Subgroup Analyses from the Phase 3 PULSAR Trial of Aflibercept 8 mg in Patients with Treatment-Naïve Neovascular Age-Related Macular Degeneration

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Disclosures

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  - **SS**: receives funding/fees from Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, EyeBiotech, Novartis, Optos, and Roche.**TM**: Employee of Bayer AG. **XZ** and **SL**: Employees of Bayer Consumer Care AG
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- Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
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PULSAR Study Design

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Multicenter, randomized, double-masked study in patients with treatment-naïve nAMD
Randomized at baseline 1 (2q8) : 1 (8q12) : 1 (8q16)

2q8
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections
n=336

8q12
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections
n=335

8q16
Aflibercept 8 mg every 16 weeks after 3 initial monthly injections
n=338

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

Key secondary endpoint at Week 16
Proportion of patients without IRF and SRF in the center subfield

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

Subgroups were determined post hoc and subgroup analyses were exploratory:
For example, baseline BCVA, CST, CNV type and race

2q8, aflibercept 2 mg every 8 weeks; **8q12**, aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **BCVA**, best-corrected visual acuity; **CNV**, choroidal neovascularization; **CST**, central subfield thickness; **IRF**, intraretinal fluid; **nAMD**, neovascular age-related macular degeneration; **SRF**, subretinal fluid.

PULSAR: Dosing Schedule and Regimen Modification in Year 1

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	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	o	X	o	X	o	X	o	X
8q12	X	X	X		o	X	o	o	X	o	o	X	o
8q16	X	X	X		o	o	X	o	o	o	X	o	o

DRM criteria for shortening dosing interval

- >5-letter loss in BCVA compared with Week 12, due to persistent or worsening nAMD

AND

- >25 µm increase in CST compared with Week 12, or new-onset foveal neovascularization, or foveal hemorrhage

DRM in Year 1

Intervals can only be **shortened**

Multiple opportunities to shorten interval

Minimum interval for all patients was **Q8**

- **Weeks 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
- **Weeks 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 injection. Note: Table does not reflect all dosing options once a patient's dosing interval is shortened.
DRM, dose regimen modification; **Q8**, every 8 weeks; **Q12**, every 12 weeks; **Wk**, week.

BCVA by Baseline BCVA Categories (ETDRS Letters): At Week 48

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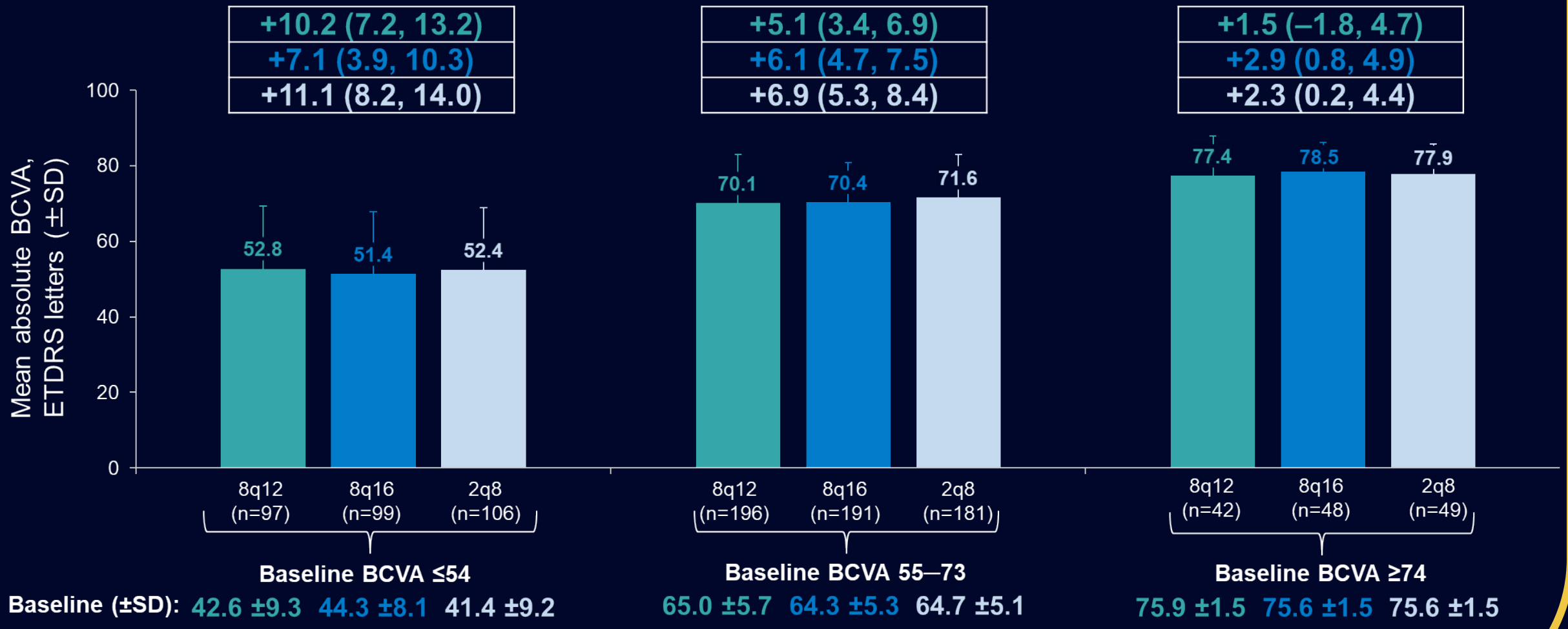
Change from Baseline at Week 48[a]



