Use Case	PPT slides	PDF file	Notes
Provision to external physicians upon request	✗	✓	Non-editable PTT or PDF versions only
Presentation (by MA/MSL) to individual or small physician group upon request	✓	✓	In accordance with local rules / regulations
Presentation at local symposia or other large audience meetings (proactive communication)			Seek guidance from local compliance and follow guidance regarding unpublished data
Presentation during an Advisory Board	✓	✓	Under confidentiality
Internal medical training	✓	✓	In accordance with local rules / regulations; distribute PDF only
Internal sales training			Medical to conduct training in accordance with local rules / regulations; distribute PDF only
Internal distribution for information only	✓	✓	Medical colleagues only; best to refer to final version on SharePoint

Legend	✓	Yes		Seek further guidance	✗	No

Rapid Fluid Resolution With Aflibercept 8 mg may be Associated With Extended Dosing Intervals at Week 96 in nAMD: A PULSAR Post Hoc Analysis

Michael W. Stewart,[1*] Paolo Lanzetta,[2,3] Richard Gale,[4] Javier Zarranz-Ventura,[5] Sergio Leal,[6] Tobias Machewitz,[7] Xin Zhang,[6] on behalf of the PULSAR study investigators

[1]Mayo Clinic College of Medicine and Department of Ophthalmology, Mayo Clinic, Jacksonville, FL, USA
[2]Department of Medicine – Ophthalmology, University of Udine, Udine, Italy
[3]Istituto Europeo di Microchirurgia Oculare (IEMO), Udine and Milan, Italy
[4]York and Scarborough Teaching Hospital NHS Foundation Trust, York, UK
[5]Hospital Clínic de Barcelona Institut Clinic de Oftalmología (ICOF), Barcelona, Spain
[6]Bayer Consumer Care AG, Basel, Switzerland
[7]Bayer AG, Berlin, Germany

*Presenter email: Stewart.Michael@mayo.edu

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PULSAR: Multicenter, Double-masked Study in Patients With Treatment-naïve nAMD

Patients were randomly assigned (1:1:1) to receive aflibercept 8q12 (n=335), 8q16 (n=338), or 2q8 (n=336), each after 3 initial monthly injections

- At W48, treatment with aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with nAMD,[1] with a consistent safety profile to aflibercept 2 mg
- At W96, treatment with aflibercept 8 mg maintained improvements in visual and anatomic outcomes with extended dosing intervals, demonstrating long-term efficacy with a consistent safety profile to aflibercept 8 mg

	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	–

[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

Figure does not reflect all dosing options once a patient's dosing interval is shortened or extended. Stippled boxes = initial treatment phase; X = active injection; o = sham injections.
2q8, aflibercept 2 mg every 8 weeks; **8q12**, aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **Q(n)**, every n weeks; **BCVA**, best-corrected visual acuity; **CRT**, central retinal thickness; **DRM**, dose regimen modification; **nAMD**, neovascular age-related macular degeneration; **OCT**, optical coherence tomography; **W**, week. 1. Lanzetta P, et al. *Lancet*. 2024;403:1141–1152.

Analysis of Early Fluid Resolution and its Association with the Last Assigned Dosing Interval at Week 96 in the Aflibercept 8-mg Groups

Objective:

To determine whether early fluid resolution is associated with last assigned dosing interval at W96 in patients treated with aflibercept 8 mg

Methods:

