Aflibercept 8 mg in Neovascular Age-Related Macular Degeneration: 156-Week Results From the PULSAR Extension

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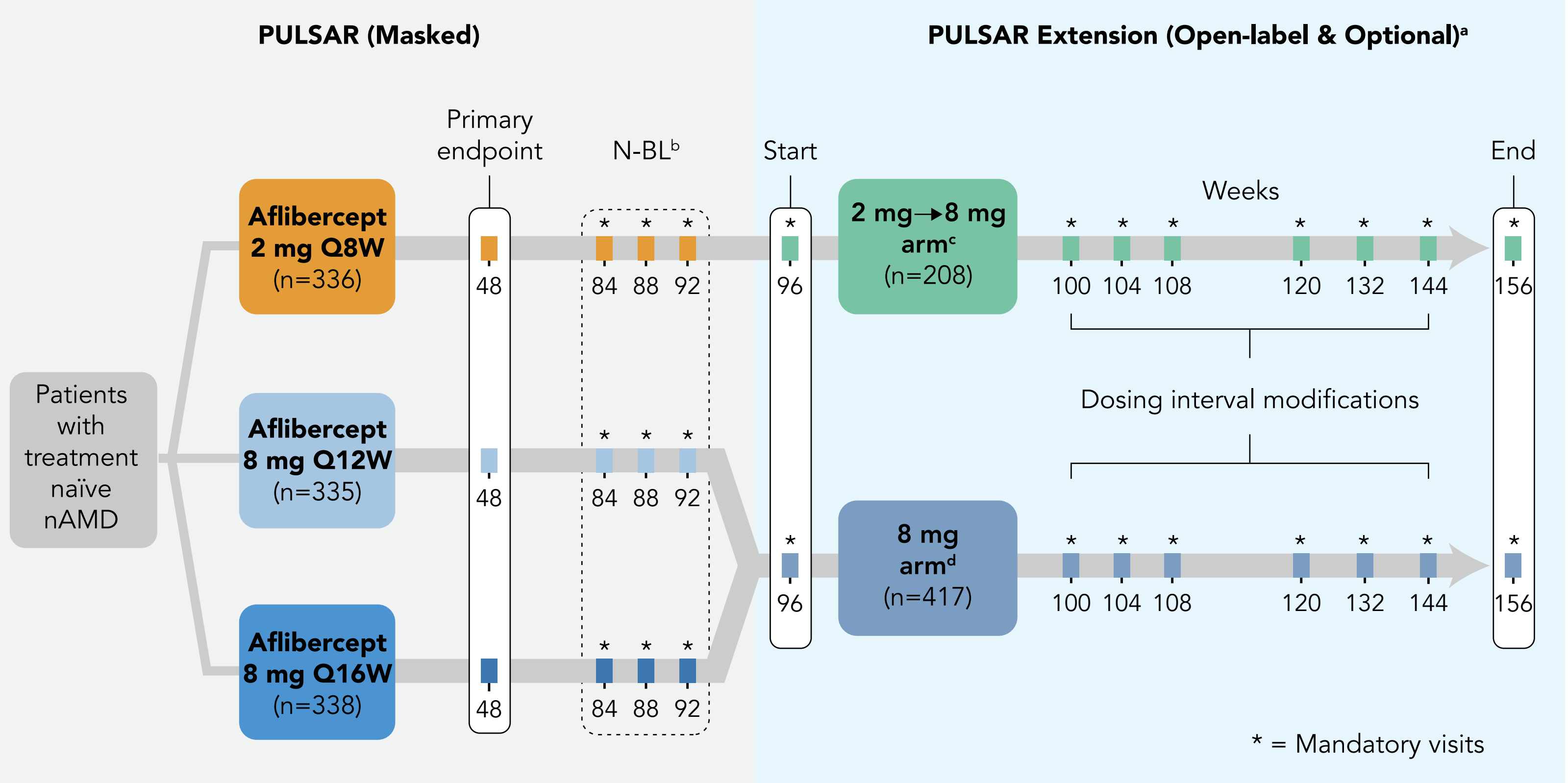
https://congresspublications.bayer.com/download/RGN_ENCORE_Mac%20Soc%202025_PULSAR%20156-WK_WONG_ORAL_07FEB25.pdf