FAS, LOCF. Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding.

[a]Mean (95% CI) change from baseline to Week 48. **CI**, confidence interval; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set; **LOCF**, last observation carried forward; SD, standard deviation.

BCVA by Baseline CST Categories (µm): At Week 48

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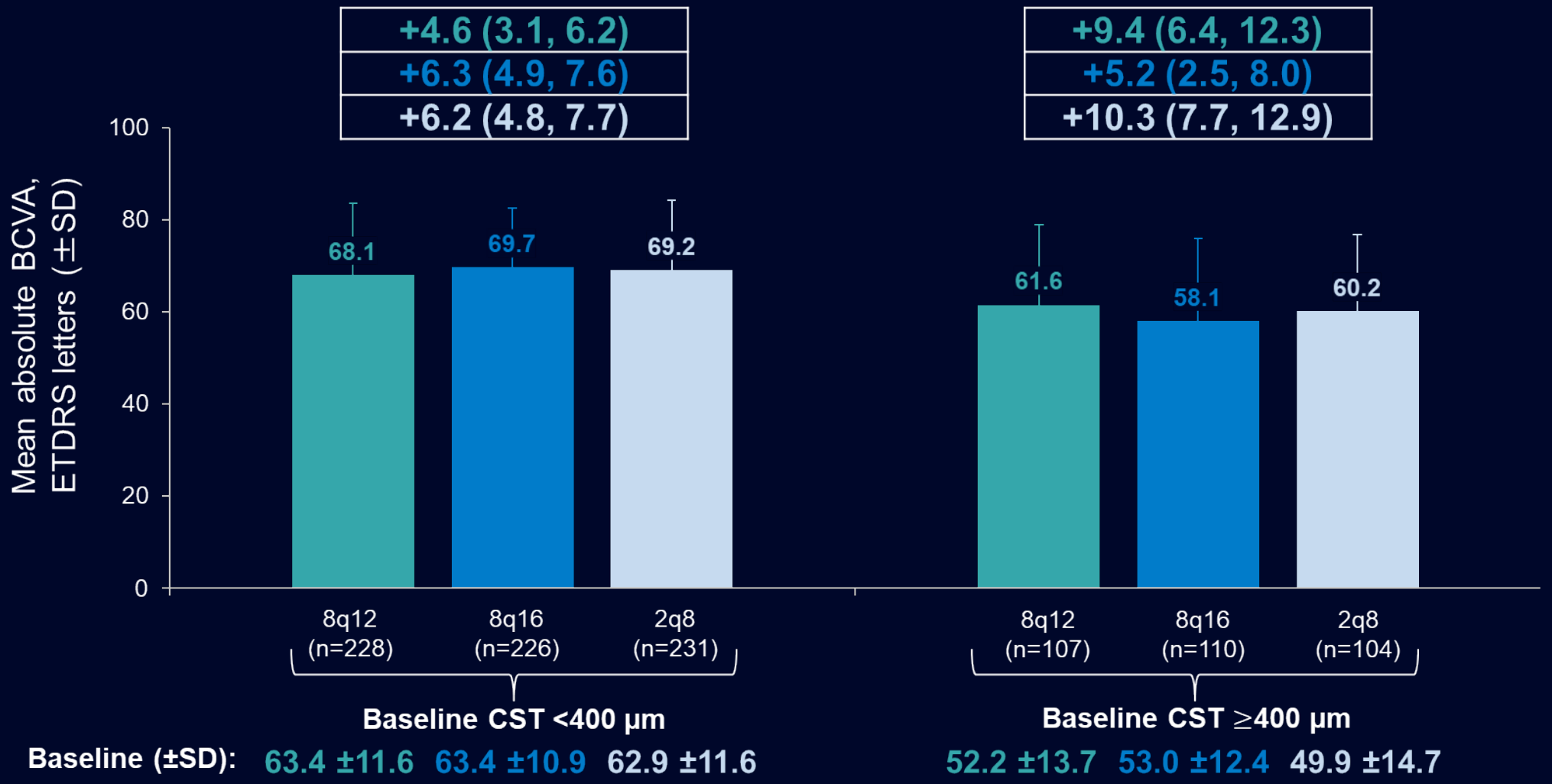
Change from Baseline at Week 48[a]



