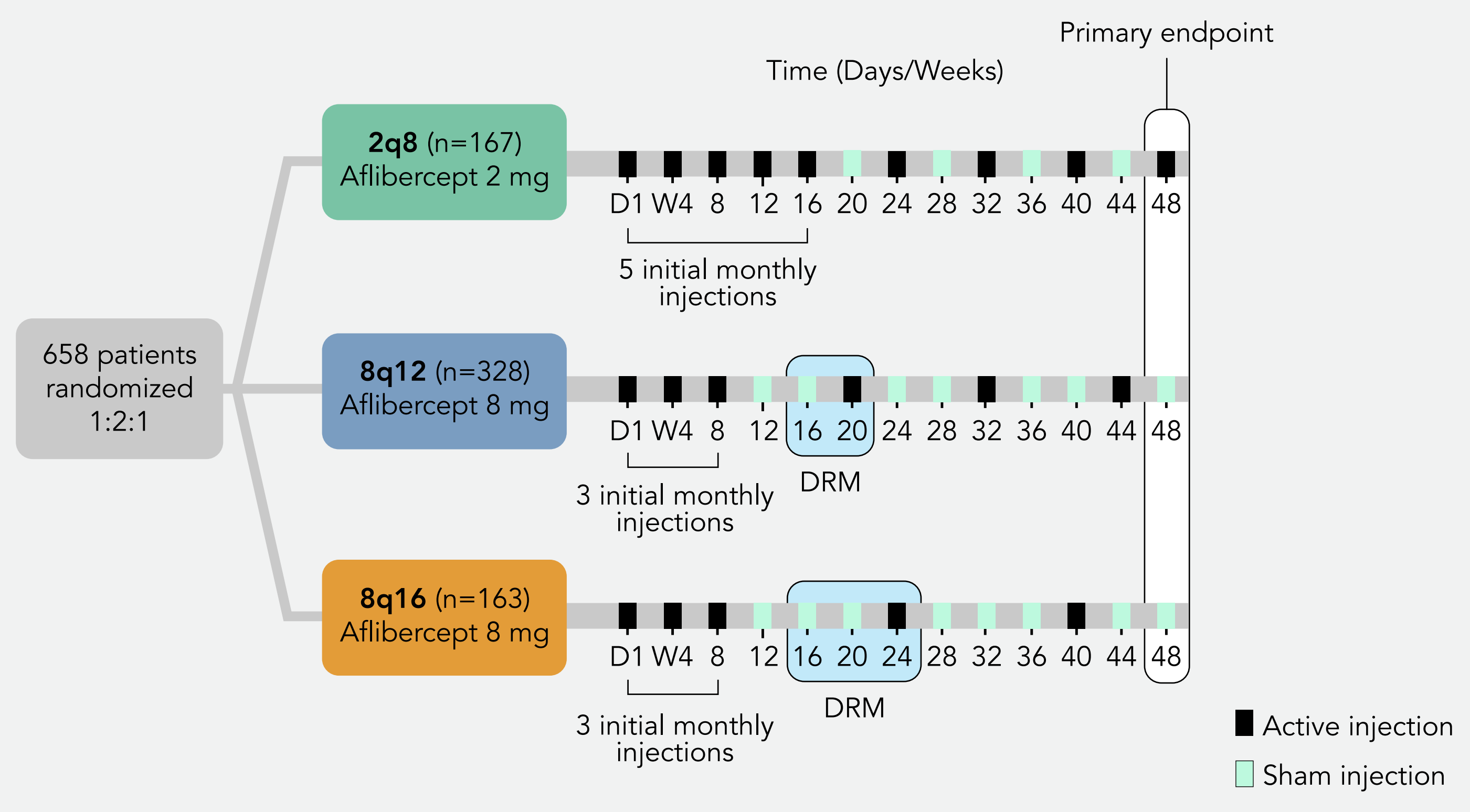
Intravitreal aflibercept 8 mg injection for DME: 48-week results from the Phase 2/3 PHOTON trial

Intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy is the current standard of care for center-involving diabetic macular edema (CI-DME). However the requirement for frequent monitoring and injections may limit the real-world effectiveness of these medications. Using 4-times higher molar dose compared to aflibercept 2 mg is hypothesized to provide longer effective vitreal concentration and enable more sustained effect on VEGF signaling. The Phase 2/3 PHOTON evaluates the efficacy and safety of aflibercept 8 mg vs 2 mg in patients with DME. This global study in ongoing and conducted across 138 sites in 7 countries.

