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Long-Term Safety and Efficacy of Revakinagene Taroretcel (NT-501) Ciliary Neurotrophic Factor Implant for Macular Telangiectasia Type 2

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- Funding was provided by Neurotech
- This study includes research conducted on human subjects. Institutional Review Board approval was obtained prior to study initiation

Take Home Points

- NT-501 was generally **well tolerated for up to 108 months** after implantation. Two of 51 NT-501 eyes were explanted (6.5 and 9.6 years after implantation).
- NT-501–treated eyes showed **less ellipsoid zone area loss** than eyes receiving sham treatment for up to 72 months (n=26 NT-501 eyes, n=18 sham eyes) in Cohort 2 or untreated fellow eyes for up to 96 months in 5 subjects and up to 108 months in 2 subjects in Cohort 1

NT-501, revakinagene taroretcel.

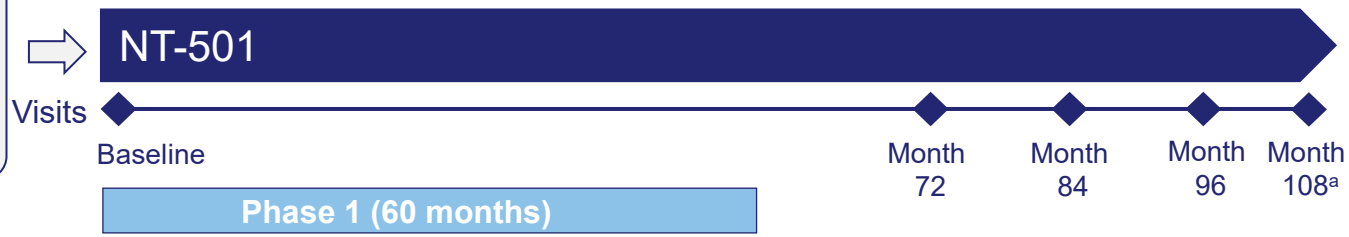
Phase 1 and Phase 2 Extension Trial: A Prospective, Multicenter, Single-Masked, Sham-Controlled Extension Study

Objective: To assess the long-term safety and efficacy of NT-501 in participants with MacTel who were previously enrolled in the Phase 1 or Phase 2 clinical trial

Inclusion Criteria

- Completed Month 60 of Phase 1
  - 7 participants enrolled; 7 completed the study
- NT-501 implanted in 1 eye

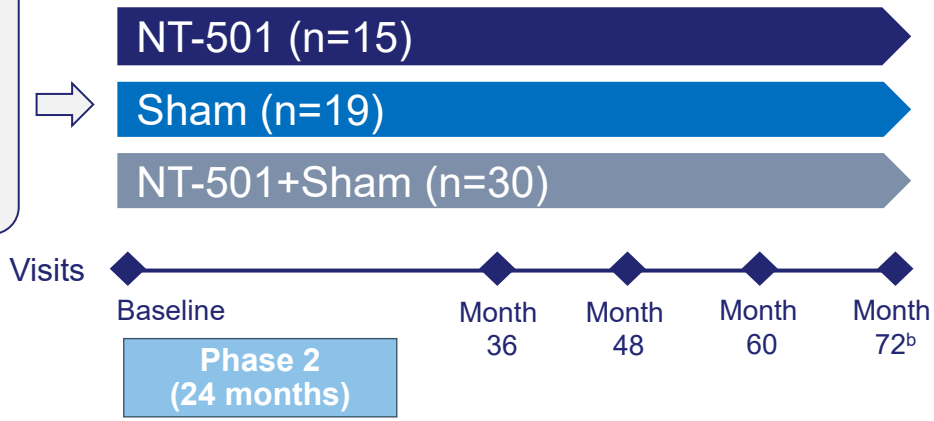
Cohort 1 (n=6)



Inclusion Criteria

- Completed Month 24 of Phase 2
  - 67 participants enrolled; 65 completed the study
- NT-501 implanted in 1 eye and/or underwent sham procedure

Cohort 2 (n=64)



- In Phase 2, participants with 1 eligible eye were randomized 1:1 to receive NT-501 or sham. In participants with 2 eligible eyes, the right eye was randomized 1:1 to NT-501 or sham and the left eye received the alternative treatment

MacTel, macular telangiectasia type 2; NT-501, revakinagene taroretcel.
[a]Of the 6 patients in Cohort 1, 3 were missing EZ area at the M108 timepoint due to delay in visit during COVID-19 pandemic. [b]At Month 72 in Cohort 2, n=58.

