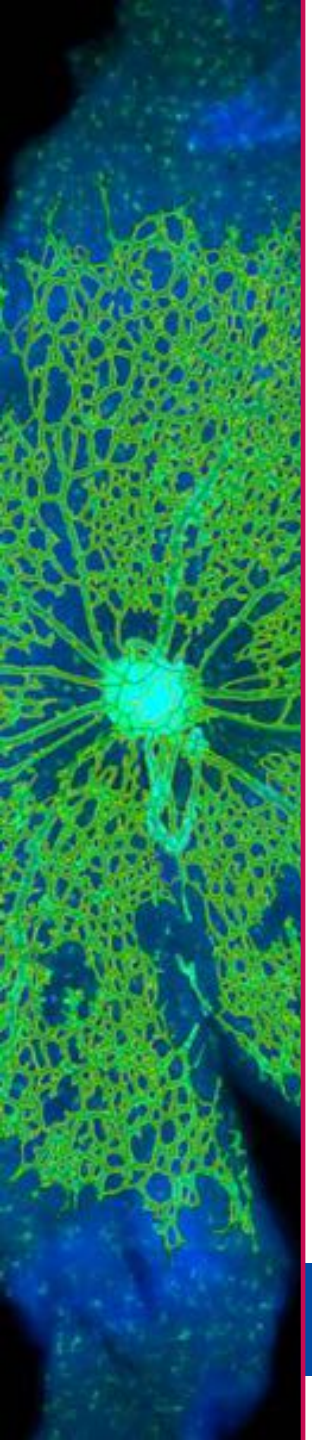

Clinical Trial Versus Real-world Outcomes With Anti–Vascular Endothelial Growth Factor Therapy for Central Retinal Vein Occlusion

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- **Study disclosures**
  - This study includes research conducted on human subjects
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Key Takeaways

- We assessed the impact of close monitoring and anti-VEGF injection frequency on vision outcomes in patients with macular edema due to CRVO
- Cross-trial comparisons found that patients in real-world studies had less frequent visits, received fewer injections, and did not achieve vision gains observed in clinical trials
- Similarly, patients in long-term extension (LTE) studies had less frequent visits, received fewer injections, and did not maintain vision gains initially achieved during core clinical trials
- Our post hoc analysis found that patients with greater injection need during the CRUISE core trial consequently lost vision with less frequent monitoring and PRN treatment during the HORIZON LTE study
- These data collectively highlight the need for new strategies that extend the durability of treatment for macular edema in CRVO, reduce treatment burden, and improve real-world vision outcomes

CRVO, central retinal vein occlusion; LTE, long-term extension; PRN, pro re nata (as-needed); VEGF, vascular endothelial growth factor.