Aflibercept 8 mg is a new intravitreal anti-VEGF formulation, delivering a concentrated 4-fold higher molar dose than aflibercept 2 mg in a 70-μL injection. The PULSAR trial was a phase 3, randomized, double-masked, active-controlled clinical trial design to evaluate the safety and efficacy of aflibercept 8 mg with extended dosing intervals (Q12W or Q16W) compared to 2 mg Q8W in treatment-naïve neovascular age-related macular degeneration (nAMD) over 96 weeks.

Following the initial 96-week period, an optional open-label extension study was conducted to week 156 to assess the long-term safety, efficacy, and durability of aflibercept 8 mg. Not all patients were able to enroll due to time constraints.

The PULSAR Extension is a multicenter, open-label, optional study to evaluate changes from Week 96 to Week 156



a To be eligible for the Extension phase, patients had to have ≥1 best-corrected visual acuity (BCVA) and central subfield retinal thickness (CRT) assessments between Week 84 and Week 92.
b New baseline (N-BL) was an average of values from Weeks 84, 88, and 92.
c Patients originally assigned to 2 mg Q8W switched to aflibercept 8 mg Q12W.
d Patients originally assigned to 8 mg Q12W or 8 mg Q16W continued aflibercept 8 mg on last assigned dosing interval.

Dosing Regimen Modification Criteria During the PULSAR Extension in Year 3 (E-DRM)

Interval Shortening

- Patients were assessed at ***any visit*** beginning at Week 100
- **Criteria for interval shortening:**
  - >5-letter loss in BCVA from N-BL due to persistent or worsening nAMD **AND either:**
    - >25 μm increase in CRT from N-BL **OR**
    - New onset of foveal neovascularization **OR**
    - New foveal hemorrhage
  - **OR** 10-letter loss in BCVA from N-BL due to worsening nAMD
- Dosing intervals shortened by **2-week** increments to a **minimum of Q8W**

