Differential anatomic response to aflibercept 8 mg versus 2 mg during the matched dosing phase of the PHOTON trial in patients with diabetic macular edema who subsequently met criteria for shortening

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- Rosangela Lattanzio serves as a consultant for AbbVie, Bayer, Roche, and Novartis
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- Edoardo Midena reports no disclosures
- Dilsher S. Dhoot serves as a consultant for Alimera, Allergan, Alkeus, Apellis, Annexon, Bausch + Lomb, Bayer, Biocryst, Coherus, EyePoint Pharmaceuticals, Genentech, IvericBio, Neurotech, Novartis, Ocular Therapeutix, Oculis, Optos, Outlook Therapeutics, Oxular, Regeneron Pharmaceuticals, Inc., REGENXBIO, and Roche
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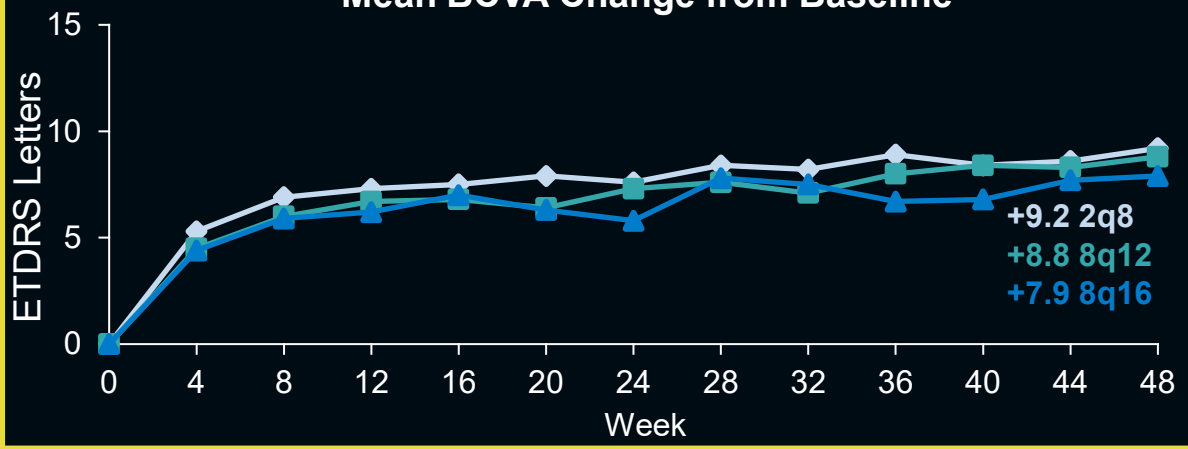
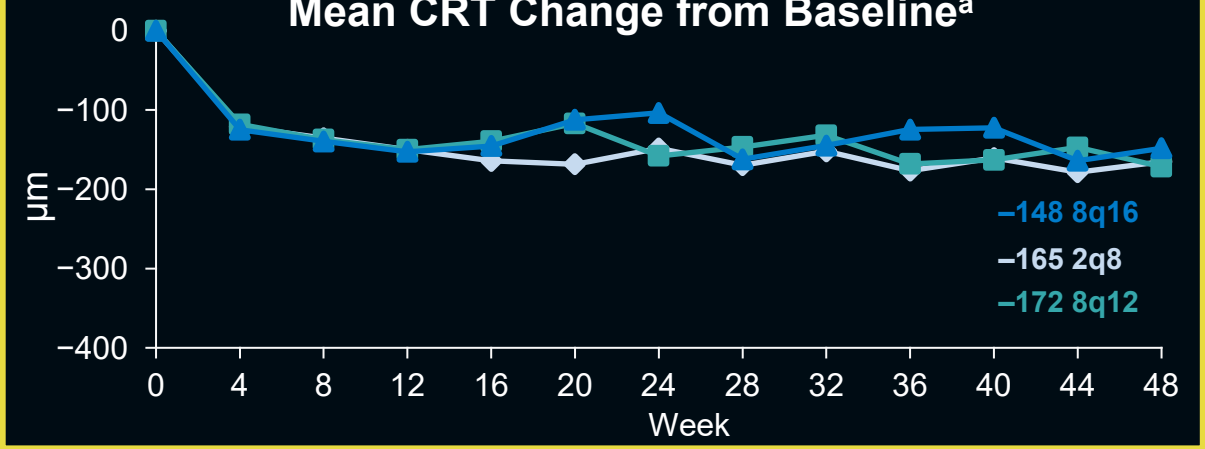
PHOTON Key Outcomes Through Week 48

DME

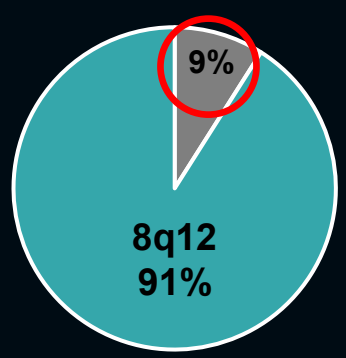
Mean BCVA Change from Baseline[a]



