PULSAR Subgroup Analysis: Aflibercept 8 mg Efficacy in CNV Subtypes Including PCV over 96 Weeks with Ability to Extend Dosing Intervals to >16 Weeks

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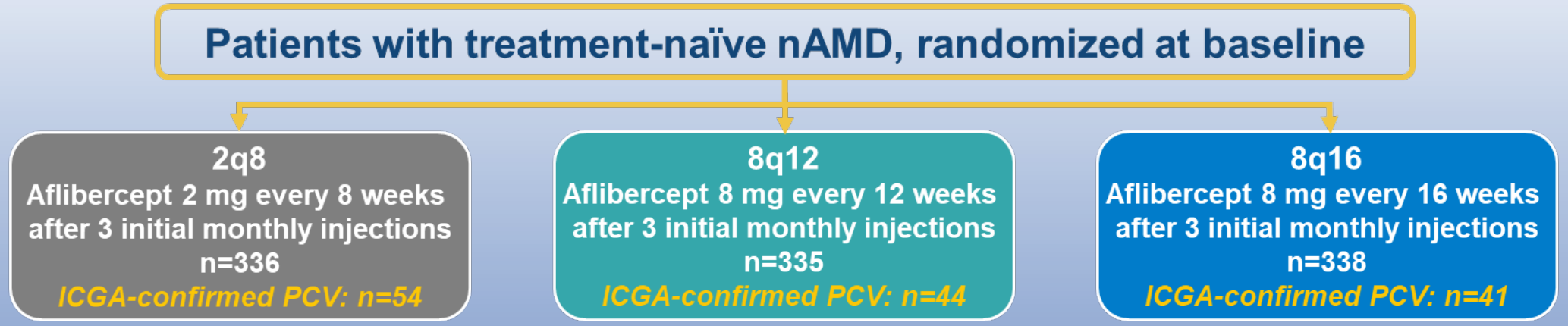
METHODS

PULSAR: 2-year multicenter, randomized, double-masked study (NCT04423718)

- PULSAR was a global study 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

