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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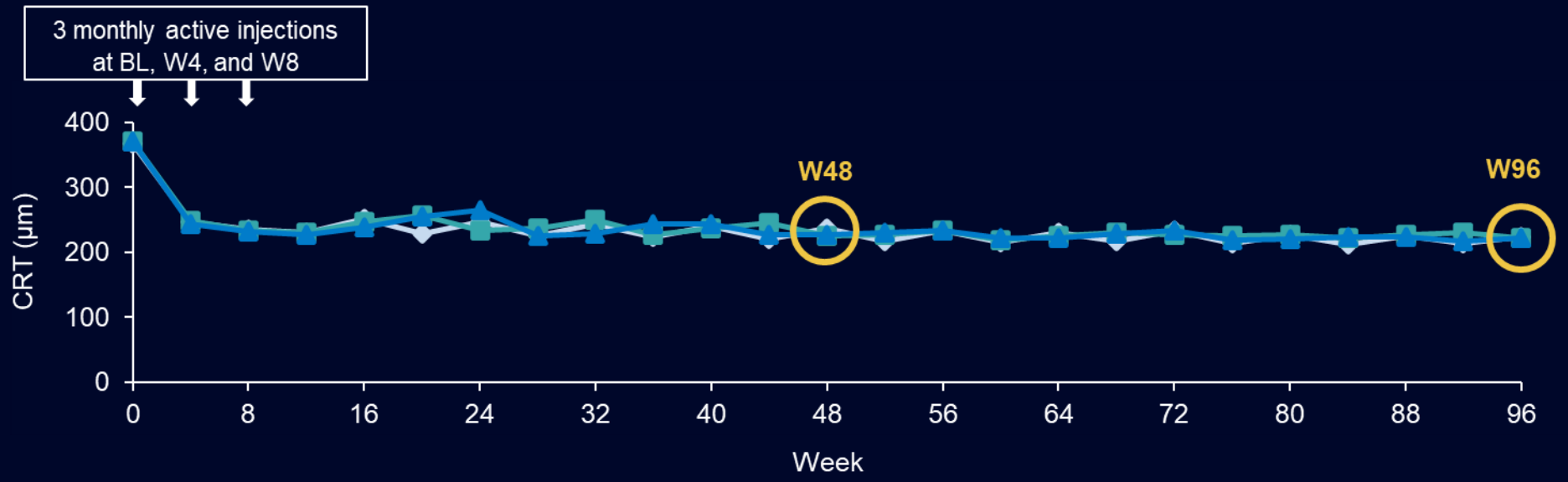
PULSAR: 96-Week, Multicenter, Double-masked Study in Patients with Treatment-naïve nAMD

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)

