



# Intravitreal Aflibercept 8 mg in Patients with Polypoidal Choroidal Vasculopathy (PCV): A Phase 3 PULSAR Trial Subgroup Analysis

Chui Ming Gemmy Cheung,<sup>1</sup> Tien Y Wong,<sup>2</sup> Jeffrey S Heier,<sup>3</sup> Xin Zhang,<sup>4</sup> Tobias Machewitz,<sup>5</sup>  
Andrea Schulze,<sup>5</sup> Sergio Leal,<sup>4</sup> on behalf of the PULSAR study investigators

<sup>1</sup>Duke-NUS Medical School, National University of Singapore, Singapore

<sup>2</sup>Singapore Eye Research Institute, Singapore National Eye Centre, Singapore; Tsinghua Medicine, Tsinghua University, Beijing, China

<sup>3</sup>Ophthalmic Consultants of Boston, Boston, MA, USA

<sup>4</sup>Bayer Consumer Care AG, Basel, Switzerland

<sup>5</sup>Bayer AG, Berlin, Germany

# Disclosures



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  - **TYW:** Consultant fees from Aldropika Therapeutics, Bayer, Boehringer Ingelheim, Genentech, Iveric Bio, Novartis, Oxurion, Plano, Roche, Sanofi, and Shanghai Henlius; holds patents and cofounder of EyRiS and Visre. **JSH:** Consulting fees from 4DMT, Abpro, Adverum, Affamed, AGTC, Akouos, Allegro, Annexon, Apellis, Asclepix, Bausch & Lomb, Biovisics, Clearside, Curacle, DTx Pharma, Genentech/Roche, Glaukos, Gyroscope, Immunogen, Iveric, Janssen R&D, jCyte, Kriya, Nanoscope, NGM, Notal Vision, Novartis, Ocular Therapeutix, OcuPhire, OcuTerra, Olix, ONL Therapeutics, Palatin, Perceive, Ray Therapeutics, Regeneron, Regenxbio, RetinAI, RevOpsis, Stealth, Thea, and Vanotech; Research funding from Annexon, Apellis, AsclepiX, Bayer, Genentech/Roche, Gyroscope, Iveric, Kodiak, NGM, Notal Vision, Regeneron, and Regenxbio; Equity in Adverum, Aldeyra, Allegro, Aviceda, DTx Pharma, jCyte, OcuPhire, Ocular Therapeutix, RevOpsis, Vinci, Vitranu; Member of the Board of Directors of Ocular Therapeutix. **XZ and SL:** Employees of Bayer Consumer Care AG. **TM and AS:** Employees of Bayer AG
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- Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
- The results of the PULSAR polypoidal choroidal vasculopathy subgroup were previously presented at: the APOA Congress, February 23–26, 2023; the ARVO Annual Meeting, April 23–27, 2023; and the ASRS Annual Meeting, July 28–Aug 1, 2023
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# PULSAR Study Design and Dosing Schedule



96-week, multicenter, randomized, double-masked study in patients with treatment-naïve nAMD  
 Randomized at baseline 1 (2q8) : 1 (8q12) : 1 (8q16)

Key secondary endpoint:  
 Proportion of patients without IRF and  
 SRF in the central subfield

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

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48
2q8 (n=336)	X	X	X		X	o	X	o	X	o	X	o	X
8q12 (n=335)	X	X	X		o	X	o	o	X	o	o	X	o
8q16 (n=338)	X	X	X		o	o	X	o	o	o	X	o	o

## DRM Criteria for Shortening Dosing Interval

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

## DRM in Year 1

Intervals can only be shortened

Multiple opportunities to shorten interval

Minimum interval for all patients was Q8

Week 16 and 20: Patients on 8q12 and 8q16 meeting DRM criteria shortened to Q8

Week 24: Patients on 8q16 meeting DRM criteria shortened to Q12

Week 32 and 44 for 8q12 and Week 40 for 8q16: Treatment interval shortened by 4 weeks for patients meeting DRM criteria

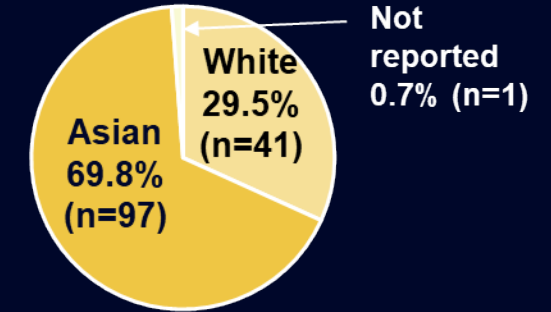
Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Note: Table does not reflect all dosing options once a patient's dosing interval is shortened. 2q8, aflibercept 2 mg every 8 weeks after 3 initial monthly injections; 8q12, aflibercept 8 mg every 12 weeks after 3 initial monthly injections; 8q16, aflibercept 8 mg every 16 weeks after 3 initial monthly injections; BCVA, best-corrected visual acuity; CST, central subfield thickness; DRM, dose regimen modification; IRF, intraretinal fluid; nAMD, neovascular age-related macular degeneration; Q8, every 8 weeks; Q12, every 12 weeks; SRF, subretinal fluid; Wk, week.

