Aflibercept 8 mg Monotherapy Results in Regression of Polypoidal Lesions That is Maintained Over 96 Weeks in Patients With PCV in the PULSAR Phase 3 Trial

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Disclosures

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PULSAR: Subgroup Analysis in Patients With PCV

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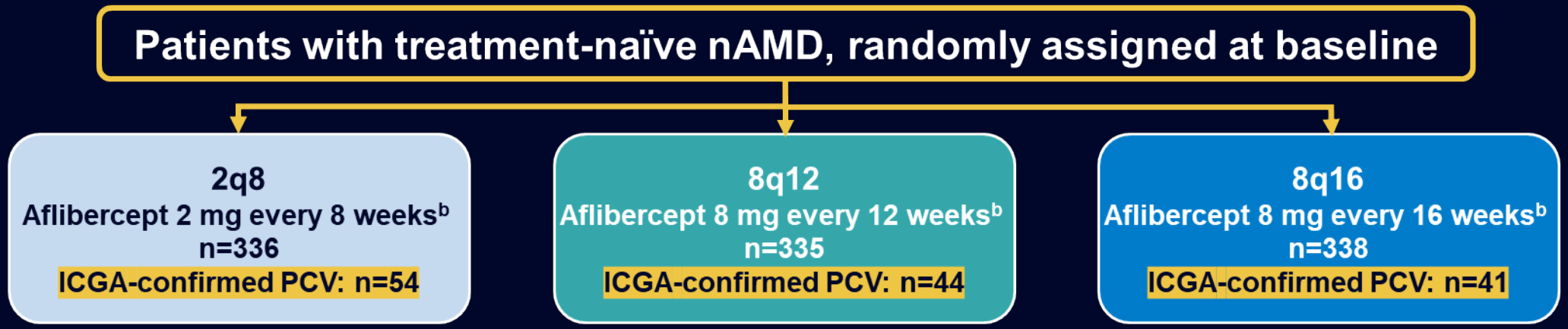
- **PULSAR:** 2-year multicenter, randomized, double-masked study (NCT04423718)
  - PULSAR was conducted across 223 sites in 27 countries
  - **ICGA was optional** and conducted in **296 patients[a] in 13 countries**; data from **139 patients with ICGA-confirmed PCV** are reported here



- **Primary endpoint:** Mean change in BCVA from baseline at Week 48 (4-letter non-inferiority vs 2q8)
  - In Year 1, only dosing interval shortening was allowed
  - In Year 2, dosing interval shortening AND extension were allowed

[a]PCV could not be graded in 3 patients. [b]After 3 initial monthly doses. **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; **ICGA**, indocyanine green angiography; **nAMD**, neovascular age-related macular degeneration; **PCV**, polypoidal choroidal vasculopathy.

Comparable BCVA Gains Observed Through Week 96 With Aflibercept 8 mg and 2 mg

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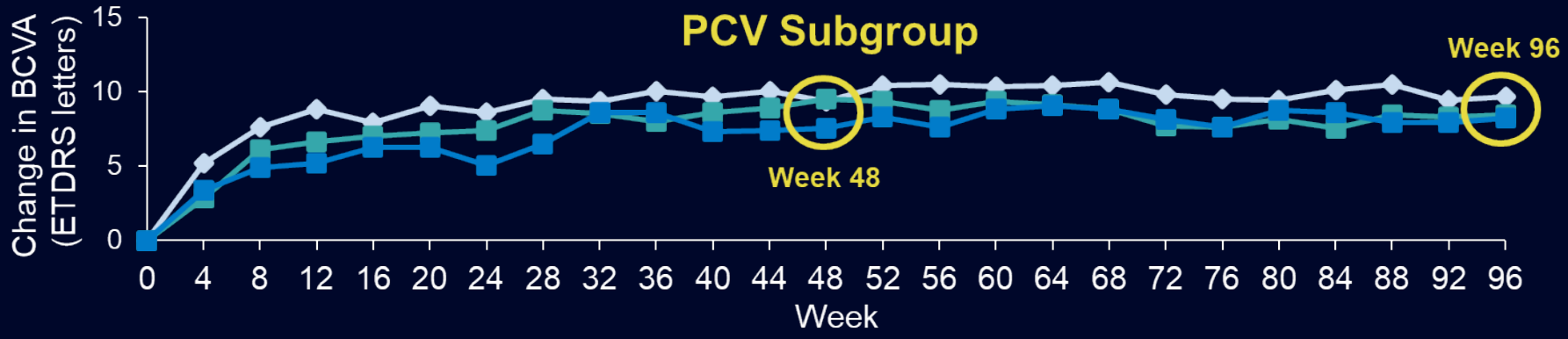
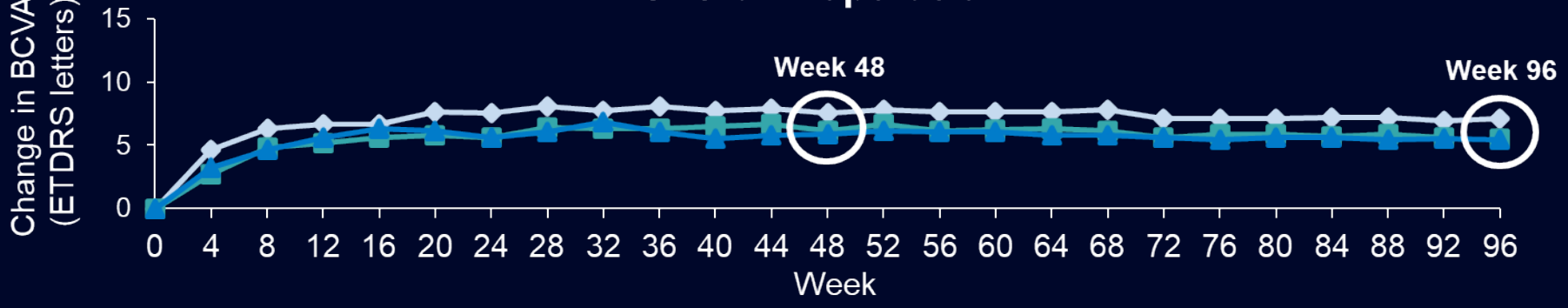
PCV Subgroup