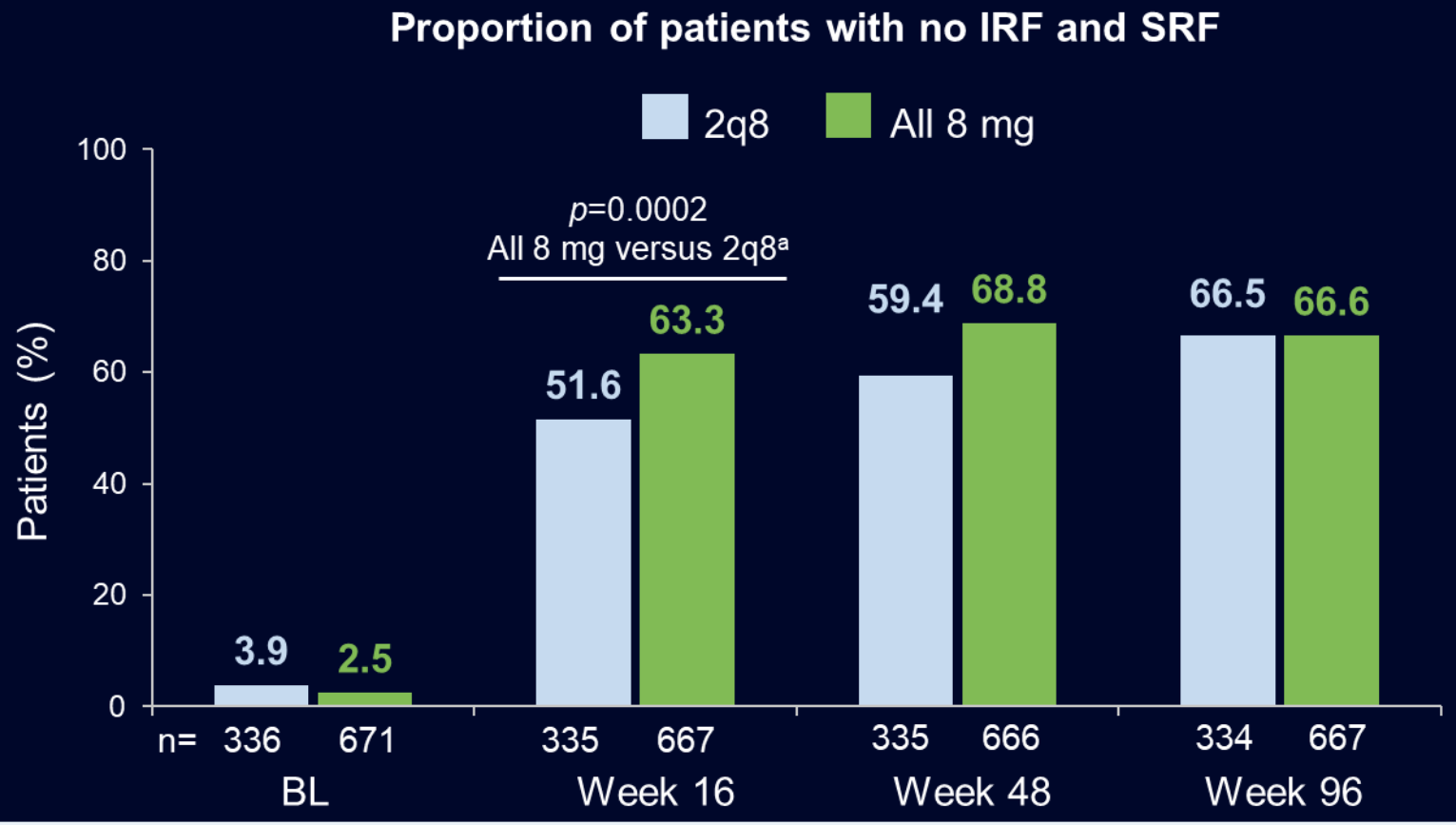


LS means CRT (µm) change from BL[a,b]

	W48	W96
2q8	–136	–147
8q12	–147	–152
8q16	–147	–149

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.

Patients with IRF and SRF Resolution Through Week 96



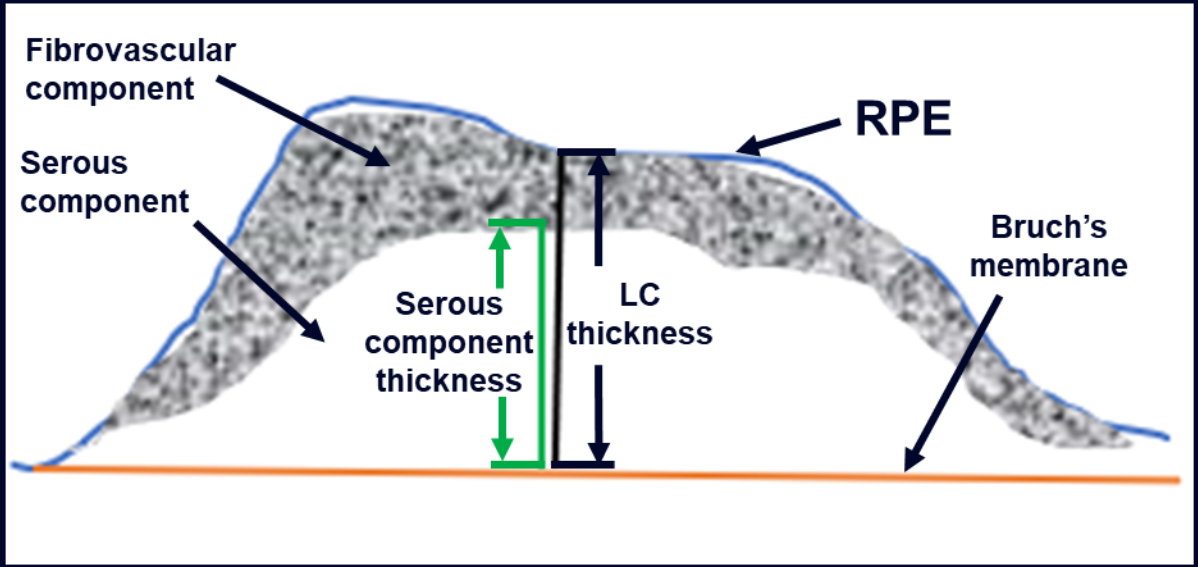
	Mean number of injections from BL	
	2 mg	8 mg
W48	6.9	5.6
W96	12.8	9.0

- The aflibercept **all 8 mg group** showed **superiority in the absence of IRF and SRF fluid** in the central subfield **at Week 16** compared with aflibercept 2 mg
- **Resilient fluid control** at 1 and 2 years was **achieved** with **fewer injections** in the **aflibercept all 8 mg** group **than** the **aflibercept 2 mg** group

FAS, LOCF (censoring data post ICE); FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338; all 8 mg n=673. [a]1-sided superiority, p-value: 1-sided CMH test; weighting scheme adjusted by geographic region and BL BCVA (<60 vs ≥60). [b]In patients completing Week 48 and Week 96, respectively. **2q8**, aflibercept 2 mg every 8 weeks; **BL**, baseline; **CMH**, Cochran-Mantel-Haenszel; **FAS**, full analysis set; **IRF**, intraretinal fluid; **LOCF,** last observation carried forward; **SRF**, subretinal fluid.

