PULSAR Extension: Clinical Improvements Sustained Over 156 Weeks With Aflibercept 8 mg in Patients With Neovascular Age-Related Macular Degeneration

David T. Wong,[1] Timothy Y.Y. Lai,[2] Tien Y. Wong,[3,4] Paolo Lanzetta,[5,6] Jean-François Korobelnik,[7,8] Frank G. Holz,[9] Taiji Sakamoto,[10] Sobha Sivaprasad,[11] Andrea Schulze,[12] Ursula M. Schmidt-Ott,[12] Xin Zhang,[13] Alyson J. Berliner,[14] Karen W. Chu,[14] Sergio Leal[13] on behalf of the PULSAR Extension investigators

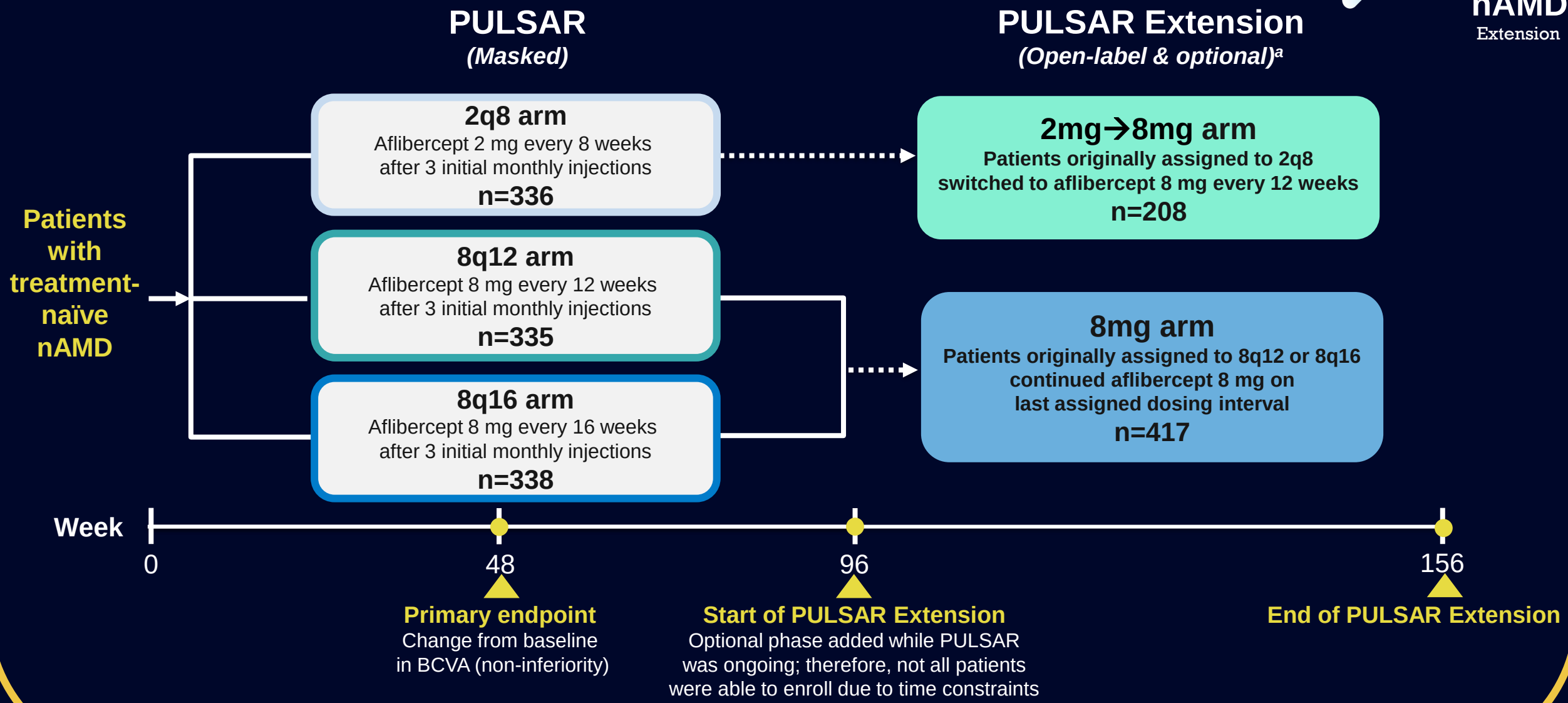
[1]Unity Health Toronto – St. Michael's Hospital, University of Toronto, Toronto, ON, Canada; [2]Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong, [3]Tsinghua Medicine, Tsinghua University, Beijing, China; [4]Singapore Eye Research Institute, Singapore National Eye Centre, Singapore; [5]Department of Medicine – Ophthalmology, University of Udine, Udine, Italy; [6]Istituto Europeo di Microchirurgia Oculare (IEMO), Udine-Milan, Italy; [7]CHU Bordeaux, Service d'Ophtalmologie, Bordeaux, France; [8]Univ. Bordeaux, INSERM, BPH, UMR1219, F-33000, Bordeaux, France; [9]Department of Ophthalmology, University of Bonn, Bonn, Germany; [10]Department of Ophthalmology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan; [11]NIHR Moorfields Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UK; [12]Bayer AG, Berlin, Germany; [13]Bayer Consumer Care AG, Basel, Switzerland; [14]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