	BL	Week 48	Week 96
2q8 (n=54)	57.6	+9.3	+9.6
8q12 (n=44)	56.3	+9.5	+8.4
8q16 (n=41)	60.1	+7.5	+8.2

Overall Population



	BL	Week 48	Week 96
2q8 (n=336)	58.9	+7.5	+7.1
8q12 (n=335)	59.9	+6.1	+5.5
8q16 (n=338)	60.0	+5.9	+5.4

PCV subgroup	Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI	Overall population	Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	+9.6 ± 12.1	6.3, 12.9	2q8	+7.1 ± 13.0	5.7, 8.5
8q12	+8.4 ± 12.8	4.5, 12.3	8q12	+5.5 ± 14.9	3.9, 7.1
8q16	+8.2 ± 9.0	5.4, 11.1	8q16	+5.4 ± 13.3	4.0, 6.8

FAS, LOCF (last available observed value prior to ICE was used to impute missing data; ICE were handled according to sensitivity estimand strategy for continuous endpoints, as described). N values are number of patients with BCVA assessments at baseline. **BL**, baseline; **CI**, confidence interval; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set; **ICE**, intercurrent event; **LOCF**, last observation carried forward; **SD**, standard deviation.

Comparable CRT Improvements Observed Through Week 96 With Aflibercept 8 mg and 2 mg

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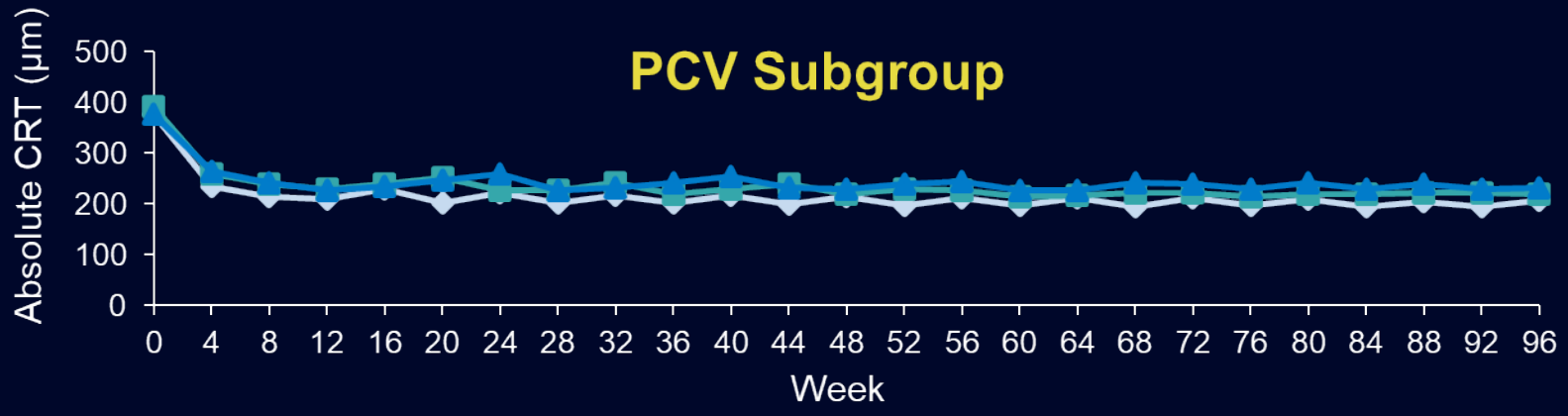
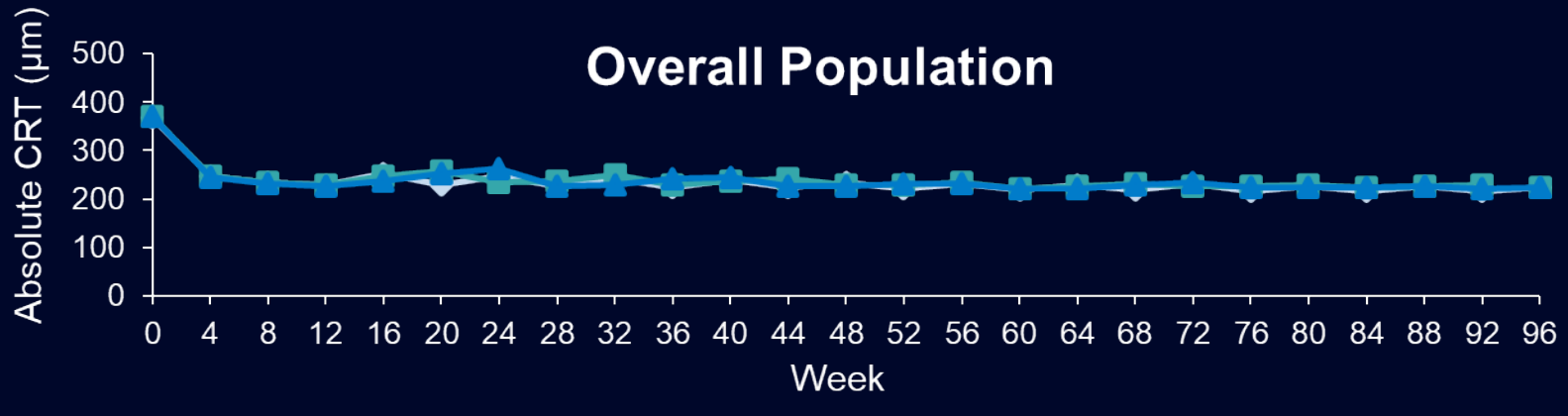
PCV Subgroup