Objective and Methods

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
- In this analysis, the sub-RPE fluid is representative of the serous component of PED

Objective:

- To evaluate the impact of aflibercept 8 mg and 2 mg treatments on PED outcomes in the PULSAR trial

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

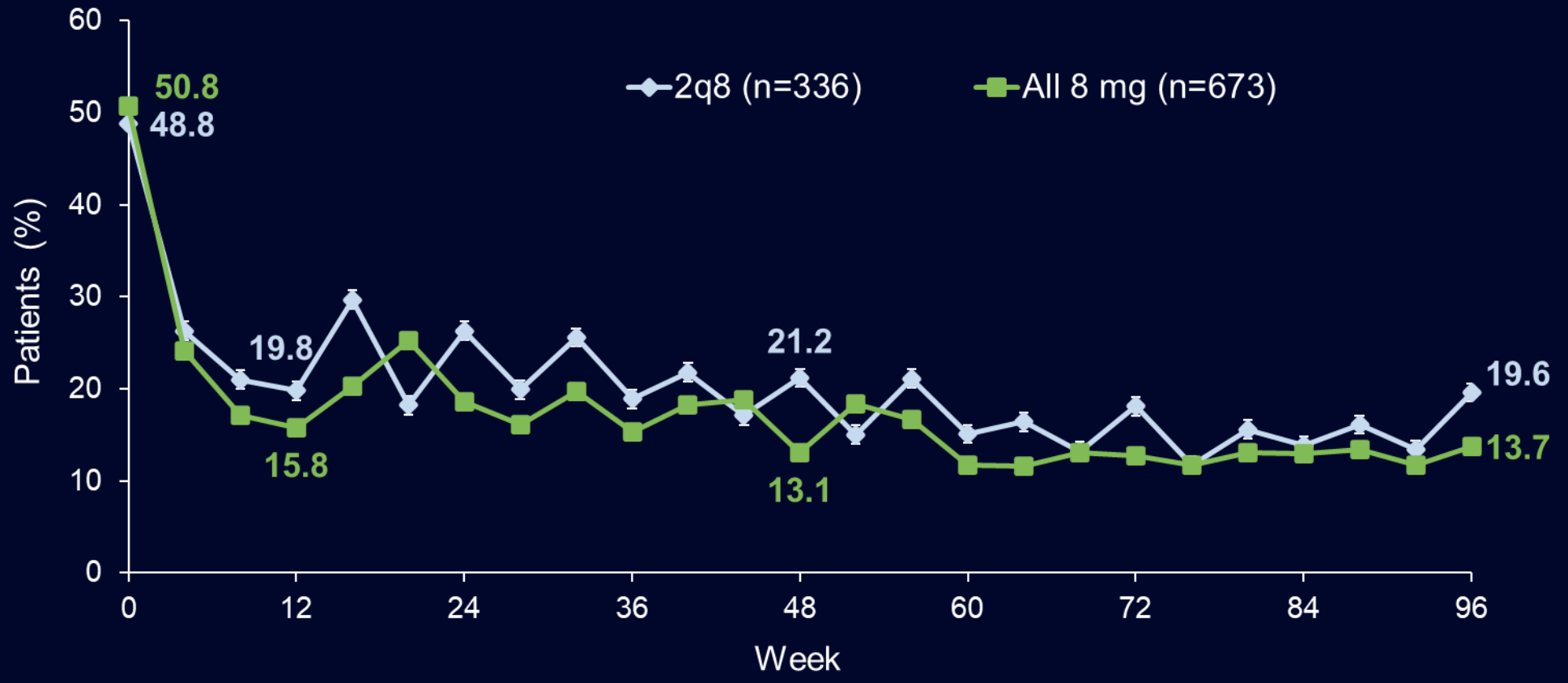
[a]Assessed using SD-OCT at Wisconsin Reading Center. **LC**, lesion complex; **PED**, pigment epithelial detachment, **RPE**, retinal pigment epithelium.

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)

FAS, OC. 2**q8**, aflibercept 2 mg every 8 weeks; **8q12**, aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **FAS**, full analysis set; **LC**, lesion complex; **OC**, observed cases; **PED**, pigment epithelial detachment, **RPE**, retinal pigment epithelium.