Presented at the Retina World Congress (RWC), Fort Lauderdale, FL, USA, May 8–11, 2025

Disclosures

- **David T. Wong:** Research grants from AbbVie, Alcon, Apellis, ArcticDX, Bausch Health, Bayer, Biogen, Boehringer Ingelheim, Novartis, Ripple Therapeutics, Roche, Topcon, Zeiss, and 20/20 Innovation Hub
  - **TYYL:** Research grants from Bayer, Chengdu Kanghong Biotech, Novartis, and Roche; consulting fees from Astellas, Bayer, Boehringer Ingelheim, Iveric Bio/Astellas Pharma, Novartis, Ocular Therapeutix, Oculis, and Roche; and lecture fees from Alcon, Bayer, Chengdu Kanghong Biotech, Gaush Meditech, Novartis, and Roche. **TYW:** Consulting fees from Aldropika Therapeutics, Bayer, Boehringer Ingelheim, Eden Ophthalmic, Genentech, Iveric Bio/Astellas Pharma, Novartis, Oxurion, Plano, Roche, Sanofi, Shanghai Henlius, and Zhaoke Pharmaceutical; and holds patents and is the co-founder of EyRiS and Visre. **PL:** Consulting fees from Aerie, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Genentech, I-Care, Novartis, Outlook Therapeutics, and Roche. **JFK:** Consulting fees from AbbVie, Apellis, Bayer, Eyepoint Pharma, Ocuphire, Ocular Therapeutix, Opthea, Roche, Thea, and Carl Zeiss Meditec; and member of a data safety monitoring board for Alexion, Novo Nordisk, and Opthea. **FGH:** Grants from Acucela, Allergan, Apellis, Bayer, Belite Bio, Bioeq, Centervue, Geuder, Heidelberg Engineering, Iveric Bio/Astellas Pharma, NightStarx, Novartis, Roche/Genentech, and Zeiss; and consulting fees from Acucela, Alcon, Alexion, Alzheon, Apellis, Bayer, Boehringer Ingelheim, Janssen, Genentech/Roche, Grayburg Vision, Heidelberg Engineering, Iveric Bio/Astellas Pharma, Lin Bioscience, Novartis, Oculis, Oxurion, PixiumScience, Stealth Biotherapeutics, and Zeiss. **TS:** Consulting fees from Bayer, Boehringer Ingelheim, Chugai/Roche, Novartis, and Senju. **SS:** Consulting fees from AbbVie, Alimera Science, Amgen, Astellas, Bayer, Biogen, Boehringer Ingelheim, Clearside Biomedical, Eyebiotech, Eyepoint Phamaceuticals, Iveric Bio/Astellas Pharma, Janssen Pharmaceuticals, Kriya Therapeutics, Nova Nordisk, Ocular Therapeutix, OcuTerra, Optos, Ripple Therapeutics, Roche, Stealth Biotherapeutics, and Sanofi. **AJB** and **KWC:** Employees and stockholders of Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA. **XZ** and **SL:** Employees of Bayer Consumer Care AG, Basel, Switzerland. **AS** and **UMS-O:** Employees and stockholders of Bayer AG, Berlin, Germany
- The PULSAR study (NCT04423718) was sponsored by Bayer AG (Leverkusen, Germany) and co-funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this presentation
- Study disclosures: This study includes research conducted on human patients, and Institutional Review Board approval was obtained prior to study initiation
- The data in this presentation were originally presented at the Angiogenesis 2025 Virtual Edition, February 8, 2025
- Medical writing support, under the direction of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG (Basel, Switzerland), in accordance with Good Publication Practice (GPP) guidance (*Ann Intern Med* 2022;175:1298–1304)

