Pigment Epithelial Detachment Outcomes with Aflibercept 8 mg versus Aflibercept 2 mg in the PULSAR trial: A 96-Week Post hoc Analysis

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Disclosures

- **Michael Singer:** Consultant for Aerie, Allegro, Alimera, Allergan, Eyepoint, Genentech, Kodiak, Novartis, Regeneron Pharmaceuticals, Inc., and Santen; speaker bureau member for Allergan, Eyepoint, Genentech, Novartis, Regeneron Pharmaceuticals, Inc., and Spark; contracted research with Aerie, Allegro, Allergan, Alimera, DRCR, Genentech, Icon, Ionis, Kalvista, Kodiak, Novartis, Opthea, Optos, Regeneron Pharmaceuticals, Inc., Santen, Senju, Sydnexis, and Ribomic; and equity in Aviceda, Nanoscope, and Inflammasome;
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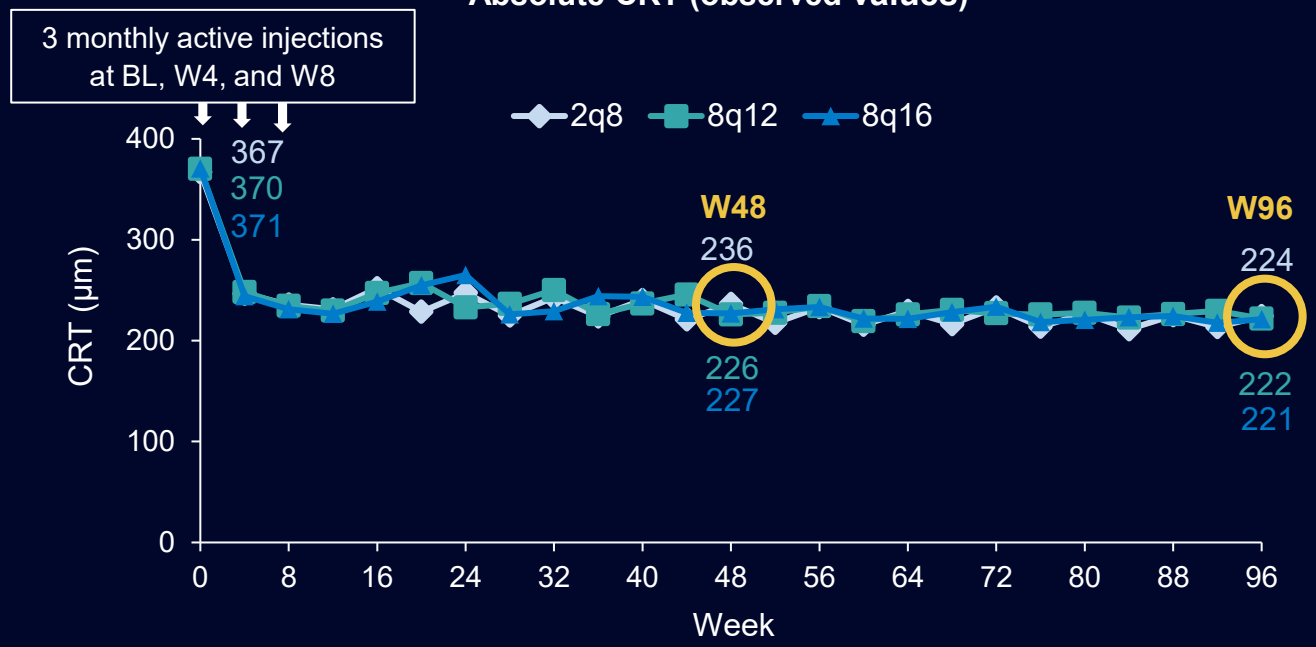
PULSAR: 96-Week, Multicenter, Double-masked Study in Patients with Treatment-naïve nAMD