Brown DM on behalf of the PHOTON study investigators. Presented at The Retina Society 55th Annual Scientific Meeting; November 2-5, 2022; Pasadena, CA.

Patients with center-involving DME were randomized and double-masked over a study period of 96 weeks, with primary endpoint at Week 48.



Dose Regimen

- **2q8:** Aflibercept 2 mg every 8 weeks after 5 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

Dose Regimen Modifications (DRM)

- **DRM criteria** for shortening dosing interval:
  >10-letter loss in BCVA from week 12 due to persistent or worsening DME + >50-micron increase in CRT from week 12
- **Weeks 16 or 20:** 8q12 or 8q16 patients meeting DRM criteria had treatment interval shortened **to every 8 weeks**
- **Week 24:** 8q16 patients meeting DRM criteria had treatment interval shortened **to every 12 weeks**
- **Subsequent dosing visits:** patients on 8 mg meeting DRM criteria had treatment interval shortened **by 4 weeks**

DME = diabetic macular edema; BCVA = best corrected visual acuity; CRT = central retinal thickness.

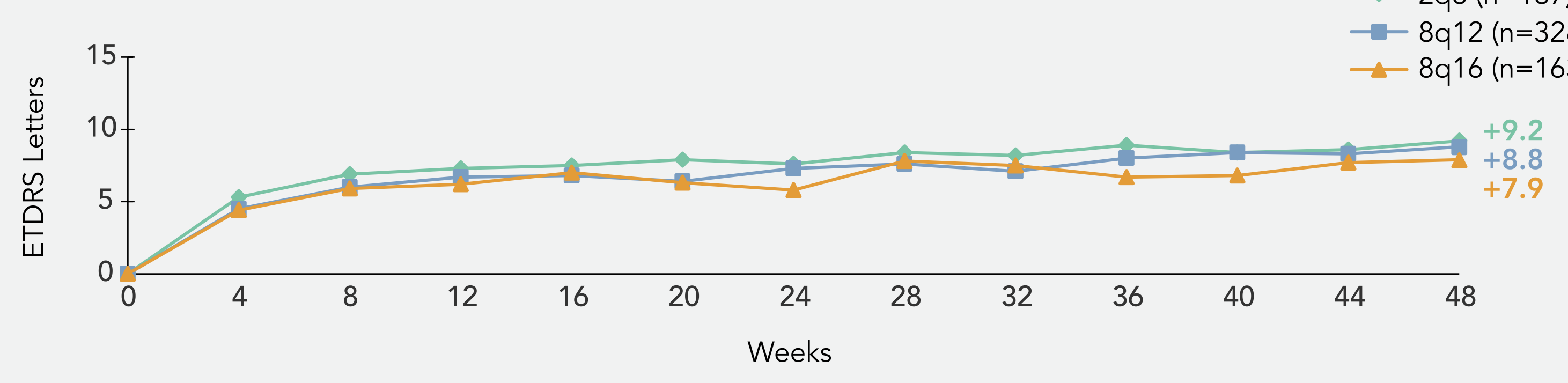
Baseline characteristics of the PHOTON study eye.

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
BCVA (ETDRS letters)	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
Snellen equivalent	20/63	20/50	20/63	20/63
20/32 (>73 to 78 letters)	12.0%	18.0%	14.1%	15.5%
20/40 or worse (≤73 letters)	88.0%	82.0%	85.9%	84.5%
CRT (μm)	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)
Prior treatment for DME (%)	44.3%	43.6%	43.6%	43.8%
DRSS categories (%)				
Better or equal to level 43	62.9%	60.1%	65.6%	62.2%
Level 47 or worse	31.7%	34.5%	28.2%	32.4%
Missing/ungradable	5.4%	5.5%	6.1%	5.6%

Data are mean (SD) unless otherwise indicated. ETDRS = Early Treatment of Diabetic Retinopathy Study.

The BCVA primary endpoint was met in both 8 mg groups after 48 weeks.