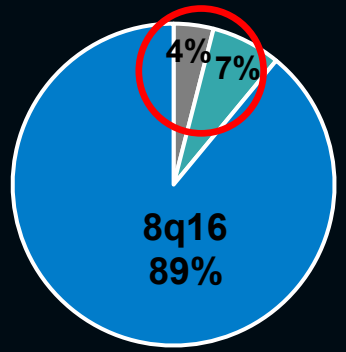
Mean CRT Change from Baseline[a]



Patients Maintained Their Randomized Dosing Intervals

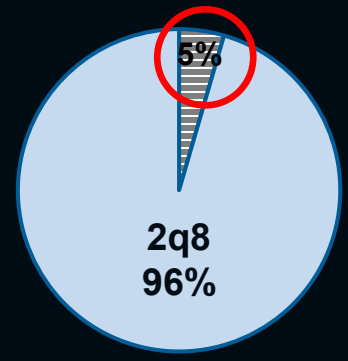


8q12 (n=300)[b]



8q16 (n=156)[b]

Patients Hypothetically Met Shortening Criteria



2q8 (n=157)[b]

[a]FAS, observed values (censoring data post-ICE). [b]FAS, patients who completed Week 48 visit.
2q8, aflibercept 2 mg every 8 weeks after 5 initial monthly doses; 8q12, aflibercept 8 mg every 12 weeks after 3 initial monthly doses; 8q16, aflibercept 8 mg every 16 weeks after 3 initial monthly doses; BCVA, best-corrected visual acuity; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set; ICE, intercurrent event.

PHOTON: Dosing Schedule and Dose Regimen Modifications in Year 1

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DME

	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	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16	X	X	X	o	o	o	X	o	o	o	X	o	o

DRM Criteria for Shortening Dosing Interval*

- >10-letter loss in BCVA due to persistent or worsening DME

AND

- >50-micron increase in CRT

*All assessments compared to Week 12

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 36[a] and 40 for 8q16: Treatment interval shortened by 4 weeks for patients meeting DRM criteria

- This post hoc analysis assessed visual and anatomic outcomes over the matched dosing phase of PHOTON through Week 12 among patients with DME who did or did not meet the dosing interval shortening criteria any time from Weeks 16 through 48

Yellow boxes indicate visits at which patients were assessed for DRM. Orange boxes indicate visits at which patients were assessed for hypothetical shortening during this study. Stippled boxes = initial treatment phase; X = active injection; o = sham injections. Note: Figure does not reflect all dosing options once a patient is shortened.[a]At Week 36, patients on 8q16 who were previously shortened to Q12 could have been shortened to Q8. DME, diabetic macular edema; DRM, dose regimen modification; Q8, every 8 weeks, Q12, every 12 weeks; Wk, Week.

Mean Change in BCVA and CRT Through Week 12 in Patients Who Met Shortening Criteria

