Pigment Epithelial Detachment Outcomes Over 156 Weeks in Patients with nAMD Receiving Aflibercept 8 mg or Switching from Aflibercept 2 mg to 8 mg

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Disclosures

- **Michael Javaheri reports consulting for Genentech, Regeneron Pharmaceuticals, Inc., and Apellis; research grants from Regeneron Pharmaceuticals, Inc.; speaker for Regeneron Pharmaceuticals, Inc., and Apellis**
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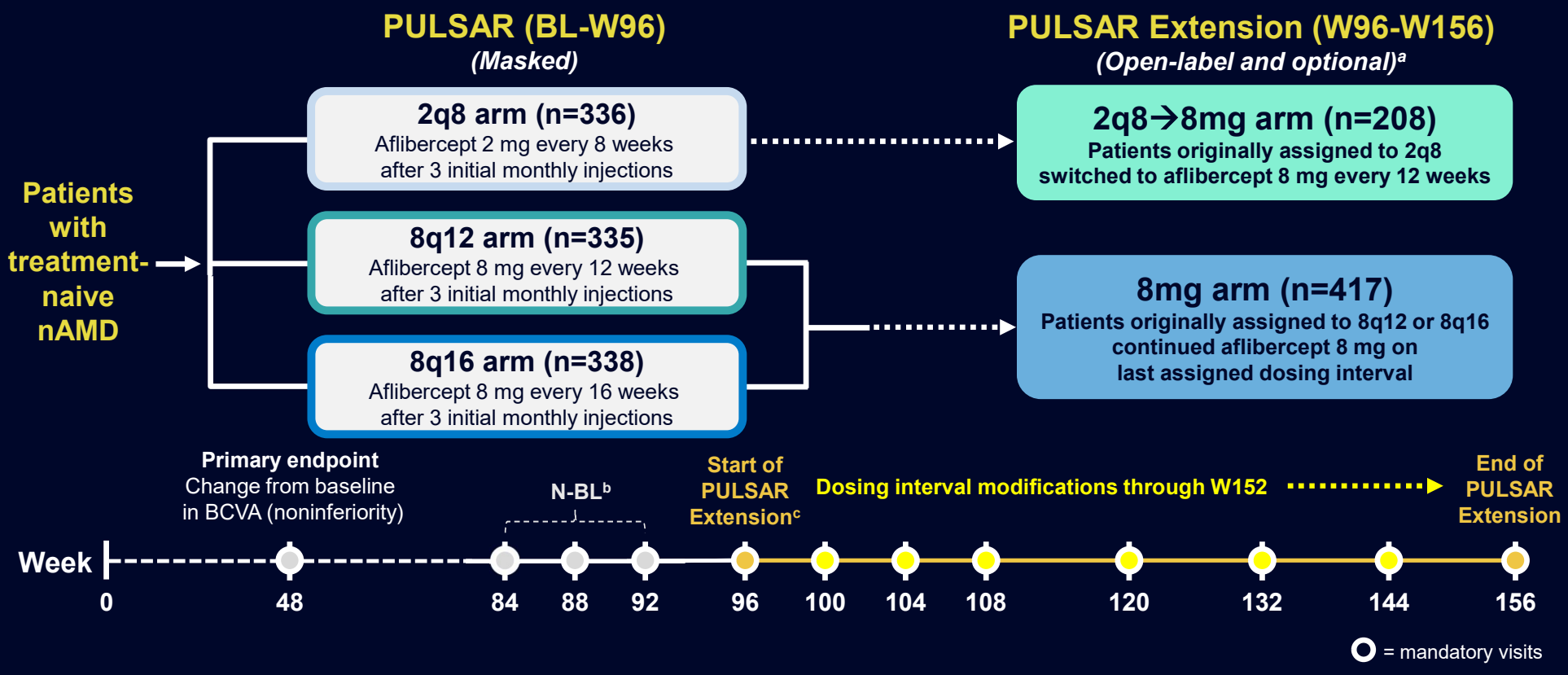
PULSAR Extension Study Design



