PULSAR Extension Phase: Fluid Resolution over 156 Weeks in Patients with Neovascular Age-related Macular Degeneration Receiving Aflibercept 8 mg and in Patients Switching from Aflibercept 2 mg to 8 mg

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Disclosures

pulsar
nAMD
Extension

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PULSAR Extension Design

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PULSAR *(Masked)*

Patients with treatment-naïve nAMD

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

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

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

PULSAR Extension *(Open-label and optional)*[a]

2q8→8mg arm
Patients originally assigned to 2q8 switched to aflibercept 8 mg every 12 weeks
n=208

8mg arm
Patients originally assigned to 8q12 or 8q16 continued aflibercept 8 mg on last assigned dosing interval
n=417

Week

0 — 48 — 96 — 156

Primary endpoint
Change from baseline in BCVA (non-inferiority)

Start of PULSAR Extension
Optional phase added while PULSAR was ongoing; therefore, not all patients were able to enroll due to time constraints

End of PULSAR Extension

[a]To be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessments between Week 84 and Week 92. The masked transition period (Week 96–108) was followed by the open-label part (Week 108–156). **BCVA**, best-corrected visual acuity; **CRT**, central retinal subfield thickness; **nAMD**, neovascular age-related macular degeneration.

PULSAR Extension Design

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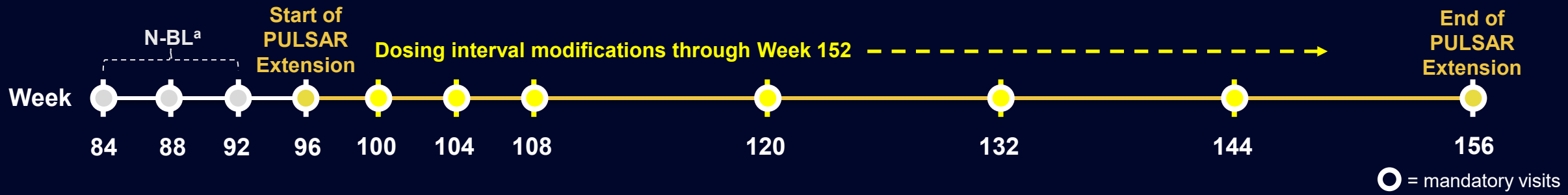
2q8→8mg
n=208

Patients initially treated with aflibercept 2q8 were switched to aflibercept 8 mg at Week 96 and immediately assigned to a 12-week dosing interval

8mg
n=417

Patients initially treated with aflibercept 8q12 or 8q16 continued with aflibercept 8 mg at their last assigned dosing interval



