Aflibercept 8 mg for Diabetic Macular Edema: 2-Year Results of the Phase 2/3 PHOTON Trial

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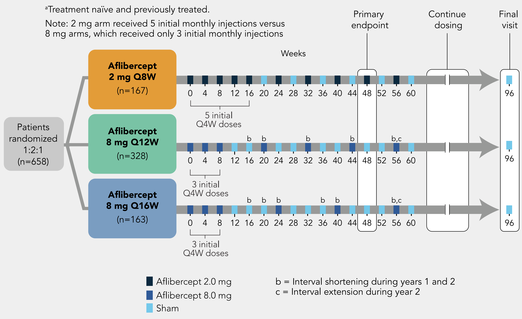
Aflibercept 8 mg is a novel intravitreal anti-VEGF formulation, delivering a 4-fold higher molar dose than aflibercept 2 mg in a 70-µL injection. The PHOTON phase 2/3 clinical trial was designed to measure safety and efficacy of aflibercept 8 mg as compared to 2 mg dosing at intervals of ≥12 weeks in DME. The primary endpoint was non-inferiority of 8 mg dosing measured by BCVA.

VEGF, vascular endothelial growth factor; DME, diabetic macular edema

PHOTON is a multicentered, randomized, double-masked study in patients with DME[a] to evaluate changes from baseline over 96 weeks.

[a]Treatment naïve and previously treated.

Note: 2 mg arm received 5 initial monthly injections versus 8 mg arms, which received only 3 initial monthly injections



Aflibercept 2.0 mg
Aflibercept 8.0 mg
Sham

b = Interval shortening during years 1 and 2
c = Interval extension during year 2

Dose Regimen Modification (DRM) Criteria

[b]Interval Shortening During Years 1 and 2

>10-letter loss in BCVA from Week 12 due to persistent or worsening DME
and
>50 µm increase in CRT from Week 12

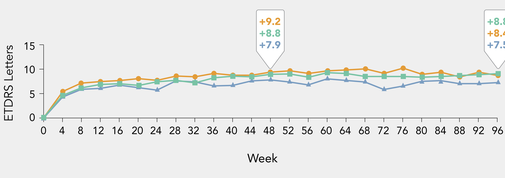
[c]Interval Extension During Year 2

The maximum assigned interval was Q24W

BCVA, best-corrected visual acuity; CRT, central retinal thickness

At Week 48, patients in the 2Q8W treatment arm had a mean change in BCVA of +9.2, whereas the 8Q12W treatment arm showed sustained results of +8.8 at week 48 and 96.

Mean Change in BCVA at Week 96



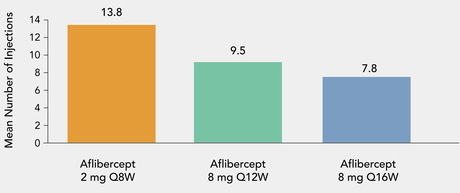
Aflibercept 2 mg Q8W
Aflibercept 8 mg Q12W
Aflibercept 8 mg Q16W

Data shown in the figure represent observed values (censoring data post-ICE); FAS: 2Q8W n=167; 8Q12W n=328; 8Q16W n=163 (at baseline).

ICE, intercurrent event; FAS, full analysis set

Through Week 96, the mean number of injections was highest in the 2Q8W treatment arm and lowest in the 8Q16W treatment arm.

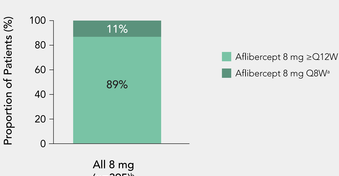
Mean Number of Injections Through Week 96



FAS, patients completing Week 96: 2Q8W n=139; 8Q12W n=256; 8Q16W n=139.

A large majority of Aflibercept 8 mg patients maintained randomized intervals through Week 96.

Portion of 8 mg Patients That Maintained Dosing Intervals ≥12 Weeks

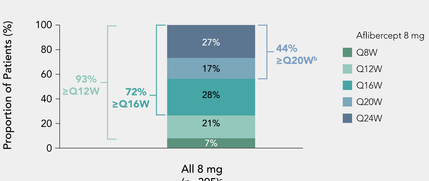


FAS, patients completing Week 96: 2Q8W n=139; 8Q12W n=256; 8Q16W n=139.

[a]Patients met DRM criteria for dosing interval shortening at some point through Week 96.
[b]Patients completing Week 96.
Values may not add up to 100% due to rounding.

Almost half of all 8 mg patients had assigned dosing intervals of ≥20 weeks at Week 96.

Last Assigned Dosing Interval at Week 96[a]



[a]Dosing intervals were extended in Year 2 if patients had <5-letter loss in BCVA from Week 12 **and** CRT <300 µm (or <320 µm on Spectralis).
[b]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.
[c]Patients completing Week 96.
Values may not add up to 100% due to rounding.

Conclusions

Results of the PHOTON trial at 96 weeks met the primary endpoint, with non-inferior BCVA in the 8Q12 and 8Q16 arms as compared to the 2Q8 arm, with up to six fewer injections. 89% of patients on 8 mg dosing maintained ≥12-week dosing intervals through Week 96, with comparable safety to 2 mg dosing in patients with DME.