Introduction

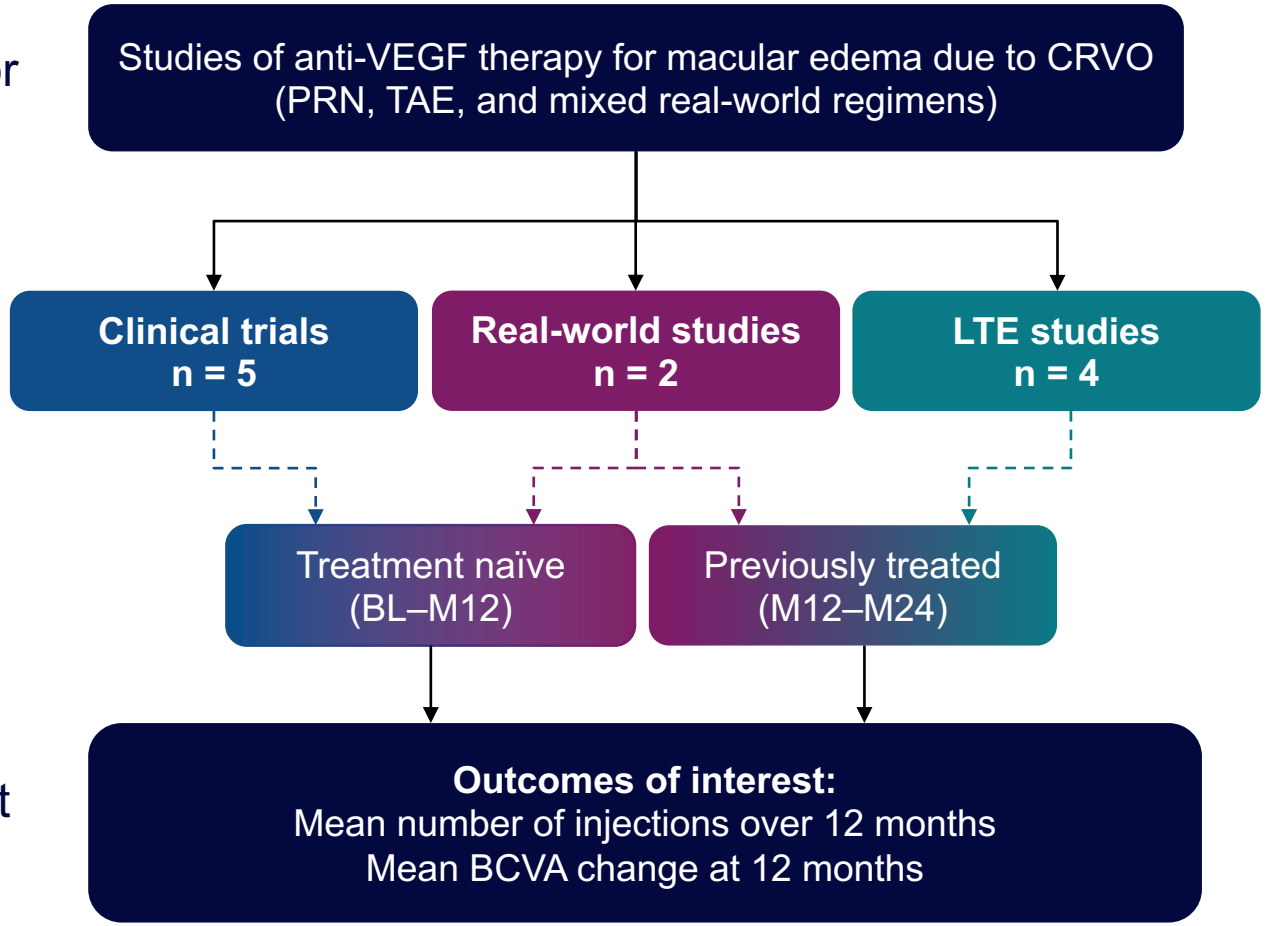
- Intravitreal anti-VEGF therapy is the first-line treatment strategy for patients with macular edema associated with RVO[1]
- Landmark trials that inform clinical guidance have demonstrated that clinically significant vision gains are achievable with frequent injections and close monitoring[2-5]
- These practices are burdensome for patients, caregivers, and physicians; therefore, alternative regimens (eg, PRN and TAE) are often adopted in real-world clinical practice[6]

1. Flaxel CJ et al. *Ophthalmology*. 2020;127(2):P288-P320. 2. Thach AB et al. *Ophthalmology*. 2014;121(5):1059-1066. 3. Korobelnik J-F et al. *Ophthalmology*. 2014;121(1):202-208.
4. Heier JS et al. *Ophthalmology*. 2014;121(7):1414-1420.e1. 5. Clark WL et al. *Ophthalmology*. 2016;123(2):330-336. 6. Callizo J et al. *Clin Ophthalmol*. 2019;13:2167-2179.
PRN, pro re nata (as-needed); RVO, retinal vein occlusion; TAE, treat-and-extend; VEGF, vascular endothelial growth factor.

What is the impact of close monitoring and injection frequency on vision outcomes in patients receiving anti-VEGF therapy for macular edema due to CRVO?

Aim 1: Compare Anti-VEGF Injection Frequencies and Vision Outcomes Between Clinical Trials, Long-term Extension (LTE) Studies, and Real-world Studies

- Cross-trial comparison of studies that assessed PRN, TAE, and mixed real-world (per investigator discretion) anti-VEGF regimens in patients with macular edema due to CRVO
- Studies with publicly available outcomes at 12 months were included
- Average 12-month injection frequencies and vision outcomes were compared between treatment-naïve patients in clinical trials and real-world studies (BL–M12), and between previously treated patients in real-world studies and LTE studies (M12–M24)
- Comparisons were limited by variations in patient population, sample size, and treatment protocols across studies