# PCV in PULSAR



- PULSAR is a global study conducted across 223 sites in 27 countries
- **ICGA** was optional and **conducted in 295 patients in 12 countries<sup>a</sup>**
  - PCV present, n=139; PCV absent, n=153
  - Data missing, n=3

PCV subgroup by race<sup>b</sup>

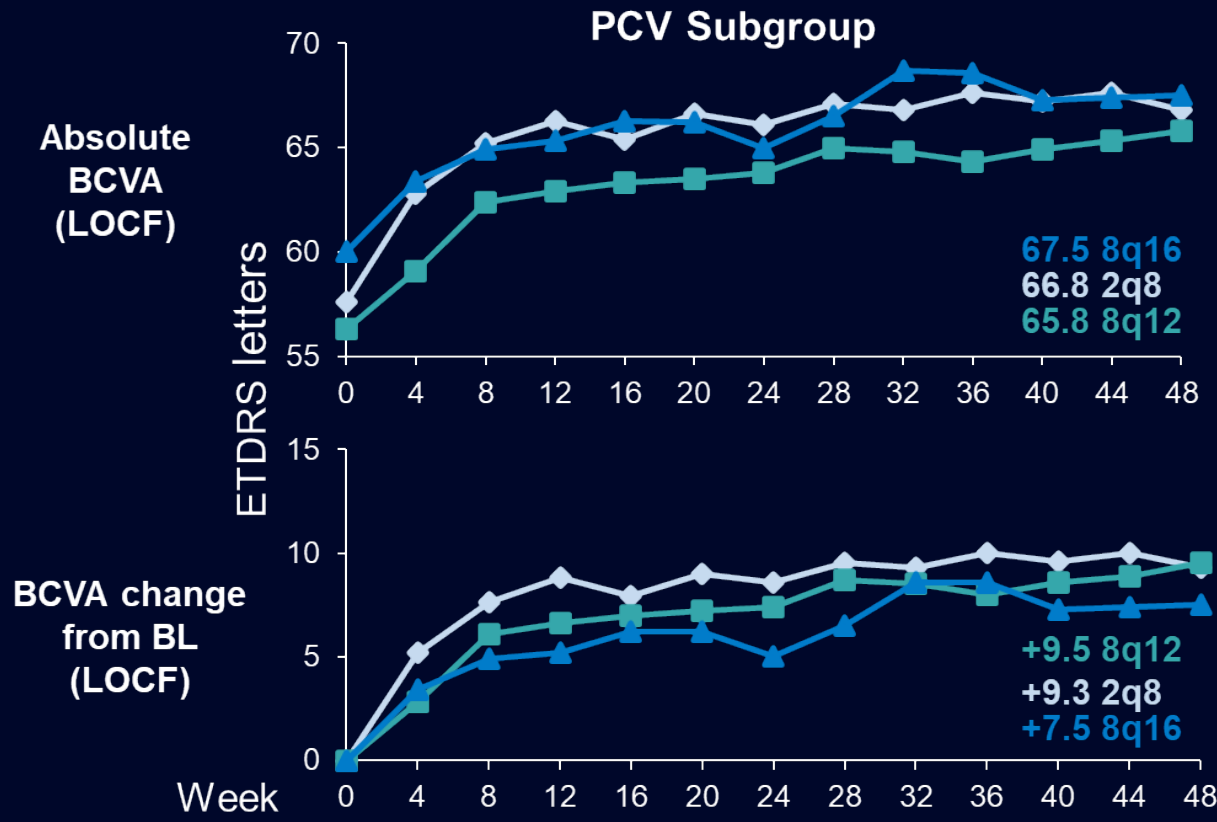


BL demographics and disease characteristics	PCV subgroup (ICGA-confirmed)				Overall population			
	2q8	8q12	8q16	All 8 mg	2q8	8q12	8q16	All 8 mg
	n=54	n=44	n=41	n=85	n=336	n=335	n=338	n=673
Age, years	72.6 (8.2)	72.2 (8.1)	73.2 (8.7)	72.7 (8.3)	74.2 (8.8)	74.7 (7.9)	74.5(8.5)	74.6 (8.2)
Female, %	31.5	50.0	36.6	43.5	56.0	54.3	53.3	53.8
BCVA, ETDRS letters	57.6 (15.5)	56.3 (13.3)	60.1 (11.5)	58.1 (12.5)	58.9 (14.0)	59.9 (13.4)	60.0 (12.4)	59.9 (12.9)
