in treating this condition.[1-3] However, its mechanism of action is not yet fully understood.[4]
Methods: A 36-year-old Caucasian male, with spastic tetraparesis sequential to a traumatic brain injury, complained of increasing left hamstring muscle pain, refractory to any therapeutic modality. Botulinum toxin was administered to the left lower limb.
A systematic assessment of passive range of motion of both hips, knees, and tibiotarsal joints was performed before injection. Reassessment of the same joints was performed 4 weeks postinjection. The contralateral side was also assessed. Pain status was monitored with the Verbal Numeric Scale (VNS).
Results: Throughout the treatment, there was improvement in range of motion on hip flexion and left foot dorsiflexion beginning after the first injection and persisting through the following evaluations. Gait performance also improved. Pain assessment showed progressive improvement over the course of treatment, with total absence of pain after 6 months.
Conclusion: In addition to spasticity, botulinum toxin has additional applications in management of chronic pain. There is much debate regarding its mechanism of action in this indication: it appears to act by an indirect effect in reducing excess dysfunctional muscle activity and also through a potential direct pharmacological effect on peripheral nociceptors. This case report clearly emphasizes the benefit of considering botulinum toxin in pain control, especially when other therapies have proved ineffective.
Keywords: Botulinum toxin; Pain; Spasticity

References
1. Wissel J, Müller J, Dressnandt J, et al. Management of spasticity associated pain with botulinum toxin A. *J Pain Symptom Manage.* 2000;20(1): 44-49.
2. Aoki KR. Pharmacology and immunology of botulinum toxin serotypes. *J Neurol.* 2001; 248(suppl 1):3-10.
3. Sheean, G. Botulinum toxin for the treatment of musculoskeletal pain and spasm. *Curr Pain Headache Rep.* 2002;6(6):460-469.
4. Matak I, Bölcskei K, Bach-Rojecky L, Helyes Z. Mechanisms of botulinum toxin type A action on pain. *Toxins (Basel).* 2019; 11(8):459.

EFFICACY AND SAFETY OF INCOBOTULINUMTOXINA IN THE TREATMENT OF LOWER-LIMB SPASTICITY IN ADULTS: THE PATTERN CUSTOMIZED STUDY DESIGN

Gerard E. Francisco[a,*], Jörg Wissel[b], Marta Banach[c], Hanna Dersch[d], Thorin Geister[d], Michael Althaus[d], Djamel Bensmail[e], Franco Molteni[f], Alberto Esquenazi[g], Michael Munin[h]. [a] *University of Texas McGovern Medical School and TIRR Memorial Hermann, Houston, TX, USA;* [b] *Vivantes Hospital Spandau, Berlin, Germany;* [c] *Department of Neurology, Jagiellonian University Medical College, Krakow, Poland;* [d] *Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany;* [e] *Raymond-Poincaré Hospital, University of Versailles Saint Quentin, Garches, France;* [f] *Villa Beretta Rehabilitation Center, Valduce Hospital, Costa Masnaga, Lecco, Italy;* [g] *MossRehab and Albert Einstein Medical Center, Elkins Park, PA, USA;* [h] *University of Pittsburgh School of Medicine, Pittsburgh, PA, USA*

E-mail address: gerard.e.francisco@uth.tmc.edu

* Corresponding author: University of Texas McGovern Medical School and TIRR Memorial Hermann, 1333 Moursund Street, Houston, TX 77030, USA.

Introduction: The Phase 3 PATTERN study (NCT03992404) will assess the efficacy and safety of incobotulinumtoxinA for lower- or lower- and upper-limb spasticity due to stroke or traumatic brain injury. We introduce the study design and its new innovative features.
Methods: PATTERN is an ongoing randomized, double-blind, placebo-controlled, multicenter study, with an open-label extension (OLEX) period. An estimated 600 adults with lower-limb spasticity (Modified Ashworth Scale [MAS] ankle score 2 or 3), with/without upper-limb spasticity of the same body side, will be enrolled. Subjects will receive incobotulinumtoxinA 400 U or placebo into lower-limb muscles in the main period (1 injection cycle [IC]) and ≤800 U into lower-limb muscles with combined upper-limb treatment, if indicated, in the OLEX (4-5 ICs). A two-stage adaptive design with interim sample size reassessment after 360 subjects will be applied. Primary and co-primary endpoints are change from baseline in derived MAS ankle score and physician's Global Impression of Change Scale score at Weeks 4-6. Safety will be assessed. A goal catalog derived from physicians' and patients' qualitative interviews will be incorporated into the goal attainment scale treatment evaluation.
Results: The PATTERN study design allows for the observation of up to 6 consecutive ICs, with the OLEX including a multi-pattern, patient-centric approach, if clinically indicated.
Conclusions: This novel study design, utilizing pre-specified sample size adaptation based on an interim analysis, demonstrates an innovative approach to the challenge of lower-limb spasticity clinical studies. To our knowledge, this is the first time such an adaptive design has been used in a BoNT study in this indication. A goal catalog specifically developed for this population is expected to overcome the difficulties of comparable high-quality SMART treatment goal setting and follow up in a large Phase 3 trial.
Funding: Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany
Keywords: IncobotulinumtoxinA; Lower-limb spasticity; Stroke