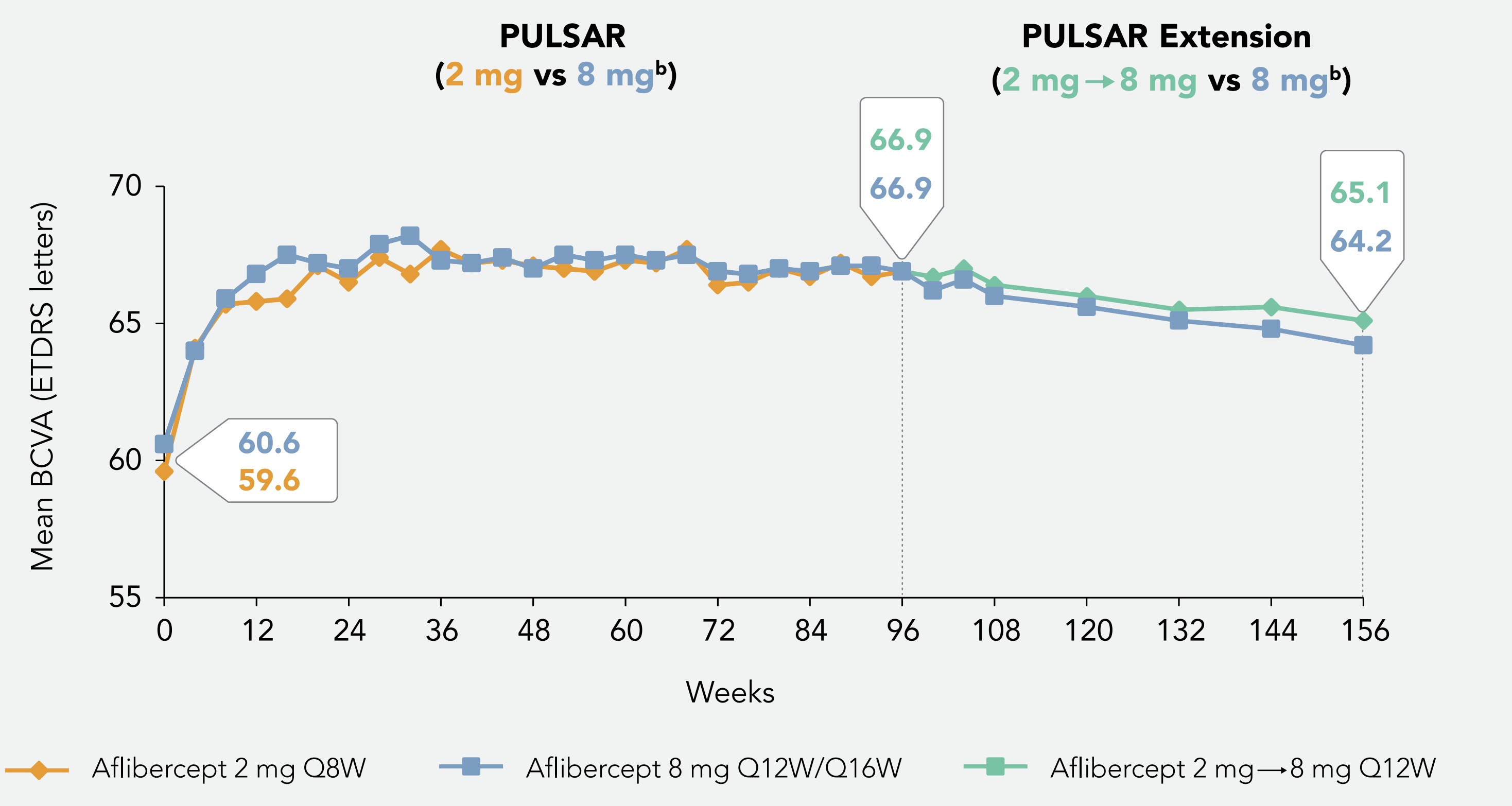
Interval Extension

- Patients were assessed at ***dosing visits*** beginning at Week 100
- **Criteria for interval extension:**
  - <5-letter loss in BCVA from N-BL **AND**
  - No fluid (IRF or SRF) in the central subfield on OCT **AND**
  - No new onset foveal neovascularization or foveal hemorrhage
- Dosing intervals extended by **2-week** increments to a **maximum of Q24W**

Q8W, every 8 weeks; Q24W, every 24 weeks;
E-DRM, dosing regimen modification criteria during the PULSAR Extension; EOS, end of study; IRF, intraretinal fluid; OCT, optical coherence tomography; SRF, subretinal fluid.

