

The Effect of Baseline Ellipsoid Zone Area Loss on Treatment Response of Revakinagene Taroretcet-Lwey (NT-501) in Macular Telangiectasia Type 2

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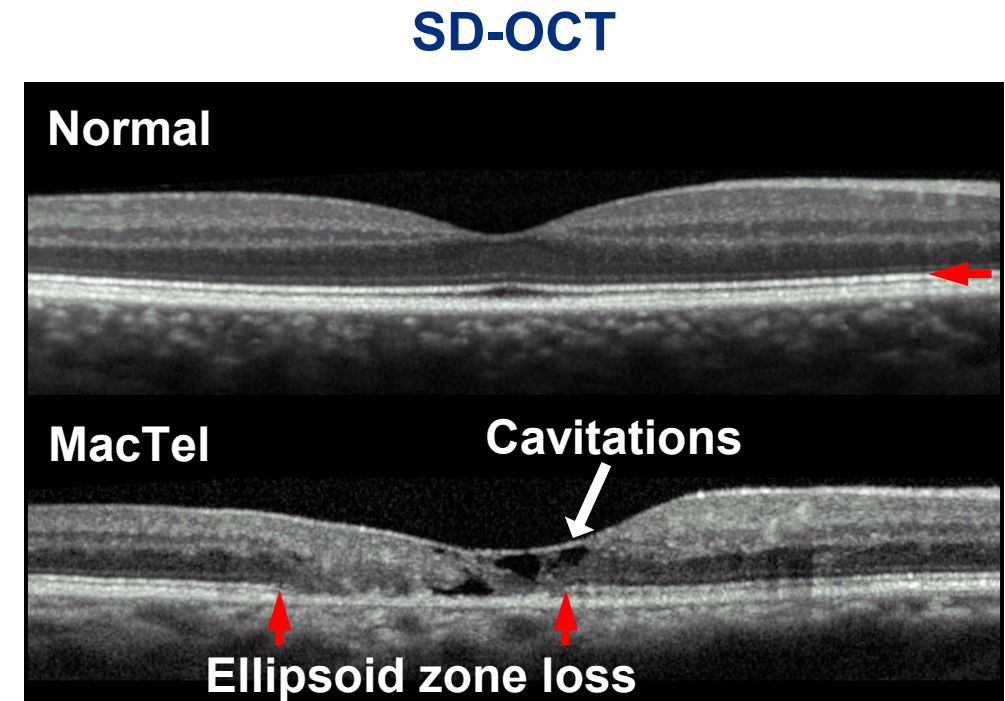
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- This study includes research conducted on human subjects; institutional review board approval was obtained prior to study initiation

Macular Telangiectasia Type 2 (MacTel) Is a Neurodegenerative Disease That Leads to Vision Loss^{1,2}

- MacTel is a bilateral, progressive, retinal neurodegenerative disease¹
 - Associated with abnormalities in Müller glia, RPE, and photoreceptors in the central retina^{2,3}
 - Progressive loss of the ellipsoid zone^{2,4,5}
- Müller cells produce many neurotrophic factors, including ciliary neurotrophic factor (CNTF), which protects and preserves photoreceptors⁴⁻⁶
 - In preclinical models of retinal degeneration, photoreceptors can be rescued with intravitreal injection of CNTF^{4,5}



