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Ciliary Neurotrophic Factor (CNTF) for Macular Telangiectasia Type 2 (MacTel): Results from a phase I safety trial

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Abstract

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[‡]The list of all Participating Centers and Investigators in the MacTel CNTF Safety Study can be found in the Appendix.

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Design of the Study: EYC, TEC, AB, TP, FS

Conduct of the Study: TEC, TP, LS, SS, AI

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PURPOSE—To evaluate the safety and tolerability of intraocular delivery of ciliary neurotrophic factor (CNTF) using an encapsulated cell implant for the treatment of macular telangiectasia type 2.

DESIGN—An open-labeled safety trial conducted in 2 centers enrolling 7 participants with macular telangiectasia type 2.

METHODS—The participant's more severely affected eye (worse baseline visual acuity) received the high dose implant of CNTF. Patients were followed for a period of 36 months. The primary safety outcome was a change in the parameters of the electroretinogram (ERG). Secondary efficacy outcomes were changes in visual acuity, en face measurements of the optical coherence tomography of the disruption in the ellipsoid zone, and microperimetry when compared with baseline.

RESULTS—The ERG findings demonstrated a reduction in the amplitude of the scotopic b-wave in 4 participants 3 months after implantation (month 3). All parameters returned to baseline values by month 12 and remained so at month 36 with no clinical impact on dark adaptation. There was no change in visual acuity compared with baseline. The area of the defect as measured functionally by microperimetry and structurally by the en face OCT imaging of the ellipsoid zone loss appeared unchanged from baseline.

CONCLUSIONS—The intraocular delivery of CNTF in the encapsulated cell implant appeared to be safe and well tolerated in eyes with macular telangiectasia type 2. Further evaluation in a randomized controlled clinical trial is warranted to test for efficacy.

INTRODUCTION

Idiopathic macular telangiectasia type 2 (MacTel) is a bilateral degenerative condition of unknown etiology with characteristic neurosensory atrophy and perifoveal telangiectatic vessels which leak on fluorescein angiography.¹ Other characteristic lesions include loss of retinal transparency, crystalline deposits, a decrease or absence of macular pigment and hyperplasia of the retinal pigment epithelium (RPE) in the macular area. The spectral-domain optical coherence tomography (OCT) assessments show disruption of the photoreceptor inner segment–outer segment junction line (IS/OS line) or ellipsoid zone (EZ), and hyporeflective cavities in both the inner and outer retina. The natural course is a gradual progressive bilateral loss of vision, occasionally accompanied by subretinal neovascularization, leading to severe vision loss.¹ Genetic studies have suggested a MacTel gene locus on chromosome 1.²

The natural course of gradual visual acuity loss in MacTel patients is approximately 1 letter per year (Clemons TE et al. IOVS, 2012;53:ARVO e-abstract 982); however, affected individuals have profoundly reduced visual function compared to a normal age-matched reference group.^{3,4} This may be due to the presence of bilateral lesions of photoreceptor disruption that begin temporal to the fovea, resulting in bilateral nasal scotomas and consequent pre-fixational blindness. A study correlating these visual field defects detected by microperimetry with OCT shows that the defects are closely associated with cavitation of the outer retina, indicating that loss of vision in MacTel is associated with structural changes at the level of photoreceptors.^{5,6} Current evidence suggests that photoreceptor cell loss is

intrinsic to the disorder rather than being consequent to the vascular changes.⁷ Photoreceptor abnormality occurs early in the disorder and progression of photoreceptor cell loss may be detected on OCT with the loss of the IS/OS layer (ellipsoid zone). Measurement of the missing ellipsoid zone, captured as “en face” images, has been proposed as a potential outcome measurement for treatment studies.⁸ These OCT abnormalities have been associated with functional changes found on microperimetry, providing a structure-function index of severity in this disorder.⁹

To date, there is no effective treatment for MacTel although a variety of therapies including steroids, photodynamic therapy and laser photocoagulation have been evaluated.^{10–14} Modulation of the leakage from the telangiectatic vessels with the use of anti-vascular endothelial growth factor (anti-VEGF) agents including bevacizumab and ranibizumab also been shown to be ineffective in halting visual loss.^{15–17}