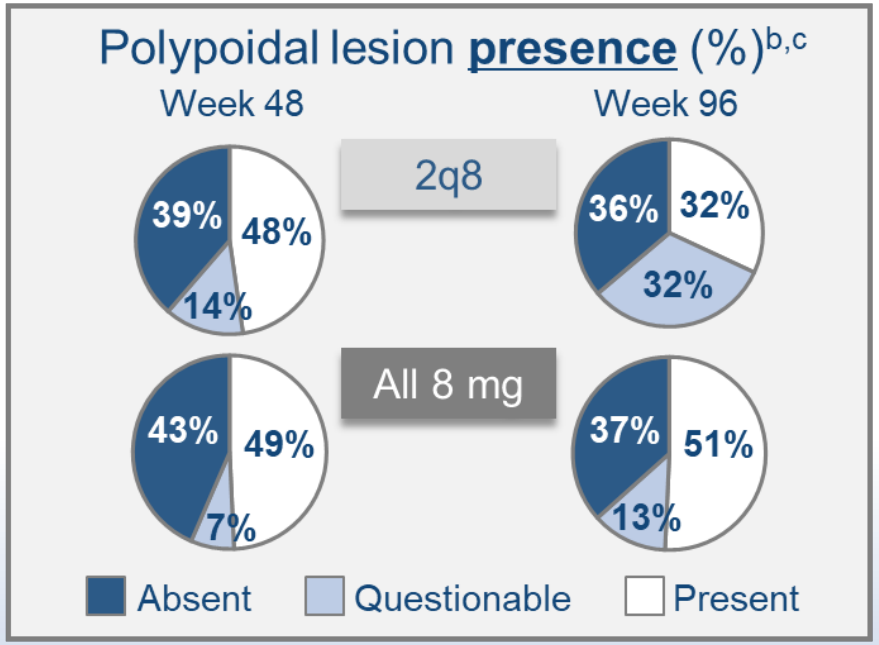


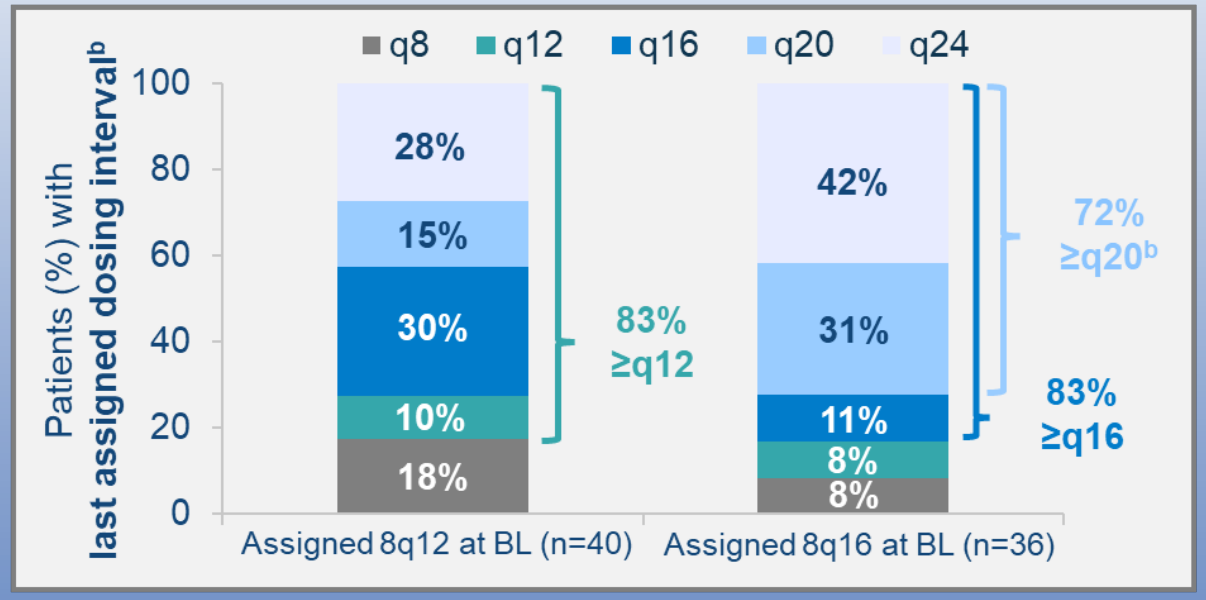
- **Primary endpoint:** Mean change in BCVA from baseline at Week 48 (4-letter non-inferiority vs 2q8)
  - In Year 1, only dosing interval shortening was allowed
  - In Year 2, dosing interval shortening AND extension were allowed

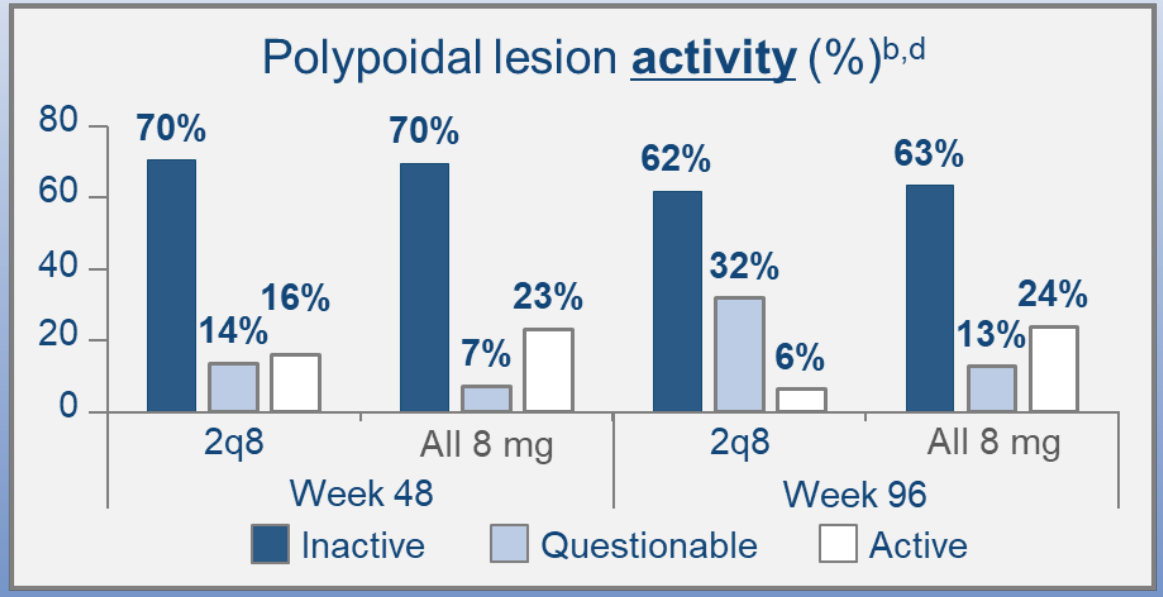
[a]PCV could not be graded in 3 patients. **q8**, every 8 weeks; **q12**, every 12 weeks; **q16**, every 16 weeks; **BCVA**, best-corrected visual acuity; **ICGA**, indocyanine green angiography; **nAMD**, neovascular age-related macular degeneration; **PCV**, polypoidal choroidal vasculopathy.