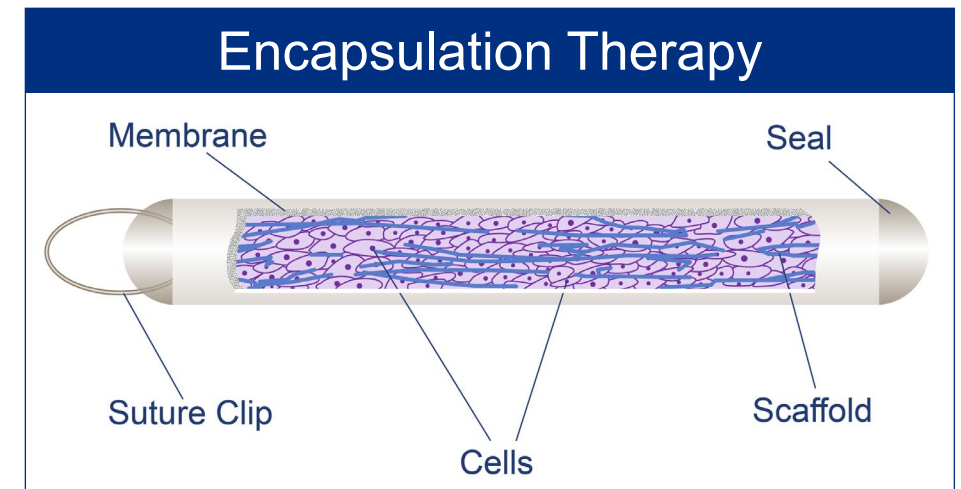
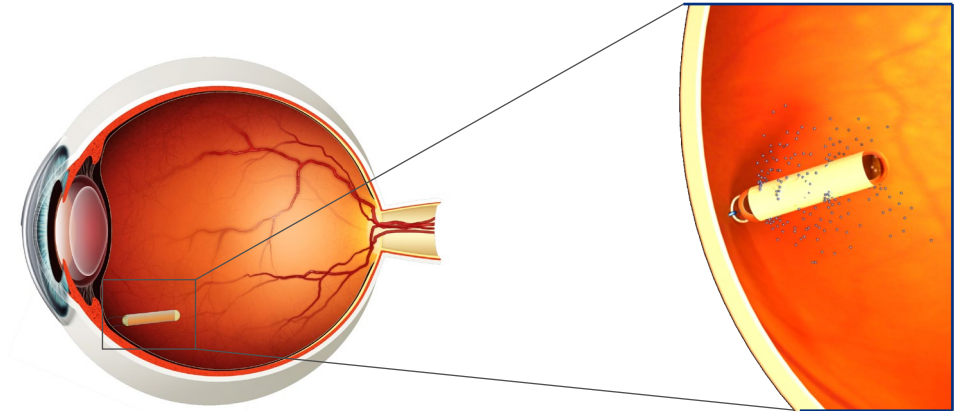
RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography.

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4. Shen W, et al. *J Neurosci*. 2012;32(45):15715-15727. 5. Tao W, et al. *Invest Ophthalmol Vis Sci*. 2002;43(10):3292-3298. 6. Sleeman MW, et al. *Pharm Acta Helv*. 2000;74(2-3):265-272.

Encapsulated Cell Therapy (ECT): Intravitreal Sustained CNTF Delivery System

- Revakinagene taroretcel-lwey (NT-501) is a first-in-class ECT¹⁻³
 - Houses NTC-201-6A cells¹
 - Allogeneic RPE cells with an expression vector for CNTF release¹
 - Cells remain alive and productive for many years⁴
 - Cells obtain oxygen and nutrients from vitreous⁴
 - Sequestered from the immune system⁴
 - Surgically implanted into the vitreous cavity² and attached to the sclera (for stability)⁵
 - Produces sustained long-term levels of CNTF²
- **NT-501 was approved by the FDA for the treatment of adults with MacTel on March 5, 2025**



CNTF, ciliary neurotrophic factor; FDA, US Food and Drug Administration; MacTel, macular telangiectasia type 2; RPE, retinal pigment epithelium.

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NT-501 Was Studied in Two Identical Phase 3 Trials Involving More Than 200 Participants

Key inclusion criteria

- Diagnosis of MacTel
- Aged >21 to <80 years
- EZ break between 0.16 and 2.00 mm²
- BCVA of ≥54 ETDRS letters (Snellen 20/80 or better)

NTMT-03-A (mITT population^a)

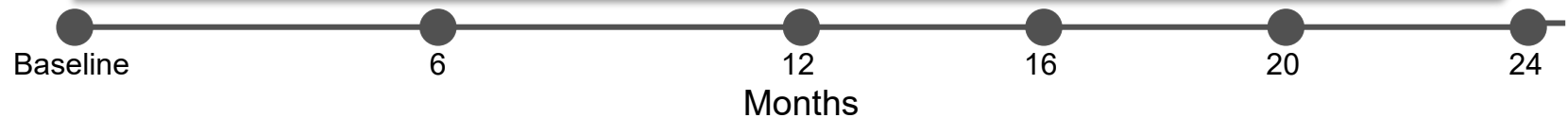
NT-501 (n=58)

Sham (n=57)

NTMT-03-B (mITT population^a)

NT-501 (n=59)

Sham (n=54)



Primary endpoint: Rate of change in EZ area loss from baseline through Month 24

Secondary endpoints: Changes in retinal sensitivity and reading speed at Month 24

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2; mITT, modified intent-to-treat; NT-501, revakinagene taroretcel-lwey.

