

Timing of Ocular Adverse Events in Pooled Analysis of Two Phase 3 Trials of Revakinagene Taroretcel-Lwey (NT-501) in Macular Telangiectasia Type 2

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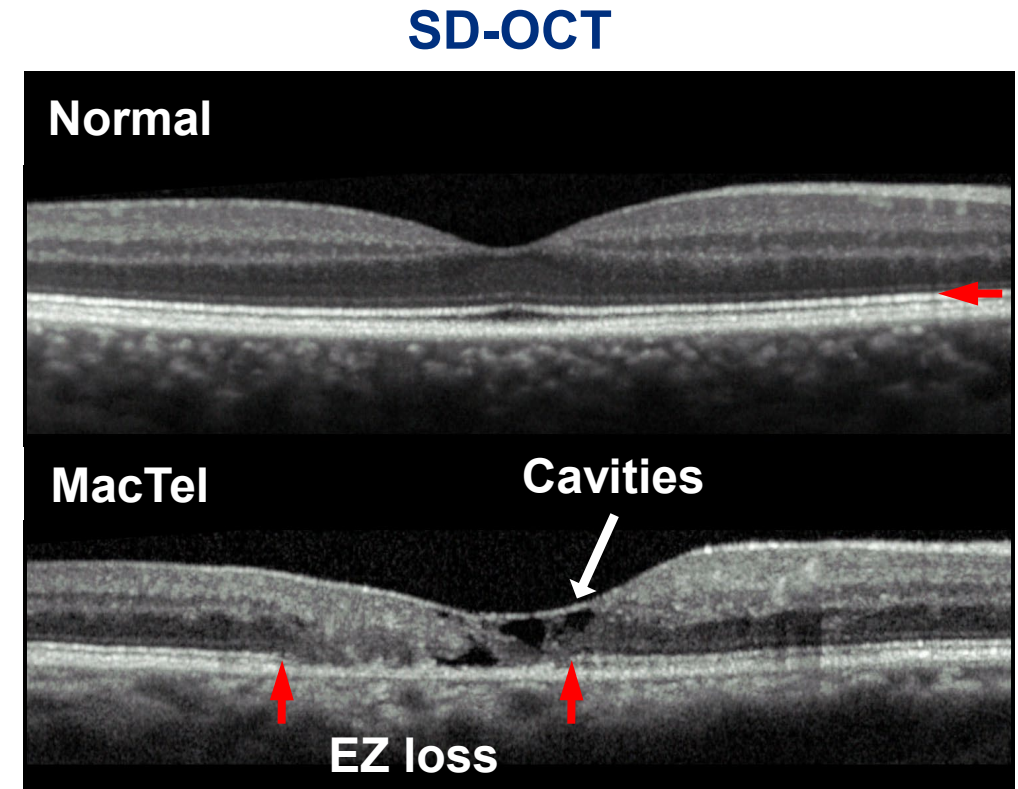
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Disclosures