[a]To be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessment between W84 and W92. Masked transition period (W96-W108) was followed by open-label part (W108-W156).
[b]N-BL was an average of values from W84, W88, and W92. [c]Optional phase added while PULSAR was ongoing; therefore, not all patients were able to enroll due to time constraints.
2q8, aflibercept 2 mg every 8 weeks after 3 initial monthly doses; 8q12, aflibercept 8 mg every 12 weeks after 3 initial monthly doses; 8q16, aflibercept 8 mg every 16 weeks after 3 initial monthly doses; BCVA, best-corrected visual acuity; BL, baseline; CRT, central retinal thickness; nAMD, neovascular age-related macular degeneration; N-BL, new baseline; W, week.

Dose Regimen Modification Criteria

Interval shortening during PULSAR Extension

Criteria for interval shortening

- >5-letter loss in BCVA compared with N-BL due to persistent or worsening nAMD **AND EITHER**
- >25-µm increase in CRT compared with N-BL, **OR** new onset foveal neovascularization, **OR** new foveal hemorrhage

- Patients who met DRM criteria **Weeks 100 through 156** had dosing intervals shortened by 2-week increments
  - The minimum assigned dosing interval was q8

Interval extension during PULSAR Extension

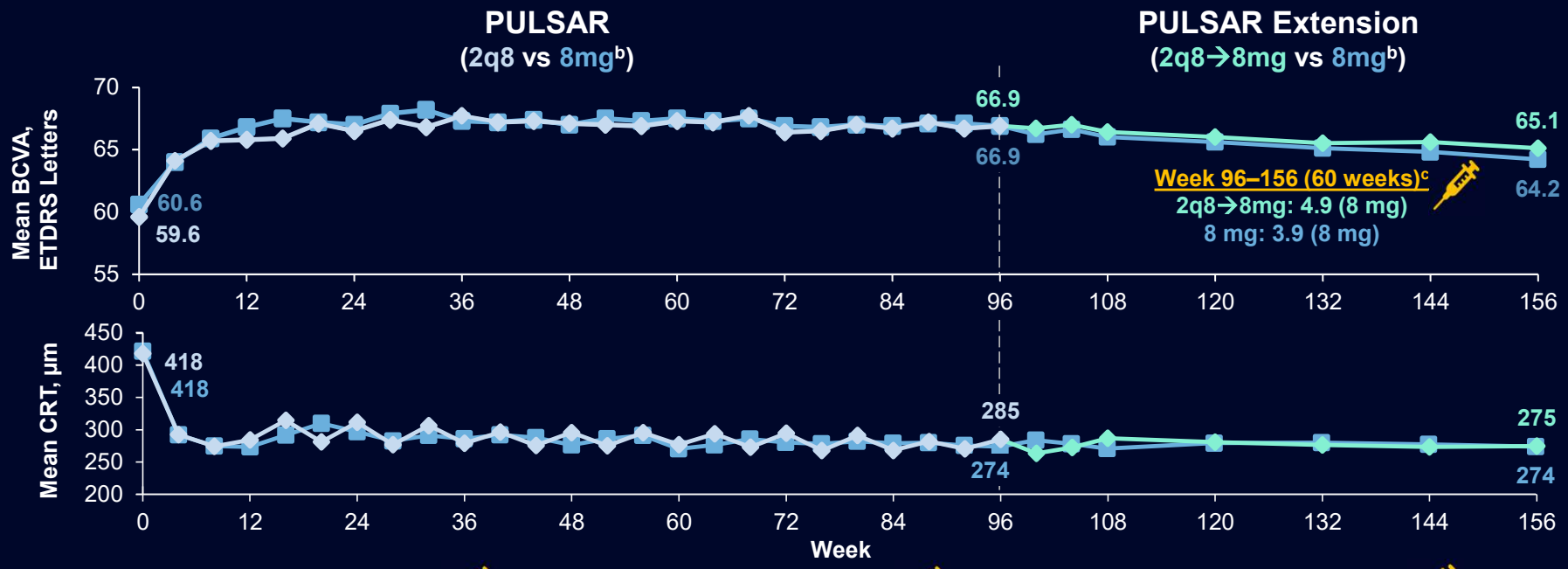
Criteria for interval extension

- <5-letter loss in BCVA compared with N-BL **AND**
- No fluid at the center subfield on OCT **AND**
- No new onset foveal hemorrhage or foveal neovascularization

- Patients who met DRM criteria from **Weeks 100 through 156** had dosing intervals extended by 2-week increments
  - The maximum assigned dosing interval was q24

DRM, dose regimen modification.

Mean BCVA and CRT Through Week 156[a]



