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### Analyzing Clinical Trial Data: Part 2

#### Dr. Elliott:

This is CME on ReachMD. I'm Dr. Dean Elliott, and here with me today is Dr. Charles Wykoff.

Revakinagene taroretcel is a new cell-based therapy approved for the treatment of idiopathic macular telangiectasia, or Mac-Tel type 2.

Charlie, how safe is it and what do the long-term data show?

#### Dr. Wykoff:

Thanks, Dean. Great to be here with you. So, I'll first start with the long-term durability of reva – revakinagene taroretcel, which has been studied now for over a decade. Data comes from 65 patients with explanted devices, who were enrolled in Phase 1 and Phase 2 trials for treatment of retinitis pigmentosa and atrophic macular degeneration.

Two, really, main points to make. The first is that time to explantation range from 6 months to over 14-and-a-half years. So, we really have really good long-term data with multiple patients past a decade.

And structurally, there was no obvious breakdown of material. There was no visible discoloration. There was no adherent tissue, and integrity of the semipermeable membrane was fully intact. And then, related to this, there was consistent CNTF production. Remember, this treatment modality is made to produce CNTF and the production was consistent with an implant before it was implanted, at about 1.7 plus or minus .7 nanograms per day.

The second major point is that morphologically, the cells inside of these implants, that have been taken out up to, again, 14.6 years after implantation, were indistinguishable from the reference device. That meant, the number of cells, the cell morphology, the viability, were all very consistent with no evidence of ability to distinguish between the reference and the devices that had been explanted later. And critically, no evidence of cell neoplasia.

#### Dr. Elliott:

Thanks, Charlie. We know the engineered RPE cells are healthy and active for over 14 years, based on the explantation data you just mentioned. What about the safety of the implant?

#### Dr. Wykoff:

Yeah, super important. So, first of all, the majority of adverse events in the trial were mild to moderate. You can see that in these graphs, here. And overall, 90% of the surgical group and 78% of the sham group experienced at least one treatment-emergent adverse event. Remember, the sham group in this trial actually underwent sham surgery. They went to the operating room. They received ocular anesthesia, and the sham surgery – all steps of the implant surgery – were followed except for scleral incision and implant placement.

This slide shows the types of ocular treatment-emergent adverse events experienced by 10% or greater of study eyes. And the ones I

want to draw your attention to are on the far right. Delayed dark adaptation and meiosis are known potential adverse events associated with CNTF treatment and they were observed in 19 and 16% of treated patients, respectively, compared to 3 and 0% of the sham-treated patients.

Suture-related complications were also observed in 11% of treated patients, compared to 2% of the sham eyes.

Importantly, there were serious treatment-emergent adverse events. There were 6% in the treated arm. And almost all of these were related to the surgical procedure or suture-related complications. Importantly, 3 of the implants, or 1.4%, were explanted over the course of the trial.

When we look, however, at visual function loss over time, we saw that there were similar rates of 15 or greater letter-loss between the sham arm and the NT-501 arm; 12% in sham and 14% with NT-501. And about half of these patients subsequently experienced improvement in their letter-loss at subsequent visits. Those that did not experience improvement in their visual acuity overtime, in most cases had an explanation. For example, cataract progression or VMT.

**Dr. Elliott:**

Thank you, Charlie. So, the key takeaways; overall, there were minimal serious adverse events, patients can expect some transient adverse events related to the surgical procedure, and there's a potential for an increase in delayed dark adaptation and meiosis due to the CNTF. CNTF production by revakinagene taroetcel is durable for over a decade.

Stay tuned for our next episode where we talk about the practical steps for integrating this into real-world practice. Thank you to our audience, and thank you for being here today, Charlie.