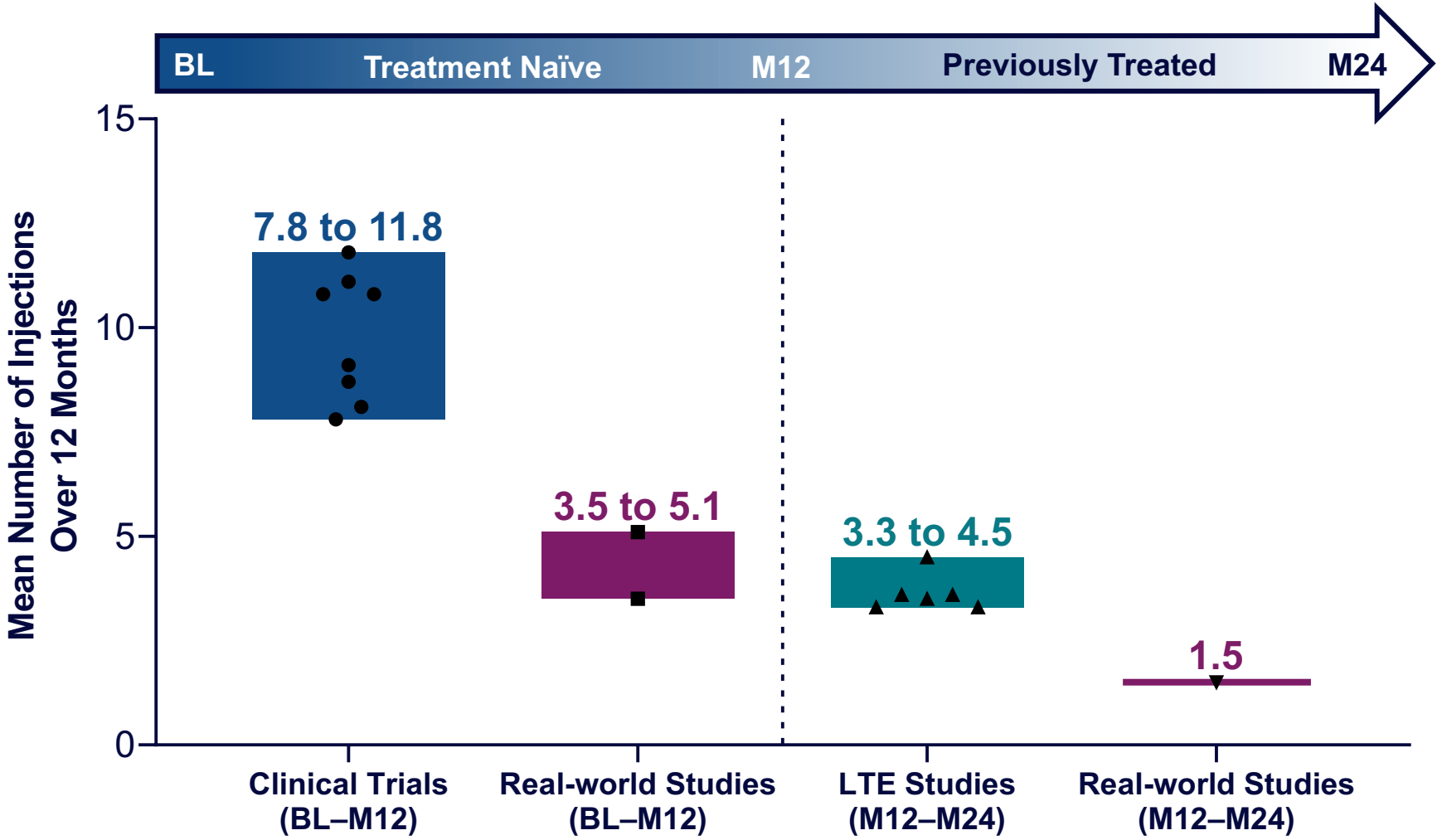
BCVA, best-corrected visual acuity; BL, baseline; CRVO, central retinal vein occlusion; LTE, long-term extension; M, month; PRN, pro re nata (as-needed); TAE, treat-and-extend; VEGF, vascular endothelial growth factor.

Studies of PRN, TAE, and Mixed Real-world Anti-VEGF Therapy in Patients With CRVO