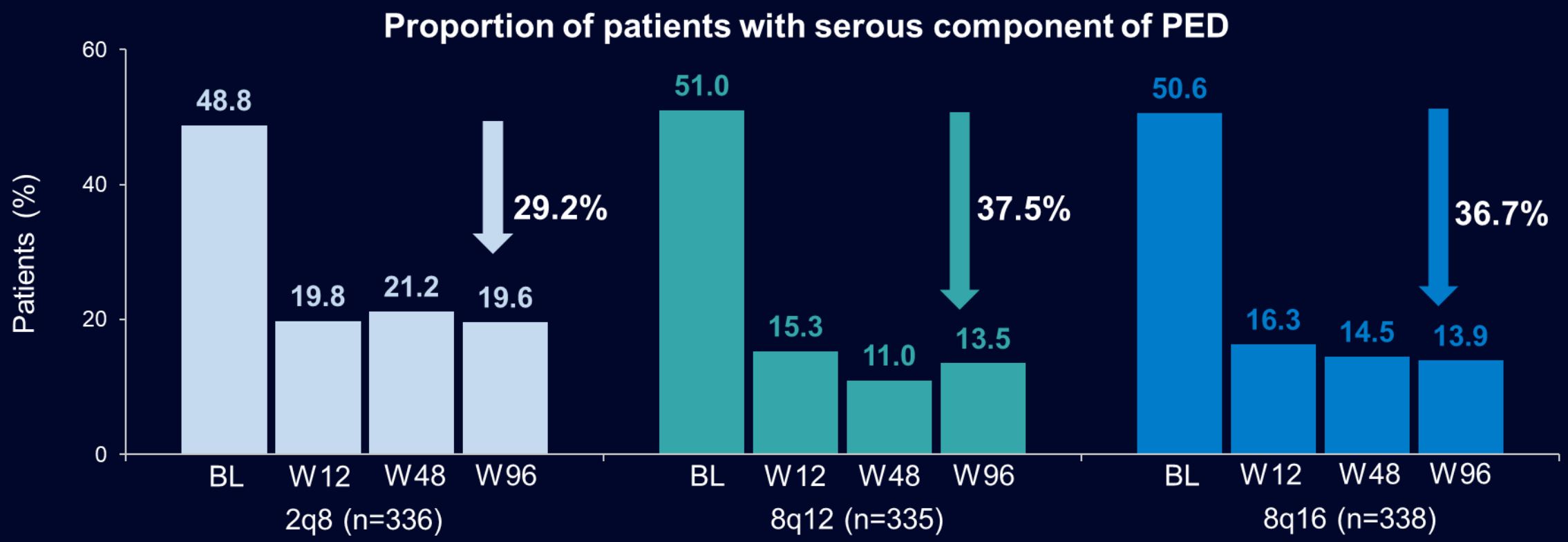
Proportion of Patients with Serous Component of PED Through Week 96



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.

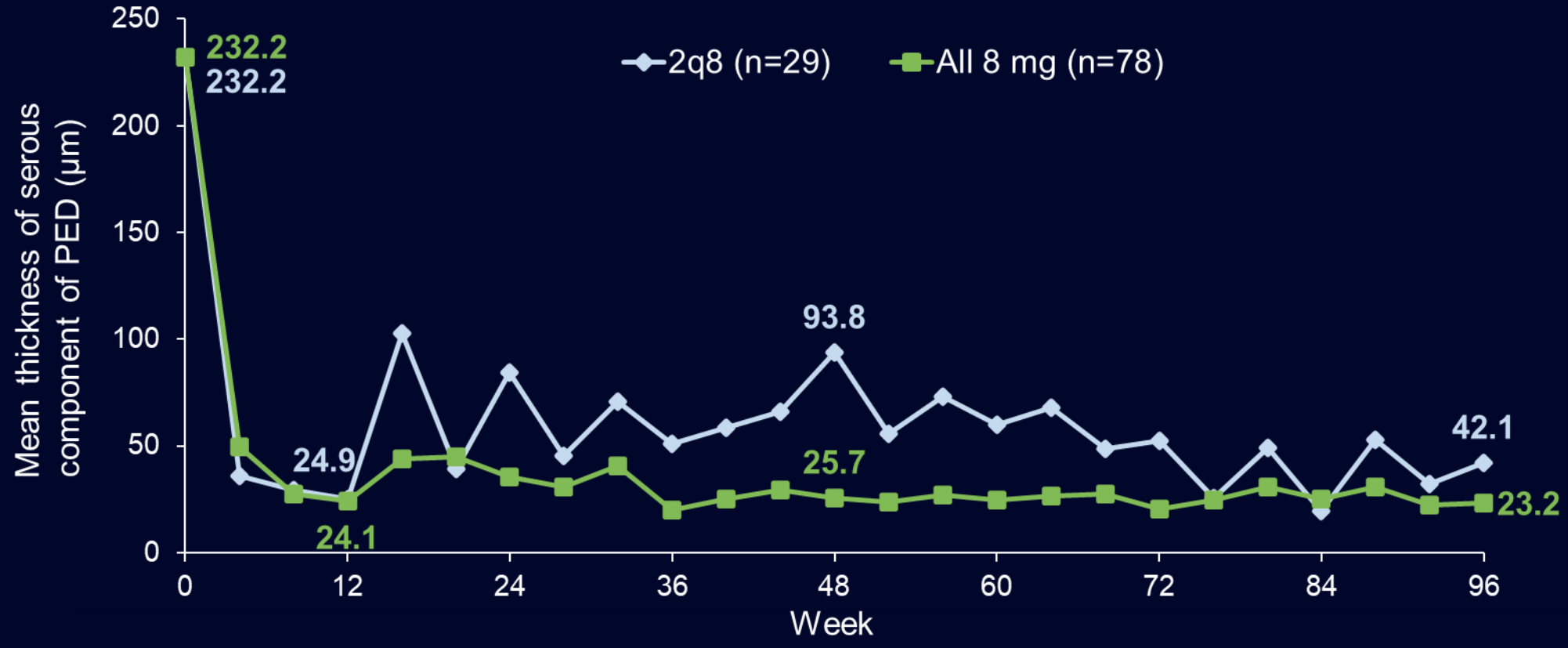
Reduction of Proportion of Patients with Serous Component of PED at Key Timepoints