PULSAR Extension Design



[a]To be eligible for the Extension phase, patients had to have ≥1 BCVA and CRT assessments between Week 84 and Week 92.
BCVA, best-corrected visual acuity; **CRT**, central subfield retinal thickness; **nAMD**, neovascular age-related macular degeneration.

PULSAR Extension Design

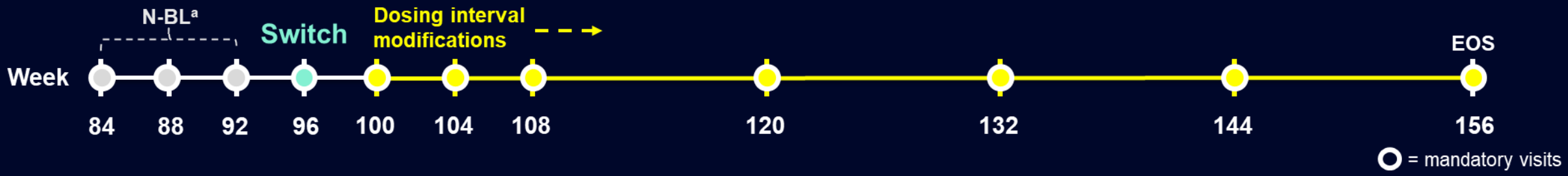
pulsar nAMD Extension

2mg→8mg
n=208

Patients initially treated with aflibercept 2q8 were switched to aflibercept 8 mg at Week 96 and immediately assigned to a 12-week dosing interval

8mg
n=417

Patients initially treated with aflibercept 8q12 or 8q16 continued with aflibercept 8 mg at their last assigned dosing interval



E-DRM: Interval Shortening During Year 3

- Patients were assessed at ***any visit*** beginning at Week 100
- **Criteria for interval shortening:**
  - >5-letter loss in BCVA from N-BL due to persistent or worsening nAMD **AND** either:
    - >25 µm increase in CRT from N-BL **OR**
    - New onset of foveal neovascularization **OR**
    - New foveal hemorrhage
  - **OR** >10-letter loss in BCVA from N-BL due to worsening nAMD
- Dosing intervals shortened by **2-week** increments to a **minimum of Q8**

E-DRM: Interval Extension During Year 3

- Patients were assessed at ***dosing visits*** beginning at Week 100
- **Criteria for interval extension:**
  - <5-letter loss in BCVA from N-BL **AND**
  - No fluid (IRF or SRF) in the central subfield on OCT **AND**
  - No new onset foveal neovascularization or foveal hemorrhage
- Dosing intervals extended by **2-week** increments to a **maximum of Q24**

[a]N-BL was an average of values from Weeks 84, 88, and 92. **BCVA**, best-corrected visual acuity; **CRT**, central subfield retinal thickness; **E-DRM**, dosing regimen modification criteria during the PULSAR Extension; **EOS**, end of study; **IRF**, intraretinal fluid; **SRF**, subretinal fluid; **N-BL**, new baseline; **OCT**, optical coherence tomography; **Q8**, every 8 weeks; **Q24**, every 24 weeks.