The class of molecules called “neurotrophic factors” has been demonstrated to slow the loss of photoreceptor cells during retinal degeneration. One of these factors, ciliary neurotrophic factor (CNTF), was found to be effective in slowing vision loss from photoreceptor cell death in animal models of outer retinal degeneration.^{18–20} Similarly, delivery of a neurotrophic factor to the outer retina in a mouse model that shares many phenotypic MacTel characteristics showed profound functional and anatomic photoreceptor cell rescue with no effect on the associated vascular abnormalities.²¹ In addition, there is evidence that CNTF can cause regeneration of cone outer segments in rats expressing a mutant rhodopsin transgene.²² The delivery of CNTF to the retina is challenging as the blood-retinal barrier prevents penetration of a variety of agents from the plasma. To surmount such a barrier, intraocular implant (NT-501), using encapsulated cell technology, was loaded with human RPE cells that were transfected with the *CNTF* gene. The CNTF was targeted for secretion by fusing the genomic murine Ig signal peptide in frame to the 5' end of the hCNTF gene to produce CNTF. The NT-501 implant (Neurotech USA, Cumberland, Rhode Island, USA) was developed specifically using encapsulated cell technology with a semipermeable membrane, which allows CNTF to diffuse into the vitreous and nutrients to diffuse into the implant but prevents the host immune system from attacking the cells within the implant, allowing a supply of CNTF over an extended period of time.²³ The technology also limits extraocular exposure of CNTF. The implant is surgically anchored into the eye and may be explanted if necessary. Encapsulated cell delivery of CNTF has been tested in three human Phase 2 studies of treatment for retinal dystrophies^{24–25} and geographic atrophy associated with age-related macular disease.²⁶ The use of this device appear to be safe while there was some limited suggestion of potential benefit in these studies.^{24–27} Since data from the mouse model with some MacTel phenotypes and data from various animal models of retinal degeneration suggested beneficial effect of CNTF in anatomic rescue of the photoreceptor cell,^{18, 20–22} the use of neurotrophic molecules may provide a therapeutic benefit for patients with MacTel, which has no proven therapy. We now report the results from a phase 1 trial that evaluated the safety and tolerability of CNTF delivered over 36-month period by encapsulated cell devices (NT-501) for the treatment of eyes with MacTel.

MATERIALS AND METHODS

Study Design

This non-randomized, uncontrolled phase 1 clinical trial, registered with ClinicalTrials.gov (NCT01327911), was conducted according to the guidelines of the Declaration of Helsinki. The protocol was approved by the Institutional Review Boards (IRBs) of the two participating sites, the Western IRB and the University of California Los Angeles (UCLA) IRB. Each participant provided signed informed consent. A Data and Safety Monitoring Committee (DSMC) was established to monitor participant safety. This was an open label, nonrandomized Phase I study conducted at two retinal centers: the Retina Associates of Cleveland, Inc. and the Jules Stein Eye Institute, University of California Los Angeles. The EMMES Corporation (Rockville, MD) served as the coordinating center for the study.

Primary Safety Outcomes—The primary outcome was ocular safety after implantation of the CNTF capsule. Safety was measured by evaluating electroretinogram (ERG) responses and visual acuity assessments. Given the typical variability in ERG measurements, a persistent reduction of 30% in any of the ERG parameters was considered a potential safety concern. Additional safety factors were the presence of inflammation in anterior segment or posterior segment (vitreous and retina) on clinical examination at the slit-lamp or on dilated ophthalmoscopy. Along with the persistent 30% reduction of ERG measurements, the following adverse outcomes were specifically designated in the study protocol for the implanted eye: visual acuity decrease of 15 or more Early Treatment Diabetic Retinopathy Study (ETDRS) chart letters compared with baseline, development of subretinal neovascularization, or peri-implant fibrosis which either blocks the visual axis of the implanted eye or affects the lens or retina. Other safety measures include the rejection or extrusion of the NT-501 device, the detection of serum CNTF levels, or the presence of circulating antibodies to CNTF and/or to NTC-201 cells. All adverse events were collected regardless of severity or potential relationship to the implant, CNTF, or surgical procedure.

Secondary Efficacy Outcomes—Secondary outcomes were best-corrected visual acuity (BCVA) and retinal sensitivity as measured by microperimetry. A secondary structural outcome of efficacy was the assessment of the photoreceptor IS/OS layer (or ellipsoid zone) loss as measured by topographical analysis of spectral-domain OCT volume scans and OCT thickness measurements. Two of the participants also had cone photoreceptor imaging using adaptive optics scanning laser ophthalmoscopy obtained at baseline and at the months 12, 24 and 36 follow-up visits.

