Clinical Outcomes with Aflibercept 8 mg and Aflibercept 2 mg are Generally Comparable in Patients Grouped by CNV Type: A Post hoc Analysis of the 96-Week PULSAR Trial

Sobha Sivaprasad,[1] Marion R. Munk,[2–4] Michael W. Stewart,[5] Justus G. Garweg,[6] Amitha Domalpally,[7] Sergio Leal,[8] Tobias Machewitz,[9] Xin Zhang[8] on behalf of the PULSAR study investigators

[1]NIHR Moorfields Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, UK; [2]Augenarzt-Praxisgemeinschaft Gutblick AG, Pfäffikon, Switzerland; [3]Department of Ophthalmology, University Hospital, Bern, Switzerland; [4]Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [5]Mayo Clinic College of Medicine and Science, Department of Ophthalmology, Mayo Clinic, Jacksonville, FL, USA; [6]Swiss Eye Institute and Clinic for Vitreoretinal Diseases, Berner Augenklinik, Bern, Switzerland; [7]Wisconsin Reading Center, University of Wisconsin-Madison, Madison, WI, USA; [8]Bayer Consumer Care AG, Basel, Switzerland; [9]Bayer AG, Berlin, Germany

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

Disclosures

pulsar
nAMD

- **Sobha Sivaprasad:** Consulting fees from AbbVie, Alimera Science, Amgen, Astellas, Bayer, Biogen, Boehringer Ingelheim, Clearside Biomedical, Eyebiotech, Eyepoint Pharmaceuticals, Iveric Bio, Janssen Pharmaceuticals, Novo Nordisk, Optos, Ocular Therapeutix, Kriya Therapeutics, OcuTerra, Ripple Therapeutics, Roche, Stealth Biotherapeutics, and Sanofi
  - **MRM:** Consulting fees from AbbVie, Allergan, Apellis, Aviceda Therapeutics, Bayer, Boehringer Ingelheim, Dandelion, Eyepoint, Gensight, Iveric Bio, Isarna Therapeutics, Kubota, Lumithera, Novartis, Oculis, Ocular Therapeutix, Ocuterra, RetinAI, Roche, and Zeiss. **MWS:** Funding from Allergan, Chengdu Kanghong Pharmaceutical Group, and Regeneron Pharmaceuticals, Inc.; and consulting fees from Alkahest, Biogen, Regeneron, and Bayer. **JGG:** Consultant/speaker for AbbVie, Bayer, Novartis, and Roche; and research funding from Bayer, Novartis, and Roche. **AD:** No disclosures. **SL** and **XZ:** Employees of Bayer Consumer Care AG. **TM:** Employee of Bayer AG
- The PULSAR study (NCT04423718) was sponsored by Bayer AG (Leverkusen, Germany) and co-funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA). The sponsors 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 ARVO Congress, Salt Lake City, UT, USA, May 4–8, 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)

Background and Methods

pulsar nAMD

PULSAR: Multicenter, Randomized, Double-masked

- **2q8** n=336
- **8q12** n=335
- **8q16** n=338

	YEAR 1													YEAR 2										
	Day 1	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48	W52	W56	W60	W64	W68	W72	W76	W80	W84	W88	W92	W96
2q8	X	X	X		X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	–
8q12	X	X	X		o[a]	X[a]	o	o	X[a]	o	o	X[a]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	–
8q16	X	X	X		o[a]	o[a]	X[a]	o	o	o	X[a]	o	o	o	X[a,b]	o	o	o	X[a,b]	o	o	o	X[a,b]	o	–

Primary endpoint at W48: Mean change in BCVA (non-inferiority)

End of study at W96 with optional ~1-year extension through W156

[a]DRM: Interval Shortening During Years 1 and 2

Criteria for interval shortening

- >5-letter loss in BCVA compared with **Week 12** due to persistent or worsening nAMD **AND**
- >25 µm increase in CRT compared with **Week 12**, **OR** new foveal neovascularization, **OR** new foveal hemorrhage