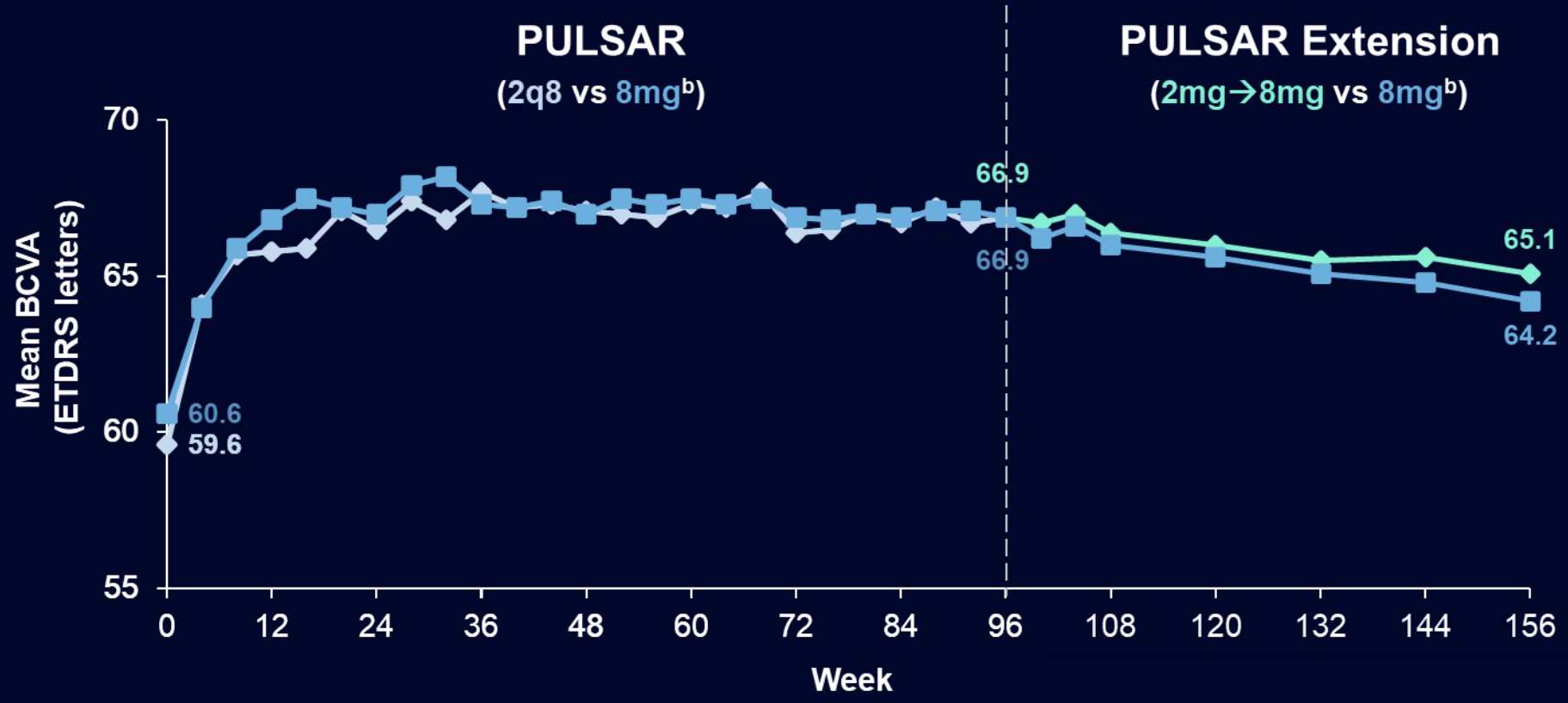
Patient Disposition & Baseline Characteristics

