P04.227

Cervical Dystonia Patient Registry for Observation of BOTOX® Efficacy (CD PROBE): Interim Results of Physician-Reported Outcomes

Joseph Jankovic[1], P. David Charles[2], Charles H Adler[3], Mark Stacy[4], Cynthia Comella[5], Lee Ming Boo[6], Mitchell F Brin[7], Spyridon Papapetropoulos[7] (on behalf of CD PROBE Study Group)

[1]Baylor College of Medicine, Department of Neurology, Houston, TX; [2]Neurology, Vanderbilt University Medical Center, Nashville, TN; [3]Neurology, Mayo Clinic, Scottsdale, AZ; [4]Duke University Medical Center, Durham, NC; [5]Department of Neurology/Movement Disorder Section, Rush University Medical Center, Chicago, IL; [6]Biosense Webster, Diamond Bar, CA; [7]Allergan, Inc., Irvine, CA

INTRODUCTION

- The most common form of adult-onset focal dystonia is cervical dystonia (CD).[1]
- Since the introduction of botulinum toxin for the treatment of CD over 25 years ago,[2] botulinum toxin has become the treatment of choice to provide relief from the abnormal head position and pain.[3]
- Despite clinical evidence from randomized controlled trials and use in thousands of patients, there is a lack of consensus regarding the optimal use of botulinum toxin for CD.[4]
- CD PROBE, an ongoing clinical registry of patients with CD treated with onabotulinumtoxinA across a broad range of physicians, may provide invaluable data about how best to treat this chronic, disabling neurologic condition.

OBJECTIVE

- To report an interim analysis of physician-reported outcomes of efficacy with repeat injections of onabotulinumtoxinA in patients with CD.

METHODS

Study Design

- This is a multicenter, open-label, prospective, standard of care, observational clinical registry of patients with CD treated with onabotulinumtoxinA (ClinicalTrials.gov, NCT00836017).
- Subjects were administered 3 injections of onabotulinumtoxinA separated by >90 days; dose and treatment intervals were based on the physician's standard of care.
- Subjects were followed over 3 treatment cycles and evaluated at baseline (injection 1), each injection, and 4–6 weeks after each injection (peak effect).
- Physicians assessed outcomes included the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and Clinical Global Impression of Change (CGIC) questionnaire.

Subjects

- 499 Patients enrolled as of October 11, 2010 (**Tables 1 & 2**).
- Inclusion criteria
  - ≥1 of the following: new to principle physician's practice; new to botulinum toxin therapy; or, if previously participated in a botulinum toxin clinical trial, did not receive botulinum toxin for ≥16
  - Informed consent obtained
- Exclusion criteria
  - Planning elective surgery during the observational study period
  - Pregnant, nursing, or planning a pregnancy

RESULTS

Table 1. Baseline Demographic Characteristics

Enrollment as of October 11, 2010, N		499
Female		384 (77.0)
Race/ethnicity		
	White	408 (93.8)
	Hispanic	13 (2.6)
	Asian	10 (2)
	Black	6 (1.2)
	Native American	1 (0.2)
	Other	1 (0.2)
Age, y		57.5 ± 14.3 (20–90)
Height, in		65.8 ± 7.7 (56–78)
Weight, lb		160.8 ± 38.6 (66–335)
Body mass index, kg/m^2		26.3 ± 5.5 (4–50)

Data are presented as n (%) or mean ± standard deviation (range) unless noted.
SD = standard deviation.

Table 2. Baseline Disease Characteristics

Age at symptom onset, y		48.2 ± 16.1 (0–89)
Time to CD diagnosis, y		5.4 ± 8.6 (0–53)
Time to 1st injection of botulinum toxin after diagnosis, y		1.0 ± 3.7 (–23 to 53)
Received botulinum toxin in the past		177 (35.5)
Predominant feature of CD, % (CI)		
	Torticollis	44.2 (39.9, 48.6)
	Lateralcollis	42.2 (37.9, 46.6)
	Retrocollis	5.9 (4.1, 8.3)
	Anterocollis	4.7 (3.1, 6.9)
	Other	3.0 (1.9, 5.0)
TWSTRS scores		
	Severity	16.9 ± 5.5 (1–32)
	Disability	10.7 ± 6.5 (0–30)
	Pain	10.4 ± 5.2 (0–20)
	Total	38.0 ± 13.4 (4–77)
Physician assessment of CD severity (n=493), %		
Mild / Moderate / Severe		40.2 / 48.7 / 11.2

Data are presented as n (%) or mean ± standard deviation (range) unless noted.
CD = cervical dystonia; SD = standard deviation; TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale.

- At baseline, 89.6% (440/491) of subjects reported pain.
- 495, 312, and 194 subjects have received 1, 2, or 3 injections of onabotulinumtoxinA, respectively.
  - The mean (SD) interval between the 1st and 2nd injections was 100.4 (±22.9) days and 100.0 (±22.3) days between the 2nd and 3rd injections.

