PULSAR Extension: Week 156 outcomes with aflibercept 8 mg in patients with nAMD grouped by baseline BCVA, CRT, and MNV lesion type

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Disclosures

- **Rufino Silva:** Consultant for Bayer and Roche; member of advisory board for Alimera, Bayer, Novartis, Roche, and Thea
    - **LK:** Consultant for AbbVie, Alimera-Horus, Bayer, Celltrion Inc., Krys, MS Pharma, Novartis, Roche, and Thea. **JGG:** Consultant/speaker for AbbVie, Bayer, Novartis, and Roche; and has received research funding from Bayer, Novartis, and Roche. **PL:** Consulting fees from 4DMT, Aerie Pharmaceuticals, Adverum, Allergan, Annexon, Apellis, Bausch + Lomb, Bayer, Biogen, Boehringer Ingelheim, EyePoint Pharmaceuticals, Genentech, I-Care, Novartis, Ocular Therapeutix, Outlook Therapeutics, Roche, and TowardPi. **MWS:** Consultant for Alkahest and Bayer; receives funding from Allergan, Kanghong, and Regeneron. **RG:** Consultant for AbbVie, Allergan, Apellis, Astellas, Bayer, Biogen, Boehringer Ingelheim, Novartis, Ocular Therapeutix, Roche, and Santen, and conducts research for Bayer, Novartis, and Roche. **YC:** Speaker for AbbVie, Bayer, Chengdu Kanghong, 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. **CMGC:** Consulting fees, speaker fees, and grants from Avirmax, Bayer, Boehringer Ingelheim, Janssen, Novartis, Roche, Topcon, and Zeiss. **WKL:** Consulting and lecturing fees from Bayer, Novartis, and Roche. TI: Consulting fees from Bayer Yakuhin, Chugai Pharmaceutical, Janssen Pharmaceutical, Kyowa Kirin, Nippon Boehringer Ingelheim, Novartis Pharma, and Senju Pharmaceutical; grants from Alcon Japan, AMO Pharma, HOYA, NIDEK, Novartis, Santen Pharmaceutical, Senju Pharmaceutical, and Topcon Healthcare; honoraria from Alcon Japan, Bayer Yakuhin, Canon, Chugai Pharmaceutical, NIDEK, Nikon, Novartis Pharma, Otsuka Pharmaceutical, Santen Pharmaceutical, Senju Pharmaceutical, and Topcon; patent from Topcon; and other financial remuneration from Kyowa Kirin. **SS**: Funding/fees from Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, EyeBiotech, Novartis, Optos, and Roche. MRM: Consulting fees from AbbVie, Allergan, Apellis, Aviceda Therapeutics, Bayer, Boehringer Ingelheim, Dandelion, Eyepoint, Gensight Biologics, Iveric Bio, Isarna Therapeutics, Kubota, LumiThera, Novartis, Ocular Therapeutix, Oculis, OcuTerra Therapeutix, RetinAI, Roche, and Zeiss. **MRM**: Consulting fees for AbbVie, Alcon, Alimera, Allergan, Amgen, Apellis Pharmaceuticals, Astellas, Aviceda Therapeutics, Bayer, Boehringer Ingelheim, Dandelione, Evolve Medical Education, Eye.gnos consulting, EyePoint Pharmaceuticals, GenSight Biologics, Isarna Therapeutics, Iveric Bio, Kubota, LumiThera, Novartis, Ocular Therapeutics, Oculis, OcuTerra Therapeutix, OD-OS, ONL Therapeutics, RetinAI, Roche, Sitalis, UBS Analytics, and Zeiss. **AD**: No disclosures. **SL**, **XZ**, and **PMW**: Employees of Bayer Consumer Care AG. **TM**: Employee and stockholder of Bayer AG
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PULSAR Extension Design

pulsar nAMD Extension

PULSAR (BL–W96)
(Masked)

Patients with treatment-naïve nAMD

2q8 group (n=336)
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections

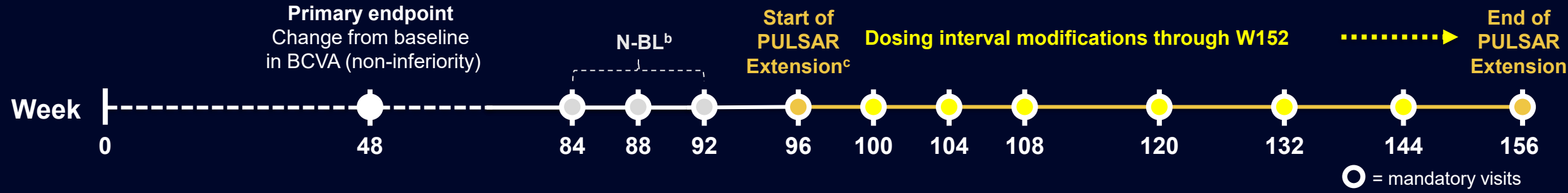
8q12 group (n=335)
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections

8q16 group (n=338)
Aflibercept 8 mg every 16 weeks after 3 initial monthly injections

PULSAR Extension (W96–W156)
(Open label and optional)[a]

2q8→8mg group (n=208)
Patients originally assigned to 2q8 switched to aflibercept 8 mg every 12 weeks

