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Topically applied neurotoxin addresses wrinkles without needles

By Jane Schwanke



Dr. Kane

New York — A groundbreaking topically applied neurotoxin now in phase 2 trials would provide a painless, injection-free wrinkle-relaxing alternative if it is eventually approved by regulators, investigators say.

"The product is being developed by Revance and would offer an additional choice for the clinician and the patient," says Michael A.C. Kane, M.D., of Kane Plastic Surgery, New York, and an investigator with the trial. "Many people are needle-phobic and would probably prefer a topical over an injection."

How it works

Neurotoxins are large molecules, and, until now, it's been impossible to get them through the skin without injecting them. The technology of Revance is a transport system that involves a positively charged lysine chain carrier. Since botulinum toxin type A molecules are negatively charged, they attract each other.

On the ends of the lysine chains are protein transduction domains (PTDs). These PTDs attach to the membrane of cells and allow the large complex to slide through, creating an opening in the cell membrane that allows the large payload to come through.

"Once it penetrates the skin and gets down to the nerves and muscle, these neurotoxins are then released and go to work," Dr. Kane says. "Thus, the treatment crosses the skin barrier without needles."

Study results

The phase 2 trial included several dose-ranging studies, followed by a study that broke down the gel and the toxin and the peptide carriers. Several human studies have been conducted on the crow's feet area at multiple centers.

Dr. Kane says all of the studies to date have only looked to ease lateral canthal lines. While the studies have focused only on this area of the face, it's possible that the product will be useful on other facial areas.

The first study enrolled 90 subjects and used a primary composite endpoint that included ratings by both the investigator and the patient on validated wrinkle severity scales. Each of the subjects had to demonstrate a >2-point improvement on both sides of the face.

Principal investigator Fredric Brandt, M.D., reported that a treatment showing such promising results would appeal to a wide variety of new patients, many of whom do not like having a needle so close to their eyes.

Results of the second study, including 180 subjects, suggested that the peptide carrier is necessary for topically applied botulinum toxin to achieve positive results.

In one of the phase 2 studies, the product longevity had a 115-day duration of effect before returning to baseline.

Phase 2 is nearing completion, with phase 3 trials slated to begin soon. So far, data is very good, with a low incidence of adverse effects. When compared to controls, efficacy is statistically significant, Dr. Kane says.

Studies confirmed there was no evidence of spread or diffusion away from the target muscle observed. Adverse events were unrelated to study treatment as rated by the investigators and were generally mild or moderate and transient.

Product delivery

Revance is a gel that becomes more viscous once it touches the body. Body temperature causes the gel to become very thick within a few seconds. The product is delivered to the crow's feet area with a gloved finger and is rubbed in.

Current plans are for Revance to be administered in doctors' offices by medical professionals. The gel is applied, left to sit for 30 minutes and then wiped off.

To date, Revance has completed extensive development work on the gel product for lateral canthal lines and has completed 11 clinical trials, treating more than 550 subjects.

Psychological bonus

For patients who are hesitant to go under the knife or the needle, a topically applied neurotoxin may be incentive for them to seek aesthetic treatments.

"I think that there are lots of barriers to patients being treated in the office," Dr. Kane says, "and one of the reasons that injectables have done so well over the past two decades is that there is a barrier in people's minds when it comes to surgery. The barrier for injectables is much lower. I think that the other barrier is that some people won't do anything if it's invasive.

"I believe that (with the introduction of this product) patients won't have such a high barrier for something that's topically applied to their skin," Dr. Kane says.

Disclosures: Dr. Kane has served as a consultant and currently serves as an investigator for Revance Therapeutics.

Dr. Kane



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