CST, $\mu\text{m}$	378 (163)	392 (129)	377 (139)	384 (134)	367 (134)	370 (124)	371 (133)	371 (128)
CNV size, $\text{mm}^2$	5.8 (4.7)	5.1 (3.8)	5.2 (4.5)	5.1 (4.2)	6.4 (5.0)	6.0 (4.8)	6.5 (5.5)	6.3 (5.2)

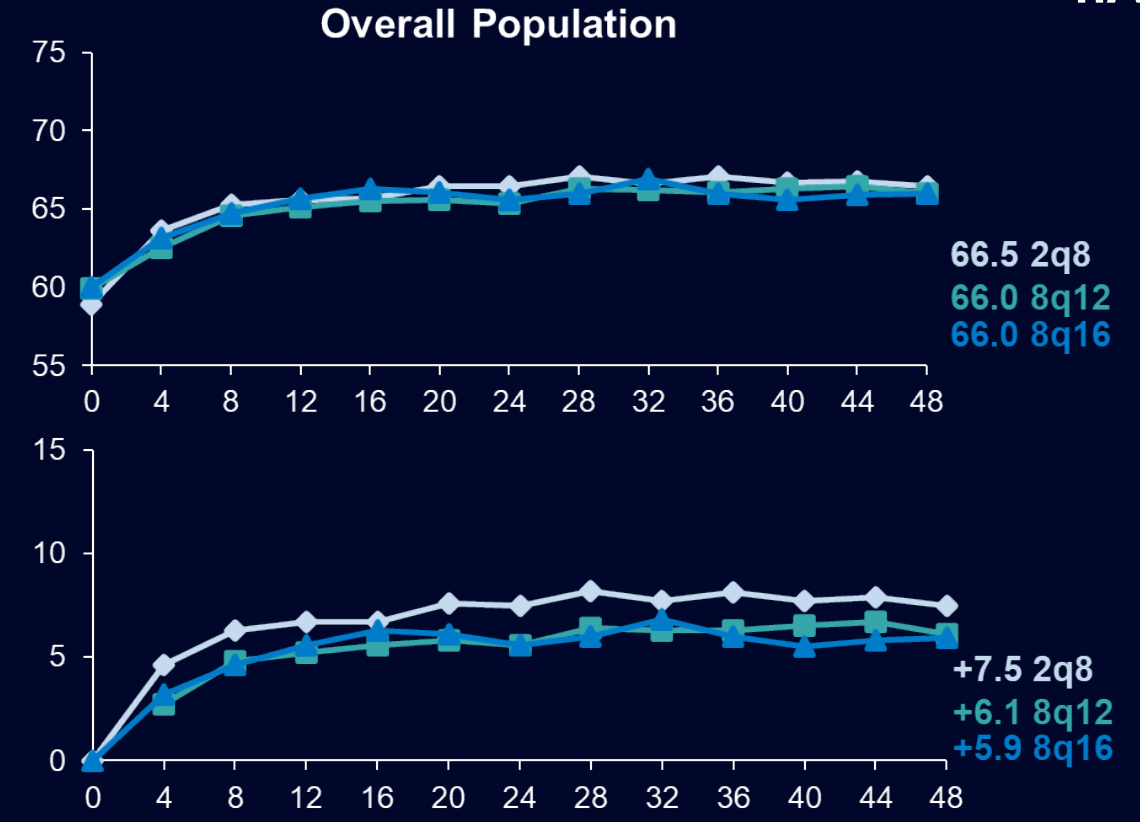
ICGA images were graded by the reading center. FAS, data are mean (SD) unless otherwise indicated. <sup>a</sup>Australia (n=15); Austria (n=7); France (n=2); Italy (n=22); Japan (n=71); Korea (n=26); Latvia (n=2); mainland China (n=66); Singapore (n=1); Spain (n=3); Switzerland (n=3); USA (n=77). <sup>b</sup>No patients were reported as Black or African American, or multi-racial.

BL, baseline; CNV, choroidal neovascularization; ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set; ICGA, indocyanine green angiography; PCV, polypoidal choroidal vasculopathy; SD, standard deviation.

