

# Reading Speed Outcomes in Macular Telangiectasia Type 2: Sham-Control Data From the Revakinogene Taroretcel-Iwey Phase 3 Clinical Trials

Lydia Sauer,<sup>1</sup> Dean Elliott,<sup>2</sup> Kensington A. Hatcher,<sup>3</sup> Michael J. DelGiodice,<sup>3</sup> Muna I. Bitar,<sup>3</sup> Emily Chew,<sup>4</sup> Thomas M. Aaberg, Jr<sup>3,5</sup>

<sup>1</sup>Associated Retinal Consultants, Royal Oak, MI, USA; <sup>2</sup>Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA; <sup>3</sup>Neurotech Pharmaceuticals, Cumberland, RI, USA; <sup>4</sup>National Eye Institute/National Institutes of Health, Bethesda, MD, USA; <sup>5</sup>Foundation for Vision Research, Grand Rapids, MI, USA

## Purpose



To evaluate the association between BCVA and reading speed in sham-treated eyes from two Phase 3 clinical trials



To assess reading speed as a sensitive marker of functional decline in MacTel

## Conclusions

- Reading speed, which reflects both foveal and parafoveal function,<sup>4</sup> declined significantly over 24 months, even when BCVA remained stable
  - 1-letter loss in BCVA = ~2 wpm decrease in reading speed
  - ~20 wpm decrease over 24 months with stable BCVA
- Left eyes were more likely to have a greater loss in reading speed than right eyes
- Reading speed may provide a sensitive, clinically meaningful measure to monitor MacTel progression, evaluate treatment effects, and quantify functional vision loss in routine practice

### References

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### Disclosures

LS: Nothing to disclose. DE: Consultant: Alcon, Aldeyra, Allergan, Apellis, GelMedix, Genentech, InGel, Neurotech Pharmaceuticals, Pykus Therapeutics, and RetMap; DMSB member: AsclepiX, Avicoda, Clearside Biomedical, EyeBio, and Ocular Therapeutics; Stockholder: Aldeyra, InGel, Pykus Therapeutics, and RetMap. KAH: Employee: Neurotech Pharmaceuticals. MJ.D: Employee: Neurotech Pharmaceuticals. MB: Employee: Neurotech Pharmaceuticals. EC: Nothing to disclose. TMA: Employee: Foundation for Vision Research and Neurotech Pharmaceuticals; Consulting fees: Castle Biosciences and Regeneron.

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## Background

- Macular telangiectasia type 2 (MacTel) is a progressive retinal disease in which best-corrected visual acuity (BCVA) may remain relatively preserved despite functional decline, limiting its sensitivity as a marker of progression<sup>1-3</sup>
- A more patient-relevant functional assessment could be beneficial in the monitoring of MacTel disease progression
- The average reading speed in individuals with normal vision is ~190–230 words per minute (wpm),<sup>4,5</sup> whereas those with MacTel have exhibited marked impairment in reading speed (~95 wpm) in Phase 3 clinical trials<sup>6</sup>
- Reading speed may better capture functional impairment, potentially reflecting the development of parafoveal scotomas in MacTel and their impact on visual function<sup>4</sup>
  - Parafoveal scotomas may differ by eye laterality and affect left-to-right reading outcome<sup>7</sup>

## Methods

- Two prospective Phase 3 clinical trials evaluated revakinogene taroretcel-Iwey treatment vs sham surgery in adults with MacTel<sup>6</sup>
- This retrospective longitudinal analysis evaluated reading speed (wpm, measured by the International Reading Speed Test) and BCVA among patients in the sham group over 24 months<sup>5</sup>
- To assess functional impact in patients with preserved visual stability, stable BCVA was defined as a change of <5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters from baseline to Month 24
  - The mean within-group change in reading speed in this cohort was assessed using a one-sample *t*-test
- A reduced linear regression model was used and Pearson correlation coefficients calculated to assess the relationship between structural progression and functional decline
- The association between eye laterality (right vs left eye) and 24-month reading speed was evaluated using analysis of covariance (ANCOVA), with baseline reading speed and BCVA included as covariates
  - A two-sided alpha level of 0.05 was used
- All analyses were performed with R version 4.4.2