- 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.

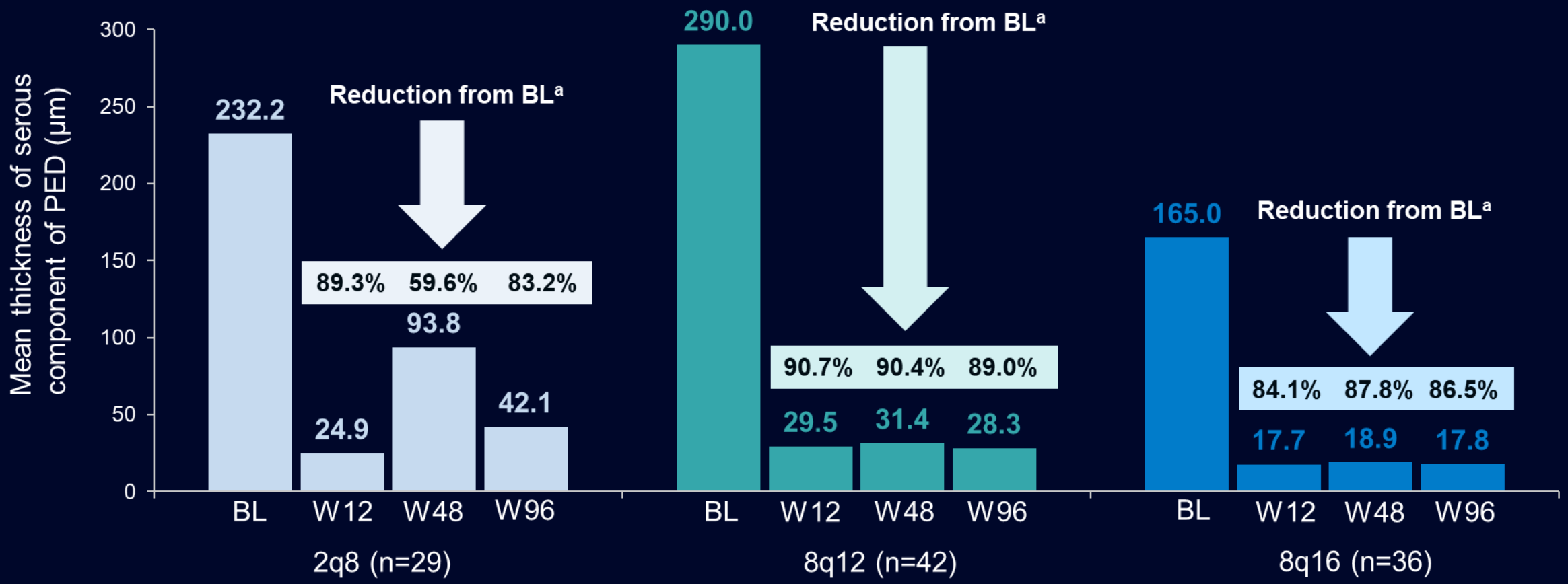
Thickness of Serous Component of PED Involving the Foveal Center Through Week 96



- **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.