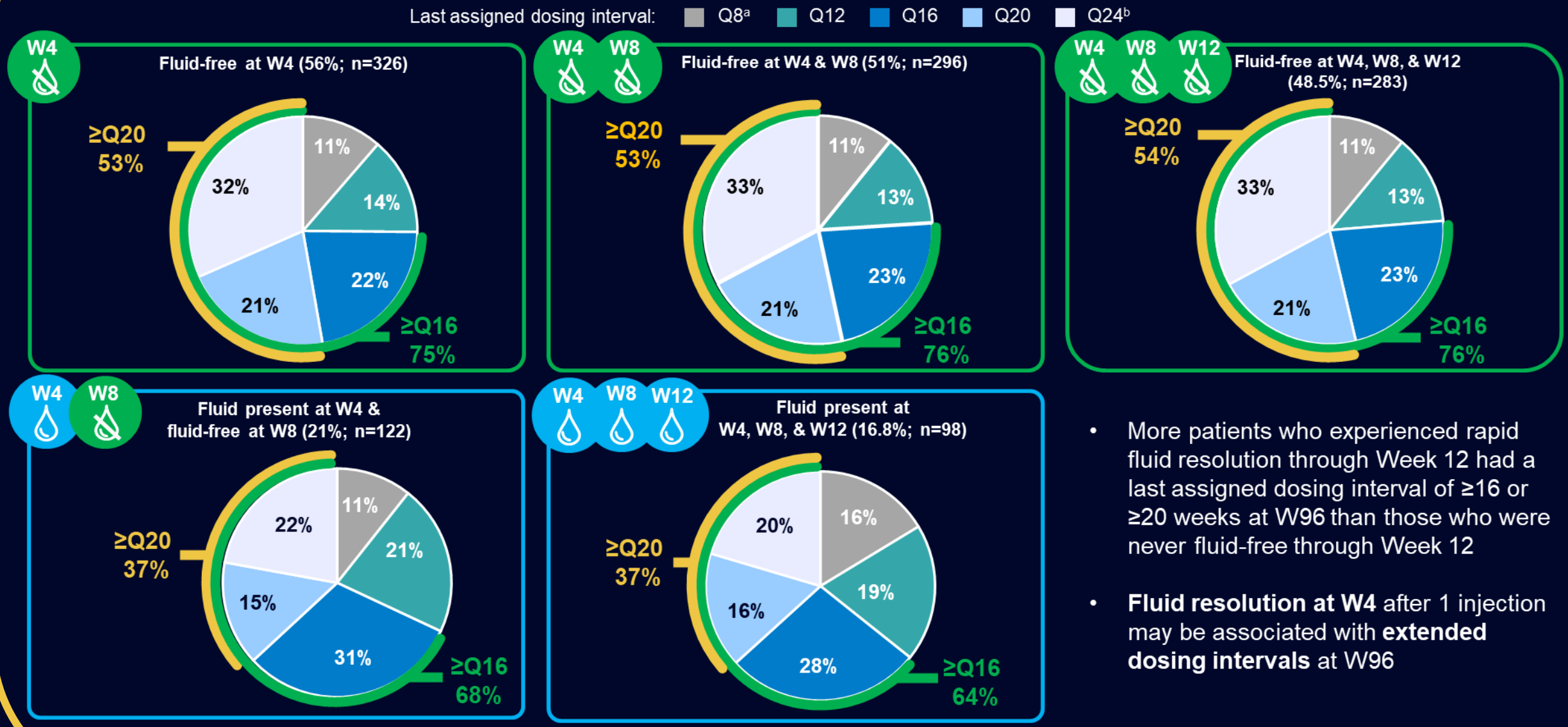
The association between fluid resolution at W4, W8, and W12 (4 weeks after each initial monthly injection) and the last assigned dosing interval at W96 in patients who received aflibercept 8 mg (8q12 and 8q16 groups) was analyzed, regardless of fluid outcomes at other timepoints

Analyzed patient groups	Day 1	W4	W8	W12
Three initial monthly injections in both aflibercept 8 mg and 2 mg groups				
Fluid-free at W4			/	/
Fluid-free at W4 and W8				/
Fluid-free at W4, W8, and W12				
Fluid present at W4 and fluid-free at W8				/
Fluid present at W4, W8, and W12				

Fluid-free **Fluid present**

Fluid status was not assessed on Day 1 but was evaluated pre-injection at W4 and W8. It was defined as the absence of IRF and SRF (fluid-free) or presence of fluid (fluid present) in the center subfield.
/ = patients who were either fluid-free, not fluid-free, or with unknown fluid status. **IRF**, intraretinal fluid; **SRF**, subretinal fluid.

Last Assigned Dosing Interval at Week 96 of the Aflibercept 8-mg Groups Based on Early Fluid Status



- More patients who experienced rapid fluid resolution through Week 12 had a last assigned dosing interval of ≥16 or ≥20 weeks at W96 than those who were never fluid-free through Week 12
- **Fluid resolution at W4** after 1 injection may be associated with **extended dosing intervals** at W96

