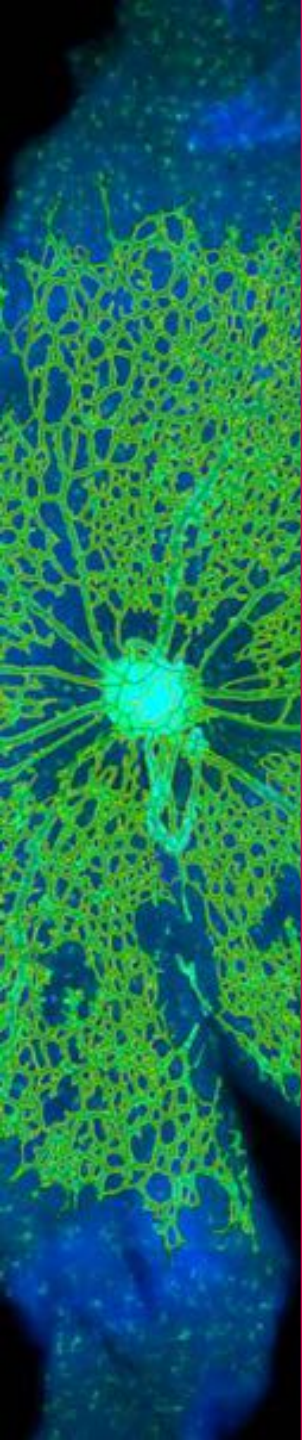




Does Month 3 Response to Ranibizumab Predict Long-term Response to Treatment in Patients With Age-Related Macular Degeneration?

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Disclosures

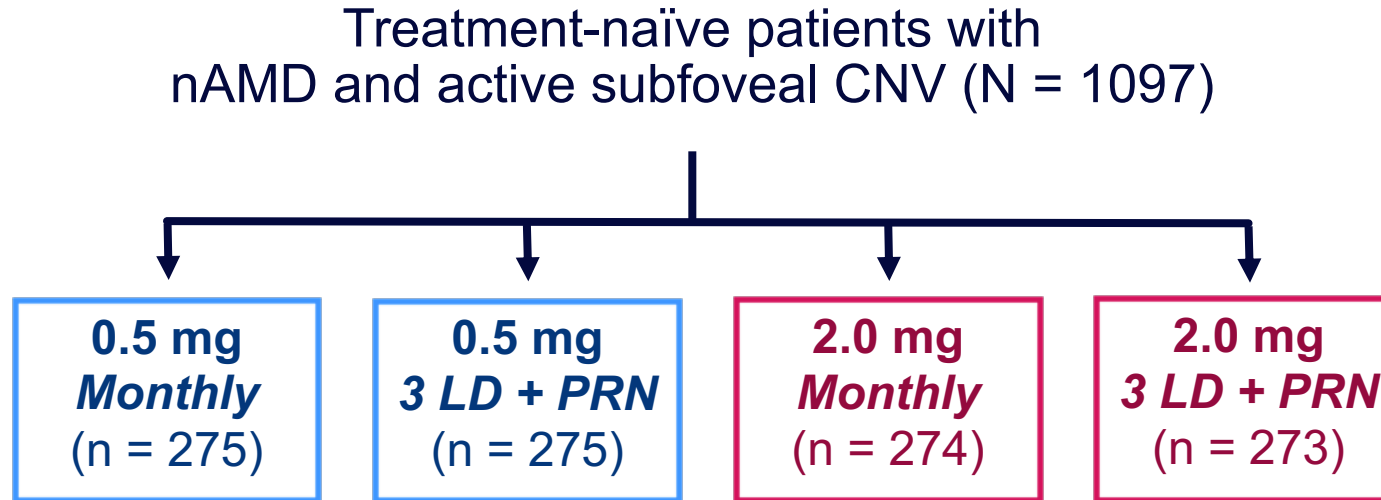
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 - PH: Consultant: Allergan; Consultant: Dutch Ophthalmic DORC; Consultant/Speaker: Genentech, Inc.
 - MT, SB, IS: Employee: Genentech, Inc.
- Study disclosures:
 - This study includes research conducted on human subjects
 - Institutional Review Board approval was obtained prior to study initiation
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Summary