## Results

### Study Population

- Of the 111 enrolled sham eyes, 104 had complete datasets for evaluation
- Baseline demographics and clinical characteristics are shown in **Table 1**

**Table 1: Baseline Demographics and Clinical Characteristics**

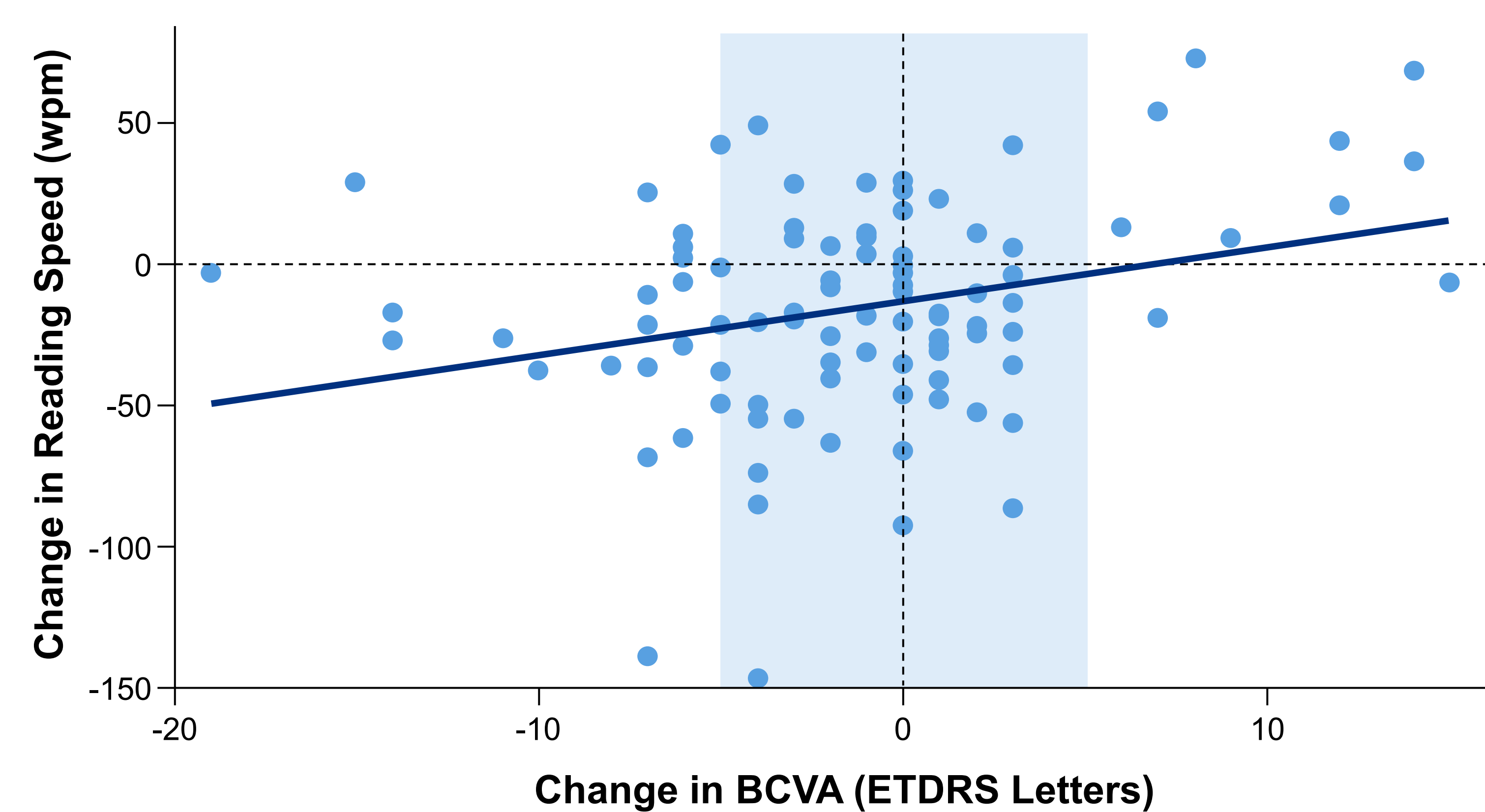
Characteristics	Sham-Treated Participants (n=104)
<b>Age, mean (SD), years</b>	59.1 (8.6)
<b>Female, n (%)</b>	71 (68.3)
<b>Baseline BCVA, mean ETDRS letters [Snellen equivalent] (SD)</b>	73.6 [20/32] (8.9)
OD	71.6 [20/40] (9.7)
OS	75.1 [20/32] (8.0)
<b>Baseline reading speed, mean (SD), wpm</b>	96.4 (48.4)
OD	98.7 (44.5)
OS	94.6 (51.6)
<b>Eye laterality, OD/OS, n</b>	45/59
<b>Baseline EZ loss area, mean (SD), mm<sup>2</sup></b>	0.47 (0.33)
OD	0.50 (0.36)
OS	0.46 (0.30)