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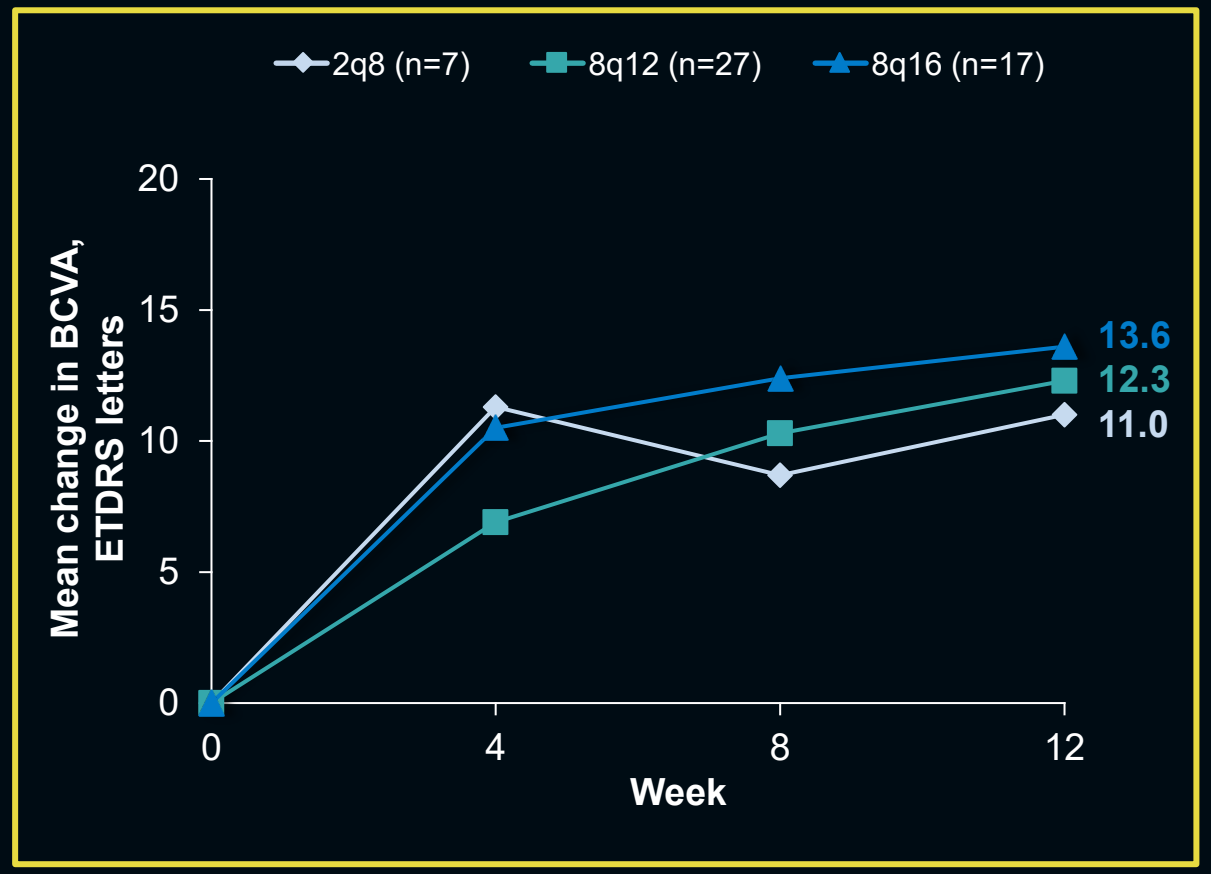
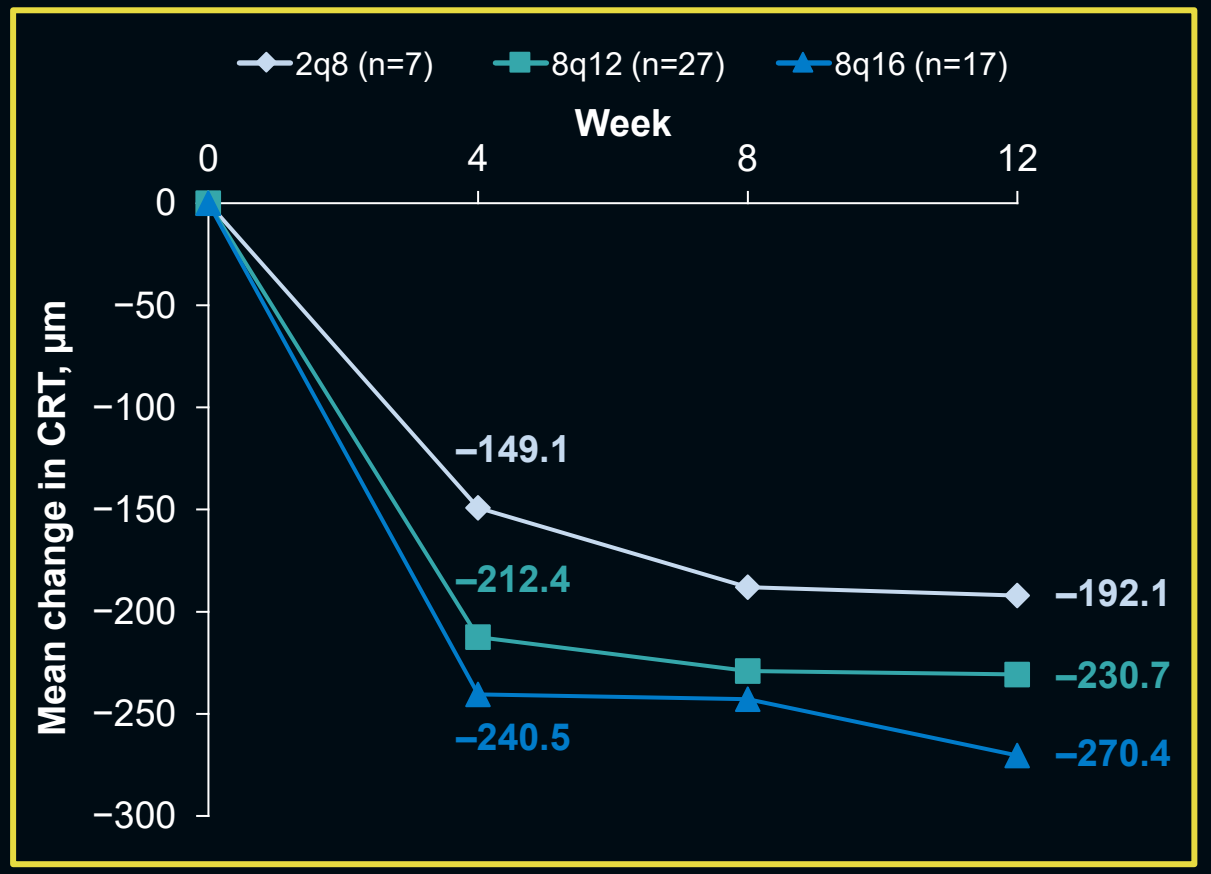
DME

BCVA



CRT



In patients who met shortening criteria, CRT improvements were relatively greater with aflibercept 8 mg than 2 mg, with similar BCVA gains across treatment groups

FAS, patients who completed Week 48 visit, observed cases (data post-ICE were excluded).

