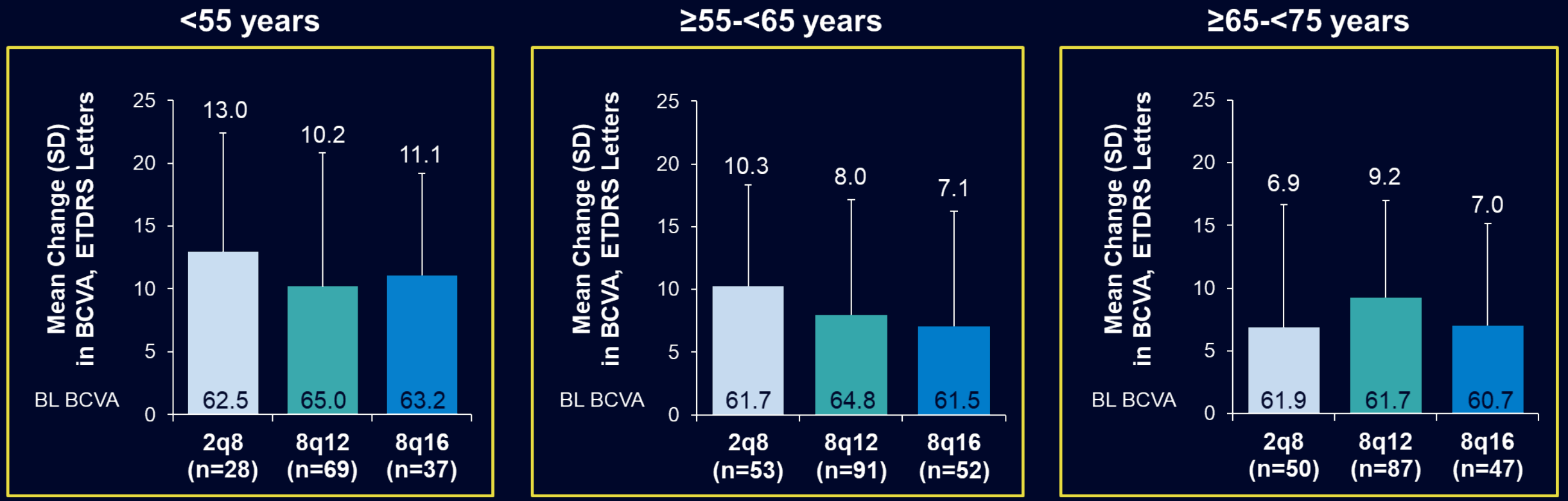
Mean Change in BCVA Through Week 48[a]



	LS mean change from baseline[b]	Difference in LS means vs. aflibercept 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	8.7	—	—	—
8q12	8.1	-0.57	-2.26, 1.13	p < 0.0001
8q16	7.2	-1.44	-3.27, 0.39	p = 0.0031

