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

Christina Y. Weng MD, MBA, FASRS on behalf of the CANDELA, PHOTON, and PULSAR study investigators

Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, USA

Financial Disclosures:
Dr. Weng has served as a consultant for Alcon, Alimera, Allergan/AbbVie, Apellis, DORC, EyePoint, Genentech, Astellas/Iveric Bio, Novartis, Regeneron Pharmaceuticals, Inc., and REGENXBIO; received research support from AGTC, Alimera, and DRCR Retina Network; and received royalties from Springer Publishers

METHODS

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

Trial Design

CANDELA

Phase 2, multi-center, randomized, single-masked study in patients with nAMD

- Aflibercept 2 mg[a] n=53
- Aflibercept 8 mg[a] n=53

End of study at Week 44

Primary endpoint at Week 16
Proportion of patients without fluid in the center subfield

PULSAR and PHOTON

Multi-center, randomized, double-masked studies in patients with nAMD (PULSAR) or DME (PHOTON)

- 2q8[b] n=336 (PULSAR) n=167 (PHOTON)
- 8q12[c] n=335 (PULSAR) n=328 (PHOTON)
- 8q16[d] n=338 (PULSAR) n=163 (PHOTON)

End of study at Week 96

Primary endpoint at Week 48
Mean change in BCVA (non-inferiority)

[a]Three initial monthly injections followed by injections at Weeks 20 and 32.
[b]Aflibercept 2q8 after 3 (PULSAR) or 5 (PHOTON) initial monthly injections.
[c]Aflibercept 8q12 after 3 initial monthly injections.
[d]Aflibercept 8q16 after 3 initial monthly injections.

Aflibercept Exposure

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled (n=1217)
Total number of injections	6464	10,067
Number of injections, mean (SD)	11.6 (3.1)	8.3 (2.1)
Treatment duration, mean (SD), weeks	84.1 (24.5)	86.8 (22.6)

2q8, 2 mg every 8 weeks, 8q12, 8 mg every 12 weeks, 8q16, 8 mg every 16 weeks, BCVA, best-corrected visual acuity, DME, diabetic macular edema, nAMD, neovascular age-related macular degeneration, SD, standard deviation

RESULTS

Ocular and Serious TEAEs Through Week 96

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled (n=1217)
Any ocular TEAEs, n (%)	263 (47.3)	583 (47.9)
Any ocular TEAEs in ≥5% of patients in any treatment group, n (%)		
Cataract[a]	53 (9.5)	140 (11.5)
Visual acuity reduced	30 (5.4)	53 (4.4)
Any serious ocular TEAEs, n (%)	7 (1.3)	28 (2.3)
Any serious ocular TEAEs in ≥3 patients in any treatment group, n (%)		
Cataract[b]	1 (0.2)	7 (0.6)
Retinal detachment	1 (0.2)	6 (0.5)
Retinal hemorrhage	1 (0.2)	4 (0.3)
Intraocular pressure increased	0	3 (0.2)
Vitreous hemorrhage	0	3 (0.2)

- **No cases of ION were reported with aflibercept 8 mg, and 1 case of ION was reported with aflibercept 2 mg**

[a]Includes cataract, cataract cortical, cataract nuclear, cataract operation, cataract subcapsular, lenticular opacities, and posterior capsule opacification although not all terms met the ≥5% threshold.
[b]Includes cataract, cataract nuclear, and cataract subcapsular although these terms did not meet the 3-patient threshold.

IOI Through Week 96

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled (n=1217)
Any intraocular inflammation, n (%)	11 (2.0)	16 (1.3)
Iridocyclitis	2 (0.4)	4 (0.3)
Iritis	0	3 (0.2)
Anterior chamber cell	1 (0.2)	2 (0.2)
Uveitis	2 (0.4)	2 (0.2)
Vitreal cells	2 (0.4)	2 (0.2)
Vitritis	0	2 (0.2)
Chorioretinitis	0	1 (<0.1)
Endophthalmitis	2 (0.4)	0
Eye inflammation	1 (0.2)	0
Hypopyon	1 (0.2)	0

- Most IOI cases were non-serious and mild or moderate in severity
- No cases of endophthalmitis were reported with aflibercept 8 mg, and 2 cases of endophthalmitis were reported with aflibercept 2 mg
- **No cases of occlusive retinal vasculitis were reported in the trials**

Non-ocular TEAEs, APTC events, and Deaths Through Week 96

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled (n=1217)
Any non-ocular TEAEs, n (%)	396 (71.2)	884 (72.6)
Any serious non-ocular TEAEs, n (%)	112 (20.1)	256 (21.0)
APTC events,[c] n (%)	23 (4.1)	45 (3.7)
Any death,[c] n (%)	17 (3.1)	33 (2.7)

[c]Treatment-emergent.

APTC, Anti Platelet Trialists' Collaboration; IOI, intraocular inflammation; ION, ischemic optic neuropathy; TEAE, treatment emergent adverse event.

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APTC, Anti-Platelet Trialists' Collaboration; IOI, intraocular inflammation

SUMMARY POINTS

- In this pooled analysis, **aflibercept 8 mg demonstrated comparable safety to aflibercept 2 mg** for up to 96 weeks across the CANDELA, PULSAR, and PHOTON trials
  - Incidence of IOI was low and similar between aflibercept 8 mg and 2 mg
  - No cases of endophthalmitis were reported with aflibercept 8 mg; 2 cases of endophthalmitis were reported with aflibercept 2 mg
  - No cases of ION were reported with aflibercept 8 mg; 1 case of ION was reported with aflibercept 2 mg
  - Incidence of non-ocular TEAEs, including serious TEAEs, APTC events, and deaths, was similar between aflibercept 8 mg and 2 mg