Mean Change in BCVA and CRT Through Week 12 in Patients who Did Not Meet Shortening Criteria

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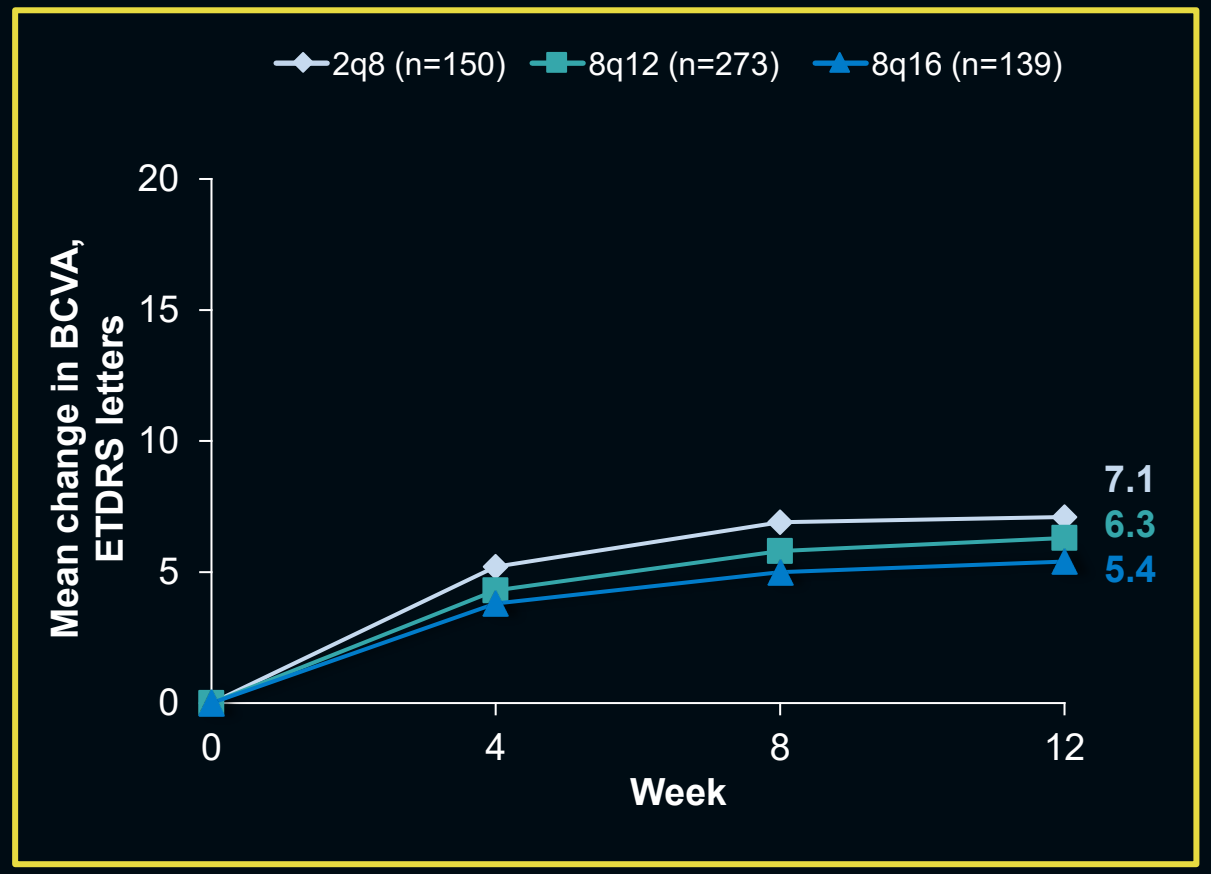
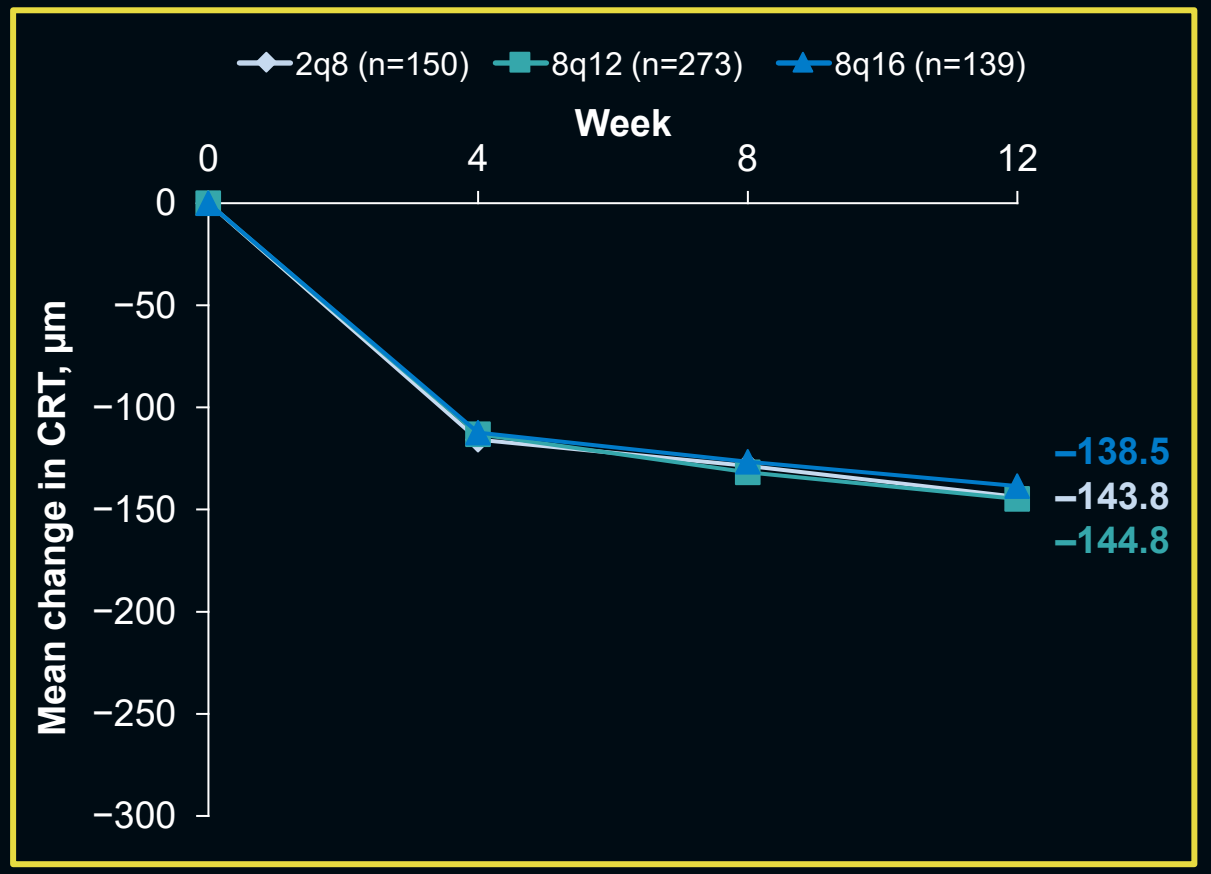
DME