	Week 48	Week 96
2q8 (n=54)	216	207
8q12 (n=44)	219	219
8q16 (n=41)	230	232

Overall Population



	Week 48	Week 96
2q8 (n=335)	236	225
8q12 (n=333)	228	223
8q16 (n=334)	227	225

PCV subgroup	Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI	Overall population	Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	−157 ± 140	−195, −118	2q8	−141 ± 132	−155, −126
8q12	−172 ± 139	−215, −130	8q12	−147 ± 128	−161, −133
8q16	−145 ± 142	−190, −100	8q16	−145 ± 135	−160, −131

FAS, LOCF. N values are number of patients with CRT assessments at baseline. **CRT**, central subfield retinal thickness.

Dosing Interval Extension in Year 2[a]: Most Patients With PCV Qualified for Extension

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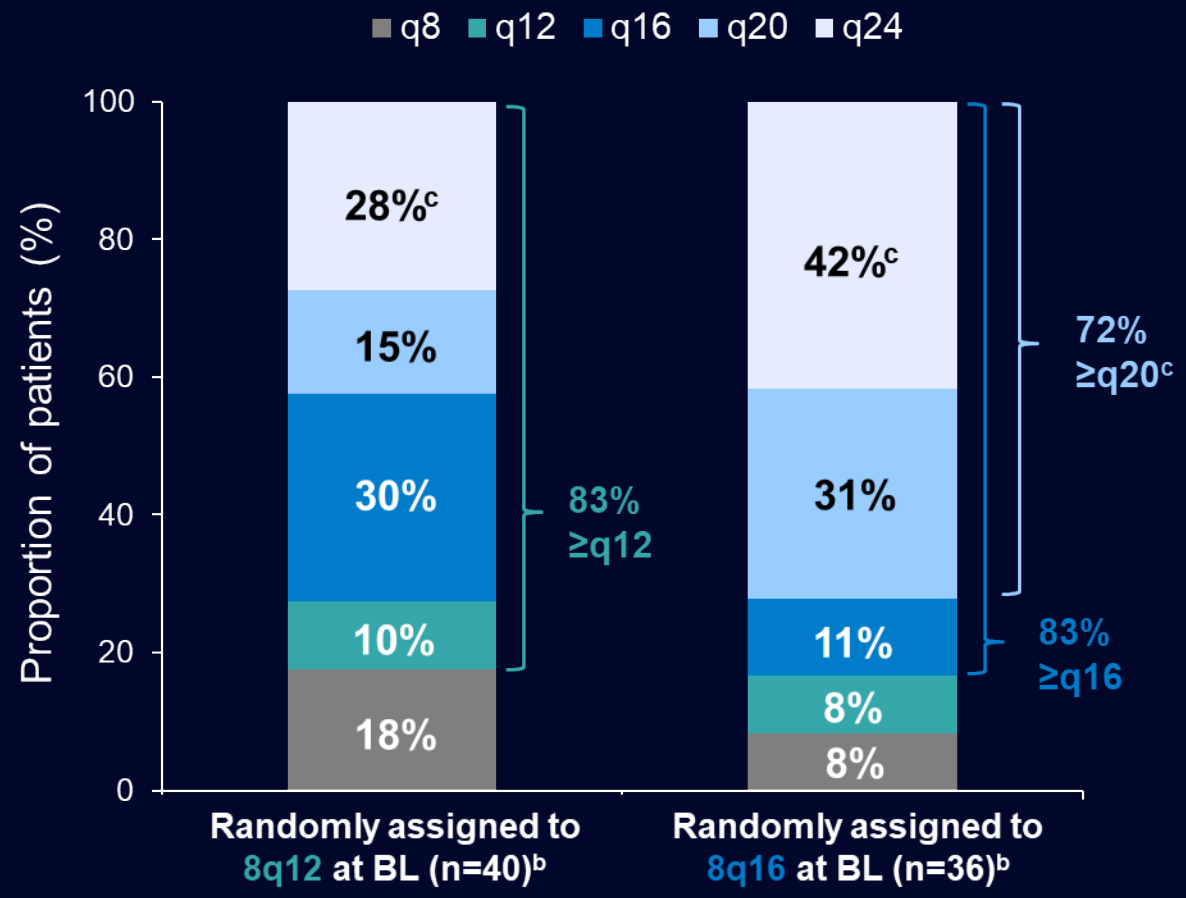
Last Assigned Dosing Interval (PCV Subgroup)



