1-2022

Improvement of Spasticity-Related Pain With IncobotulinumtoxinA Treatment in Children/Adolescents With Cerebral Palsy: Pooled Analysis of 3 Phase 3 Studies

Florian Heinen

Petr Kanovsky

A Sebastian Schroeder

Henry G. Chambers

Edward Dabrowski
Beaumont Health

See next page for additional authors

Recommended Citation

Heinen F, Kanovsky P, Schroeder AS, Chambers HG, Dabrowski E, Geister TL, et al. Improvement of spasticity-related pain with incobotulinumtoxinA treatment in children/adolescents with cerebral palsy: pooled analysis of 3 phase 3 studies. Dev Med Child Neurol. 2022 Jan;64(Suppl 1):48. doi:10.1111/dmcn.15123.

Authors

Florian Heinen, Petr Kanovsky, A Sebastian Schroeder, Henry G. Chambers, Edward Dabrowski, Thorin L. Geister, Hanna Dersch, Irena Pulte, Michael Althaus, Marta Banach, and Deborah Gaebler-Spirag

Patients received total body incobotulinumtoxinA doses of 16 U/kg body weight (BW, ≤400 U) for LL spasticity in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL/UL treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Adverse events (AEs) were assessed in the pooled population.

Results: In total, 907 patients (59.6% male, mean [SD] age 6.7 [4.2] years, BW 23.3 [13.9] kg) received multipattern treatment; 753 patients (83.0%) completed the studies and received up to 6 ICs. Across all ICs, 363 (40.0%) experienced an AE; 33 (3.6%) had ≥1 treatment-related AE. The most common AEs were nasopharyngitis, bronchitis, and upper-respiratory tract infection. Serious AEs (SAEs) and AEs of special interest (AESIs) were reported for 49 (5.4%) and 18 (2.0%) patients, respectively. AESIs reported in >1 patient were muscular weakness (6 patients, 0.7%), dyspnea, constipation, and dysphagia (3 patients, 0.3% each). There was no increased incidence of AEs, SAEs, or AESIs with repeated dose. No deaths were reported in these studies.

Conclusions: IncobotulinumtoxinA was safe and well tolerated for LL, UL, or combined multipattern treatment over up to 6 ICs in a comprehensive population of ambulant and non-ambulant pediatric patients with spasticity (GMFCS levels I-V).

Poster 097

Improvement of spasticity-related pain with Incobotulinumtoxina treatment in children/adolescents with cerebral palsy: pooled analysis of 3 phase 3 studies

F HEINEN[1], P KAŇOVSKY[2], AS SCHROEDERA[3], HG CHAMBERS[4], E DABROWSKI[5], TL GEISTER[6], H DERSCH[6], I PULTE[6], M ALTHAUS[6], M BANACH[7], D GAEBLER-SPIRAG[8]

[1]Division of Paediatric Neurology and Developmental Medicine, Dr. von Hauner Children's Hospital, Munich, Germany; [2]Faculty of Medicine and Dentistry and University Hospital, Palacký University Olomouc, Olomouc, Czech Republic; [3]Dr. von Hauner Children's Hospital, Ludwig Maximilian University of Munich, Munich, Germany; [4]Rady Children's Hospital, San Diego, USA; [5]Beaumont Pediatric Physical Medicine and Rehabilitation, Royal Oak, USA; [6]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany; [7]Department of Neurology, Jagiellonian University Medical College, Krakow, Poland; [8]Shirley Ryan AbilityLab, Northwestern Feinberg School of Medicine, Chicago, USA

Introduction: Spasticity-related pain (SRP) in children and adolescents with cerebral palsy (CP) is common, often neglected, and impacts daily quality of life. We assessed the effect of incobotulinumtoxinA on SRP using pooled data from 3 large Phase 3 pediatric studies.

Methods: Ambulant and non-ambulant patients (2–17 years of age; uni- or bilateral CP; Ashworth Scale score ≥2 in clinical patterns for treatment) were enrolled. Patients received total body incobotulinumtoxinA doses of ≤16 U/kg (≤400 U) for lower-limb (LL) treatment in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL and upper-limb (UL) treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Changes in self-reported (child/adolescent) or observed (parent/caregiver) SRP were assessed using the Questionnaire on Pain caused by Spasticity (QPS) in patients with LL (TIM, TIMO, and XARA) and UL treatment (TIMO and XARA).

Results: Assessments for 849 patients with LL and 454 patients with UL treatment were included. Of these, 340 (40.0%, LL: 61.2% male, mean [SD] age 9.3 [3.8], body weight [BW] 32.6 [14.8] kg) and 160 (35.2%, UL: (61.9% male, mean [SD] age 10.3 [3.7] years, BW 36.8 [16.5] kg) were able to assess SRP by interviewer- or self-administered QPS. Most (81.9% LL; 69.7% UL) reported pain at baseline for ≥1 activity. SRP increased with activity demands. Complete SRP relief at Week 4 post-treatment in each IC was seen (Table) and was highest in IC4. Observed SRP frequency was consistent with self-reported SRP and was supported by respective QPS item scores (all $P<0.001$ for responder rates).

Conclusions: In this large, pooled analysis, repeated incobotulinumtoxinA injections led to sustained pain reduction in children and adolescents with spasticity, with complete pain relief in the injected limb during activities in ≤54.8% of patients.

Poster 098

Common features in children with known genetic cause for cerebral palsy.

K SAJIP[1,3], K BURTON[2]

[1]Addenbrookes Hospital, Cambridge, UK; [2]Cambridgeshire Community Services NHS Trust, Cambridge, UK; [3]Cambridge University Clinical School, Cambridge, UK

Background: Cerebral palsy (CP) has a complex aetiology with several contributing factors such as prematurity, infection and hypoxic-ischaemic injury which are well understood and have guided clinical treatment and prevention, reducing prevalence. There is an emerging understanding of the genetics behind this complex disorder with Increasing knowledge of both genetic susceptibility genes, copy number variants and rarer monogenic mutations, which can drive research towards targets for intervention and precision medicine.

Objectives: To characterise the clinical presentation of children with an underlying genetic cause for their cerebral palsy and to identify common features possibly predictive of underlying genetic abnormality.

Methods: From a cohort of 221 patients in Cambridgeshire aged 0–18 years who all had a clinical presentation consistent with CP, we identified 11 cases with a genetic diagnosis identified. We analysed their clinical records to identify common themes likely from literature to be atypical.

Results: Of 9 patients, 4 were male (36.3%) and 7 were female (63.6%). Identified features more likely to be seen in genetic CP included: normal gestation and delivery, epilepsy type or severe intellectual disability out of keeping with presentation, congenital abnormalities, dysmorphic features, atypical MRI findings and a family history. 9/11 (81.8%) patients had at least 4 of the 7 features we have identified in total and 6/11 (54.5%) patients had at least 5 out of the 7 features we have identified in total. The most common features included: unexpected severe intellectual disability (9/11 patients), normal gestation and delivery (8/11 patients), dysmorphic features (9/11 patients) and atypical MRI findings (9/11 patients).

Conclusions: In patients with a genetic underlying cause identified for their cerebral palsy, there are a number of common features