	Study	Anti-VEGF Agent	Treatment Regimen	Monitoring Frequency	n
Clinical Trials	**CRUISE (year 1)**[1,2] NCT00485836	RBZ 0.5 mg	Q4W from BL through M6, then PRN through M12	Q4W	130
	GALILEO (year 1)[3] NCT01012973	AFL 2.0 mg	Q4W from BL through M6, then PRN through M12	Q4W	103
	COPERNICUS (year 1)[4] NCT00943072	AFL 2.0 mg	Q4W from BL through M6, then PRN through M12	Q4W	114
	SCORE2 (year 1)[5,6] NCT01969708	AFL 2.0 mg	Q4W from BL through M6, then protocol-defined treatment (Q4W or TAE) through M12 (good responders)	4–10 weeks	117
		AFL 2.0 mg	Q4W from BL through M6, then dexamethasone 700 µg PRN through M12 (poor responders)	NR	14
		BEV 1.25 mg	Q4W from BL through M6, then protocol-defined treatment (Q4W or TAE) through M12 (good responders)	4–10 weeks	119
		BEV 1.25 mg → AFL 2.0 mg	BEV Q4W from BL through M6, then AFL (Q4W or TAE) through M12 (poor responders)	NR	35
	CRYSTAL (year 1)[7] NCT01535261	RBZ 0.5 mg	Q4W from BL through M3, then PRN through M12	Q4W	357
LTE Studies	**HORIZON**[8] NCT00379795	RBZ 0.5 mg	PRN from LTE BL through M12 (RBZ 0.5 mg arm; CRVO subgroup)	≥ Q12W	51
	RETAIN[9] NCT01198327	RBZ 0.5 mg	PRN from LTE BL through M12 (CRVO subgroup)	Q4W	32
		RBZ 0.5 mg	PRN from M12 through M24 (CRVO subgroup)	≥ Q12W	32
	COPERNICUS (year 2)[4] NCT00943072	AFL 2.0 mg	PRN from M12 through week 100	≥ Q12W	114
	SCORE2 (year 2)[5] NCT01969708	Any (post AFL)	Per investigator discretion from M12 through M24 (AFL arm; good responders during year 1)	Per investigator	117
		Any (post BEV)	Per investigator discretion from M12 through M24 (BEV arm; good responders during year 1)	Per investigator	119
Real-world Studies	**LUMINOUS**[10] NCT01318941	RBZ	PRN (per investigator discretion) from BL through M12 (overall CRVO subgroup)	Per investigator	31
	OCEAN[11] NCT02194803	RBZ	PRN (per investigator discretion) from BL through M12 (CRVO subgroup)	Per investigator	71
		RBZ	PRN (per investigator discretion) from M12 through M24 (CRVO subgroup)	Per investigator	47