Mean number of injections[c]

BL-Week 48[d]
2q8: 6.9 (2 mg)
8q12: 6.1 (8 mg)
8q16: 5.2 (8 mg)

Week 48-96[d]
2q8: 5.9 (2 mg)
8q12: 3.6 (8 mg)
8q16: 3.1 (8 mg)

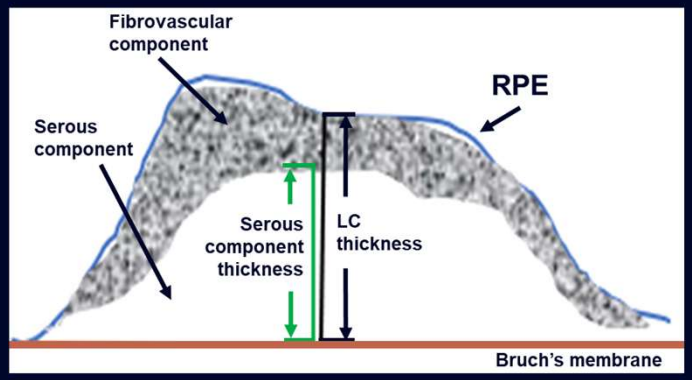
Week 96-156 (48 weeks)[d]
2q8→8mg: 3.9 (8 mg)
8mg: 3.1 (8 mg)

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. [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). [d]Injections at the end of the indicated timeframe (i.e. Week 48 and Week 96, respectively) are not included in the calculation of number of active injections for this timeframe. [e]Calculated as the number of active injections from Week 96 through Week 156, divided by 60 and multiplied by 48. BL, baseline; CI, confidence interval; eSAF, safety analysis set in the PULSAR Extension; ETDRS, Early Treatment Diabetic Retinopathy Study; LS, least squares; MMRM, mixed model for repeated measures.

Objective and Outcome Measures

This analysis sought to determine PED outcomes in patients with nAMD treated with aflibercept 8 mg or those switched from aflibercept 2 mg to 8 mg

- The following **outcome measures**[a] were evaluated by treatment arm:
  - Proportion of patients with sub-RPE fluid (representative of serous component of PED)
  - Mean thickness of sub-RPE fluid involving the foveal center
- Outcomes were evaluated descriptively



- PED is characterized by the separation of the RPE from the Bruch's membrane
- The neovascular LC is comprised of the serous (sub-RPE fluid) and fibrovascular component of the PED

[a]Assessed using spectral domain optical coherence tomography at Wisconsin Reading Center.
LC, lesion complex; PED, pigment epithelial detachment; RPE, retinal pigment epithelium.