PCV subgroup	Mean number of injections	
	BL to Week 48[d]	BL to Week 96[b]
2q8	7.0	12.7
8q12	6.1	9.7
8q16	5.1	7.7

The safety profiles of aflibercept 8 mg and 2 mg were comparable in the PCV subgroup; **no new safety signals were observed in patients with PCV**

Values may not add up to 100% due to rounding. [a]Dosing intervals were extended in Year 2 if patients had <5-letter loss in BCVA from Week 12 **AND** no fluid at the central subfield **AND** no new foveal hemorrhage or neovascularization. [b]Patients completing Week 96. [c]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period. [d]Patients completing Week 48. **q8**, every 8 weeks; **q12**, every 12 weeks; **q16**, every 16 weeks; **q20**, every 20 weeks; **q24**, every 24 weeks.

Polypoidal Lesions Through Week 96

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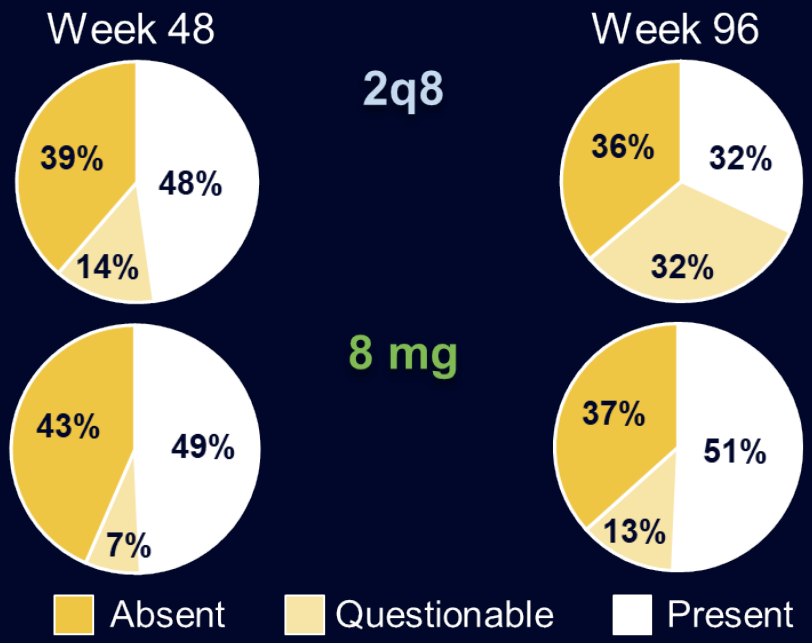
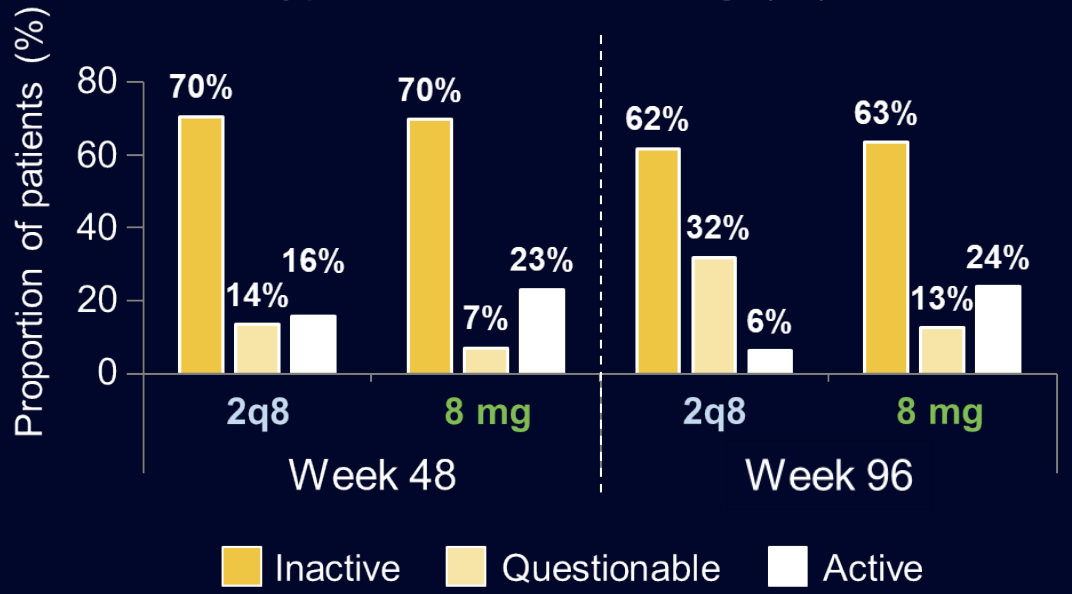
~36% of patients had no polypoidal lesions present at Week 96