- Vision gains in patients with nAMD treated with ranibizumab in the HARBOR (NCT00891735) clinical trial were examined
 - Patients were categorized based on their vision response from baseline at Month 3
- At first glance, mean BCVA gains (at a population level) may appear stable across 24 months
- However, analysis of individual patient responses demonstrates considerable variation over the 24-month period

Month 3 vision outcomes for an individual nAMD patient are not highly predictive of long-term outcomes

The HARBOR Trial Compared Monthly and PRN Ranibizumab in nAMD for 24 Months



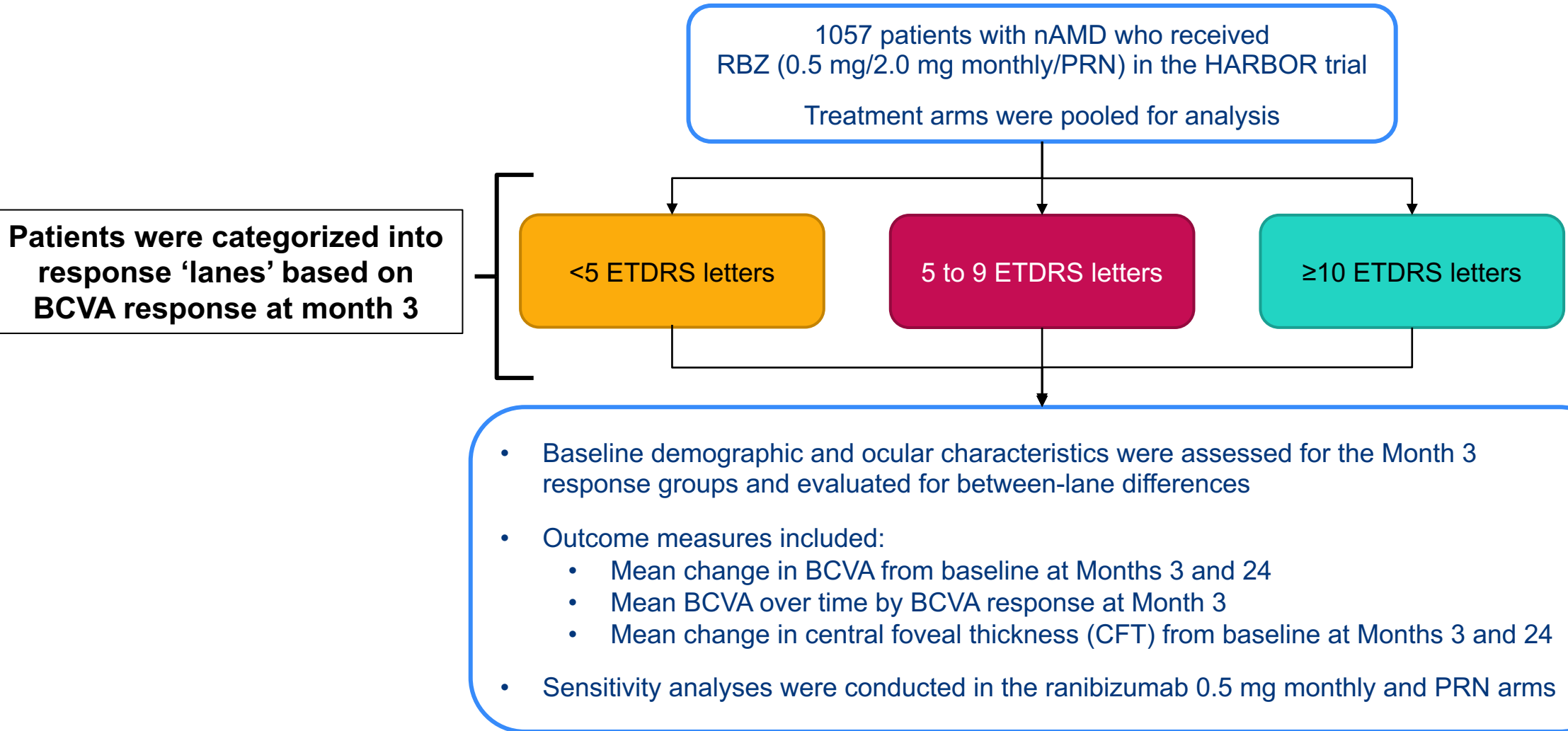
Re-treatment criteria for the PRN groups:

≥ 5-letter decrease in BCVA from previous visit
or any evidence of disease activity on SD-OCT
(SRF, IRF, or subretinal pigment epiretinal fluid)

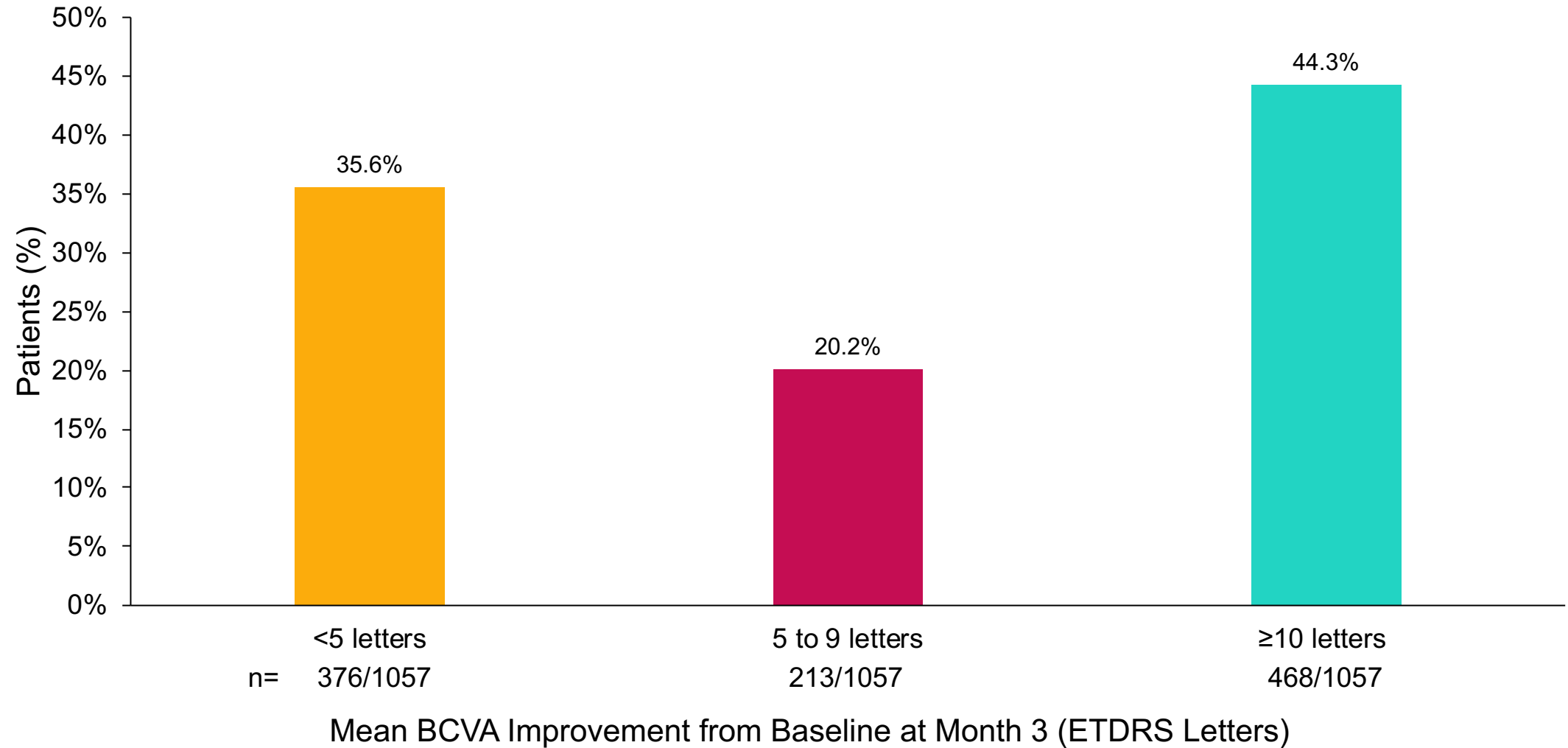
Key Clinical Question

Do Month 3 vision outcomes in patients with neovascular age-related macular degeneration predict long-term outcomes?