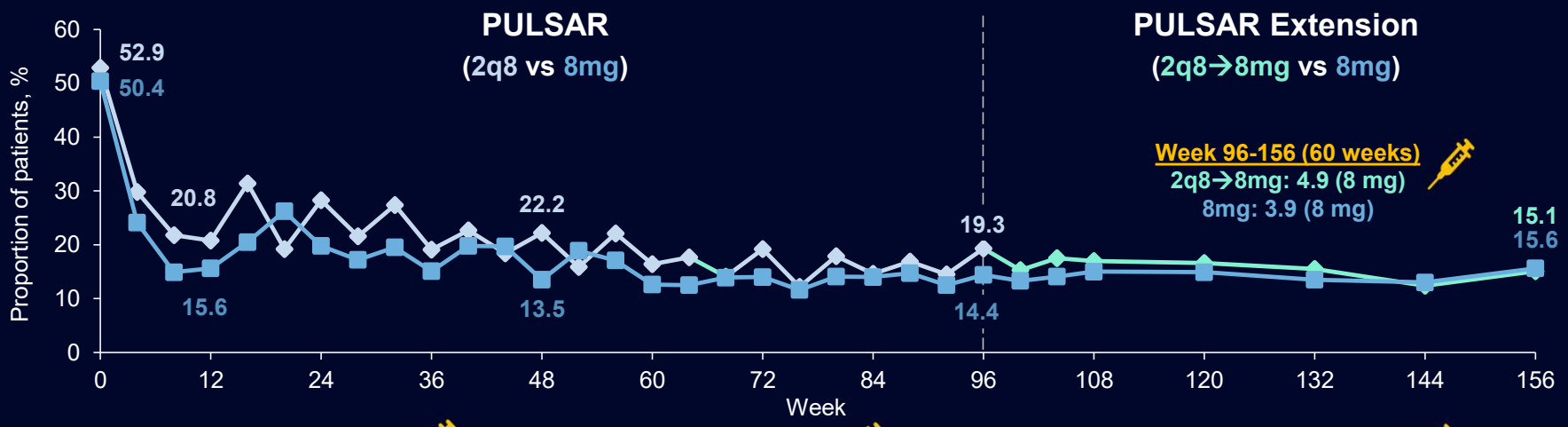
PED Characteristics at PULSAR Baseline

	Aflibercept 2q8→8mg (n=208)	**Aflibercept All 8 mg** (n=417)
Patients with sub-RPE fluid, n (%)	110 (52.9)	210 (50.4)
Patients with sub-RPE fluid involving the foveal center, n (%)	24 (11.5)	52 (12.5)

Approximately 50% of patients had sub-RPE fluid and ~12% had sub-RPE fluid involving the foveal center

eFAS.
eFAS, extension full analysis set.

Proportion of Patients with Presence of Sub-RPE Fluid Through Week 156[a]



Mean number of injections[b]

BL-Week 48[c]
2q8: 6.9 (2 mg)
8mg: 5.7 (8 mg)

Week 48-96[c]
2q8: 5.9 (2 mg)
8mg: 3.4 (8 mg)

