

Botox and Reloxin Are Similar but Different

BY DAMIAN McNAMARA

MIAMI BEACH — Dosing, speed of onset, and extent of spread are among differences to anticipate with a second botulinum toxin expected to reach the U.S. market soon, according to physicians who evaluated its safety and efficacy in preclinical trials.

The Food and Drug Administration is reviewing data for Reloxin (botulinum toxin, Ipsen). “This is really exciting—the first new toxin in the market since Botox,” Dr. Mark Nestor said at the South Beach Symposium. “We are hoping it will be approved in the next few months.”

“The starting out point for us, especially if it comes in a 300-unit vial, is to do the same thing you do now with Botox,” said Dr. Nestor, a dermatologist in private practice in Aventura, Fla., and clinical associate professor of dermatology and cutaneous surgery at the University of Miami. “Start out conservatively, and you will finesse this over time.” Dr. Nestor is a speaker and consultant for and has received research grants from Medicis. He is also an advisory board member and speaker for Allergan.

There are four important studies that demonstrate its safety and efficacy, said Dr. Joel L. Cohen, principal investigator of one and assistant clinical professor of dermatology at the University of Colorado, Denver. Two studies assessed patient response to a single 50-U treatment and two others to repeat injections over time. Dr. Cohen is a consultant for Medicis and Allergan.

Median time to onset of effect was 2 days in a study of 300 patients who received Reloxin or placebo to treat the glabellar area. At 3 days, about half of patients felt an effect, and by 7 days, cumulative response was 90%, according to patient diaries. Investigators reported median response duration of 117 days. Nine patients had eye problems, including ptosis. A total of five patients experienced serious adverse events, but none were considered related to treatment, said Dr. Cohen, who is also in private practice in Englewood, Colo. Incidence of headache and injection site bleeding were similar to placebo.

A 90% response was also reported in another single treatment trial with 158 patients receiving either the toxin or placebo. There were some slight differences in efficacy compared to the other single treatment trial. Patient diaries indicated median time to effect of 3 days. Researchers found an 85-day median duration of effect. Reloxin also was well tolerated in this study, Dr. Cohen said.

Up to five repeat treatment sessions were allowed in an open-label,

multicenter study. Researchers found a greater proportion of responders at each follow-up evaluation. They reported an overall 93% response and 73% of participants had at least a two-grade improvement. Patients older than 65 years were less likely to respond to Reloxin, as were those with severe ratings at baseline. In addition, the toxin appeared to work better in women, compared with men. Repeat injections were well tolerated, Dr. Cohen said.

The majority of treatment-emergent adverse events were mild. Injection site events, ocular events, and headaches were the most common. There were 72 severe adverse events during the study, including 1 death by gunshot, all unrelated to treatment.

Dr. Cohen and his colleagues also conducted a repeat injection study that found no difference between toxin and placebo patients in terms of vital signs or serum assays (no patient developed antibodies). This study included 768 patients allowed up to eight repeat treatments over 2 years. The multiple cycles were well-tolerated and effective, he said. Injection site pain and nasopharyngitis were the most common adverse events. A total of 37 participants had at least one treatment-emergent adverse event, 2% of which were severe.

The injection technique and pattern will be similar because the mechanism of action is the same for Reloxin and Botox (Allergan), Dr. Michael A.C. Kane said. He has served as an adviser and consultant to Medicis and Allergan.

“The dose-response curves are not parallel, so there is no simple conversion between Reloxin and Botox. “It cannot be a simple number multiplier, period,” according to Dr. Kane, attending plastic surgeon at the Manhattan Eye, Ear and Throat Hospital in New York City.

Patients who have had both Botox and Reloxin say Botox is a gradual change over days, Dr. Kane said. “The biggest difference [with Reloxin] patients say it’s almost like a sledgehammer hits them—a much more abrupt feeling—they really feel it kick in.”

“Migration is probably the biggest issue we will hear,” Dr. Kane said. Tissue migration may be related to complex size, and Botox is a larger 900 kd, compared with 500-600 kd for Reloxin. “We know bigger things move more slowly in muscle. But they would have you believe the smaller molecules of Reloxin will spread all over the place.”

