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

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- Dr Marcus has served as a consultant for Regenxbio, Genentech/Roche, Regeneron, Clearside, Vial, Coherus, and Vantage Biosciences and has received research grants from Amgen, Ionis, Xplore, Mylan, Opthea, Clearside, Iveric, Outlook, Gemini, Genentech, Graybug, Topcon, Gyroscope, Stealth Spiam, Apellis, Roche, Xplore, Regenxbio, Kodiak, Annexon, Oculis, Alexion, Oxurion, and Regeneron Pharmaceuticals, Inc.
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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

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- Aflibercept 8 mg, a novel intravitreal formulation that delivers a 4-times higher molar dose than aflibercept 2 mg, has demonstrated improved functional and anatomic outcomes at dosing intervals of ≥12 weeks in ongoing clinical trials
- These findings supported regulatory approval of aflibercept 8 mg for the treatment of nAMD, DME, and DR in the United States[1]
- The influence of baseline patient demographics and ocular characteristics on the treatment effects of aflibercept 8 mg in patients DME have yet to be evaluated

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

DME, diabetic macular degeneration; DR, diabetic retinopathy; nAMD, neovascular age-related macular degeneration.

1. EYLEA® HD (aflibercept) injection, for intravitreal use. Highlights of prescribing information. Regeneron Pharmaceuticals, Inc.; 2023. Accessed September 14, 2023. https://www.regeneron.com/downloads/eyleahd_fpi

PHOTON Study Design

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DME

Multi-center, randomized, double-masked study in patients with DME[a]
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

[a]Treatment naïve and previously treated.
BCVA, best-corrected visual acuity.

PHOTON: Dose Regimen Modifications in Year 1

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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 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.
CRT, central retinal thickness; DRM, dose regimen modification.

Baseline Demographics

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	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

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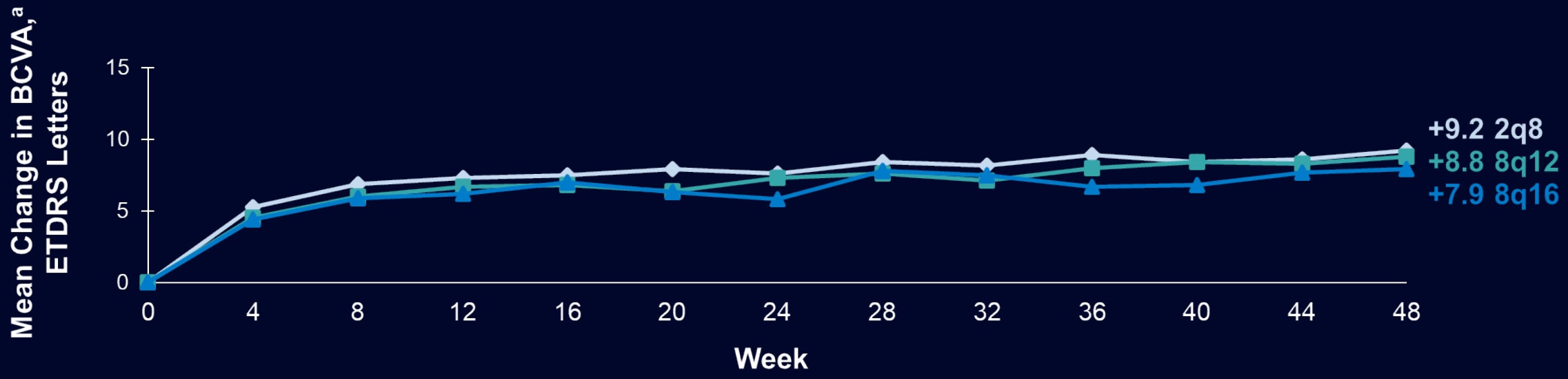
DME

	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.92

Mean Change in BCVA Through Week 48[a]

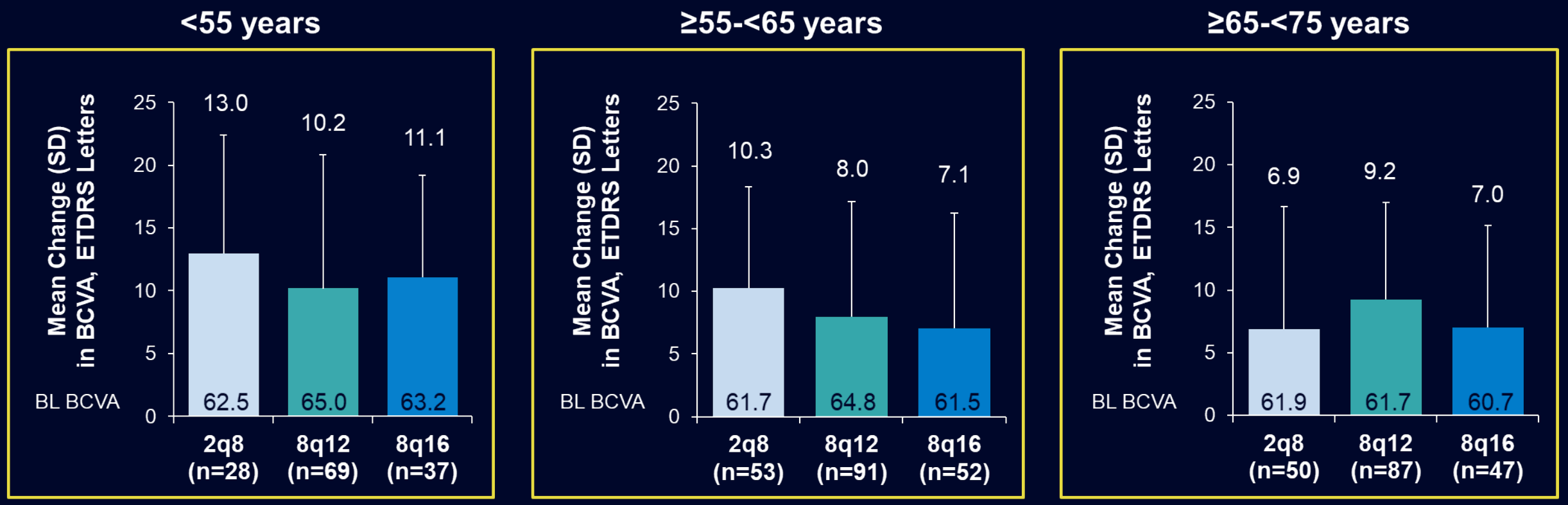


	LS mean change from baseline[b]	Difference in LS means vs. aflibercept 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	8.7	—	—	—
8q12	8.1	-0.57	-2.26, 1.13	p < 0.0001
8q16	7.2	-1.44	-3.27, 0.39	p = 0.0031

[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.