E-DRM: Interval Shortening During Year 3

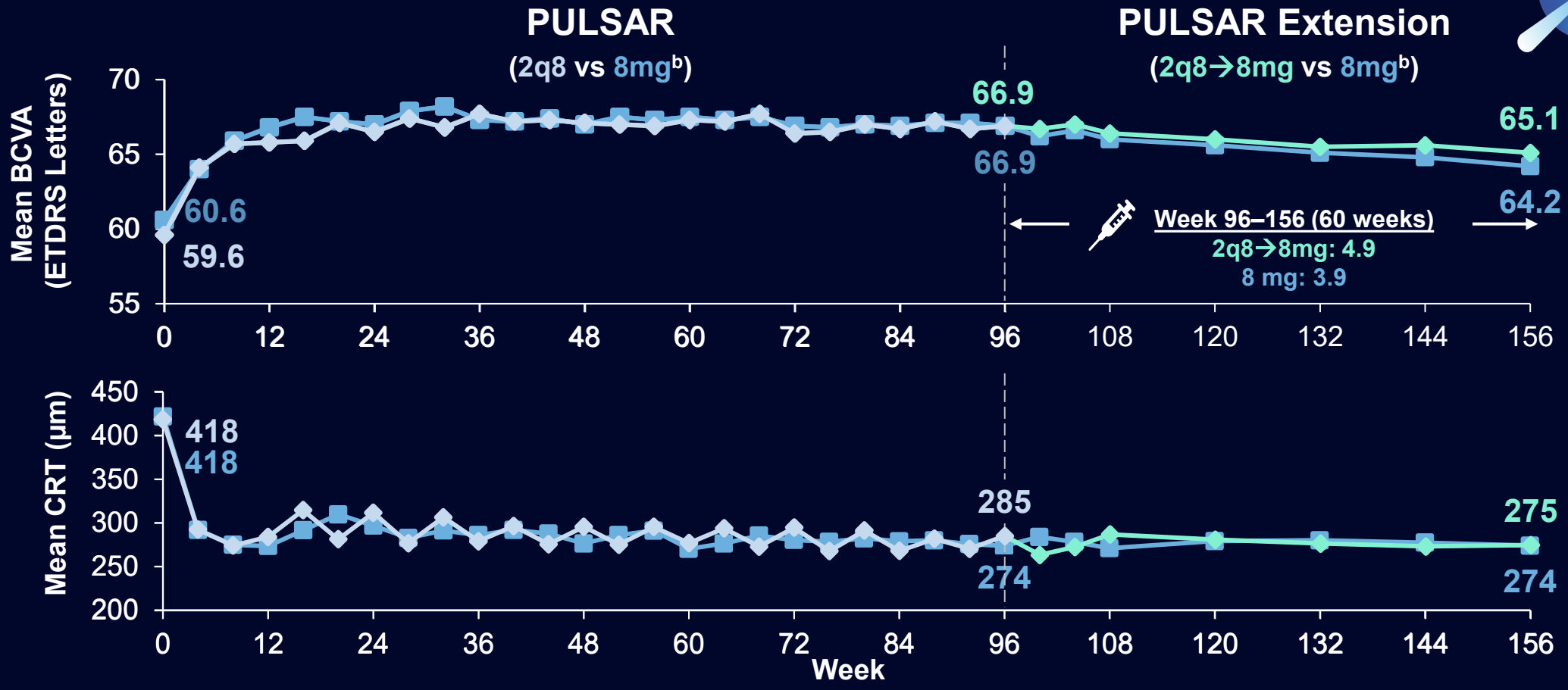
- Patients were assessed at ***any visit*** beginning at Week 100
- **Criteria for interval shortening:**
  - >5-letter loss in BCVA from N-BL due to persistent or worsening nAMD **AND either:**
    - >25 µm increase in CRT from N-BL **OR**
    - New onset of foveal neovascularization **OR**
    - New 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 Q8**

E-DRM: Interval Extension During Year 3

- 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 of foveal neovascularization or foveal hemorrhage
- Dosing intervals extended by **2-week** increments to a **maximum of Q24**

[a]N-BL was an average of values from Weeks 84, 88, and 92. **E-DRM**, dosing regimen modification criteria during the PULSAR Extension; **IRF**, intraretinal fluid; **N-BL**, new baseline; **OCT**, optical coherence tomography; **Q8**, every 8 weeks; **Q24**, every 24 weeks; **SRF**, subretinal fluid.

Mean BCVA and CRT Through Week 156[a]



Mean number of active injections over 48-week periods:[c]

