Pooled Safety Analysis of Aflibercept 8 mg in the CANDELA, PHOTON, and PULSAR Trials

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Disclosures

- Justus G. Garweg has served as an advisor and speaker for AbbVie, Bayer, Novartis and Roche; and as investigator in multicenter randomized controlled trials for Bayer, Novartis, and Roche
  - **ES** is a consultant and investigator for Carl Zeiss Meditec, Inc. and Notal Vision. **AJB, KWC, KR, RR, and RV** are employees and stockholders of Regeneron Pharmaceuticals, Inc. **AS, CT, and USO** are employees of Bayer AG. **XZ and SL** are employees of Bayer Consumer Care AG
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- Study disclosures: These studies include research conducted on human patients; Institutional Review Board approval was obtained prior to study initiation
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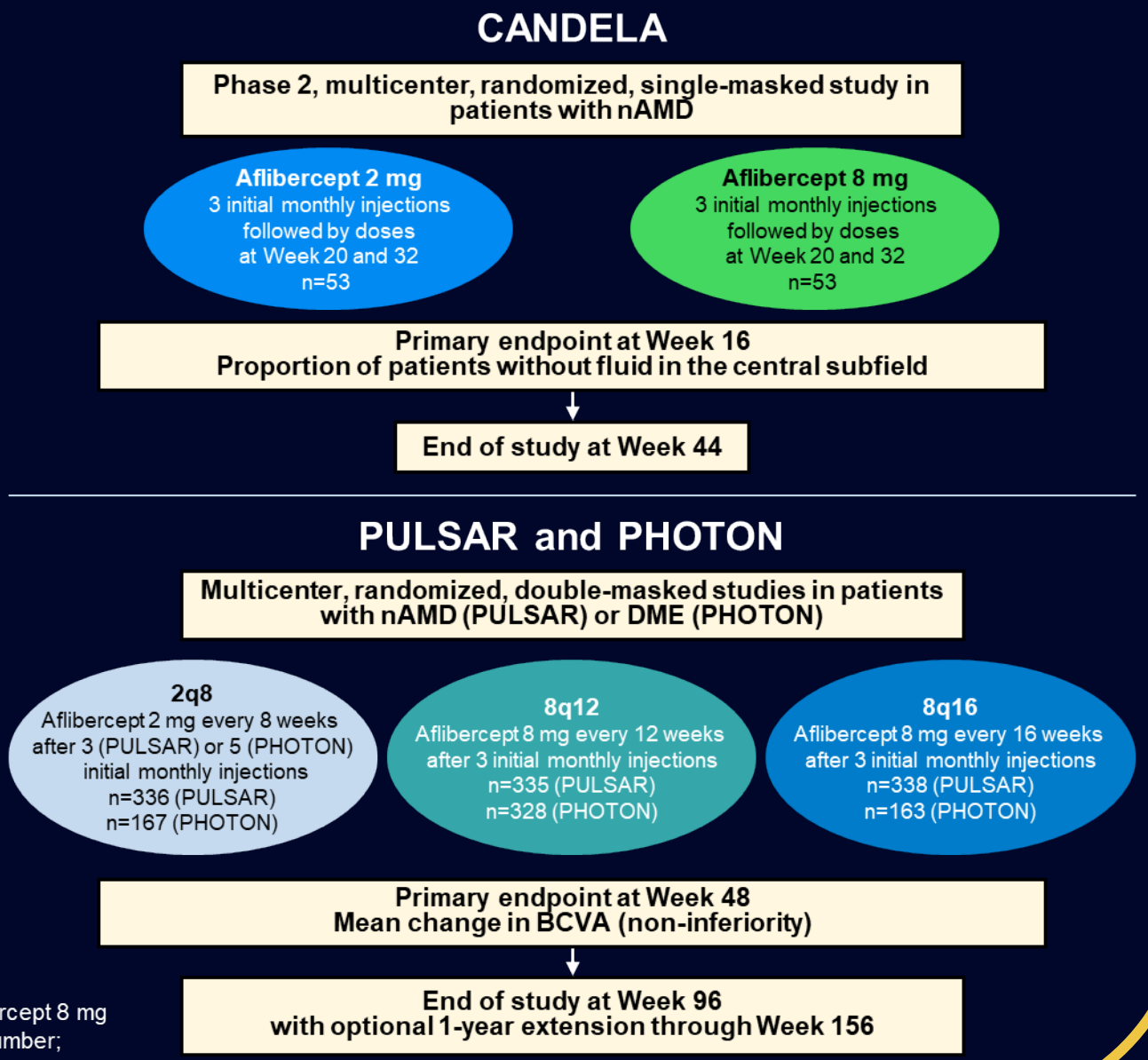
Background and Methods