- Victor H. Gonzalez is a consultant for AbbVie, Alcon/Novartis, Alimera Sciences, Allergan, Astellas Institute for Regenerative Medicine, Bausch & Lomb, Beaver-Visitech International, Genentech, Ocuphire Pharma, Oxurion (subsidiary of ThromboGenics), Regeneron, Santen, TOPCON, and Valeant; has personal financial interest in Alimera Sciences, Aviceda Therapeutics, Eclipse Life Sciences, Nanoscope Observational, PANOPTICA, Restore, and Starlight; receives financial support from 4DMT, 60° Pharmaceuticals, Adverum, AiViva Biopharma, Alcon/Novartis, Alimera Sciences, Allergan, Allgenesis Biotherapeutics, Alluvium, Alnylam, American Genomics, Annexin, Apellis Gale, Astellas Institute for Regenerative Medicine, Aviceda Therapeutics, Avonelle-X, Boehringer Ingelheim CRIMSON/1436-0007, Boehringer Ingelheim Pharma GmbH & Co. KG, Chengdu Kanghong Biotechnology, Concerto, CONDOR, Curacle, DAVIO2 EYP-1901, Eclipse Life Sciences, Endogena Therapeutics, Envision UBX, EyeBio EYE103-101, Genentech, Graybug Vision, Iconic Therapeutics, IMVT 1401-3201, INSITE, IONIS, IQVIA RDS, Johnson & Johnson Surgical Vision, KLRS-100, LEOPARD, Lightsite III, Mallinckrodt ARD, Ocu410-101, Oculis Diamond (Stage 1), Oculis Diamond (Stage 2), Ocuphire Pharma, OcuTerra Therapeutics, ONL Therapeutics, OPTHEA, Oxurion (subsidiary of ThromboGenics), Oxular Limited, Regeneron, Rezolute, Rhone-X, RIBOMIC USA, RxSight, Santen, SPIAM-301, the SYNCHRONICITY Study, Valeant, Vista, and Voyage
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- This study includes research conducted on human participants; institutional review board approval was obtained prior to study initiation

Macular Telangiectasia Type 2

- Bilateral, progressive, retinal neurodegenerative disease that leads to central vision loss and functional impairment^{1,2}
 - Progressive loss of the EZ:
~0.08 mm²/year³
- Associated with abnormalities in Müller glia, retinal pigment epithelia, and photoreceptors in the central retina corresponding with degenerative hyporeflective cavities⁴



EZ, ellipsoid zone; MacTel, macular telangiectasia type 2; SD-OCT, spectral domain-optical coherence tomography.

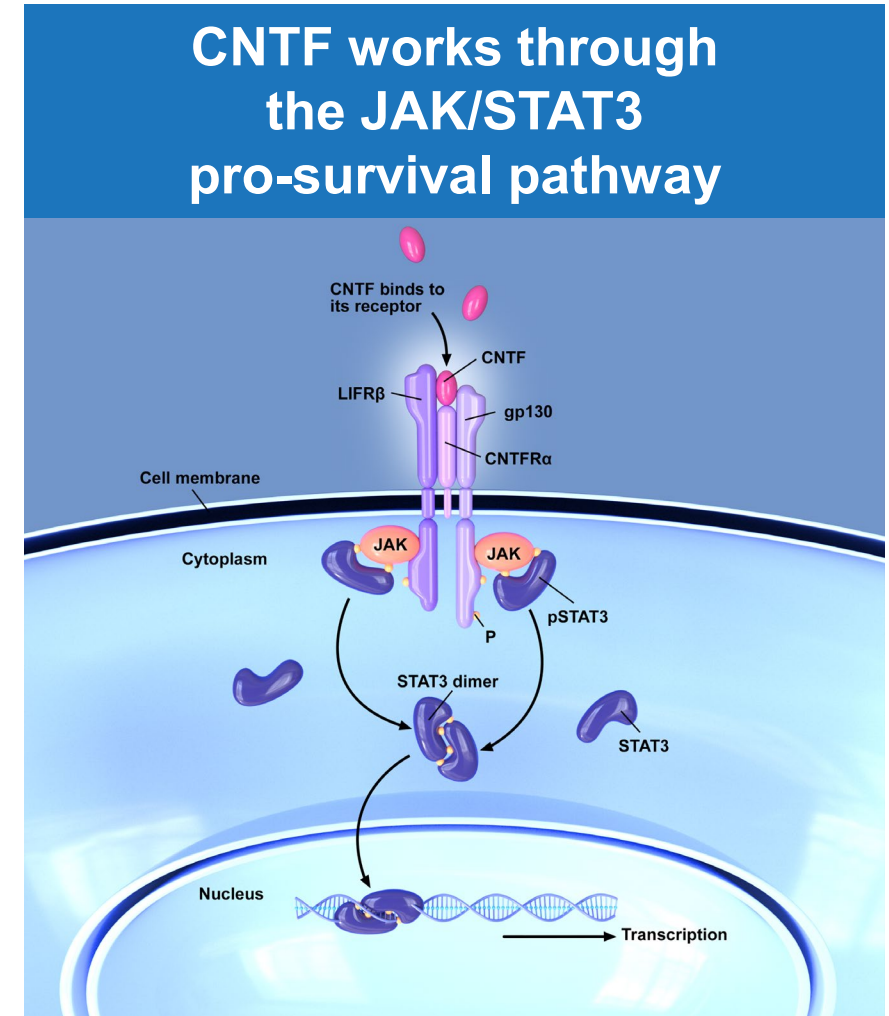
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3. Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. 4. Kedariseti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