FAS, LOCF. Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding.
[a]Mean (95% CI) change from baseline to Week 48.

BCVA by Baseline CNV Type: At Week 48

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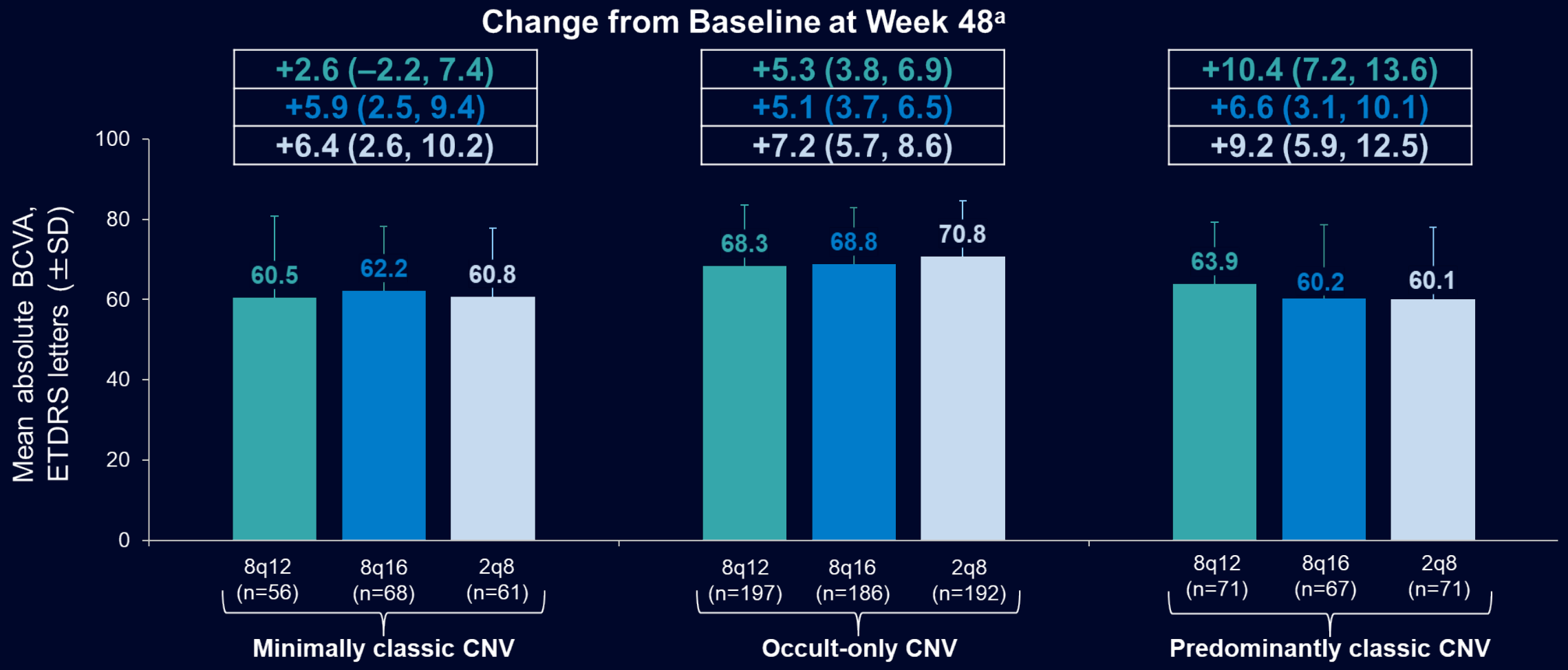

FAS, LOCF. Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding.
[a]Mean (95% CI) change from baseline to Week 48.