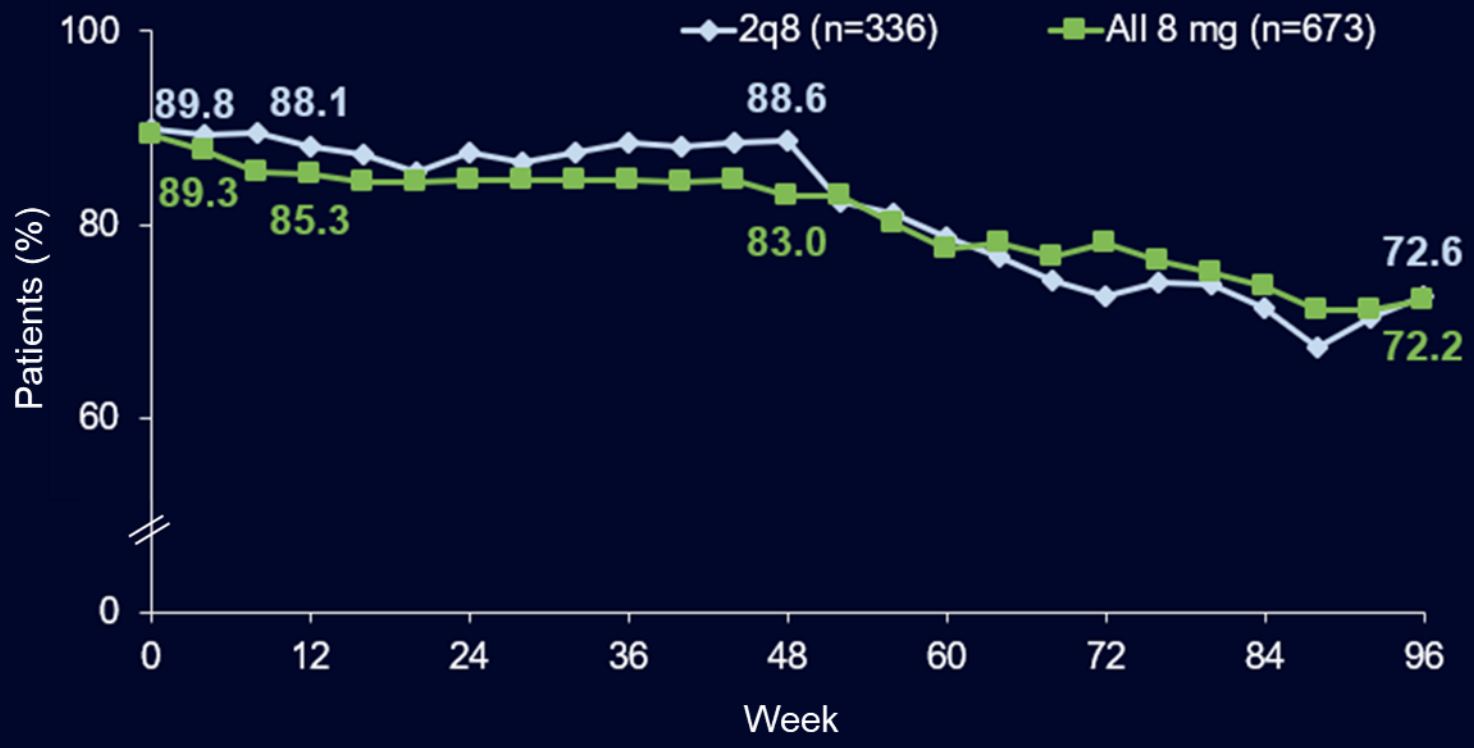
Reductions in Thickness of Serous Component of PED Involving the Foveal Center at Key Timepoints



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

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.

Proportion of Patients with Neovascular LC Involving the Foveal Center Through Week 96