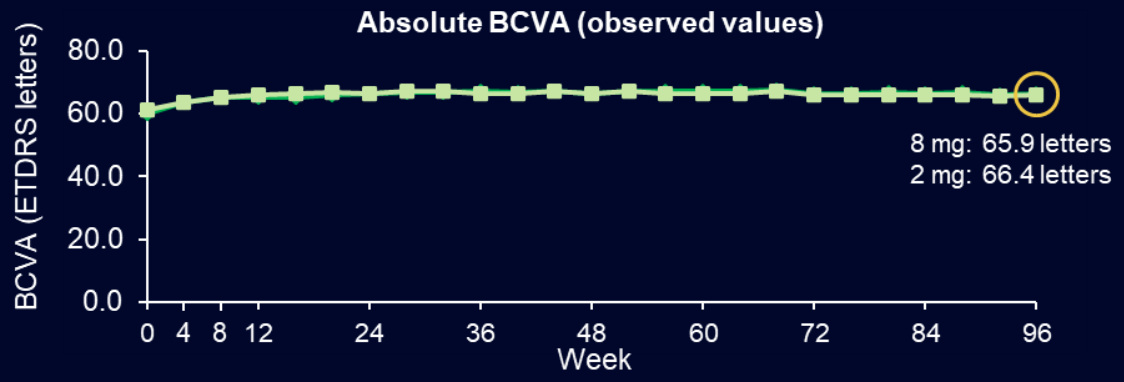
FAS. Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding. [a]Patients had their dosing interval shortened based on DRM assessments at some point through W96. [b]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period. [c]FAS. OC prior to ICE. **ETDRS**, Early Treatment Diabetic Retinopathy Study; **ICE**, intercurrent event; **OC**, observed cases.

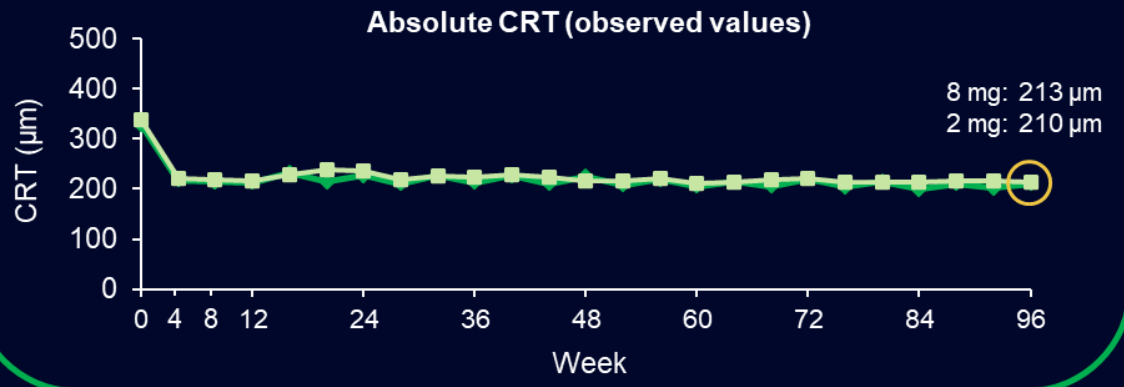
BCVA and CRT Outcomes in the Aflibercept 8-mg and 2-mg Groups Through Week 96 Based on Early Fluid Status