BCVA



CRT



In patients who did not meet shortening criteria, BCVA and CRT improvements were comparable across all treatment groups

FAS, patients who completed Week 48 visit, observed cases (data post-ICE were excluded).

Proportion of Patients With no IRF and SRF in the Center Subfield at Baseline and Week 12

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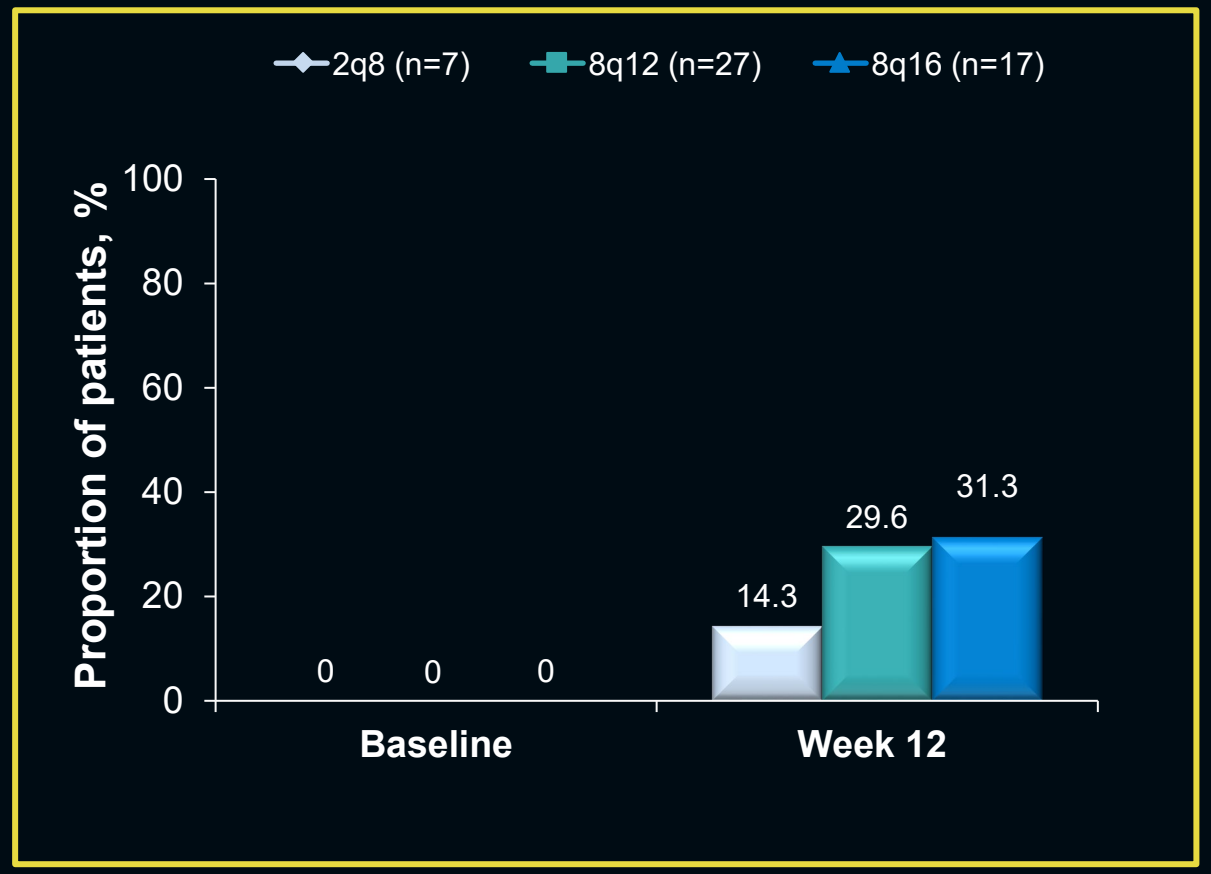
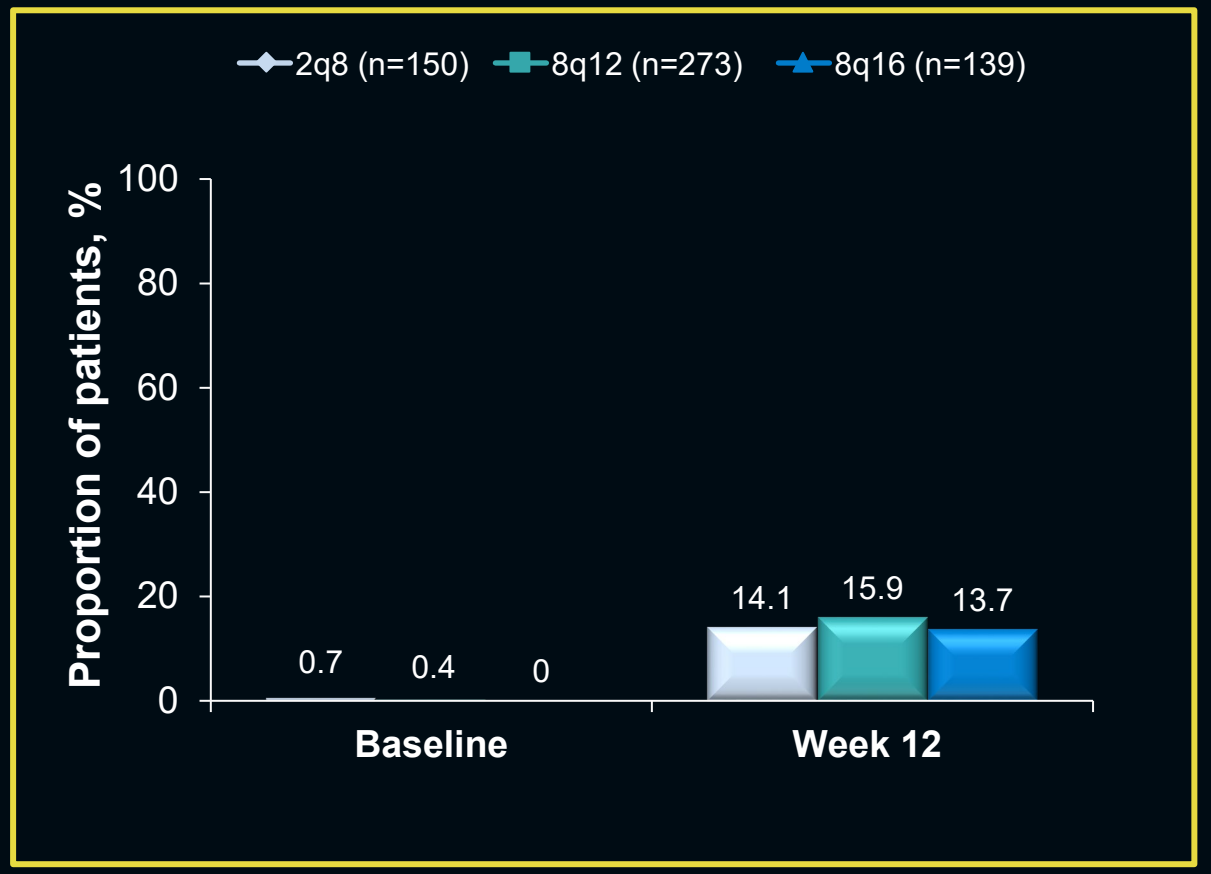
DME