Phase 1 and Phase 2 Extension Trial: Study Design and Endpoints

Study design

- Safety and efficacy were assessed at 4 annual visits
- All safety data presented represent events reported from the start of the extension study
- 16 of 19 participants in the sham group in Phase 2 elected to have NT-501 implanted during the extension study. These subjects are excluded from the data presented to provide a better understanding of the long-term safety and efficacy of NT-501 by eliminating the impact of the treatment switch
- 4 participants did not continue in the extension, 2 due to death (n=1, NT-501; n=1 NT-501+sham) and 2 for participant withdrawal for other reasons (n=1, NT-501 [Cohort 1]; n=1 NT-501+sham)

Primary endpoint:

- Long-term safety, evaluated by AEs, SAEs, TEAEs that occurred during the extension study

Secondary endpoint:

- Proportion of study eyes with ≥35% increase from baseline in EZ area loss, as measured by SD-OCT

AE, adverse event; EZ, ellipsoid zone; NT-501, revakinagene taroretcel; SAE, serious adverse event; SD-OCT, spectral domain-optical coherence tomography; TEAE, treatment-emergent adverse event.

Baseline Characteristics Were Well Balanced Across Cohorts and Treatment Arms

By participant	Cohort 1 NT-501 (n=6)	Cohort 2[a] NT-501 (n=15)	Sham (n=19)	Sham[b] (n=3)	NT-501+sham (n=30)
Female, n (%)	4 (67)	9 (60)	11 (58)	1 (33)	20 (67)
Mean age, years (SD)	53.8 (5.1)	59.5 (10.8)	59.4 (7.6)	56.0 (13.1)	63.6 (8.6)
Race, n (%)					
White	4 (67)	11 (73)	16 (84)	2 (67)	28 (93)
Asian	1 (17)	0	1 (5)	0	0
Black or African American	0	0	0	0	1 (3)
Other	1 (17)	4 (27)	2 (11)	1 (33)	1 (3)
Ethnicity, n (%)					
Hispanic or Latino	0	1 (7)	0	0	1 (3)

By eye	Cohort 1 NT-501 (n=6)	Cohort 1 Fellow eye (n=6)	Cohort 2[a] NT-501 (n=45)	Sham[b] (n=33)	Sham (n=49)
EZ area loss, mm^2					
Mean (SD)	0.63 (0.81)	0.70 (0.83)	0.70 (0.42)	0.79 (0.47)	0.77 (0.55)
Median (minimum, maximum)	0.24 (0,1.86)	0.36 (0, 1.93)	0.60 (0.19, 1.98)	0.68 (0.18, 2.41)	0.62 (0.15, 2.79)
Mean BCVA, ETDRS letters (SD)	75.0 (7.9)	80.5 (7.3)	77.4 (5.7)	78.2 (7.1)	77.1 (7.3)
Snellen equivalent	20/32	20/25	20/32	20/32	20/32

Participants were primarily White, non-Hispanic, and female, had a mean age of ~60 years, and had a baseline visual acuity of approximately 20/32

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; NT-501, revakinagene taroretcel; SD, standard deviation.
[a]Baseline characteristics from the NTMT-02 study are presented. [b]Subjects in the sham treatment group that received intervention (NT-501) during the extension study are excluded (n=16).

Most TEAEs Were Mild or Moderate in Severity

By eye	Cohort 1		Cohort 2[b]		
	NT-501 (n=6)	Fellow eye (n=6)	NT-501 (n=45)	Sham (n=33)	Fellow eye (n=18)
≥1 ocular TEAE, n (%)	4 (67)	3 (50)	30 (67)	16 (49)	6 (33)
Ocular TEAE by maximum severity, n (%)					
Mild	2 (33)	1 (17)	12 (27)	9 (27)	4 (22)
Moderate	2 (33)	2 (33)	15 (33)	7 (21)	2 (11)
Severe	0	0	3 (7)	0	0
Ocular TEAE by relationship,[a] n (%)					
Surgery	1 (17)	—	3 (7)	0	—
NT-501	0	—	5 (11)	0	—
CNTF	0	—	4 (9)	1 (3)	—
Ocular TEAE leading to explantation, n (%)	1 (17)	0	1 (2)	0	0

Cohort 1

- 67% of eyes implanted with NT-501 had ≥1 ocular TEAE, none of which were serious or severe
  - 1 eye had a suture-related complication that led to explantation approximately 9.6 years after implantation
- 83% of participants had ≥1 non-ocular TEAE
  - 3 (in 2 participants) were severe
  - None were related to surgery, NT-501, or CNTF