W4

Patients who were fluid-free at Week 4

8-mg groups 2-mg group

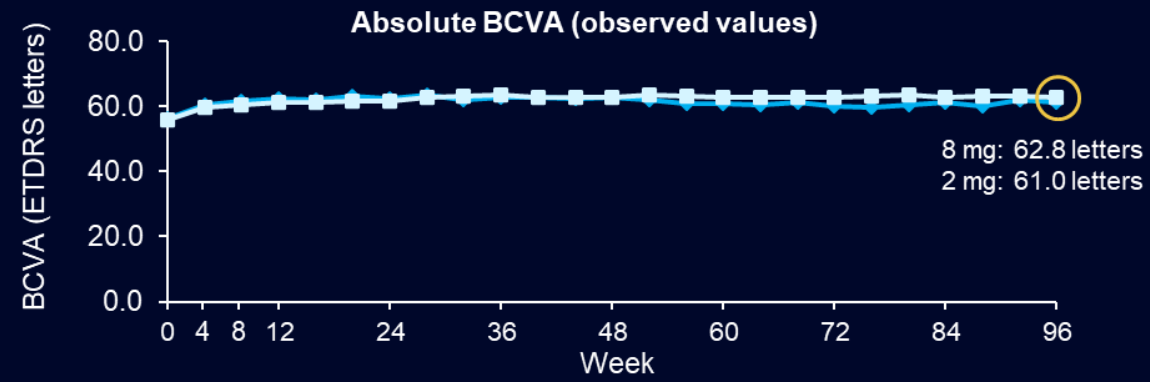


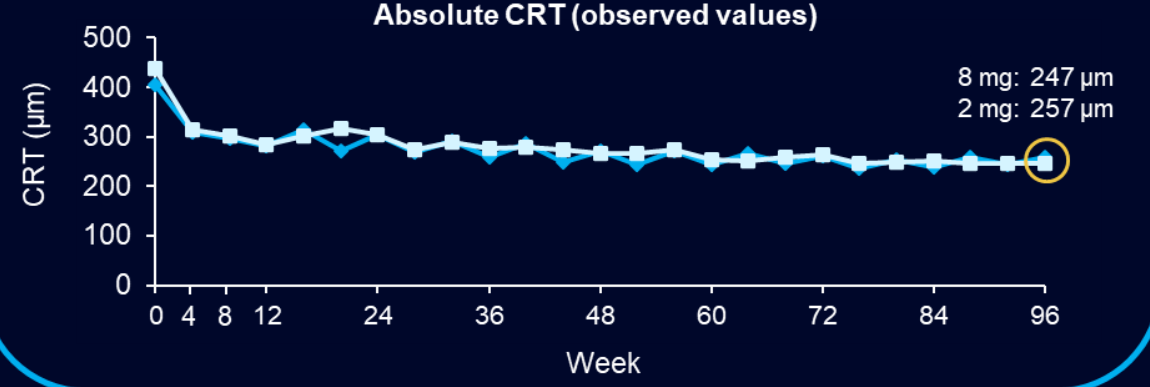


W4 W8 W12

Patients who had fluid at Weeks 4, 8, and 12

8-mg groups 2-mg group



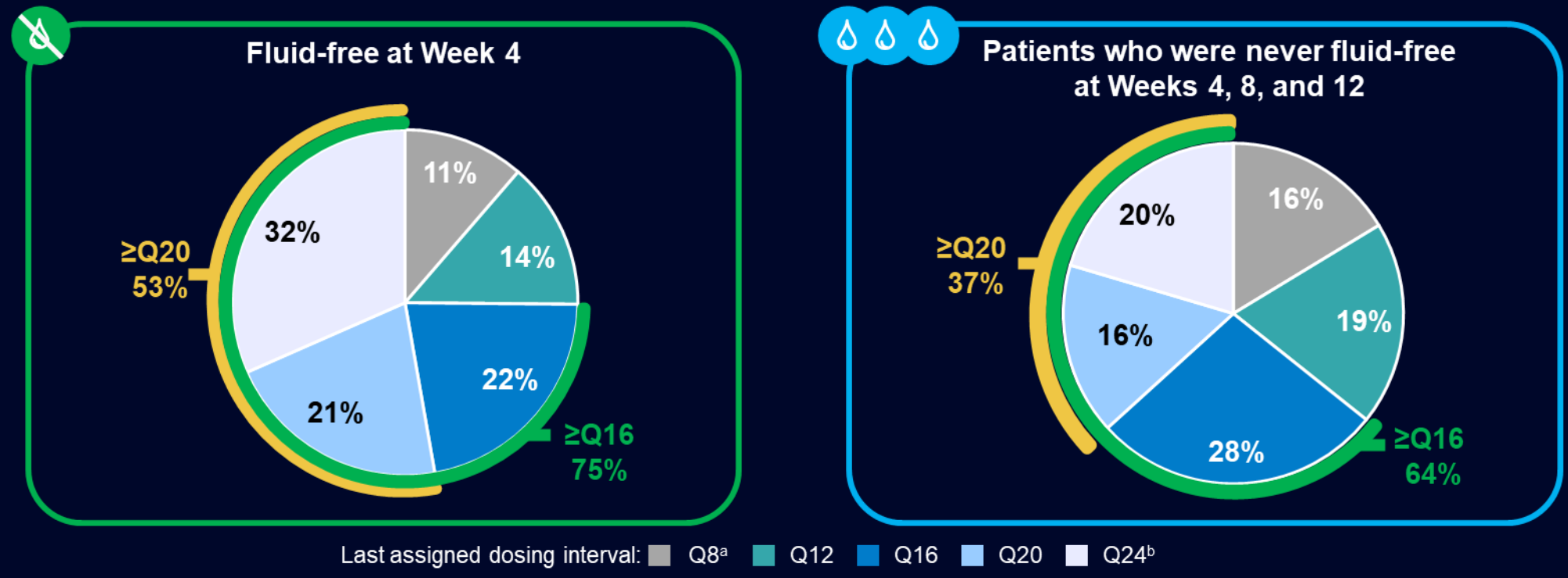


- Rapid BCVA gains and CRT reductions were observed after the first injection and were sustained over 96 weeks

FAS (OC prior to ICE).

Conclusion

- **Rapid fluid resolution** during the initial monthly treatment phase – particularly at Week 4 after the first injection – may be associated **with extended dosing intervals in patients who received aflibercept 8 mg** for nAMD
- Patients in the 8-mg groups who had early fluid resolution were able to achieve extended dosing intervals **without compromising visual and anatomic outcomes**



FAS. Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding. [a]Patients had their dosing intervals shortened based on DRM assessments at some point through W96. [b]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.