Pooled Safety Analysis of Aflibercept 8 mg for up to 96 Weeks in the CANDELA, PHOTON, and PULSAR Trials

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Disclosures

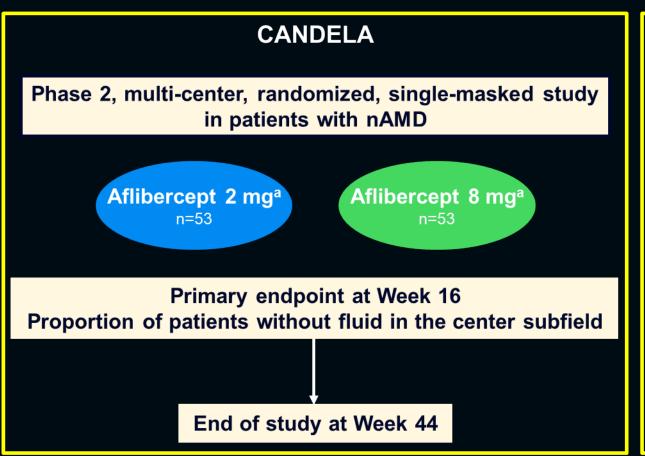
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- These trials include research conducted on human patients. Institutional review board approval was obtained prior to initiation of all trials
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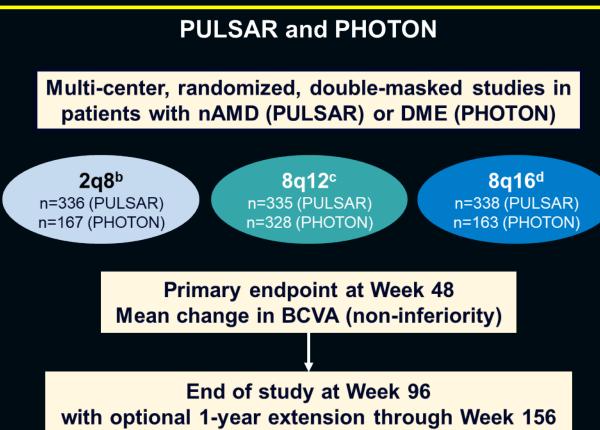
Background

- Aflibercept 8 mg is a novel formulation that delivers a 4-fold higher molar dose than aflibercept 2 mg, potentially suppressing VEGF signaling over a longer duration
- Aflibercept 8 mg demonstrated comparable efficacy and safety to aflibercept 2 mg in the proof-ofconcept Phase 2 CANDELA trial in nAMD, the pivotal Phase 3 PULSAR trial in nAMD, and the pivotal Phase 3 PHOTON trial in DME¹⁻³
- The present analysis, including >1200 patients who received >10,000 injections of aflibercept 8 mg over
 2 years, was conducted to further assess safety with aflibercept 8 mg

This analysis evaluated the safety of aflibercept 8 mg and 2 mg for up to 96 weeks across the CANDELA, PULSAR, and PHOTON trials

Study Designs





^aThree initial monthly injections followed by injections at Weeks 20 and 32.

^bAflibercept 2 mg every 8 weeks after 3 (PULSAR) or 5 (PHOTON) initial monthly injections.

^cAflibercept 8 mg every 12 weeks after 3 initial monthly injections.

^dAflibercept 8 mg every 16 weeks after 3 initial monthly injections. BCVA, best-corrected visual acuity.

Aflibercept Exposure Through Week 96

Total number of injections
Number of injections, mean (SD)
Treatment duration, mean (SD), weeks

Aflibercept 2 mg pooled (n=556)
6464
11.6 (3.1)
84.1 (24.5)

Aflibercept 8 mg pooled (n=1217)
10,067
8.3 (2.1)
86.8 (22.6)

Ocular TEAEs

Aflibercept

Aflibercept

	2 mg pooled (n=556)	8 mg pooled (n=1217)
Ocular TEAEs, n (%)	263 (47.3)	583 (47.9)
Ocular TEAEs in ≥3% of patients in any treatment group, n (%)		
Cataract ^a	53 (9.5)	140 (11.5)
Visual acuity reduced	30 (5.4)	53 (4.4)
Vitreous floaters	22 (4.0)	49 (4.0)
Conjunctival hemorrhage	17 (3.1)	46 (3.8)
Vitreous detachment	16 (2.9)	45 (3.7)
Retinal hemorrhage	22 (4.0)	44 (3.6)
Intraocular pressure increased	17 (3.1)	34 (2.8)
Subretinal fluid	17 (3.1)	24 (2.0)