- Patients who met DRM criteria had dosing intervals shortened to q8 at **Weeks 16** and **20** or by 4-week increments from **Week 24**
  - The minimum assigned dosing interval was q8

[b]DRM: Interval Extension During Year 2

Criteria for interval extension

- <5-letter loss in BCVA compared with **Week 12 AND**
- No fluid at the center subfield on OCT **AND**
- No new foveal hemorrhage or foveal neovascularization

- Patients who met DRM criteria from **Weeks 52 through 96** had dosing intervals extended by 4-week increments
  - The maximum assigned dosing interval was q24

Stippled boxes = initial treatment phase; X = active injection; o = sham injections.
2q8, aflibercept 2 mg every 8 weeks after 3 initial monthly injections; **8q12**, aflibercept 8 mg every 12 weeks after 3 initial monthly injections; **8q16**, aflibercept 8 mg every 16 weeks after 3 initial monthly injections; **q8**, every 8 weeks; **q24**, every 24 weeks; **BCVA,** best-corrected visual acuity; **CRT**, central subfield retinal thickness; **DRM**, dose regimen modification; **nAMD**, neovascular age-related macular degeneration; **OCT**, optical coherence tomography; **W**, week.

Baseline Demographics and Disease Characteristics of the CNV Type Subgroups

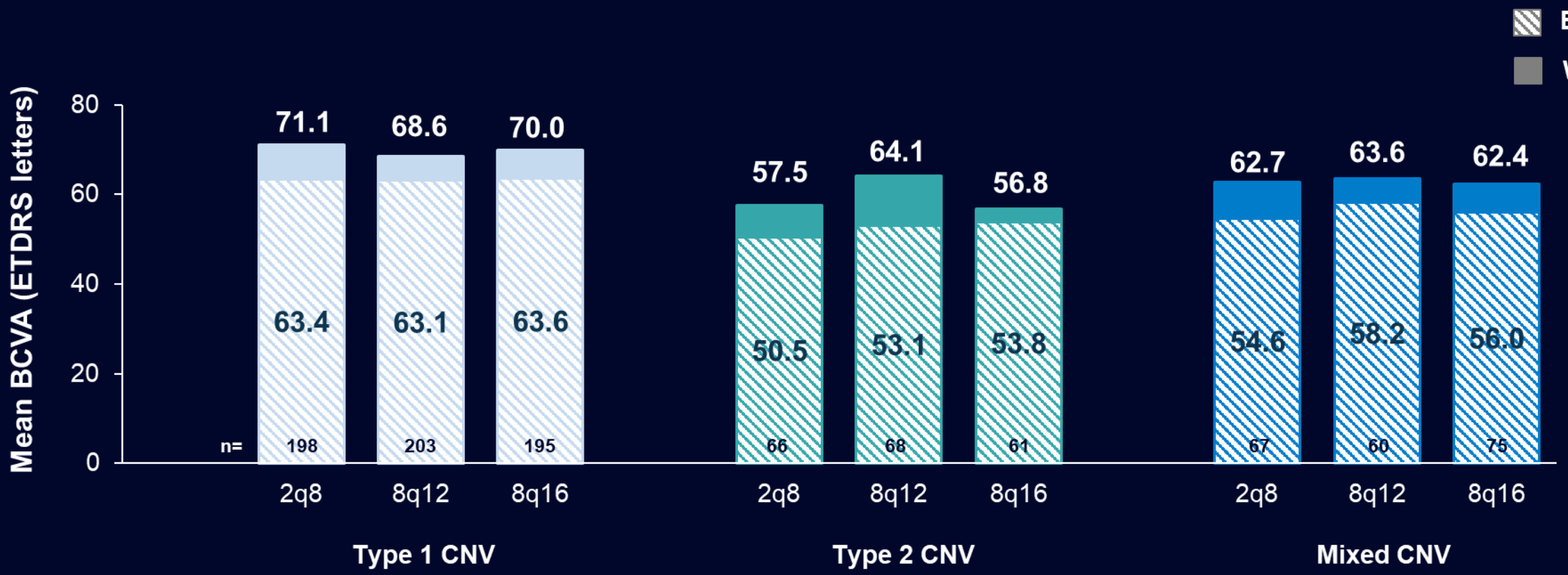
pulsar nAMD

CNV Type		2q8	8q12	8q16
Type 1 n=596 (59.1%)	n	198	203	195
	Female, %	58.1	57.6	54.4
	BCVA, ETDRS letters (SD)	63.4 (11.9)	63.1 (12.4)	63.6 (11.4)
	CRT, µm (SD)	327 (108)	338 (107)	338 (119)
	CNV size, mm^2 (SD)	7.1 (5.3)	6.3 (4.5)	7.0 (5.5)
Type 2 n=195 (19.3%)	n	66	68	61
	Female, %	50.0	50.0	50.8
	BCVA, ETDRS letters (SD)	50.5 (15.0)	53.1 (12.8)	53.8 (12.6)
	CRT, µm (SD)	442 (148)	429 (140)	419 (155)
	CNV size, mm^2 (SD)	3.6 (3.1)	3.2 (3.6)	3.1 (3.9)
Mixed[a] n=202 (20.0%)	n	67	60	75
	Female, %	53.7	46.7	52.0
	BCVA, ETDRS letters (SD)	54.6 (13.7)	58.2 (12.6)	56.0 (11.7)
	CRT, µm (SD)	406 (141)	398 (114)	416 (126)
	CNV size, mm^2 (SD)	6.9 (4.9)	8.0 (5.7)	8.2 (5.6)
Type 3 n=14 (1.4%)	n	5	4	5

FAS. [a]Mixed CNV type consists of Type 1 and Type 2 CNV types.
CNV, choroidal neovascularization type; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set; **SD**, standard deviation.