The mean BCVA was comparable at Week 156 between the 2 mg→8 mg and 8 mg groups

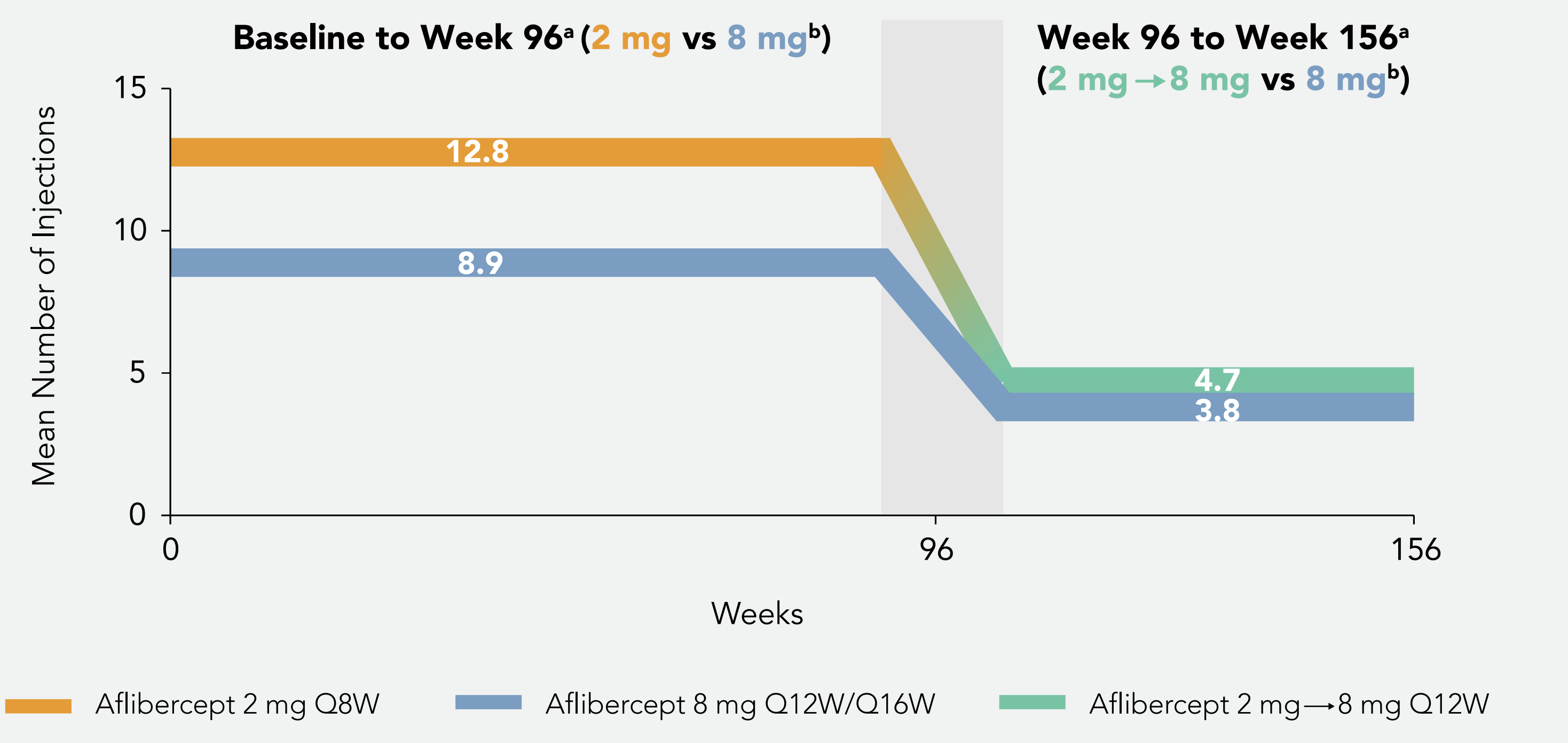
Mean BCVA[a] through Week 156



a eFAS (observed cases).
b Patients who were randomly assigned to the 8 mg Q12W or 8 mg Q16W groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension.

The mean number of injections between both treatment groups decreased from Week 96 to Week 156