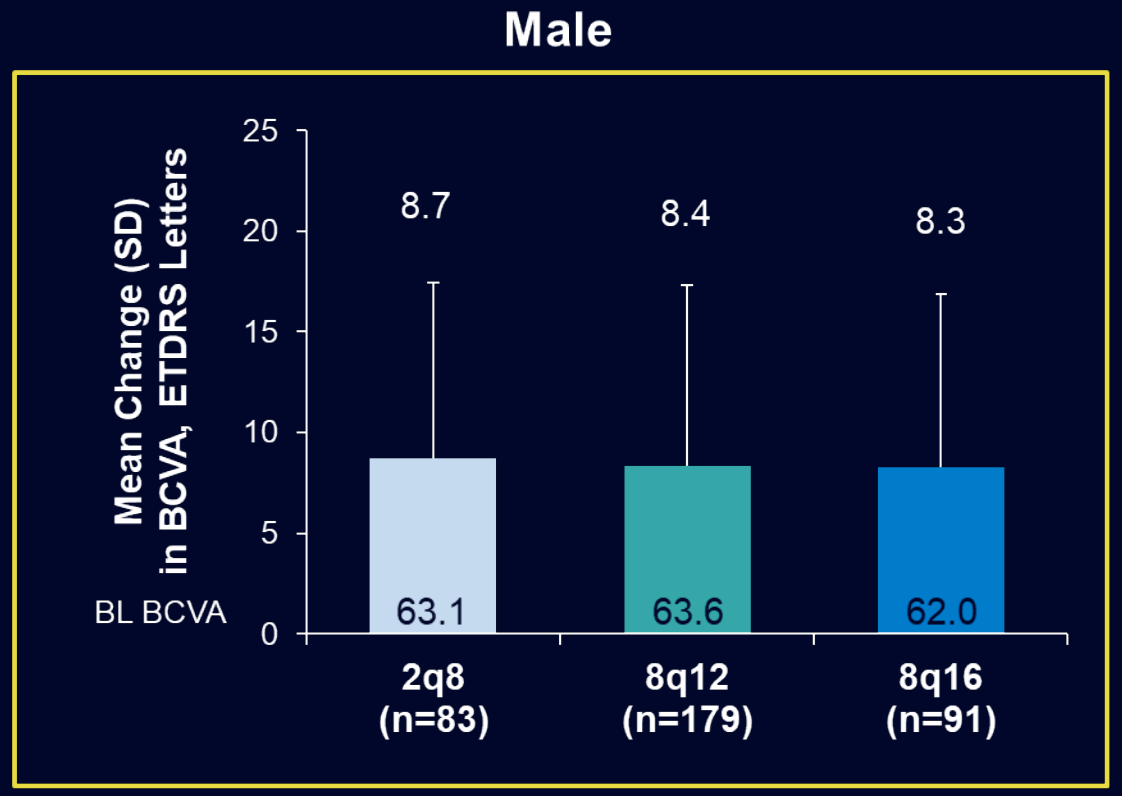
Mean Change in BCVA at Week 48 by Age[a]

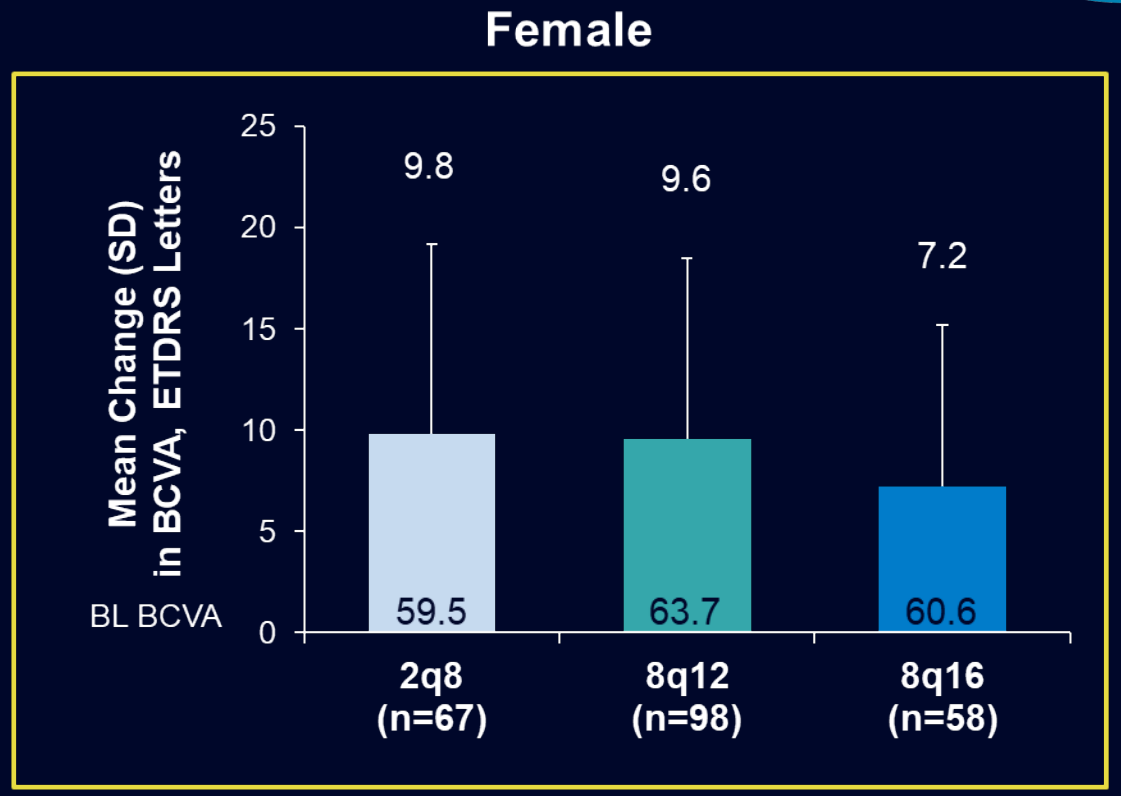
DME



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.