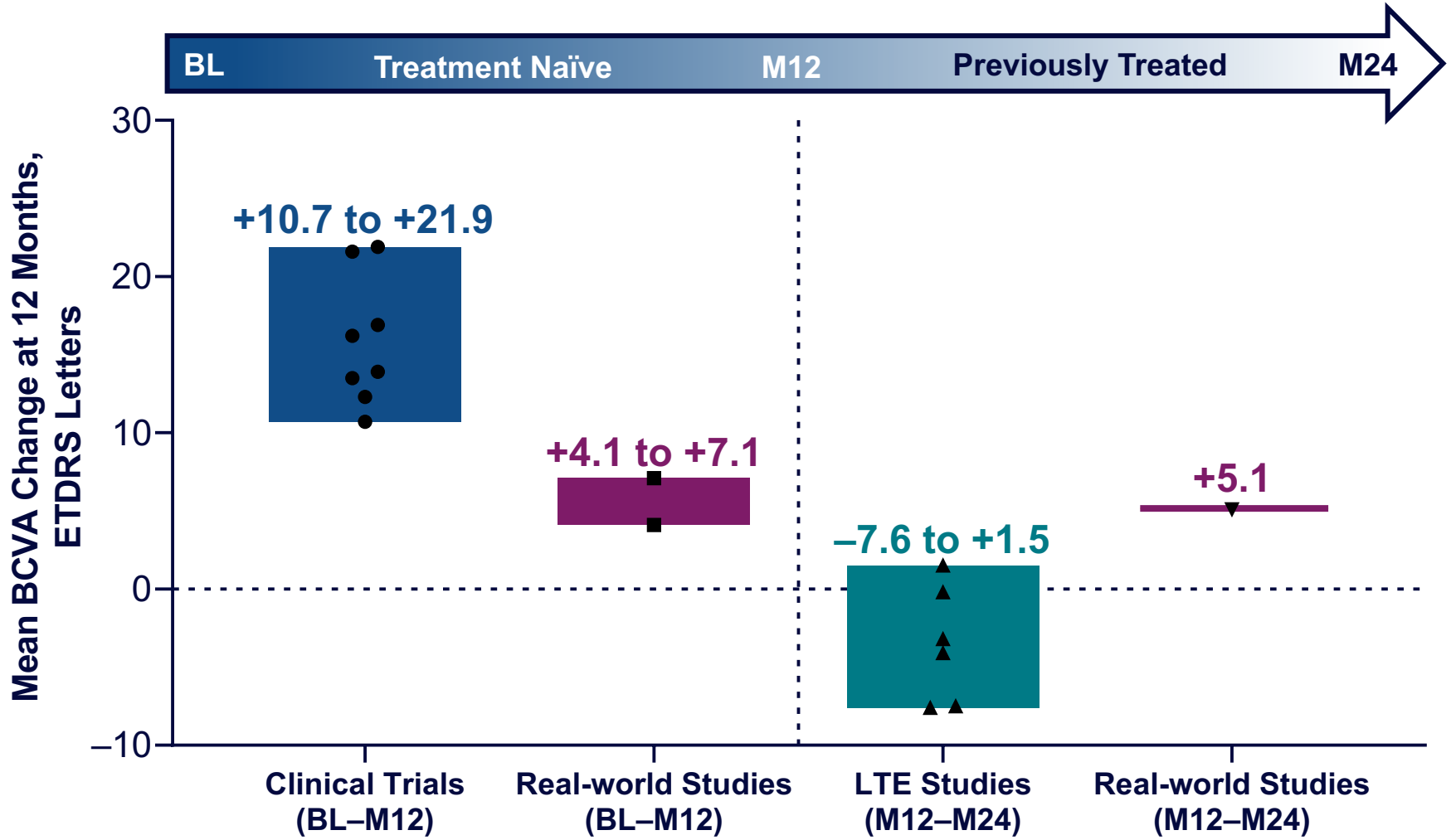
1. Ho AC et al. *Invest Ophthalmol Vis Sci*. 2010;51(13):6452. 2. Thach AB et al. *Ophthalmology*. 2014;121(5):1059-1066. 3. Korobelnik J-F et al. *Ophthalmology*. 2014;121(1):202-208. 4. Heier JS et al. *Ophthalmology*. 2014;121(7):1414-1420.e1. 5. Scott IU et al. *JAMA Ophthalmol*. 2019;137(12):1389-1398. 6. Ip MS et al. *JAMA Ophthalmol*. 2019;137(3):281-287. 7. Larsen M et al. *Ophthalmology*. 2016;123(5):1101-1111. 8. Heier JS et al. *Ophthalmology*. 2012;119(4):802-809. 9. Campochiaro PA et al. *Ophthalmology*. 2014;121(1):209-219. 10. Pearce IA et al. *Invest Ophthalmol Vis Sci*. 2015;56(7):3743. 11. Callizo J et al. *Clin Ophthalmol*. 2019;13:2167-2179. AFL, aflibercept; BEV, bevacizumab; BL, baseline; CRVO, central retinal vein occlusion; LTE, long-term extension; M, month; NR, not reported; Q4W, every 4 weeks; Q12W, every 12 weeks; PRN, pro re nata (as-needed); RBZ, ranibizumab; TAE, treat-and-extend; VEGF, vascular endothelial growth factor.

Patients in Real-world Studies Received Fewer Mean Injections Than Those in Clinical Trials or LTE Studies



BL, baseline; LTE, long-term extension; M, month.