Physician-Reported Outcomes

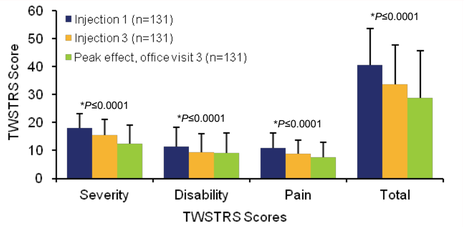
- Mean (SD) total dose for injection 1 was 175.6 (±104.9) units. The mean (SD) doses for injection 1 differed significantly based on the physician assessments of CD severity (P<0.0001) (**Table 3**).

Table 3. Mean Dose of OnabotulinumtoxinA at Baseline (Injection 1) by Physician-Assessed Severity

Severity	n	Dose, Mean ± SD (Units)
Mild	188	154.7 ± 94.1
Moderate	225	181.3 ± 112.0
Severe	52	226.0 ± 90.4

SD = standard deviation.

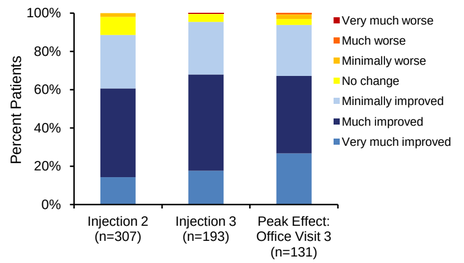
Figure 1. Assessment of TWSTRS Total Score and Subscales



*Repeated measures (ANOVA); all available data for each time point.

- Among subjects with assessments following 3 injections, TWSTRS total score (SD) decreased from 40.5 (±13.2) at baseline to 28.9 (±16.8) at Injection 3 peak effect (P<0.0001 vs baseline).

Figure 2. Clinicians' Global Impression of Change



All available data for each time point.

- According to CGIC assessments, physicians rated 93.4% of subjects with some improvement at injection 3.
  - >60% of patients were much/very much improved following injection 2 and injection 3 compared with baseline.

Adverse Events

- Severe adverse events (SAEs) were reported for 17 patients.
  - In 16 patients, the SAE was considered not related to treatment
  - In 1 patient, the SAE (pyrexia) was considered unlikely due to the treatment .

Table 4. Number of Patients Withdrawn From the Study and Reasons for Withdrawal (n=96)

Reason for withdrawal	Number of patients
Lack of response after first or second injection	9
Lost to follow-up	25
Patient withdrew consent	30
Physician discretion	5
Other	18
Adverse event*	9

*Neck weakness (3 patients) and mild dysphagia (2 patients) were the most frequent adverse events leading to withdrawal

CONCLUSIONS

- OnabotulinumtoxinA treatment resulted in clinical improvement of CD symptoms, as indicated by multiple physician-assessed measures.
- The benefits of treatment with onabotulinumtoxinA, without serious adverse effects, were sustained during this observational study with injections administered at 100-day intervals.

CD PROBE Study Group

Lefko Aftonomos, CA; Pinky Agarwal, WA; Fahd Amjad, DC; Angela Applebee, VT; Kristin Appleby, DC; Richard Barbano, NY; Peter Barbour, PA; Brandon Barton, IL; Jay Bhatt, IN; Kevin Biglan, NY; David Bowers, TN; James Boyd, VT; Allison Brashear, NC; Mary Caire, TX; Barbara Changizi, NY; Mahan Chehrenama, VA; Shilpa Chitnis, TX; Cynthia C Cullis, MI; Khashayar Dashtipour, CA; Lisa Davidson, MN; Thomas Davis, TN; J Antonelle De Marcaida, CT; Christina Drafta, NY; Drake Duane, AZ; Richard Dubinsky, KS; Jeffrey Esper, PA; Virgilio Evidente, AZ; Rez Farid, MO; Grace Forde, NY; Timothy Fries, VT; Ramon Gil, FL; John Goudreau, MI; David Greeley, WA; Alida Griffith, WA; Laurie Gutmann, WV; Gregory Hanes, FL; Robert Hauser, FL; Vanessa Hinson, SC; Patrick Hogan, WA; Tomas Holmlund, NY; Allan Ingenito, MN; Stuart Isaacson, FL; Bahman Jabbari, CT; Sandra Jacobson, AZ; Paul Jett, TN; John Kelemen, NY; Katie Kompoliti, IL; Daniel Kremens, PA; Rajeev Kumar, CO; Eugene Lai, TZ; Julie Leegwater-Kim, MA; Kenneth Levin, NJ; Peter LeWitt, MI; Tsao-Wei Liang, PA; Steven Lo, DC; Duarte Machado, CT; Padma Mahant, AZ; Zoltan Mari, MD; Anthony May, PA; Davis McDonald, FL; Stephen McGuire, TX; Emilio Melchionna, MA; Eric Molho, NY; Fatta Nahab, FL; Srinivas Nalamachu, KS; Anthony Nicholas, AL; Suneetha Nuthalapaty, TN; William Ondo, TX; Padraig O'Suilleabhain, TX; Fernando Pagan, DC; Atul Patel, KS; Gauri Pawar, WV; Diana Pollock, FL; Ben Renfroe, FL; Diana Richardson, CT; Perry Richardson, DC; Michael Rivner, GA; Jason Rosenberg, SC; David Ross, FL; Michael Rossen, MA; Kyle Ruffing, FL; Marwan Sabbagh, AZ; Johan Samanta, AZ; Cenk Sengun, FL; Aliya Sarwar, TX; Kapil Sethi, GA; Scott Sherman, AZ; Holly Shill, AZ; Tanya Simuni, IL; Carlos Singer, FL; Rodney Sorensen, WI; Michael Sorrell, MA; Natividad Stover, AL; Thyagarajan Subramanian, PA; William Sunter, FL; David Swope, CA; Tamara Miller, CO; Martin Taylor, OH; Margaret Tilton, NH; Bruno Tolge, NY; Richard Trosch, MI; Winona Tse, NY; Miodrag Velickovic, NY; Maureen Watts, TX; Robert Yapundich, NC; Cindy Zadikoff, IL; Lin Zhang, CA; Chong-Hao Zhao, CA