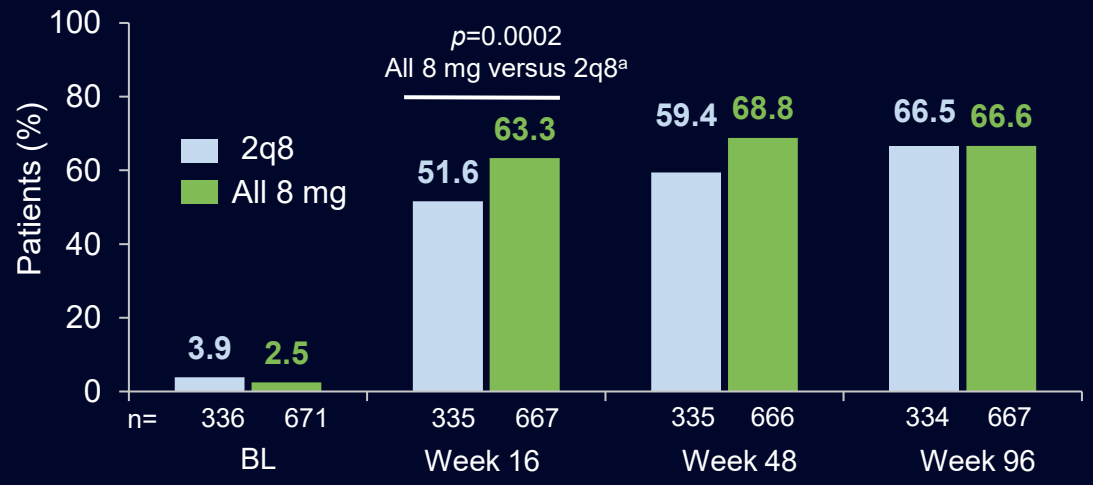
Patients were randomly assigned (1:1:1) to receive aflibercept 8q12 (n=335), 8q16 (n=338), or 2q8 (n=336) each after 3 monthly injections

At W48, treatment with aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with nAMD,[1] with no new safety signals
At W96, treatment with aflibercept 8 mg maintained improvements in visual and anatomic outcomes with extended dosing intervals, demonstrating long-term efficacy with no new safety signals

Absolute CRT (observed values)



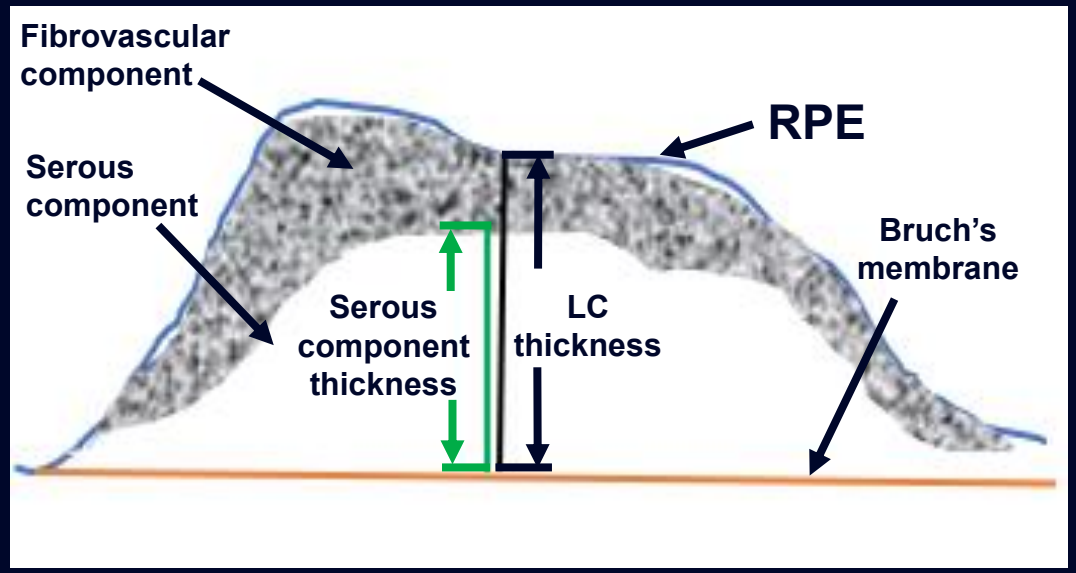
Patients with no IRF and SRF



	Mean number of injections from BL	
	2 mg	8 mg
W48	6.9	5.6
W96	12.8	9.0

FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338 (at BL). [a]LS mean values (post-ICE data were censored). [b]LS means were generated using MRMM, with BL CRT measured as a covariate; fixed factors included treatment group (aflibercept 2q8, 8q12, 8q16), visit, and stratification variables (geographic region [Japan vs Rest of World] and BL BCVA [<60 vs ≥60]); and interaction terms were included for BL and visit and for treatment and visit. **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; **BL**, baseline; **CRT**, central subfield retinal thickness; **FAS**, full analysis set; **ICE**, intercurrent event; **LS**, least squares; **MMRM**, mixed model for repeated measures; **nAMD**, neovascular age-related macular degeneration; **W**, week. [1]Lanzetta P, et al. *Lancet*. 2024;403:1141–1152.

