pulsar Extension

PULSAR Extension: Pigment Epithelial Detachment Outcomes over 156 weeks in Patients with Neovascular Age-related Macular Degeneration Receiving Aflibercept 8 mg or Switching from Aflibercept 2 mg to 8 mg

Paolo Lanzetta,[1] Aude Ambresin,[2] Michael Singer,[3] Timothy Y. Y. Lai,[4] Xin Zhang,[5] David T. Wong,[6] Ehsan Rahimy,[7] Michael Javaheri,[8] Jean-François Korobelnik,[9,10] Javier Zarranz-Ventura,[11] Tobias Machewitz,[12] Sergio Leal,[5] on behalf of the PULSAR study investigators

[1]Department of Medicine – Ophthalmology, University of Udine, and Istituto Europeo di Microchirurgia Oculare – IEMO, Udine, Italy; [2]Swiss Visio Montchoisi, Lausanne, Switzerland; [3]University of Texas Health Science Center, San Antonio, TX, USA; [4]Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong; [5]Bayer Consumer Care AG, Basel, Switzerland; [6]Unity Health Toronto – St. Michael's Hospital, University of Toronto, Toronto, ON, Canada; [7]Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, USA; Palo Alto Medical Foundation, Palo Alto, CA, USA; [8]Roski Eye Institute, Keck School of Medicine, University of Southern California, and Retina Specialists of Beverly Hills, Los Angeles, CA, USA; [9]CHU Bordeaux, Service d'Ophtalmologie, Bordeaux, France; [10]University of Bordeaux, INSERM, Bordeaux Population Health Research Center, UMR1219, F-33000, Bordeaux, France; [11]Hospital Clínic de Barcelona, University of Barcelona, Barcelona, Spain; [12]Bayer AG, Berlin, Germany

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pulsar nAMD Extension

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PULSAR Extension Design

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PULSAR (BL–W96)
(Masked)

Patients with treatment-naïve nAMD

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

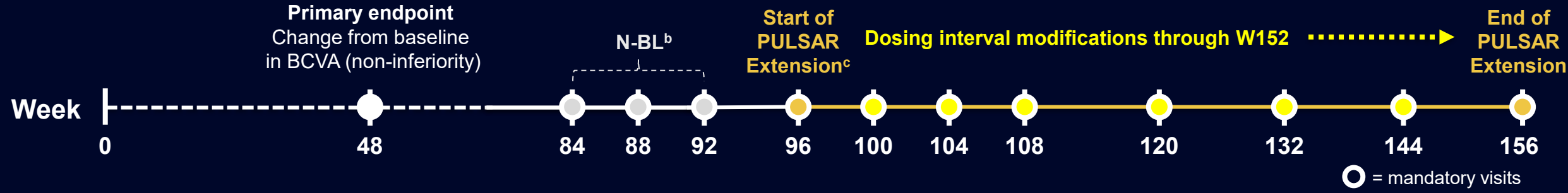
8q12 arm (n=335)
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections

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

PULSAR Extension (W96–W156)
(Open-label and optional)[a]

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

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



[a]To be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessment between Week 84 and Week 92. Masked transition period (W96–108) was followed by open-label part (W108–W156).
[b]N-BL was an average of values from W84, 88, and 92. [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; **8q12,** aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **BCVA,** best-corrected visual acuity; **CRT**, center subfield retinal thickness; **nAMD**, neovascular age-related macular degeneration; **N-BL**, new baseline; **W**, week.