Participants

Participants were eligible if they had bilateral MacTel, were 21 years or older, and likely to be followed up for the duration of the study. The participants must not have had a history of prior intraocular surgery. The ocular inclusion criteria included BCVA of 20/50 or better and the presence of a disruption in the photoreceptor IS/OS layer (or ellipsoid zone) on OCT. The eye with worse BCVA was designated as the study eye. If both eyes had the same BCVA, then the eye with the less overall favorable clinical characteristics (as determined by

the Principal Investigator) was designated as the study eye. If there was no difference between eyes, the right eye was designated as the study eye.

Encapsulated Cell Technology

The CNTF encapsulated cell implants (NT-501) were manufactured by Neurotech USA. The implant was inserted through a 2.0 mm sclerotomy made 3.75 mm posterior to the limbus in the inferotemporal quadrant. At the end of surgery, subconjunctival dexamethasone and antibiotics were administered and the eye was examined with an indirect ophthalmoscope to confirm the placement of the device into the vitreous.

Clinical follow-up

A comprehensive eye examination was performed at baseline, including BCVA testing, dilated funduscopy, intraocular pressure (IOP), ocular imaging with stereoscopic color fundus (CF) photographs, fundus autofluorescence (FAF), fluorescein angiography (FA), spectral domain OCT images, microperimetry and ERG testing. Following implant surgery, participants were evaluated at week 1 and months 1, 3, 6, 12, 18, 24, 30 and 36.

Imaging—CF and FA images were recorded digitally using fundus cameras. FAF imaging was performed using Heidelberg HRA2 or Spectralis scanning laser ophthalmoscopes (Heidelberg Engineering GmbH, Heidelberg, Germany). OCT scans were acquired at UCLA using Heidelberg Spectralis OCT (Heidelberg Engineering GmbH, Heidelberg, Germany) and in Cleveland using Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA) devices. On the Spectralis, volume scans $15^{\circ} \times 10^{\circ}$ in area with $30\mu\text{m}$ B-scan intervals were recorded. On the Zeiss Cirrus, a standard 512×128 cube scan covering a retinal area $20^{\circ} \times 20^{\circ}$ in size was acquired. Orthogonal topographic maps (“en face” images) of the inner segment/outer segment (IS/OS) layer (or ellipsoid zone) were generated as described earlier.^{8–9} In two participants, adaptive optics scanning laser ophthalmoscopy (AOSLO) testing was conducted at the U. of Rochester and UC Berkley at baseline, visits months 12, 24 and 36. These results will be presented in another report.

Functional testing—Monocular BCVAs were determined according to a standardized protocol, using ETDRS visual acuity charts starting at a distance of 4 meters. Scoring of the test was based on the number of letters read correctly. Possible scores ranged from 0 (Snellen equivalent $<20/800$) to 100 (Snellen equivalent $20/12$).^{28–29}

Fundus-correlated automated mesopic microperimetry was performed following pupil dilatation with 1.0% tropicamide and 2.5% phenylephrine hydrochloride and 5 minutes of visual dark adaptation, using Nidek MP1 microperimeters (Nidek Technologies, Albignasego, Italy). The technique has been described previously.^{30–32} Microperimetry was also performed at each visit on MAIA perimeters (CenterVue S.p.A., Padova, Italy), using a test grid and stimulus size identical to that used on the MP1. Results were reported in decibels (dB).

ERG testing was performed according to a standard protocol developed by the International Society for Clinical Electrophysiology of Vision (ISCEV).³³ A full-field ERG test was

performed at baseline and at months 3, 6, 9, 12, 18, 24, 30 and 36 including a low luminance white flash in a dark-adapted eye (DA 0.01), and the response to a “standard flash” (DA 3.0). An additional high luminance flash (DA 10.0) was used in one clinic. The standard photopic single flash (LA 3.0) and flicker ERG (LA 30 Hz) recordings were obtained in all patients at both institutions.

Measure of serum CNTF, CNTF specific antibodies and antibodies to NTC-201 cells—Blood was drawn at baseline, months 12, 24 and 36 for measurements of serum CNTF, and antibodies to CNTF or NTC-201 cells. Serum CNTF was measured using a capture ELISA (R & D Systems). By incubating the participant’s serum on a plate coated with hCNTF (R & D Systems), the CNTF specific antibody signal was detected by a secondary antibody of horseradish peroxidase-conjugated donkey anti-human IgG (Jackson ImmunoResearch Laboratories, Inc., West Grove, PA, USA). Titers for serum antibodies against the NTC-201 cells were determined by ELISA by incubating participant serum on a plate coated with NTC-201 cells for 16 hours and then probing with horseradish peroxidase-conjugated donkey anti-human IgG (Jackson ImmunoResearch Laboratories, Inc., West Grove, PA, USA).