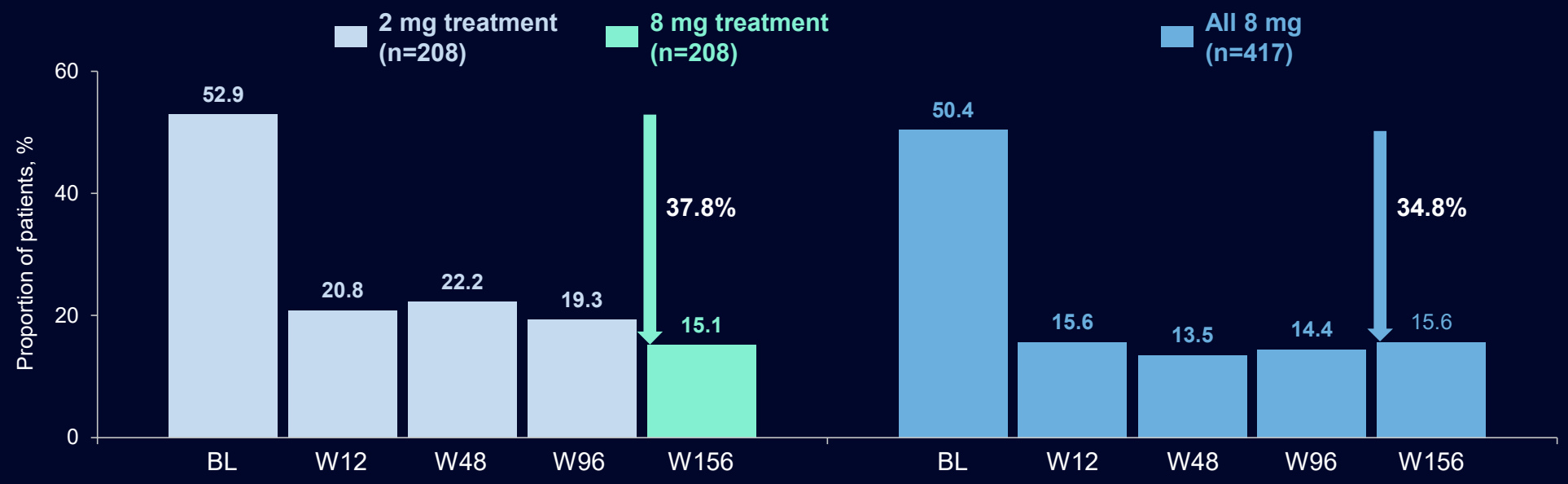
Week 96-156 (60 weeks)
2q8→8mg: 4.9 (8 mg)
8mg: 3.9 (8 mg)

Week 96-156 (48 weeks)[d]
2q8→8mg: 3.9 (8 mg)
8mg: 3.1 (8 mg)

- **Fewer** patients treated with aflibercept 8 mg versus 2 mg had presence of sub-RPE fluid through **Week 96**
- At **Week 156**, the **proportion of patients** with presence of sub-RPE fluid was **generally maintained in the 8mg group**
- Results in the **2q8→8mg** group were **comparable to the 8mg group,** with **fewer aflibercept 8 mg injections** (following the switch) than with previous aflibercept 2 mg injections over the same time periods

[a]eFAS, observed cases (2q8→8mg, n=208; 8mg, n=417); [b]eSAF (156-week completers; 2q8→8mg, n=186; 8mg, n=375). [c]Injections at the end of the indicated timeframe (i.e. Week 48 and Week 96, respectively) are not included in the calculation of number of active injections for this timeframe. [d]Calculated as the number of active injections from Week 96 through Week 156, divided by 60 and multiplied by 48.
eSAF, safety analysis set in the PULSAR Extension.