Cohort 2

- 67% of eyes implanted with NT-501 had ≥1 ocular TEAE, 2 of which were considered a treatment-emergent SAE
  - 1 eye had NT-501 explanted due to the SAE of device expulsion/extrusion approximately 6.5 years after surgery
  - 1 eye with noninfectious endophthalmitis was considered by the investigator to be related to NT-501 and resolved by the Month 72 visit
- 70% of all participants had ≥1 non-ocular TEAE, none of which were related to surgery, NT-501, or CNTF
  - 2 experienced fatal non-ocular SAEs, neither related to surgery, CNTF, NT-501

CNTF, ciliary neurotrophic factor; NT-501, revakinagene taroretcel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a]A TEAE considered by the investigator to be related to >1 category (ie, surgery, NT 501, or CNTF) was counted separately in each category.
[b]Subjects in the sham treatment group that received intervention (NT-501) during the extension study are excluded (n=16).

Ocular TEAEs of Interest (by Eye)[a]

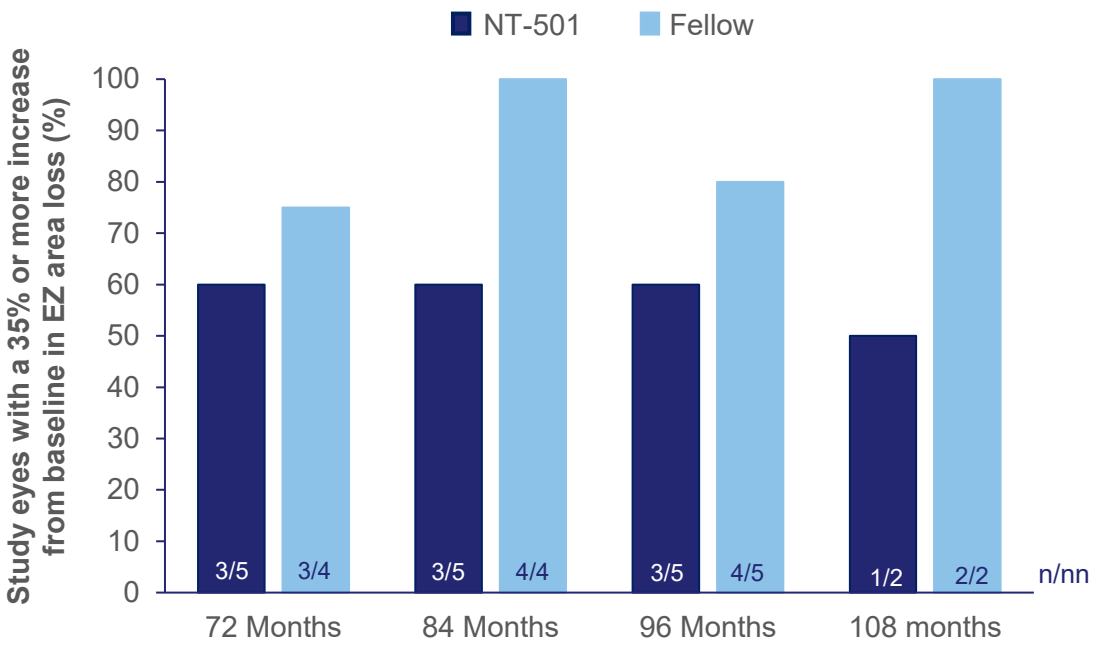
	Cohort 1 (N=6 participants)		Cohort 2[b] (N=96 eyes)		
Clinically significant ocular TEAE, n (%)	**NT-501 (n=6)**	**Fellow Eye (n=6)**	**NT-501 (n=45)**	**Sham (n=33)**	**Fellow Eye (n=18)**
Choroidal neovascularization	0	0	1 (2.2)	1 (3.0)	1 (5.6)
Fluid leakage[c]	0	0	1 (2.2)	1 (3.0)	0
Subconjunctival hemorrhage	0	0	0	0	0
Fibrosis	0	0	1 (2.2)[d]	1 (3.0)[d]	0
Vitreal inflammation	0	0	1 (2.2)	0	0
Sectorial lens opacification	0	0	1 (2.2)	1 (3.0)	0
Intraocular hemorrhage	0	0	3 (6.7)	0	0
Dry eye	0	0	3 (6.7)	1 (3.0)	1 (5.6)
Change in dark adaptation	0	0	1 (2.2)	1 (3.0)	0
Miosis	0	0	3 (6.7)	0	0

CNV, choroidal neovascularization; NT-501, revakinagene taroretcel; TEAE, treatment emergent adverse event.
[a]Safety events reported from the start of the extension trial. No safety events from the antecedent study are reported. [b]Subjects in the sham treatment group that received intervention (NT-501) during the extension study are excluded (n=16). [c]Fluid leakage refers to new intraretinal or subretinal fluid. Fluid leakage occurred in the study eye of 1 subject in the sham group (002-081) and in the NT-501 implanted eye of 1 subject in the NT-501+sham group (002-017). In both instances, fluid leakage was associated with the development of CNV. [d]Subretinal fibrosis at the macula was observed for both eyes of 1 subject (011-184) in the NT-501+sham group..

