

MERZ PHARMACEUTICALS ANNOUNCES RESULTS OF THREE CLINICAL TRIALS WITH NT-201 (BOTULINUM NEUROTOXIN TYPE A FREE FROM COMPLEXING PROTEINS) IN MOVEMENT DISORDER PATIENTS

April 28, 2009, Seattle – Results from two prospective, double-blind placebo controlled multi-center studies in patients with cervical dystonia and blepharospasm, and pooled European efficacy and safety data in patients with focal dystonia and upper limb spasticity will be presented at the American Academy of Neurology's (AAN) 61st annual meeting in Seattle. The studies were sponsored by Merz Pharmaceuticals, which plans to file a Biologic License Application (BLA) for NT-201 in the USA in the near future.

“The data to be presented at AAN compliment the European data. We now have robust U.S. data for Xeomin (the brand name for NT-201 in Europe) for the symptomatic management of movement disorders.” said Eric Pappert, MD, Vice President of Medical Affairs, Merz Pharmaceuticals, USA.

NT-201 is a botulinum neurotoxin type A free from complexing proteins approved for marketing in Europe since 2007 to treat various movement disorders, and recently approved in Canada for the indications of symptomatic management of blepharospasm, cervical dystonia and post-stroke spasticity of the upper limb. Through advanced manufacturing processes, NT-201 combines high biologic activity with low bacterial protein load, making it a neurotoxin therapy free from complexing proteins. In pre-clinical work, the exposure to complexing proteins has been found to heighten the immune system response to botulinum toxin.

“Xeomin – the proposed brand name for NT-201 - potentially offers a new option to treat movement disorders. Because Xeomin combines high biologic activity with low protein load, it is a neurotoxin that is free from complexing proteins,” said David M. Simpson, M.D., Professor of Neurology and Neuromuscular Diseases at Mount Sinai Medical Center in New York and a leading botulinum neurotoxin researcher.

The NT-201 data will be presented at the AAN's annual meeting. The data include poster p07.088, *Efficacy and safety of NT 201 (Botulinum neurotoxin free from complexing proteins) in cervical dystonia*, poster p07.081, *Clinical efficacy in focal dystonia and overall tolerability of NT 201 (botulinum neurotoxin free from complexing proteins)* and poster p07.091, *Efficacy and safety of NT-201 (Botulinum neurotoxin free from complexing proteins) in Blepharospasm*.

Joseph Jankovic, M.D. Professor of Neurology, Distinguished Chair in Movement Disorders, and Director of the Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine in Houston and a lead investigator of the blepharospasm study noted that “these promising data indicate that following approval, Xeomin will become an important treatment option for movement disorders.”

About the Studies

Efficacy and safety of NT-201 (Botulinum neurotoxin free from complexing proteins) in cervical dystonia. Presented by Cynthia Comella of Rush University in Chicago.

Method

This prospective, double-blind, placebo-controlled, multi-center study evaluated the safety and efficacy of NT-201 [Botulinum neurotoxin A (BoNT A) free from complexing proteins], compared to placebo in subjects with cervical dystonia (CD). There were 233 CD patients (66% women, age 52.8 years, CD duration 51.9 months), 39% not previously treated with BoNT. Patients were randomized to placebo (N= 74), 120 U NT 201 (N= 78), and 240U NT 201 (N= 81). Following injection, patients were evaluated at 4 weeks using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS); adverse events (AEs) were also collected. The primary outcome was the change from Baseline to week 4 for the TWSTRS-Total score analyzed using an ANCOVA model.

Results

The change in total TWSTRS from baseline to week 4 was -2.2 ± 7.3 points (placebo group); -9.9 ± 10.4 points (120 U group) and -10.9 ± 11.7 points (240 U group) ($p < 0.001$). AEs occurred in 41.9% of the placebo group, 56.4% of the 120 U group and 55.6% of the 240 U group. AEs reported most frequently for each group respectively were dysphagia (2.7% vs 12.8% vs 18.5%), neck pain (4.1% vs 6.4%, vs 14.8%), and muscular weakness (1.4% vs 6.4% vs 11.1%).