Image and Data analysis

Study images were assessed and graded by a central reading center (The NIHR Biomedical Research Centre for Ophthalmology, at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology). ERG data were evaluated by Drs. GH and NP.

Statistical analyses

The analyses were performed using all available data. For changes in BCVA and the ellipsoid zone as measured by OCT, within-participant and between study/fellow eye comparisons were based on paired Student’s t-tests. McNemar’s χ^2 tests were used to examine the difference in the proportion of the increase or decrease in dB as measured by microperimetry between study and fellow eyes. All analyses were carried out using commercially available statistical software (SAS version 9.2; SAS Institute, Cary, NC). This safety study was not powered to evaluate efficacy.

RESULTS

A total of seven participants were enrolled and surgery was performed between August 26, 2011, and September 16, 2011. Two participants were male and five female, ages ranging from 48 to 67 years. Five were Caucasian, one was Asian and one identified as other race. All participants completed the 36 month follow-up.

Primary Safety Outcomes

No implant was rejected or extruded, and no severe ocular inflammation occurred. One participant had a BCVA decrease of 15 or more letters immediately after surgery and returned to pre-implant level at month 3. Surgical complications included one participant who had decreased IOP following a wound leak, while another had an elevation of IOP to 36 mmHg post-operatively. In both cases, IOP returned to the normal range by the 1 week visit

and remained normal throughout the study. There were no protocol-defined adverse outcomes. However, 5 of the 7 participants developed miosis in the implanted eye and this persisted throughout the study. One of these 5 participants with miosis experienced difficulties with dark adaptation despite ERG findings that were not changed from baseline.

Measurement of serum CNTF, CNTF specific antibodies and antibodies to NTC-201 cells—No CNTF or antibodies to CNTF or NTC-201 cells were detected in the serum of participants at any time point (baseline, months 12, 24 and 36).

Electroretinogram—At months 3 and 6, a total of 4 participants demonstrated reduced amplitude in the ERG b-wave obtained from study eyes to a dark-adapted dim flash (DA 0.01) (Figure 1). The responses of these study eyes to high luminance flashes were preserved, as were photopic single flash and 30 Hz flicker ERGs. Fellow eyes showed no change in ERG amplitude from baseline. At month 9, 1 of the 4 affected study eyes had returned to the normal range, and in 2 of the 4 eyes, the asymmetry between the study and fellow eyes had decreased. By month 12, none of the 4 treated eyes demonstrated a reduction in amplitude of the ERG-b wave to the dark-adapted dim flash stimulus condition. During the period of the reduction in the amplitude of the dark-adapted dim flash response, none of the 4 participants were symptomatic. However, another participant with no evidence of ERG changes complained of abnormal dark adaptation. As noted earlier, this patient had miosis.

Secondary Efficacy Outcomes

Best Corrected Visual Acuity (BCVA)—The mean $\pm$ standard deviation (SD) BCVA was 73.7 ± 8.0 letters for study eyes and 78.6 ± 8.4 letters for fellow eyes. The mean change $\pm$ standard error (SE) in BCVA from baseline to month 12 was 0.7 ± 1.9 ($p=0.73$) letters in the study eyes and 1.7 ± 0.8 ($p=0.09$) letters in the fellow eyes. The differences in mean change between study and fellow eyes did not meet statistical significance (mean $\pm$ SE difference = 1.0 ± 2.1 ; 95% CI: $-4.2 - 6.2$; $p=0.66$). The mean $\pm$ SE change in BCVA from baseline to month 26 was 1.14 ± 1.45 ($p=0.46$) letters in the study eyes and 3.1 ± 1.2 ($p=0.04$) letters in the fellow eyes. The differences between study and fellow eyes did not meet statistical significance (mean $\pm$ SE difference = 2.0 ± 1.7 ; 95% CI: $-2.1 - 6.1$; $p=0.28$).