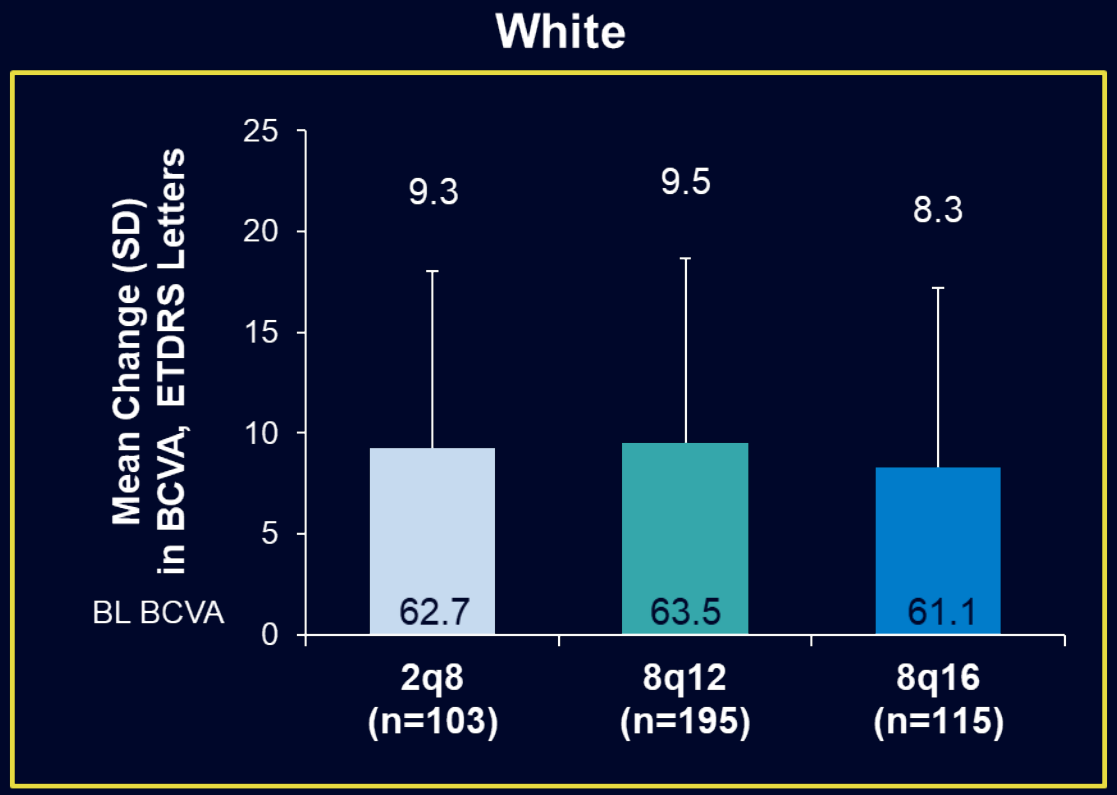
Mean Change in BCVA at Week 48 by Sex

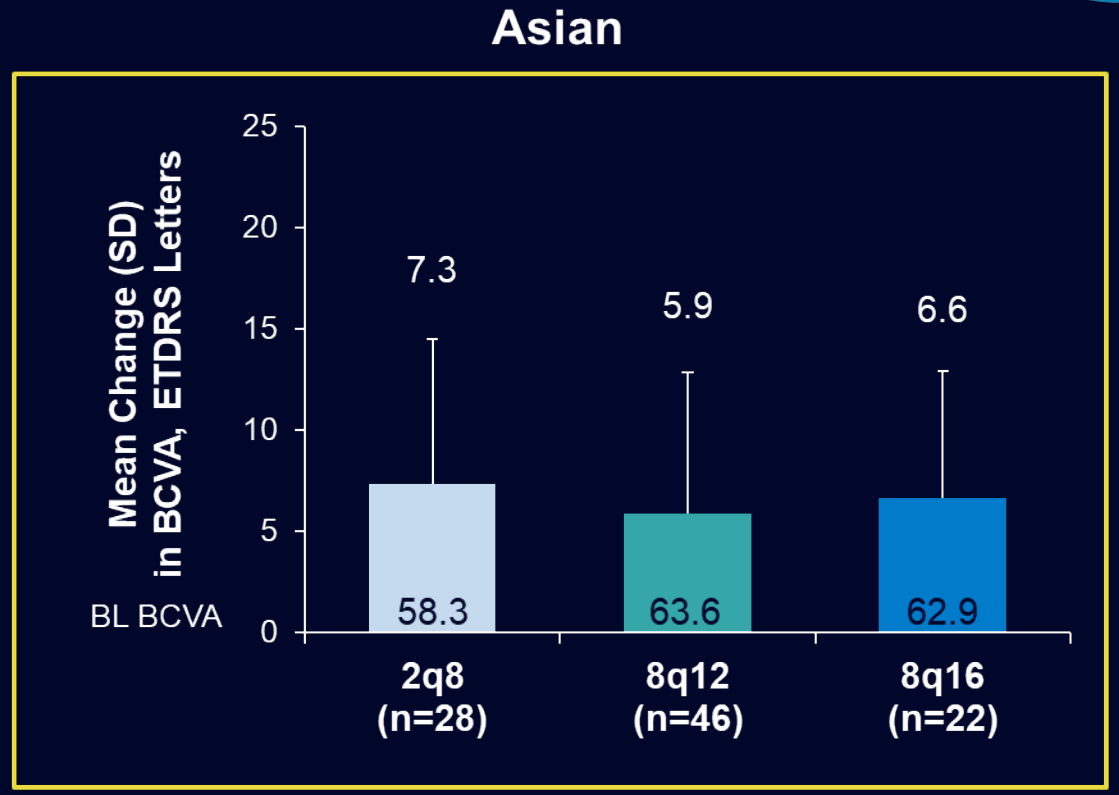




FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

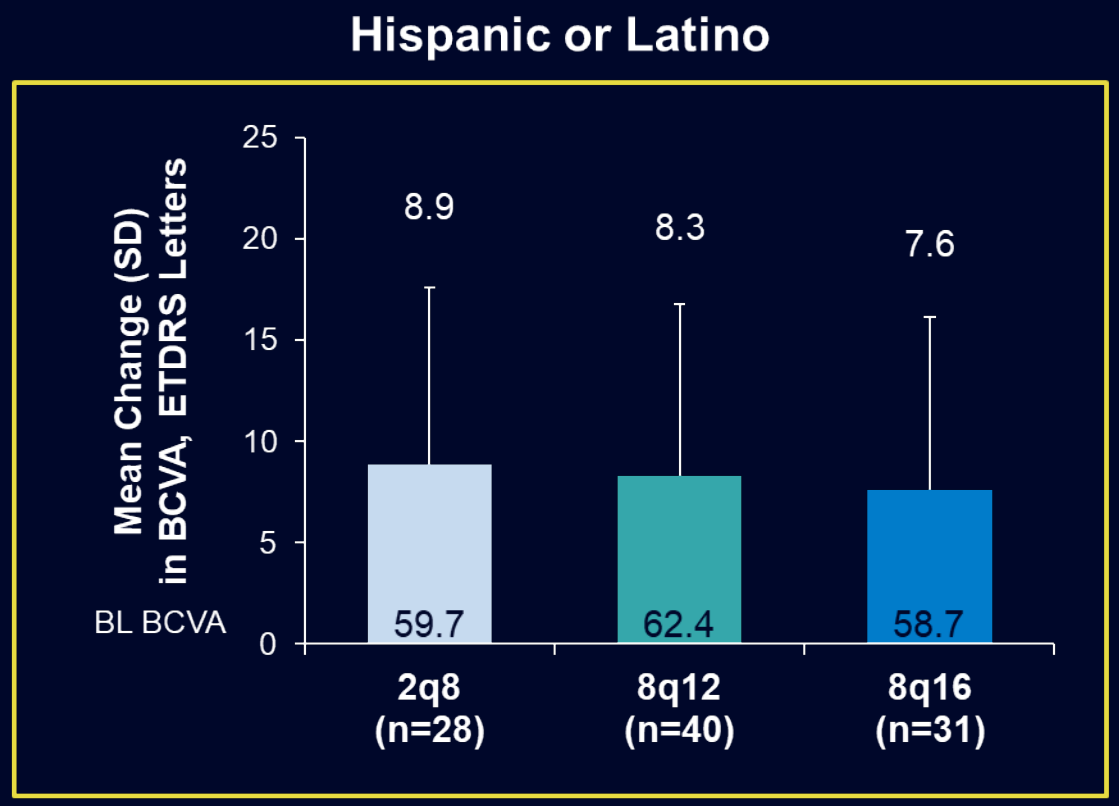
Mean Change in BCVA at Week 48 by Race[a]