Methods



Response Lanes Were Determined by Month 3 Vision Improvements From Baseline

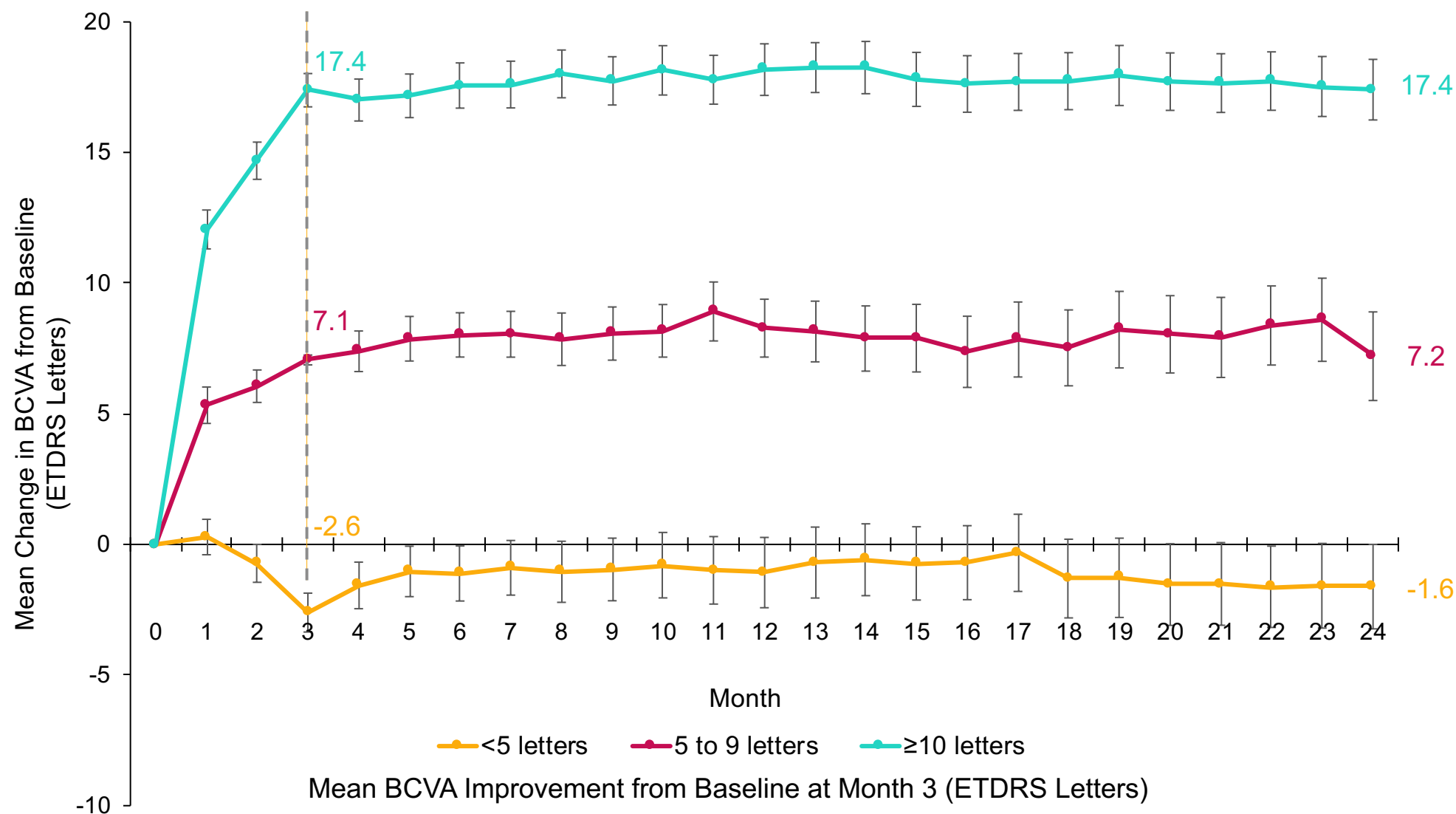


Baseline Characteristics Were Similar Between Patients Improving <5 and 5 to 9 ETDRS Letters From Baseline at Month 3