Mean BCVA at Baseline and Week 96

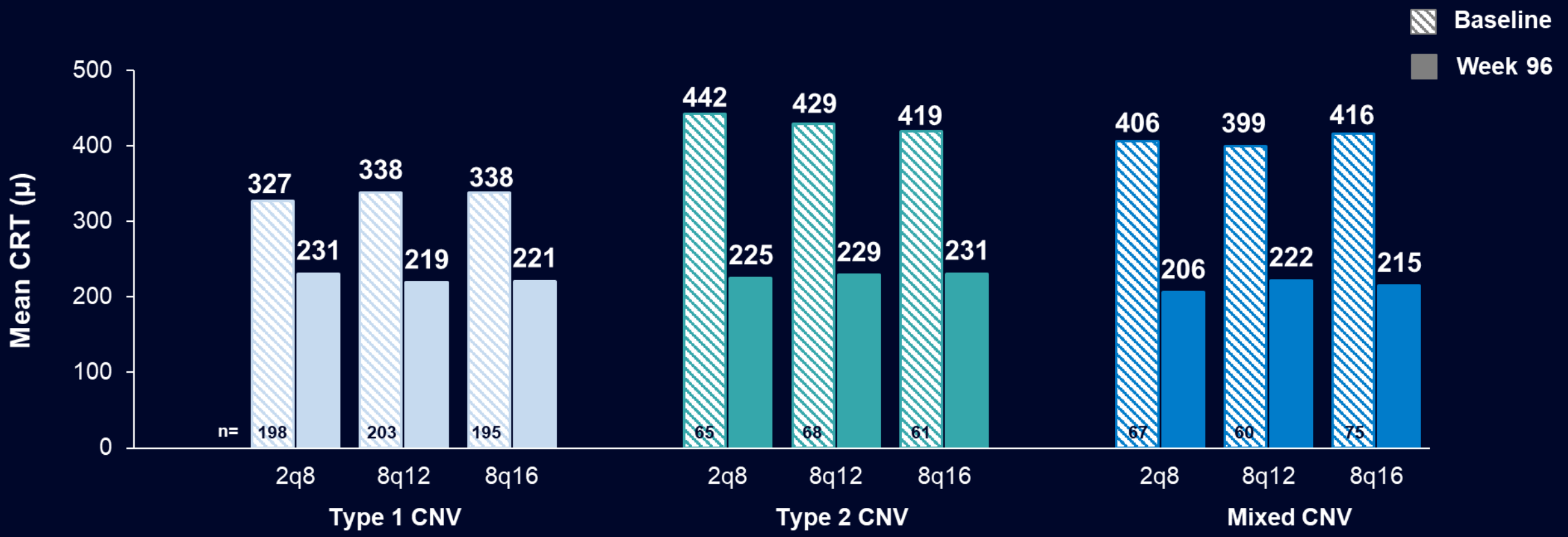
pulsar
nAMD



FAS (observed cases prior to intercurrent events); n values represent the number of patients at baseline. LS mean changes[a] from baseline at Week 96 in the 2q8, 8q12, and 8q16 arms were 6.6, 4.0, and 5.8 letters for Type 1, 6.5, 10.3, and 3.6 letters for Type 2, and 7.3, 5.7, and 6.7 letters for Mixed, respectively. [a]LS mean values were generated using MMRM, with baseline BVCA measurement as a covariate, and treatment group (aflibercept 2q8, 8q12, 8q16), visit, and stratification variables (geographic region [Japan vs Rest of World] and baseline BCVA [<60 vs ≥60]) as fixed factors, and interaction terms for baseline and visit and for treatment and visit.
LS, least squares; **MMRM**, mixed model repeated measures.