^aThe mITT population includes all randomized participants who underwent surgery (NT-501 or sham); this was the primary population for efficacy evaluations.

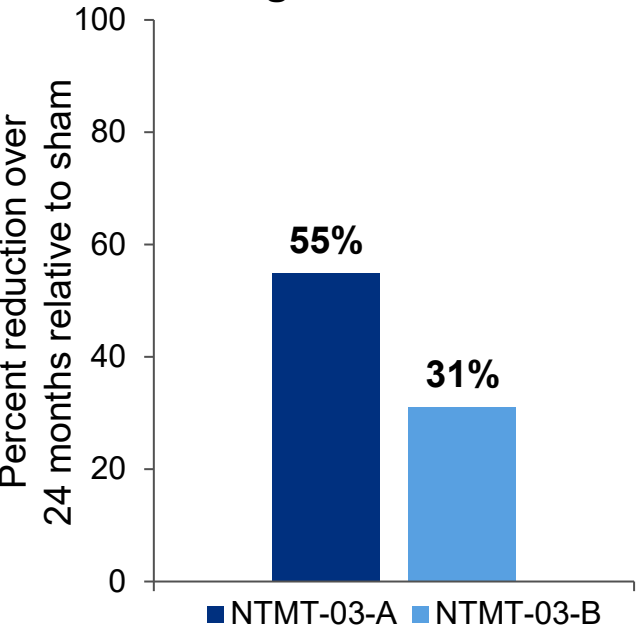
Baseline Characteristics Were Well Balanced Across Treatment Arms Within Each Study

Characteristic in mITT population	NTMT-03-A		NTMT-03-B		Pooled	
	NT-501 (n=58)	Sham (n=57)	NT-501 (n=59)	Sham (n=54)	NT-501 (n=117)	Sham (n=111)
Female, n (%)	39 (67)	40 (70)	46 (78)	36 (67)	85 (73)	76 (68)
Mean (SD) age, years	61.1 (8.0)	60.2 (8.4)	58.5 (7.6)	58.7 (8.9)	59.8 (7.9)	59.5 (8.6)
Age category, n (%)						
<65 years	37 (64)	37 (65)	42 (71)	36 (67)	79 (68)	73 (66)
≥65 years	21 (36)	20 (35)	17 (29)	18 (33)	38 (32)	38 (34)
Race, n (%)						
White	50 (86)	48 (84)	55 (93)	47 (87)	105 (90)	95 (86)
Asian	2 (3)	3 (5)	3 (5)	1 (2)	5 (4)	4 (4)
Black or African American	1 (2)	2 (4)	0	0	1 (1)	2 (2)
American Indian or Alaska Native	0	1 (2)	0	0	0	1 (1)
Other	5 (9)	3 (5)	1 (2)	6 (11)	6 (5)	9 (8)
EZ area loss, mm²						
Mean (SD)	0.51 (0.48)	0.49 (0.36)	0.52 (0.31)	0.48 (0.29)	0.52 (0.40)	0.48 (0.33)
Median (minimum, maximum)	0.35 (0.15, 1.99)	0.36 (0.16, 1.70)	0.48 (0.16, 1.63)	0.40 (0.16, 1.38)	0.42 (0.15, 1.99)	0.37 (0.16, 1.70)
Mean (SD) BCVA, ETDRS letters						
Snellen equivalent	70.8 (9.1) 20/40	73.3 (8.6) 20/40	74.4 (7.8) 20/32	73.6 (9.2) 20/32	72.6 (8.6) 20/40	73.4 (8.9) 20/40
Foveal involvement, n (%)						
No	17 (29)	15 (26)	15 (25)	22 (41)	32 (27)	37 (33)
Unknown	1 (2)	0	0	0	1 (1)	0
Yes	40 (69)	42 (74)	44 (75)	32 (59)	84 (72)	74 (67)
History of diabetes, n (%)						
Yes	27 (47)	19 (33)	22 (37)	16 (30)	49 (42)	35 (32)
No	31 (53)	38 (67)	37 (63)	38 (70)	68 (58)	76 (68)