Image provided by Dr. Thomas Aaberg.

Ciliary Neurotrophic Factor Is a Potent Neuroprotectant¹⁻³

- In response to injury, Müller glial cells release the neuroprotective factor CNTF¹
- **CNTF protects and preserves photoreceptors²⁻⁴**
- In preclinical models of retinal degeneration, photoreceptors can be rescued with intravitreal injection of CNTF^{2,4}

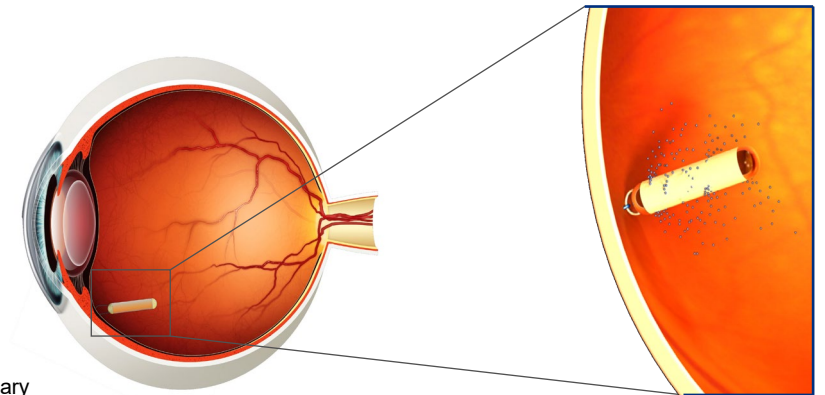
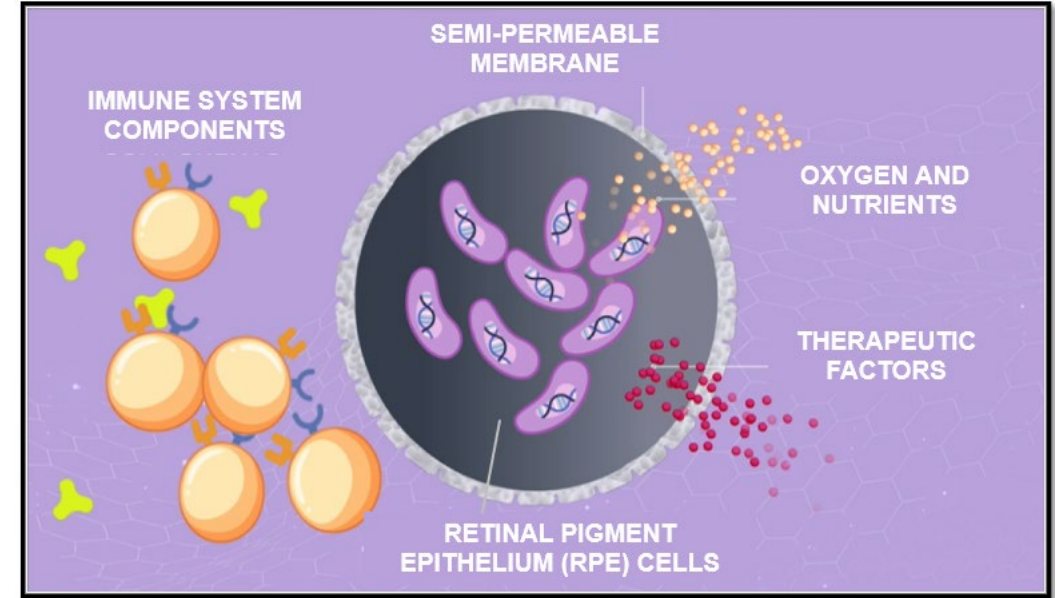


