No effective pharmacologic treatment is currently available for prevention of vision loss associated with geographic atrophy (GA) as a result of dry age-related macular degeneration (AMD). Ciliary neurotrophic factor (CNTF), a protein that in humans is encoded by the CNTF gene, has been investigated for treatment of motor neuron disease. NT-501 (Neurotech, Lincoln, RI) is an intraocular implant containing encapsulated cells genetically modified to secrete CNTF and deliver it to the posterior segment. This device has been shown to be capable of delivering CNTF to the vitreous for at least 1 year and to increase thickness of the retina and to protect photoreceptors in animal models.2

The safety of this extended-release device is being assessed in a phase 2, multicenter, double-masked, randomized controlled dose-ranging clinical trial in patients with GA associated with dry AMD.3 The trial is also seeking to identify efficacy trends and to help identify endpoints for future clinical trials. Interim 18-month results of this study were recently presented,4 and top-line data are summarized here.

CLINICAL TRIAL DESIGN

In the NT-501 clinical trial, 48 enrolled participants were randomized 2:1:1 to receive an intravitreal NT-501 implant with high or low output of CNTF or sham surgery.

NT-501 has been shown to be capable of delivering CNTF to the vitreous for at least 1 year.

The primary endpoint was increase in best corrected visual acuity (BCVA) from baseline to 1 year. Secondary endpoints included the mean, median, and distribution of change in BCVA over the 18-month follow-up period, change in ERG between baseline and months 12 and 18, change in area of geographic atrophy from baseline to months 12 and 18, and change in retinal thickness from baseline to months 12 and 18.

Visual acuity was measured using the Electronic Visual Acuity (EVA) Tester technology with Early Treatment Diabetic Retinopathy Study protocol. Retinal thickness was measured by time-domain optical coherence tomography (OCT), and lesion size was measured by fundus photography. Each was performed at 4, 6, 12, and 18 months after placement of the implant.

The investigator could remove the implant after the 12-month visit with the consent of the patient. CNTF release from explanted implants was measured using ELISA.

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RESULTS

Stability of visual function was defined as less than 15 letters (three lines) of visual acuity loss. Visual function was stabilized in the high-dose treatment group, as compared with the sham and low-dose groups, at 12 and 18 months. In eyes with a baseline BCVA of 20/63 or better, the mean BCVA in the high-dose group was 10.5 and 10.0 letters greater than the low-dose and sham groups at 12 and 18 months, respectively. This difference was statistically significant at 12 months ($P=.03$).

Structural changes accompanied stabilized visual acuity. A dose-dependent increase in retinal thickness was seen as early as 4 months after implantation, and this increase was maintained through the 6-, 12-, and 18-month visits ($P<.001$).

The rate of GA lesion area growth was reduced in the treatment groups at both 12 and 18 months.

Regarding safety, the NT-501 implant and the implantation procedure were both well tolerated. No serious adverse events associated with either the implant or the procedure were reported.

Five patients allowed their devices to be explanted after 1 year. All contained viable CNTF cells and continued to release CNTF for up to 18 months.

CONCLUSIONS

The intraocular delivery of the neurotrophic protein CNTF via encapsulated cell technology with the NT-501 device produced long-term stabilization of visual acuity and increased retinal thickness in eyes with GA associated with dry AMD. The device was well-tolerated with no serious adverse events reported. The results of this phase 2 trial support next-stage clinical study in a larger patient population.

Glenn J. Jaffe, MD, is a Professor of Ophthalmology in the Vitreoretinal Service at Duke University Eye Center, Durham, NC. Dr. Jaffe is a Retina Today Editorial Board member. He reports that he is a consultant to Neurotech. Dr. Jaffe may be reached at jaffe001@mc.duke.edu.