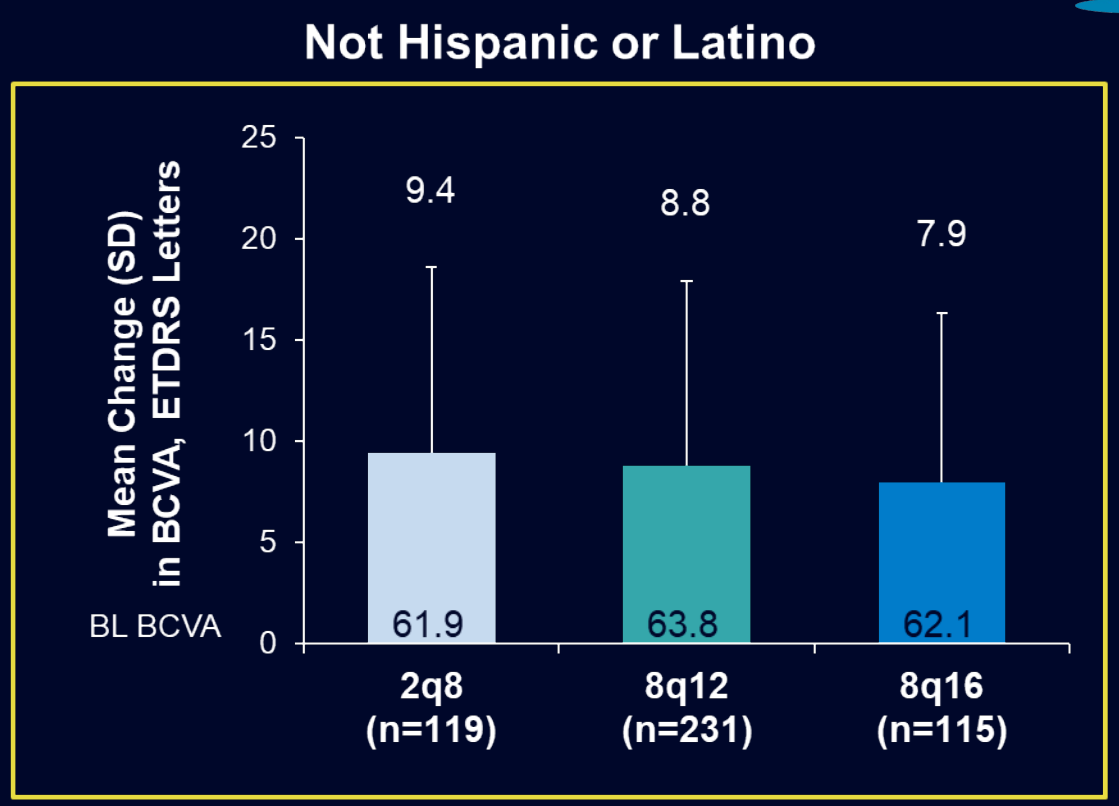




FAS.
[a]The subgroup Black or African American race could not be evaluated due to small sample size (<15 patients in the 2q8 and 8q16 groups).
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

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).