BCVA, best-corrected visual acuity; EZ, ellipsoid zone; OD, right eye; OS, left eye; SD, standard deviation; wpm, words per minute.

### Reading Speed and BCVA

- Mean (SD) 24-month reading speed change was -15.4 (38.3) wpm and mean (SD) 24-month BCVA change was -1.2 (5.8) letters
  - This represents a 16.0% loss in reading speed compared with a 1.6% loss in visual acuity
- Reading speed decreased by **2.13 wpm** for every **1-letter loss in BCVA** ( $P<0.0001$ ) (**Figure 1**)
  - This was independent of laterality, baseline reading speed, and baseline BCVA
- Table 2** shows coefficients of the reduced multiple linear regression model
- Despite minimal changes in acuity, 68 eyes with stable BCVA experienced a statistically significant decline in reading speed of **19.39 wpm** over 24 months ( $P<0.0001$ )

**Figure 1: Dissociation Between Reading Speed Change and BCVA Change (24 Months)**



BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; wpm, words per minute. Each blue circle represents one study eye; the solid blue line is the linear regression showing the correlation; the dashed black lines mark zero change for both metrics; and the light blue area denotes the zone of stable BCVA (change of <5 ETDRS letters).

**Table 2: Coefficients of Predictors for 24-Month Reading Speed (Multiple Linear Regression)**

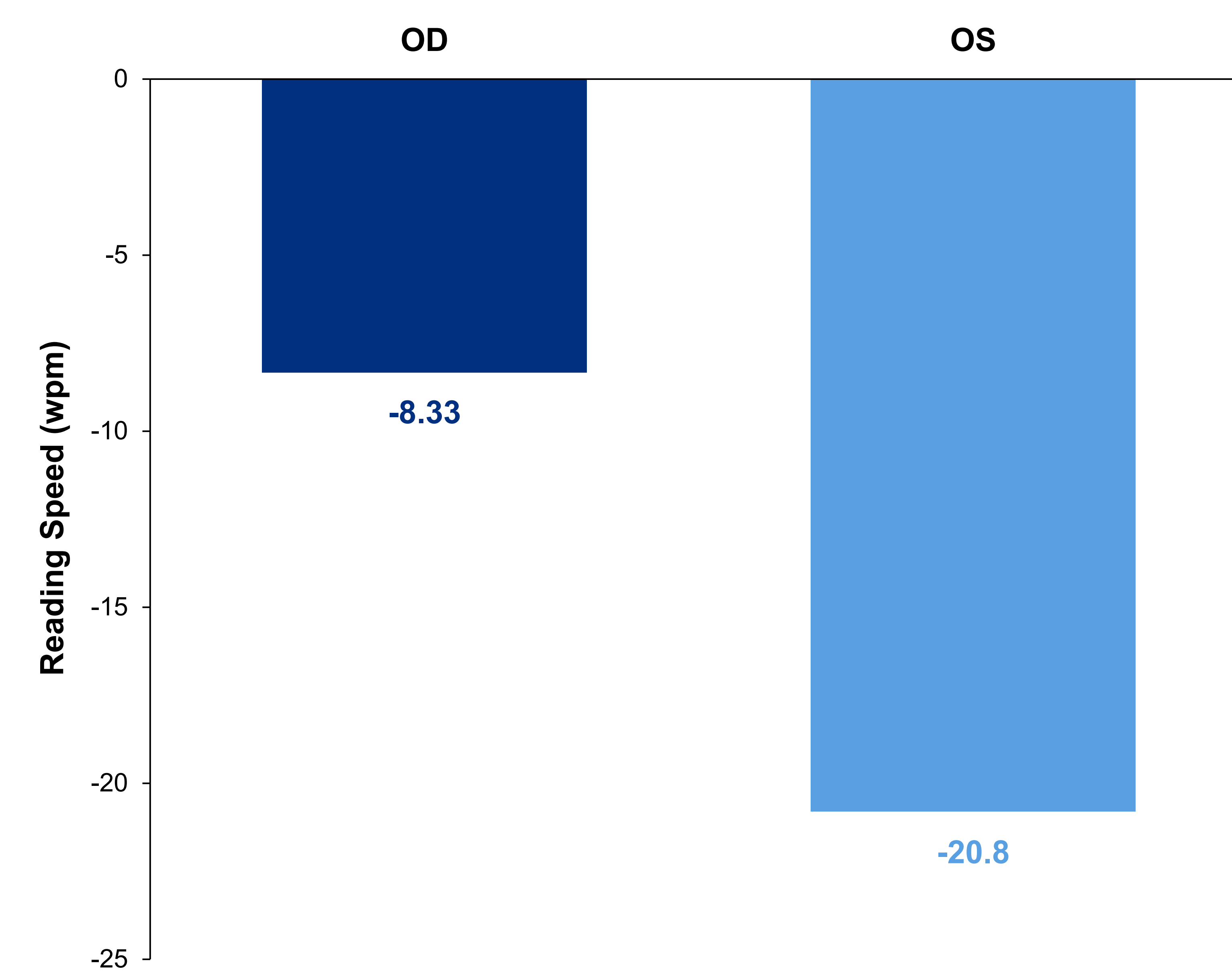
Variable	Coefficient (Estimate)	Standard Error	T	P
<b>Baseline reading speed, wpm</b>	-0.54	0.07	-8.04	<0.0001