Objective and Methods



Objective:

- Evaluate the impact of aflibercept 8 mg and 2 mg on PED outcomes in the PULSAR trial

Definition:

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

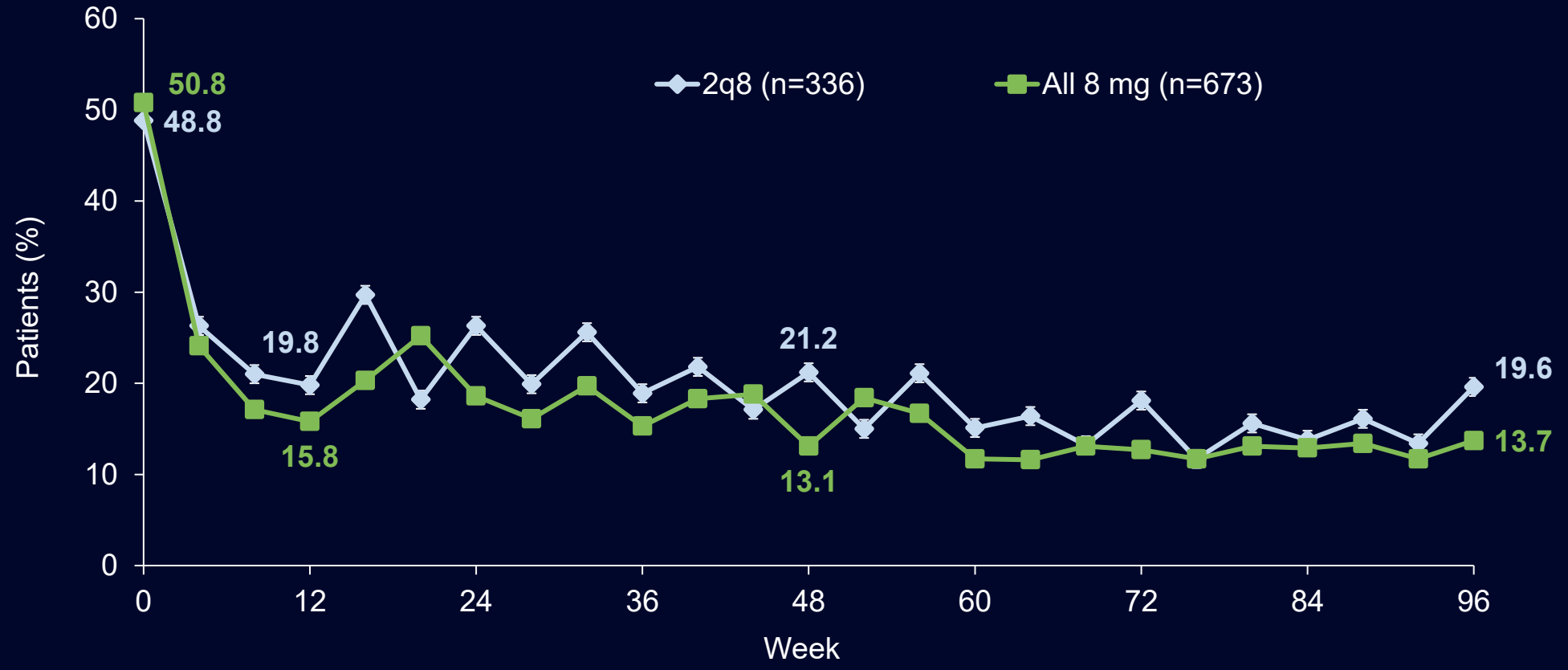
Outcomes:

- Presence and location of serous component of PED and neovascular LC through Week 96[a]
- Thickness of serous component of PED and neovascular LC in patients with serous component of PED and neovascular LC with involvement of the foveal center

Presence and Location of PED at Baseline	2q8 (n=336)	8q12 (n=335)	8q16 (n=338)	All 8 mg (n=673)
Presence of serous component of PED, n (%)	164 (48.8)	171 (51.0)	171 (50.6)	342 (50.8)
Serous component of PED with involvement of foveal center, n (%)	29 (8.6)	42 (12.5)	36 (10.7)	78 (11.6)
Neovascular LC with involvement of foveal center, n (%)	299 (89.8)	299 (90.1)	296 (88.6)	595 (89.3)

[a]Assessed using SD-OCT at Wisconsin Reading Center. **LC**, lesion complex; **PED**, pigment epithelial detachment, **RPE**, retinal pigment epithelium.