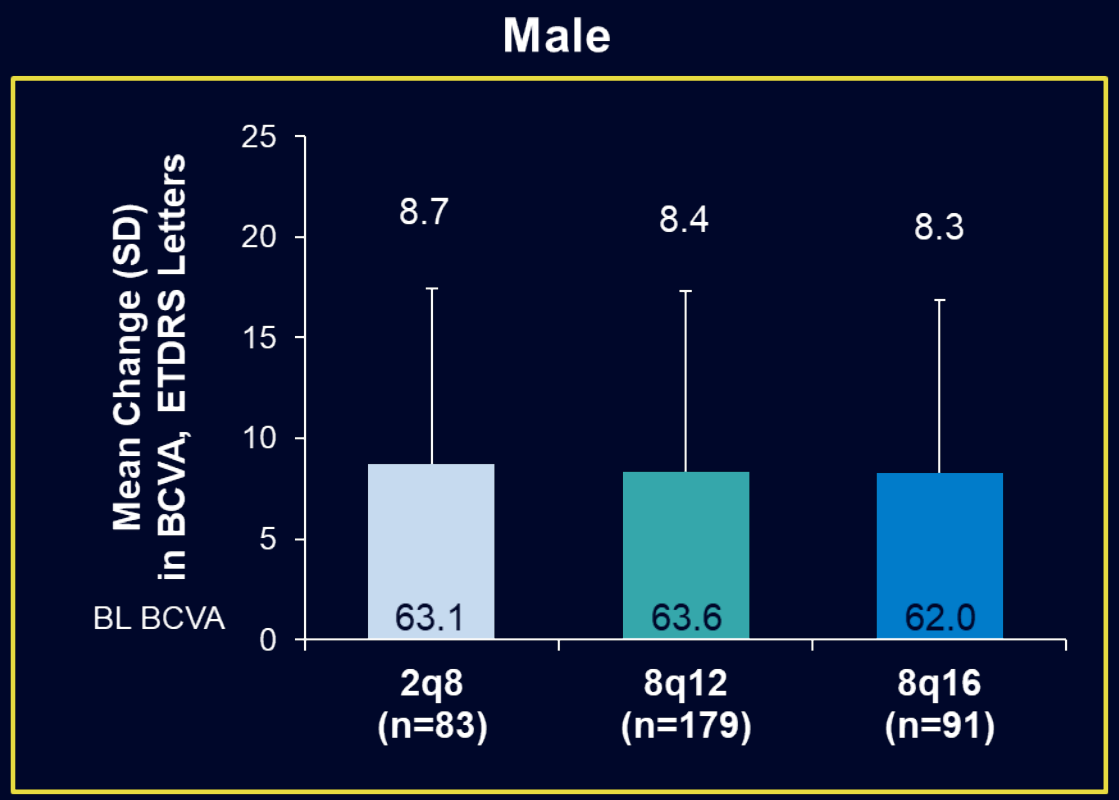
[a]Based on observed values (censoring data post-ICE).
[b]Estimated using MMRM.
FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163.
FAS, full analysis set; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

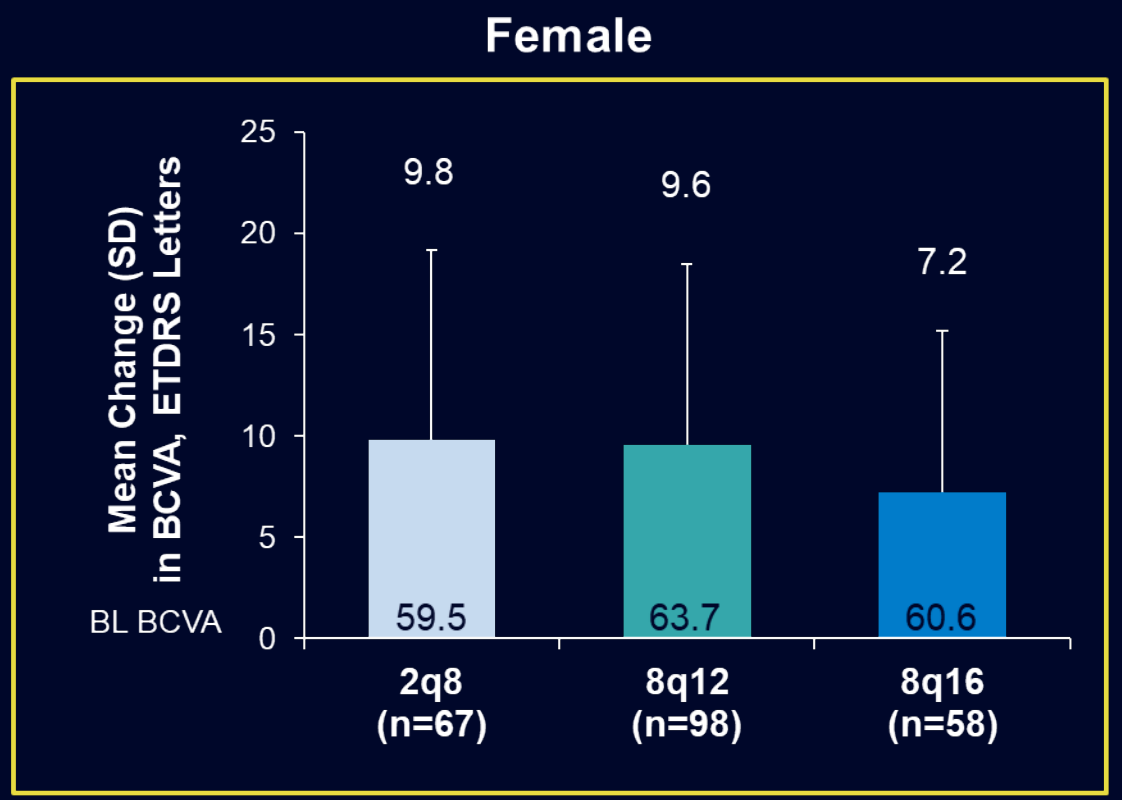
Mean Change in BCVA at Week 48 by Age[a]



FAS.
[a]The subgroup age ≥75 years could not be evaluated due to small sample size (<15 patients in the 8q16 treatment group).
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).
BL, baseline.

