Intravitreal Aflibercept 8 mg Injection in Patients With Neovascular Age-Related Macular Degeneration: 60-Week and 96-Week Results from the Phase 3 PULSAR Trial

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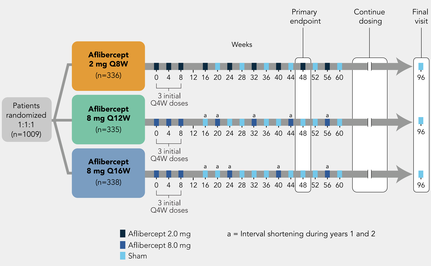
Aflibercept 8 mg is a new intravitreal anti-VEGF formulation, delivering a concentrated 4-fold higher molar dose than aflibercept 2 mg in a 70-µL injection. The double masked, active-controlled, 96-week, non-inferiority, three-group, PULSAR phase 3 clinical trial was designed to measure safety and efficacy of aflibercept 8 mg as compared to 2 mg dosing at intervals of ≥12 weeks in neovascular age-related macular degeneration (nAMD). The primary endpoint was non-inferiority of 8 mg dosing measured by BCVA.

PULSAR is a multicenter, randomized, double-masked study in patients with treatment-naïve nAMD to evaluate changes from baseline over 60 weeks.



Dose Regimen Modification (DRM) Criteria

[a]**Interval Shortening During Years 1 and 2**

>5-letter loss in BCVA compared with Week 12 due to persistent or worsening nAMD

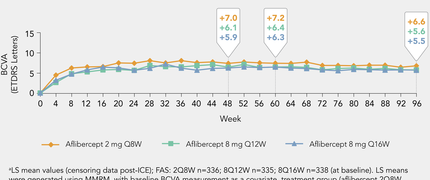
and

>25 µm increase in CST compared with Week 12, **or** new-onset foveal neovascularization, **or** foveal hemorrhage

Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks;
nAMD, neovascular age-related macular degeneration; BCVA, best-corrected visual acuity; CST, central subfield thickness.

Afibercept 8 mg groups achieved similar BCVA gains compared with 2 mg groups at Weeks 60 and 96.

BCVA Change from Baseline (LS Means)[a]

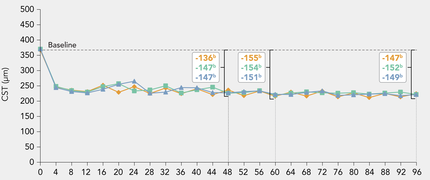


[a]LS mean values (censoring data post-ICE); FAS: 2Q8W n=336; 8Q12W n=335; 8Q16W n=338 (at baseline). LS means were generated using MMRM, with baseline BCVA measurement as a covariate, treatment group (aflibercept 2Q8W, 8Q12W, 8Q16W), visit, and stratification variables (geographic region [Japan vs Rest of World] and baseline BCVA [<60 vs ≥60] as fixed factors, and interaction terms for baseline and visit and for treatment and visit.

ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

Change in CST was similar in the three treatment arms, with minimal fluctuations over the course of treatment.

Absolute CST (Observed Values)[a]

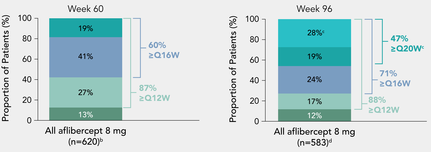


[a]Observed values (censoring data post-ICE); FAS: 2Q8W n=336; 8Q12W n=335; 8Q16W n=338 (at baseline).
[b]LS mean values (censoring data post-ICE); FAS: 2Q8W n=336; 8Q12W n=335; 8Q16W n=338 (at baseline). LS means were generated using MRMM, with BLCST measurement as a covariate, treatment group (aflibercept 2Q8W, 8Q12W, 8Q16W), visit and stratification variables (geographic region [Japan vs Rest of World] and baseline BCVA [<60 vs ≥60]) as fixed factors, and interaction terms for baseline and visit and for treatment and visit.

ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

At Weeks 60 and 96 respectively, 91% and 89% of patients receiving aflibercept 8q16 achieved ≥Q12 dosing intervals and 77% and 78% achieved ≥Q16 intervals.

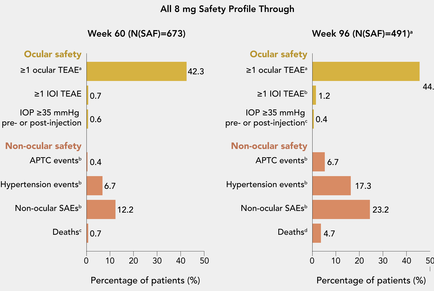
Last Assigned Dosing Interval at Week 60 and Week 96[a]



[a]Dosing intervals were extended in Year 2 if patients had <5-letter loss in BCVA from Week 12 **and** no fluid at the center subfield **and** no new foveal hemorrhage or neovascularization.
[b]Patients completing Week 60.
[c]Patients were assigned to 24-week dosing intervals if they continued to meet extension criteria but did not have enough time to complete the interval within the 96-week study period.
[d]Patients completing Week 96. Values may not add up to 100% due to rounding.

The safety profile of aflibercept 8 mg at Week 96 is comparable to that at Week 60, and also with aflibercept 2 mg.

All 8 mg Safety Profile Through



[a]In the study eye
[b]Treatment emergent
[c]All events

[a]In the study eye
[b]Treatment emergent
[c]IOP was measured in the study eye
[d]All events

[a]Diana V. Do, on behalf of the PHOTON study investigators
Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, USA
Presented at American Society of Retina Specialists 2023 Meeting, July 28–August 1, 2023

APTC = Anti-Platelet Trialists' Collaboration; IOI = intraocular inflammation; IOP = intraocular pressure; SAE = serious adverse event; SAF = safety analysis set; TEAE = treatment-emergent adverse event.

Conclusions

In PULSAR, the high-dose formulation of intravitreal aflibercept (8 mg), with extended dosing intervals, resulted in non-inferior vision gains and superior anatomic outcomes at weeks 60 and 96 compared with aflibercept 2 mg.

At Weeks 60 and 96 respectively, 91% and 89% of patients receiving aflibercept 8Q16 achieved ≥Q12 dosing intervals and 77% and 78% achieved ≥Q16 intervals.

The safety profile of aflibercept 8 mg was comparable to aflibercept 2 mg over 96 weeks, with no new safety concerns identified.

Aflibercept 8 mg could fulfill an important unmet need by allowing patients to safely achieve sustained disease control over longer dosing intervals and, ultimately, by optimizing the management of nAMD.