BL–Week 48
2 mg: 6.9
8q12: 6.1
8q16: 5.2

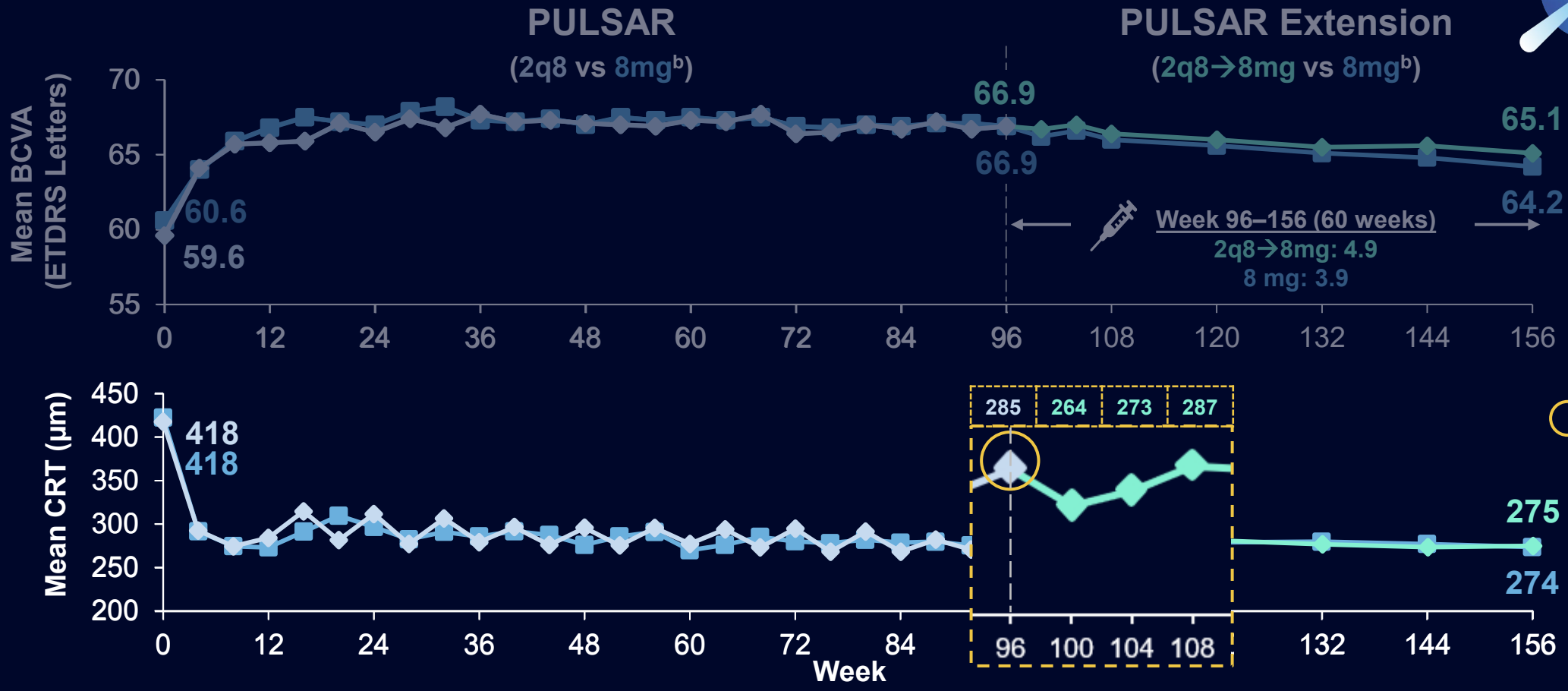
Week 48–96
2 mg: 5.9
8q12: 3.6
8q16: 3.1

Week 108–156
8 mg: 2.9
8 mg: 2.9

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from BL (MMRM) in BCVA of +4.6 (2.6, 6.6) letters and +3.4 (1.9, 4.9) letters, respectively, and in CRT of −145 (−155, −136) µm and −148 (−156, −140) µm, respectively. MMRM was used to generate BCVA/CRT LS means for the eFAS with BL BCVA/CRT as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and BL BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and BL BCVA/CRT and the interaction between visit and treatment. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **BL**, baseline; **CI,** confidence interval; **eSAF**, safety analysis set in the PULSAR Extension; **LS**, least squares; **MMRM,** mixed model for repeated measures.

Mean BCVA and CRT Through Week 156[a]

pulsar nAMD Extension



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Patients with Fluid Resolution in the Aflibercept 2q8→8mg and 8 mg Groups at Week 156