Patients with ≥10 letter gain at month 3 were on average: younger, had worse BCVA, had thicker retinas, and had a smaller lesion size

	<5 Letters (n = 376)	5 to 9 Letters (n = 213)	≥10 Letters (n = 468)
Age, years, mean (SD)	80.0 (8.2)	78.9 (8.2)	77.6 (8.3)
Mean BCVA (ETDRS letters)	55.1 (13.0)	55.4 (12.0)	52.5 (12.8)
Mean CFT, μm (SD)	333.3 (146.8)	326.8 (129.7)	362.0 (146.6)
Mean CST, μm (SD)	372.4 (129.9)	361.6 (105.6)	392.7 (119.3)
Total area of lesion, μm ³ (SD)	3.8 (2.4)	3.4 (2.1)	2.9 (2.0)
Total area of CNV, μm ³ (SD)	3.6 (2.3)	3.3 (2.06)	2.8 (2.0)

At the Population Level Patients Stay in Their Lanes



All treatment groups pooled (RBZ 0.5 mg monthly, 0.5 mg PRN, 2 mg monthly, 2 mg PRN). Mean change and 95% confidence intervals.
BCVA, best-corrected visual acuity. ETDRS, Early Treatment Diabetic Retinopathy Study, PRN, as-needed.

At the Individual Patient Level There is Notable Movement Between Lanes

All Treatments Pooled		Change in BCVA at Month 24		
Change in BCVA at Month 3	<5 Letters	5 to 9 Letters	≥10 Letters	Total
<5 Letters	62% (n=202)	17% (n=54)	21% (n=69)	n=325
5 to 9 Letters	35% (n=66)	20% (n=37)	45% (n=83)	n=186
≥10 Letters	11% (n=45)	9% (n=38)	80% (n=337)	n=420
Total	n=313	n=129	n=489	n=931

	Moved up lane(s)
	Stayed in lane
	Moved down lane(s)

BCVA response shows notable movement between response groups from M3 to M24 (numbers in red text). All patients with BCVA score at both M3 and M24 included in analysis. Data from HARBOR trial. All treatment groups pooled (RBZ 0.5 mg monthly, 0.5 mg PRN, 2 mg monthly, 2 mg PRN)

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In total, 38% (355/931) of patients switched lanes by Month 24

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	Stayed in lane
	Moved down lane(s)

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In total, 38% (355/931) of patients switched lanes by Month 24
Of these, 58% (206/355) moved to higher lanes

 Moved up lane(s)
 Stayed in lane
 Moved down lane(s)