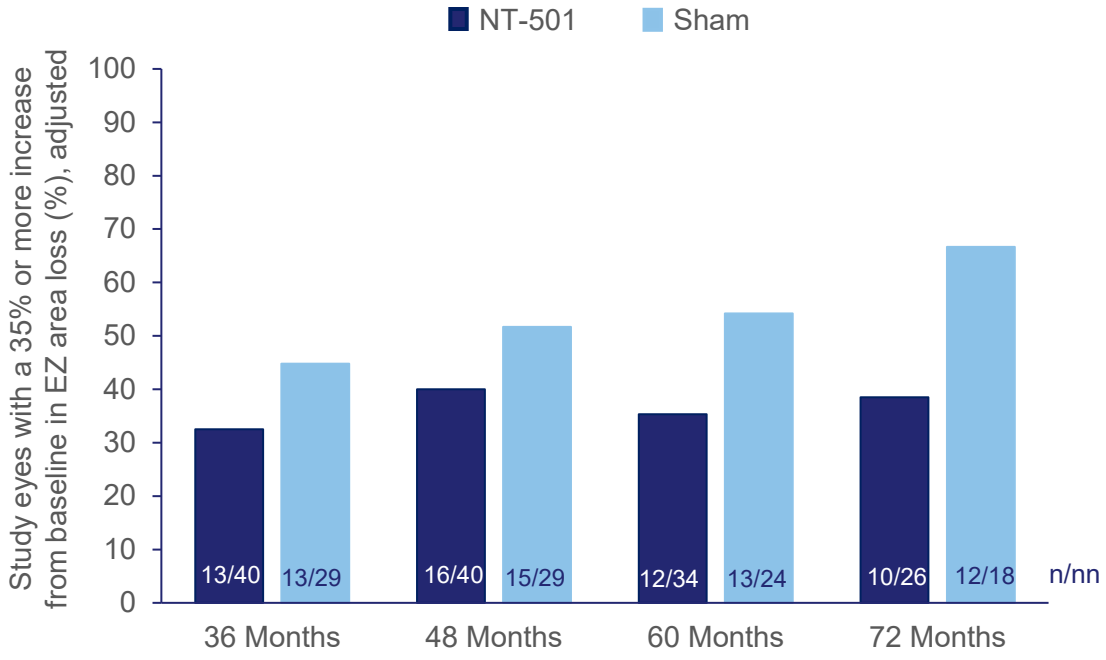
Percentage of Eyes With ≥35% Increase in EZ Area Loss Was Lower for Eyes With NT-501 Than Sham-Treated or Fellow Eyes

Percentages of study eyes with ≥35% increase from baseline in EZ area loss

Cohort 1[a]



Cohort 2[b]



EZ, ellipsoid zone; ITT, intent-to-treat; n=number of eyes with at least 35% increase from baseline; nn=number of eyes observed; NT-501, revakinagene taroretcel; PP, per-protocol.
[a]For Cohort 1, EZ area loss is reported in the ITT population. [b]For Cohort 2, EZ area loss is reported in the PP population, which included all subjects in the ITT population who had no major protocol infractions (defined prior to unmasking of the study); for Cohort 2, a total of 20 participants, including all 16 in the sham group implanted with NT-501 during the extension study, were excluded from the PP analysis. The PP analysis provides a better understanding of the long-term efficacy of NT-501 by eliminating the impact of the treatment switch.

Take Home Points

- NT-501 was generally **well tolerated for up to 108 months** after implantation. Two of 51 NT-501 eyes were explanted (6.5 and 9.6 years after implantation).
- NT-501–treated eyes showed **less ellipsoid zone area loss** than eyes receiving sham treatment for up to 72 months in Cohort 2 or untreated fellow eyes for up to 96 months in 5 subjects and up to 108 months in 2 subjects in Cohort 1

EZ, ellipsoid zone; NT-501, revakinagene taroretcel.

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