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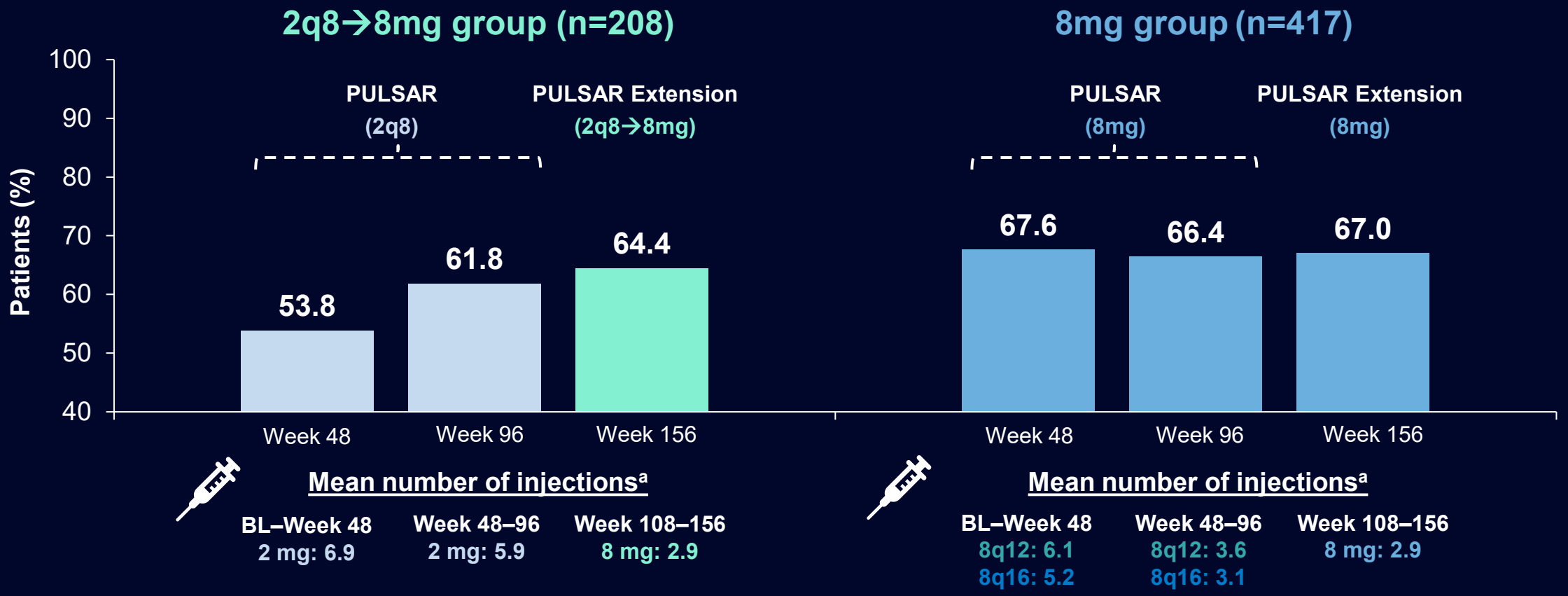

- The proportion of patients with fluid resolution was maintained in the **aflibercept 2q8→8mg** group through 96 weeks, and was **sustained after switching to 8 mg** through Week 156
- **Long-term fluid resolution** was observed in the 8mg group with extended dosing intervals through Week 156
- The proportion of patients with fluid resolution was **similar in the 2q8→8mg and 8 mg groups** at Week 156

eFAS (LOCF). Fluid resolution defined as no IRF and no SRF in central subfield. Fluid status was evaluated pre-injection. eFAS (LOCF). [a]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **LOCF**, last observation carried forward.

2q8→8mg Group: Patients with Fluid Resolution 4 and 8 Weeks After Active Injections