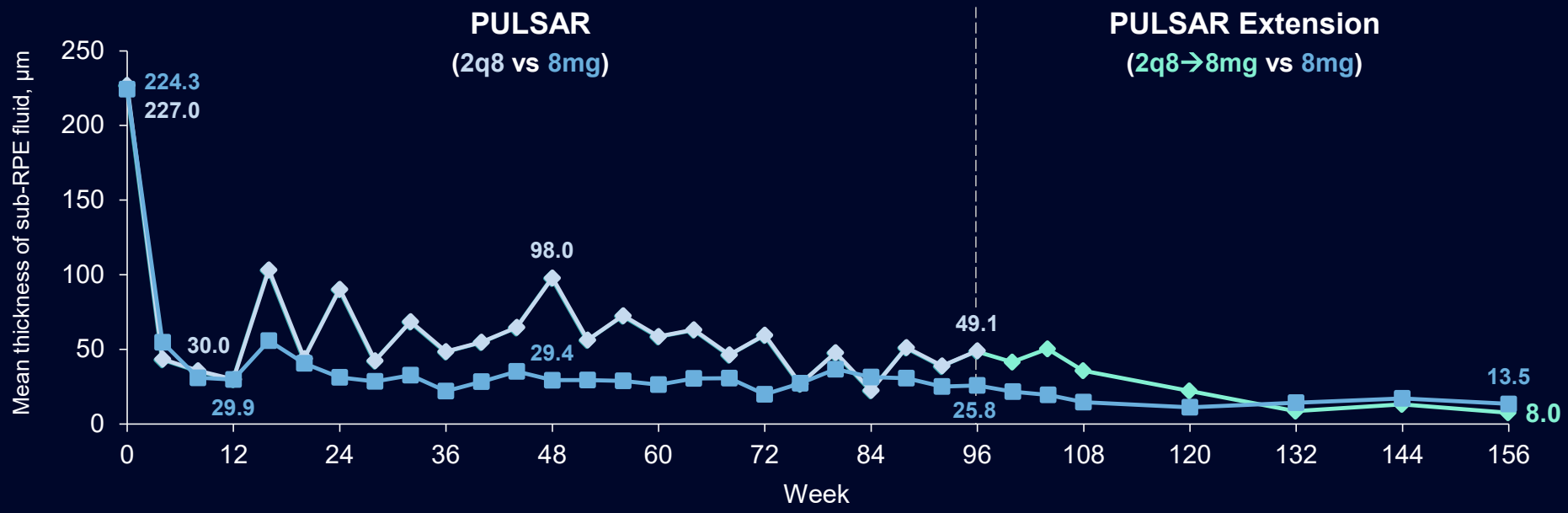
Reduction in Proportion of Patients with Presence of Sub-RPE Fluid at Key Timepoints



- The proportion of patients with presence of **sub-RPE fluid decreased from ~50% at BL to 19.3% and 14.4% at Week 96** in patients receiving **aflibercept 2 mg and 8 mg**, respectively
- From Week 96 to Week 156, the proportion of patients with presence of sub-RPE fluid in the **2q8→8mg group decreased by 4.2% following switch to aflibercept 8 mg**, while the proportion of patients in the 8mg group remained stable

eFAS, observed cases (2q8→8mg, n=208; 8mg, n=417).

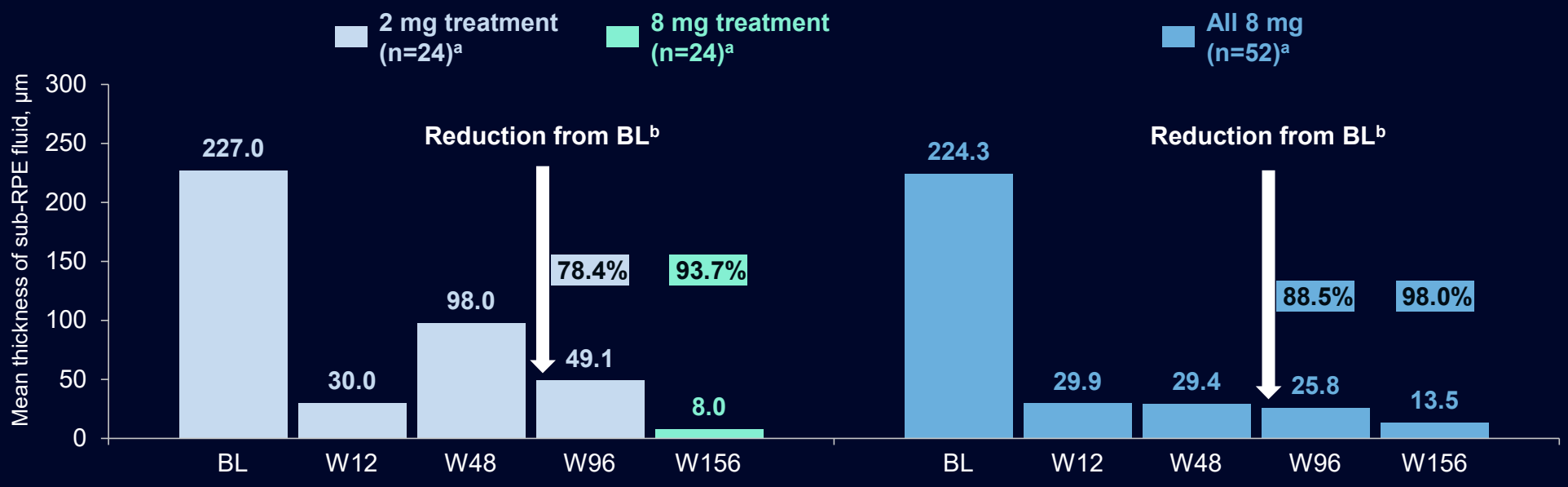
Thickness of Sub-RPE Fluid Involving the Foveal Center Through Week 156