CNTF, ciliary neurotrophic factor; CNTFRα, ciliary neurotrophic factor receptor-alpha; gp130, glycoprotein 130; JAK/STAT3, Janus kinase/signal transducer and activator of transcription 3; LIFRβ, leukemia inhibitory factor β; P, phosphorous; STAT3, signal transducer and activator of transcription 3.

1. Bringmann A, et al. *Prog Retin Eye Res.* 2009;28:423-445. 2. Shen W, et al. *J Neurosci.* 2012;32:15715-15727. 3. Sleeman MW, et al. *Pharm Acta Helv.* 2000;74:265-272. 4. Tao W, et al. *Invest Ophthalmol Vis Sci.* 2002;43:3292-3298.

Encapsulated Cell Therapy Is Designed to Deliver Sustained Levels of CNTF

- Revakinagene taroretcel-lwey (NT-501) is a first-in-class encapsulated cell therapy^{1,2}
 - Houses NTC-201-6A cells¹
 - Allogeneic retinal pigment epithelial cells expressing recombinant human CNTF¹
 - Surgically implanted into the vitreous cavity and stably anchored to the sclera¹
 - Developed to produce long-term sustained levels of CNTF³
 - **NT-501 was approved by the FDA for the treatment of MacTel on March 5, 2025**



CNTF, ciliary neurotrophic factor; FDA, Food and Drug Administration; MacTel, macular telangiectasia type 2.

1. ENCELTO [package insert]. Cumberland, RI: Neurotech Pharmaceuticals, Inc; March 2025. 2. Lally D, Elliott D. Phase 2 safety study of bilateral ciliary neurotrophic factor-producing revakinagene taroretcel in participants with macular telangiectasia type 2 [abstract]. Presented at: Annual EURETINA; September 19-22, 2024; Barcelona, Spain. 3. Kauper K, et al. *Invest Ophthalmol Vis Sci.* 2023;64:3680.