# PCV Subgroup: Absolute and Change from Baseline in BCVA through Week 48 (LOCF)



	Mean ± SD change from BL to Week 48 (LOCF)	Two-sided 95% CI
<b>2q8</b>	+9.3 ± 11.1	6.2, 12.3
<b>8q12</b>	+9.5 ± 13.0	5.5, 13.4
<b>8q16</b>	+7.5 ± 7.6	5.1, 9.9



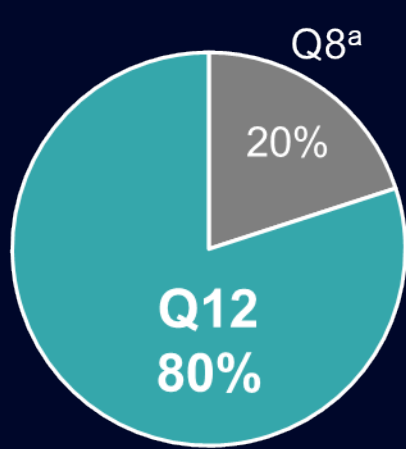
	Mean ± SD change from BL to Week 48 (LOCF)	Two-sided 95% CI
<b>2q8</b>	+7.5 ± 12.0	6.2, 8.8
<b>8q12</b>	+6.1 ± 13.2	4.7, 7.6
<b>8q16</b>	+5.9 ± 11.8	4.6, 7.2

LOCF: last available observed value prior to ICE will be used to impute missing data. ICE will be handled according to sensitivity estimand strategy for continuous endpoints as described; FAS (PCV subgroup): 2q8 n=54; 8q12 n=44; 8q16 n=41 (at baseline), (overall population): 2q8 n=336; 8q12 n=335; 8q16 n=338 (at baseline). CI, confidence interval; ICE, intercurrent event; LOCF, last observation carried forward;

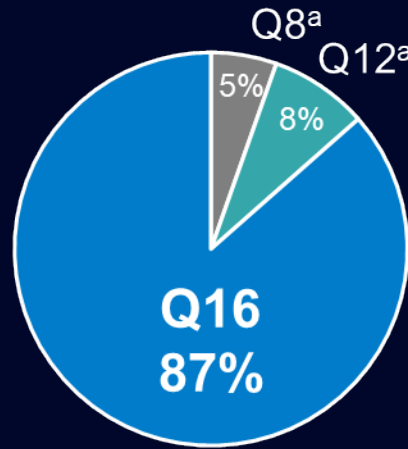
# PCV Subgroup: Proportions of Patients Maintained on Q12 and Q16 Dosing Intervals through Week 48



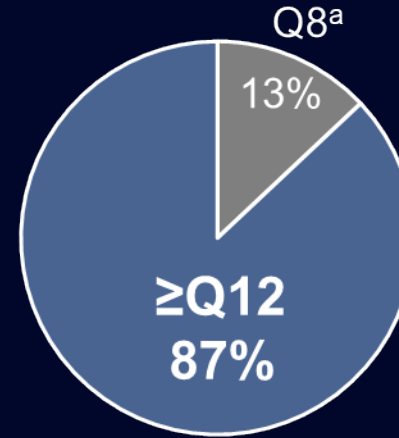
## PCV subgroup



**8q12** n=41<sup>b</sup>



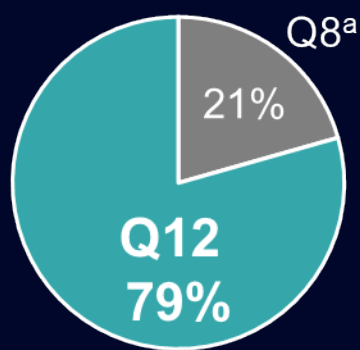
**8q16** n=37<sup>b</sup>



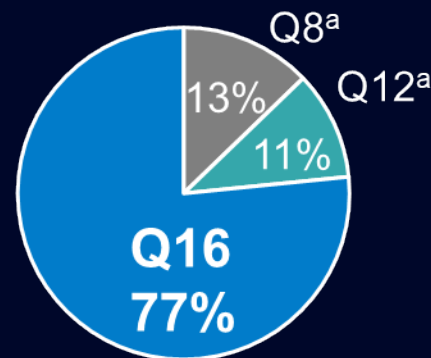
**All aflibercept 8 mg** n=78<sup>b</sup>