Participants were primarily White and female, had a mean age of approximately 60 years, and had a baseline visual acuity of approximately 20/40

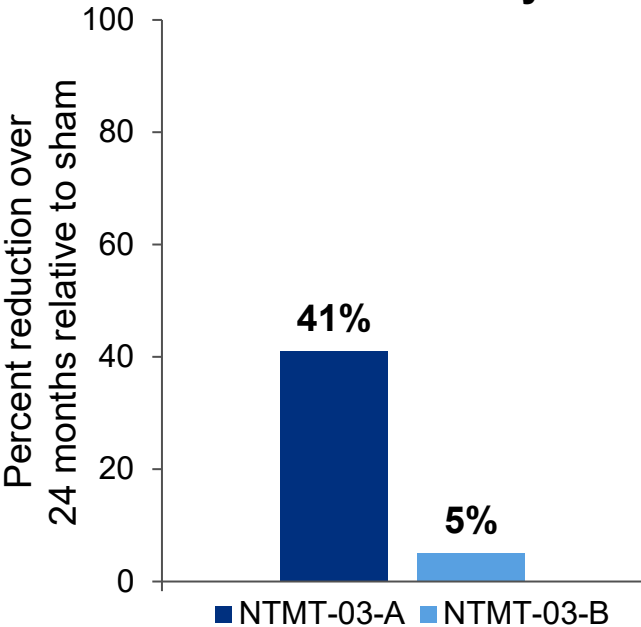
Key Efficacy Outcomes at 2 Years: NT-501 Led to Reductions in Loss of EZ Area, Retinal Sensitivity, and Reading Speed When Compared with Sham

**Primary Endpoint:
Reduction in Rate of
Change in EZ Area Loss^a**



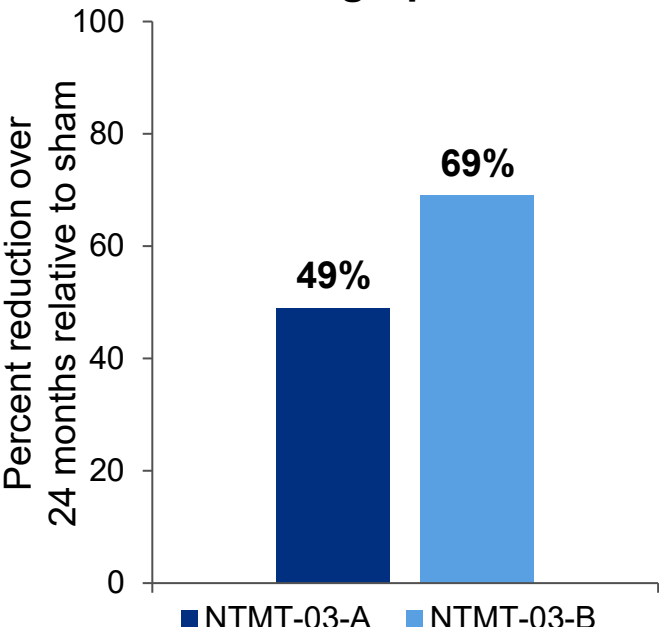
NT-501 reduced the rate of change in **EZ area loss** by **55%** in NTMT-03-A ($P<0.001^{b,c}$) and **31%** in NTMT-03-B ($P=0.0186^{b,c}$), relative to sham treatment

**Secondary Endpoint:
Reduction in
Retinal Sensitivity Loss^a**



NT-501 reduced **retinal sensitivity** loss by **41%** in NTMT-03-A ($P=0.020^{b,d}$) and **5%** in NTMT-03-B ($P=0.835^{b,d}$), relative to sham treatment

**Secondary Endpoint:
Reduction in
Reading Speed Loss^a**



NT-501 reduced **reading speed** loss by **49%** in NTMT-03-A ($P=0.385^{b,d}$) and **69%** in NTMT-03-B ($P=0.033^{b,d,e}$), relative to sham treatment

EZ, ellipsoid zone; mITT, modified intent-to-treat; NT-501, revakinagene tarorectel-lwey.