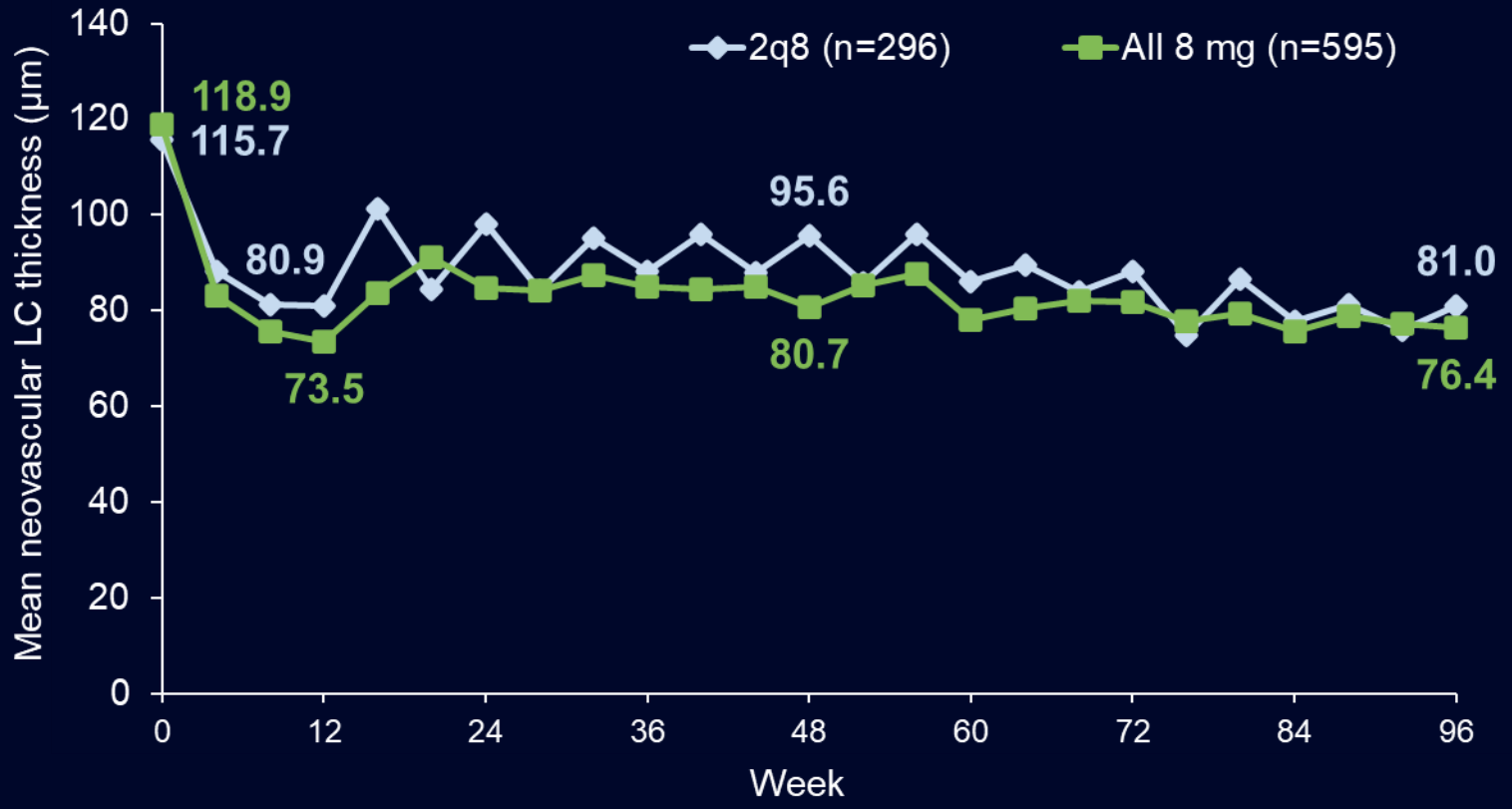
Proportion of patients with neovascular LC (%)

	BL	W12	W48	W96
2q8	89.8	88.1	88.6	72.6
8q12	90.1	86.2	85.4	73.3
8q16	88.6	84.3	80.5	71.1

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**

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

Thickness of Neovascular LC Involving the Foveal Center



Mean neovascular LC thickness (µm)

	BL	W12	W48	W96
2q8	115.7	80.9	95.6	81.0
8q12	125.6	76.2	80.4	79.8
8q16	112.2	70.8	80.9	72.9

Percent reduction from BL in mean neovascular LC thickness[a] (%)

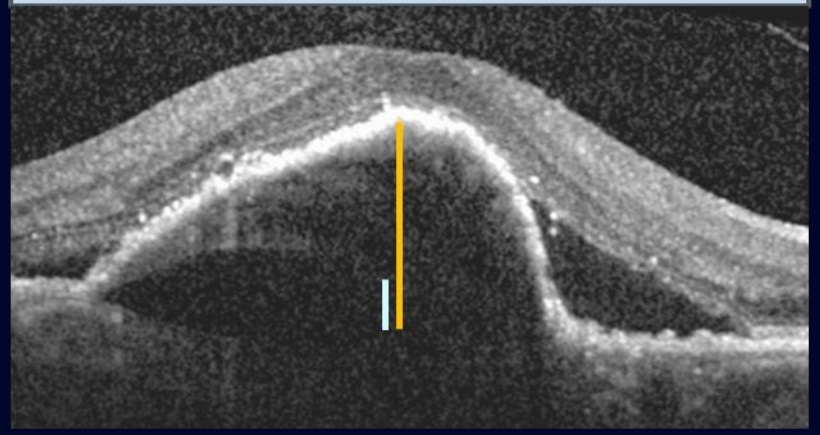
	W12	W48	W96
2q8	29.6	18.8	28.8
8q12	39.6	31.3	30.3
8q16	31.2	20.6	28.8

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. [a]Calculated as the mean change from BL in neovascular LC thickness at a particular timepoint divided by the BL value. **BL**, baseline; **FAS**, full analysis set; **LC**, lesion complex; **OC**, observed cases; **W**, week.