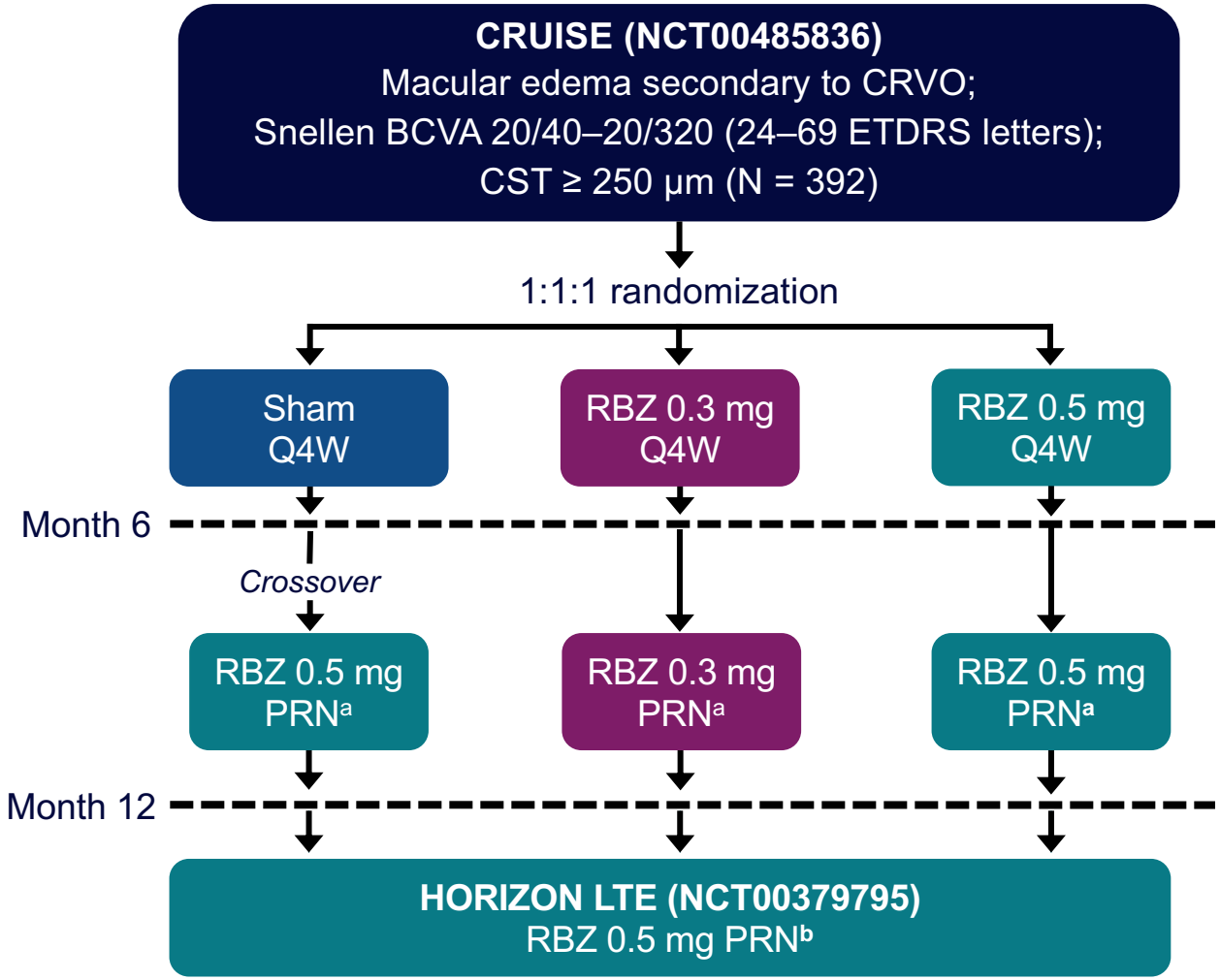
Patients in LTE Studies Did Not Maintain Vision Gains Achieved in Core Clinical Trials, and Patients in Real-world Studies Did Not Achieve Clinically Significant Vision Gains



BCVA, best-corrected visual acuity; BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study; LTE, long-term extension; M, month.

Aim 2: Examine the Relationship Between Injection Need and Vision Outcomes in the HORIZON LTE Study

