A pooled analysis of the CANDELA, PHOTON, and PULSAR trials: Comparably low intraocular inflammation-related events with aflibercept 8 mg and 2 mg

Jordana G. Fein,[1,2] W. Lloyd Clark,[3,4] Justus G. Garweg,[5] Diana V. Do,[6] Jean-Francois Korobelnik,[7,8] Sobha Sivaprasad,[9] Sergio Leal,[10] Alyson J. Berliner,[11] Karen W. Chu,[11] Andreas Stahl,[12] John A. Wells,[3,4] Claudia Tueckmantel,[13] Ajla Dupljak,[11] Maggie Hymowitz,[11] Xin Zhang,[10] Peter Morgan-Warren,[10] April J. McCullough,[11] Anna Portnoy,[11] Ursula M. Schmidt-Ott,[14] on behalf of the CANDELA, PHOTON, and PULSAR study investigators

[1]Retina Group of Washington, Fairfax, VA, USA; [2]Georgetown University School of Medicine, Washington, DC, USA; [3]Palmetto Retina Center, Prima Health Medical Group, Columbia, SC, USA; [3]University of South Carolina School of Medicine Columbia, Columbia, SC, USA; [5]Swiss Eye Institute and Berner Augenklinik, Bern, Switzerland; [6]Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, USA; [7]CHU Bordeaux, Service d'Ophtalmologie, Bordeaux, France; [8]University of Bordeaux, INSERM, Bordeaux Population Health, Bordeaux, France; [9]Moorfields Eye Hospital, London, UK; [10]Bayer Consumer Care AG, Basel, Switzerland; [11]Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; [12]Department of Ophthalmology, University Medicine Greifswald, Greifswald, Germany; [13]Bayer AG, Wuppertal, Germany; [14]Bayer AG, Berlin, Germany

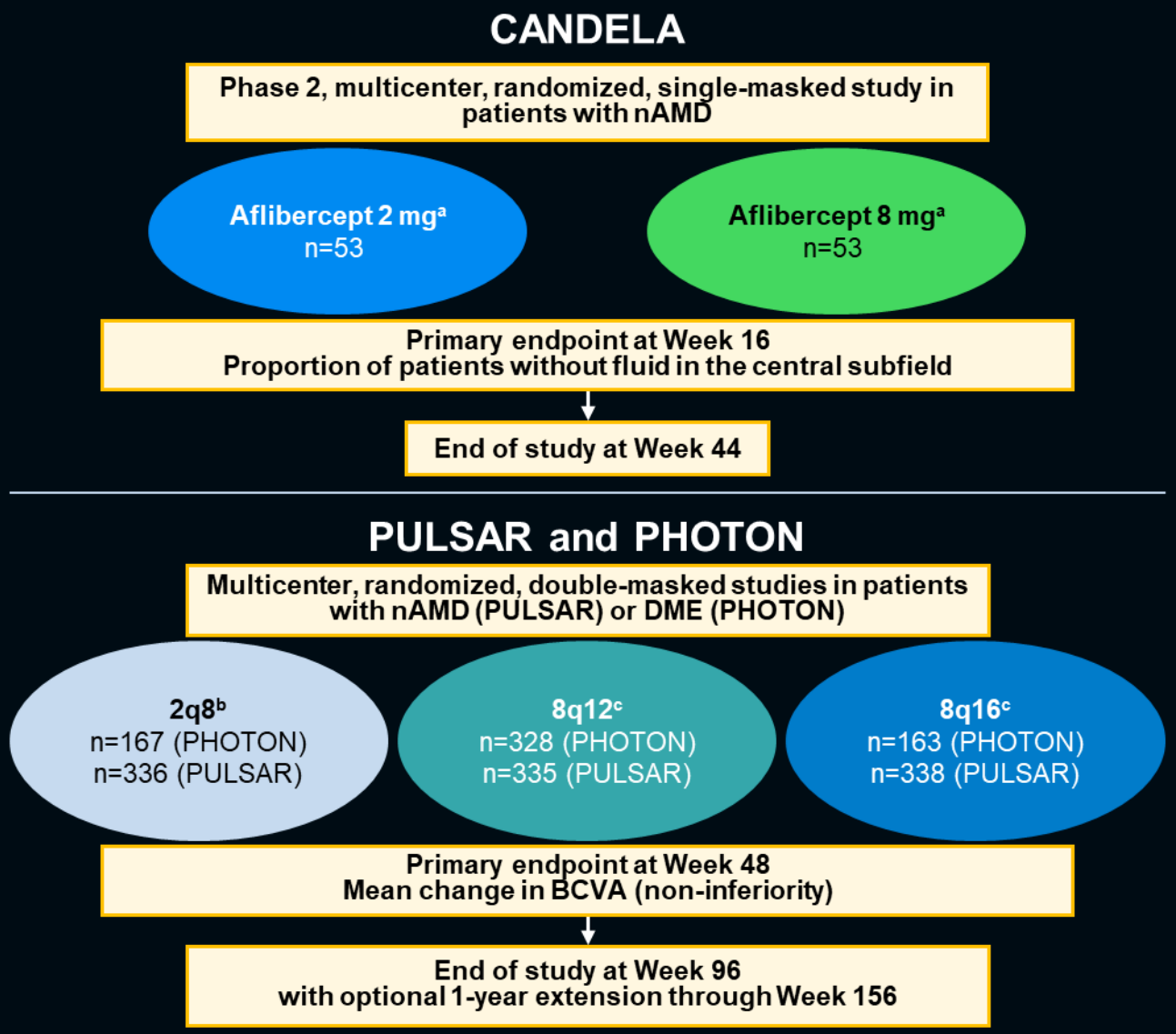
Presented at the American Society of Retina Specialists 43rd Annual Scientific Meeting, Long Beach, CA, USA, July 30–August 2, 2025