Polypoidal lesion **presence** (%)[a,b]



~62% of patients had no active polypoidal lesions at Week 96

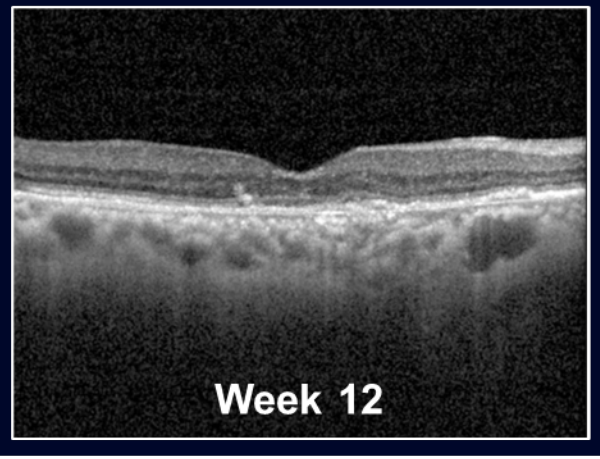
Polypoidal lesion **activity** (%)[a,c]

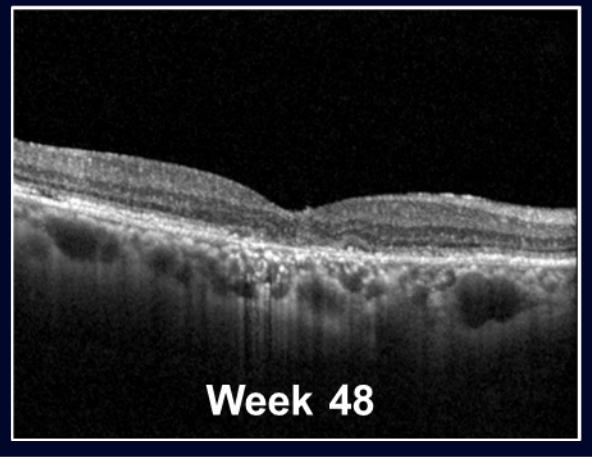


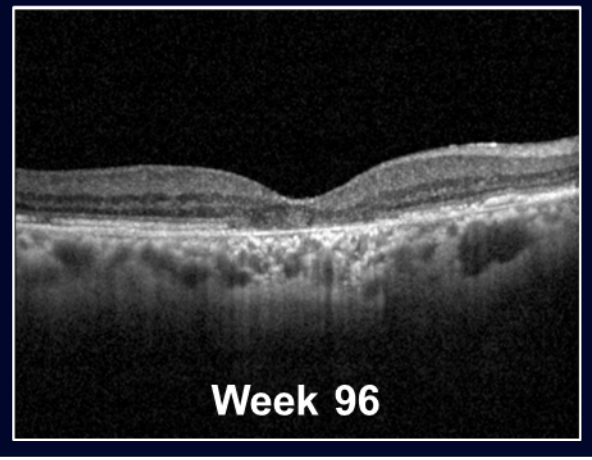
[a]W96 completers only; percentages calculated based on number of completers who underwent assessment. [b]W48, n=44 (2q8) and n=69 (8 mg); at W96, n=47 (2q8) and n=71 (8 mg). [c]W48, n=44 (2q8) and n=69 (8 mg); at W96, n=47 (2q8) and n=71 (8 mg); patients with inactive polypoidal lesions were defined as those with no polypoidal lesions present OR patients with polypoidal lesions present but both IRF and SRF known to be absent. **IRF**, intraretinal fluid; **SRF**, subretinal fluid; **W**, week.