<b>BCVA change (Month 24 – baseline), letters</b>	+2.13	0.51	4.18	<0.0001
<b>Baseline BCVA, letters</b>	+1.44	0.37	3.89	0.0002
<b>Eye, OS</b>	-14.76	5.95	-2.48	0.0150

BCVA, best-corrected visual acuity; OS, left eye; wpm, words per minute. Model fit: The model accounts for a substantial proportion of the variance in the 24-month reading speed (adjusted  $R^2=0.43$ ,  $P<0.0001$ ). Note: The intercept was omitted because it represents a nonphysiological condition and is not clinically interpretable.

### Impact of Laterality on Reading Speed Loss

- A two-sample *t*-test found a non-significant trend toward greater reading speed decline in left eyes compared with right eyes over 24 months ( $P=0.097$ ) (**Figure 2**)
- After adjusting for baseline factors, ANCOVA indicated that left eyes were predicted to read **~18.52 wpm slower** than right eyes at Month 24, aligning with the known pathophysiology of MacTel<sup>4</sup>
  - Temporal retinal damage creates a nasal visual field scotoma<sup>8,9</sup>
  - In the left eye, this blocks the text coming up next and reduces left-to-right reading speed because the eye has difficulty anticipating upcoming words<sup>7,10</sup>
  - In contrast, the right eye's scotoma lies away from the reading direction, which may explain the smaller impact on the right eye's reading performance<sup>7,10</sup>

**Figure 2: Average Reading Speed Loss Over 24 Months (OD vs OS)**



OD, right eye; OS, left eye; wpm, words per minute.