- The purpose of the current analysis was to evaluate the safety of aflibercept 8 mg in a large patient population by pooling safety data across clinical trials of aflibercept 8 mg
- Data from 3 multicenter clinical trials comparing the efficacy and safety of aflibercept 8 mg versus aflibercept 2 mg were pooled:
  - Phase 2 **CANDELA trial** in treatment-naïve patients with nAMD
  - Phase 3 **PULSAR trial** in treatment-naïve patients with nAMD
  - Phase 2/3 **PHOTON trial** in treatment-naïve and previously treated patients with DME
- Data were pooled through Week 44 of the CANDELA trial and through Week 48 of the PULSAR and PHOTON trials



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; **DME**, diabetic macular edema; **n**, number; **nAMD**, neovascular age-related macular degeneration.

Baseline Demographics and Aflibercept Exposure in the Pooled Safety Analysis

Overall, safety data for **1773 patients were evaluated**

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
CANDELA, n	53	53
PULSAR, n	336	673
PHOTON, n	167	491
Total, n	**556**	**1217**

		Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n		**556**	**1217**
Age group, n (%)	<65 years	141 (25.4%)	349 (28.7%)
	≥65–<75 years	196 (35.3%)	441 (36.2%)
	≥75 years	219 (39.4%)	427 (35.1%)
Female, n (%)		299 (53.8%)	574 (47.2%)
White, n (%)		412 (74.1%)	927 (76.2%)
Hispanic or Latino, n (%)		47 (8.5%)	106 (8.7%)
Aflibercept exposure			
Number of injections, mean (SD)		6.9 (1.1)	5.5 (0.9)
Treatment duration, mean (SD), weeks		45.5 (7.4)	45.9 (7.5)

[a]Aflibercept 8q12 and 8q16 combined. **SD**, standard deviation.

Ocular TEAEs in the Study Eye

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n	556	1217
Patients with **≥1 ocular TEAE**	196 (35.3%)	428 (35.2%)
Ocular TEAEs in ≥2% of patients, n (%)		
Cataract	12 (2.2%)	37 (3.0%)
Conjunctival hemorrhage	13 (2.3%)	36 (3.0%)
Intraocular pressure increased	13 (2.3%)	28 (2.3%)
Vitreous floaters	15 (2.7%)	36 (3.0%)
Reduced visual acuity	25 (4.5%)	35 (2.9%)
Vitreous detachment	9 (1.6%)	33 (2.7%)
Retinal hemorrhage	17 (3.1%)	28 (2.3%)
Subretinal fluid	12 (2.2%)	16 (1.3%)

Ocular TEAE incidences in the study eye were **similar across treatment groups**; no endophthalmitis, occlusive retinal vasculitis, or ischemic optic neuropathy cases were reported through Week 48

[a]Aflibercept 8q12 and 8q16 combined. **TEAE**, treatment-emergent adverse event.

Intraocular Inflammation and Intraocular Pressure Increase Events in the Study Eye

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n	556	1217
Patients with **≥1 event of IOI**, n (%)	3 (0.5%)	10 (0.8%)

Reported IOI terms: iridocyclitis, iritis, vitreal cells (each in 3 patients overall), vitritis (in 2 patients overall), chorioretinitis, and uveitis (each in 1 patient overall)

n	556	1217
Patients with **≥1 event of IOP increase**, n (%)	15 (2.7%)	36 (3.0%)
Intraocular pressure increased	13 (2.3%)	28 (2.3%)
Ocular hypertension	2 (0.4%)	10 (0.8%)

A patient is counted only once within each safety topic and preferred term.
[a]Aflibercept 8q12 and 8q16 combined. [b]All IOI cases are mild and moderate. **IOI,** intraocular inflammation; **IOP,** intraocular pressure.