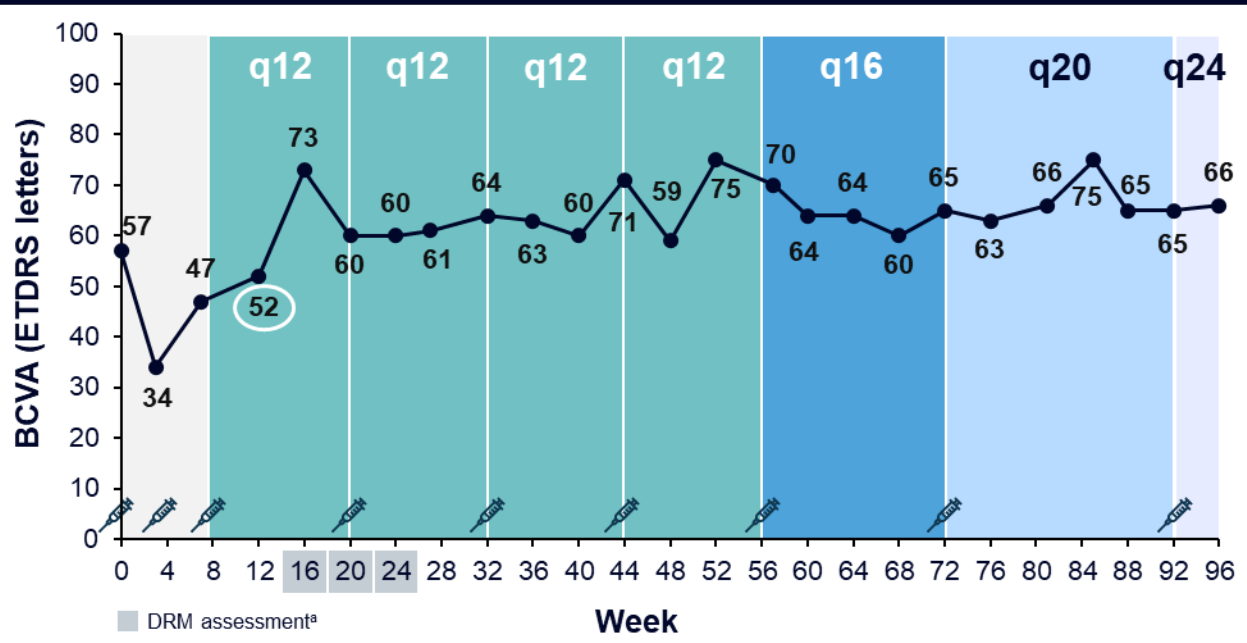
PCV Case Study 1

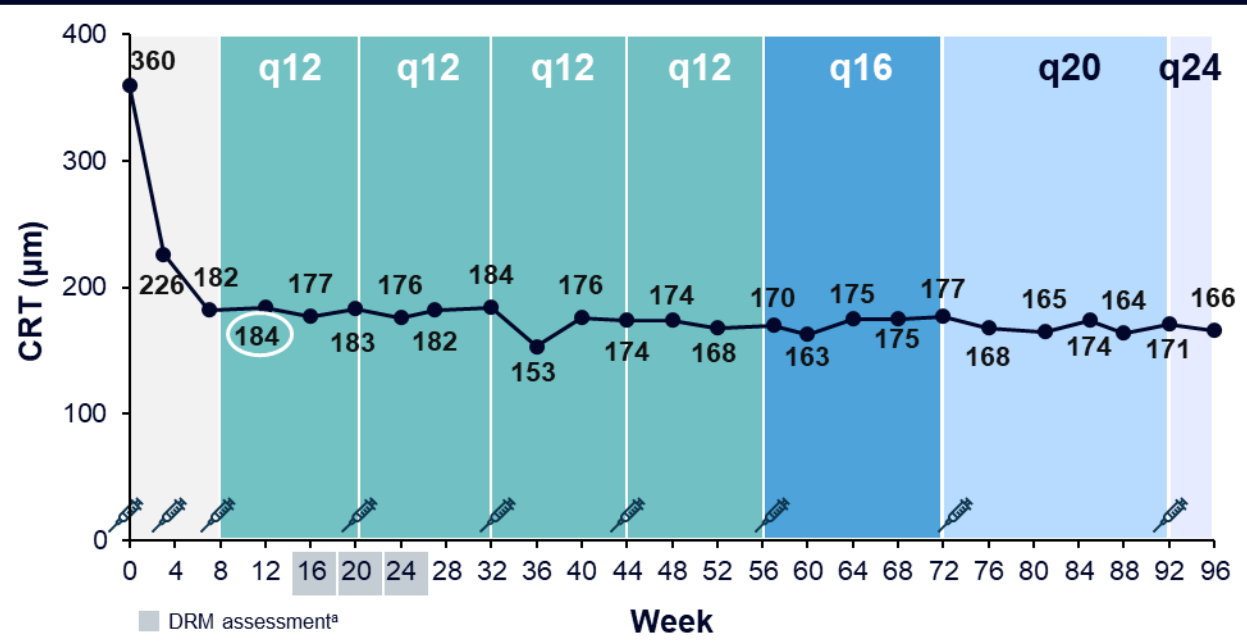
Age (years)	74
Gender	Male
Race	Asian
Treatment arm	8q12
Baseline BCVA (ETDRS letters)	57
Baseline CRT (µm)	360