Optical Coherence Tomography (OCT)—A secondary efficacy outcome was change in break area measured by OCT topographical maps of the IS/OS layer. The mean $\pm$ SD ellipsoid zone measurement at baseline was 0.90 ± 0.34 mm² in the study eyes and 1.01 ± 0.36 in the fellow eyes. One participant was excluded from the analysis because no definite break in the IS/OS layer was detectable at baseline although a thinning of the ellipsoid band was present, but a break occurred at month 18. The mean $\pm$ SE change in break area at month 12 was 0.06 ± 0.04 mm² ($p=0.15$) in the study eyes and 0.12 ± 0.07 mm² ($p=0.15$) in the fellow eyes. The differences between study and fellow eyes did not meet statistical significance (mean $\pm$ SE difference = -0.06 ± 0.05 ; 95% CI: $-0.19 - 0.07$; $p=0.29$). The mean $\pm$ SE change in break area at month 36 was 0.33 ± 0.15 mm² ($p=0.08$) in the study eyes and 0.37 ± 0.15 mm² ($p=0.05$) in the fellow eyes. Again, this difference did not meet statistical significance (mean difference = -0.04 ± 0.07 ; 95% CI: $-0.22 - 0.16$; $p=0.58$).

Figure 2 provides a graph of the means and standard errors by study and fellow eye at baseline and month 36.

Retinal thickness was also measured in 9 zones according to the ETDRS grid that was placed on the fundus photographs (Figure 3). The mean changes in microns are depicted in Figure 4. The x-axis is divided into 9 zones as shown in Figure 4. The eyes that had the CNTF implant had the greatest increases in zones 6 to 9 (ranging from 20.0 to 23.0 microns) and the lowest increases in the zones 1 to 5 with means ranging from 6.3 microns to 11.1 microns. The fellow eyes had minimal increase while zones 1, 2 and 5 exhibited decrease in retina thickness. There was no marked increase in the retinal thickness in the fellow eyes during the course of the study.

Microperimetry—Change of retinal sensitivity by 10 dB in at least one point either adjacent to a pre-existing scotoma or in a new area within the central 10° at month 12 or month 36 was assessed by microperimetry. At month 12, increased sensitivity by 10 dB was recorded in 3 study eyes (43%) and 4 fellow eyes (57%) ($p=0.32$); decreased sensitivity by 10dB was recorded 3 study eyes (43%) and 3 fellow eyes (43%) ($p = 1.00$). At month 36, increased sensitivity of 10 dB in at least one point was recorded in all study eyes (100%) and 5 fellow eye (71%) ($p=0.16$) while a decrease of 10 dB in at least one point occurred in 3 study eyes (43%) and 3 fellow eyes (43%). The p-value could not be computed for the latter comparison as there was perfect agreement between study and fellow eyes within participants.

The mean $\pm$ SE change in microperimetry sensitivity from baseline to 12 months was 0.9 ± 0.8 ($p=0.31$) dB in the study eyes and 0.4 ± 0.4 ($p=0.37$) dB in the fellow eyes. The difference between study and fellow eyes did not meet statistical significance (mean $\pm$ SE difference = 0.5 ± 0.6 dB; 95% CI: $-1.0 - 2.0$; $p=0.44$). The mean change in sensitivity from baseline to month 36 was 2.1 ± 0.8 ($p=0.05$) dB in the study eyes and 1.2 ± 0.4 ($p=0.02$) dB in the fellow eyes. The difference between study and fellow eyes was not statistically significant (mean $\pm$ SE difference = 0.9 ± 0.5 dB; 95% CI: $-0.3 - 2.2$; $p=0.12$). It is important to note that the microperimetric sensitivity changes observed were ultimately within the expected level of variability (< 5.56 dB) for MP1 microperimetry.³⁴ Similar findings were obtained with the MAIA microperimetry.

DISCUSSION

The NT-501 implant in eyes with Mac Tel type 2 appeared to be well tolerated as no implants required criteria driven explantation. No implants were extruded. Three of the seven eyes studied developed miosis that persisted throughout the observation period. The only outcomes changed in implanted eyes were transiently reduced BCVA in one participant and transient reduced ERG amplitude in four participants. The one occurrence of BCVA reduction resolved within one month. The ERG reductions resolved over a longer time frame. Animal studies have established that CNTF can reduce ERG amplitude without induced cellular degeneration.^{35–37} In animal models, the mechanism is thought to involve a down regulation of phototransduction and to involve both rod and cone photoreceptors. In this study, ERG reductions were only noted for the dark-adapted condition where the

response is dominated by the b-wave, and reductions in the a-wave or cone ERG were not noted. In the absence of non-human primate studies with CNTF, it is not possible to determine if this specificity reflects a species difference or some other factor. In this phase I study, ERG abnormalities were defined to be a reduction of 30% from baseline. This criterion is more restrictive than that applied by the US Food and Drug Administration (FDA) which suggests monitoring for a 50% or greater reduction from baseline (personal communication). The particular ERG protocol used here, which incorporated the ISCEV standard including the response to a low luminance stimulus in the dark-adapted state, was the first to be conducted in evaluations of CNTF therapy. These findings may help with the planning and execution of future studies of CNTF.