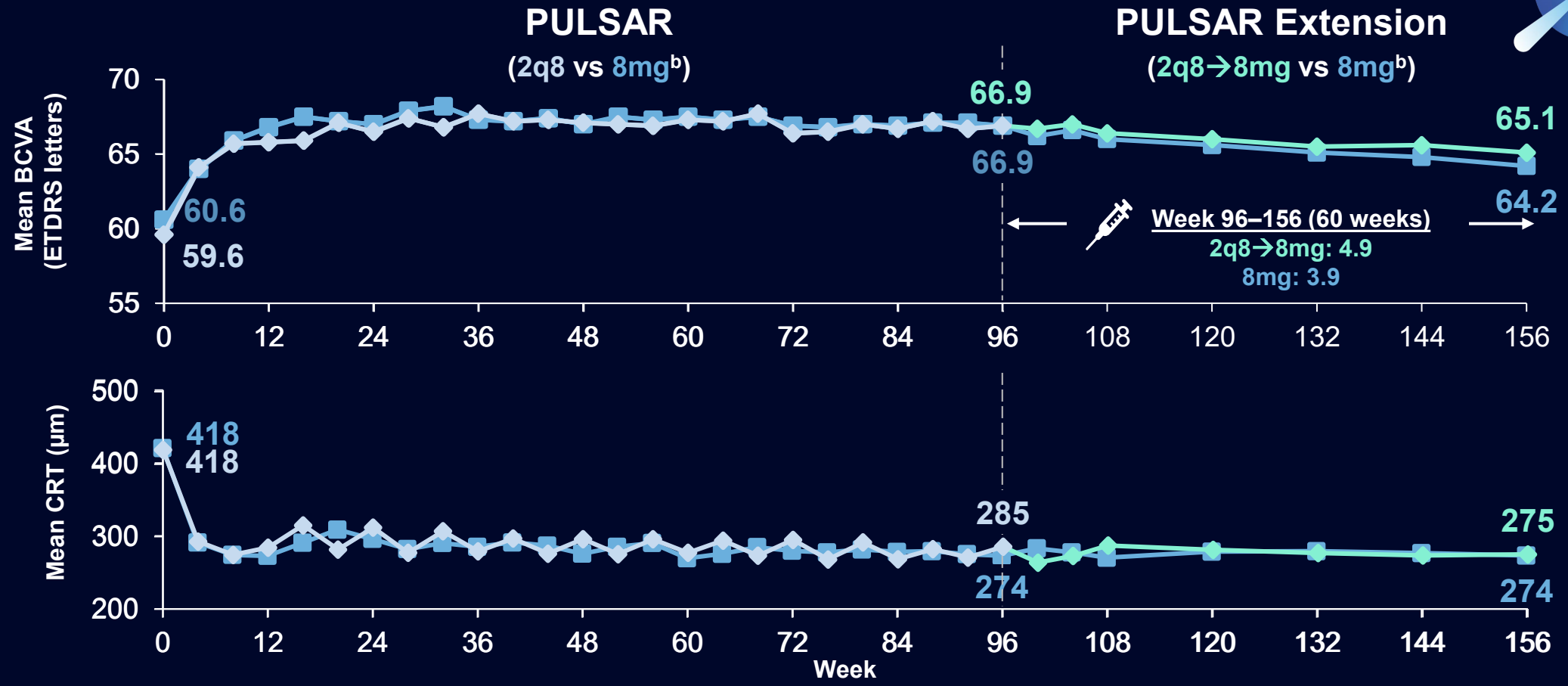
8mg group (n=417)
Patients originally assigned to 8q12 or 8q16 continued aflibercept 8 mg on last assigned dosing interval



[a]To be eligible for PULSAR Extension, patients were required to have ≥1 BCVA and CRT assessments between Week 84 and Week 92. Masked transition period (W96–W108) was followed by open-label part (W108–W156).
[b]N-BL was an average of values from W84, W88, and W92. [c]Optional phase added while PULSAR was ongoing; therefore, not all patients were able to enroll due to time constraints.
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; **BL,** baseline; **CRT**, central subfield retinal thickness; **nAMD**, neovascular age-related macular degeneration; **N-BL**, new baseline; **W**, week.

Mean BCVA and CRT Through Week 156[a]

pulsar nAMD Extension



Mean number of active injections over 48-week periods:[c]

BL–Week 48
2 mg: 6.9
8q12: 6.1
8q16: 5.2

Week 48–96
2 mg: 5.9
8q12: 3.6
8q16: 3.1

Week 108–156
8 mg: 3.9
8 mg: 3.1

No new safety signals were identified through 156 weeks. The safety profile remained consistent with previous findings.

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from baseline (MMRM) in BCVA of +4.6 (2.6, 6.6) letters and +3.4 (1.9, 4.9) letters, respectively, and in CRT of −145 (−155, −136) µm and −148 (−156, −140) µm, respectively. MMRM was used to generate BCVA/CRT LS means for the eFAS with baseline BCVA/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 BCVA/CRT and the interaction between visit and treatment. [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 (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **CI**, confidence interval; eFAS, full analysis set in the PULSAR extension; **eSAF**, safety analysis set in the PULSAR Extension; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **LS**, least squares; **MMRM**, mixed model for repeated measures.

Week 156 outcomes with aflibercept 8 mg by baseline BCVA

Sustained Improvement in BCVA and CRT Through Week 156 in Patients Continuing or Switching to Aflibercept 8 mg by Baseline BCVA