REAL-LIFE USE OF BOTULINUM TOXIN TYPE A IN POSTSTROKE SPASTICITY: IS THERE A TIME WINDOW TO START TREATMENT?

Margarida Freitas[a,*], Susana Rosa[b], Bruno Guimarães[c], Joana Martins[d], José Luís Mesquita[e], Daniel Cardoso[f], Jorge Jacinto[f]. [a] *Department of Physical and Rehabilitation Medicine, Hospital Garcia de Orta, Almada, Portugal;* [b] *Department of Physical and Rehabilitation Medicine, Centro Hospitalar Universitário de Lisboa Central (CHULC), Lisbon, Portugal;* [c] *Department of Physical and Rehabilitation Medicine, Centro Hospitalar Entre o Douro e Vouga (CHEDV), Santa Maria da Feira, Portugal;* [d] *Department of Physical and Rehabilitation Medicine, Centro Hospitalar e Universitário de Coimbra (CHUC), Lisbon, Portugal;* [e] *Department of Physical and Rehabilitation Medicine, Centro Hospitalar Universitário de Lisboa Norte (CHULN), Lisbon, Portugal;* [f] *Centro de Medicina de Reabilitação de Alcoitão, Department of Adult Rehabilitation, Cascais, Portugal*

E-mail address: margaridafmfreitas@gmail.com

* Corresponding author: Department of Physical and Rehabilitation Medicine, Hospital Garcia de Orta, Avenida Torrado da Silva, 2805-267, Almada, Portugal.

Introduction: Spasticity can occur following stroke, causing disability and a negative impact on quality of life. Botulinum toxin type A (BoNT-A) is the first-line treatment for post-stroke spasticity. Goal Attainment Scaling (GAS) is a method of rating the extent to which patients' individual goals are achieved. This study aims to compare the therapeutic effects of BoNT-A in spastic patients starting treatment within 1 year after stroke and 3 years after stroke.
Methods: A sample of 216 patients (98 females) diagnosed with poststroke spasticity – encompassing a total of 2083 injection sessions – was divided into 3 groups: patients who started BoNT-A in the first year post-stroke (Group 1; n = 1009 injections); patients who started BoNT-A between 1 and 3 years post-stroke (Group 2; n= 749 injections); and patients who started BoNT-A after 3 years post-stroke (Group 3; n= 308 injections). We excluded 17 injections that lacked valid information. We characterized the sample according to gender, age, and BoNT-A formulation administered. Treatment efficacy was measured by goal achievement/overachievement, using GAS as the primary outcome measure for all goals. Success was defined as a GAS score ≥0 per goal.
Results: BoNT-A was very effective in all groups of patients (GAS≥ 0 in over 80% of the injections), regardless of the time the treatment was started. Group 3 had better treatment efficacy for secondary goals, with statistically significant results. When comparing the results between the various BoNT-A preparations used, we found no statistically significant differences in GAS scores.
Conclusions: Our findings suggest that BoNT-A is very effective in post-stroke spasticity. BoNT-A can be started even after 3 years post-stroke for well-selected patients, with realistic, individualized goals. Patients in Group 3 had long-standing, established, and well recognized deficits, with easily identifiable needs. It may be easier to set viable objectives for these patients, enabling better results in goal attainment.
Keywords: AbobotulinumtoxinA; Botulinum toxin; GAS score; IncobotulinumtoxinA; OnabotulinumtoxinA; Poststroke spasticity