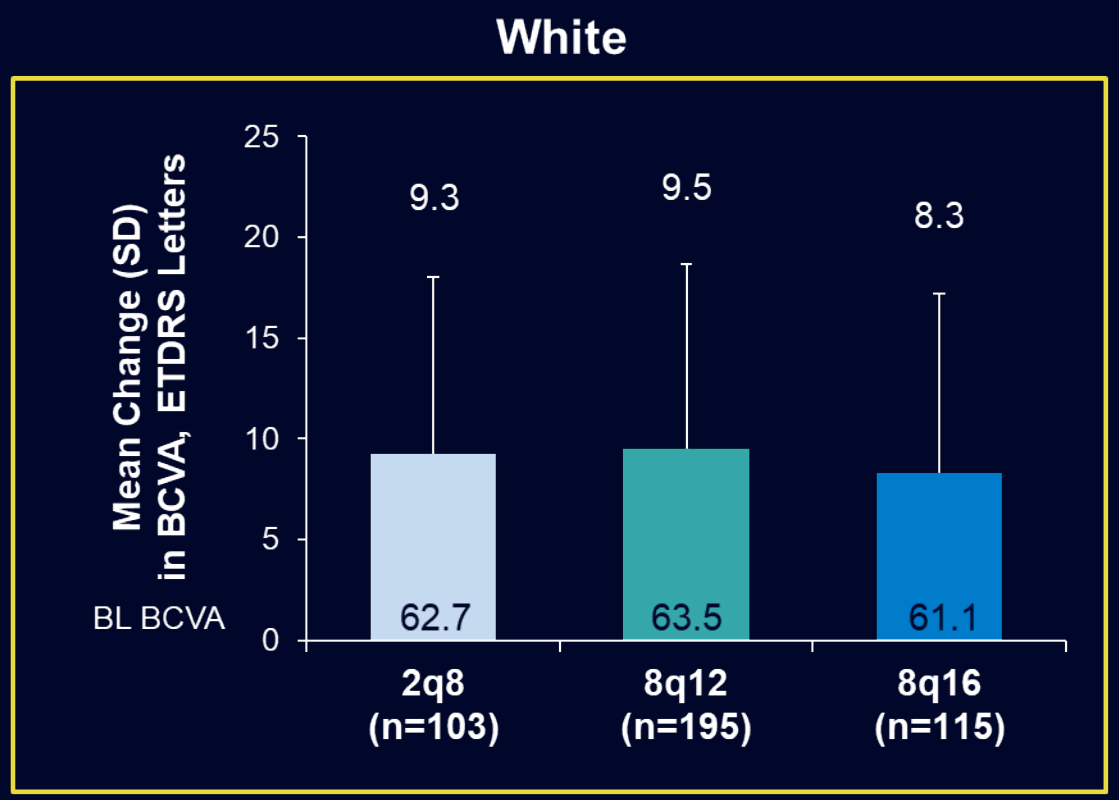
Mean Change in BCVA at Week 48 by Sex

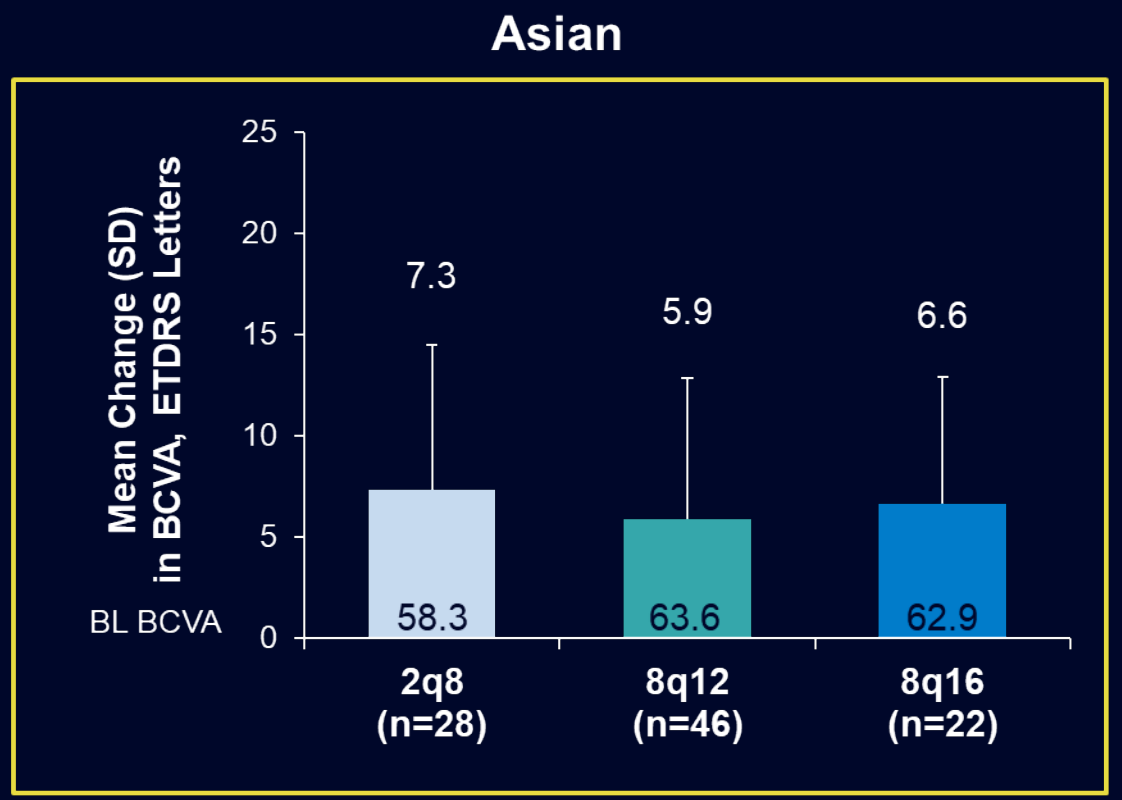




FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

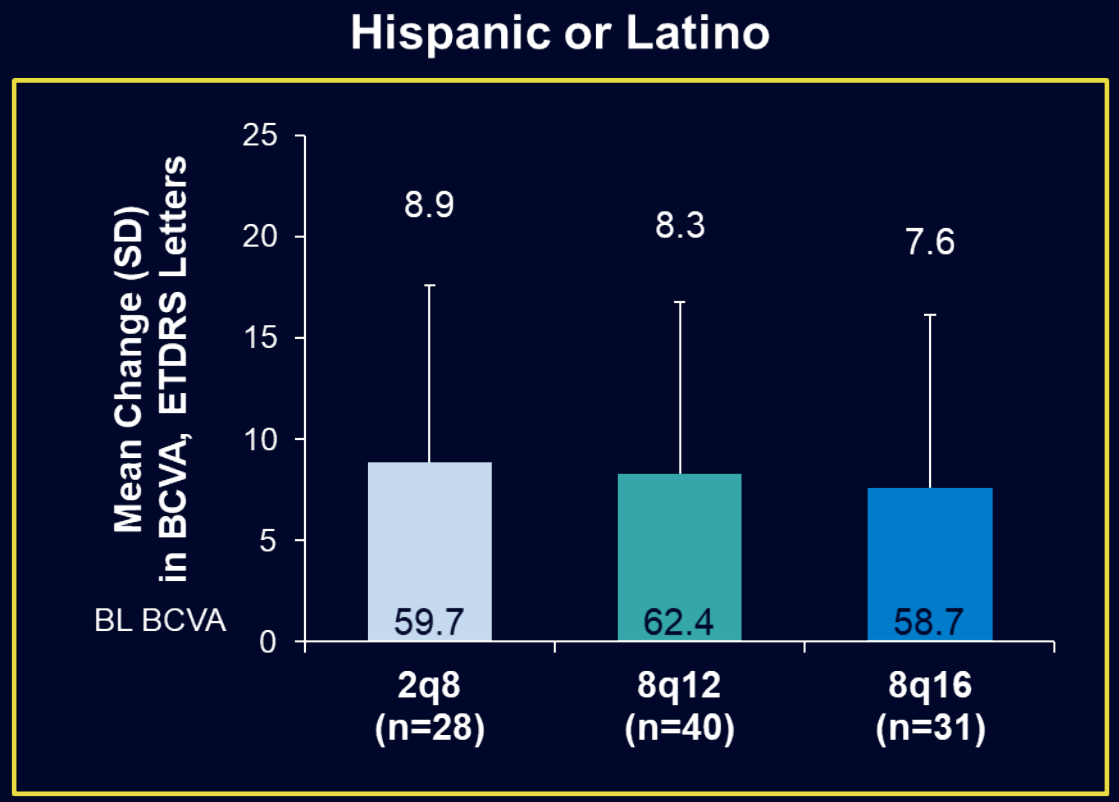
Mean Change in BCVA at Week 48 by Race[a]