pulsar
nAMD
Extension

BCVA Outcomes

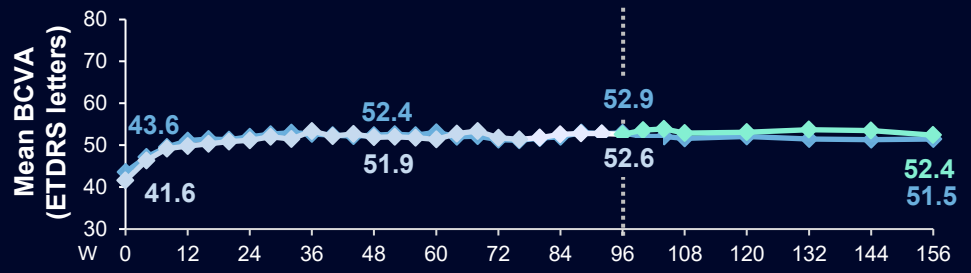
CRT Outcomes

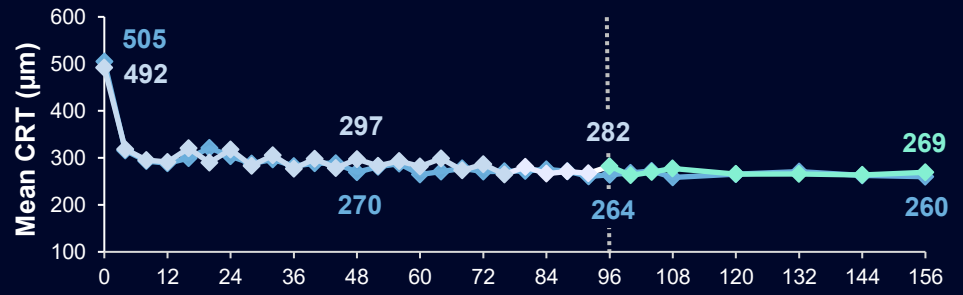
PULSAR
2q8 vs 8mg

PULSAR Extension
2q8→8mg vs 8mg

Baseline BCVA

≤54 ETDRS letters (n=61, n=114)



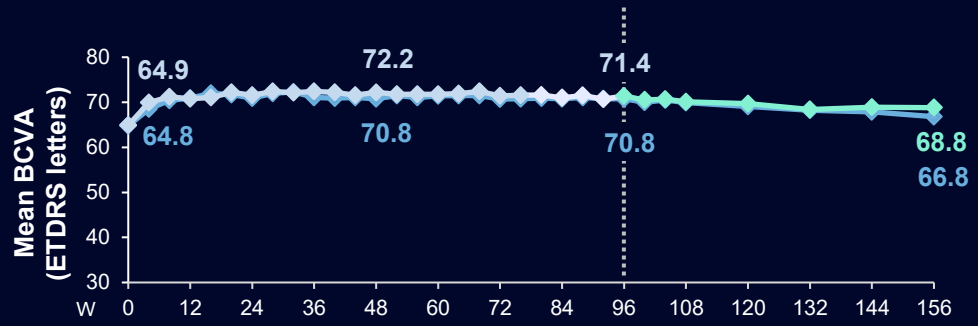


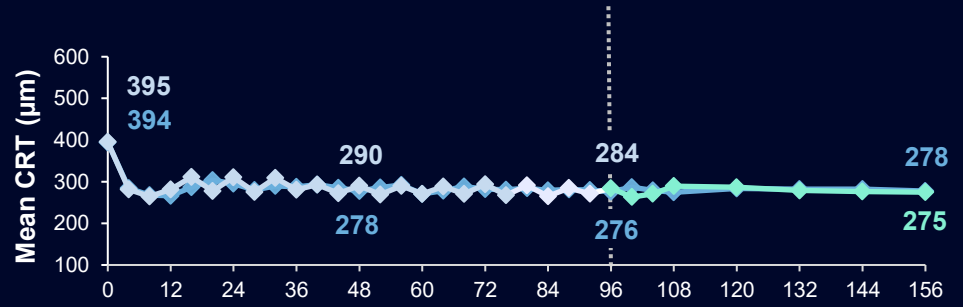
Mean no. of injections[a]

BL–W96
12.9 vs **9.2**

W96–W156
4.7 vs **3.8**

55–73 ETDRS letters (n=117, n=242)

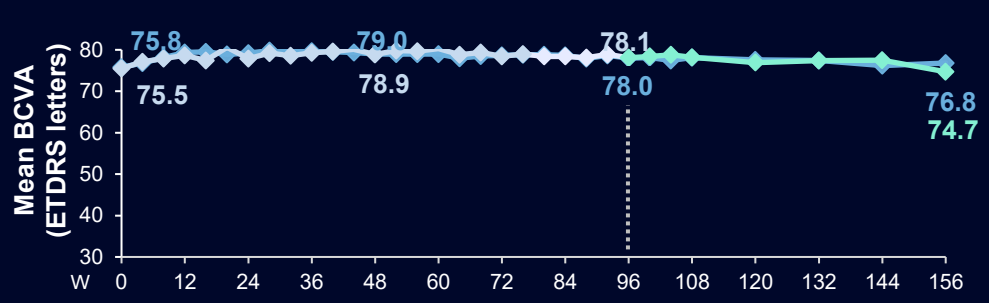


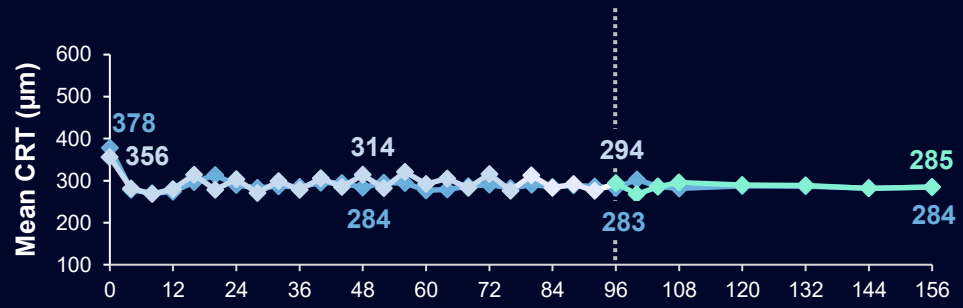


BL–W96
12.8 vs **9.0**

W96–W156
4.9 vs **3.9**

≥74 ETDRS letters (n=30, n=61)