PED Outcomes: Objectives and Methods

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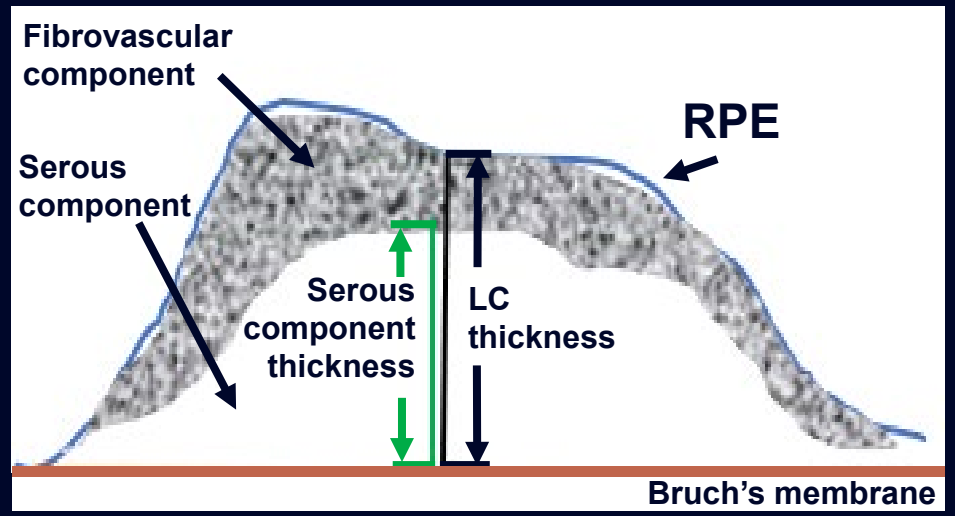
- Pigment epithelial detachment (PED) is characterized by the separation of the RPE from the Bruch's membrane, resulting in a space that can be filled with fluid, blood, drusen, or fibrovascular material
- The neovascular lesion complex (LC) is comprised of the serous (sub-RPE fluid) and fibrovascular component of the PED



Objective:

To evaluate PED outcomes over 156 weeks in patients who switched from aflibercept 2 mg to 8 mg, and who stayed on aflibercept 8 mg.

Outcome measures[a]:

- Percentage of patients with sub-RPE fluid (representative of serous component of PED)
  - Mean thickness of serous component in patients with serous component of PED involving the foveal center
- Percentage of patients with neovascular LC with involvement of foveal center
  - Mean thickness of neovascular LC at the foveal center

PED characteristics at PULSAR baseline[b]	2q8→8mg (n=208)	All 8 mg (n=417)
Patients with serous component of PED, n (%)	110 (52.9)	210 (50.4)
Patients with serous component of PED with involvement of foveal center, n (%)	24 (11.5)	52 (12.5)
Patients with neovascular LC with involvement of foveal center, n (%)	186 (89.4)	362 (86.8)

[a]Assessed using SD-OCT at Wisconsin Reading Center. [b]eFAS. **eFAS**, extension full analysis set; **RPE**, retinal pigment epithelium; **SD-OCT**, Spectral Domain Optical Coherence Tomography.

Patients with Serous Component of PED Through Week 156[a]

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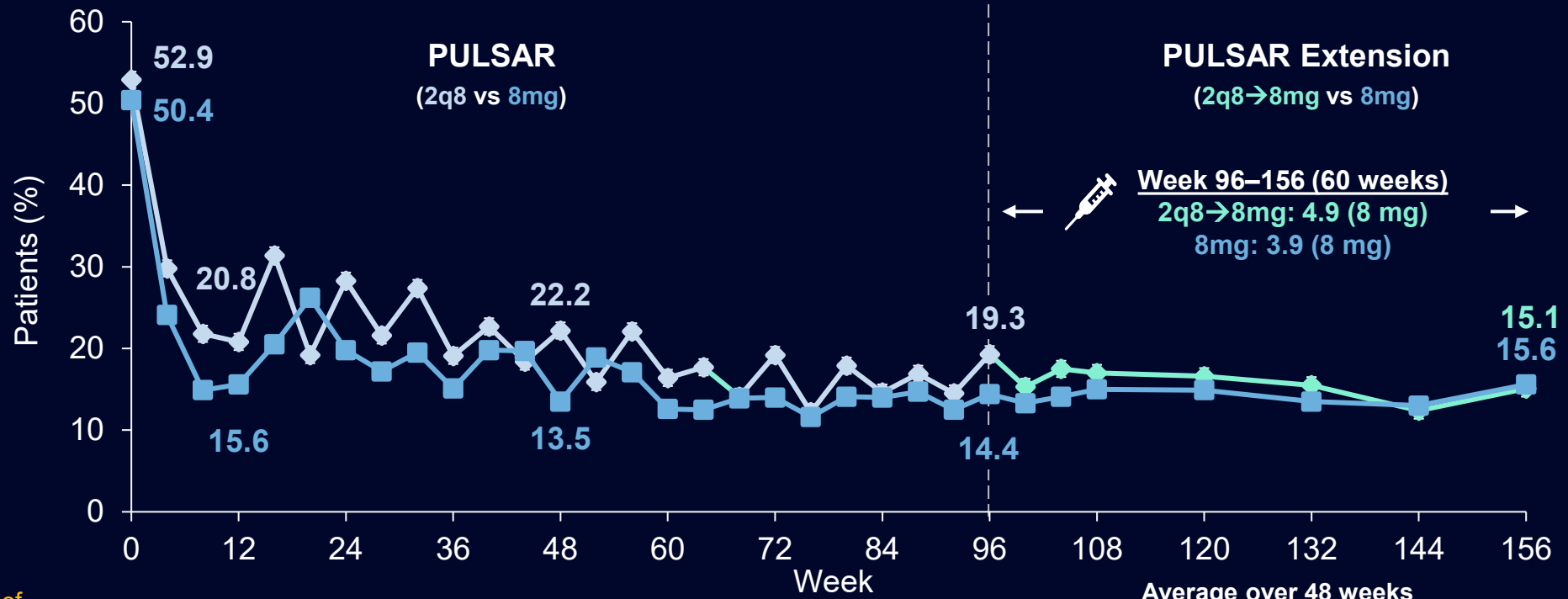