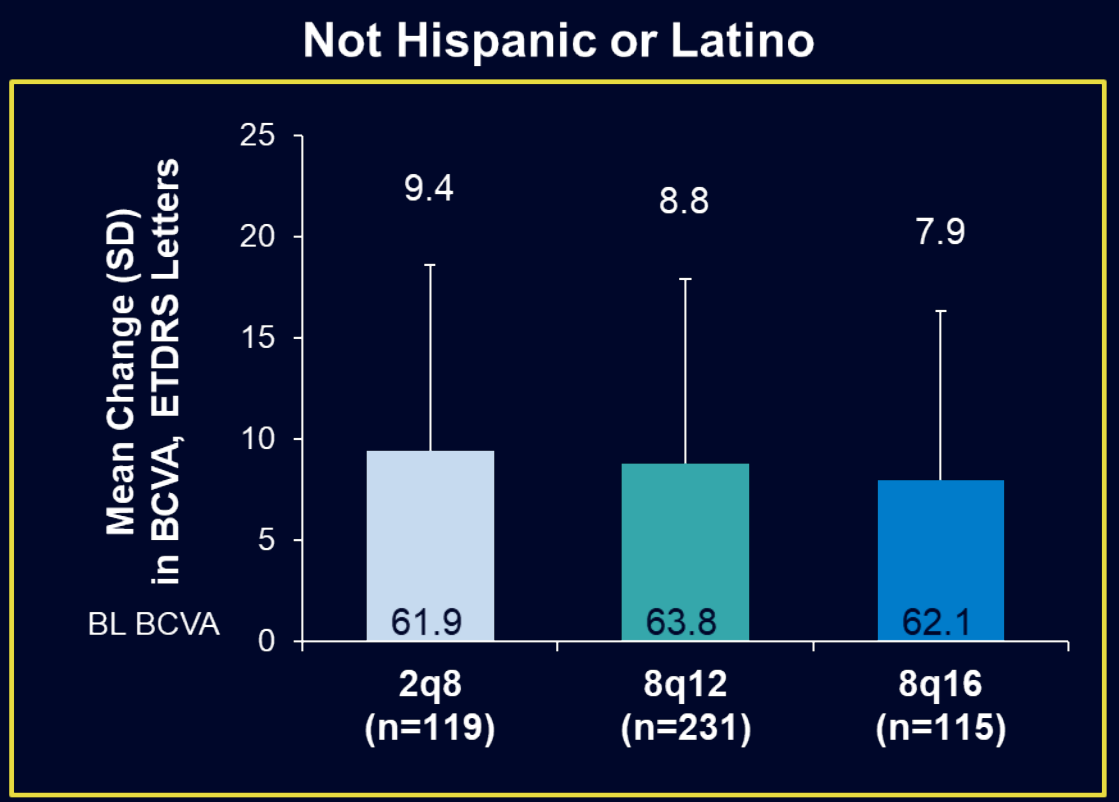




FAS.
[a]The subgroup Black or African American race could not be evaluated due to small sample size (<15 patients in the 2q8 and 8q16 groups).
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

