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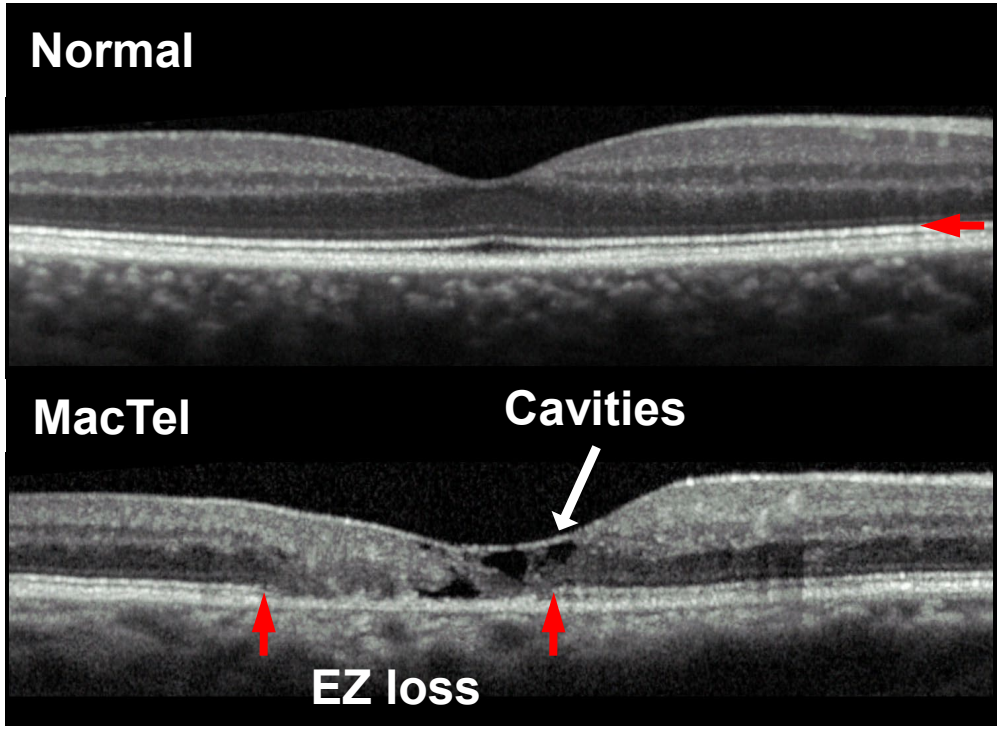
- This study includes research conducted on human participants; institutional review board approval was obtained prior to study initiation

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 mm^2/year[3]
- Associated with abnormalities in Müller glia, retinal pigment epithelia, and photoreceptors in the central retina corresponding with degenerative hyporeflective cavities[4]

SD-OCT



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

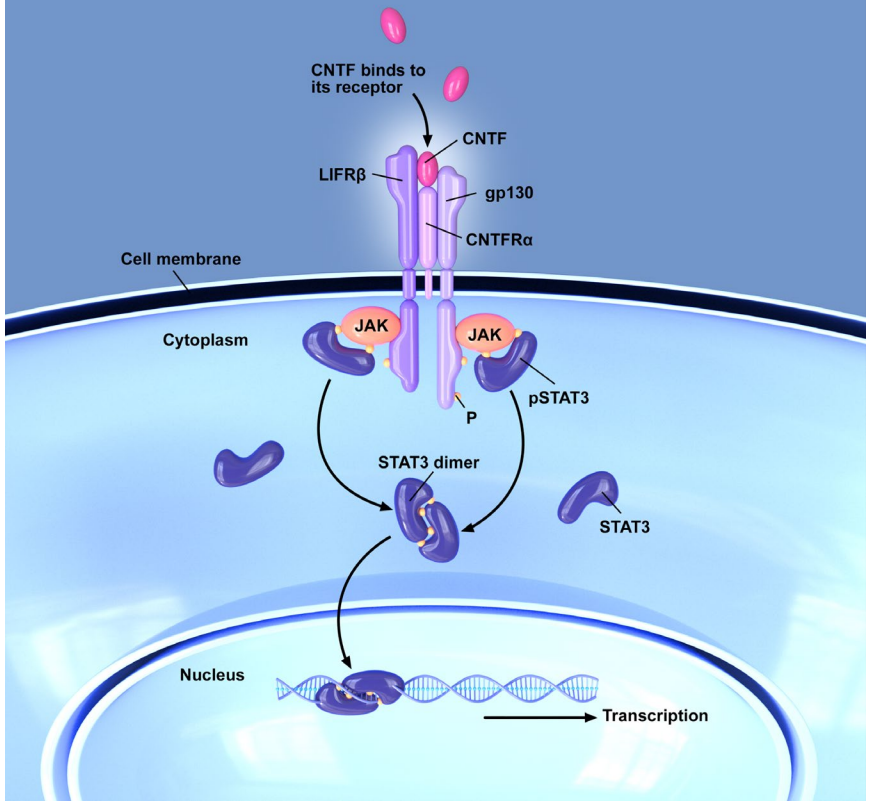
1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Hereen TFC, et al. *Ophthalmology*. 2020;127:1539-1548. **3.** Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. **4.** Kedarisetti KC, et al. *Clin Ophthalmol.* 2022;16:3297-3309.