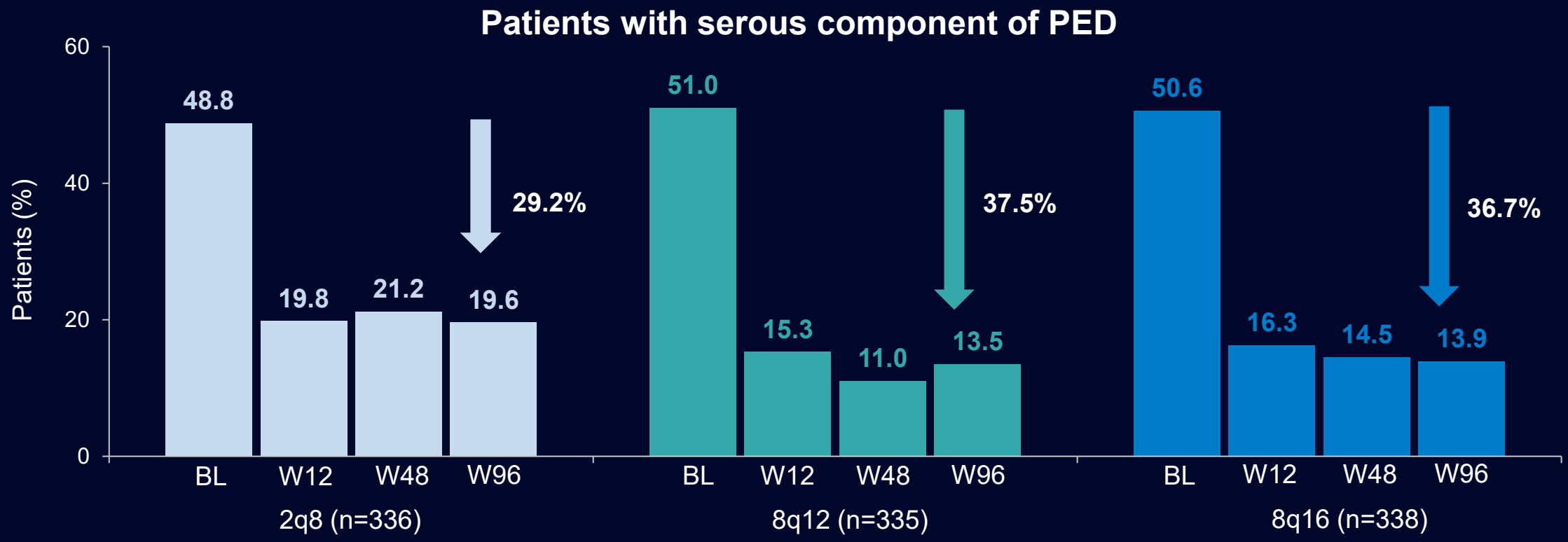
Patients with Serous Component of PED Through Week 96



Lower proportion of patients had **serous component of PED** with **aflibercept 8 mg** than with **aflibercept 2 mg** through **Week 96**

FAS, OC. **FAS**, full analysis set; **OC**, observed cases; **PED**, pigment epithelial detachment.