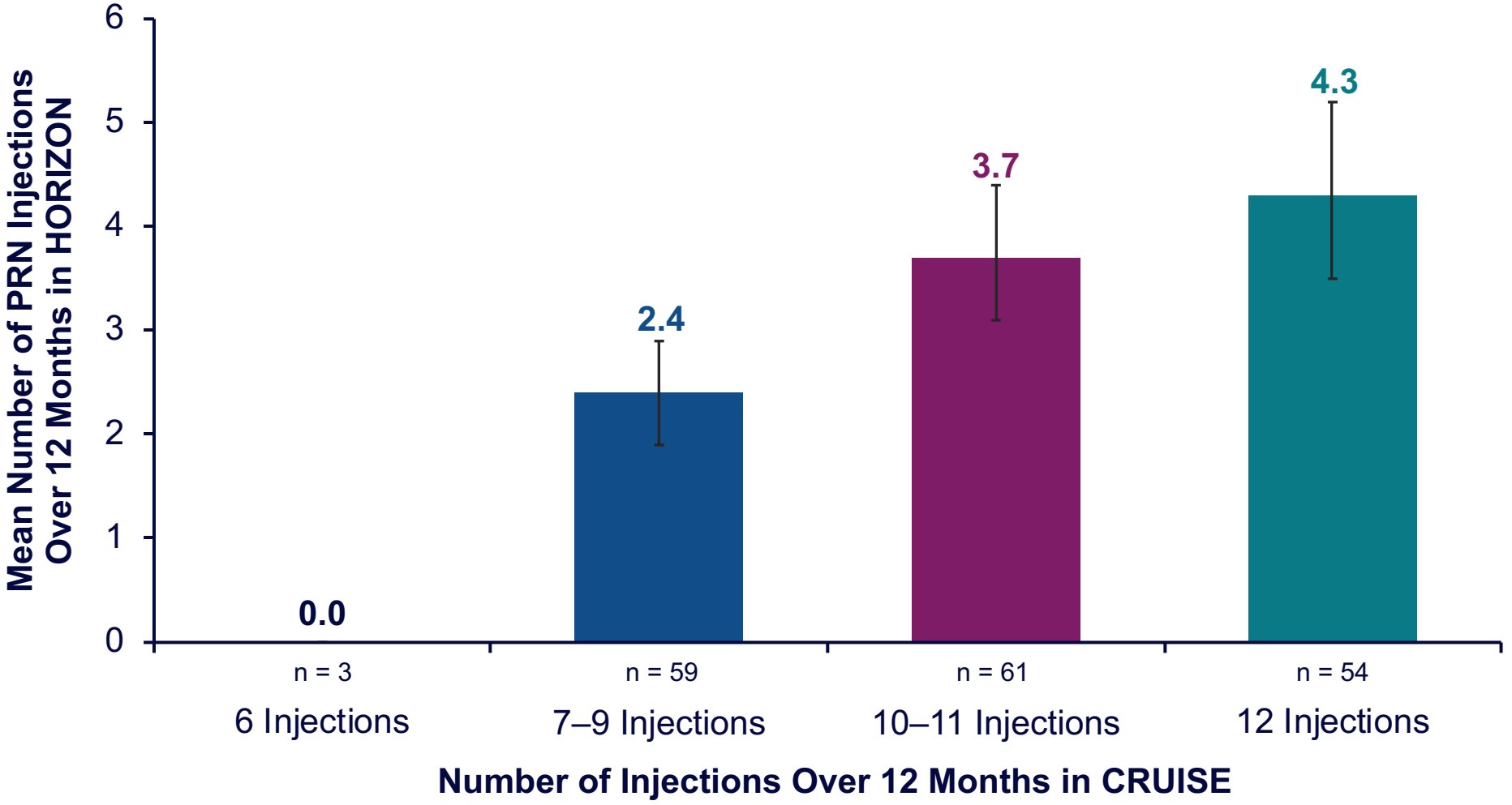
- Post hoc analysis of patients with CRVO who entered HORIZON LTE (all CRUISE treatment arms pooled)
- Outcomes of interest during HORIZON:
  - Mean number of PRN injections over 12 months
  - Mean BCVA change from HORIZON baseline at months 3, 6, 9, and 12
- Patients were stratified by injection frequency over 12 months in CRUISE
  - 6 injections (6 monthly + 0 PRN)
  - 7–9 injections (6 monthly + 1–3 PRN)
  - 10–11 injections (6 monthly + 4–5 PRN)
  - 12 injections (6 monthly + 6 PRN)



[a] During the PRN phase of CRUISE, patients were monitored monthly and received re-treatment if Snellen BCVA was worse than 20/40, or if mean central subfield thickness (CST) was > 250 µm according to time-domain optical coherence tomography. [b] During HORIZON, patients were monitored at least every 3 months and received re-treatment if mean CST was ≥ 250 µm, or if persistent or recurrent macular edema was deemed to be affecting visual acuity.