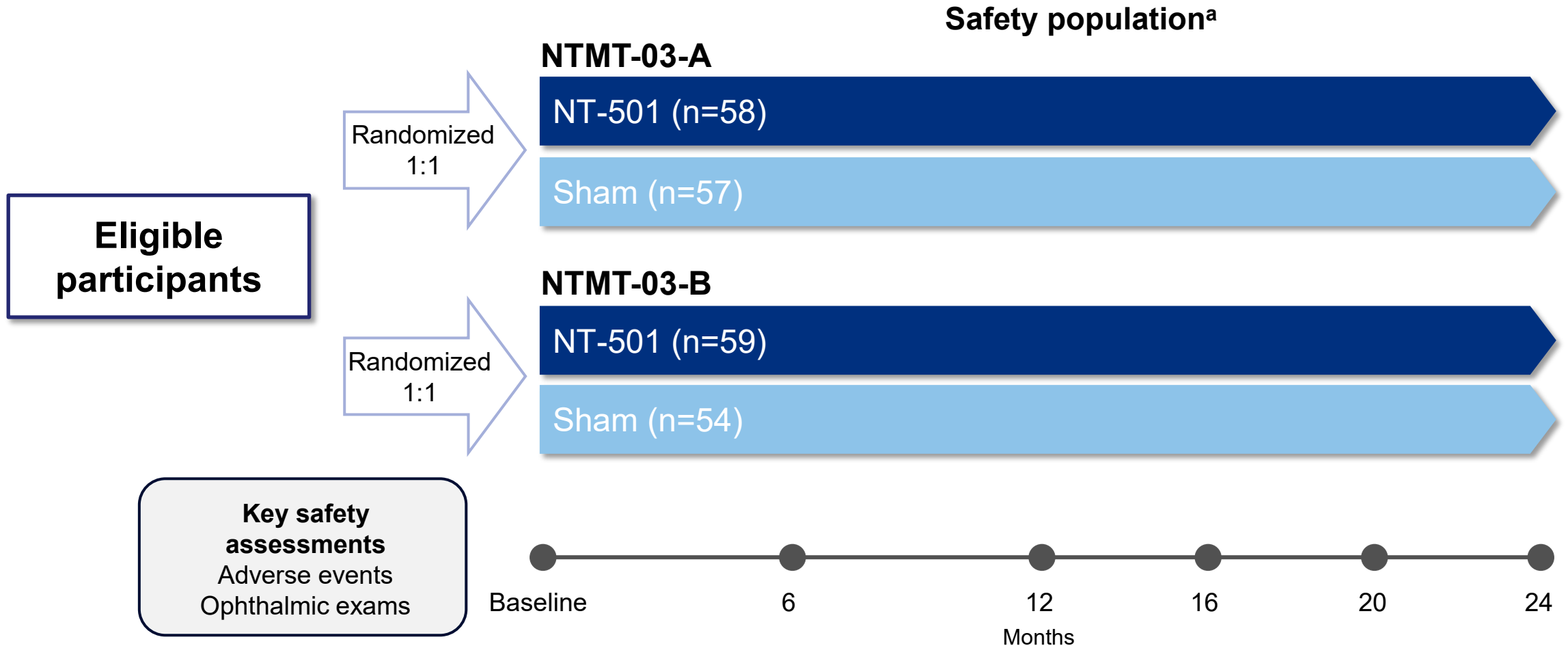
NT-501 Was Studied in Two Identical Phase 3 Clinical Trials

- In both NTMT-03A and NTMT-03B, NT-501 preserved photoreceptors, as indicated by a significant reduction in the rate of EZ area loss through 2 years compared with sham treatment
 - Both trials met their primary endpoints
- NT-501 was generally well tolerated

The objective of this analysis was to examine the incidence and timing of ocular TEAEs across the two Phase 3 trials of NT-501

NTMT-03-A and NTMT-03-B (Identical Study Designs)