Image provided by Dr. Thomas Aaberg.

Ciliary Neurotrophic Factor Is a Potent Neuroprotectant[1-3]

- In response to injury, Müller glial cells release the neuroprotective factor CNTF[1]
- **CNTF protects and preserves photoreceptors[2-4]**
- In preclinical models of retinal degeneration, photoreceptors can be rescued with intravitreal injection of CNTF[2,4]

CNTF works through the JAK/STAT3 pro-survival pathway

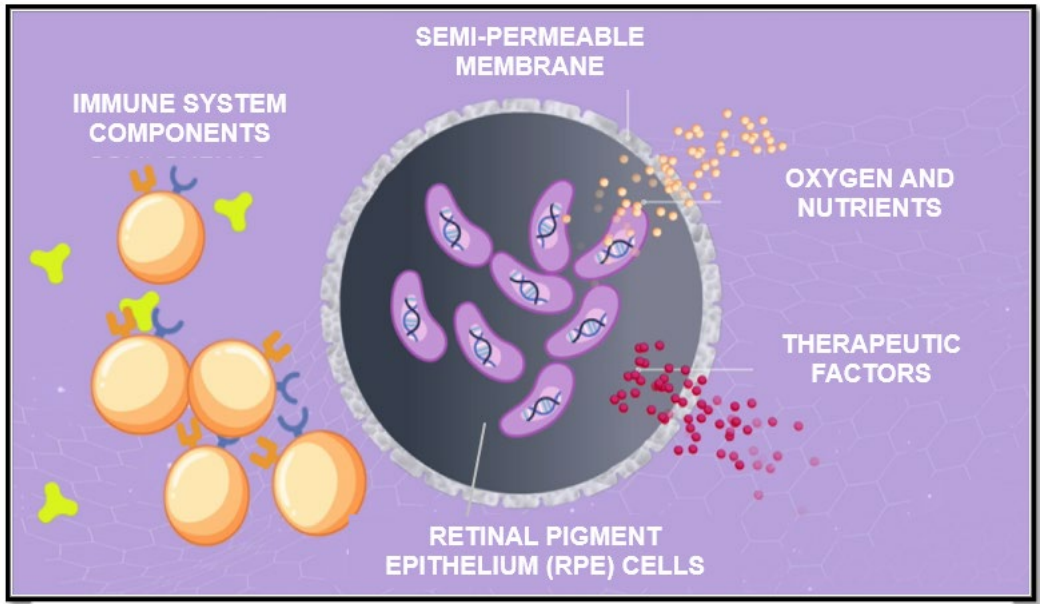


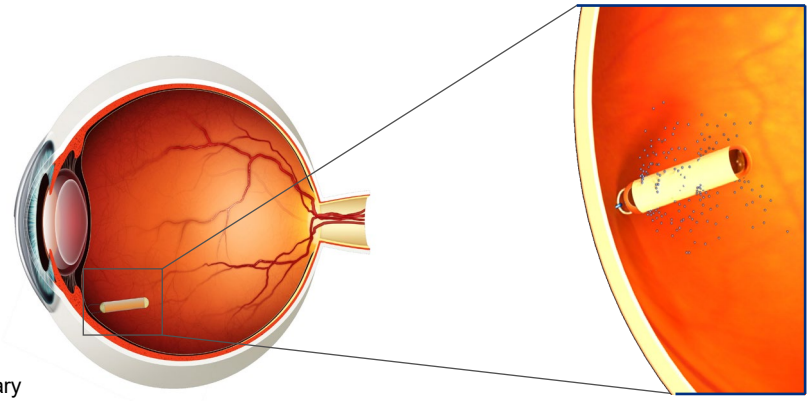
CNTF, ciliary neurotrophic factor; CNTFRα, ciliary neurotrophic factor receptor-alpha; gp130, glycoprotein 130; JAK/STAT3, Janus kinase/signal transducer and activator of transcription 3; LIFRβ, leukemia inhibitory factor ß; P, phosphorous; STAT3, signal transducer and activator of transcription 3.