BCVA by Race: At Week 48

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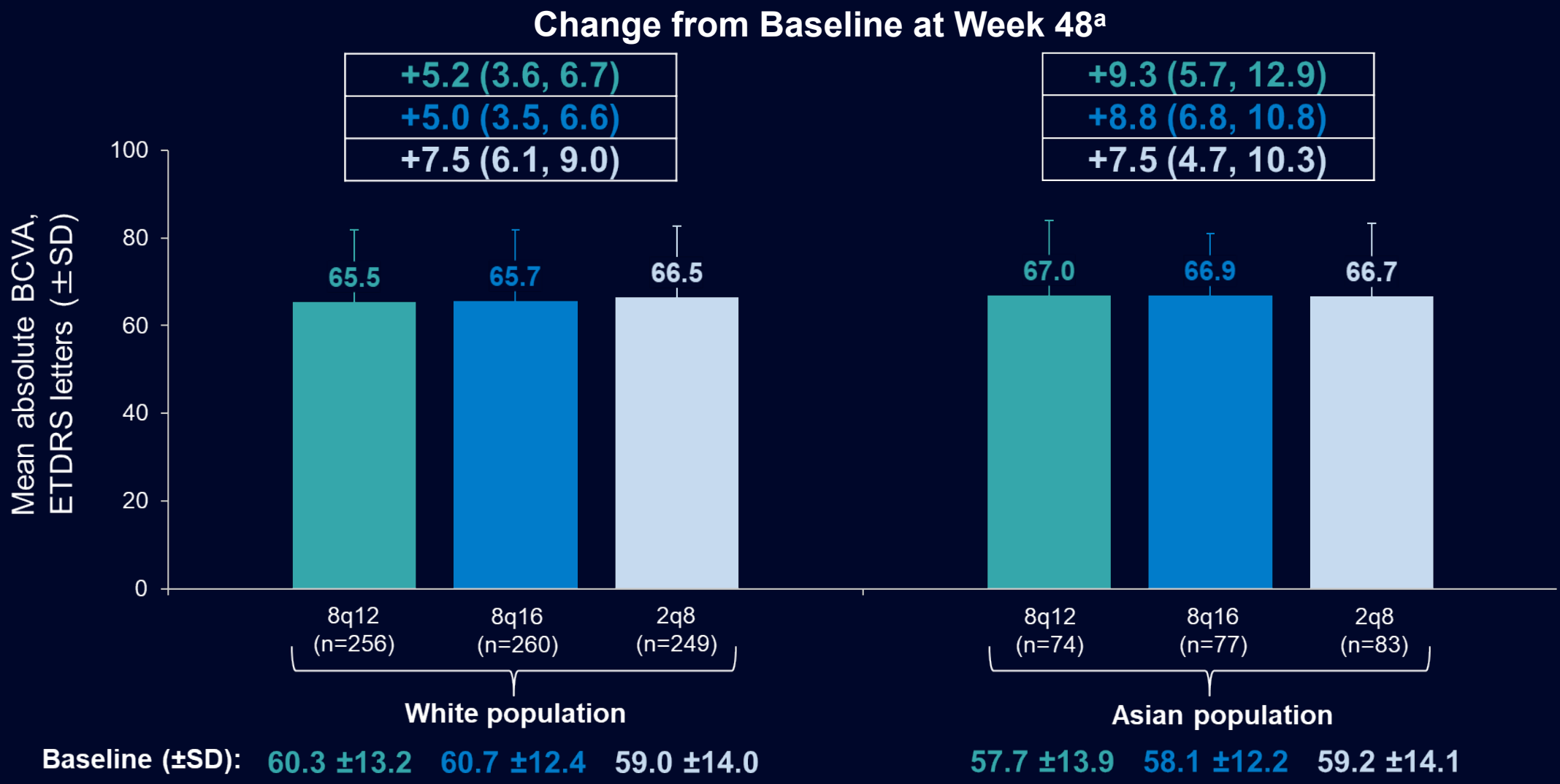

FAS, LOCF. Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding. Data are not reported for Black or African American patients due to small sample size (n=2). [a]Mean (95% CI) change from baseline to Week 48.