Mean Change in BCVA at Week 48 by Baseline BCVA

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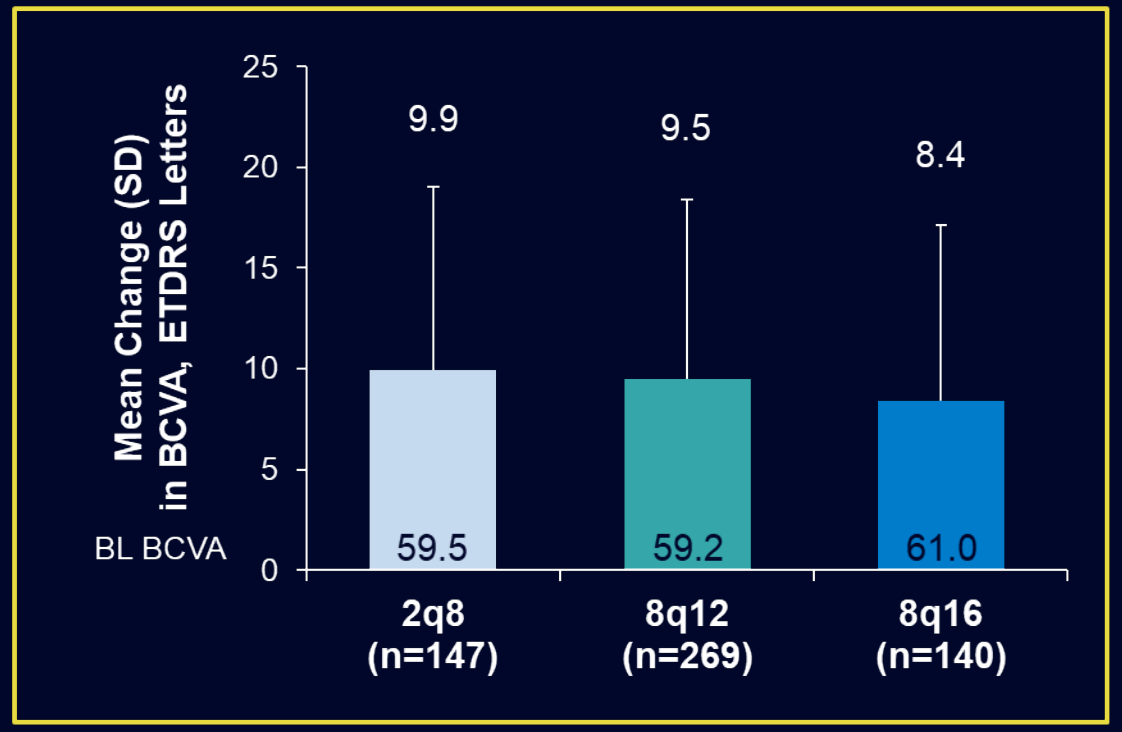
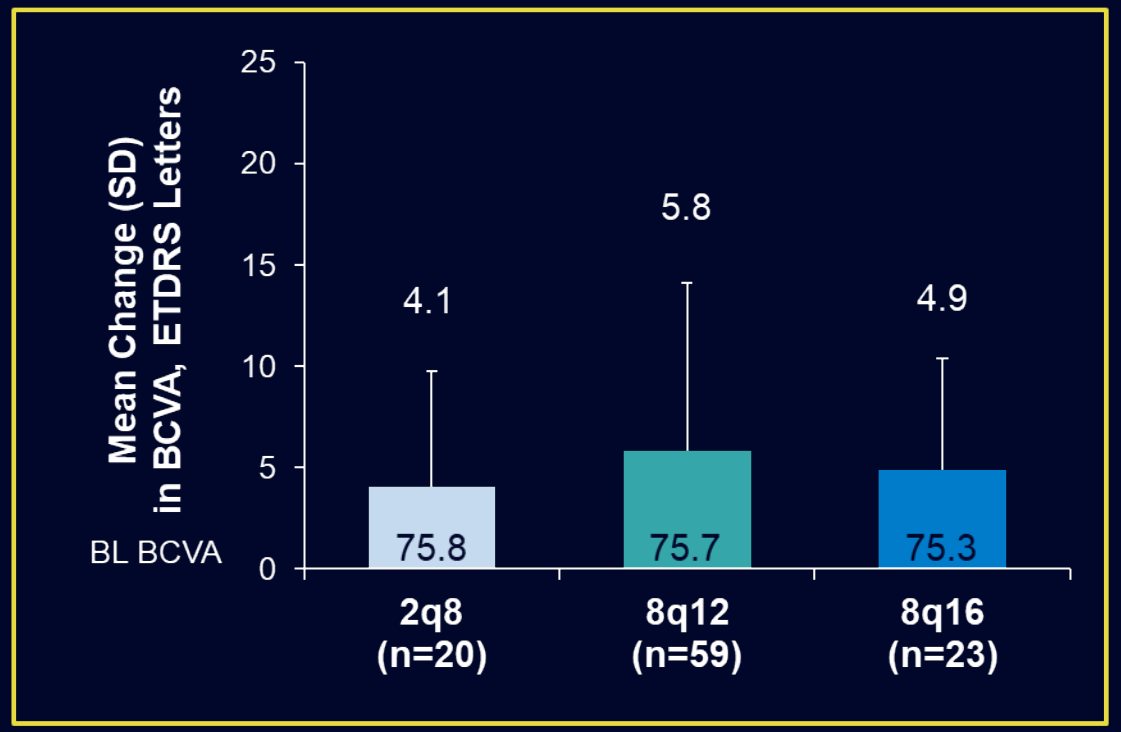
Baseline BCVA ≤ 73 letters