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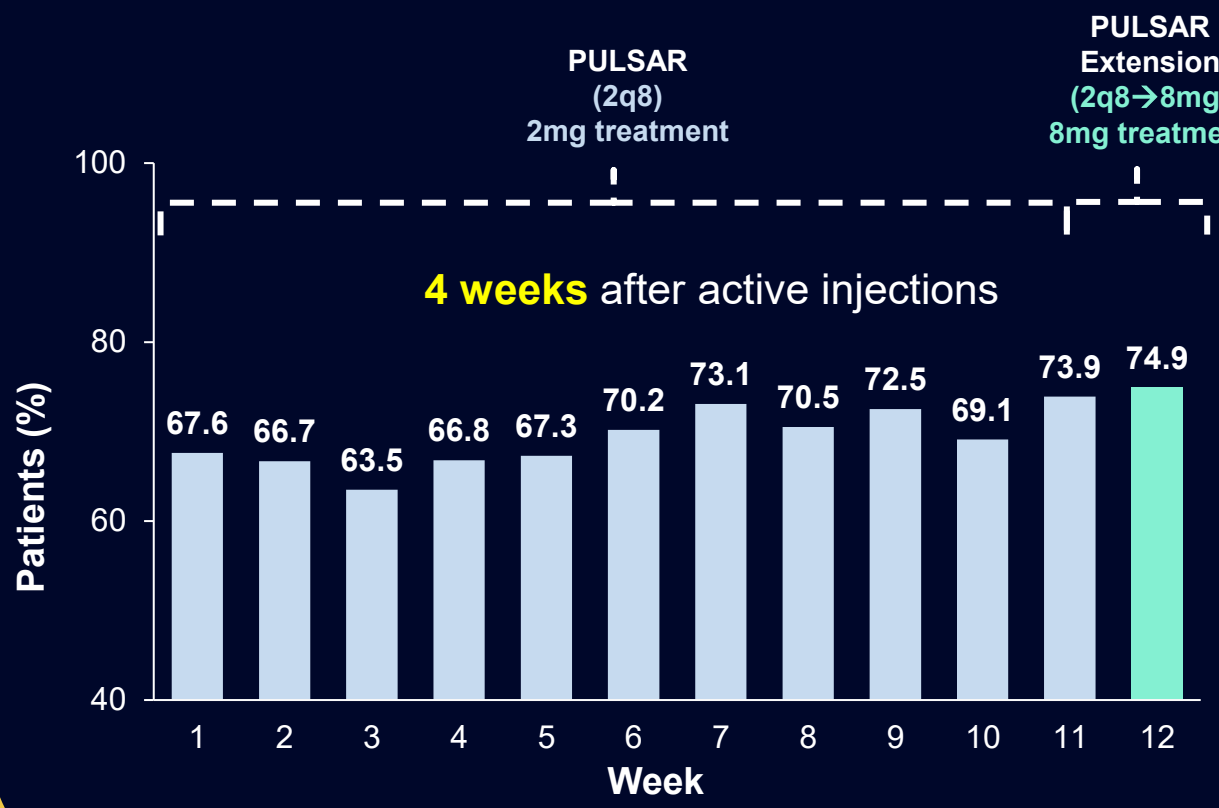
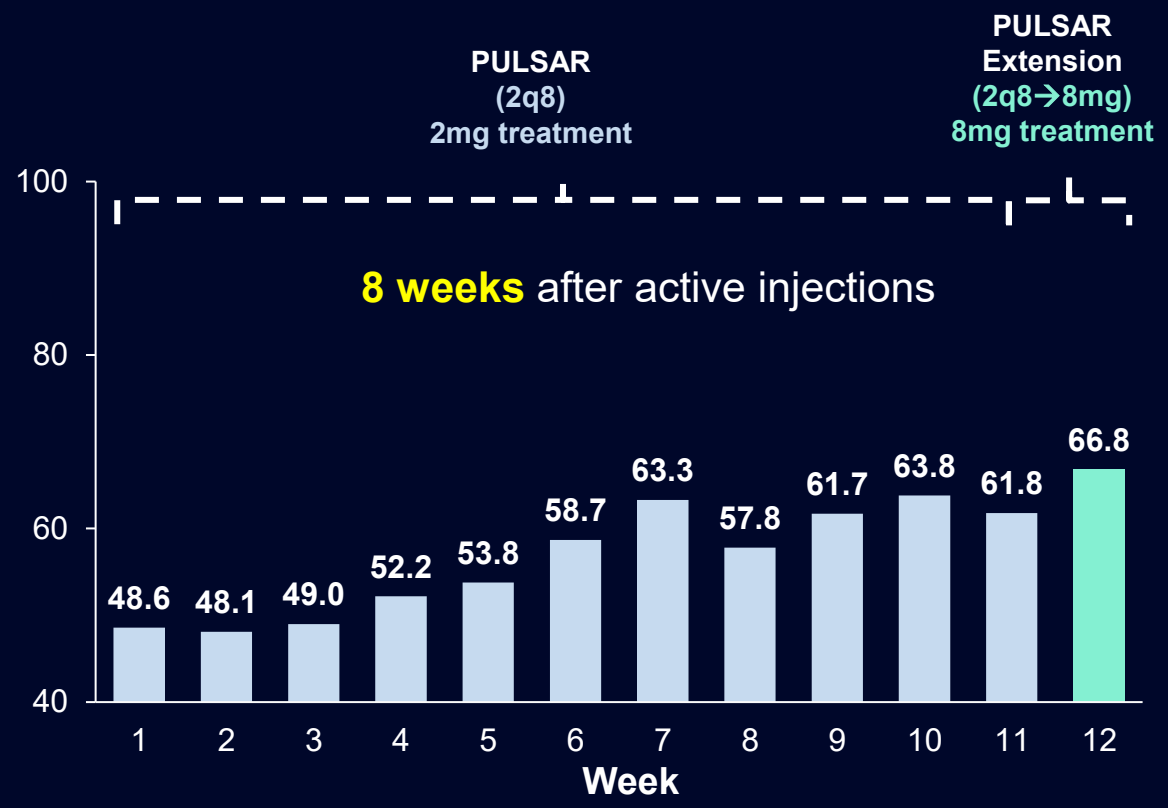
Aflibercept 2q8 dosing regimen through Week 96 of PULSAR																							
Day 1	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48	W52	W56	W60	W64	W68	W72	W76	W80	W84	W88	W92	W96
X	X	X		X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X