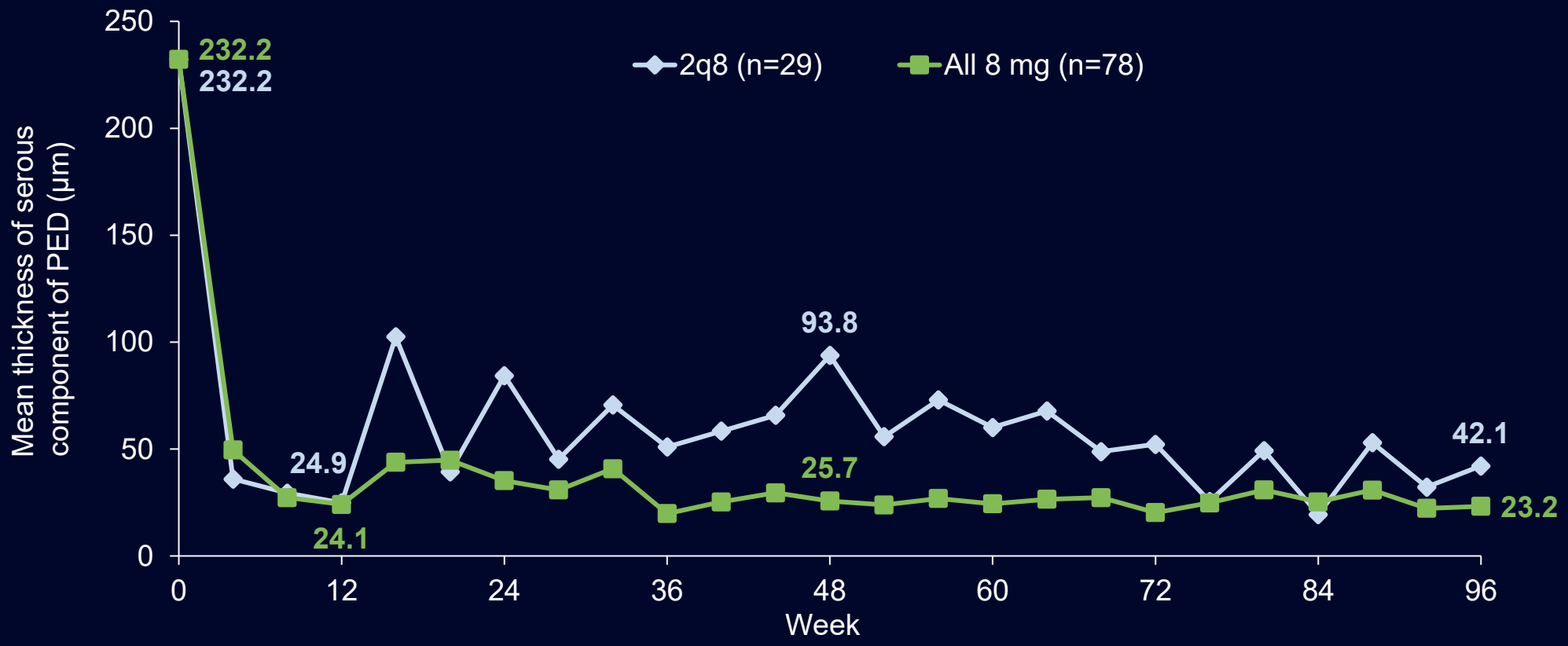
Reduction of Proportion of Patients with Serous Component of PED at Key Timepoints



- The proportion of patients with serous component of PED decreased by 29.2%, 37.5%, and 36.7% in the 2q8, 8q12, and 8q16 groups, respectively, from BL to Week 96

FAS, OC. **BL**, baseline; **FAS**, full analysis set; **OC**, observed cases; **PED**, pigment epithelial detachment; **W**, week.