Financial Disclosures

- **Jordana G. Fein** has served as a consultant/speaker for Regeneron, Inc., Apellis, Bausch and Lomb, and Genentech/Roche; and has received institutional research funding from Alexion, Apellis, Clearside, Kyowa Kirin, Notal Vision, Ophthea, and Regeneron, Inc.
  - **WLC** is a **c**onsultant for Genentech and Regeneron Pharmaceuticals; has received research support form Genentech; is a speaker for Bayer, Genentech, and Regeneron Pharmaceuticals; and has received travel support from Bayer, Genentech, and Regeneron. **JGG** is a consultant/speaker for AbbVie, Bayer, Novartis, and Roche; and has received research funding from Bayer, Novartis, and Roche. **DVD** is a consultant for Boehringer Ingelheim, Genentech, Kodiak Sciences, Kriya, and Regeneron Pharmaceuticals, Inc.; has received research funding from Boehringer Ingelheim, Genentech, Kriya, and Regeneron Pharmaceuticals, Inc.; and has stock options from Kodiak Sciences. **J-FK** is a consultant for AbbVie, Apellis, Bayer, Carl Zeiss Meditec AG, Eyepoint Pharma, Ocular Therapeutix, Ocuphire, Opthea, Roche, and Théa Pharmaceuticals; and serves on the data safety monitoring/advisory board for Alexion, Novo Nordisk, and Opthea. **SS** has received funding/fees from Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, EyeBiotech, Novartis, Optos, and Roche. **SL** is an employee, investor, and patent holder of Bayer Consumer Care AG. **AJB**, **AD**, **MH**, **AJM**, and **AP** are employees of Regeneron, Inc. **KWC** is a former employee of Regeneron, Inc. **AS** is a consultant for Allergan, Apellis, Bayer, Novartis, and Roche. **JAW** is a consultant for 4DMT, Genentech/Roche, Neurotech, and Ocular Therapeutix; and has received research support from 4DMT, Adverum, Astellas, Aviceda, Bayer, Eyebiotech, Eyepoint, Genentech, Iveric, Kalaris, Kodiak, Lowy MRI, Neurotech, Ocular Therapeutix, Oculis, Opthea, Outlook Therapeutics, Regeneron, and Roche. **CT** is an employee of Bayer AG. **XZ** is an employee and investor of Bayer Consumer Care AG. **PM-W** is an employee of Bayer Consumer Care AG. **UMS-O** was an employee of Bayer AG at the time of the analyses
- The CANDELA and PHOTON studies were sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY), and the PULSAR study was funded by Bayer AG (Leverkusen, Germany). The sponsor participated in the design and conduct of the studies, analysis of the data, and preparation of this presentation
- Study disclosures: These studies include research conducted on human patients; Institutional Review Board approval was obtained prior to study initiation
- The pooled safety analysis of intravitreal aflibercept 8 mg from CANDELA, PHOTON, and PULSAR was previously presented at the ARVO Annual Meeting, May 4–8, 2025, Salt Lake City, UT, USA
- Medical writing support, under the directions of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG, Basel, Switzerland, in accordance with Good Publication Practice (GPP) guidelines (*Ann Intern Med.* 2022;175:1298–1304)

Background and Methods

- The objective of this analysis was to evaluate the safety of aflibercept 8 mg, with a focus on treatment-emergent adverse events associated with IOI through up to 96 weeks in a large patient population
- 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 2/3 **PHOTON trial** in treatment-naïve and previously treated patients with DME
  - Phase 3 **PULSAR trial** in treatment-naïve patients with nAMD



[a]Three initial monthly injections followed by injections at Weeks 20 and 32. [b]After 3 (PULSAR) or 5 (PHOTON) initial monthly injections. [c]After 3 initial monthly injections. **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; **IOI**, intraocular inflammation; **nAMD**, neovascular age-related macular degeneration.