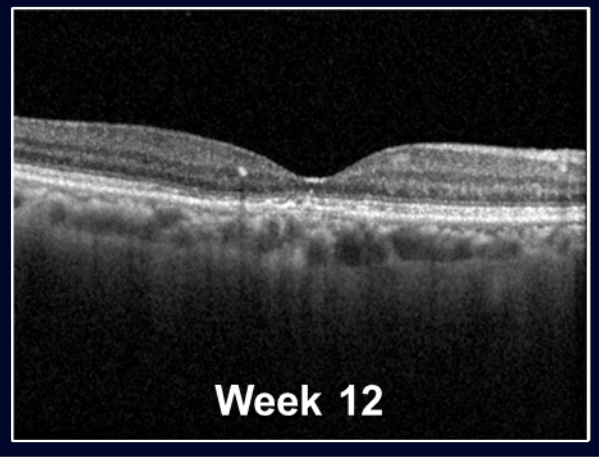


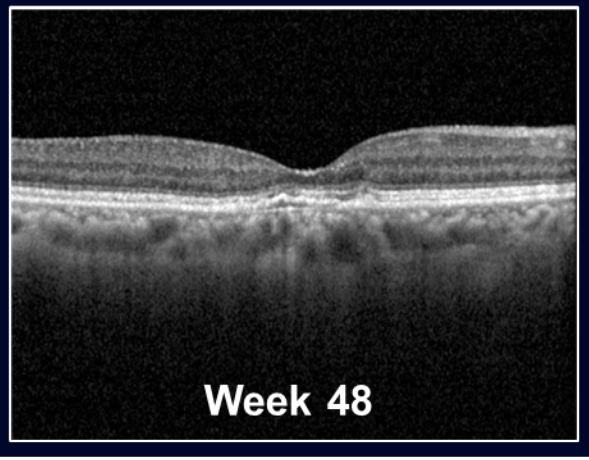


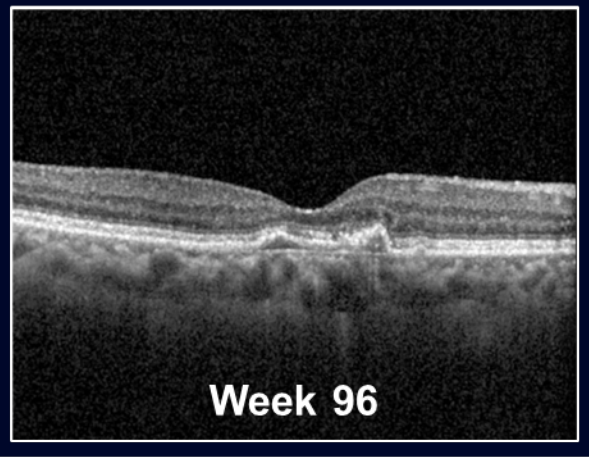
This patient case is taken from the Phase 3 PULSAR study (NCT04423718). [a]DRM assessments occurred at injection visits after Week 24 in the 8q12 treatment arm.
DRM, dose regimen modification.