BL–W96
13.0 vs **9.0**

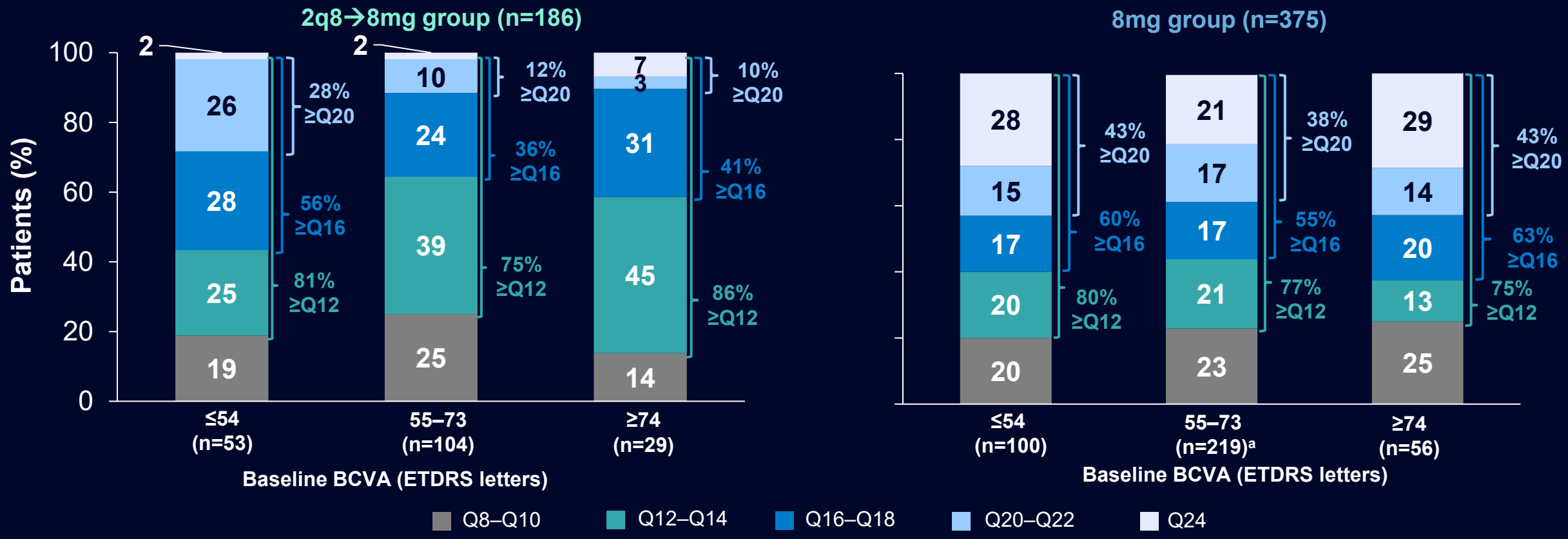
W96–W156
5.1 vs **3.9**

eFAS; observed cases. [a]eSAF.

Most Patients Achieved Extended Dosing Intervals at Week 156 Regardless of Baseline BCVA

pulsar nAMD Extension

Last assigned dosing intervals at Week 156



- Most patients (75–86%) continuing or switching to aflibercept 8 mg achieved ≥12-week dosing intervals at Week 156 regardless of baseline BCVA
- In the **2q8→8mg** group, **36–56%** of patients across subgroups achieved **≥16-week** dosing intervals
- In the **8mg** group, **38–43%** of patients across subgroups achieved **≥20-week** dosing intervals

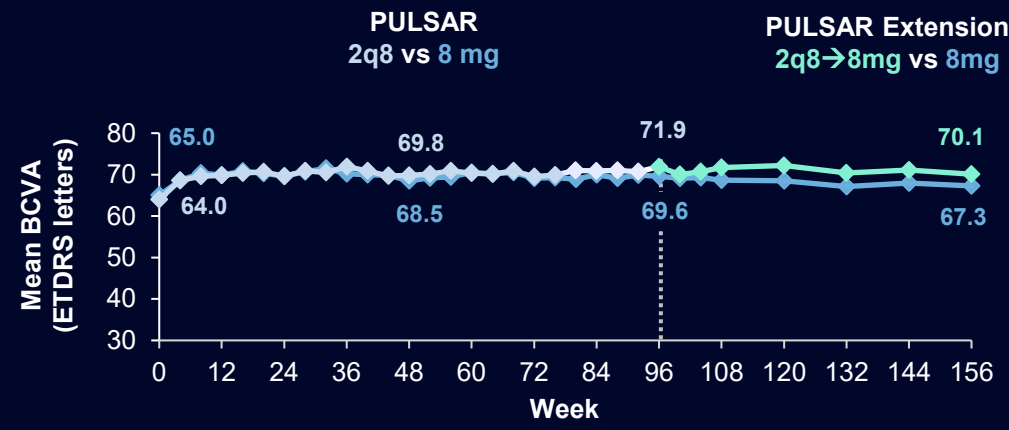
eSAF, participants who completed 156 weeks of treatment. Values may not add up to 100% due to rounding. [a]One patient was missing from the analysis. **Qn**, n-weekly interval.

Week 156 outcomes with aflibercept 8 mg by baseline CRT

Sustained Improvement in BCVA Through Week 156 in Patients Continuing or Switching to Aflibercept 8 mg by Baseline CRT

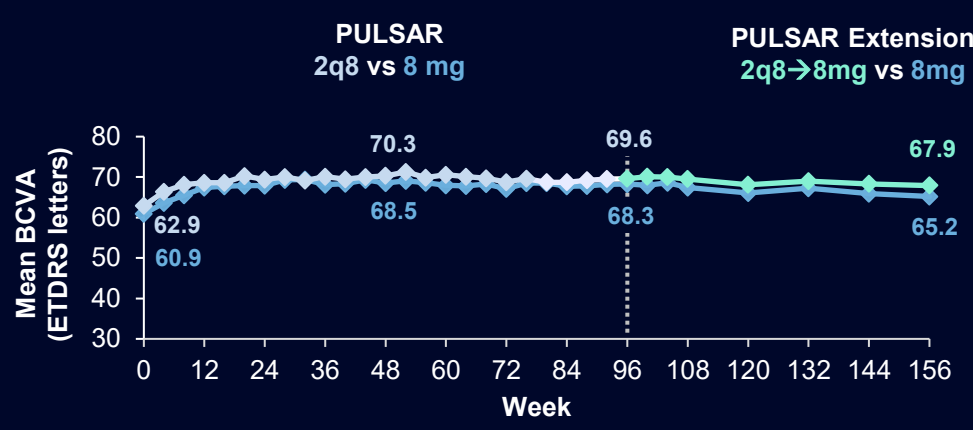
pulsar
nAMD
Extension

Baseline CRT Q1: <326 µm (n=48, n=108)