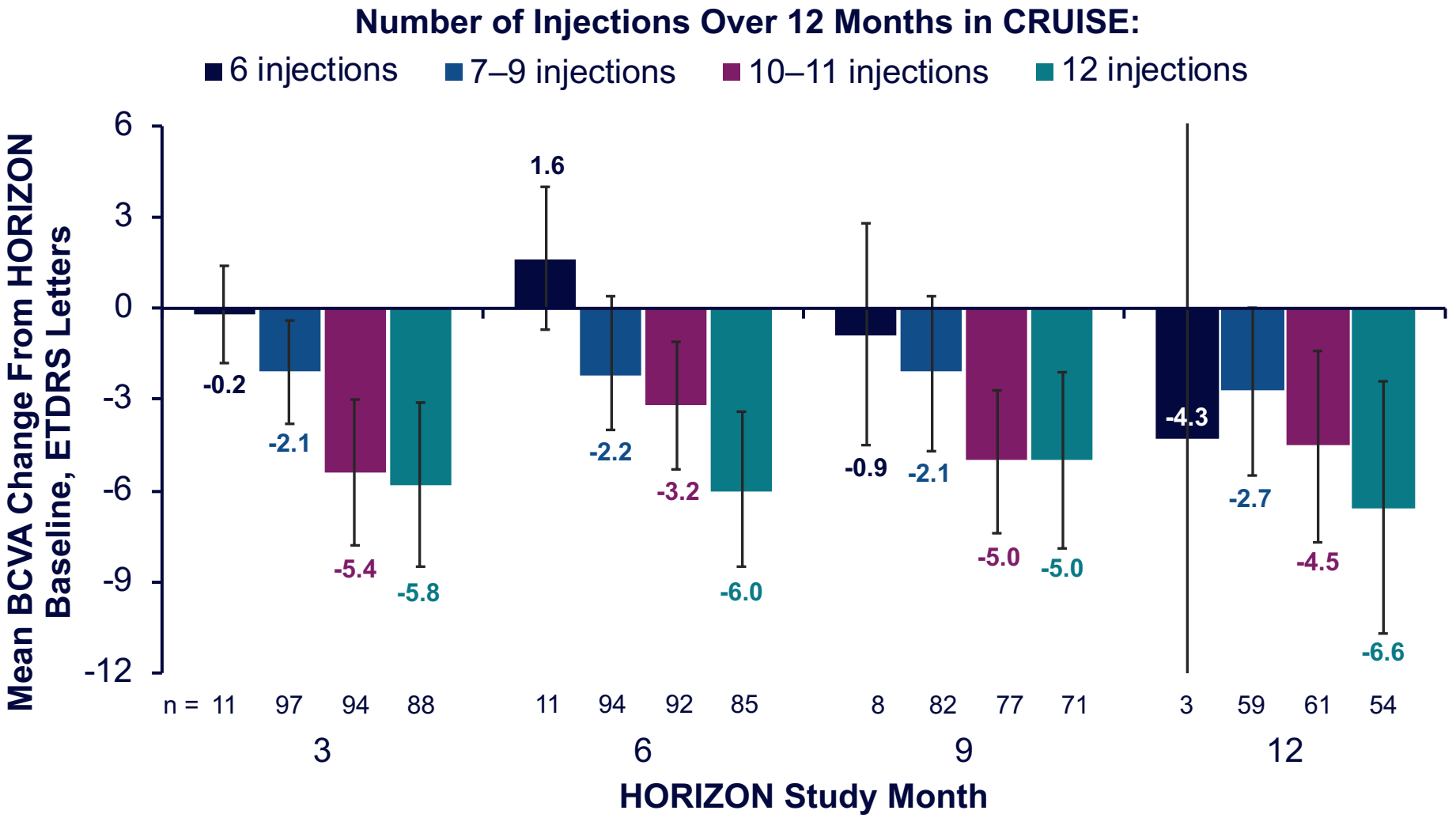
BCVA, best-corrected visual acuity; CRVO, central retinal vein occlusion; ETDRS, Early Treatment Diabetic Retinopathy Study; LTE, long-term extension; PRN, pro re nata (as-needed); Q4W, every 4 weeks; RBZ, ranibizumab.

Relative to CRUISE, Patients Received Significantly Fewer Injections With Less Frequent Monitoring During HORIZON LTE



Analyses included patients with best-corrected visual acuity data available at baseline and month 12 of HORIZON (observed data). Error bars represent 95% CI.
LTE, long-term extension; PRN, pro re nata (as-needed).

Patients With Greater Injection Need During CRUISE Lost Vision With Less Frequent Monitoring During HORIZON LTE



Analyses included patients with BCVA data available at baseline and at each time point of HORIZON (observed data). Error bars represent 95% CI.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; LTE, long-term extension.

Conclusions

- With frequent anti-VEGF injections and near-monthly monitoring, patients with CRVO reliably achieved clinically significant vision improvements from baseline in controlled clinical trials
- In LTE and real-world studies, patients with CRVO were monitored less frequently, received fewer anti-VEGF injections, and subsequently did not achieve or maintain vision gains observed in clinical trials
- Post hoc analyses similarly showed that patients with greater injection need during CRUISE consequently lost vision with less frequent monitoring and PRN treatment during HORIZON LTE
- These data collectively highlight the need for new strategies that extend the durability of treatment for macular edema in CRVO, reduce treatment burden, and improve real-world vision outcomes

CRVO, central retinal vein occlusion; LTE, long-term extension; PRN, pro re nata (as-needed); VEGF, vascular endothelial growth factor.