BCVA change from baseline



	Mean change from baseline at week 48 (MMRM)	Difference in LS means vs. 2q8 (95% CI)	1-sided test for non-inferiority at 4-letter margin
2q8	8.7		
8q12	8.1	-0.57 (-2.26, 1.13)	*P*< .0001
8q16	7.2	-1.44 (-3.27, 0.39)	*P*= .0031

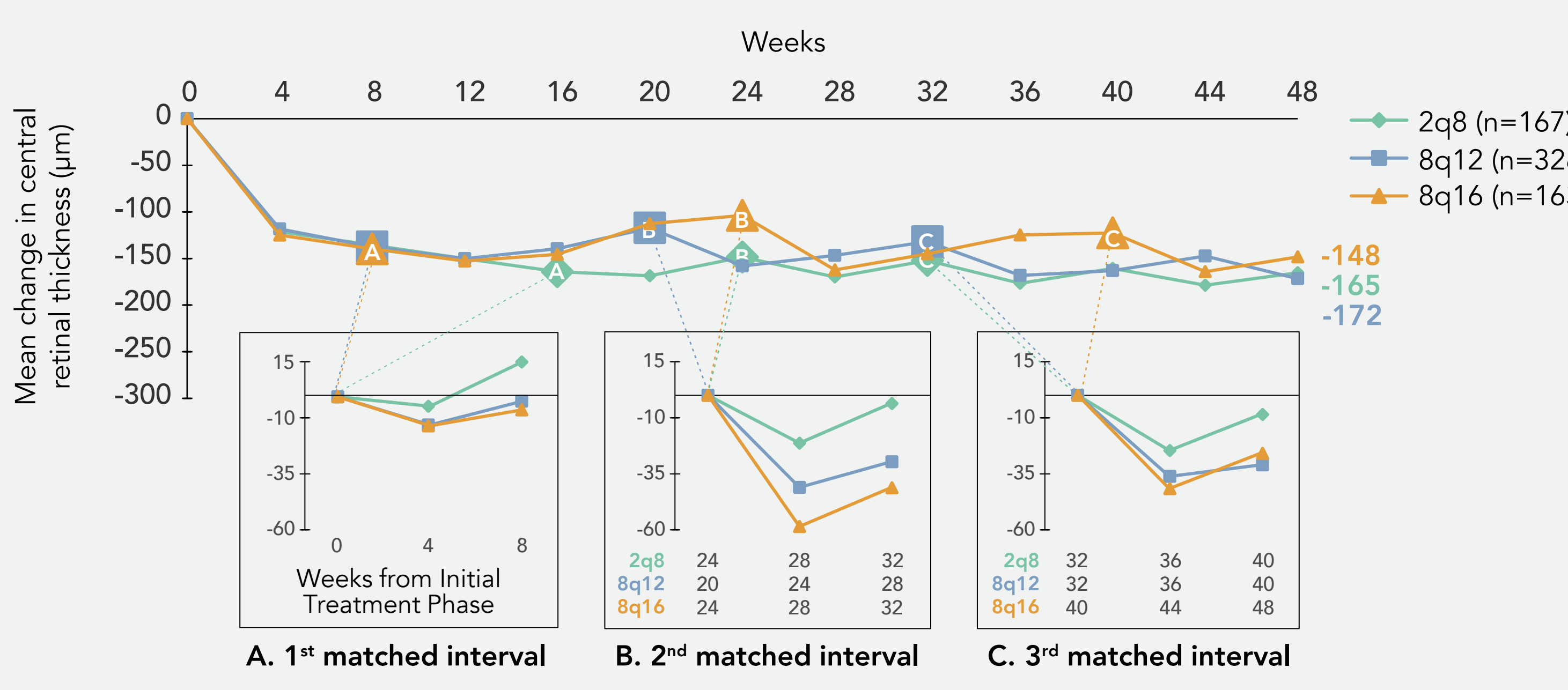
At Week 48

- Both 8 mg groups had non-inferior BCVA compared to 2q8
- 8q12 group met the non-inferiority margin of 15% in the proportion of patients with ≥2-step improvement in DRSS

MMRM = mixed model for repeated measurements.

Despite fewer initial monthly doses, 8 mg groups exhibited longer duration at each matched interval, thus achieving similar retinal thickness to 2 mg by week 48.

