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AbobotulinumtoxinA Efficacy and Safety in Children With Upper Limb Spasticity Previously Treated With Botulinum Toxin

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in 49.8% (n=1312), systemic medication in 12.4% (n=329), and transcutaneous electrical nerve stimulation (TENS) in 1.4% (n=37) of patients. Most patients used one (30.7%, n=810), two (36.9%, n=971), or three (19.2%; n=505) adjuvant strategies. Due to missing data, 1230 treatment sessions were included in a subanalysis investigating the role of adjuvant therapies to BoNTA for treatment success.
Patients in the G1 group received 101, and those in G2, 1129 injections. In both groups most patients had an expected or greater than expected outcome on their Goal Attainment Scaling (GAS) assessment (Table). Analysis by goal category showed higher success rates for the G2 group in all goal categories except for involuntary movements, where the G1 group scored higher (91.2% vs 79.2%, respectively). The G2 group advantage was more evident in goals related to pain (88.6% vs 76.5%) and range of motion (88.8% vs 80.0%), suggesting the relevance of a multimodal approach to pain management and the prominent role of stretching techniques for maintenance of range of motion (ROM).
Conclusions: In our 20 years of clinical practice in PSS management with BoNTA, there is a very high percentage of patients using different adjuvant therapies and treatment success rates tend to be higher in this group, except for goals related to involuntary movements.

Table
GAS Results According to Group Distribution.

		Treatment with BoNTA and Adjuvant Therapies (N=1129)	Treatment With BoNTA Monotherapy (N=101)
GAS	**T-Score Achieved**	48.7 ± 4.8	48.3 ± 5.1
	Goal ≥0	812 (71.9%)	65 (64.4%)
	Goal <0	317 (28.1%)	36 (35.6%)
	Change	11.7 ± 4.9	11.5 ± 5.1
	Change in GAS score ≥10	840 (74.4%)	71 (70.4%)
	Change in GAS score <10	289 (25.6%)	30 (29.6%)
Goals with GAS score ≥0	**ROM maintenance**	103 (88.8%)	4 (80.0%)
	Pain	187 (88.6%)	13 (76.5%)
	Involuntary movement	251 (79.2%)	31 (91.2%)
	Active function	92 (82.1%)	14 (77.7%)
	Passive function	118 (89.46%)	5 (83.3%)
	Mobility	194 (81.6%)	17 (81.0%)
	Treatment facilitation	4 (100.0%)	0 (0.0%)

Keywords: Adjuvant therapies; Botulinum toxin; Spasticity; Stroke; Treatment success

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Study Design of LONG RUN: A LONGitudinal Evaluation and Real-World Evidence of Uniquely Purified IncobotulinumtoxinA in Treatment-Naïve Participants

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Introduction: IncobotulinumtoxinA (INCO) is approved for the temporary improvement of moderate-to-severe upper facial lines (UFL), in the North American, Latin American, European, and Asia-Pacific regions (specific indications vary with country). Though widely used since 2010, clinical data on the long-term effectiveness, safety, and participant satisfaction with INCO in aesthetic management is limited. Here, we describe the design of an open-label, prospective, observational study, aimed at capturing long-term, real-world evidence and clinically-relevant data of INCO use in clinical practice in a global population.
Methods: Insight regarding protocol development was provided by an external study advisory committee. Participants 18 years of age or older, who have never received prior botulinum neurotoxin type A (BoNT-A) treatment, and are seeking treatment with INCO for UFL, will be enrolled at approximately 25 clinical sites in approximately 12 countries. Participants will be treated with INCO according to standard of care, and treatment, safety, and available effectiveness data will be collected. At each treatment visit, treatment variables will be recorded. Self-perception of age will be assessed using the validated FACE-Q Aging Appraisal Form and the Patient-Perceived Age Visual Analogue Scale. Severity of UFLs will be assessed by investigator's live assessment, and by participant self-assessment using the validated 5-point Merz aesthetic scales.
A global assessment of aesthetic improvement in appearance of UFL compared to the status prior to INCO treatment will be assessed by the participants using the Global Aesthetic Improvement Scale. Participant satisfaction with treatment will be assessed by direct questioning. Participants will undergo repeated treatments as needed and according to standard of care for up to 3 years, and will be contacted by phone, email, or site visit 4 to 6 weeks after each treatment to assess satisfaction. A blood sample will be collected from participants at the end-of study visit for the assessment of neutralizing antibodies.
Conclusions: The study design described here is, to our knowledge, the first of its kind for a real-world-evidence, observational study, which will follow the treatment journey of BoNT-naïve participants receiving facial cosmetic procedures for up to 3 years continuously. Data collected in this clinical study will enable a general assessment of the long-term safety, efficacy, and patient satisfaction associated with continuous treatments with INCO administered as needed according to physician and participant discretion for UFLs under real-world conditions. Data from this study will also provide insight into aesthetic uses of INCO in a global patient population, and exploration of the potential effects of neutralizing antibodies.
Funding: This study is sponsored by Merz Aesthetics.
Keywords: Aesthetics; Clinical study; Efficacy; IncobotulinumtoxinA; Patient satisfaction

