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ONABOTULINUMTOXINA SIGNIFICANTLY DECREASES URINARY INCONTINENCE AND PROVIDES TREATMENT BENEFIT IN PATIENTS WITH IDIOPATHIC OVERACTIVE BLADDER

Hypothesis / aims of study
To evaluate the efficacy and safety of onabotulinumtoxinA 100U compared with placebo for the treatment of overactive bladder (OAB) patients with urinary incontinence (UI) who have had an inadequate response to or experienced intolerable side effects with anticholinergic therapy.

Study design, materials and methods
In this pivotal, multicenter, double-blind, randomized, placebo-controlled, phase 3 study (ClinicalTrials.gov identifier NCT00910520), eligible patients had idiopathic OAB and experienced ≥3 urgency UI episodes over 3-day period and an average of 8 micturitions per day. All patients were not adequately managed by prior anticholinergic therapy. Patients were randomized 1:1 to onabotulinumtoxinA 100U (n=277) or placebo (n=271), which was administered via cystoscopy as 20 intradetrusor injections (0.5 mL per injection site), avoiding the trigone. Patients were followed for at least 24 weeks post-treatment and could receive an additional treatment of onabotulinumtoxinA 100U. Co-primary efficacy variables were the change from baseline in the daily average frequency of UI episodes and the proportion of patients with a positive treatment response on the Treatment Benefit Scale (TBS). All other OAB symptoms 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). The primary timepoint was Week 12. The study provided 82% power to detect a between group difference in change from baseline of 2.3 UI episodes/day (sd 8.5), assuming an alpha of 0.05.

Results
A total of 548 patients were randomized into the study (277 to onabotulinumtoxinA 100U and 271 to placebo). There were no significant differences between groups in baseline demographic or clinical characteristics. Intradetrusor injection of onabotulinumtoxinA100U significantly reduced the daily frequency of urinary incontinence episodes compared with placebo. Reductions from baseline at week 12 were -2.95 and -1.03 episodes/day in the onabotulinumtoxinA 100 U and placebo groups, respectively ($p<0.001$). The proportion of patients with a positive response on the TBS (ie. rated their condition as 'greatly improved' or 'improved') was significantly higher in the onabotulinumtoxinA 100U group (62.8%) than placebo (26.8%; $p<0.001$).

All other studied OAB symptoms were also significantly improved following treatment with onabotulinumtoxinA 100U compared to placebo, including reductions in the daily frequency of micturition, urinary urgency and nocturia episodes and increases in the volume voided per micturition ($p<0.001$ at week 12 for all parameters).

The most frequently reported adverse events were urologic, which were higher in the onabotulinumtoxinA 100U group: UTI (24.1 vs. 9.6%), bacteriuria (6.2 vs. 3.3%), dysuria (5.8 vs. 4.1%), and urinary retention (5.8 vs. 0.4%). The majority were reported in the first 12 weeks. The mean increase from baseline in PVR was 25.9 mL in the onabotulinumtoxinA 100U group compared to 5.8 mL in the placebo group ($p<0.001$). Correspondingly, the proportion of patients who initiated CIC was also low; 6.9% in the onabotulinumtoxinA 100U group compared to 0.7% in the placebo group.

Interpretation of results
This study met its objectives, demonstrating the superior and clinically relevant efficacy of onabotulinumtoxinA 100U over placebo in all OAB symptoms. This was also reflected in the patient's perception of an improvement in their condition. The majority of adverse events were localized urological events and the proportion of patients with a PVR increase requiring catheterization was low.

Concluding message
OnabotulinumtoxinA 100U provides a new treatment option for patients with OAB and urinary incontinence who are not adequately managed by anticholinergic therapy.

Disclosures
Funding: Allergan **Clinical Trial:** Yes **Public Registry:** Yes **Registration Number:** www.clinicaltrials.gov NCT00910520 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** institutional review boards and/or ethics committees at each study center approved the study **Helsinki:** Yes **Informed Consent:** Yes