Met shortening criteria



Did not meet shortening criteria

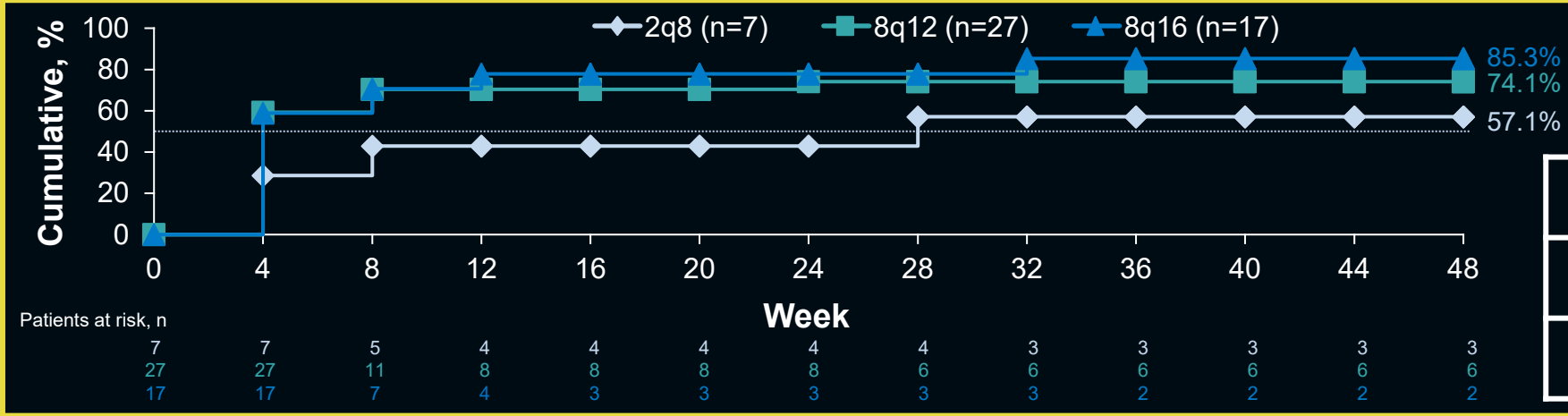


In patients who met shortening criteria, a relatively greater proportion of patients treated with aflibercept 8 mg had no retinal fluid at Week 12

FAS, patients who completed Week 48 visit, observed cases (data post-ICE were excluded). IRF, intraretinal fluid; SRF, subretinal fluid.

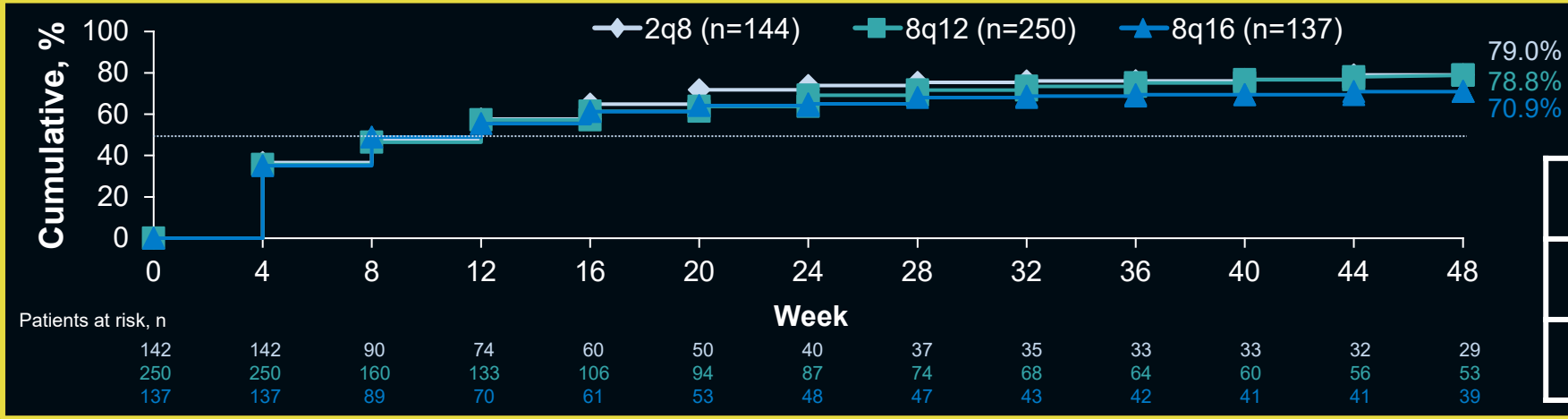
Time to CRT <300 µm Through Week 48[a]

Met shortening criteria



	2q8 (n=7)	8q12 (n=27)	8q16 (n=17)
Median time, weeks	28	4	4
Hazard ratio (95% CI)	-	1.71 (0.56, 5.18)	1.86 (0.58, 5.94)
Nominal *P*-value	-	0.3436	0.2938

Did not meet shortening criteria



	2q8 (n=144)	8q12 (n=250)	8q16 (n=137)
Median time, weeks	12	12	12
Hazard ratio (95% CI)	-	0.99 (0.78, 1.25)	0.86 (0.65, 1.13)
Nominal *P*-value	-	0.9022	0.2654