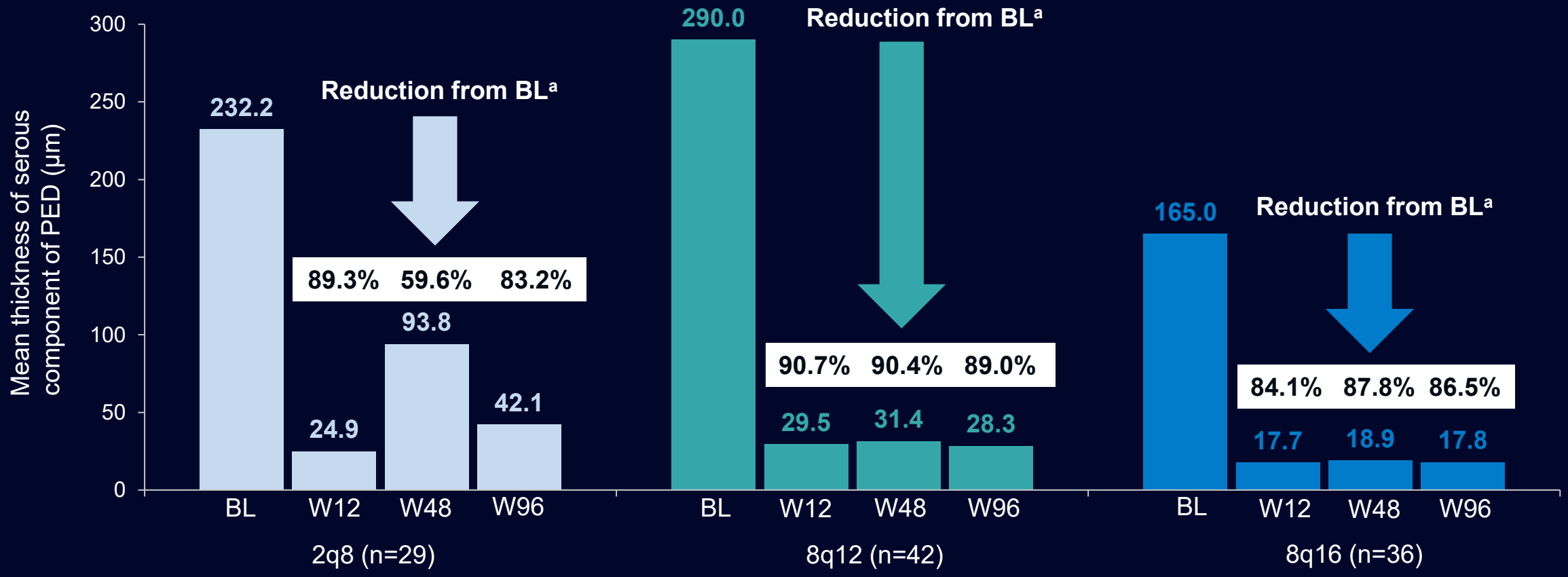
Thickness of Serous Component of PED Involving the Foveal Center Through Week 96



- **Marked reductions** in **thickness of the serous component of PED** involving the foveal center were achieved with **aflibercept 8 mg and 2 mg** at **Week 12**
- **Reductions** in **thickness of the serous component of PED** involving the foveal center were **sustained** through **Week 96**

FAS, OC. **FAS**, full analysis set; **OC**, observed cases; **PED**, pigment epithelial detachment.

Reductions in Thickness of Serous Component of PED Involving the Foveal Center at Key Timepoints

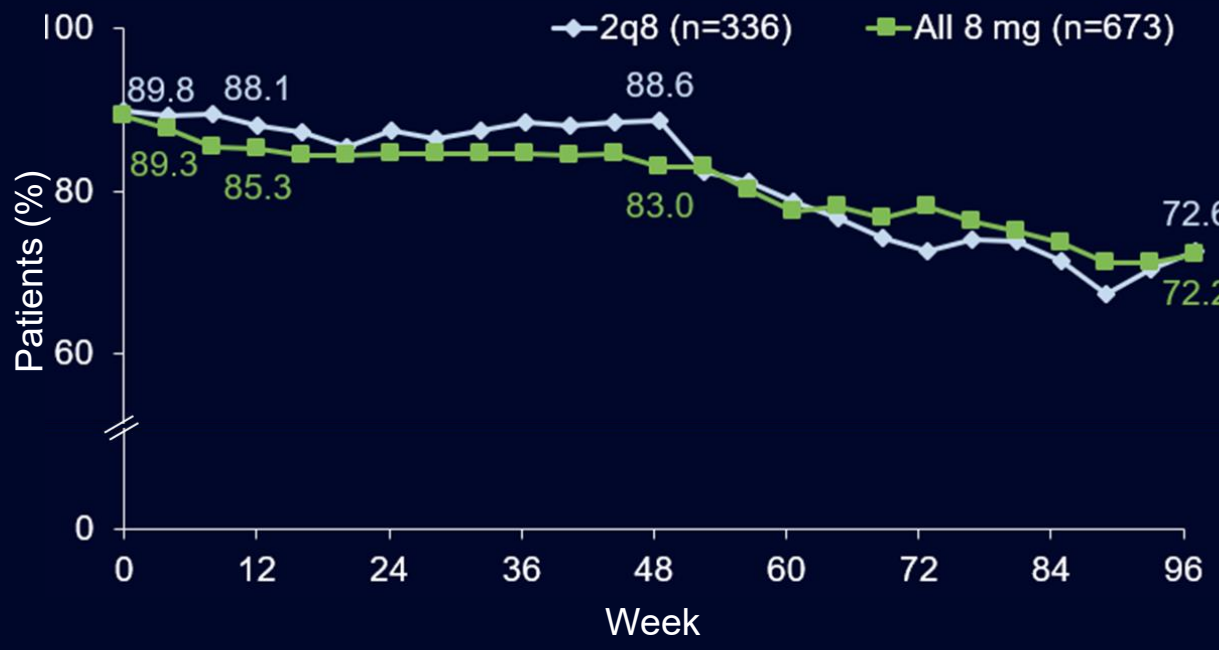


Marked reductions in **thickness of the serous component of PED** involving the foveal center at **Week 12** were **sustained** through **Week 96** in the **aflibercept 8q12, 8q16, and 2q8 groups**