pulsar nAMD Extension

	PULSAR	PULSAR Extension		
	Total	2mg→8mg	8mg	Total
Patients entering PULSAR study (FAS), n	1009	–	–	–
Patients entering PULSAR Extension (eFAS), n (%)	–	208 (61.9)[a]	417 (62.0)[a]	625 (61.9)[a]
Completion rate at Week 96, %	85.9	–	–	–
Completion rate at Week 156, %	–	89.9[b]	90.4[b]	90.2[b]
Age (years)	74 (8.4)	73.9 (8.2)	74.0 (8.1)	74.0 (8.1)
Female, %	54.5	58.7	55.2	56.3
Race, %				
White	75.8	77.4	77.5	77.4
Black or African American	0.4	0.5	0.5	0.5
Asian	23.2	22.1	21.1	21.4
Other[c]	0.6	0	1.0	0.6
History of hypertension, %	64.3	63.0	65.0	64.3
BCVA (ETDRS letters)	59.6 (13.3)	59.6 (13.7)	60.6 (12.7)	60.3 (13.0)
CRT (μm)[d]	369 (130)	365 (139)	375 (132)	371 (134)
Total lesion area, mm^2	6.7 (5.4)	6.8 (5.0)	6.4 (5.2)	6.6 (5.1)
Lesion type, %				
Occult	58.2	57.7	57.1	57.5
Predominantly classic	20.7	23.1	22.4	18.8
Minimally classic	18.6	15.9	18.1	20.3

Data are mean±SD unless otherwise stated; data are for patients in the FAS (PULSAR) and eFAS (PULSAR Extension) at the main study baseline. [a]Proportions were calculated based on the number of patients who initially entered the main PULSAR study. [b]Completion rate for PULSAR Extension based on eFAS. [c]Other includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple races, and unreported race. [d]Data as assessed by reading center. **eFAS**, PULSAR Extension FAS; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set, **SD**, standard deviation.

Mean BCVA[a] Through Week 156



Mean number of injections from baseline to Week 96[c]

2q8: 12.8

8q12/8q16: 8.9

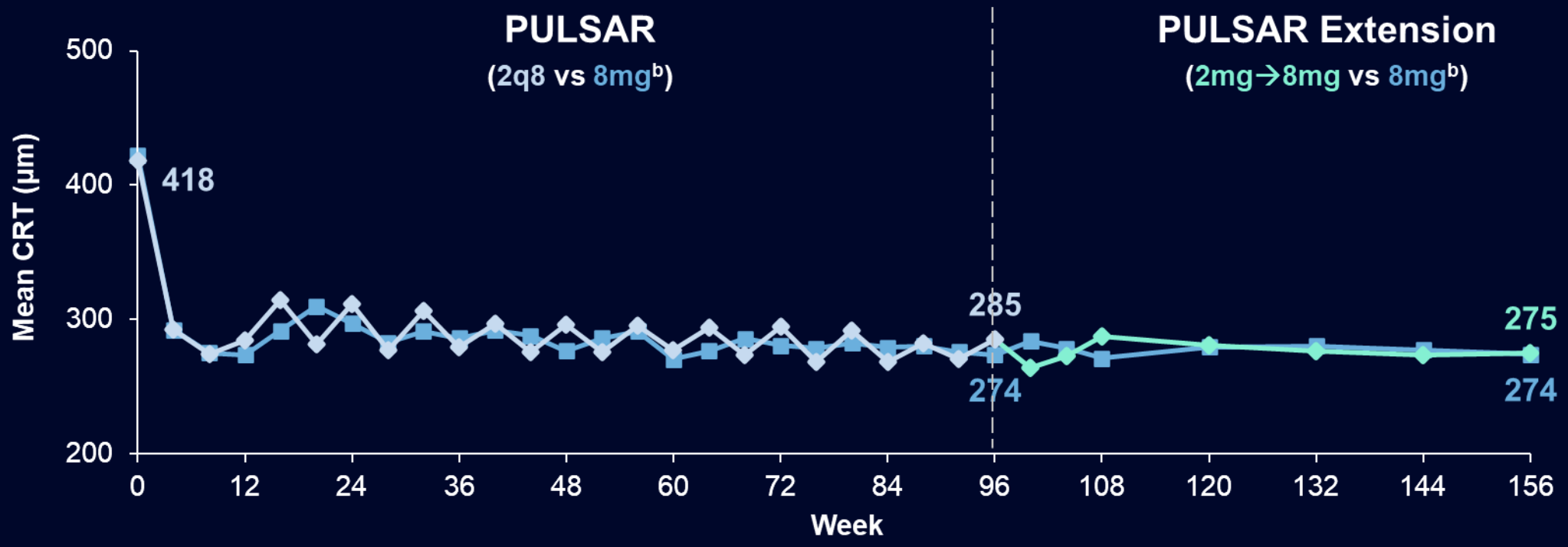
Mean number of injections from Week 96 to Week 156[c]

