There is currently no effective or approved treatment for vision loss associated with geographic atrophy (GA) in nonexudative age-related macular degeneration (AMD). Ciliary neurotrophic factor (CNTF) is a neurotrophic factor that has been shown to increase thickness of the retina, in particular the outer nuclear layer of photoreceptors, in animal models. NT-501 (Neurotech) is an intraocular implant containing encapsulated cells genetically modified to secrete CNTF and deliver it to the posterior segment.

A phase 2, randomized, double-masked, controlled, multicenter dose-ranging study was performed to assess the safety profile of the NT-501 encapsulated cell technology in subjects with geographic atrophy. A secondary purpose of the study was to identify efficacy trends in terms of structure and function, to help determine primary endpoints for future clinical studies of efficacy.

The study included 51 subjects at eight sites, randomized 2:1:1 to receive a high- or low-dose NT-501 intravitreal implant or sham surgery. After 1-year follow-up, the primary study endpoint, the investigator could remove the device if the patient so desired. Then patients were followed for an additional 6 months. Patients were included if they were 50 years old or more, had best corrected visual acuity (BCVA) of 20/50 to 20/200, and had GA-associated vision loss in the study eye. GA was defined as one or more well-defined circular patches of pigmented retinal pigment epithelium greater than 350 µm in diameter.

Optical coherence tomography (Stratus OCT; Carl Zeiss Meditec, Jena, Germany) scans were analyzed at the Duke Reading Center for quantitative and morphologic changes. Quantitative measures included average thickness at center point, total macular volume, and average thickness in nine subfields. Morphologic factors included intraretinal cysts, subretinal fluid, choroidal neovascularization (CNV), epiretinal membrane (ERM), and vitreomacular traction.

**WELL-TOLERATED**

The NT-501 was well-tolerated. No serious adverse events were attributed to the implant. No endophthalmitis or retinal detachment occurred, and there...
was no increase in intraocular pressure, CNV, or serum antibodies to either the CNTF or the encapsulated cells.

CNTF treatment resulted in dose-dependent changes in retinal thickness as early as 4 months after implantation, with changes maintained through 6 and 12 months. There was a statistically significant increase in total macular volume in the group with high-dose–releasing implants compared with the low-releasing group and the sham surgery group.

The significant increase in retinal thickness persisted when possible mitigating factors were controlled for, including toxic effects related to cysts, ERM, CNV, and vitreomacular traction. These results are consistent with the preclinical studies. The increase could have been due to increases in size of photoreceptor cells or in the number of cells, but with the resolution of the time-domain Stratus OCT it was not possible to determine this.

**STABILIZED BCVA**

The anatomic changes were associated with stabilization of BCVA (less than 15 letters lost) in the high-dose group compared with low-dose and sham groups at 12 months. In post-hoc subgroup analysis, in the eyes that started with better BCVA at baseline (20/63 or better), there was a greater difference between the high-dose group and the other two groups in preservation of visual acuity. None of the eyes in the high-dose group lost 15 letters of BCVA, and the mean BCVA in the high-dose group was 10.5 letters greater than the BCVA in the low-dose and sham groups combined.

Five patients allowed their implants to be explanted after 1 year, and those implants were evaluated. All of them contained viable cells and continued to release CNTF for up to 18 months.

In summary, safe, sustained intraocular delivery of CNTF with encapsulated cell technology was demonstrated in a multicenter clinical trial. A potential for a therapeutic effect in eyes with GA in nonexudative AMD was identified in terms of both retinal thickness change and visual function, especially in eyes with better BCVA at baseline. These data should be helpful in designing subsequent clinical trials in larger patient populations.

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