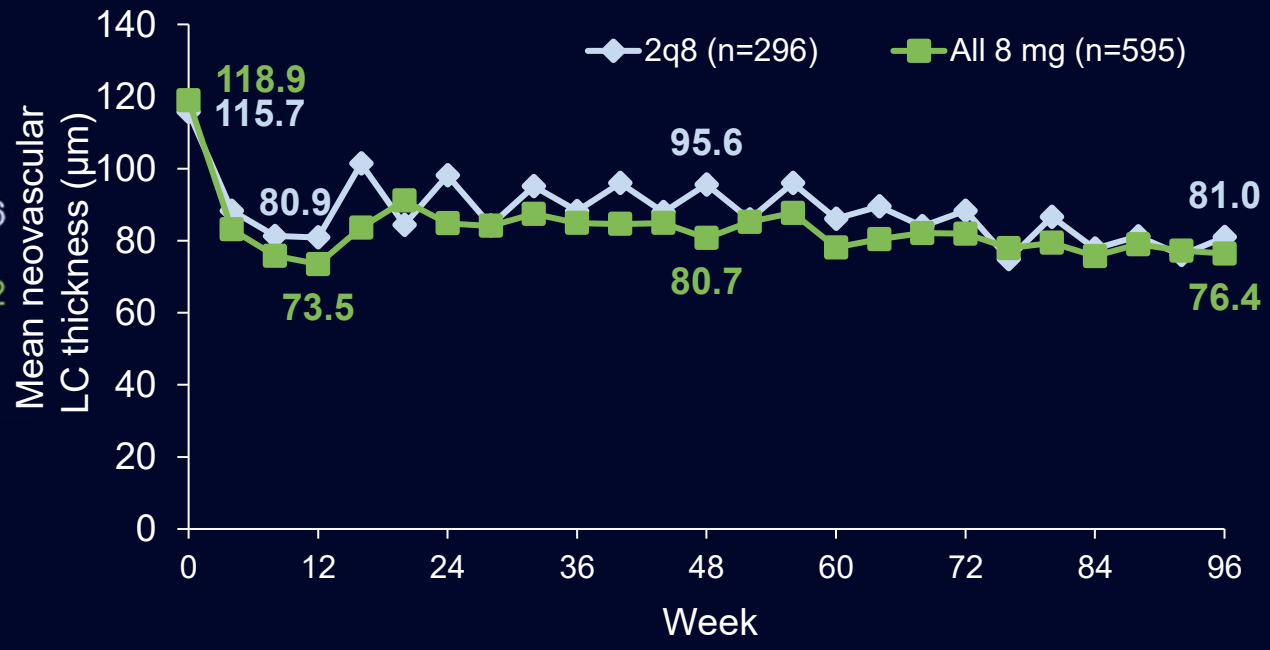
FAS, OC. [a]Calculated as the mean change from BL in thickness of serous component of PED at a particular timepoint divided by the BL value. **BL**, baseline; **OC**, observed cases; **PED**, pigment epithelial detachment; **W**, week.