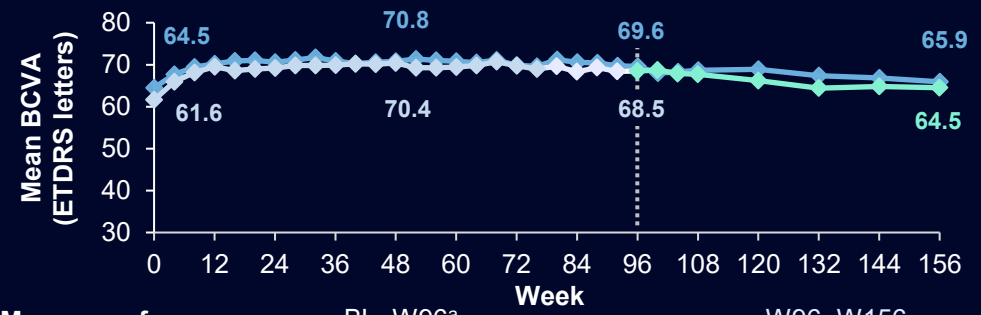
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.9 vs 8.6	4.8 vs 3.6

Baseline CRT Q3: ≥396 to <483 µm (n=56, n=100)



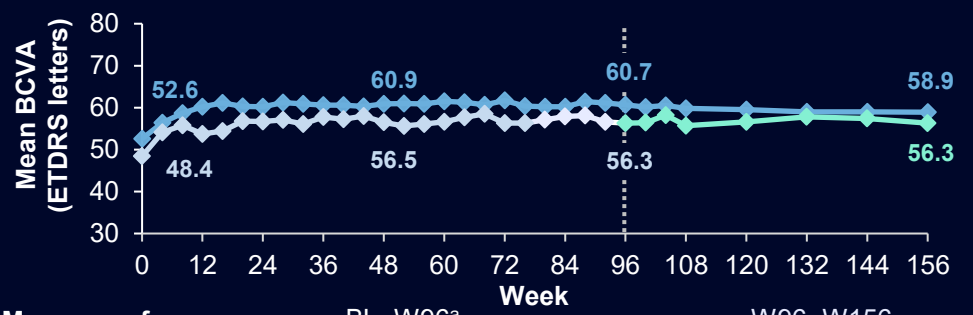
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.8 vs 9.2	4.9 vs 3.9

Baseline CRT Q2: ≥326 to <396 µm (n=58, n=98)



Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.8 vs 8.8	5.0 vs 3.7

Baseline CRT Q4: ≥483 µm (n=46, n=111)



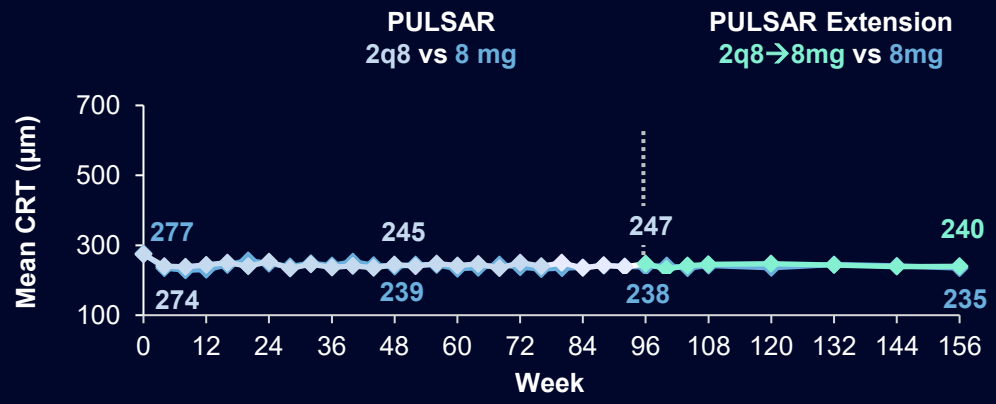
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.9 vs 9.4	4.8 vs 4.2

eFAS; observed cases. [a]eSAF. Qn, quartile number.

Sustained Improvement in CRT Through Week 156 in Patients Continuing or Switching to Aflibercept 8 mg by Baseline CRT

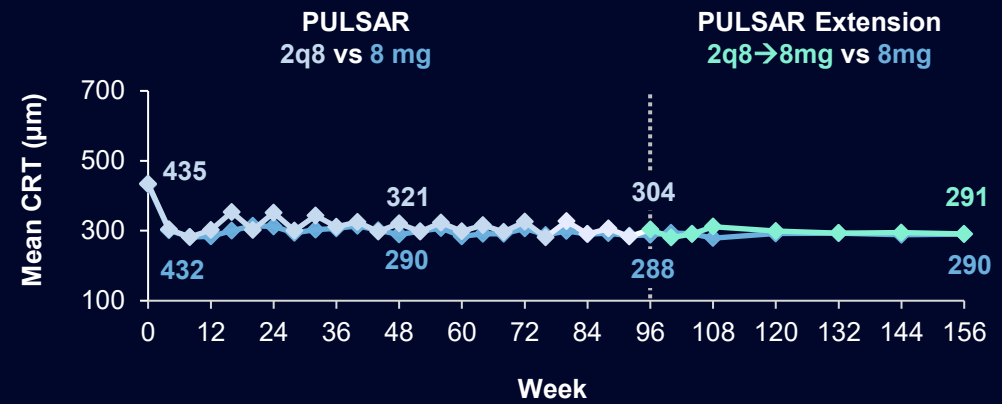
pulsar
nAMD Extension

Baseline CRT Q1: <326 µm (n=48, n=108)