Week 96–156 (60 weeks)
2q8→8mg: 4.9 (8 mg)
8mg: 3.9 (8 mg)

Mean number of active injections over 48-week periods for treatment groups:[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)

Average over 48 weeks in PULSAR Extension[d]
2q8→8mg: 3.9 (8 mg)
8mg: 3.1 (8 mg)

- At **Week 96**, a **lower proportion** of patients had serous component of PED **with aflibercept 8 mg** than with aflibercept 2 mg
- At **Week 156**, the **proportion of patients** with serous component of PED was **generally maintained in the 8mg group**
- Results in the **2q8→8mg** group were **comparable to the 8 mg 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 of Proportion of Patients with Serous Component of PED at Key Timepoints

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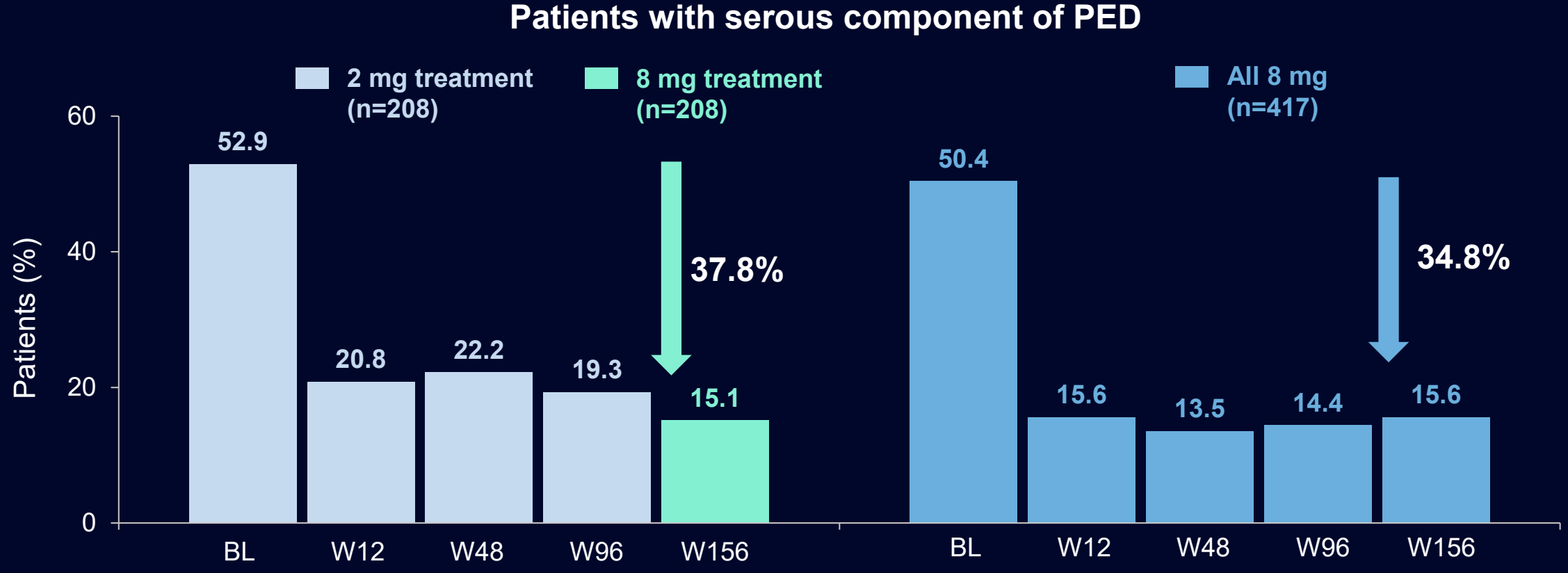