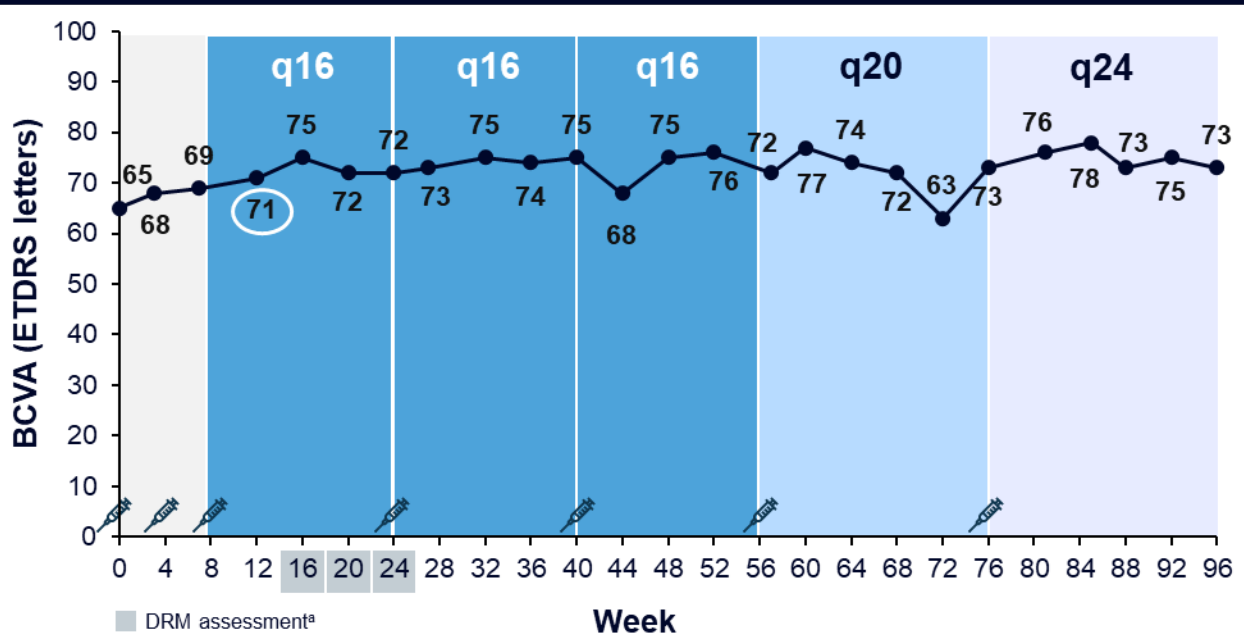
PCV Case Study 2

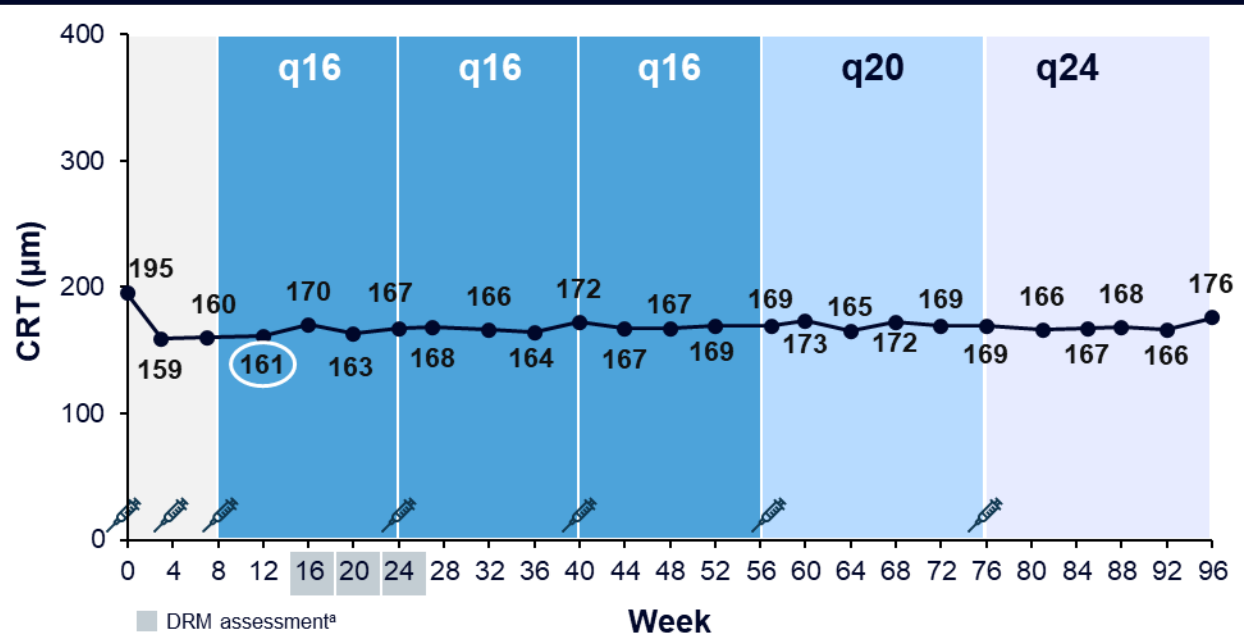
Age (years)	61
Gender	Female
Race	Asian
Treatment arm	8q16
Baseline BCVA (ETDRS letters)	65
Baseline CRT (µm)	195











This patient case is taken from the Phase 3 PULSAR study (NCT04423718). [a]DRM assessments occurred at injection visits after Week 24 in the 8q16 treatment arm.

Conclusions: Aflibercept 8 mg Monotherapy in PCV

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Aflibercept 8 mg monotherapy[a] maintained efficacy in PCV over 2 years

- **Efficacy** was **maintained** with **aflibercept 8 mg monotherapy**[a] in patients with **PCV over 2 years**
  - Mean change in BCVA and CRT was comparable among the 2q8, 8q12, and 8q16 treatment arms
- Aflibercept 8 mg **markedly reduced** the proportion of patients with **any polypoidal lesions** or **active polypoidal lesions** through 96 weeks

Extended durability

- At Week 96, **72%** of patients with PCV in the 8q16 treatment arm qualified for an **extended dosing interval of ≥20 weeks**, suggesting **extended durability of aflibercept 8 mg** compared with aflibercept 2 mg

Comparable safety profile for aflibercept 8 mg versus 2 mg

- The **safety profiles** of aflibercept 8 mg and 2 mg were **comparable** in the PCV subgroup; **no new safety signals** were observed in patients with PCV

[a]Without active rescue photodynamic therapy.