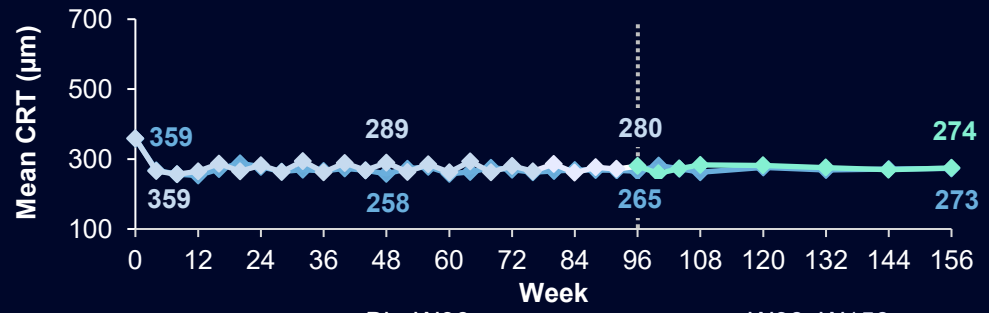
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.9 vs 8.6	4.8 vs 3.6

Baseline CRT Q3: ≥396 to <483 µm (n=56, n=100)



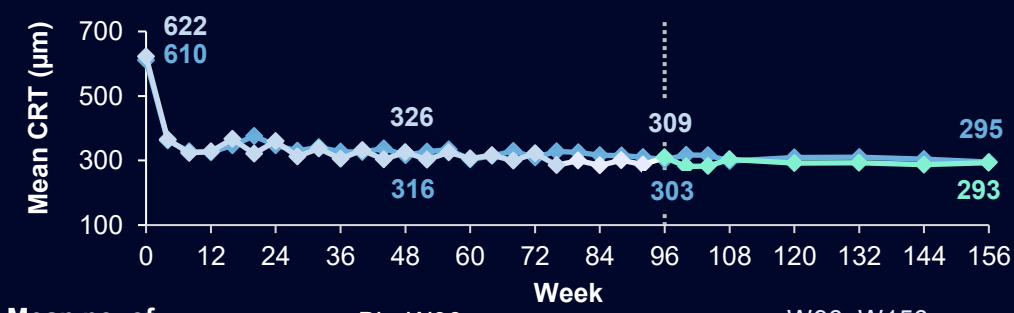
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.8 vs 9.2	4.9 vs 3.9

Baseline CRT Q2: ≥326 to <396 µm (n=58, n=98)



Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.8 vs 8.8	5.0 vs 3.7

Baseline CRT Q4: ≥483 µm (n=46, n=111)



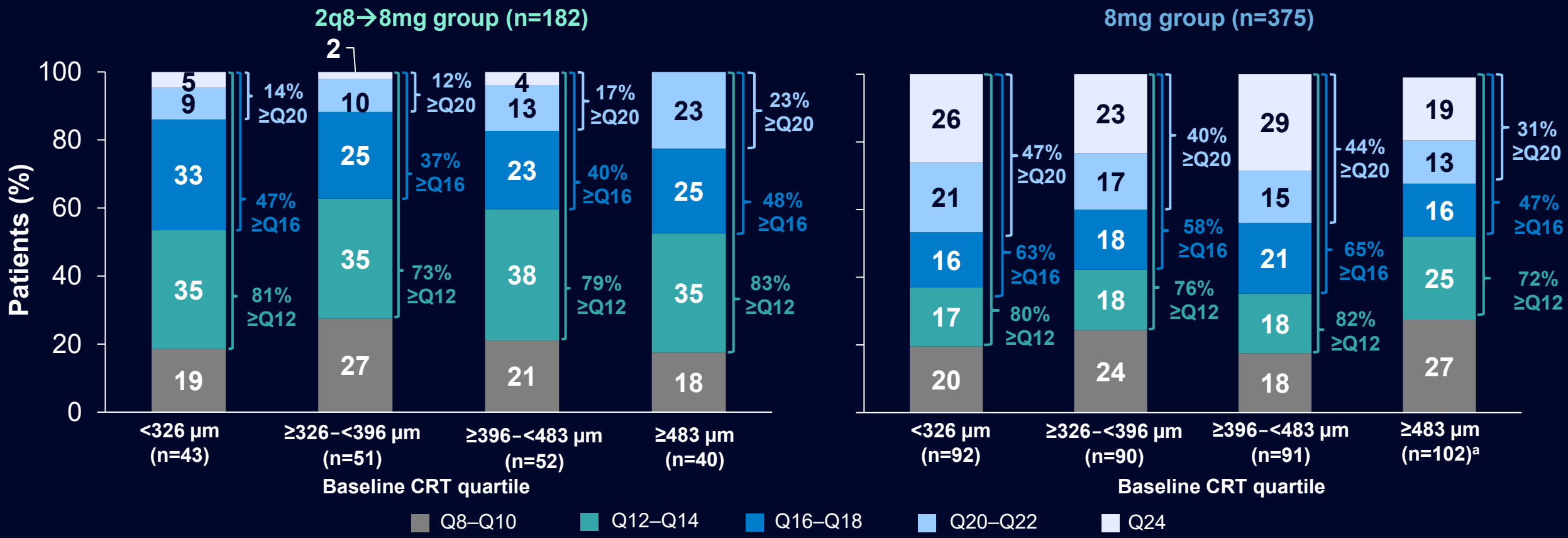
Mean no. of injections[a]	BL–W96[a]	W96–W156
	12.9 vs 9.4	4.8 vs 4.2

eFAS; observed cases. [a]eSAF.