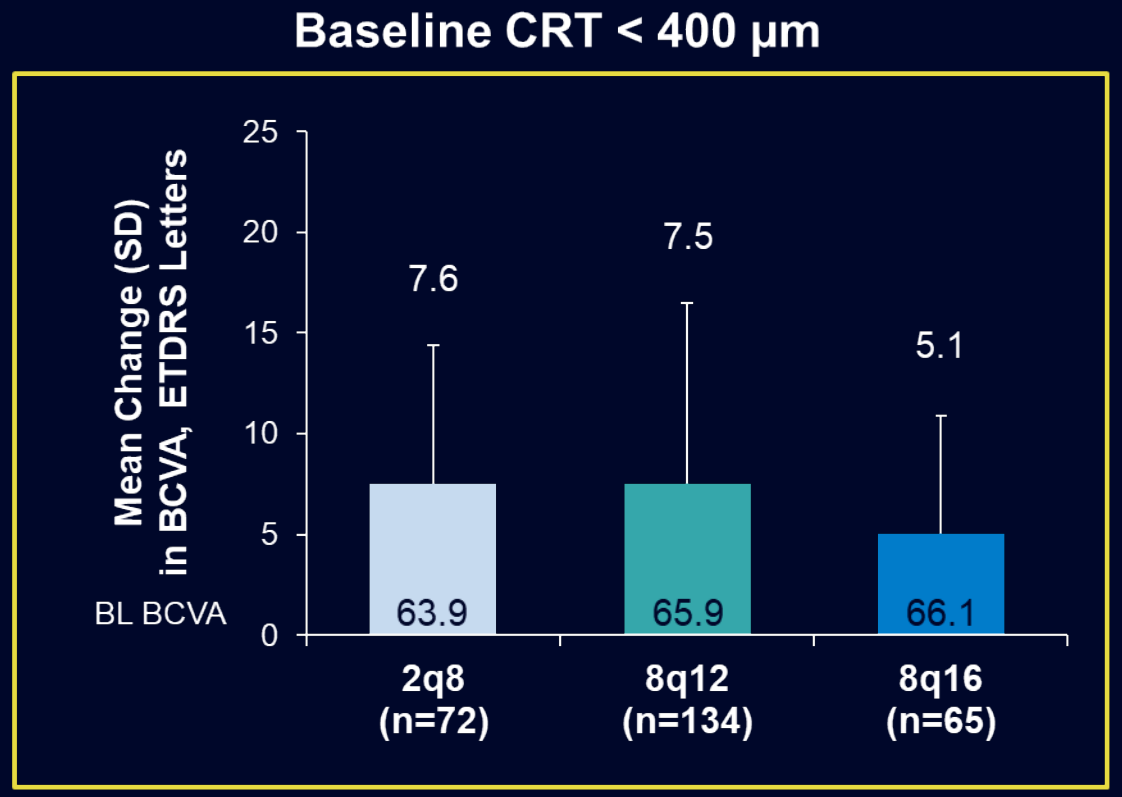


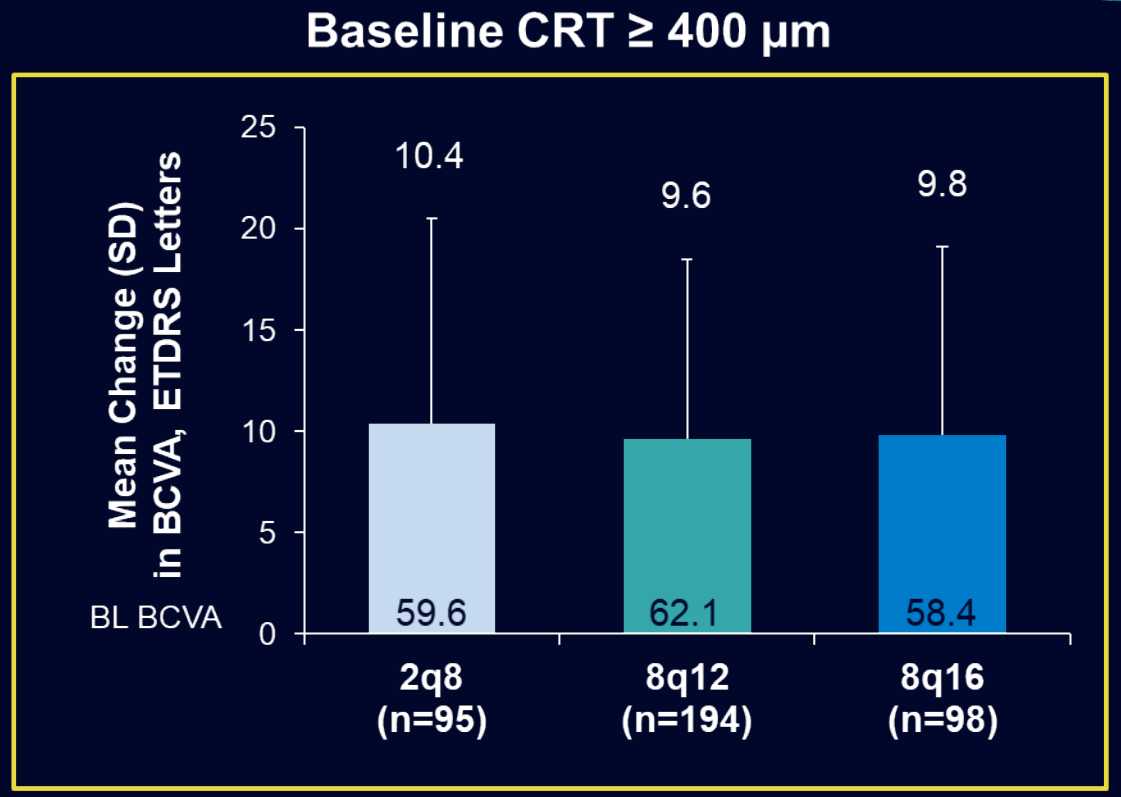
Baseline BCVA > 73 letters



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

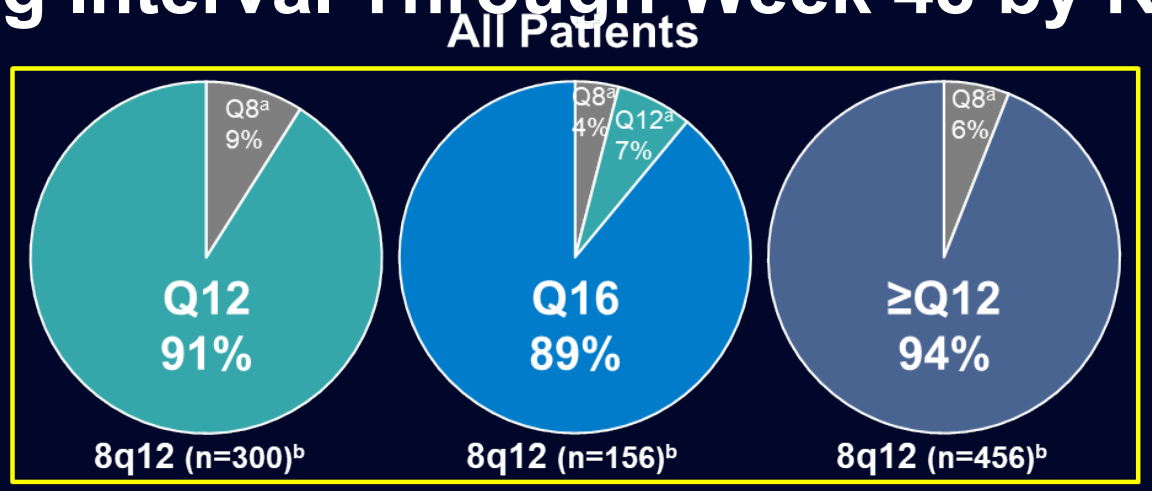
Mean Change in BCVA at Week 48 by Baseline CRT