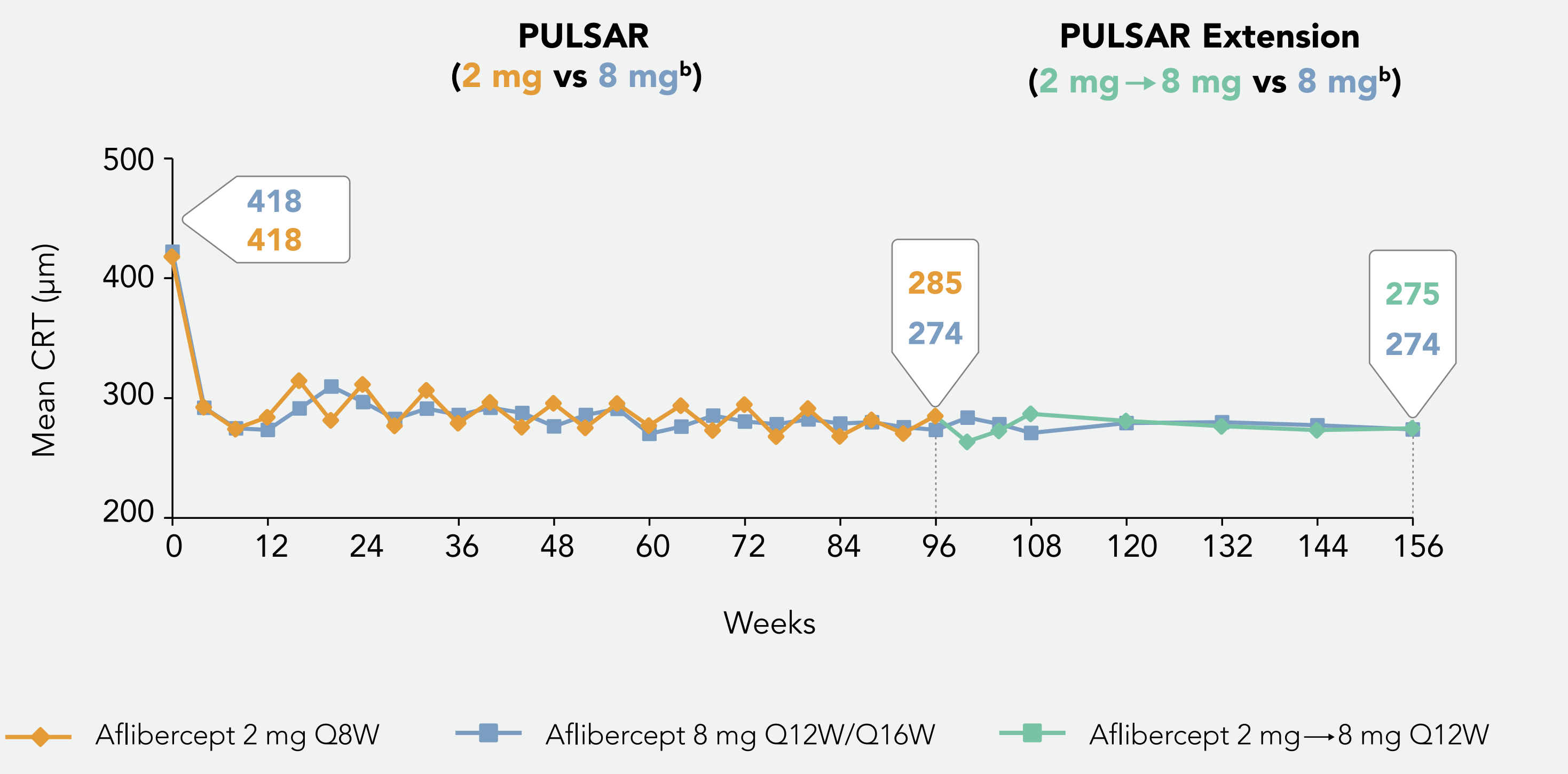
Mean number of injections

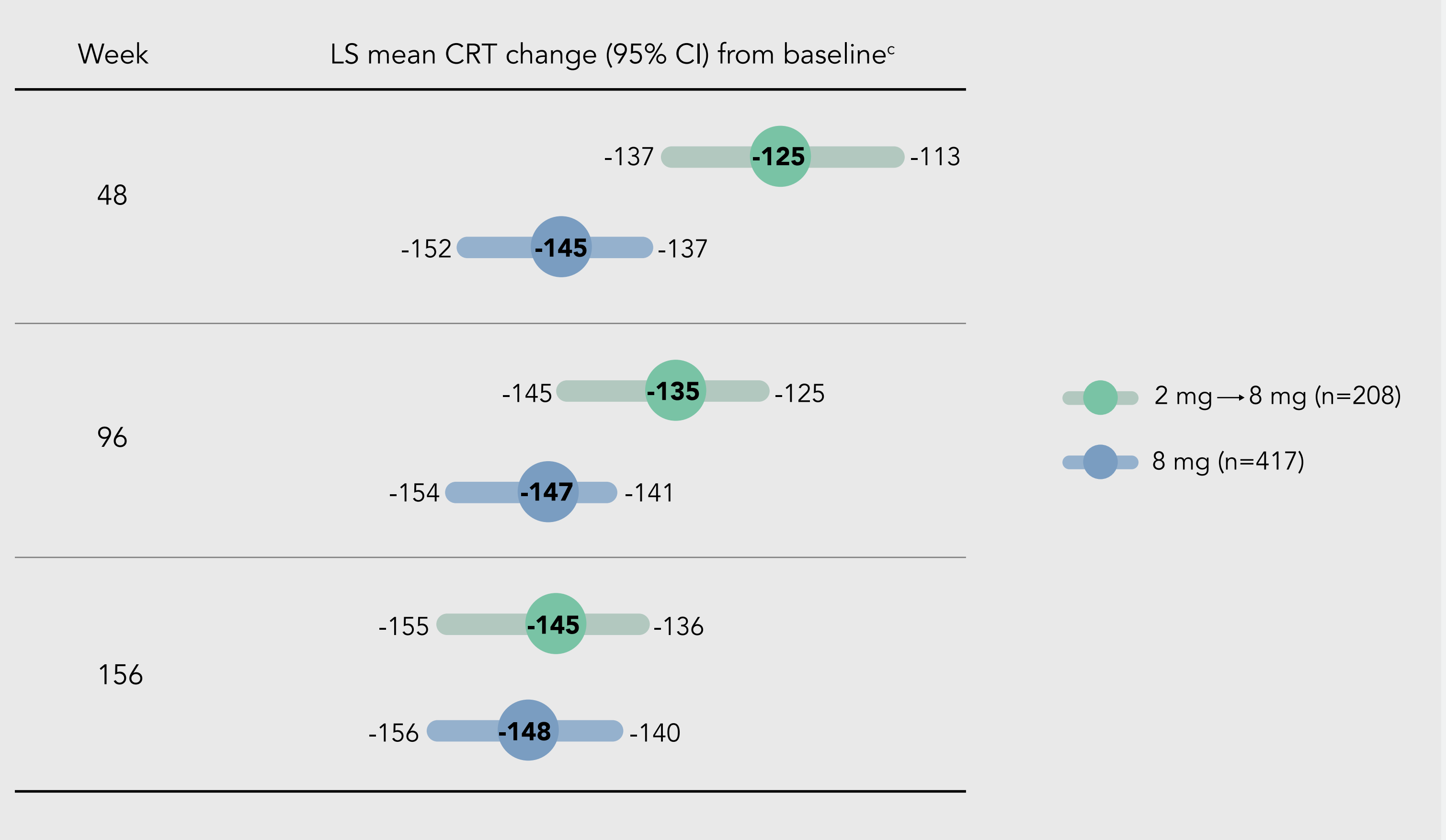


a eSAF, safety analysis set in the PULSAR Extension.
b Patients who were randomly assigned to the 8 mg Q12W or 8 mg Q16W groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension.