- The proportion of patients with **serous component of PED decreased from around 50% at BL to 19.3% and 14.4% at W96** in patients receiving **aflibercept 2 mg and 8 mg**, respectively
- From W96 to W156, the proportion of patients with serous component of PED in the **2q8→8mg group decreased by 4.2% following switch to aflibercept 8 mg,** while the proportion of patients in the 8 mg group remained stable

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

Thickness of Serous Component of PED Involving the Foveal Center Through Week 156

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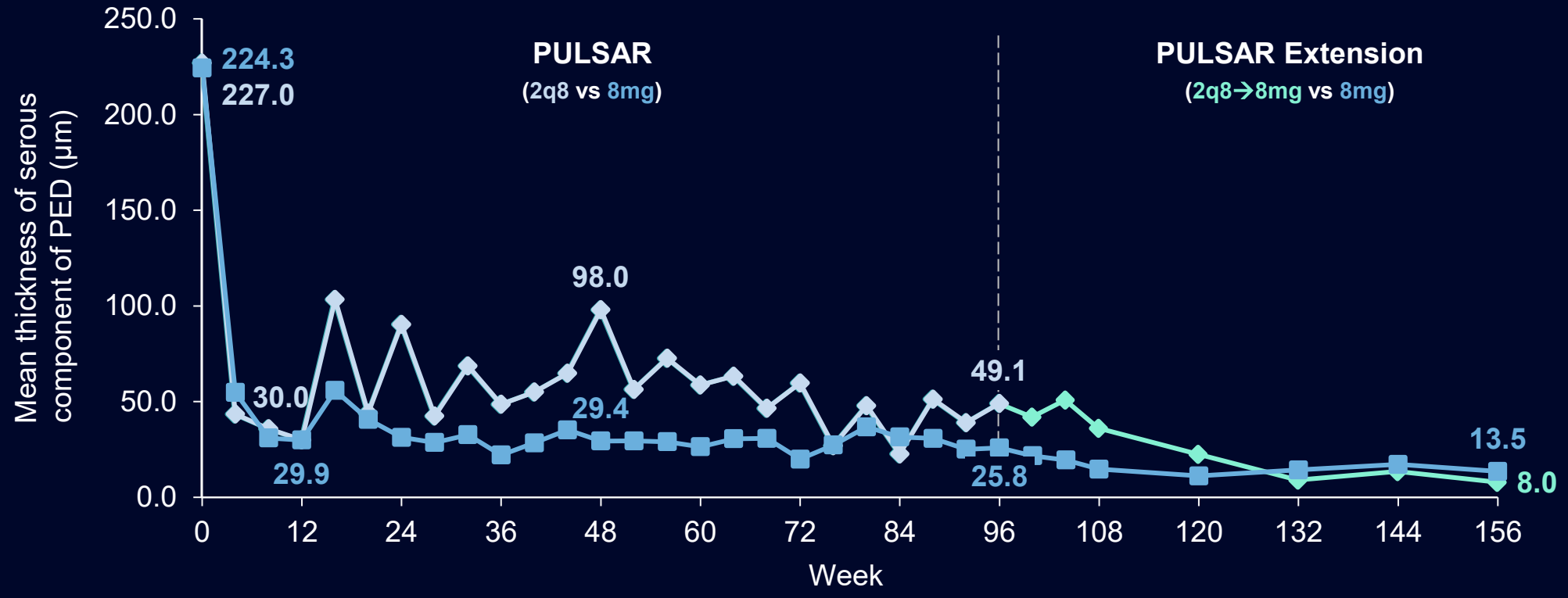

- **Marked reductions** in **thickness of the serous component of PED** involving the foveal center were achieved with **aflibercept 2 mg and 8 mg** at **Week 12 and sustained** through **Week 96**
- **Further reductions** were observed **at Week 156** in patients who **switched** from **aflibercept 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 Serous Component of PED Involving the Foveal Center at Key Timepoints