To put the differences in perspective, Dr. Kane said, “The hyaluronic acid fillers will vary by a greater degree than the differences between the different toxins.” ■

Silicone or Saline? Expert Takes a Long-Term View

BY BRUCE JANCIN

SCOTTSDALE, ARIZ. — Silicone or saline?

With 550,000 breast augmentations performed each year in the United States, it’s a question physicians and surgeons get asked a lot.

Today, most women choose silicone. Indeed, silicone gel breast implants have dominated the marketplace since November 2006, when the Food and Drug Administration lifted its moratorium on their primary cosmetic use. Silicone gel now accounts for 56% of all breast implants; saline implants, for 44%. But many women who opt for silicone gel implants don’t fully appreciate the higher long-term complication rate, one expert said at the annual meeting of the American Academy of Cosmetic Surgery.

“It’s really important for these young ladies to understand what they’re getting in for 10-20 years from now, because often the complications are not reversible,” explained Dr. Erik J. Nuveen, an Oklahoma City cosmetic surgeon who has performed more than 4,000 breast augmentations.

Dr. Nuveen uses both silicone and saline implants. In presurgical counseling, he has witnessed how the tactile experience of handling the silicone devices in the consultation room can influence the selection. This makes it all the more critical, he stressed, that a woman fully understands the pros and cons of both implant types before making her decision.

“The silicone gel implants are softer, more natural feeling. It’s alluring to place one on the table and then put it in the patient’s hand. You put a saline [implant] in the other hand and, sure enough, 99% of patients say, ‘I’ve got to get that silicone gel,’” he said.

Silicone breast implants’ purported association with connective tissue diseases—the debunked controversy that prompted the former FDA moratorium—has distracted attention from other, very real problems with silicone gel implants, he said.

An estimated 45% of women receiving silicone implants undergo reoperations within 10 years. In practical terms, this means that among women receiving silicone gel breast implants this year, there will be 138,600 reoperations for device rupture, contracture, pain, or loss of shape within the coming decade.

In contrast, the 10-year reoperation rate with saline implants is 20%-26%—roughly half the rate for silicone gel implants.

“These numbers are really important to me. They directly impact how I advise patients in order to minimize complications in their lives at 10 years,” Dr. Nuveen continued.

Extracapsular rupture of a silicone gel

implant with resultant migration of a silicone stream is a major problem. The silicone must be surgically removed before it can reach the lungs or other vital organs—and that involves a lumpectomy or mastectomy.

The extracapsular rupture rate is 1% at the time of implantation, 7% at 5 years, and estimated at 10% at 10 years.

In contrast, rupture of a saline implant is less problematic. Implant deflation is immediately apparent, and the saline is readily absorbed by surrounding tissue. There is no need to remove substantial breast tissue. The rupture rate with saline implants is 3%-10% at 10 years, depending largely on surgeon expertise.

The reoperation rate for capsular contraction is substantially lower with saline implants than silicone gel.

Silicone gel implants require a larger



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placement incision—a minimum of 5 cm—because they go in full. The implants themselves are more expensive than saline ones. Moreover, silicone gel recipients have to bear a continuing lifelong expense for FDA-mandated MRI evaluation in order to detect silent rupture. The initial MRI is required at 3 years, then every 2 years thereafter. It’s not covered by insurance.

MRI has an 89% sensitivity for detection of implant rupture. In contrast, physical examination of the breast has only 10%-30% sensitivity. Mammography is quite poor at detecting silicone implant rupture while it’s still intracapsular and therefore far more easily treated. Moreover, mammography is the No. 1 cause of implant shell failure.

These days the clinical situation in which Dr. Nuveen said he is most comfortable in recommending silicone gel is in the thinnest patients, who are more likely to find saline implants uncomfortable.

Dr. Nuveen said the future of breast augmentation may be a highly cohesive silicone gel known as style 410. It is the most widely used type of implant in Europe but remains investigational in the United States, where large clinical trials are underway. The 3-year U.S. data are encouraging, but longer follow-up is required.

Dr. Nuveen reported having no conflicts of interest. ■