Phase 3, Multicenter, Randomized, Sham-Controlled Studies

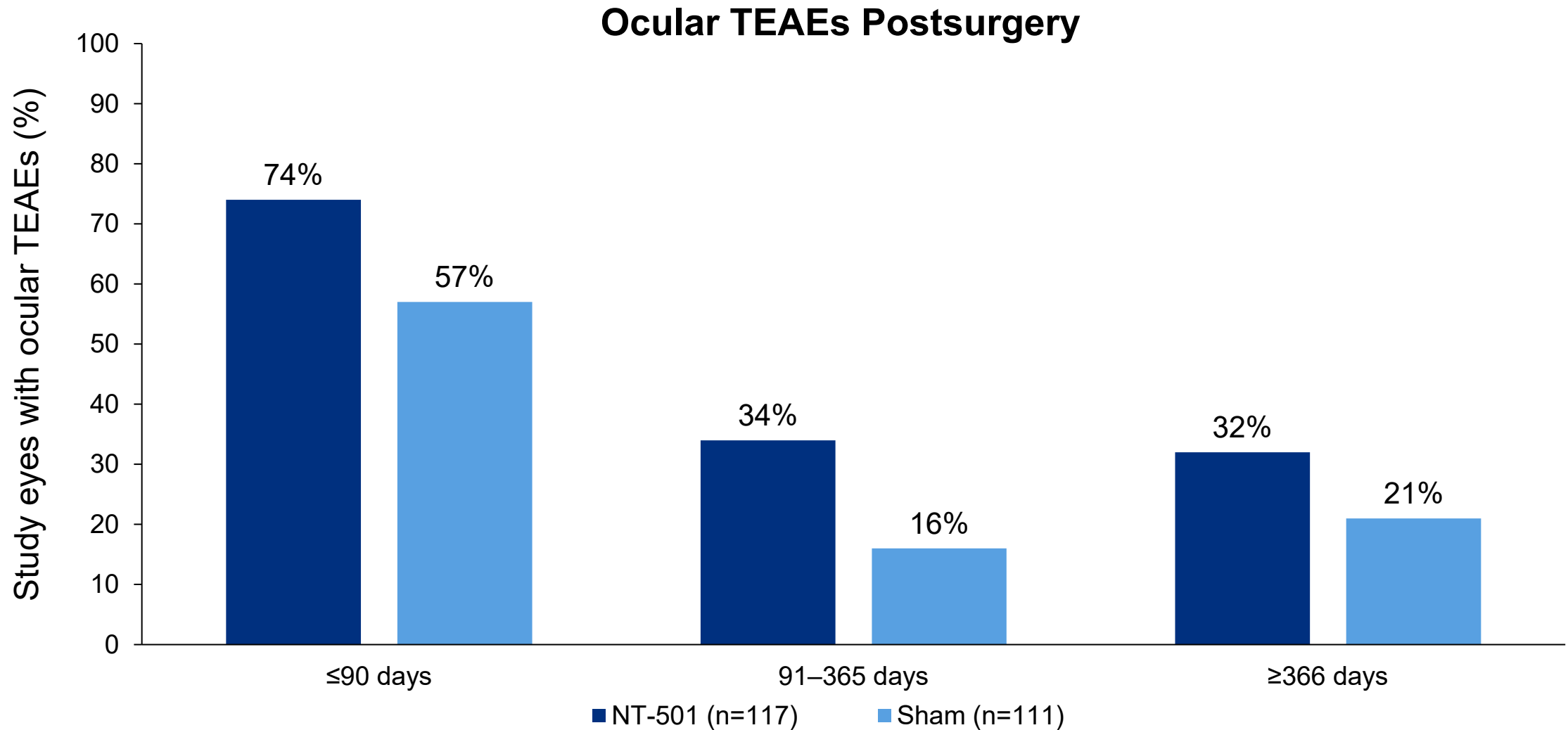


^aAll participants who received the implant or the sham surgery and had ≥ 1 safety measurement.

NTMT-03-A and NTMT-03-B Safety Analysis

- Safety data from NTMT-03A and NTMT-03B from study eyes were pooled for this analysis
- Ocular TEAEs and SAEs were stratified by time of onset postsurgery (≤ 90 days, 91–365 days, or ≥ 366 days)
 - The presence or absence of delayed dark adaptation as perceived by the participant was solicited and recorded at each study visit
 - Miosis included reported AEs and events captured during ophthalmic exams
 - Incidence rates of new onset or worsening cataracts using combined and preferred MedDRA v25.0 terms were reported and stratified by the same time periods

A Majority of Ocular TEAEs Occurred Within the First 90 Days of Surgery



TEAE, treatment-emergent adverse event.

PROVIDED IN RESPONSE TO AN UNSOLICITED REQUEST

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Most Common TEAEs Occurring ≤90 Days Postsurgery

Ocular TEAE in study eye, n (%)	NT-501 (n=117)	Sham (n=111)
Conjunctival hemorrhage	35 (29.9)	30 (27.0)
Foreign body sensation in eyes	19 (16.2)	14 (12.6)
Eye pain	19 (16.2)	10 (9.0)
Conjunctival hyperemia	13 (11.1)	9 (8.1)
Delayed dark adaptation	16 (13.7)	1 (0.9)

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The majority of TEAEs were expected postsurgical events and occurred with similar frequencies between the NT-501 and sham surgery arms