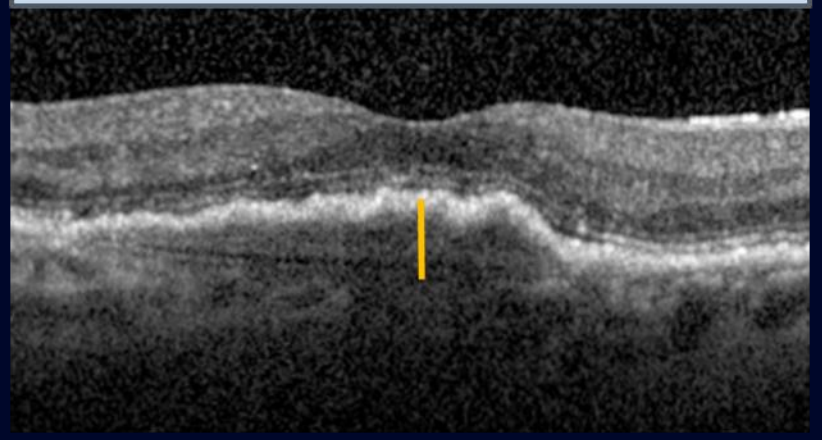
PED Outcomes Following Three Initial Monthly Doses

Baseline



Neovascular LC (670 µm)
Serous component of PED (148 µm)

Week 12



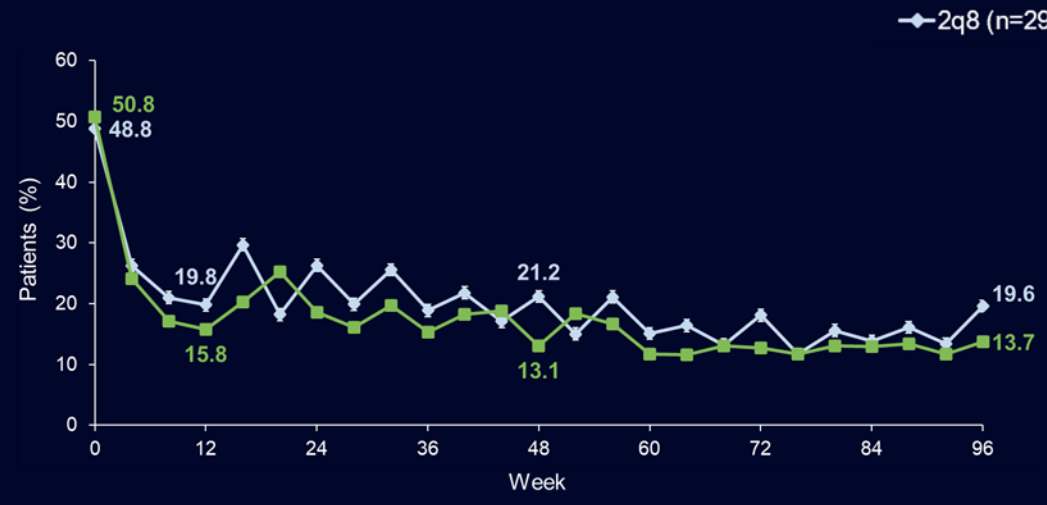
Neovascular LC (166 µm)
Serous component of PED resolved
SRF resolved

LC, lesion complex; **PED**, pigment epithelial detachment; **SRF**, subretinal fluid.

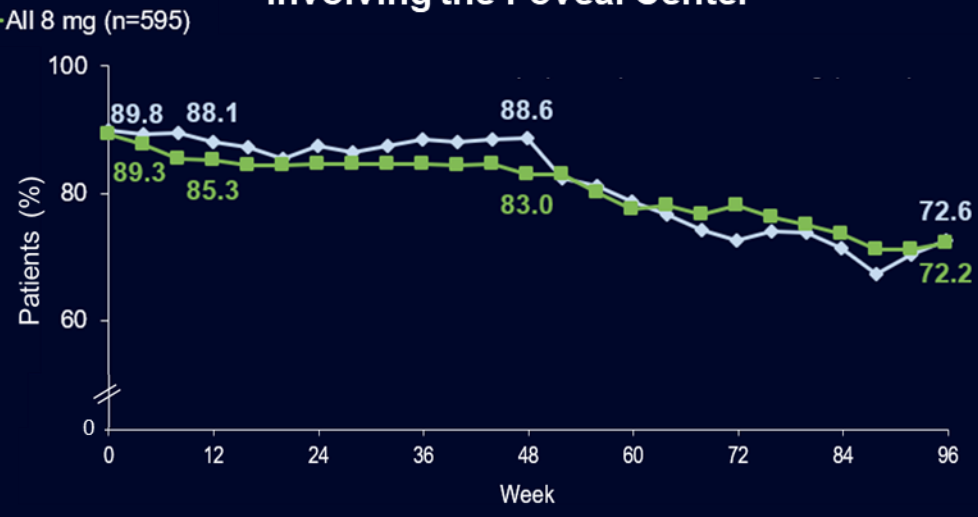
Conclusions

- 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 was achieved with aflibercept 8q12, 8q16, and 2q8
- **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

Proportion of Patients with Serous Component of PED



Proportion of 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.