2mg→8mg: 4.7

8mg: 3.8

Note: At Week 156, the 2mg→8mg group (n=208) and 8mg group (n=417) reported a LS mean change (MMRM) from baseline in BCVA of +4.6 and +3.4 letters, respectively. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF.
eSAF, safety analysis set in the PULSAR Extension; **LS**, least squares; **MMRM,** mixed model for repeated measures, used to generate least square means for the eFAS with baseline BCVA as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and baseline BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and baseline BCVA and the interaction between visit and treatment.

Mean CRT[a] Through Week 156



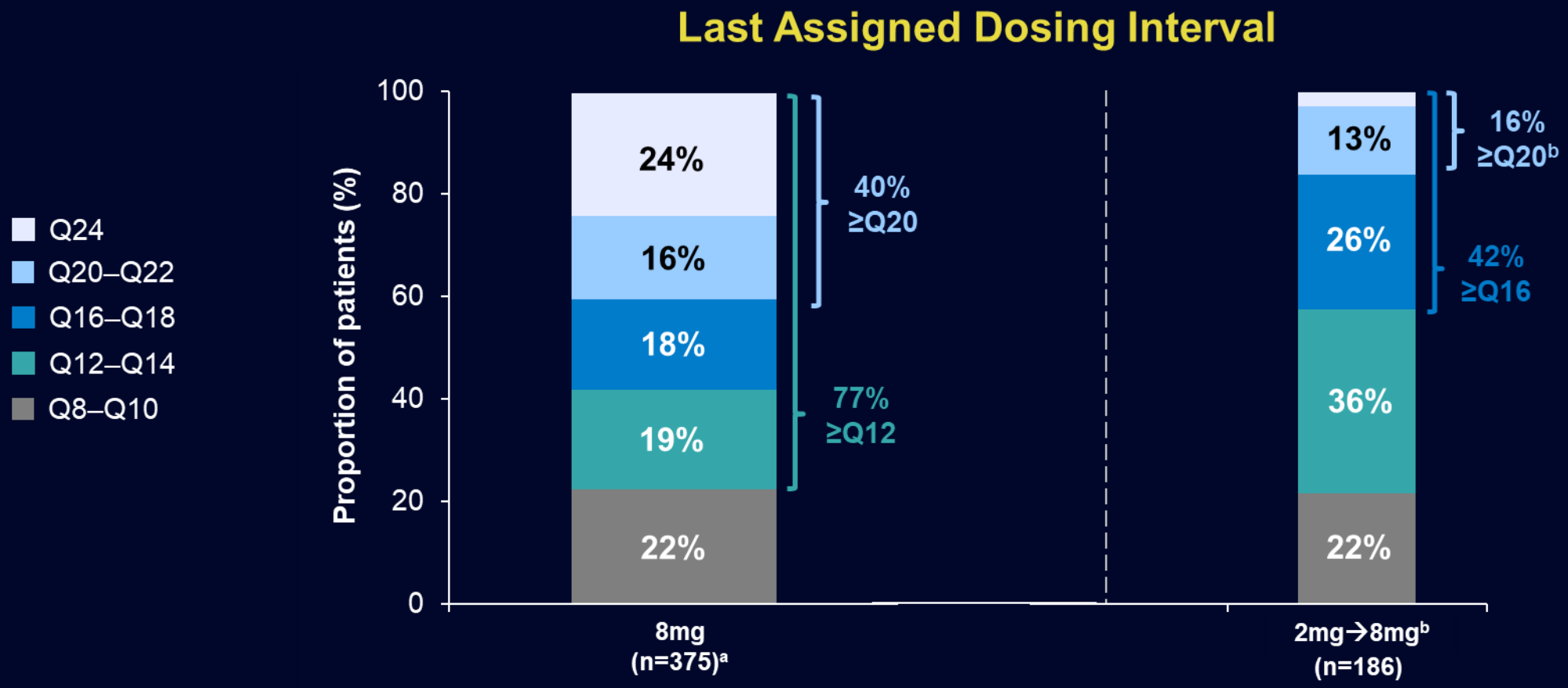
LS mean CRT change (95% CI) from baseline[c]