Mean CRT at Baseline and Week 96

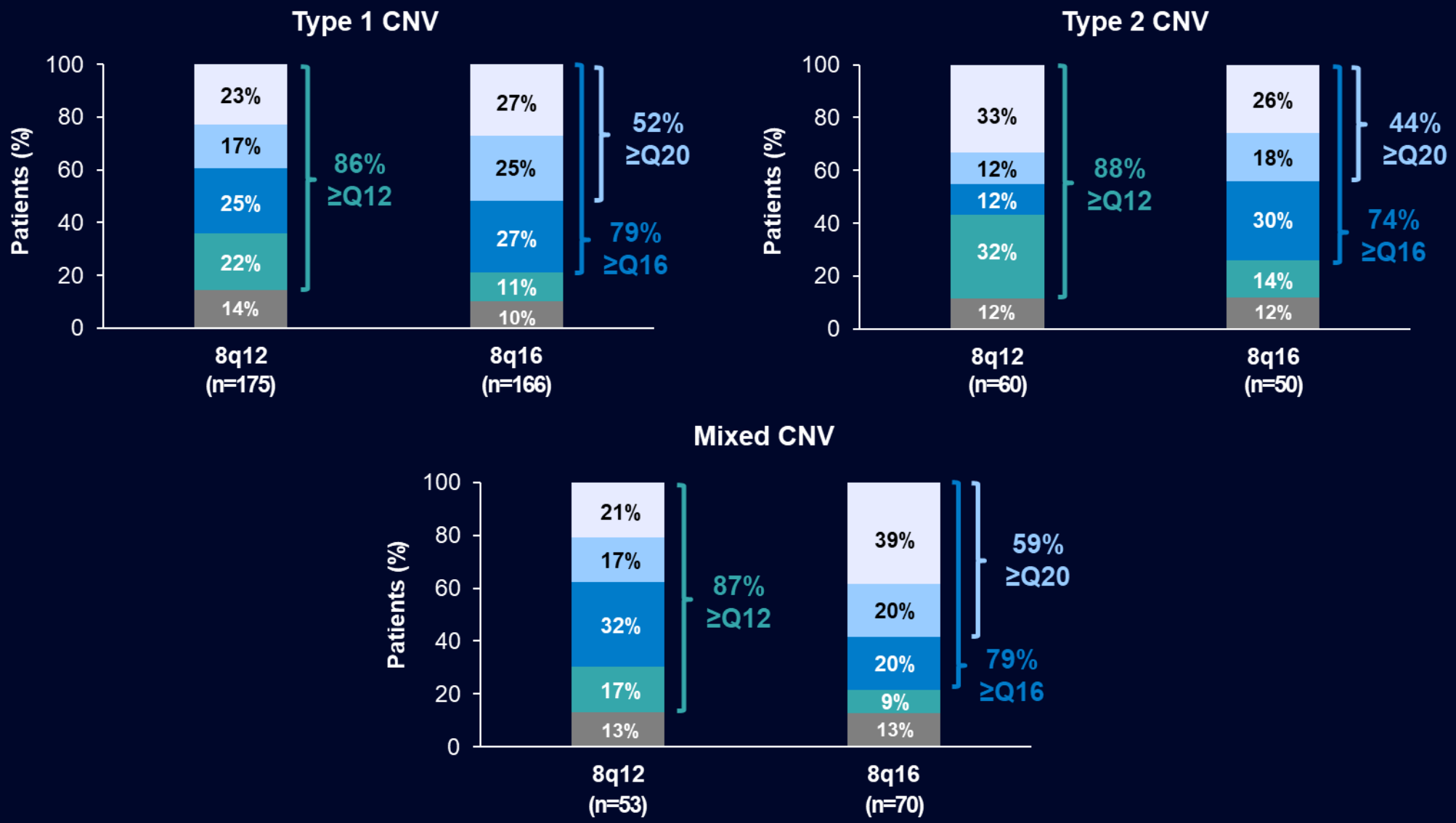
pulsar
nAMD



FAS (observed cases prior to intercurrent events); n values represent the number of patients at baseline. LS mean changes[a] from baseline at Week 96 in the 2q8, 8q12, and 8q16 arms were −104, −116, and −116 µm for Type 1, −201, −202, and −194 µm for Type 2, and −196, −181, and − 181 µm for Mixed, respectively. [a]LS mean values were generated using MMRM, with baseline CRT measurement as a covariate, and treatment group (aflibercept 2q8, 8q12, 8q16), visit, and stratification variables (geographic region [Japan vs Rest of World] and baseline BCVA [<60 vs ≥60]) as fixed factors, and interaction terms for baseline and visit and for treatment and visit.

Last Assigned Dosing Interval at Week 96

pulsar nAMD



FAS, patients completing Week 96. Values may not add up to 100% due to rounding.

Safety Through Week 96 by CNV Type

pulsar nAMD

		2q8	All 8 mg
Type 1 CNV	N (SAF)	198	398
	≥1 Ocular TEAEs, n (%)	102 (51.5)	205 (51.5)
	≥1 Serious ocular TEAEs, n (%)	3 (1.5)	10 (2.5)