Efficacy and safety of NT 201 (Botulinum neurotoxin free from complexing proteins) in Blepharospasm. Presented by Joseph Jankovic of Baylor College of Medicine in Houston, TX.

Method

This prospective, double-blind, placebo-controlled, randomized, multi-center study investigated the efficacy and safety of NT-201 [Botulinum neurotoxin A (BoNT A) free from complexing proteins], compared to placebo in pre-treated subjects with blepharospasm (BEB). The study investigated individual dose of NT-201 up to 50 units per eye compared to placebo; of the 109 randomized BEB patients 65.1% were female, mean age 61.9 years and a median BEB duration of 84 months. The mean dose was 64.8 U in the NT-201 group. Pre-treated subjects were randomized in a 2:1 ratio to NT-201 or placebo. Subjects were followed-up for up to 20 weeks. The Jankovic Rating Scale (JRS) severity subscore six weeks after injection was the primary

outcome assessed by a blinded independent investigator. Confirmatory analysis was based on the intent-to-treat (ITT) population using an ANCOVA model. AEs were collected via direct questioning.

Results

The treatment difference in the JRS severity subscore was statistically significant in favor of NT-201 ($p < 0.001$). These results were confirmed in all secondary endpoints.

AEs were reported in 70.3% subjects in the NT-201 group and 61.8% subjects in the placebo group. The most commonly reported AEs were eyelid ptosis (18.9 vs. 8.8%), dry eye (16.2 vs. 11.8%), and dry mouth (16.2 vs. 2.9%).

Clinical efficacy in focal dystonia and overall tolerability of NT-201 (botulinum neurotoxin free from complexing proteins) Presented by Susanne Grafe of Merz Pharmaceuticals GmbH, Frankfurt, Germany.

Methods

This study assessed the overall clinical efficacy and tolerability of NT-201 (botulinum neurotoxin free from complexing proteins). Efficacy analyses in focal dystonia were performed on pooled data from 2 pivotal clinical trials in blepharospasm and cervical dystonia (343 NT-201 patients; 340 BoNT patients). For the safety analyses, 6 clinical trials (blepharospasm, cervical dystonia and upper limb spasticity) were included ($n=539$ NT-201, $n=442$ BoNT and $n=75$ placebo subjects, respectively). Spontaneously reported adverse events were analyzed.

Results

In the randomized, active-controlled, double-blind studies in focal dystonia NT-201 and one other Botulinum toxin (BoNT) have been used with a dose ratio of 1:1. The results demonstrate equivalent efficacy between the two products. Onset, waning, and duration of effect were comparable. These findings have been confirmed by the Global Impression of Physician: 70.6% of BoNT patients and in 71.8% of the NT-201 patients were rated as “good” or “very good”. A total of 26.7% of patients in the NT-201 group, 26.0% in the BoNT group and 22.7% in the placebo group reported an adverse event. There were no clinically relevant differences between the two treatment groups. All adverse reactions were either already known and/or were considered unlikely to be related to NT-201 by the physician. The analysis of the 67,000 patients treated post-launch demonstrates that no new safety concerns have been identified. These analyses demonstrate that NT-201 and BoNT are comparable regarding efficacy and safety.

About Merz Pharmaceuticals, LLC

Merz is a specialty pharmaceutical company dedicated to addressing unmet medical needs with innovative healthcare solutions.

Merz USA was established in 1995 and is responsible for the North American introduction of products developed within the global Merz organization.

Merz is known worldwide for its development of original compounds and formulations for medical professionals and consumers in 90 countries.

At Merz, research is concentrated in fields that have a strong need for therapeutic innovation such as Alzheimer's disease, Parkinson's disease, tinnitus, chronic pain conditions, addictions, and neuromuscular disturbances.

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