Most Common TEAEs Occurring ≤90 Days Postsurgery

Ocular TEAE in study eye, n (%)	NT-501 (n=117)	Sham (n=111)
Conjunctival hemorrhage	35 (29.9)	30 (27.0)
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Conjunctival hyperemia	13 (11.1)	9 (8.1)
Delayed dark adaptation	16 (13.7)	1 (0.9)

Delayed dark adaptation occurred more frequently in the NT-501 arm with the majority of cases occurring within 90 days of surgery

Most Common TEAEs Occurring 91–365 Days Postsurgery

Ocular TEAE in study eye, n (%)	NT-501 (n=117)	Sham (n=111)
Delayed dark adaptation	8 (6.8)	1 (0.9)
Miosis	7 (6.0)	0
Dry eye	3 (2.6)	3 (2.7)
Visual impairment	0	5 (4.5)
Vitreous floaters	5 (4.5)	0

Most Common TEAEs Occurring 91–365 Days Postsurgery

Ocular TEAE in study eye, n (%)	NT-501 (n=117)	Sham (n=111)
Delayed dark adaptation	8 (6.8)	1 (0.9)
Miosis	7 (6.0)	0
Dry eye	3 (2.6)	3 (2.7)
Visual impairment	0	5 (4.5)
Vitreous floaters	5 (4.5)	0

- **Miosis incidence began to increase in NT-501 eyes between 91 and 365 days after implantation**
- **The occurrence of delayed dark adaptation decreased after 90 days postsurgery**

Most Common TEAEs Occurring ≥ 366 Days Postsurgery

Ocular TEAE in study eye, n (%)	NT-501 (n=117)	Sham (n=111)
Miosis	7 (6.0)	0
Dry eye	3 (2.6)	2 (1.8)
Delayed dark adaptation	3 (2.6)	1 (0.9)
Blurred vision	2 (1.7)	1 (0.9)
Choroidal neovascularization	1 (0.9)	2 (1.8)

Delayed Dark Adaptation and Miosis Were Related to CNTF

	Occurrence ≤90 days, n (%)		Occurrence 91–365 days, n (%)		Occurrence ≥366 days, n (%)		Mean (SD) Days From Surgery	Range (days)
	NT-501 (n=117)	Sham (n=111)	NT-501 (n=117)	Sham (n=111)	NT-501 (n=117)	Sham (n=111)		
Delayed dark adaptation^a	16 (13.7)	1 (0.9)	8 (6.8)	1 (0.9)	3 (2.6)	1 (0.9)	142.4 (173.24)	1–606
Miosis^a	4 (3.4)	0	7 (6.0)	0	7 (6.0)	0	358.1 (261.56) ^b	2–745

- Delayed dark adaptation occurred an average of 142 days after surgery
 - Most occurrences were seen in the first 90 days after surgery, with a decreasing frequency as time from surgery elapsed
- Miosis occurred an average of 358 days after surgery
 - Occurrences for miosis increased 4 months after surgery
- Both of these AEs were considered related to CNTF

