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ONABOTULINUMTOXINA REDUCES NOCTURNAL VOIDS AND IMPROVES QUALITY OF LIFE IN OVERACTIVE BLADDER PATIENTS WITH NOCTURIA

Hypothesis / aims of study

Nocturia is a bothersome urinary symptom in patients with overactive bladder (OAB). This is particularly true among those who experience two or more nocturia episodes/night [1] resulting in substantial impairment in their quality of life (QOL), poorer sleep quality and increased tiredness. Two phase 3 trials demonstrated that onabotulinumtoxinA significantly reduces the symptoms of OAB and improves QOL outcomes in OAB patients [2,3]. The results from these trials ultimately resulted in the approval of 100U of onabotulinumtoxinA for the treatment of patients with OAB who were inadequately managed by ≥ 1 anticholinergic. We performed a post hoc analysis of these trials to evaluate the effect of onabotulinumtoxinA on nocturia and patient-reported outcomes in OAB patients with ≥ 2 nocturia episodes/night at baseline.

Study design, materials and methods

Two phase 3 trials of onabotulinumtoxinA (NCT0091845 and NCT00910520) enrolled OAB patients (N=1105) who had experienced ≥ 3 urgency urinary incontinence episodes over a 3-day period and ≥ 8 micturitions per day. All patients were inadequately managed by ≥ 1 anticholinergic. Patients with a predominance of stress urinary incontinence were excluded. Patients were randomized 1:1 to receive onabotulinumtoxinA 100U (n=557) or placebo (n=548), via cystoscopic intradetrusor injections (20 injections at 0.5 mL/injection), sparing the trigone. Data from the two phase 3 trials, which were identical in design, were pooled for analysis. Efficacy and safety assessments were evaluated in a subpopulation of intent-to-treat (ITT) patients who reported an average of ≥ 2 nocturia episodes/night at baseline, with no more than 1 nocturia-free night, in the 3-day bladder diary (n=580). Efficacy assessments at Week 12, following a single onabotulinumtoxinA treatment, included change from baseline in nocturia episodes/night, and proportion of patients who achieved $\geq 33\%$, $\geq 50\%$, and ≥ 1 episode reduction in nocturia episodes/night. Patient-reported outcomes relevant to nocturia were assessed, including the mean change from baseline in the sleep/energy domain scores on the King's Health Questionnaire (KHQ), which was measured by patient responses to two specific questions: "Does your bladder problem affect your sleep?" and "Do you feel worn out or tired?" The clinically relevant change from baseline in KHQ, or minimally important difference (MID), was based on published literature and determined *a priori* to be a -5 point decrease. The proportion of patients reporting a positive response—improvement or great improvement in their urinary condition—on the Treatment Benefit Scale (TBS) was evaluated. Adverse events (AEs) were also assessed.

Results

Patients in the onabotulinumtoxinA and placebo groups reported an average of 3.2 and 3.0 nocturia episodes/night at baseline, and an average of 74.6 and 74.7 KHQ sleep/energy domain scores, respectively. Baseline characteristics were well matched between the treatment groups. OnabotulinumtoxinA resulted in significantly greater reductions in nocturia episodes/night, compared with placebo (-0.88 vs -0.52; $P < 0.001$). A significantly greater proportion of patients treated with onabotulinumtoxinA achieved a reduction of ≥ 1 nocturia episode(s)/night relative to placebo (51.1% vs 36.4%; $P < 0.001$). Furthermore, significantly higher proportions of onabotulinumtoxinA- versus placebo-treated patients reported $\geq 33\%$ reduction (46.5% vs 31.8%; $P < 0.001$) and $\geq 50\%$ reduction (32.4% vs 21.1%; $P = 0.003$) in nocturia episodes/night. Improvements in KHQ sleep/energy domain scores with onabotulinumtoxinA were 4 times the MID and significantly greater than placebo (-20.1 vs -5.9; $P < 0.001$). A significantly higher proportion of onabotulinumtoxinA vs placebo patients reported an improvement/great improvement in their overall urinary condition on the TBS (60.2% vs 27.4%; $P < 0.001$), which was consistent with improvements seen in the OAB pooled population from the phase 3 studies. Urinary tract infection (UTI) and dysuria were the most commonly observed AEs in this subpopulation and, similar to the pooled ITT population, occurred more frequently in the onabotulinumtoxinA group than placebo (UTI: 18.0% vs 6.2%; dysuria: 9.0% vs 4.7%). Similar efficacy and safety results were observed in the broader subpopulation of OAB patients with nocturia (i.e., ≥ 1 nocturia episode(s)/night at baseline) from the pooled phase 3 trials.

Interpretation of results

This post hoc analysis demonstrated that in OAB patients with ≥ 2 nocturia episodes/night, treatment with onabotulinumtoxinA resulted in significant reductions in episodes of nocturia, compared with placebo. These improvements in nocturia symptoms following onabotulinumtoxinA treatment were accompanied by clinically meaningful improvements in QOL outcomes, particularly in the KHQ sleep/energy domain. The incidence of AEs in the subset of patients with nocturia was consistent with the previously reported results from the phase 3 trials in the overall pooled population.

Concluding message

OnabotulinumtoxinA treatment significantly reduced nocturnal voids and resulted in clinically meaningful QOL improvements in OAB patients with nocturia who were inadequately managed by ≥ 1 anticholinergic. OnabotulinumtoxinA was well-tolerated, with an acceptable safety profile.

References

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Disclosures

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Ethics Committee: Institutional Review Board (IRB) **Helsinki:** Yes **Informed Consent:** Yes