87% of patients receiving aflibercept 8 mg maintained dosing intervals ≥12 weeks

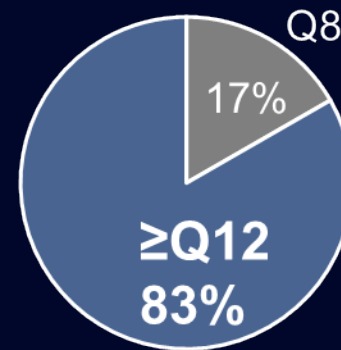
## Overall population



**8q12** n=316<sup>b</sup>



**8q16** n=312<sup>b</sup>



**All aflibercept 8 mg** n=628<sup>b</sup>

83% of patients receiving aflibercept 8 mg maintained dosing intervals ≥12 weeks

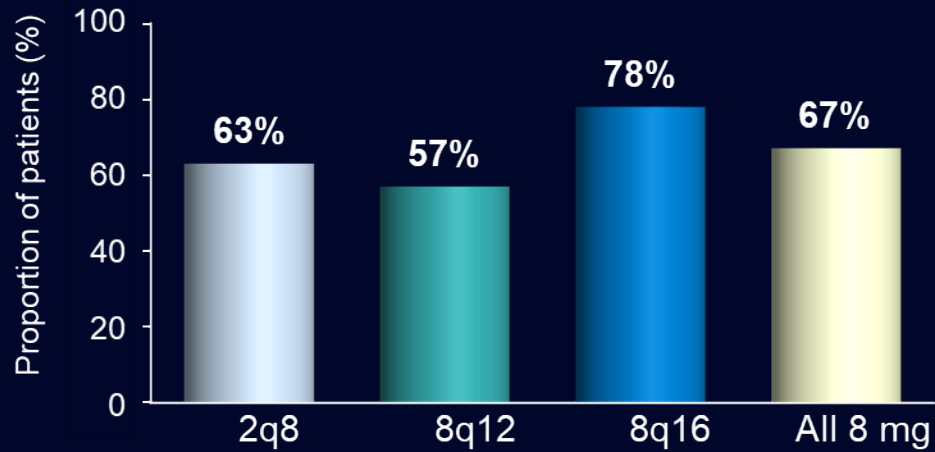
Values may not add up to 100% due to rounding.

<sup>a</sup>Patients shortened based on DRM assessments at some point through Week 48. <sup>b</sup>Patients completing Week 48.

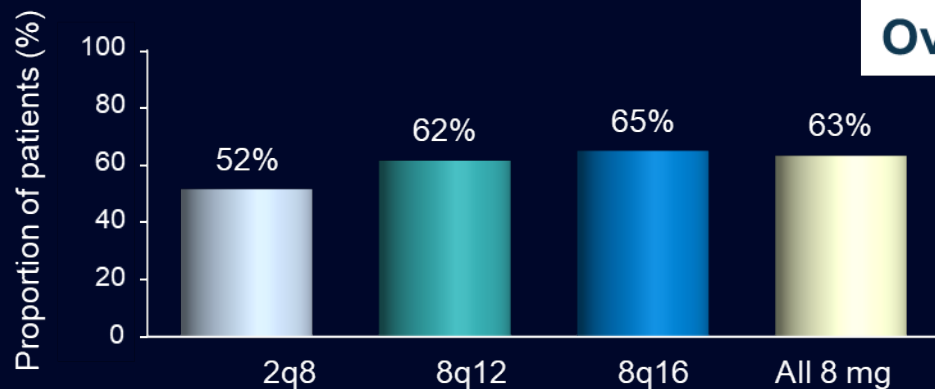
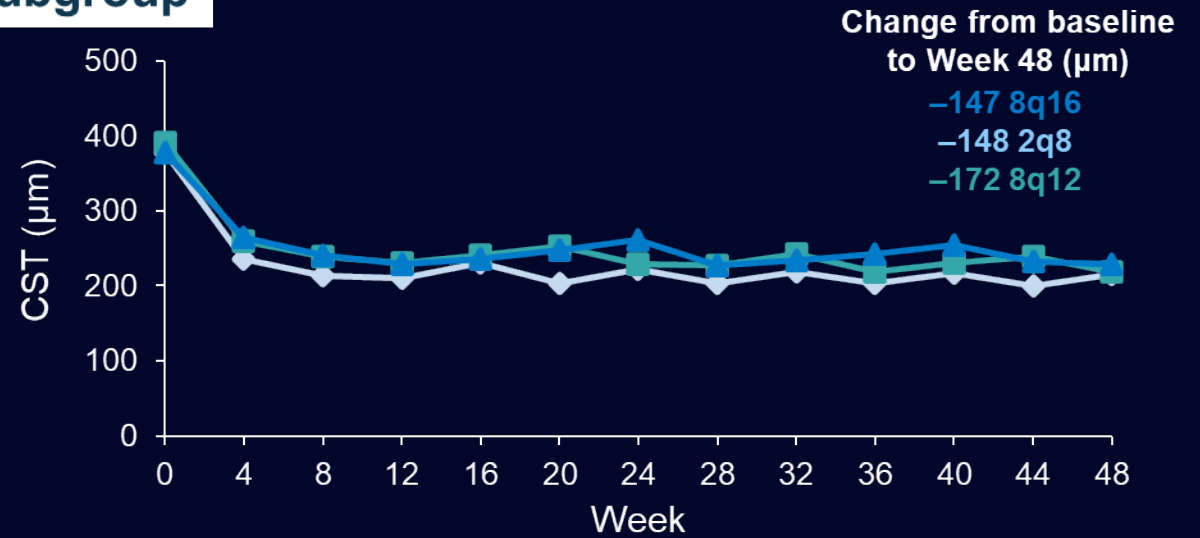
# PCV Subgroup: Anatomic Endpoints