Mean Change in BCVA at Week 48 by Ethnicity



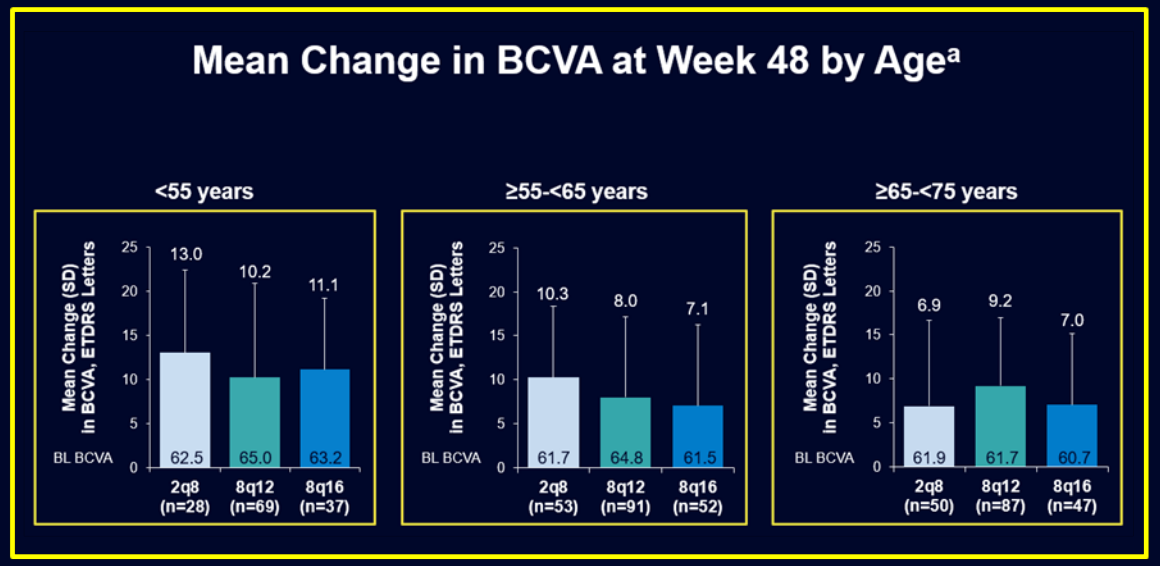


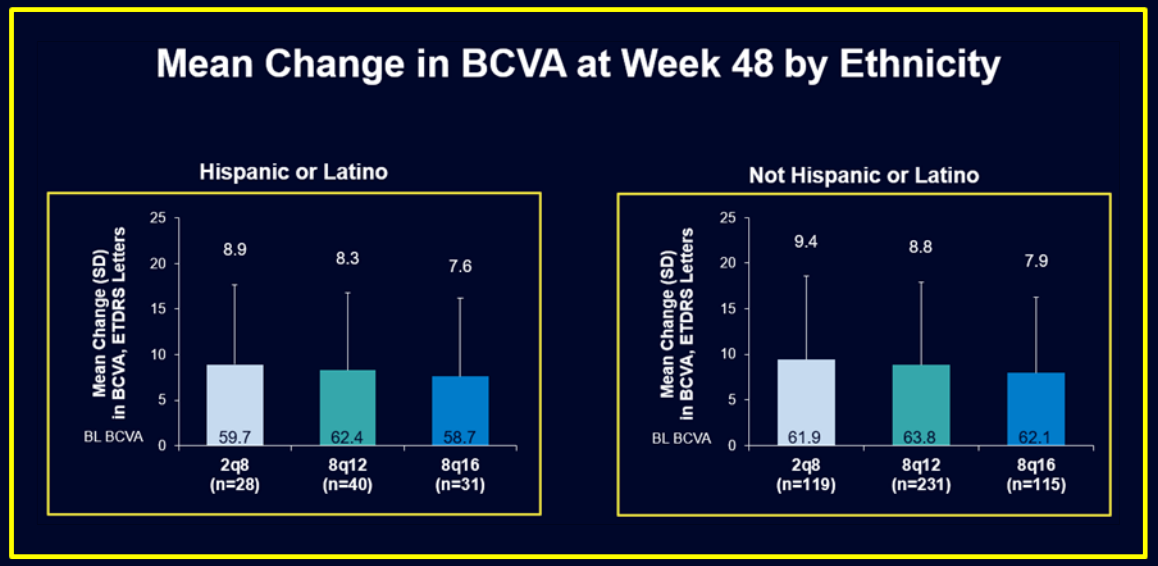
FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

Limitations

- This analysis was not designed to evaluate statistical differences within subgroups
- Select subgroups (age ≥75 years and Black or African American race) could not be evaluated due to small sample size

Conclusions





- Aflibercept 8 mg achieved meaningful BCVA gains from baseline at Week 48 in patients with DME across evaluable subgroups of age, sex, race, and ethnicity