Methods

- Data were pooled through Week 44 of the CANDELA trial and through Week 96 of the PULSAR and PHOTON trials
  - **Overall, safety data for 1773 patients were evaluated**

	Aflibercept 2 mg pooled	8q12	8q16	Aflibercept 8 mg pooled[a]
CANDELA, n	53	53	0	53
PULSAR, n	336	335	338	673
PHOTON, n	167	328	163	491
Total, n	**556**	716	501	**1217**

Safety analysis set. TEAEs of IOIs and severity grading were reported at the discretion of the investigators. **TEAE**, treatment-emergent adverse event.
[a]Aflibercept 8q12 and 8q16 combined.

Baseline Demographics and Aflibercept Exposure in the Pooled Safety Analysis

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled[a] (n=1217)
Baseline demographics		
Female, n (%)	299 (53.8)	574 (47.2)
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)
White, n (%)	412 (74.1)	927 (76.2)
Hispanic or Latino, n (%)	47 (8.5)	106 (8.7)
Aflibercept exposure		
Total number of injections	**6464**	**10,067**
Number of injections, mean (SD)	**11.6 (3.1)**	**8.3 (2.1)**
Treatment duration (weeks), mean (SD)	**84.1 (24.5)**	**86.8 (22.6)**

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

IOI-related Events in the Study Eye

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled[a] (n=1217)
Patients with ≥1 IOI-related event, n (%)	**9 (1.6)**	**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)[b]
Endophthalmitis	2 (0.4)	0
Eye inflammation	1 (0.2)	0
Hypopyon	1 (0.2)	0
Severity of IOI-related events, n (%)		
Mild	7 (1.3)	12 (1.0)
Moderate	1 (0.2)	4 (0.3)
Severe	1 (0.2)[c]	0

Safety analysis set. [a]Aflibercept 8q12 and 8q16 combined. [b]The event was considered mild and neither treatment- nor procedure-related; the dose and treatment were not changed, no remedial therapy was documented, and the patient had not recovered at the time of the analysis. [c]The patient experienced endophthalmitis; the event was considered related to be injection procedure but not treatment-related. Therapy was interrupted, remedial therapies were provided, and the patient recovered.

Treatment Status of Patients with IOI-related Events in the Study Eye

	Aflibercept 2 mg pooled (n=556)	Aflibercept 8 mg pooled[a] (n=1217)
Patients recovered or recovering from IOI-related event, n/N[b] (%)	7/9 (77.8)	11/16 (69.0)
Treatment status of patients after IOI-related event, n/N[b] (%)		
No Change	4/9 (44.4)	12/16 (75.0)[c]
Treatment interrupted	4/9 (44.4)	1/16 (6.3)
Treatment withdrawn	1/9 (11.1)[d]	2/16 (12.5)[e]
Treatment plan/study ended	0/9 (0)	1/16 (6.3)

Visual outcomes were comparable between the treatment groups for patients with IOI-related events, with mean (SD) BCVA changes from baseline to Week 96 of +0.3 (12.3) and +0.9 (14.3) letter improvements for the aflibercept 2 mg and aflibercept 8 mg groups, respectively

Safety analysis set. [a]Aflibercept 8q12 and 8q16 combined. [b]N=the number of patients with IOI-related events. [c]Three patients developed the same IOI-related event twice, both events of which recovered or resolved: aflibercept 2 mg group (vitreal cells n=1, eye inflammation n=1) and aflibercept 8 mg group (iritis n=1). [d]The patient developed a moderate case of uveitis, received remedial therapy, and their recovery status was not available at the time of the analysis. [e]One patient developed a moderate case of iridocyclitis, received remedial treatment, and had not recovered at the time of the analysis; one patient developed a moderate case of iritis, received remedial treatment, and had recovered at the time of the analysis.

Conclusions

Incidence of IOI-related events	• Incidence of IOI-related events with aflibercept 8 mg was **low and comparable** to that for aflibercept 2 mg • **No cases of endophthalmitis were reported** with aflibercept 8 mg and 2 cases of endophthalmitis were reported with aflibercept 2 mg
Severity of IOI-related events	• **Most IOI-related events were mild in severity** for both aflibercept 8 mg and 2 mg, with 1 case of severe IOI-related event reported with aflibercept 2 mg • **Most patients** receiving aflibercept 8 mg and 2 mg who developed IOI-related events **had recovered or were recovering** at the completion of the trials
Safety profile	• The findings from this pooled analysis of IOI-related safety data **further support the safety profile of aflibercept 8 mg**