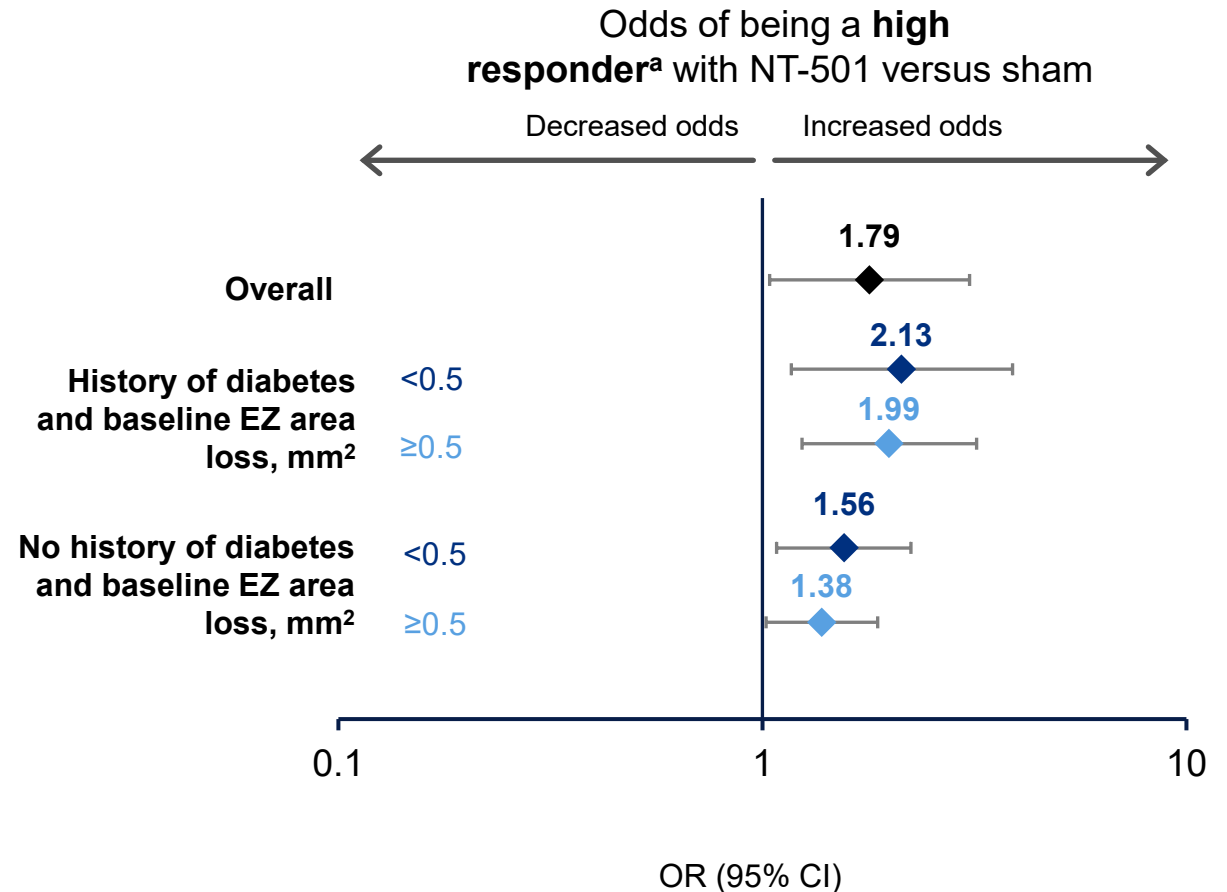
^aAnalyzed in the mITT population. ^b P values based on difference in measures of NT-501 versus sham through 24 months. ^cBased on a repeated-measures model that included baseline and Months 12, 16, 20, and 24, adjusting for study group, time (continuous), treatment $\times$ time interaction, and participant-specific random intercepts. The difference in rates of change in EZ area loss over 2 years between study groups was based on the treatment $\times$ time interaction term. ^dTwo-sample t test comparing change from baseline to Month 24 in NT-501 versus sham. ^eNominal P value.