Patients without retinal fluid  
in central subfield at Wk 16

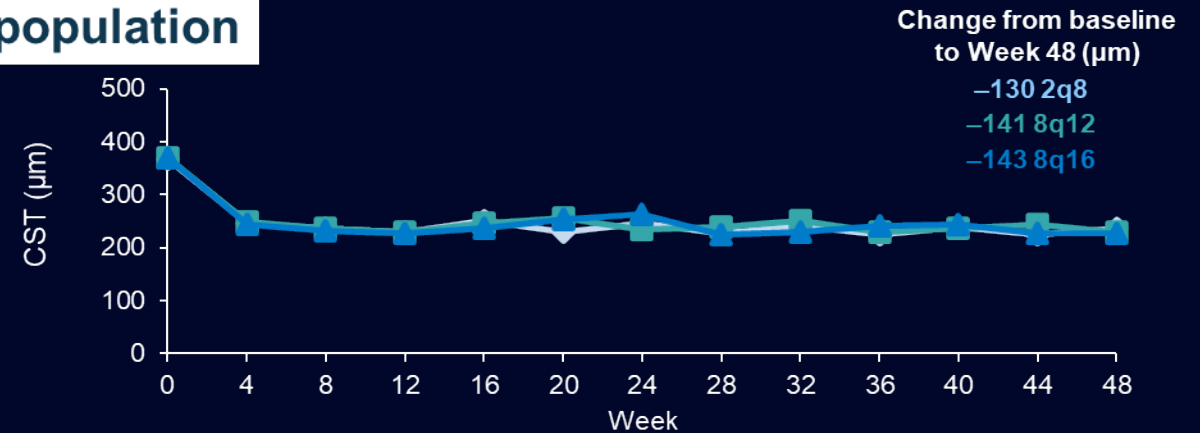
**PCV subgroup**



**Absolute CST**



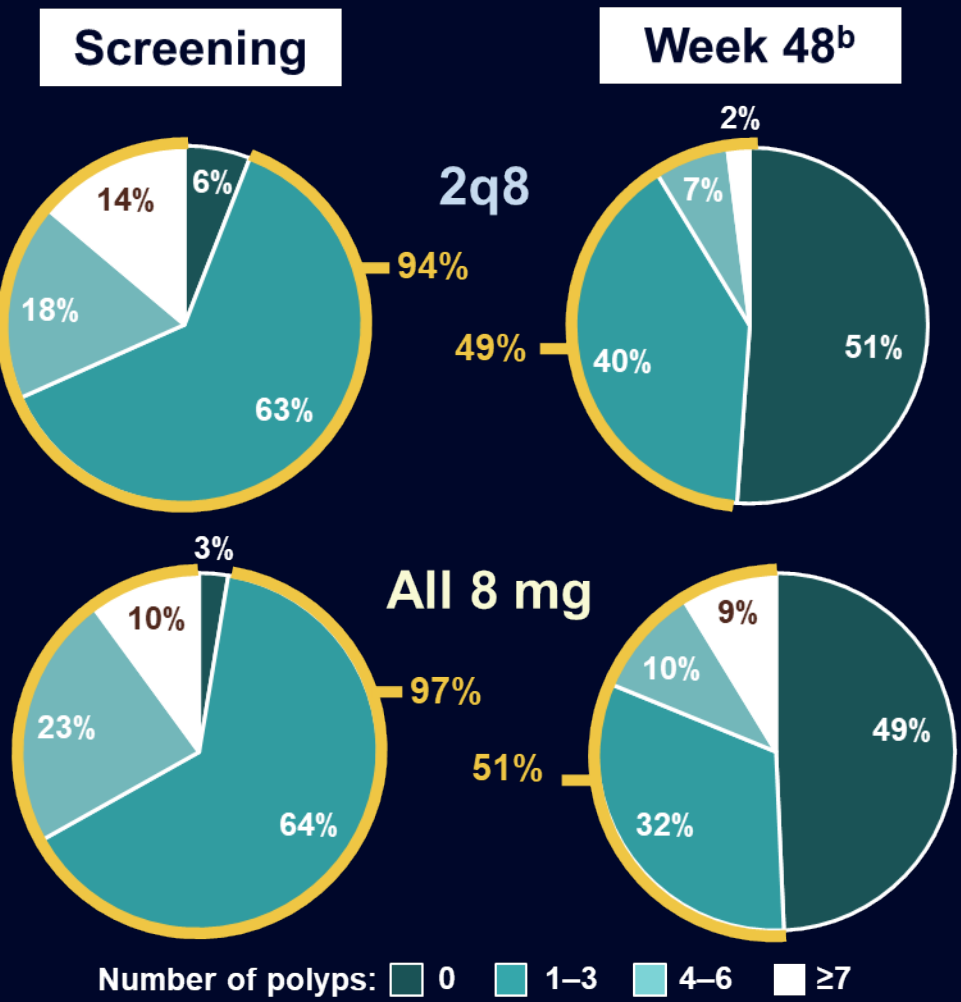
**Overall population**



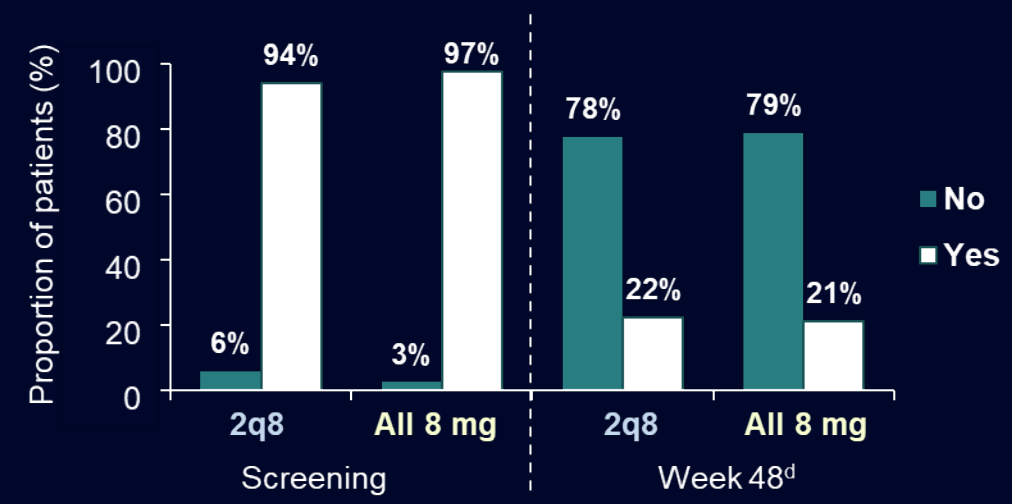
'Without retinal fluid' defined as absence of IRF and SRF in central