Serious Ocular TEAEs in the Study Eye

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n	556	1217
Patients with **≥1 serious ocular TEAE**, n (%)	4 (0.7%)	16 (1.3%)

Reported serious ocular TEAEs: retinal detachment (in 5 patients overall), intraocular pressure increased, retinal hemorrhage (each in 3 patients overall), vitreous hemorrhage, angle closure glaucoma (each in 2 patients overall), cataract, cataract subcapsular, choroidal detachment, retinal tear, skin laceration, ulcerative keratitis, visual impairment, and visual acuity reduced (each in 1 patient overall)

[a]Aflibercept 8q12 and 8q16 combined.

Non-Ocular TEAEs, APTC Events and Deaths

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n	556	1217
Patients with **≥1 non-ocular TEAE**, n (%)	281 (50.5%)	654 (53.7%)
Non-ocular TEAEs in ≥2% of patients in any treatment group, n (%)		
Hypertension	25 (4.5%)	75 (6.2%)
COVID-19	18 (3.2%)	69 (5.7%)
Nasopharyngitis	21 (3.8%)	43 (3.5%)
Back pain	17 (3.1%)	34 (2.8%)
Headache	10 (1.8%)	28 (2.3%)
Urinary tract infection	15 (2.7%)	28 (2.3%)
Atrial fibrillation	11 (2.0%)	6 (0.5%)
Patients with **≥1 APTC event**, n (%)	11 (2.0%)	18 (1.5%)
Non-fatal stroke	2 (0.4%)	9 (0.7%)
Non-fatal myocardial infarction	5 (0.9%)	5 (0.4%)
Vascular death	4 (0.7%)	4 (0.3%)
Deaths, n (%)	9 (1.6%)	14 (1.2%)

The incidences of non-ocular TEAEs, APTC events, and death were similar across treatment groups

[a]Aflibercept 8q12 and 8q16 combined.

APTC, Anti-Platelet Trialists' Collaboration; **COVID-19**, coronavirus disease 2019.

Serious Non-Ocular TEAEs

	Aflibercept 2 mg pooled	Aflibercept 8 mg pooled[a]
n	556	1217
Patients with **≥1 non-ocular serious TEAE**, n (%)	76 (13.7%)	145 (11.9%)
Non-ocular serious TEAEs in ≥4 patients in any treatment group, n (%)		
Pneumonia	2 (0.4%)	8 (0.7%)
Cerebrovascular accident	2 (0.4%)	7 (0.6%)
Myocardial infarction	3 (0.5%)	5 (0.4%)
Chest pain	1 (0.2%)	5 (0.4%)
COVID-19	1 (0.2%)	5 (0.4%)
Acute kidney injury	1 (0.2%)	5 (0.4%)
Acute respiratory failure	2 (0.4%)	4 (0.3%)
Acute left ventricular failure	4 (0.7%)	3 (0.2%)
Hyponatremia	4 (0.7%)	2 (0.2%)
Urinary tract infection	4 (0.7%)	1 (<0.1%)

The incidences of serious non-ocular TEAEs were similar across treatment groups

[a]Aflibercept 8q12 and 8q16 combined.
APTC, Anti-Platelet Trialists' Collaboration; **COVID-19**, coronavirus disease 2019.

Conclusions

- In this pooled analysis of Year 1 data, aflibercept 8 mg demonstrated similar safety to aflibercept 2 mg
- Incidences of IOI were low and similar between aflibercept 8 mg and aflibercept 2 mg, with no reports of endophthalmitis, occlusive retinal vasculitis, or ischemic optic neuropathy
- There were no relevant differences in incidence of increased IOP between aflibercept 8 mg and aflibercept 2 mg
- Non-ocular events, including serious TEAEs, APTC events, and deaths, were rare and similar between aflibercept 8 mg and aflibercept 2 mg
- This descriptive analysis is limited to the recently reported clinical trials evaluating aflibercept 8 mg in nAMD and DME