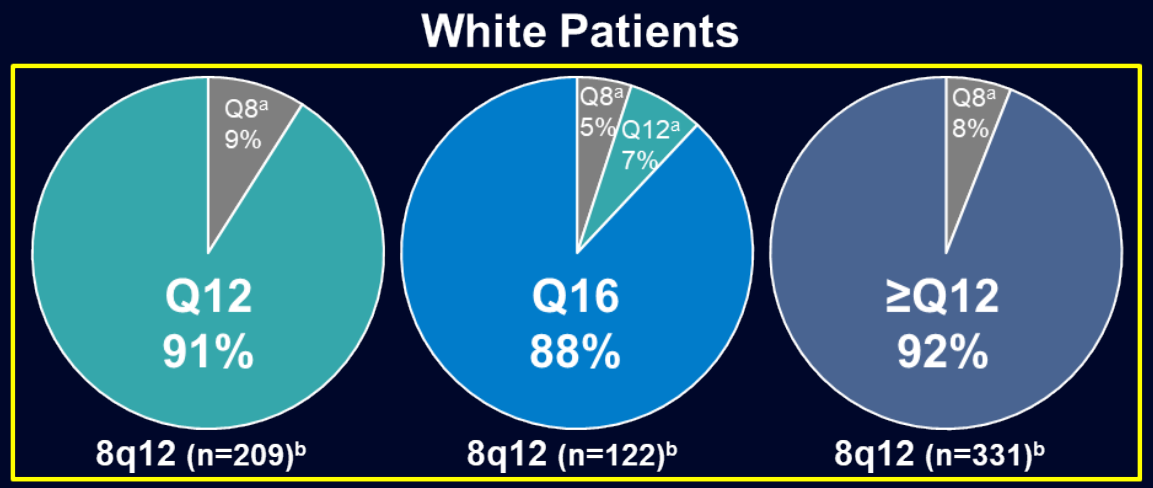


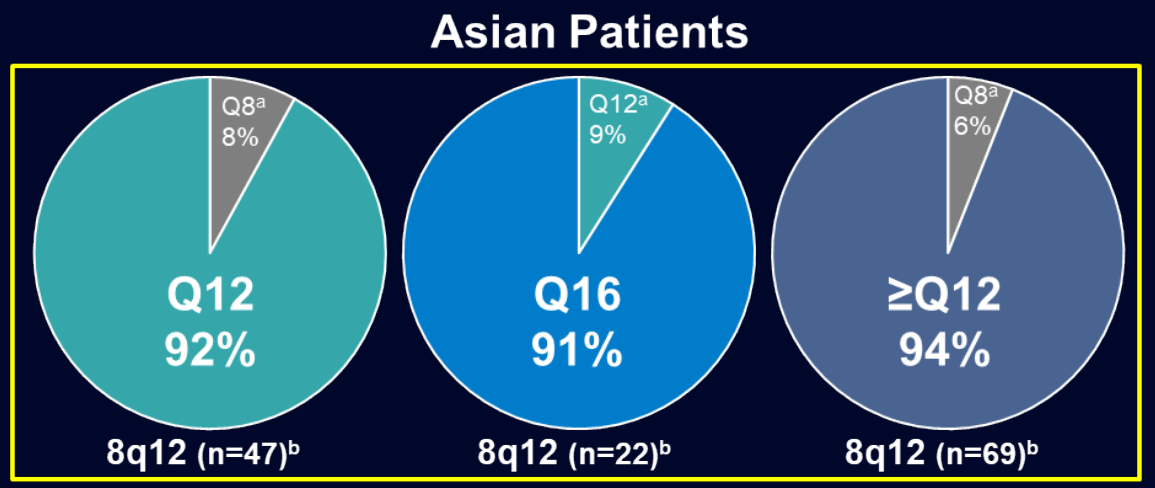


FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

Proportion of 8 mg Patients Who Maintained Randomized Dosing Interval Through Week 48 by Race







[a]Patients shortened based on DRM criteria through Week 48. [b]Patients completing Week 48.
Data are not reported for Black or African American patients due to small sample size. Values may not add up to 100 due to rounding.

Proportion of 8 mg Patients Who Maintained Randomized Dosing Interval Through Week 48 by Ethnicity

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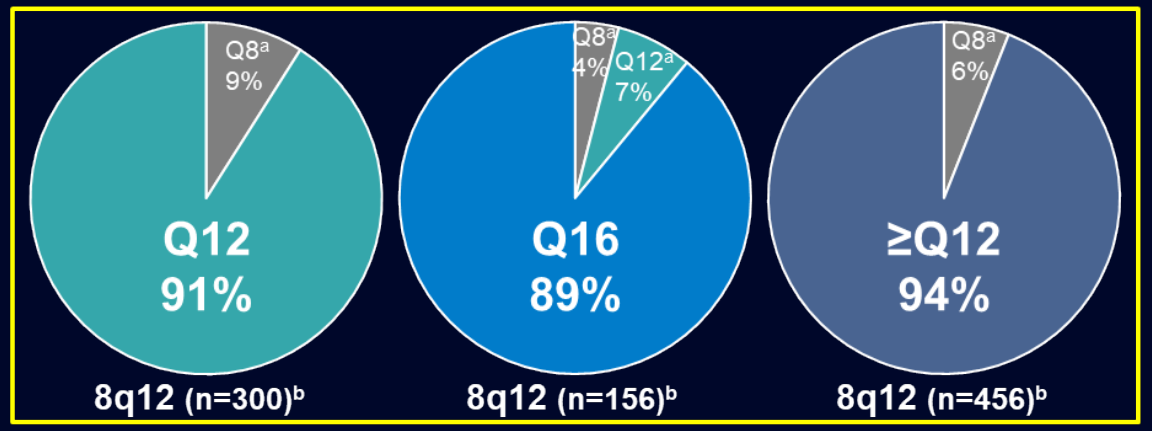
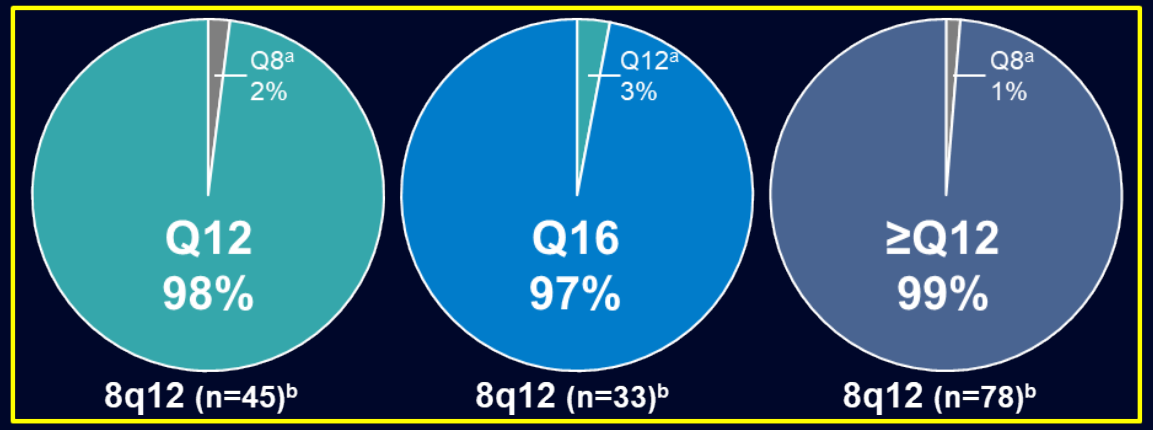
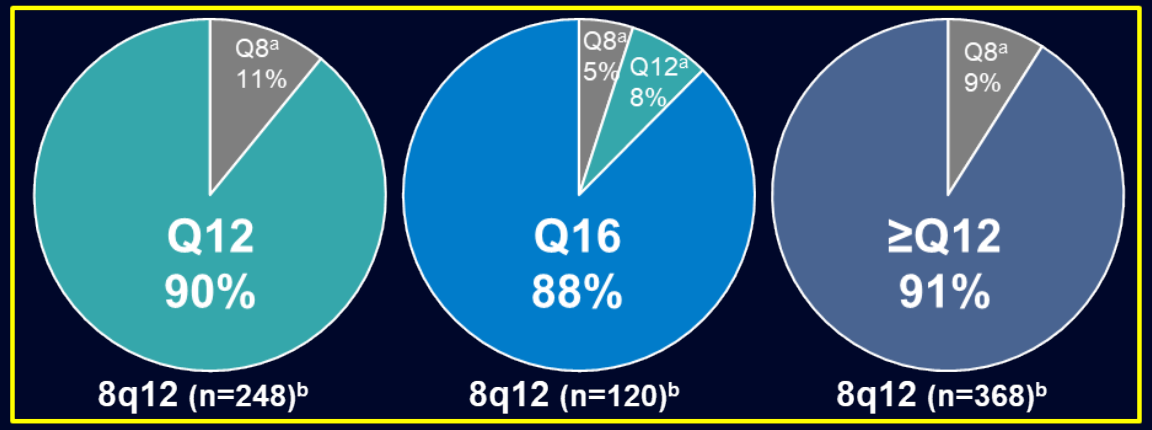
All Patients