subfield. For fluid: LOCF (censoring data post ICEs); FAS (PCV subgroup). For CST: LOCF, FAS. PCV subgroup, 2q8 n=54; 8q12 n=44; 8q16 n=41; overall population, 2q8 n=335; 8q12 n=333; 8q16 n=334.

# PCV Subgroup: Additional Analyses

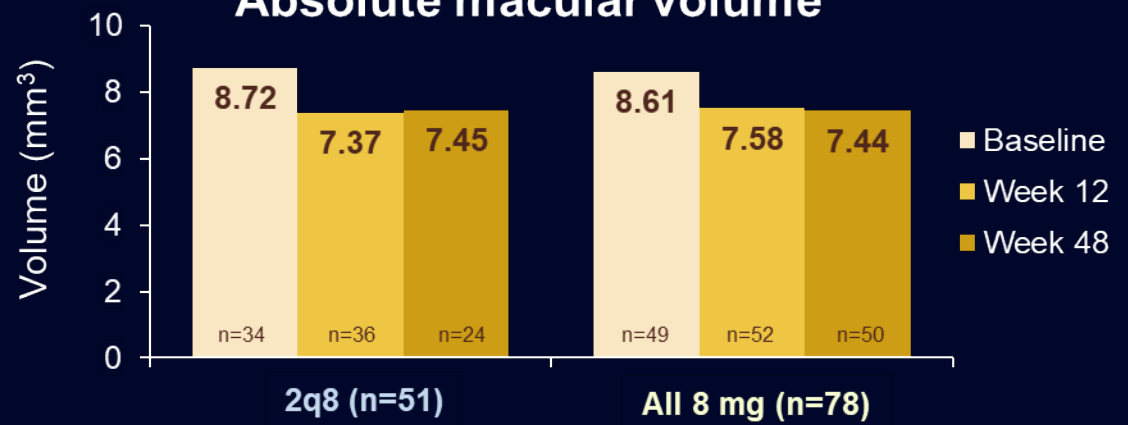
Patients with number of polyps<sup>a</sup>