Proportion of Patients Maintaining 8 mg Q12 and Q16 Treatment Intervals Up to Week 48: Categorized by Race

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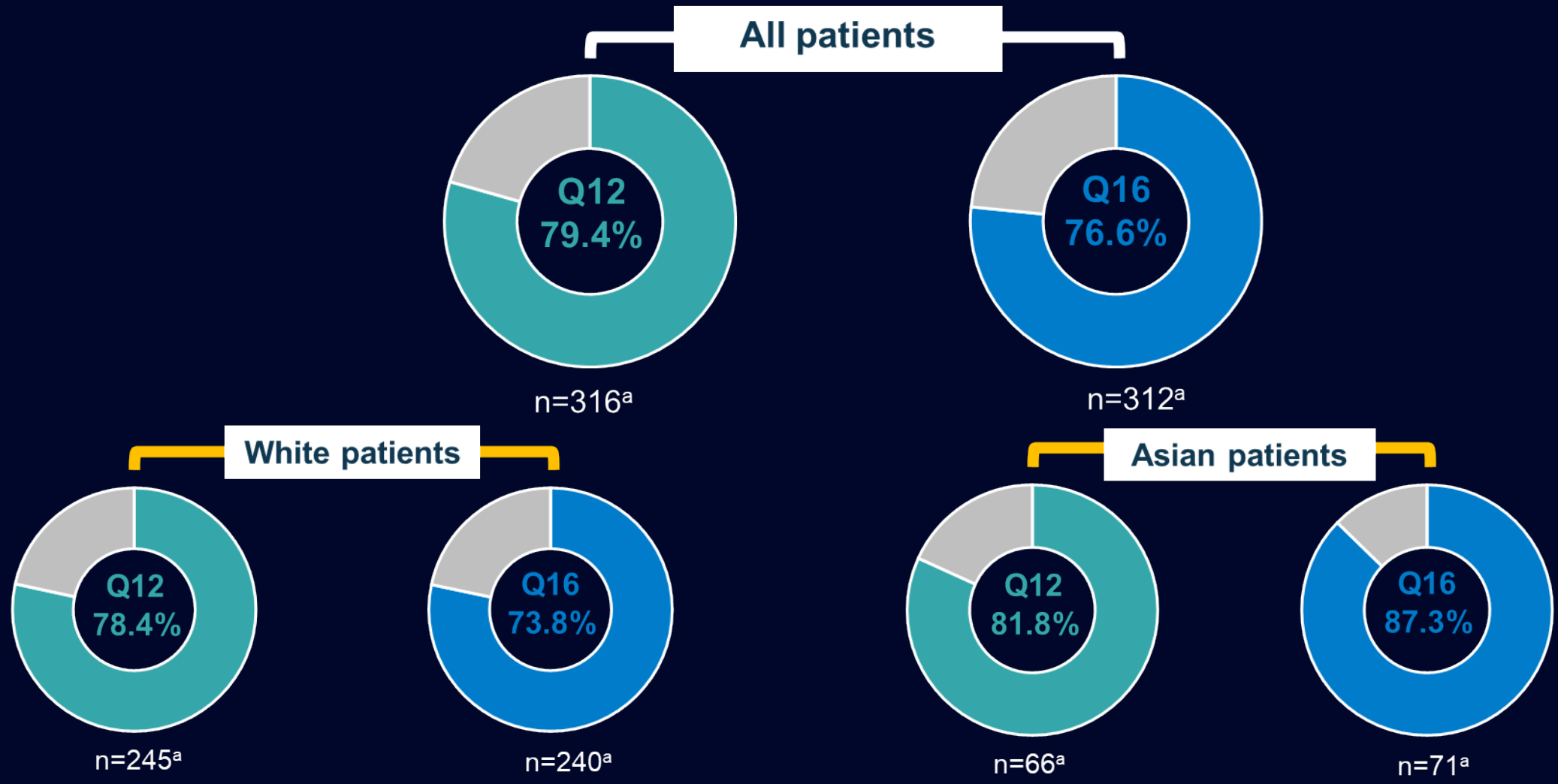

FAS, LOCF. Data are not reported for Black or African American patients due to small sample size (n=2).
[a]Patients completing Week 48.

Conclusions: Baseline Subgroup Analyses at Week 48

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- BCVA outcomes were comparable for aflibercept 8 mg vs aflibercept 2 mg among the evaluable subgroups of baseline characteristics
- Regardless of differences in baseline BCVA and BCVA change at Week 48 in some subgroups, absolute BCVA values at Week 48 were comparable
- The majority (70–80%) of White and Asian patients with nAMD treated with intravitreal aflibercept 8 mg maintained Q12 or Q16 week treatment intervals.[a] These proportions are comparable to those for the overall patient populations in the PULSAR trial

[a]Black or African American patients were excluded due to small sample size.