Patients with Neovascular LC Involving the Foveal Center Through Week 96

Patients with Neovascular LC Involving the Foveal Center



Mean Neovascular LC Thickness



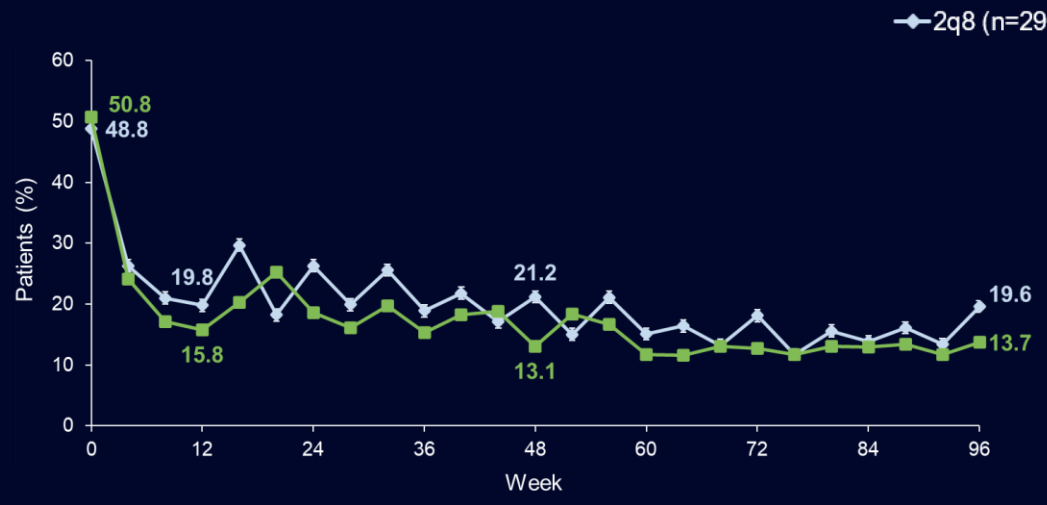
- **Decrease** in proportion of **patients with neovascular LC** involving the foveal center, from **BL to Week 96**, **was comparable in the 8 mg and 2 mg treatment groups**
- **Reduction** in **mean thickness of neovascular LC** involving the foveal center, achieved with **aflibercept 8 mg and 2 mg at Week 12**, was **sustained at Weeks 48 and 96**

FAS, OC. **BL**, baseline; **FAS**, full analysis set; **LC**, lesion complex; **OC**, observed cases; **W**, week.

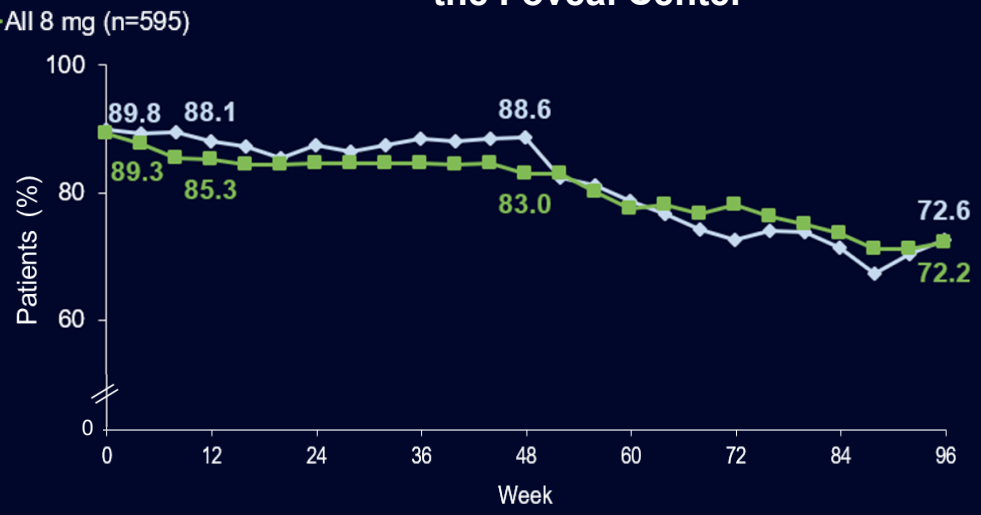
Conclusions

- A **lower proportion of patients** treated with **aflibercept 8 mg** than with aflibercept 2 mg had **serous component of PED through Week 96**
  - **Marked reductions in thickness of serous component of PED** involving the foveal center were achieved in the aflibercept 8q12, 8q16, and 2q8 groups
- **Decrease** in proportion of **patients with neovascular LC** involving the foveal center, from BL to Week 96, was **comparable in the 2 mg and 8 mg** treatment groups
  - Moderate reductions in mean neovascular LC thickness were seen across all 3 treatment groups
- All **improvements in PED outcomes were observed early at Week 12** and **maintained through Week 96**, with **fewer injections of aflibercept 8 mg** than aflibercept 2 mg

Patients with Serous Component of PED



Patients with Neovascular LC Involving the Foveal Center



FAS, OC. **BL**, baseline; **FAS**, full analysis set; **LC**, lesion complex; **OC**, observed cases; **PED**, pigment epithelial detachment.