Note: 2 mg arm received 5 initial monthly injections vs. 8 mg arms which received only 3 initial monthly injections



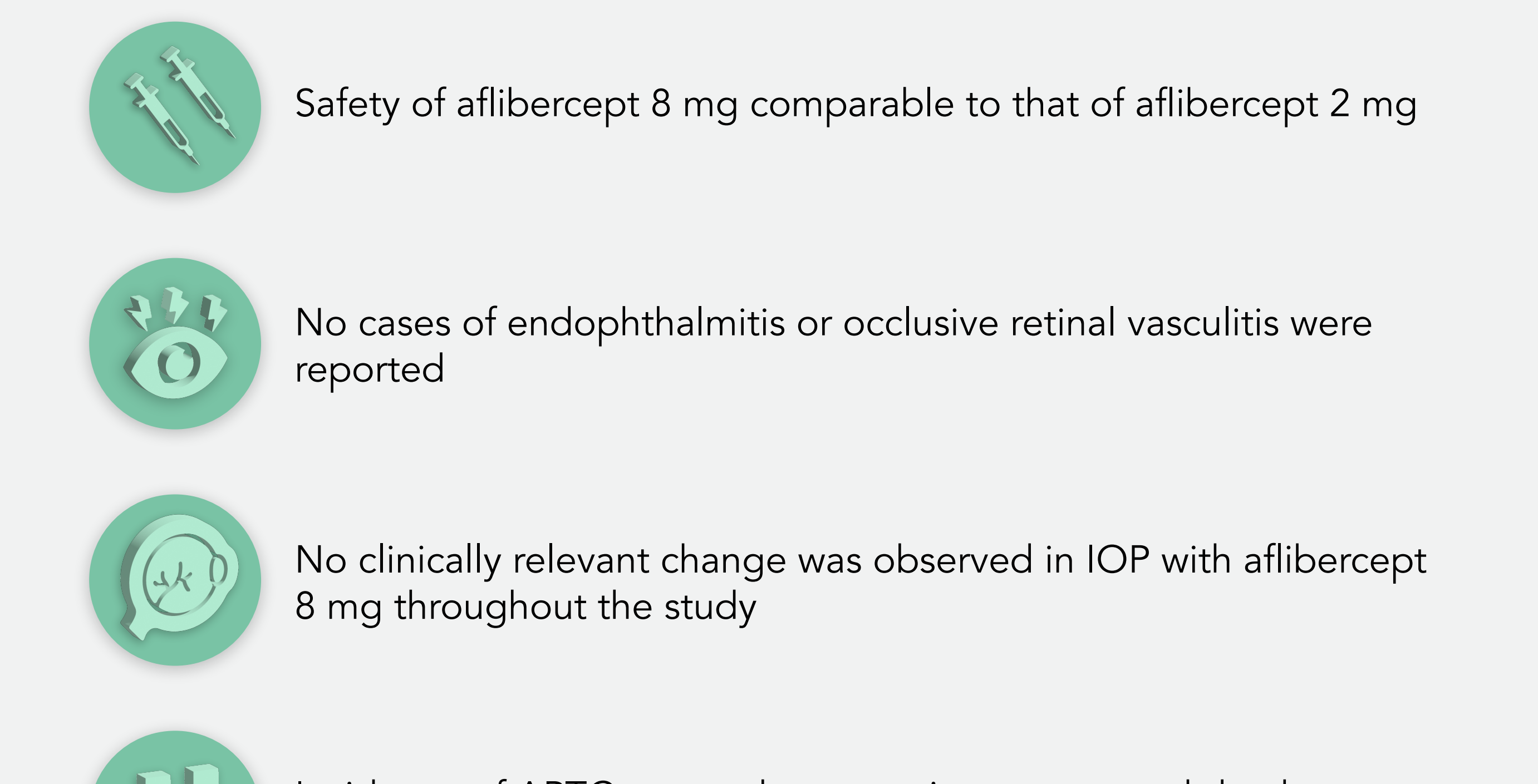
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).

PHOTON 48-week safety results.

- Safety of aflibercept 8 mg comparable to that of aflibercept 2 mg
- No cases of endophthalmitis or occlusive retinal vasculitis were reported
- No clinically relevant change was observed in IOP with aflibercept 8 mg throughout the study
- Incidence of APTC events, hypertension events, and death was similar between aflibercept 8 mg and 2 mg

IOP = intraocular pressure; APTC = Anti-Platelet Trialists' Collaboration.

A large majority of 8 mg patients maintained randomized intervals.



*Patients shortened based on DRM assessments at some point through Week 48. [a]Patients completing Week 48.

Conclusion

PHOTON Phase 2/3 trials showed that **both 8 mg aflibercept arms had non-inferior BVCA to 2 mg** every 8 weeks with comparable ocular/nonocular safety and randomized interval maintenance.