No cases of ischemic optic neuropathy were reported with aflibercept 8 mg, and 1 case of ischemic optic neuropathy was reported with aflibercept 2 mg through Week 96

alncludes cataract, cataract cortical, cataract nuclear, cataract operation, cataract subcapsular, lenticular opacities, and posterior capsule opacification although not all terms met the ≥3% threshold.

Intraocular Inflammation

IOI, n (%)
Iridocyclitis
Iritis
Anterior chamber cell
Uveitis
Vitreal cells
Vitritis
Chorioretinitis
Endophthalmitis
Eye inflammation
Hypopyon

Aflibercept 2 mg pooled (n=556)
11 (2.0)
2 (0.4)
0
1 (0.2)
2 (0.4)
2 (0.4)
0
0
2 (0.4)
1 (0.2)
1 (0.2)

Aflibercept 8 mg pooled (n=1217)
16 (1.3)
4 (0.3)
3 (0.2)
2 (0.2)
2 (0.2)
2 (0.2)
2 (0.2)
1 (<0.1)
0
0
0

- Most IOI cases were non-serious and mild or moderate in severity
- No cases of occlusive retinal vasculitis were reported through Week 96 in any treatment group

IOP in the Study Eye

IOP increase ≥10 mmHg from baseline (pre-injection), n (%)^a

IOP ≥35 mmHg pre- or post-injection, n (%)^a

Aflibercept 2 mg pooled (n=556)

15 (2.7)^b

 $4(0.7)^{d}$

Aflibercept 8 mg pooled (n=1217)

 $49 (4.0)^{c}$

 $6(0.5)^{e}$

IOP, intraocular pressure.

^aAt any visit.

bCANDELA (n=0), PULSAR (n=11), and PHOTON (n=5).

^cCANDELA (n=2), PULSAR (n=18), PHOTON (n=28).

dCANDELA (n=0), PULSAR (n=2), and PHOTON (n=2).

 $^{^{}m e}$ CANDELA (n=0), PULSAR (n=4), and PHOTON (n=2).

Serious Ocular TEAEs

Serious ocular TEAEs, n (%)
Serious ocular TEAEs in ≥2 patients in any treatment group, n (%)
Cataracta
Retinal detachment
Retinal hemorrhage
IOP increased
Vitreous hemorrhage
Retinal tear

Aflibercept 2 mg pooled (n=556)
7 (1.3)
1 (0.2)
1 (0.2)
1 (0.2)
0
0
0

Aflibercept 8 mg pooled (n=1217)
28 (2.3)
7 (0.6)
6 (0.5)
4 (0.3)
3 (0.2)
3 (0.2)
2 (0.2)

Non-Ocular TEAEs, APTC Events and Deaths

Any non-ocular TEAEs, n (%)
Any serious non-ocular TEAEs, n (%)
APTC events, n (%) ^a
Any death, n (%) ^a

Aflibercept 2 mg pooled (n=556)
396 (71.2)
112 (20.1)
23 (4.1)
17 (3.1)

Aflibercept 8 mg pooled (n=1217)
884 (72.6)
256 (21.0)
45 (3.7)
33 (2.7)

Conclusions

- In this pooled analysis, the incidence of IOI was low and similar between aflibercept 8 mg and 2 mg
 - No cases of endophthalmitis were reported with aflibercept 8 mg, whereas 2 cases were reported with aflibercept 2 mg
 - No cases of occlusive retinal vasculitis were reported through Week 96 in any treatment group
- The incidence of non-ocular TEAEs, including serious TEAEs, APTC events, and deaths, was similar between aflibercept 8 mg and 2 mg
- Overall, aflibercept 8 mg demonstrated comparable safety to aflibercept 2 mg for up to 96 weeks across the CANDELA, PULSAR, and PHOTON trials