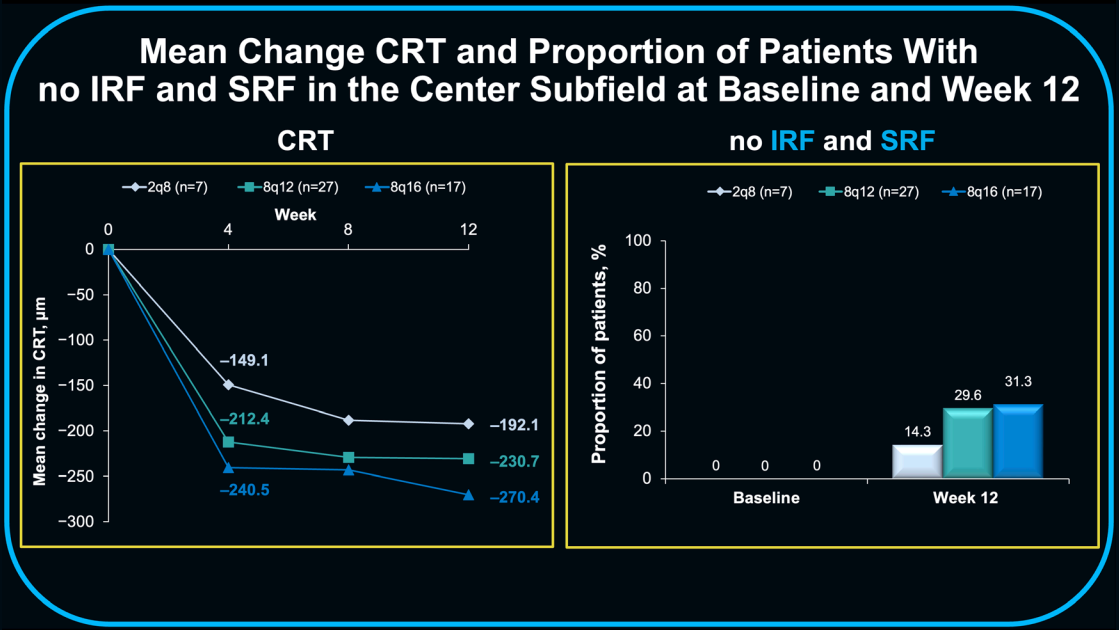
Patients treated with aflibercept 8 mg who met shortening criteria achieved CRT <300 µm relatively faster than those treated with aflibercept 2 mg in the same subgroup

FAS, patients who completed Week 48 visit. [a]Patients with baseline CRT ≥300 µm.

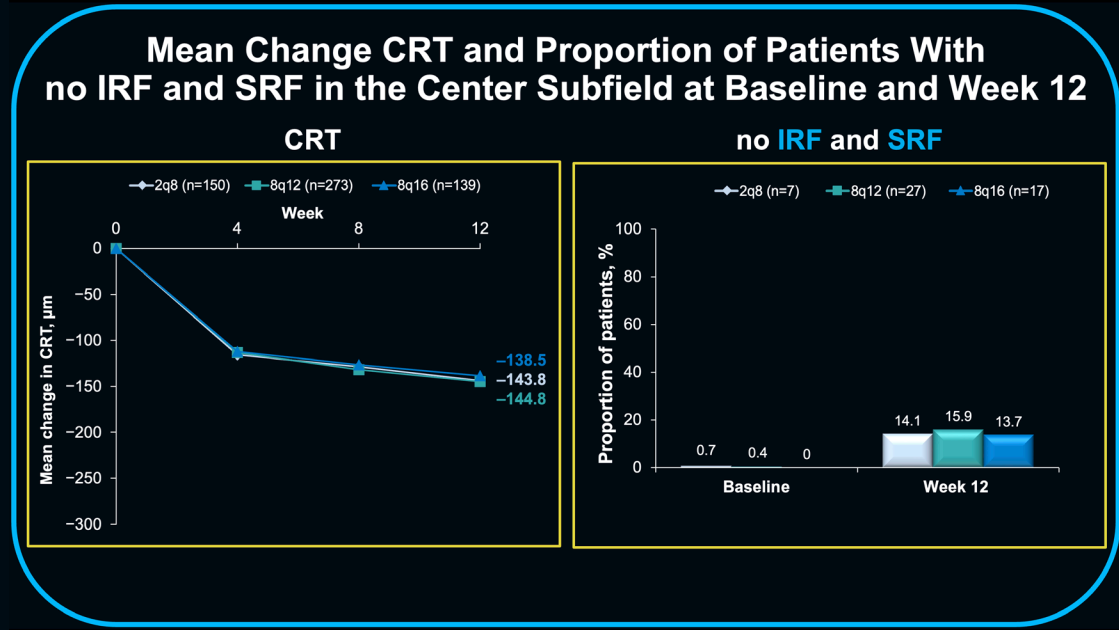
Conclusions

DME

In patients who met shortening criteria (~10%):



In patients who did not meet shortening criteria (~90%):



- Aflibercept 8 mg provided relatively greater anatomic benefit than aflibercept 2 mg, with similar BCVA gains
- Aflibercept 8 mg provided similar visual and anatomic outcomes compared with 2 mg but with fewer injections over 48 weeks, potentially reducing treatment burden

Limitations: (a) Small number of patients; (b) no adjustment for multiplicity; considered hypothesis-forming only