	≥1 Non-ocular TEAEs, n (%)	156 (78.8)	294 (73.9)
Type 2 CNV	N (SAF)	66	129
	≥1 Ocular TEAEs, n (%)	37 (56.1)	71 (55.0)
	≥1 Serious ocular TEAEs, n (%)	0	3 (2.3)
	≥1 Non-ocular TEAEs, n (%)	48 (72.7)	96 (74.4)
Mixed CNV	N (SAF)	67	135
	≥1 Ocular TEAEs, n (%)	38 (56.7)	66 (48.9)
	≥1 Serious ocular TEAEs, n (%)	1 (1.5)	7 (5.2)
	≥1 Non-ocular TEAEs, n (%)	49 (73.1)	103 (76.3)

- Safety profiles of aflibercept 2 mg and 8 mg were comparable in each of the CNV type subgroups
- Overall, the most common ocular TEAEs were cataract, retinal hemorrhage, reduced visual acuity, and vitreous floaters
  - The most common serious ocular TEAEs were retinal detachment (n=6), retinal hemorrhage (n=5), and cataract (n=4)

TEAE, treatment-emergent adverse event.

Conclusions

pulsar
nAMD

- **Improvements in BCVA and CRT** were observed at Week 96 with aflibercept 8q12, 8q16, and 2q8 **across all baseline CNV types**
- Larger variability was observed in subgroups of smaller size, limiting interpretability
- **Safety outcomes were comparable** for **aflibercept 8 mg and 2 mg** for all CNV type subgroups