- **Marked reductions** in **mean thickness of sub-RPE fluid** involving the foveal center were achieved with **aflibercept 2 mg and 8 mg** at **Week 12 and sustained** through **Week 96**
- **Further reductions** were observed **at Week 156** in patients who **switched** from **aflibercept 2 mg to 8 mg** and in patients who continued to receive **aflibercept 8 mg**

Patients with sub-RPE fluid presence at center point, observed cases (2q8→8mg, n=24; 8mg, n=52).

Reductions in Thickness of Sub-RPE Fluid Involving the Foveal Center at Key Timepoints



- From **BL to Week 96**, the **thickness in sub-RPE fluid involving the foveal center decreased** by **78.4% and 88.5%** in patients **who received aflibercept 2 mg and 8 mg, respectively**
- **At Week 156,** these values **decreased further** to **93.7%** in patients who **switched from aflibercept 2 mg to 8 mg,** and to **98.0%** in those **who received aflibercept 8 mg throughout**

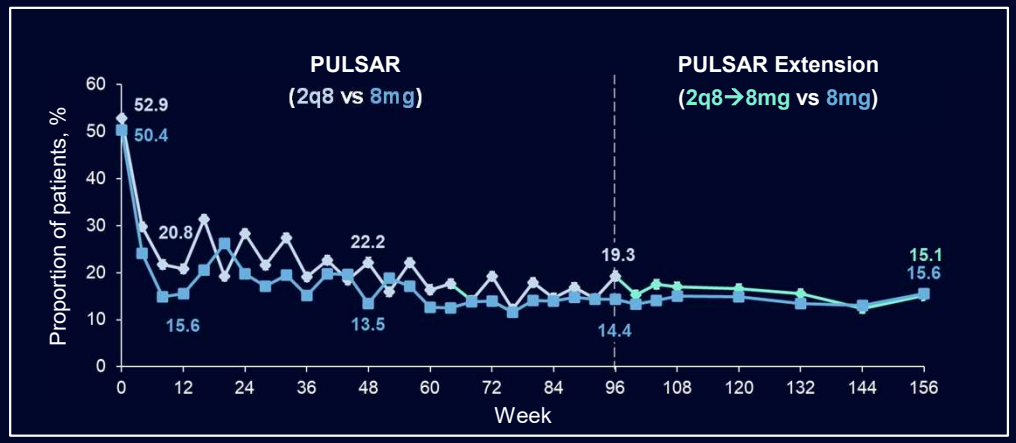
[a]Patients with sub-RPE fluid presence at center point, observed cases. [b]Calculated as the mean change from BL in thickness of serous component of PED at a particular timepoint divided by the BL value.

Conclusions

In the PULSAR Extension, early **improvements in PED outcomes seen at Week 12** were **generally maintained or improved from Week 96 to Week 156** in patients in the following groups:

- **2q8→8mg group** following switch from aflibercept 2 mg to aflibercept 8 mg, with **fewer injections**
- **8mg group** who had been receiving aflibercept 8 mg throughout the study

Proportion of Patients with Presence of Sub-RPE Fluid Through Week 156



Thickness of Sub-RPE Fluid Involving the Foveal Center Through Week 156