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ONABOTULINUMTOXINA SIGNIFICANTLY DECREASES URINARY INCONTINENCE AND PROVIDES TREATMENT BENEFIT IN PATIENTS WITH IDIOPATHIC OVERACTIVE BLADDER: A POOLED ANALYSIS OF TWO PHASE III, PLACEBO-CONTROLLED PIVOTAL TRIALS

Hypothesis / aims of study

Efficacy and safety of onabotulinumtoxinA for the treatment of patients with overactive bladder (OAB) with urinary incontinence (UI) who have been inadequately managed with anticholinergic therapies were assessed in a pooled analysis of two large, randomized, placebo-controlled, phase 3 studies (NCT00910845 and NCT00910520), which were identical in design.

Study design, materials and methods

Patients (N=1105) with idiopathic OAB with ≥3 urgency UI episodes over a 3-day period and ≥8 micturitions/day were randomized 1:1 to receive 20 cystoscopic intradetrusor injections (0.5 mL/injection) of onabotulinumtoxinA 100U (n=557) or placebo (n=548), sparing the trigone. Patients were inadequately managed with anticholinergic therapy (insufficient efficacy or intolerable side effects); those with a predominance of stress UI were excluded. Patients participated in the study for 24 weeks unless retreatment occurred. From 12 weeks onward, patients could request retreatment with onabotulinumtoxinA 100U if they had at least 2 urgency UI episodes over 3 days. The co-primary endpoints were change from baseline at week 12 (primary timepoint) in UI episodes/day and proportion of patients reporting a positive response (i.e. rating their condition as 'greatly improved' or 'improved') on the Treatment Benefit Scale (TBS). Other OAB symptoms (including episodes of micturition, urgency and nocturia) and volume voided per micturition were also assessed. Safety assessments included adverse events (AEs), post-void residual (PVR) urine volume, and initiation of clean intermittent catheterization (CIC). Each of the phase 3 studies individually provided 82% power to detect a between-group difference in change from baseline in the primary study endpoint (2.3 UI episodes/day; standard deviation of 8.5), assuming an alpha of 0.05.

Results

There were no significant differences between the treatment groups in baseline demographic or clinical characteristics. Mean daily UI episodes at baseline in onabotulinumtoxinA and placebo groups were 5.5 and 5.4, respectively. At week 12, significant reductions from baseline in daily UI episodes were observed with onabotulinumtoxinA 100U, compared with placebo (–2.80 vs. –0.95 episodes/day; p<0.001). These results were reflected in the patient perception of treatment benefit as the corresponding proportion of patients reporting a positive TBS response was significantly higher in the onabotulinumtoxinA 100U group (61.8%), than the placebo group (28.0%; p<0.001). All other OAB symptoms were significantly improved following treatment with onabotulinumtoxinA 100U compared with placebo; significant reductions from baseline were noted with onabotulinumtoxinA versus placebo, in daily episodes of micturition (–2.35 vs. –0.87), urgency (–3.3 vs. –1.2) and nocturia (–0.49 vs. –0.24) (p<0.001 vs. placebo at week 12 for all parameters). Volume voided/micturition was significantly increased with onabotulinumtoxinA compared with placebo (42.1 ml vs. 11.2 ml; p<0.001). The median time for qualification for retreatment was 24 and 21 weeks in the two phase 3 studies, respectively. AEs were primarily localized to the bladder. In the pooled safety population (all patients who received treatment analyzed by actual treatment received; N=1094), the most common AE was urinary tract infection (UTI) (25.5% with onabotulinumtoxinA vs. 9.6%). All but one case of UTI were uncomplicated with no upper urinary tract involvement. Other AEs of note that were higher in the onabotulinumtoxinA group than placebo were dysuria (10.9% vs. 7.0%), bacteriuria (8.0% vs. 3.5%), and urinary retention (5.8% vs. 0.4%). The majority of AEs were reported in the first 12 weeks following treatment. The mean increase from baseline in PVR was 29.3 mL in the onabotulinumtoxinA 100U group compared with 4.2 mL in the placebo group (p<0.001). The proportion of patients who initiated CIC was low: 6.5% (36/552) in the onabotulinumtoxinA 100U group compared with 0.4% (2/542) in the placebo group.

Interpretation of results

In OAB patients with UI who were inadequately managed with anticholinergic therapy, treatment with onabotulinumtoxinA 100U resulted in significant improvements in all evaluated symptoms of OAB. These improvements were reflected in patients' perception of treatment benefit with 62% of patients reporting their condition as improved or greatly improved following treatment with onabotulinumtoxinA. The majority of AEs were localized to the bladder and the proportion of patients with urinary retention and a PVR elevation requiring catheterization was low.

Concluding message

OnabotulinumtoxinA 100U is an important new treatment option for OAB patients with UI who are inadequately managed by anticholinergic therapy.

Disclosures

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