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 cells[1]
    - Allogeneic retinal pigment epithelial cells expressing recombinant human CNTF[1]
  - Surgically implanted into the vitreous cavity and stably anchored to the sclera[1]
  - Developed to produce long-term sustained levels of CNTF[3]
  - **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, Eliott 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.

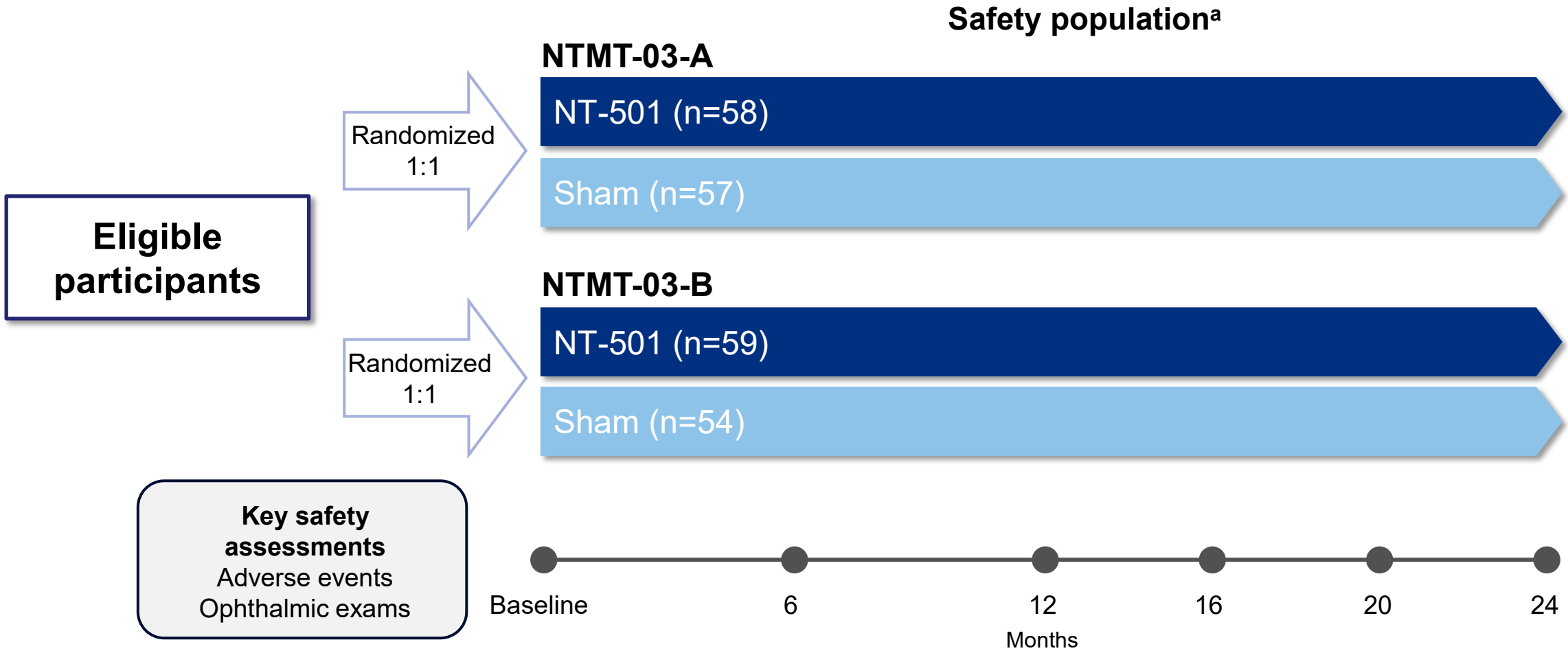
NT-501 Was Studied in Two Identical Phase 3 Clinical Trials

- 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

EZ, ellipsoid zone; TEAE, treatment-emergent adverse event.