Post Hoc Analysis to Explore Differences in Trials A and B

- Evaluated the impact of baseline characteristics on treatment responses to better understand these observed differences in the efficacy outcomes
- Treatment response was examined as *responder status*
 - Participants were considered high responders if they had a $\geq 50\%$ reduction in disease progression (based on EZ area loss) compared with the sham treatment
- Eight baseline variables were assessed using a **multivariate approach**; the following two were found to be associated with response:
 - **EZ area loss** ($< 0.5 \text{ mm}^2$ or $\geq 0.5 \text{ mm}^2$ based on the mean baseline loss in both studies [0.5 mm^2])
 - History of diabetes (yes or no based on medical history)

Both Baseline EZ Area Loss and Diabetes Were Associated With Higher Odds of Treatment Response

- In the multivariate analysis, **smaller baseline EZ area loss** and a **history of diabetes** were both associated with greater odds of achieving high responder status^a
 - Participants with diabetes had higher odds of response than those without, regardless of baseline EZ area loss
 - Participants with smaller baseline EZ area loss had higher odds of treatment response than those with larger lesion size, regardless of diabetes status

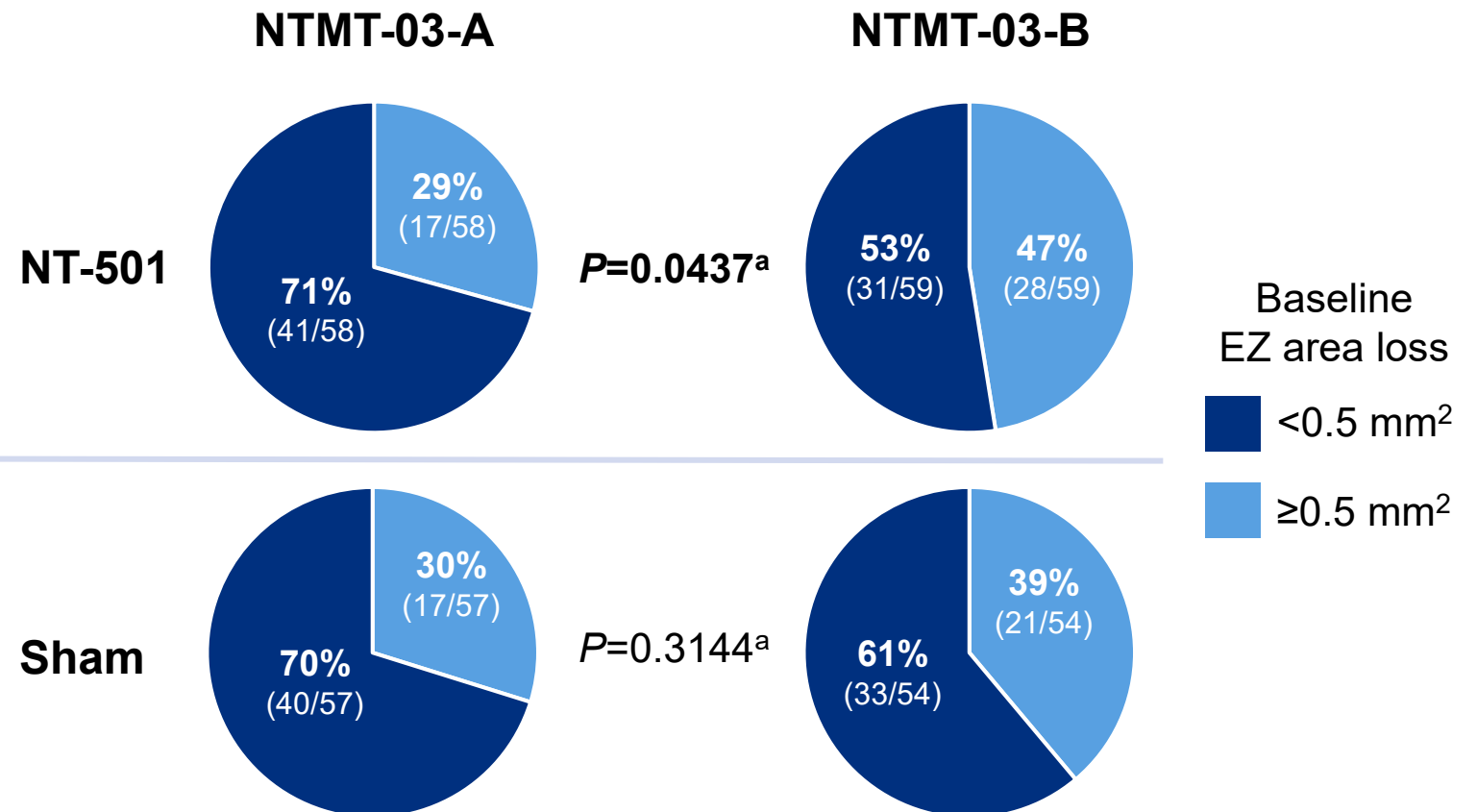


CI, confidence interval; EZ, ellipsoid zone; NT-501, revakinagene tarorectel-lwey; OR, odds ratio.
Results are pooled data from both Phase 3 clinical studies. ^aDefined as mean rate of change in EZ area ≥50% relative to mean rate of change in sham-treated group.

Distribution of Baseline Factors in the Phase 3 Trials: More Participants Treated With NT-501 in Trial A Had Smaller Baseline Lesions Versus Trial B

- Significant difference in the distribution of baseline lesion sizes in the NT-501 groups between studies
 - No significant differences between studies in sham groups
- A greater proportion of participants who received NT-501 in trial A had smaller baseline lesions compared to the NT-501 group in trial B

Baseline Lesion Size Between the Phase 3 Clinical Studies

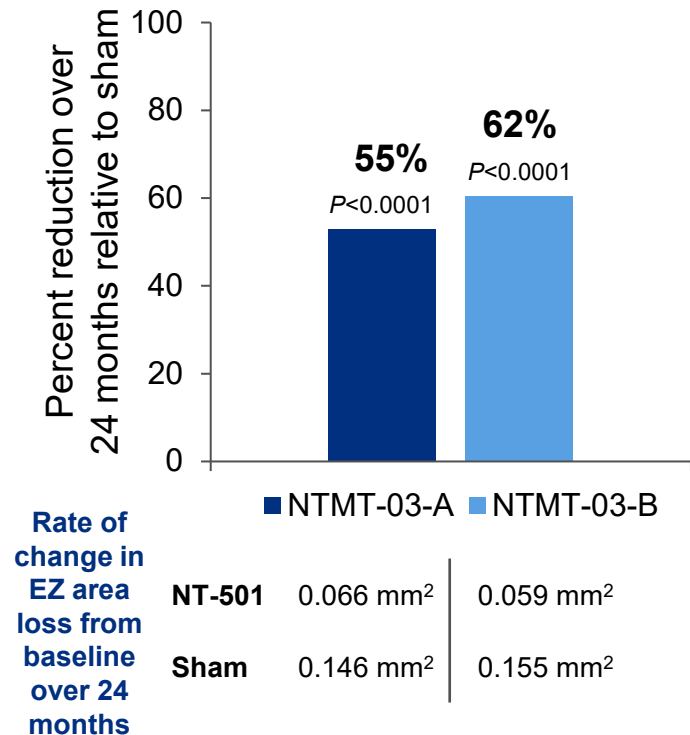


EZ, ellipsoid zone; NT-501, revakinagene tarorectel-lwey.

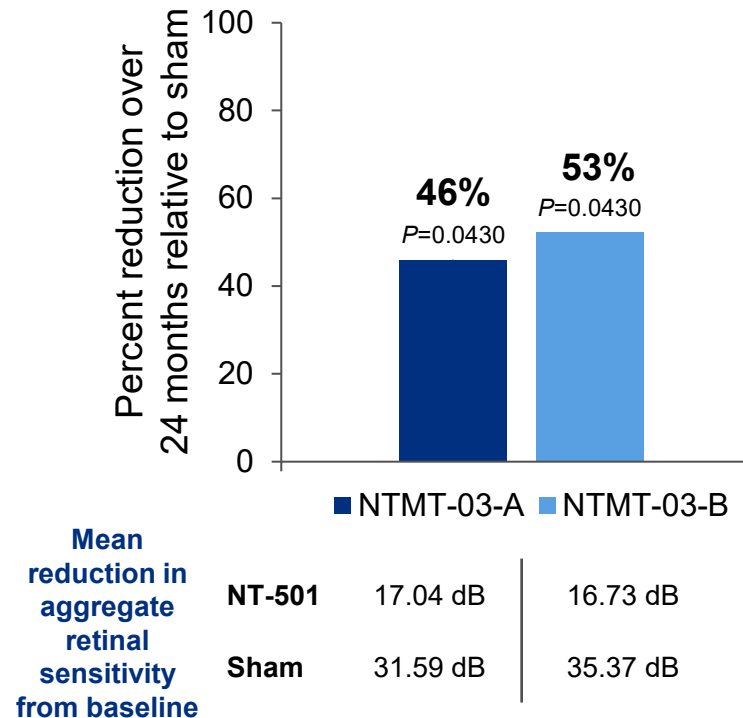
^aNominal chi-square *P* value; bolded value is statistically significant.