Patients with active polyps<sup>a,c</sup>



Absolute macular volume



Data are for patients with PCV who completed Week 48. Screening (Visit 1) occurred before the baseline visit (Visit 2). <sup>a</sup>For polyp data: 2q8, n=51; All 8 mg, n=78. % calculated based on number of patients with known number of polyps. <sup>b</sup>At Wk 48, number of polyps unknown for n=6 and n=9 in 2q8 and All 8 mg groups, respectively. <sup>c</sup>'No' active polyps defined as no polyps present OR IRF and SRF are 'absent' or 'questionable'. <sup>d</sup>At Wk 48, n=2 unknown each for 2q8 and All 8 mg groups.



# PCV Subgroup: Safety – Week 48

TEAE, n (%)	PCV subgroup				Overall population			
	2q8	8q12	8q16	All 8 mg	2q8	8q12	8q16	All 8 mg
	n=54	n=44	n=41	n=85	n=336	n=335	n=338	n=673
<b>Any ocular TEAE</b>	14 (25.9)	17 (38.6)	13 (31.7)	30 (35.3)	130 (38.7)	129 (38.5)	127 (37.6)	256 (38.0)
Reduced visual acuity	3 (5.6)	2 (4.5)	0	2 (2.4)	20 (6.0)	12 (3.6)	18 (5.3)	30 (4.5)
Cataract	2 cases of cataracts <sup>a</sup>				10 (3.0)	12 (3.6)	12 (3.6)	24 (3.6)
Retinal hemorrhage	2 (3.7)	3 (6.8)	1 (2.4)	4 (4.7)	14 (4.2)	11 (3.3)	10 (3.0)	21 (3.1)
Intraocular pressure increased	1 (1.9)	2 (4.5)	3 (7.3)	5 (5.9)	7 (2.1)	11 (3.3)	9 (2.7)	20 (3.0)
Vitreous floaters	2 (3.7)	0	3 (7.3)	3 (3.5)	11 (3.3)	4 (1.2)	12 (3.6)	16 (2.4)
Subretinal fluid	0	0	0	0	11 (3.3)	10 (3.0)	5 (1.5)	15 (2.2)
Intraocular inflammation	1 mild case <sup>a</sup>				2 (0.6)	4 (1.2)	1 (0.3)	5 (0.7)
Endophthalmitis	0	0	0	0	0	0	0	0
Occlusive retinal vasculitis	0	0	0	0	0	0	0	0

**The safety profile of aflibercept 8 mg was comparable with that of aflibercept 2 mg both in the PCV subgroup and overall population of patients with nAMD**

Data are from the SAF. TEAEs are AEs occurring from the first injection to 30 days after the last injection (active or sham); ocular TEAEs are those occurring in the study eye.

<sup>a</sup>Data presented in this way to avoid unintentional patient unmasking.

AE, adverse event; TEAE, treatment-emergent adverse event; SAF, safety analysis set.

# Conclusions: Aflibercept 8 mg Monotherapy in PCV

**Aflibercept 8 mg monotherapy<sup>a</sup> showed robust efficacy benefits**

**Robust improvements in BCVA** from baseline to Week 48 were observed in the aflibercept 8q12, 8q16, and 2q8 PCV subgroups (+9.5, +7.5, and +9.3 letters, respectively)  
At **Week 16, fluid was absent** in 67% and 63% of patients with PCV in the pooled aflibercept 8 mg group and aflibercept 2 mg group, respectively  
Aflibercept 8 mg and aflibercept 2 mg **markedly reduced** the proportion of patients with PCV with **active polyps** from baseline (97% and 94%) to Week 48 (21% and 22%), respectively

**Extended durability**

In total, **87%** of patients with PCV treated with aflibercept 8 mg were maintained on dosing intervals **≥12 weeks**, suggesting extended durability compared with aflibercept 2 mg

**Comparable safety profile with aflibercept 2 mg**

In the PULSAR study, the **safety profile** of aflibercept 8 mg was **similar** in the PCV subgroup and the overall study population, and the safety profile was comparable to that of aflibercept 2 mg<sup>1,2</sup>

<sup>a</sup>Without active rescue photodynamic therapy.

1. Heier et al. Ophthalmology 2012;119(12):2537-48; 2. Schmidt-Erfurth et al. Ophthalmology 2014;121(1):193-201.