AbobotulinumtoxinA in the Management of Hallux Valgus in Adult Patients: Results of a Randomised And Placebo-Controlled Phase 2 Trial

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Introduction/Purpose: Hallux valgus (HV) is a progressive foot deformity affecting nearly 25% of adults, characterized by pain and functional disability, and morphological changes in foot appearance due to progressive lateral deviation of the hallux. HV is initially managed with orthotic interventions, which are often ineffective. Corrective surgery can be efficacious, but is associated with significant pain, long recovery times and, potentially, recurrence. AbobotulinumtoxinA (aboBoNT-A, Dysport®) injections may correct the underlying muscle imbalance (resulting from hypertonia of specific forefoot muscles governing the hallux) thought to cause deformity, thereby reducing pain and disability associated with HV. Therefore, the aim of this phase II, placebo-controlled, parallel-group, multicenter study (NCT03569098) was to evaluate the effect of aboBoNT-A on pain and disability associated with HV in adults.

Methods: Patients were randomized (1:1:1) to receive aboBoNT-A 300U, 500U, or placebo in a ≥12-week double-blind (DB) phase, followed by a 24-week open-label (OL) phase (OL Cycle 1, 300U [all patients]; OL Cycle 2, 300U or 500U). Total doses were divided equally into four specific foot muscles involved in hallux function. Eligible patients were aged 18–75 years with an HV angle 15–30° and numeric pain rating scale (NPRS) score of ≥4 (0, no pain; 10, worst possible pain). NPRS score was self-reported for 7 days before baseline and before each post-baseline visit. The primary endpoint was change from baseline in NPRS score (7-day average) before DB Week 8. Two post-hoc endpoints were defined as the percentage of days patients' NPRS scores were: 1) lower than their lowest NPRS score before baseline; and 2) ≥2 points lower than mean baseline NPRS score. Adverse events (AEs) were monitored throughout the study.

Results: No statistically significant differences were observed for aboBoNT-A 300U (n=63) or 500U (n=60) versus placebo (n=63) in NPRS scores at DB Week 8 (least squares mean [standard error]: -1.7 [0.3], -2.4 [0.3], versus -2.0 [0.3], respectively). Scores showed a trend towards pain reduction at Week 12 for aboBoNT-A 500U (-2.4 [0.3]) versus placebo (-1.7 [0.3]; p=0.06). Scores reduced further in OL Cycle 1. Post-hoc analyses showed that patients treated with aboBoNT-A 500U spent significantly more days with reduced pain before DB Week 8 compared with those treated with placebo: analysis 1) 63% versus 38% of days, respectively (p<0.01); analysis 2) 55% versus 37% of days, respectively (p=0.06). Results were similar at DB Week 12 (analysis 1: p<0.01; analysis 2: p=0.02, respectively). No new or unexpected AEs were reported.

Conclusion: Although the primary endpoint was not met at Week 8, a trend towards significant pain reduction versus placebo was reported for patients with HV at Week 12 following aboBoNT-A 500U injection. Pain was further reduced with repeat injection. Post-hoc analyses indicate that HV patients spent a greater proportion of time with reduced pain following aboBoNT-A 500U injection compared with placebo. This may be a more clinically relevant assessment of benefit than NPRS score averaged over 7 days. Safety results were in line with the known profile of aboBoNT-A.

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