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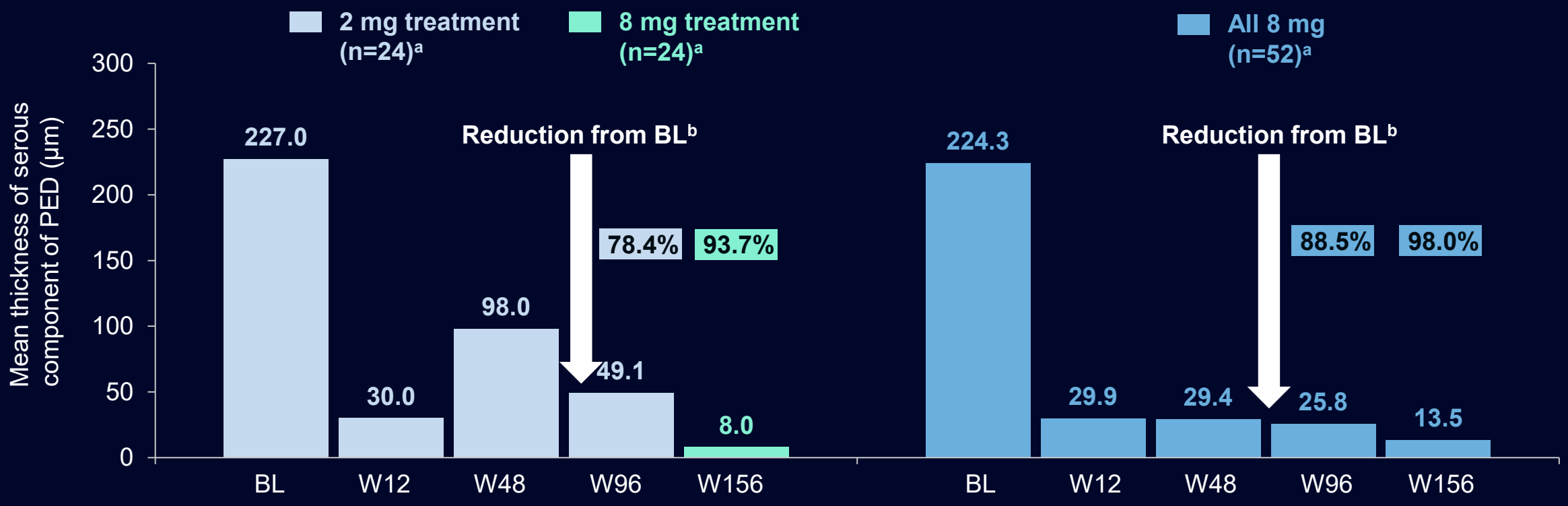

- From **BL to W96**, the **thickness in serous component of PED decreased** by **78.4% and 88.5%** in patients **who received aflibercept 2 mg and 8 mg, respectively**
- **At W156,** these values **decreased further** to 93.7% in patients who **switched from aflibercept 2 mg to 8 mg,** and to 98.0% 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

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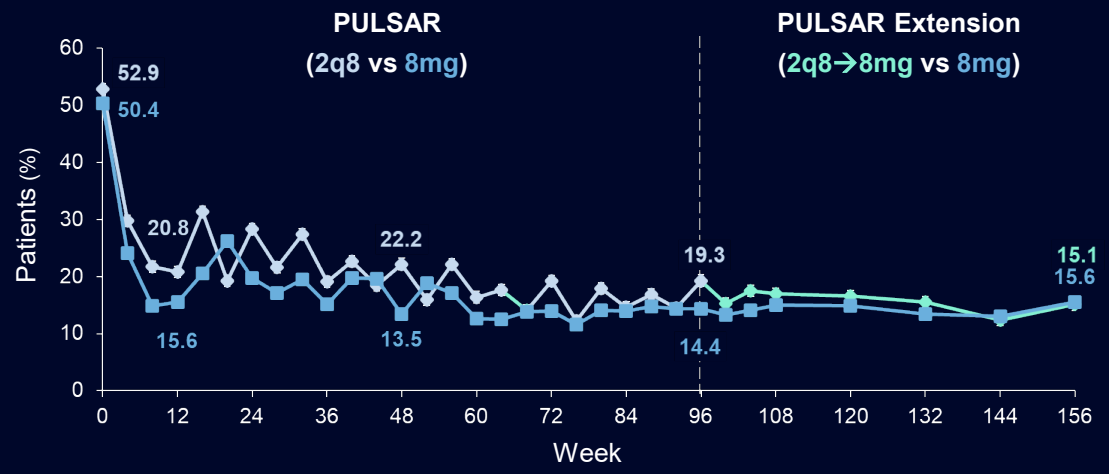
In the PULSAR Extension, early **improvements in PED outcomes seen at Week 12** were **generally maintained or improved from Week 96 to Week 156** in patients in the following groups:

- **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 serous component of PED through Week 156



Thickness of serous component of PED involving the foveal center through Week 156