Stippled boxes = initial treatment phase; X = active injection; o = sham injections.
eFAS (LOCF). Patients entering the PULSAR extension: 2q8→8mg group (n=208). Presence of fluid was evaluated prior to active injection administration. Aflibercept 2 mg injections were given at Week 0, 4 and 8, and then 8-weekly from Week 16 to Week 88. The first aflibercept 8 mg injection was administered at Week 96.

2q8→8mg Group: Proportion of Patients with Fluid Resolution 4 and 8 Weeks After Aflibercept 2 mg and 8 mg Injections

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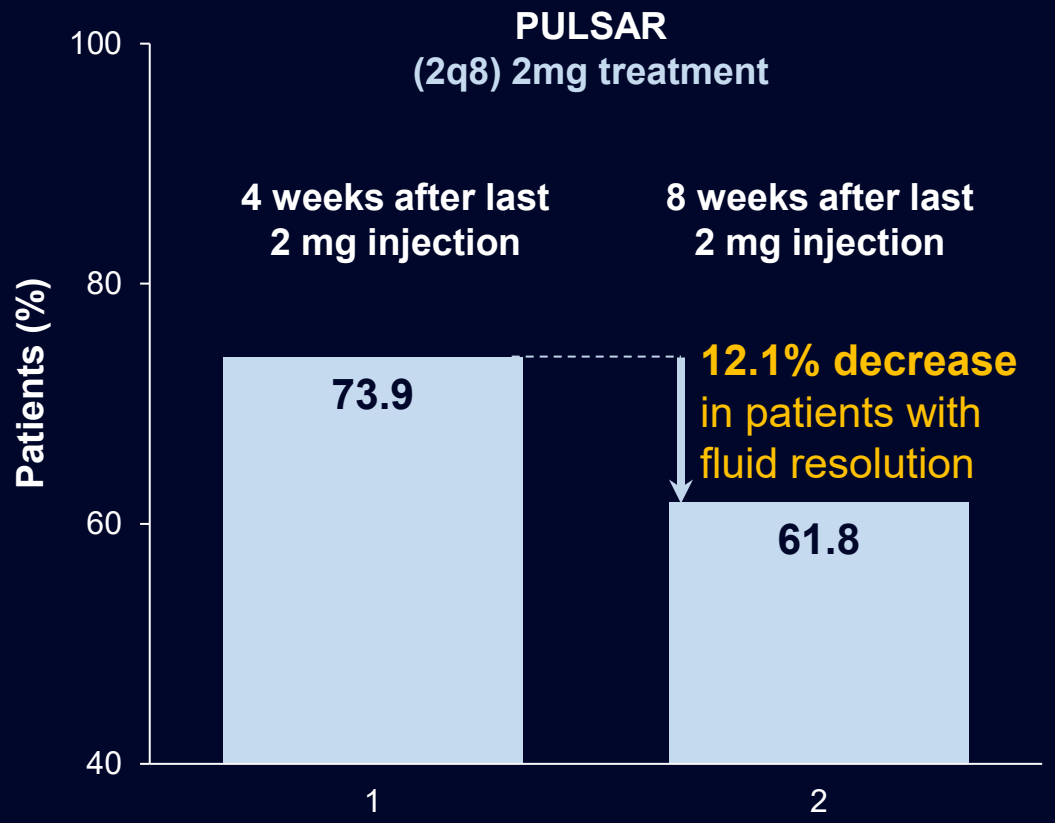
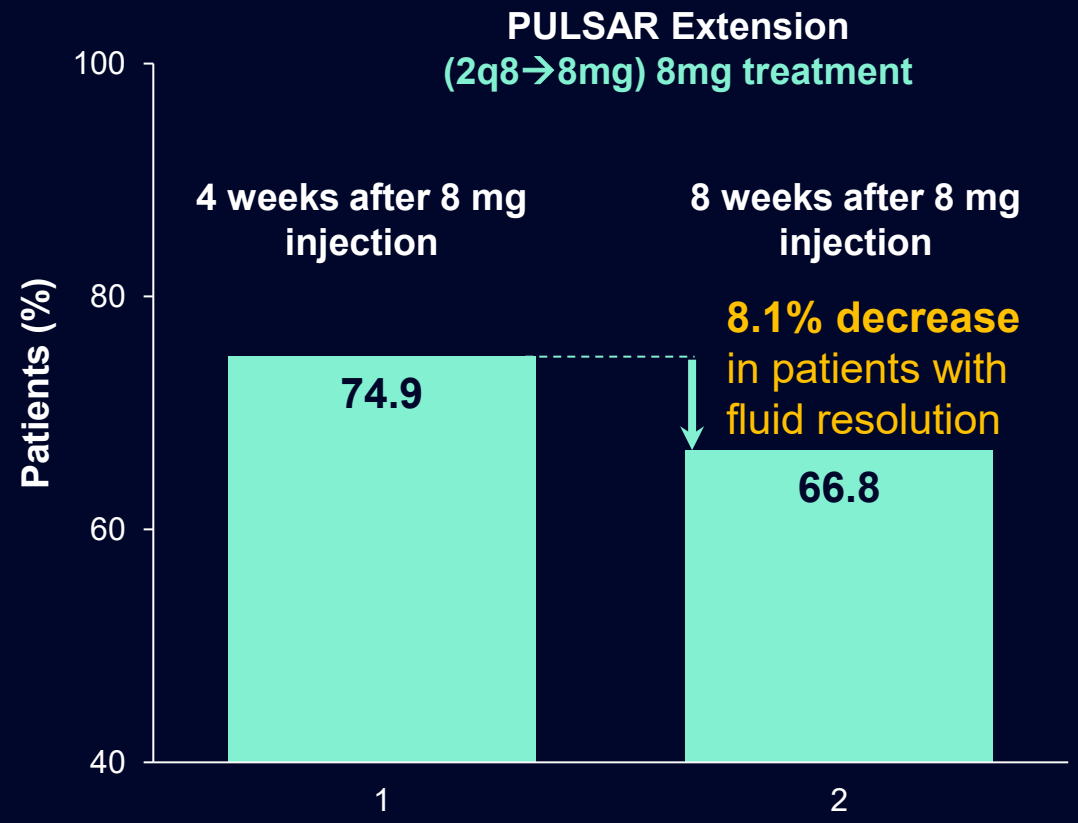
Difference in proportion of patients with fluid resolution 4 and 8 weeks after the last 2 mg injection



Difference in proportion of patients with fluid resolution 4 and 8 weeks after the first 8 mg injection



eFAS (LOCF). Patients entering the PULSAR extension: 2q8→8mg group (n=208).