Most Patients Achieved Extended Dosing Intervals at Week 156 Regardless of Baseline CRT

pulsar nAMD Extension

Last Assigned Dosing Intervals at Week 156 by Baseline CRT



- Most patients (72–83%) continuing or switching to aflibercept 8 mg achieved ≥12-week dosing intervals at Week 156 regardless of baseline CRT
- In the **2q8→8mg** group, **37–48%** of patients across subgroups achieved **≥16-week** dosing intervals
- In the **8mg** group, **31–47%** of patients across subgroups achieved **≥20-week** dosing intervals

eSAF, participants who completed 156 weeks of treatment. Values may not add up to 100% due to rounding. [a]One patient was missing from the analysis.

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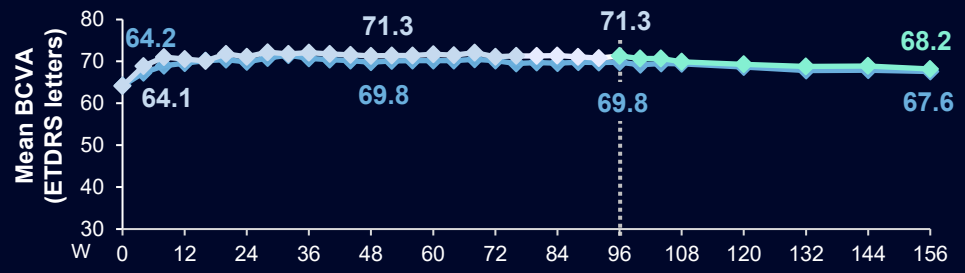
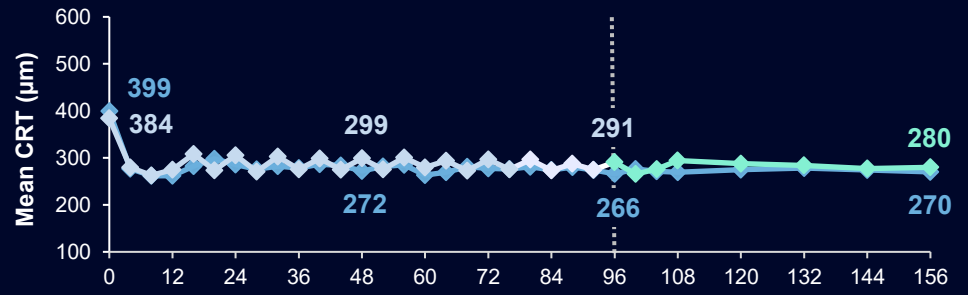
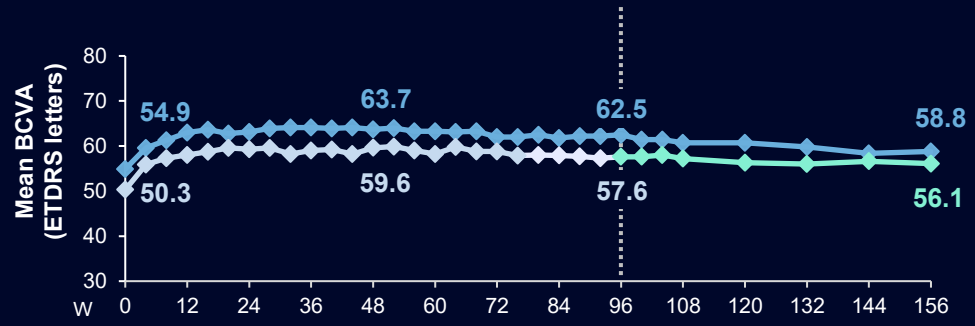
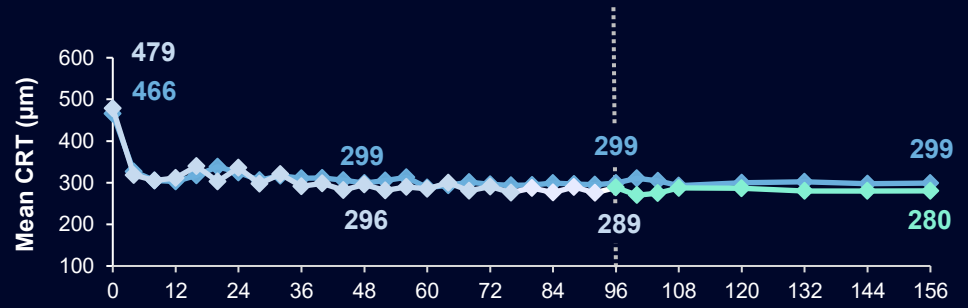
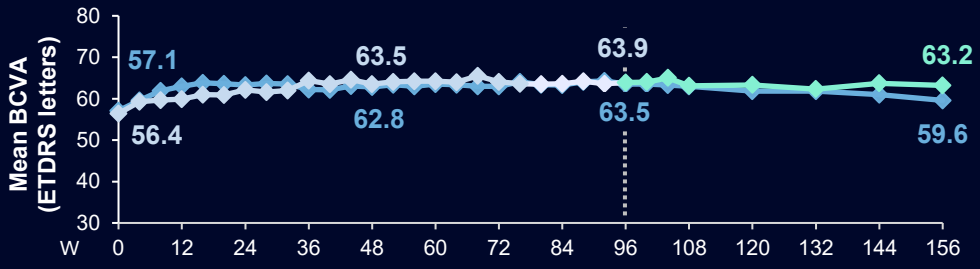
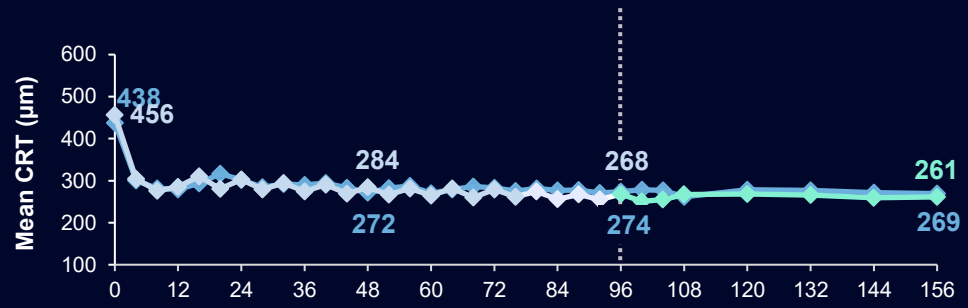
Week 156 outcomes with aflibercept 8 mg by baseline MNV Lesion Type