No other ocular safety signals were observed. Secondary measures of the structural and functional correlates with the OCT IS/OS break area findings and the microperimetry results demonstrated no statistically or clinically significant changes. However, the study was not powered to demonstrate clinically and statistically significant differences and the eyes were not randomly assigned, making it difficult to compare. Interestingly, the measures of retinal thickness by OCT showed increases in the treated eye while the untreated fellow eye had decreased retinal thickness. This is similar to studies conducted in rabbits that showed an increase in the outer nuclear layer with the implanted eyes.³⁸ Such findings were also confirmed in human studies of geographic atrophy associated with age-related macular degeneration and retinitis pigmentosa.^{25–26, 39}

MacTel is known to have a slow and gradual rate of progression, based on the natural history data obtained from an observational study conducted in more than 500 participants followed for a median of 4 years (Clemons TE et al. IOVS, 2012;53:ARVO e-abstract 982). While this pilot study was not powered to evaluate treatment efficacy, this Phase 1 safety study indicates that CNTF implants are unlikely to have a major deleterious effect in MacTel eyes. This supports the development of a phase 2 trial designed to answer the question of whether the CNTF NCT-501 implant will slow the disease time course.

The choice of outcome measurement is important for such a phase 2 trial. In view of the slow disease progression, functional changes such as visual acuity changes may not be sensitive outcome measures. Our use of an objective anatomic parameter such as an increase in the area of the break in the IS/OS layer (ellipsoid zone) measured in OCT topographic ('en face') maps of the layer, indicative of photoreceptor disruption, parallels similar studies of geographic atrophy associated with age-related macular degeneration (AMD).⁴⁰ The area of AMD-associated geographic atrophy as measured by fundus autofluorescence has been an accepted primary outcome measure by the FDA for clinical trials (Safety and Efficacy of Brimonidine Intravitreal Implant in Patients with Geographic Atrophy Due to Age-Related Macular Degeneration, NCT00658619, <http://clinicaltrials.gov>). OCT en face measurements may become an acceptable outcome measure for future studies if changes in this measure are shown to be predictive of future visual function. In addition, functional changes captured by microperimetry appear to have reasonably good correlation with the structural changes demonstrated by OCT topographic imaging of the IS/OS.⁸ We hope to confirm these correlations in our current phase 2 study of CNTF therapy for Mac Tel type 2 (NCT01949324) which is actively recruiting participants.

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Financial Disclosures:

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APPENDIX: Participating Centers and Investigators in the MacTel CNTF Safety Study

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Biography

Emily Chew is a medical retinal specialist at the National Eye Institute/National Institutes of Health. Her research interest include includes phase1/2 and phase 3 clinical trials and epidemiologic studies in retinovascular diseases such as age-related macular degeneration, diabetic retinopathy, and others. She worked extensively in large multi-centered trials headed by the staff of NEI/NIH including the Early Treatment Diabetic Retinopathy Study, the Age-Related Eye Disease Study and the Age-Related Eye Disease Study 2.

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Figure 1.

Electroretinogram (ERG) changes in eyes implanted with the ciliary neurotrophic factor (study eyes) and fellow eyes of participants with macular telangiectasia type 2 over the course of the first year of the study.

Legend: The solid circles denote the study eyes while open circles denote the fellow eyes. ERG amplitude is plotted relative to the pre-implantation baseline measure.

Figure 2. Area of the ellipsoid zone (IS/OS) break measured in the eyes treated with ciliary neurotrophic factor (study eye) and the fellow eye of participants with macular telangiectasia type 2. Legend: Data points indicate the means ($\pm$ standard error) at baseline and at 36 months post-implantation.

Figure 3. This ETDRS Grid was used to demarcate the 9 zones of the Optical Coherence Tomography Image in all study and fellow eyes of participants with macular telangiectasia type 2.

Figure 4.

Change in mean retinal thickness (in μm) on each of the 9 zones of the Ocular Coherence Tomography (OCT) at 24 months compared with baseline in study eyes and fellow eyes with macular telangiectasia type 2.

Legend: All zones except for zones 5 and 6 had p values <0.05 for the comparison of change in retinal thickness in the study eyes vs. the thickness in the fellow eyes. Bars indicate 95% confidence intervals.