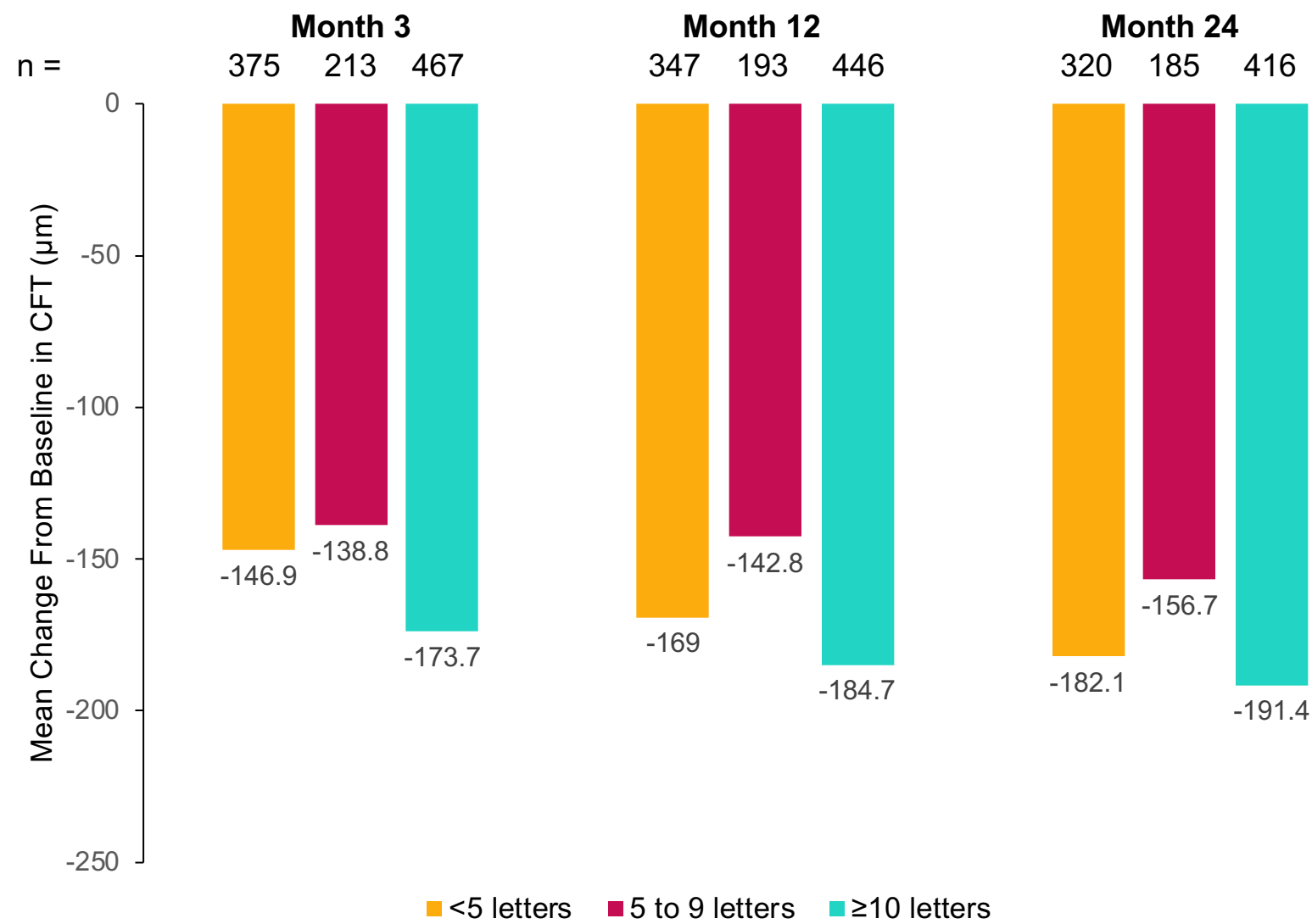
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Notably, 80% (337/420) of patients that had gained ≥10 letters at Month 3 stayed in their lane at Month 24

	Moved up lane(s)
	Stayed in lane
	Moved down lane(s)

Decreases in CFT From Baseline at Month 3 Were Maintained Through Month 24, Regardless of Month 3 Vision Response



Findings from the Ranibizumab 0.5 mg Monthly Treatment Arm Mirrored Those of the Pooled Analysis*

All Treatments Pooled	Change in BCVA at Month 24			
Change in BCVA at Month 3	<5 Letters	5-9 Letters	≥10 Letters	Total
<5 Letters	60%% (n=47)	20% (n=16)	20% (n=16)	n=79
5-9 Letters	29% (n=14)	31% (n=15)	40% (n=19)	n=48
≥10 Letters	7% (n=7)	9% (n=9)	84% (n=83)	n=99
Total	n=68	n=30	n=118	n=226

In total, 36% (81/226) of patients switched lanes by Month 24

	Moved up lane(s)
	Stayed in lane
	Moved down lane(s)

*Similar trends observed in the 0.5 mg PRN treatment arm.

BCVA response shows notable movement between response groups from M3 to M24 (numbers in red text). All patients with BCVA score at both M3 and M24 included in analysis.

BCVA, best-corrected visual acuity; M, month; PRN, as-needed.

Conclusions

- Patient-level data indicate that month 3 vision outcomes are not predictive of long-term nAMD outcomes
 - At first glance, population-level data may falsely suggest that month 3 vision outcomes are predictive
- Nearly 40% of patients changed BCVA 'lanes' after month 3, with most showing vision improvement; of these, approximately 60% changed to the higher vision gain lanes
- Further biomarkers are needed to predict the long-term nAMD outcomes and optimal timing for switching to novel-mechanism treatments when available