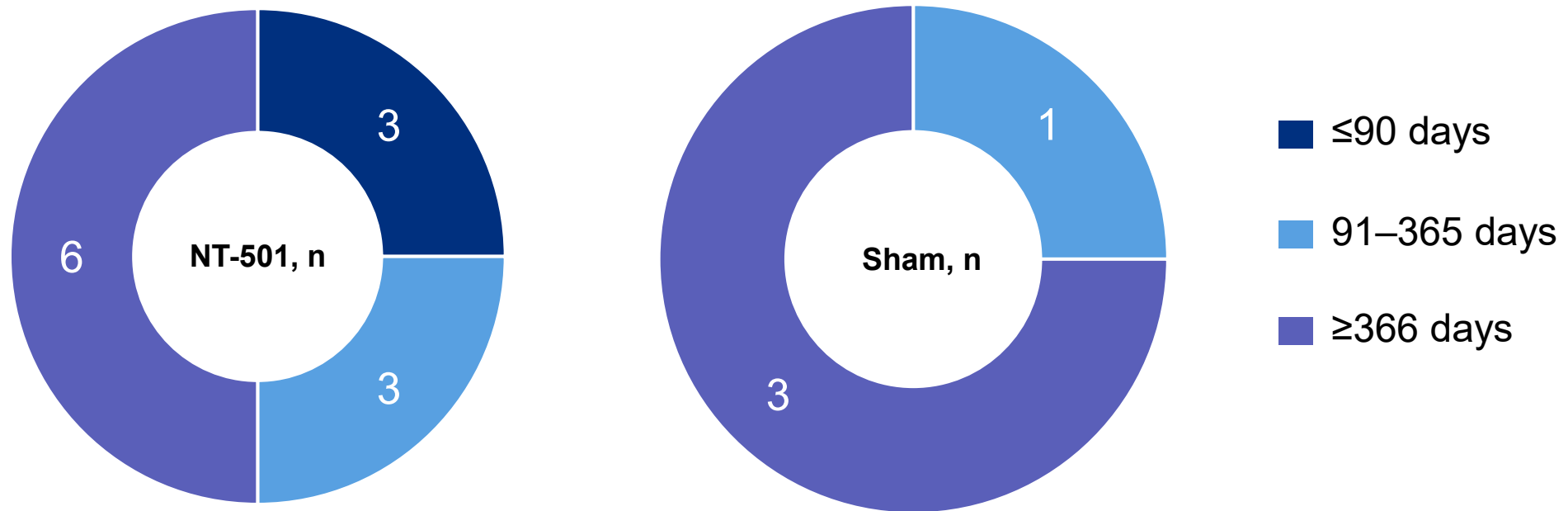
AE, adverse event; CNTF, ciliary neurotrophic factor; SD, standard deviation.

^aIf participants had ≥1 event, all instances contributed to the calculation of the mean and other descriptive statistics shown in the table.

^bIncludes 4 miosis AEs and 18 clinically significant events captured as part of ophthalmic exams.

Cataracts Occurred or Worsened in the NT-501 Group Across All 3 Time Periods

Cataract Occurrence or Worsening Postsurgery^a



Among all participants, 12 (10.3%) in the NT-501 group and 4 (3.6%) in the sham group had onset or worsening of cataracts; this was most commonly seen ≥366 days postsurgery

^aIf participants experienced ≥1 event with a given system organ class or preferred term, they were counted only once for that system organ class or preferred term.

Ocular SAEs Were Rare

- A total of 6 participants receiving NT-501 experienced ocular SAEs
 - **≤90 days postsurgery:** 1 suture-related complication (scleral wound opening)
 - **91–365 days postsurgery:** 2 suture-related complications (exposed suture and exposed metallic loop)
 - **≥366 days postsurgery:** 2 suture-related complications (exposed suture and suture eroded through conjunctiva) and 1 device extrusion
- Suture-related complications and the device extrusion were considered related to surgery

Summary

- **Based on two pooled Phase 3 trials of NT-501, a recently approved CNTF–producing encapsulated cell therapy for MacTel, we evaluated the incidence and timing of ocular TEAEs**
 - **≤90 days postsurgery:** most ocular TEAEs were related to surgery, were expected, and occurred with similar frequency between the eyes that underwent NT-501 versus sham surgery
 - **91–365 days postsurgery:** most ocular TEAEs, including delayed dark adaptation and miosis, almost exclusively were reported in eyes with NT-501 and were related to CNTF
 - **≥366 days postsurgery:** most common ocular TEAEs were miosis, dry eye, and delayed dark adaptation
 - Cataract onset or progression was not common during these studies, with most events occurring ≥366 days postsurgery
 - All but one of the ocular SAEs reported in NT-501 eyes were suture-related complications

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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