RESULTS

From BL to Week 96	2q8 (n=54)	8q12 (n=44)	8q16 (n=41)
Mean (95% CI) change in BCVA (ETDRS letters)[a]	+9.6 (6.3, 12.9)	+8.4 (4.5, 12.3)	+8.2 (5.4, 11.1)
Mean (95% CI) change in CRT (µm)[a]	−157 (−195, −118)	−172 (−215, −130)	−145 (−190, −100)
Mean±SD total injections[b]	12.7±0.7	9.7±1.4	7.7±1.2







[a]FAS, LOCF. [b]W96 completers only: 2q8, n=49; 8q12, n=40; 8q16, n=36; percentages calculated based on number of completers who underwent assessment. [c]W48, n=44 (2q8) and n=69 (All 8 mg); at W96, n=47 (2q8) and n=71 (All 8 mg). [d]W48, n=44 (2q8) and n=69 (All 8 mg); at W96, n=47 (2q8) and n=71 (All 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. **BL**, baseline; **CRT**, central retinal subfield thickness; **IRF**, intraretinal fluid; **LOCF**, last observation carried forward; **SRF**, subretinal fluid; **W**, week.

DISCUSSION

- **Efficacy** was **largely 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
- At Week 96, 72% of patients with PCV treated with aflibercept 8q16 qualified for an extended dosing interval of ≥20 weeks, suggesting **extended durability of aflibercept 8 mg** compared with aflibercept 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.

BCVA gains at Week 96 stratified by baseline PCV status and CNV classification

- **BCVA gains** at Week 96 were **numerically higher** in the **PCV subgroup** than in patients without PCV[a]
- **BCVA outcomes** at Week 96 were **similar** across patients stratified by baseline **CNV classification**[b]

PCV Subgroup (ICGA-confirmed)	n	Mean ± SD change in BCVA from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	54	**+9.6** ± 12.1	6.3, 12.9
8q12	44	**+8.4** ± 12.8	4.5, 12.3
8q16	41	**+8.2** ± 9.0	5.4, 11.1

Non-PCV Subgroup (ICGA-confirmed)	n	Mean ± SD change in BCVA from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	54	**+4.0** ± 13.4	0.3, 7.7
8q12	54	**+2.2** ± 18.5	-2.8, 7.3
8q16	46	**+4.9** ± 11.1	1.6, 8.2

Occult only CNV	n	Mean ± SD change in BCVA from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	195	**+6.6** ± 10.6	5.1, 8.1
8q12	201	**+4.4** ± 13.4	2.5, 6.2
8q16	189	**+5.2** ± 11.1	3.6, 6.8

Minimally classic CNV	n	Mean ± SD change in BCVA from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	62	**+7.4** ± 16.5	3.2, 11.6
8q12	57	**+3.5** ± 18.8	-1.5, 8.5
8q16	69	**+5.8** ± 15.8	2.0, 9.6

Predominantly classic CNV	n	Mean ± SD change in BCVA from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8	71	**+7.7** ± 15.2	4.1, 11.3
8q12	71	**+9.4** ± 14.5	6.0, 12.8
8q16	66	**+4.3** ± 16.8	0.2, 8.5

FAS, LOCF. N values represent number of patients at BL. [a]Analysis included patients with ICGA-confirmed PCV status only. [b]Determined by fluorescein angiography/fundus photography. **FAS**, full analysis set.