AbobotulinumtoxinA Efficacy and Safety in Children With Upper Limb Spasticity Previously Treated With Botulinum Toxin

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Introduction: Primary endpoint analysis of this phase 3 study confirmed abobotulinumtoxinA (aboBoNT-A 8 U/kg and 16 U/kg) significantly

reduced hypertonia versus the 2 U/kg low-dose control and was generally well tolerated (Delgado, et al, 2021). However, the impact of previous botulinum neurotoxin (BoNT) injections on treatment outcomes remains largely unexplored.
Methods: We present subgroup analyses of a phase 3 study conducted in children (aged 2-17) with cerebral palsy (Gross Motor Function Classification System [GMFCS] Levels I-IV) and spasticity in ≥1 upper limb. In the first treatment cycle, 210 children were randomized to treatment with aboBoNT-A 2 U/kg, 8 U/kg or 16 U/kg into the primary target muscle group (PTMG; elbow or wrist flexors) and additional upper limb muscles. Children could be naïve to BoNT treatment or previously treated (with any BoNT formulation).
Results: In the modified intent-to-treat (mITT) population, 138 children had been previously treated with a BoNT formulation, and 70 children were new to treatment. At Week 6, previously treated children showed mean reductions (±SD in modified Ashworth scale (MAS_{PTMG}) scores of -1.4 ±1.0 in the 2 U/kg (n=45), -1.9 ±0.9 in the 8 U/kg (n=47), and -2.0 ±1.0 in the 16 U/kg (n=46) groups vs baseline. Children who were BoNT-naïve showed MAS_{PTMG} reductions of -1.5 ±1.2 (n=24), -2.0 ±1.3 (n=22), and -2.7 ±0.7 (n=24), respectively. Treatment differences were significant vs the control group for both subgroups treated with aboBoNT-A 16 U/kg and for the previously treated subgroup who received 8 U/kg. All children (all groups) showed improvement on the Physician Global Assessment. For this global assessment, the magnitude of improvement was slightly better for BoNT-naïve children in the 8 U/kg group than in other groups (2.3 vs 1.7-2.0 grade improvements in other subgroups). Adverse events during Cycle 1 (combined doses) were reported in a similar proportion of BoNT-naïve (52.8%) and previously treated (58.0%) children and most were considered unrelated to treatment. Eight children who had all been previously treated with BoNT reported experiencing muscular weakness.
Conclusions: These results demonstrate similar aboBoNT-A efficacy and safety profiles in children with upper limb spasticity who are new to BoNT treatment compared to those previously treated.
Funding: Ipsen
Keywords: AbobotulinumtoxinA; Clinical trial; Efficacy; Pediatric; Upper limb spasticity

Reference

Delgado MR, Tilton A, Carranza-Del Rio J, et al and the Dysport in PUL Study Group. Efficacy and safety of abobotulinumtoxinA for upper limb spasticity in children with cerebral palsy: A randomized repeat-treatment study. *Dev Med Child Neurol.* 2021;63(5):592-600.