NTMT-03-A and NTMT-03-B (Identical Study Designs)
Phase 3, Multicenter, Randomized, Sham-Controlled Studies



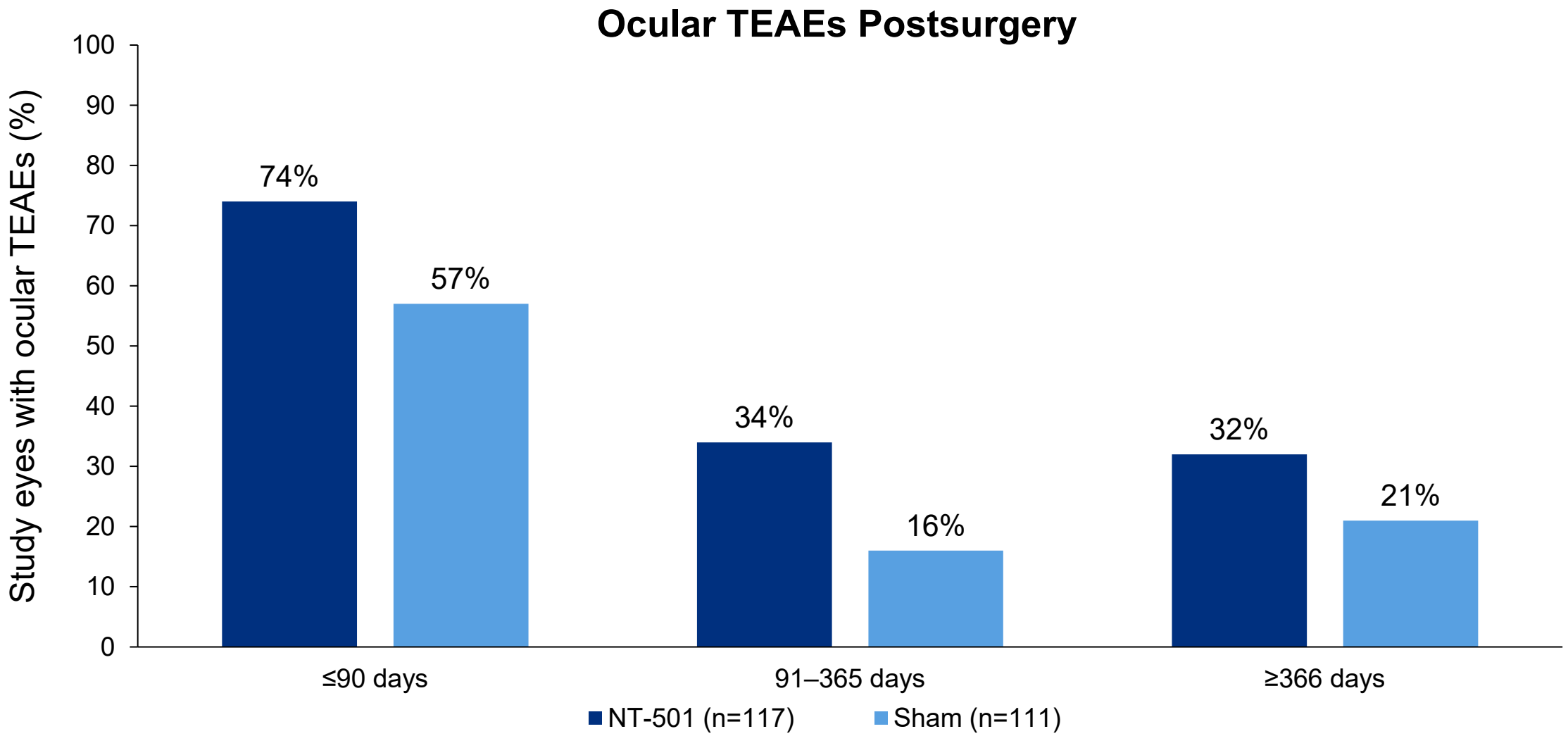
[a]All participants who received the implant or the sham surgery and had ≥1 safety measurement.