Week	2mg→8mg (n=208)	8mg (n=417)
48	−125 (−137, −113)	−145 (−152, −137)
96	−135 (−145, −125)	−147 (−154, −141)
156	−145 (−155, −136)	−148 (−156, −140)

[a]eFAS (observed cases); data as assessed by study investigators. [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]LS means were generated for the eFAS using a mixed model for repeated measures with baseline CRT as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and baseline BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and baseline CRT and the interaction between visit and treatment. **CI**, confidence intervals; **LS**, least squares.

Majority of Aflibercept 8 mg-Treated Patients Assigned Extended Dosing Intervals at Week 156

pulsar nAMD Extension



eSAF, patients completing Week 156. Values may not add up to 100% due to rounding. [a]One patient had a missing value for this assessment. [b]Per protocol, patients in the 2mg→8mg group did not have sufficient time to achieve a last assigned dosing interval of >Q20 by Week 156; patients misassigned to longer dosing intervals are included for completeness.

Ocular and Non-Ocular Safety From Main Baseline Through Week 156[a]

pulsar nAMD Extension

	2mg→8mg	8mg	Total
N (eSAF)	208	417	625
Ocular TEAEs, n (%)	130 (62.5)	251 (60.2)	381 (61.0)
Serious ocular TEAEs, n (%)	7 (3.4)	21 (5.0)	28 (4.5)
Serious non-ocular TEAEs, n (%)	43 (20.7)	106 (25.4)	149 (23.8)
Intraocular inflammation, n (%)	5 (2.4)	8 (1.9)	13 (2.1)
APTC events, n (%)	4 (1.9)	7 (1.7)	11 (1.8)
Deaths, n (%)	4 (1.9)	9 (2.2)	13 (2.1)

[a]Cumulative events in the study eye from the main PULSAR study baseline through Week 156.
APTC, Anti-Platelet Trialists' Collaboration; **TEAE**, treatment-emergent adverse event.

PULSAR Extension: Key Week 156 Results

- In the PULSAR Extension, functional and anatomic improvements were sustained through Week 156 in the **2mg→8mg and 8mg groups**
  - Patients in the **2mg→8mg group** achieved these improvements with **extended dosing intervals** and a **mean of 4.7 injections** from Week 96 through Week 156
- These findings suggest that patients with treatment-naïve nAMD can achieve **durable improvements with aflibercept 8 mg** administered over extended dosing intervals
- The safety profile of aflibercept 8 mg was comparable with that of aflibercept 2 mg