Subgroup of Participants with Smaller Baseline Lesions (<0.5 mm²)^a in Trials A and B: Efficacy Outcomes

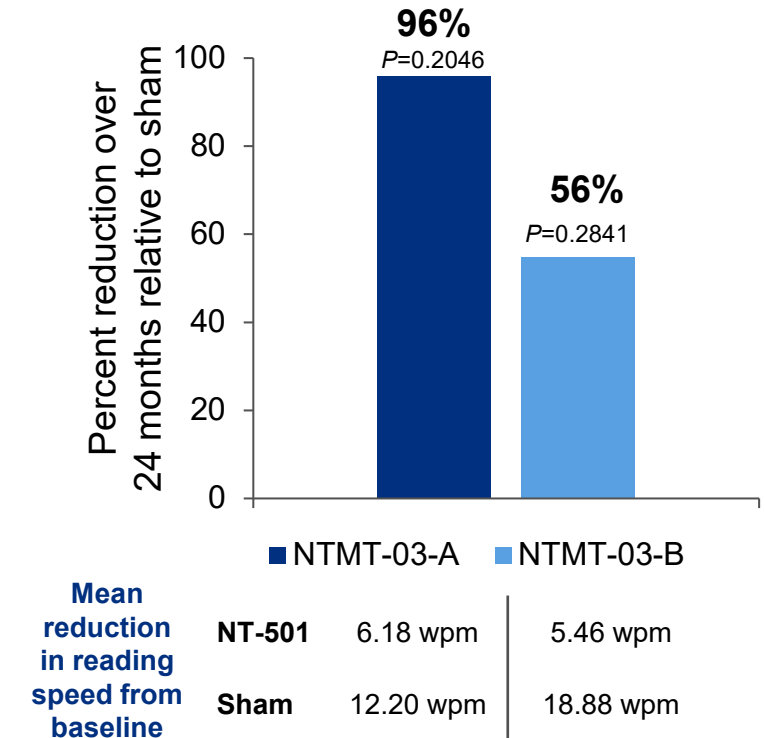
Reduction in Rate of Change in EZ Area Loss^b



Reduction in Retinal Sensitivity Loss^b



Reduction in Reading Speed Loss^b



Magnitude of reductions in EZ area loss, retinal sensitivity loss, and reading speed loss were more consistent between the studies with NT-501 treatment

dB, decibels; EZ, ellipsoid zone; mITT, modified intent-to-treat; NT-501, revakinagene tarorectel-lwey; wpm, words per minute.

All P values are nominal. ^aFor participants with baseline lesion size <0.5 mm² in NTMT-03-A, 51% (n=41) had NT-501 and 49% (n=40) had sham; in NTMT-03-B: 48% (n=31) had NT-501 and 53% (n=33) had sham.

^bAmong participants with baseline lesion size <0.5 mm² in the mITT population.

Take-Home Points

- Treatment with NT-501 versus sham **led to reductions in the rate of EZ area loss** in participants with MacTel, meeting the primary endpoint, and the implant is now FDA approved
- **Within the current post hoc analysis, smaller baseline EZ area loss and a history of diabetes appeared to independently confer greater odds of being a high responder** with NT-501 versus sham
- The treatment response difference between NTMT-03-A and NTMT-03-B appears to be **related to baseline lesion size differences**
- Among participants with **smaller baseline lesions, consistent reductions** were found in **EZ area loss, retinal sensitivity, and reading speed**
- Though the entire Phase 3 cohort had a **treatment benefit**, participants treated **earlier in the disease process** had the greatest **anatomic and functional treatment benefit**, with increased likelihood of **reducing further disease progression**

Thank You

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- MacTel Project investigators and their research teams (in the Natural History Registry Study and the Phase 1, 2, and 3 clinical trials)
- Study participants with MacTel
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