DISCLOSURE

This study and its analysis were sponsored by Allergan, Inc., Irvine, CA. Writing assistance was provided by Susan M. Kaup, PhD, of Evidence Scientific Solutions, and was funded by Allergan, Inc.

Dr Jankovic received compensation from Allergan, Inc., Chelsea Therapeutics, EMD Serono, Merz Pharmaceuticals, Lundbeck Inc., and Teva for consulting services; he received compensation from Medlink: Neurology for serving as an editorial board member; he received research support from Allergan, Inc., Allon Therapeutics, Ceregene Inc., Chelsea Therapeutics, Diana Helis Henry Medical Research Foundation, EMD Serono. Huntington's Disease Society of America, Huntington Study Group, Impax Pharmaceuticals, Ipsen Limited, Lundbeck Inc, Michael J. Fox Foundation for Parkinson Research, Medtronic, Merz Pharmaceuticals, National Institutes of Health, National Parkinson Foundation, Neurogen, St. Jude Medical, Teva Pharmaceutical Industries Ltd, University of Rochester, and Parkinson Study Group. Dr. Charles receives income from Allergan, Medtronic, and Pfizer for education and consulting services. Vanderbilt University receives income from grants and contracts with Allergan and Medtronic for research lead by Dr. Charles. Dr Adler received consulting fees from Eli Lilly, Ipsen, Medtronic, and Merck Serono. Dr Stacy received compensation from Allergan, Inc., Boehringer-Ingelheim Inc., General Electric, Novartis, Osmotica, Synosia, Schering-Plough, GlaxoSmithKline, Teva, Biogen, and Neurologix for consulting, speaker bureaus, protocol steering committee, and/or safety monitoring boards; he received royalties from Informa Press and research support from Ceregene, IMPAX, Michael J. Fox Foundation, Neuraltus, Novartis, Parkinson Study Group, and Schering-Plough. Dr Comella served as a consultant for Ipsen, Merz, Allergan, Inc., UCB, and Esai; her institution received research support from Merz, Allergan, Inc., Ipsen, and Boehringer-Ingelheim Inc. in which she was a Principal Investigator. Dr Boo received personal compensation from Allergan, Inc. as an employee; she is currently an employee of Johnson and Johnson. Dr Brin is an employee of Allergan, Inc. and receives salary, stock, and stock options from Allergan, Inc. Dr Papapetropoulos is an employee of Allergan, Inc. and receives salary, stock, and stock options from Allergan, Inc.; previously he was employed by Biogen Idec Inc. and received stock options.

References

1. Jankovic J, Tsui J, Bergeron C. *Parkinsonism Relat Disord*. 2007;13:411-416. **2.** Jankovic J. *Lancet Neurol*. 2006;5:864-872. **3.** Simpson DM, Blitzer A, Brashear A, et al. *Neurology*. 2008;70:1699-1706. **4.** Sheean G. *Neurol Clin*. 2008;26(suppl 1):66-76.

Presented at the 63rd Annual Meeting of the American Academy of Neurology (AAN), 9–16 April, 2011, Honolulu, Hawaii, USA.

The potency units of onabotulinumtoxinA are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of onabotulinumtoxinA cannot be compared with or converted into units of any other botulinum toxin products assessed with any other specific assay method.