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

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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



TEAE, treatment-emergent adverse event.

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

TEAE, treatment-emergent adverse event.

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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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)

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

TEAE, treatment-emergent adverse event.

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

TEAE, treatment-emergent adverse event.

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**

TEAE, treatment-emergent adverse event.

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)

TEAE, treatment-emergent adverse event.

Delayed Dark Adaptation and Miosis Were Related to CNTF

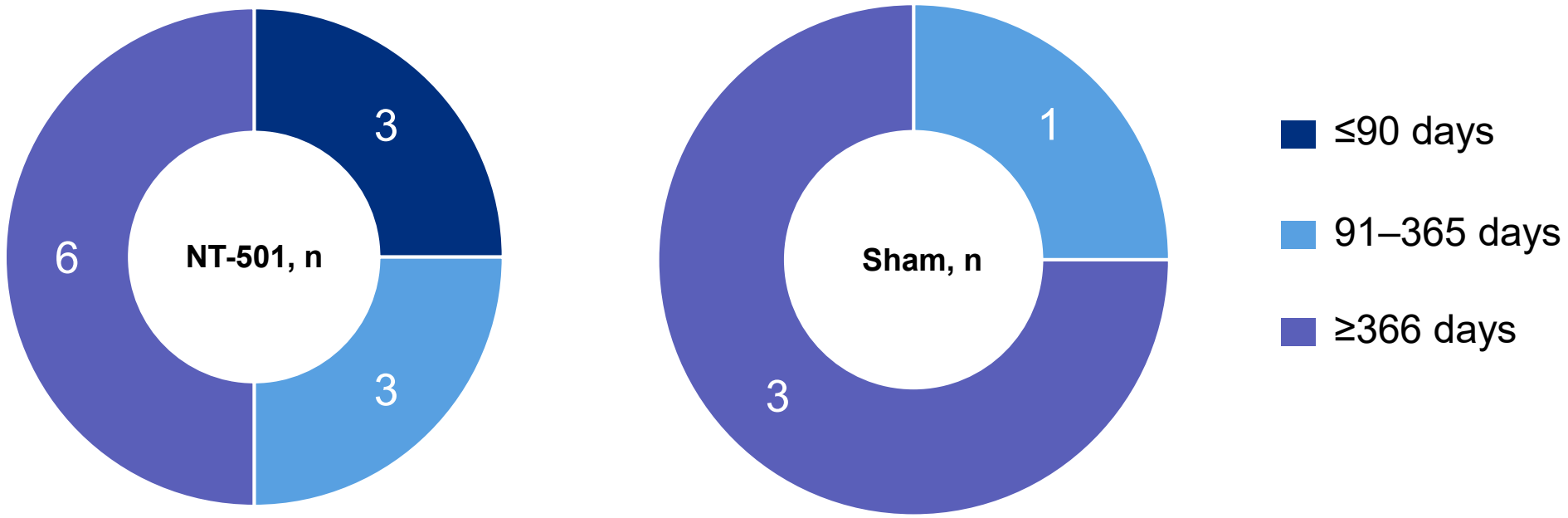
	Occurrence ≤90 days, n (%)		Occurrence 91–365 days, n (%)		Occurrence ≥366 days, n (%)		Mean (SD) Days From Surgery	Range (days)
	NT-501 (n=117)	Sham (n=111)	NT-501 (n=117)	Sham (n=111)	NT-501 (n=117)	Sham (n=111)		
Delayed dark adaptation[a]	16 (13.7)	1 (0.9)	8 (6.8)	1 (0.9)	3 (2.6)	1 (0.9)	142.4 (173.24)	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.
[a]If participants had ≥1 event, all instances contributed to the calculation of the mean and other descriptive statistics shown in the table.
[b]Includes 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

[a]If 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

SAE, serious adverse event

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

AE, adverse event; CNTF, ciliary neurotrophic factor; MacTel, macular telangiectasia type 2; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Thank You

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- Study participants with MacTel
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MacTel, macular telangiectasia type 2.