The mean CRT was comparable at Week 156 between the 2 mg→8 mg and 8 mg groups

Mean CRT[a] through Week 156

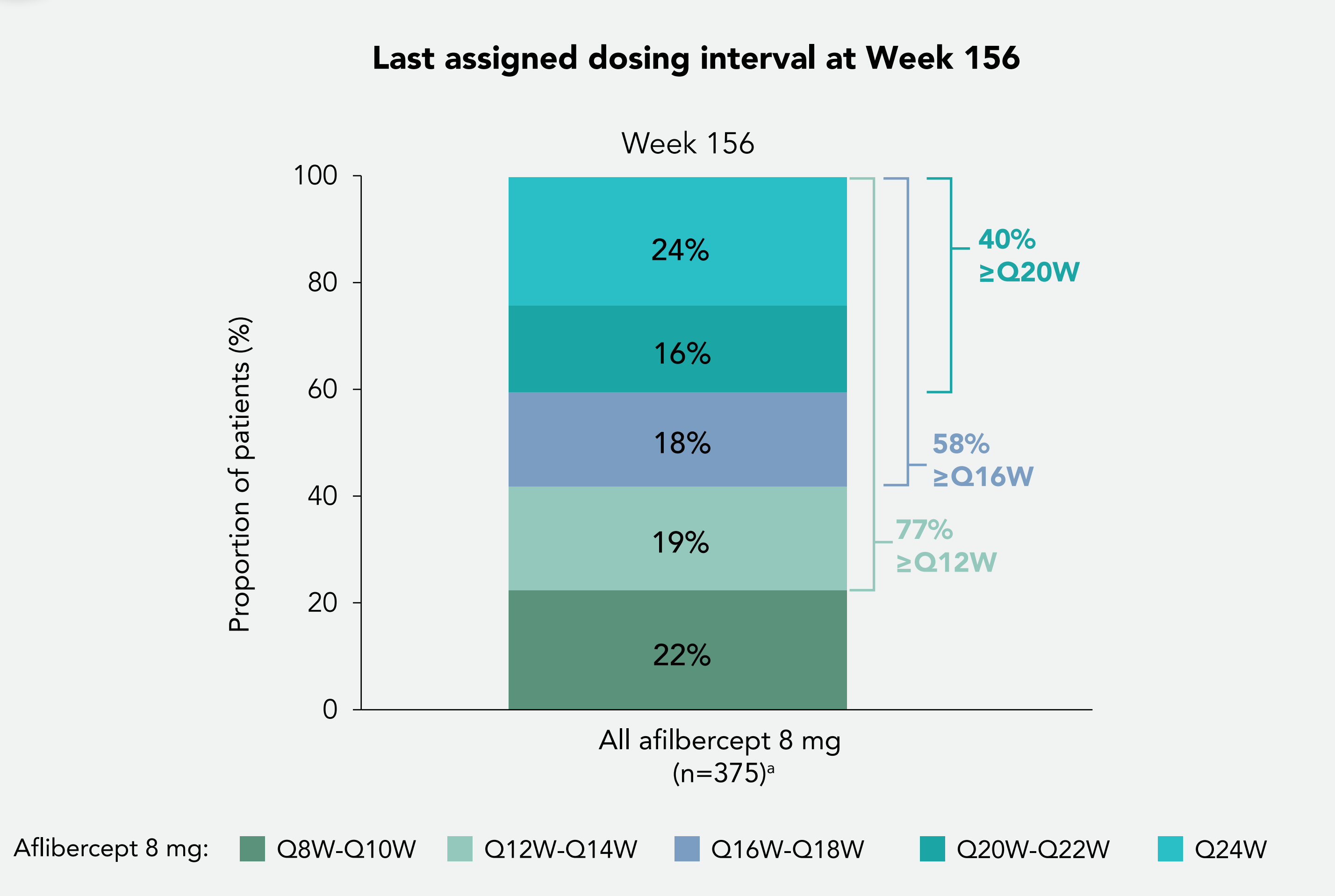




a eFAS (observed cases).
b Patients who were randomly assigned to the 8 mg Q12W or 8 mg Q16W groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension.
c LS means were generated for the eFAS using a mixed model for repeated measures with baseline CRT as a covariate; treatment group (aflibercept 8 mg Q12W, 8 mg Q16W, 2 mg Q8W), visit, and stratification variables (geographic region [Japan vs rest of the world] and baseline BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and baseline CRT and the interaction between visit and treatment.
CI, confidence intervals; CRT, central retinal thickness; LS, least squares.

The majority of patients achieved extended dosing intervals at Week 156

Last assigned dosing interval at Week 156



eSAF, patients completing Week 156. Values may not add up to 100% due to rounding.
a One patient had a missing value for this assessment.

Adverse events

No new safety signals were reported with aflibercept 8 mg through Week 156

Conclusion

Functional and anatomic improvements observed in the PULSAR trial were largely maintained through Week 156 in the PULSAR Extension with comparable mean BCVA and CRT at Week 156 between the 2 mg→8 mg and 8 mg groups. The majority of patients achieved extended dosing intervals at Week 156.