Conclusions

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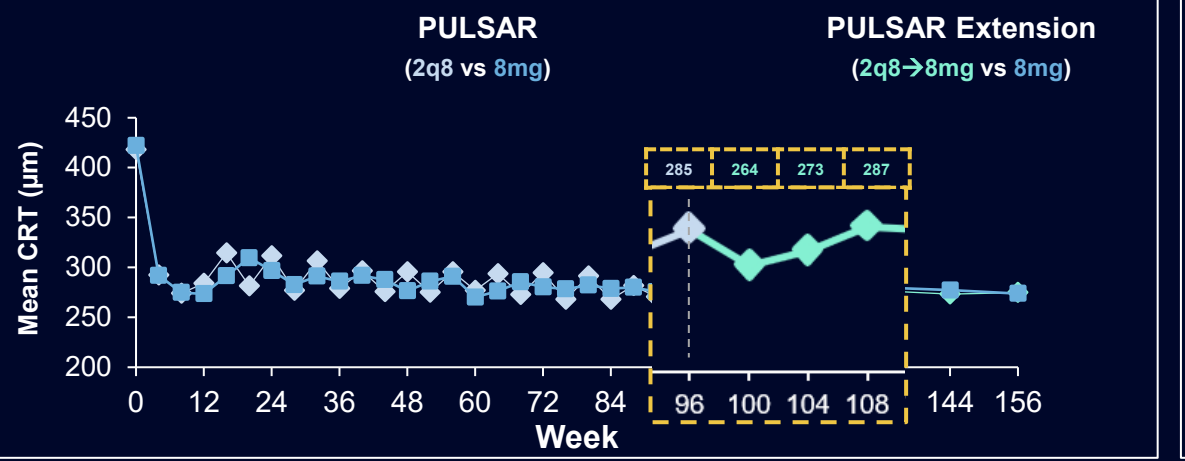
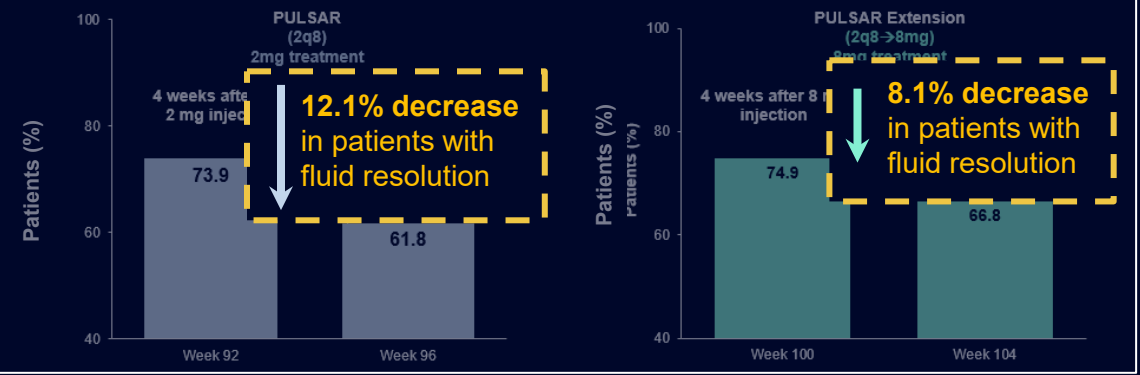
- In the PULSAR Extension, functional and anatomic improvements were sustained through Week 156 in the **2q8→8mg** and **8mg groups**
- At Week 156, the proportion of patients with fluid resolution was **comparable in the 2q8→8mg and 8mg groups**, with extended dosing intervals from Week 96 to Week 156 in the 2q8→8mg group following the switch to aflibercept 8 mg
- Findings from the 8mg group suggest that patients with treatment-naïve nAMD can achieve **durable improvements in fluid resolution with aflibercept 8 mg** administered over extended dosing intervals
- In the **2q8→8mg group**, the proportion of patients with fluid resolution was sustained from Week 96 to Week 156 following the switch to aflibercept 8 mg
  - A **lower proportion** of patients had **fluid re-accumulation** between 4 and 8 weeks **after the first 8 mg injection** in the PULSAR extension than between 4 and 8 weeks after the last 2 mg injection in PULSAR

Mean CRT Through Week 156[a]



2q8→8mg Group: Difference in Proportion of Patients with Fluid Resolution 4 and 8 Weeks After Active Injections[b]



[a]eFAS (observed cases).[b]eFAS (LOCF).