Sustained BCVA and CRT Outcomes Through Week 156 in Patients Continuing or Switching to Aflibercept 8 mg by Baseline MNV Type

pulsar nAMD Extension

BCVA outcomes

CRT outcomes

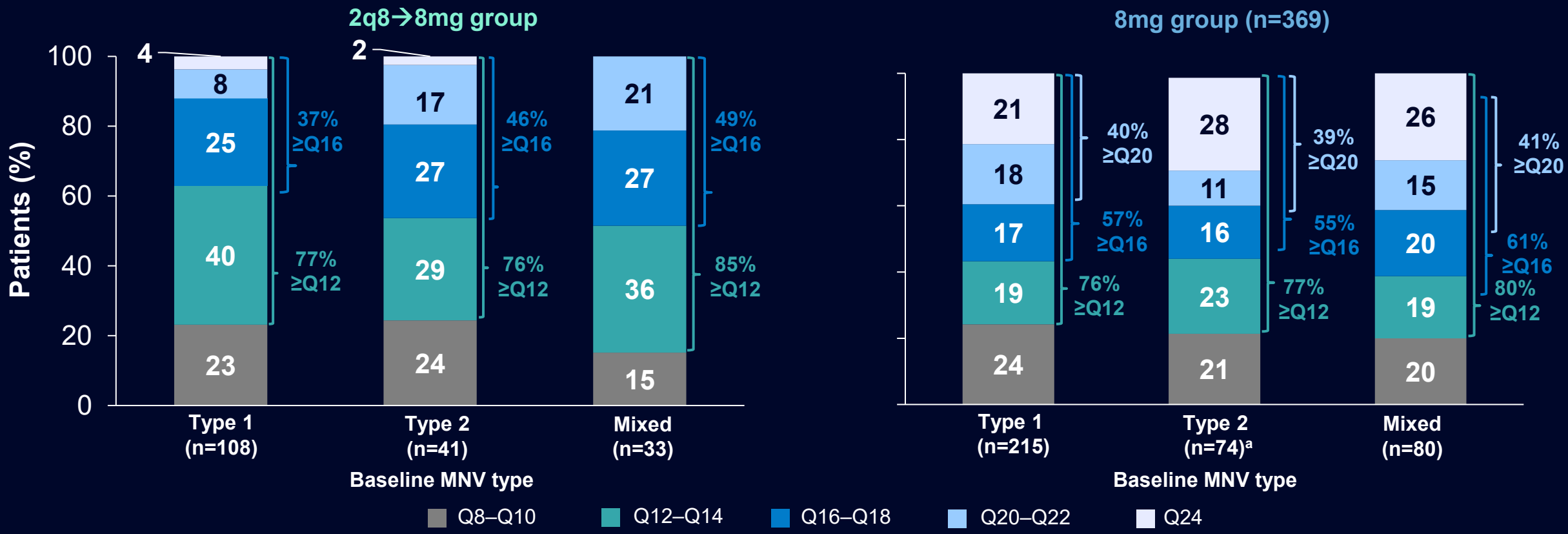
Baseline MNV type	BCVA outcomes: PULSAR 2q8 vs 8mg / PULSAR Extension 2q8→8mg vs 8mg	CRT outcomes: PULSAR 2q8 vs 8 mg / PULSAR Extension 2q8→8mg vs 8mg	Mean no. of injections[a]
Type 1 MNV (n=122, n=243)			BL–W96 **12.8** vs **9.0** W96–W156 **5.0** vs **4.0**
Type 2 MNV (n=45, n=80)			BL–W96 **12.9** vs **9.2** W96–W156 **4.8** vs **3.8**
Mixed MNV (n=37, n=87)			BL–W96 **12.9** vs **9.1** W96–W156 **4.9** vs **3.7**

eFAS; observed cases. [a]eSAF. **MNV**, macular neovascularization.

Most Patients Achieved Extended Dosing Intervals at Week 156 Irrespective of Baseline MNV Type

pulsar nAMD Extension

Last Assigned Dosing Intervals at Week 156 by Baseline MNV Type



- Most patients (76–85%) continuing or switching to aflibercept 8 mg achieved ≥12-week dosing intervals at Week 156 regardless of baseline MNV type
- In the **2q8→8mg** group, **37–49%** of patients across subgroups **achieved ≥16-week** dosing intervals
- In the **8mg** group, **39–41%** of patients across subgroups **achieved ≥20-week** dosing intervals

eSAF, patients completing Week 156; proportions calculated based on total number of completers per cohort; values may not add up to 100% due to rounding. [a]One patient was missing from this analysis.

Conclusions

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Extension

- In the PULSAR Extension, functional and anatomic improvements were sustained through Week 156 in the **2q8→8mg** and **8mg** groups
- Regardless of baseline BCVA, CRT, or MNV type, patients in the **2q8→8mg** group **maintained** BCVA gains and CRT improvements through Week 156 **after switching** to aflibercept 8 mg at Week 96
- Findings in the **8mg** group suggest that patients with treatment-naïve nAMD can achieve **durable improvements** with aflibercept 8 mg administered over extended dosing intervals, regardless of baseline BCVA, CRT, or MNV type
- At Week 156, **BCVA and CRT outcomes were comparable** in patient groups stratified by baseline BCVA, CRT, and MNV type in the **2q8→8mg** and **8mg** groups, with
  - 36–56% of patients in the 2q8→8mg group achieving ≥16-week dosing intervals, and
  - 31–47% of patients in the 8mg group achieving ≥20-week dosing intervals