Hispanic or Latino Patients



Not Hispanic or Latino Patients



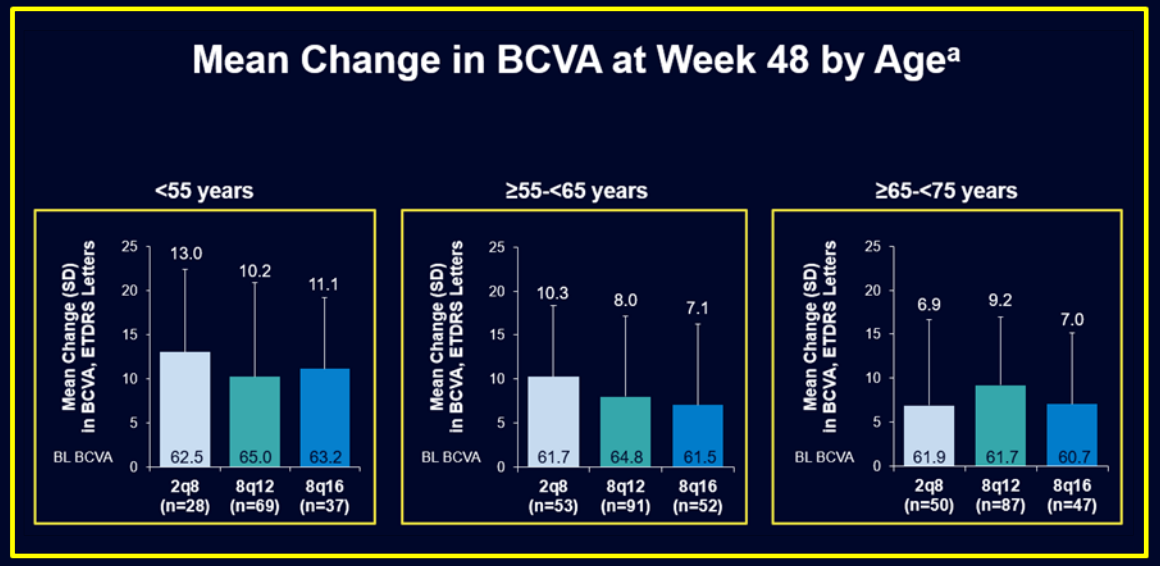
[a]Patients shortened based on DRM criteria through Week 48. [b]Patients completing Week 48.
Values may not add up to 100 due to rounding.

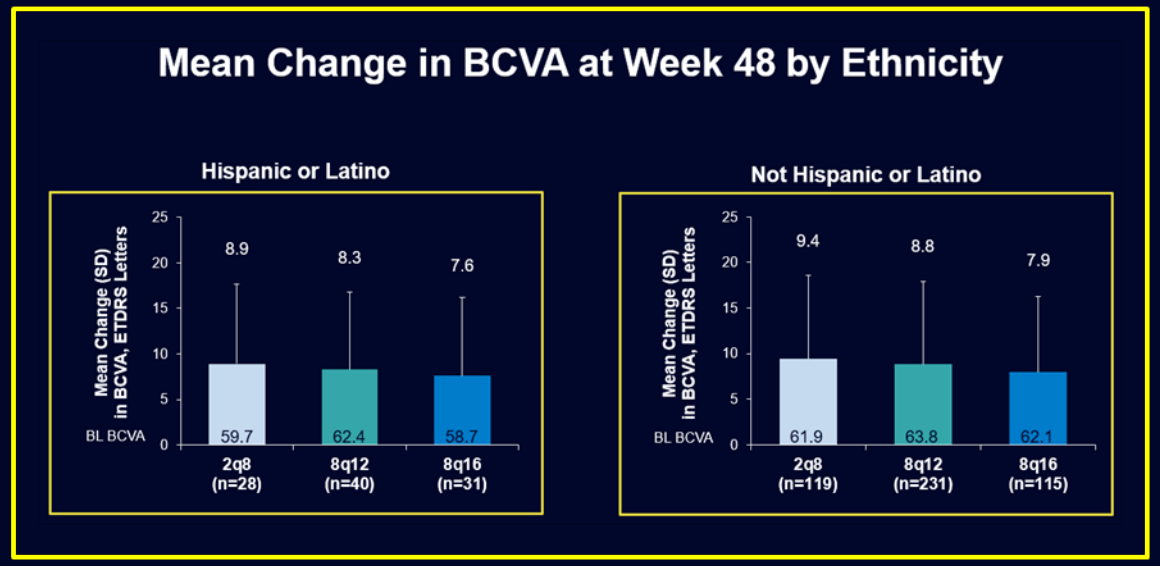
Limitations

- 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

DME





- Aflibercept 8 mg achieved meaningful BCVA gains from baseline at Week 48 in patients with DME across evaluable subgroups of age, sex, race, ethnicity, baseline BCVA, and baseline CRT
- When evaluated by race and ethnicity, the majority of patients in the 8 mg groups maintained their randomized dosing intervals