Comparative Efficacy of AbobotulinumtoxinA and OnabotulinumtoxinA for the Treatment of Refractory Neurogenic Detrusor Overactivity: An Indirect Treatment Comparison

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Introduction: Neurogenic detrusor overactivity (NDO) causes urinary incontinence (UI). AbobotulinumtoxinA (aboBoNT-A) and onabotulinumtoxinA (onaBoNT-A) reduce the frequency of weekly UI episodes. The objective was to compare the efficacy and safety of aboBoNT-A with onaBoNT-A in NDO.
Methods: The systematic literature review followed Cochrane database and National Institute for Health and Care Excellence (NICE) guidance. MEDLINE and other sources were searched for randomized controlled trials of botulinum toxin type A formulations (through August 2020). Results from two aboBoNT-A trials and four onaBoNT-A trials were included. Outcomes included mean change from baseline (CFB) in weekly UI episodes (2, 6, 12, and 24 weeks); proportion of patients with 100% reduction in UI episodes at 6 weeks; and treatment-emergent urinary tract infections (TE-UTI). Bucher indirect treatment comparisons (ITCs) were conducted.
Results: Six studies on three active interventions (aboBoNT-A 600 U, 800 U, and onaBoNT-A 200 U) were included in the ITC, connected via the comparator placebo.
Trends were consistent although not significant. aboBoNT-A 600 U had numerically greater reduction in weekly UI episodes versus onaBoNT-A, with mean (95% confidence interval [CI]) differences in CFB of -0.8 (-6.0,4.5) and -2.3 (-8.5, 3.9) at 6 and 12 weeks, respectively. At 6 weeks, aboBoNT-A 600 U had numerically greater odds of a 100% reduction in weekly UI episodes versus onaBoNT-A (odds ratio: 3.0 [95%CI: 0.60, 15.34]). Results were similar for aboBoNT-A 600 U and 800 U. Applying relative effect estimates to a common/average placebo anchor rate resulted in estimates of 54.5%, 45.9%, and 28.4% of patients achieving 100% reduction in weekly UI episodes at 6 weeks with aboBoNT-A 600 U, 800 U and onaBoNT-A 200 U, respectively. aboBoNT-A 600 U/800 U was associated with fewer TE-UTIs than onaBoNT-A 200 U (odds ratios: 0.64 [0.34,1.21] and 0.90 [0.48,1.66], respectively).
Conclusions: aboBoNT-A and onaBoNT-A offer significant efficacy in NDO, with improvement on aboBoNT-A numerically greatest, and difference in CFB between the two toxins increasing from week 6 to 12. Further studies are needed for better-powered comparisons that may find statistically significant differences.
Funding: This study was sponsored by Ipsen.
Keywords: Bladder; Botulinum neurotoxin type A; Comparative effectiveness; Neurogenic; Treatment decision; Urinary incontinence

Consecutive Headache-Free Days With OnabotulinumtoxinA Treatment in Patients With Chronic Migraine: A Pooled PREEMPT Analysis

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Introduction: The disability of chronic migraine prevents patients from performing daily activities, leading to substantial personal, societal, and familial disturbance. More consecutive days of headache freedom are associated with meaningful improvements in quality of life. The goal of this study was to evaluate the impact of onabotulinumtoxinA versus placebo on the number of consecutive headache-free days and days without moderate/severe headache in participants with chronic migraine.
Methods: This was a post hoc analysis of the phase 3, 24-week, randomized, double-blind PREEMPT clinical trials (NCT00156910, NCT00168428). A headache day was defined as a day with ≥4 continuous hours of headache, per participant diary; participants recorded headache severity as mild, moderate, or severe. Percentages of participants who experienced ≥7, ≥14, and ≥21 consecutive days without headache or without a moderate/severe headache that required acute medication were compared between onabotulinumtoxinA and placebo groups. Only diary data after the first dose were used to calculate consecutive days without headache. Data were pooled to improve precision. Two-tailed Fisher's exact tests were performed to compare onabotulinumtoxinA versus placebo during the double-blind phase.
Results: A total of 1384 participants were randomized to onabotulinumtoxinA (n=688) or placebo (n=696) in the PREEMPT trials. During the 28-day baseline screening phase, the mean number of headache days was 19.9 for onabotulinumtoxinA and 19.8 for placebo (P=0.498). During the double-blind treatment phase, significantly more participants treated with onabotulinumtoxinA than placebo experienced ≥7 (70% vs 64%; P=0.039), ≥14 (40% vs 31%; P<0.001), and ≥21 (26% vs 18%; P<0.001) consecutive headache-free days without acute medication use. Significant differences favoring onabotulinumtoxinA treatment remained when the analysis was restricted to participants who experienced ≥7 (74% vs 68%; P=0.018), ≥14 (42% vs 34%; P=0.003), and ≥21 (28% vs 21%; P=0.003) consecutive