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Cervical Dystonia Patient Registry for Observation of BOTOX® Efficacy (CD PROBE) Interim Results of Pain-Related Outcomes

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INTRODUCTION

- Cervical dystonia (CD) is one of the most common forms of adult-onset focal dystonia.
- CD is associated with abnormal contraction of neck muscles causing an abnormal head position and is commonly associated with pain.
- Pain associated with CD can lead to missed work and difficulties with activities of daily living.
- Neurotoxin injection is accepted as first line treatment for CD.[1]
- OnabotulinumtoxinA (BOTOX® Allergan Inc.) was the first neurotoxin approved by the US Food and Drug Administration for the treatment of CD.[2]
- Neurotoxin injection for CD has been utilized worldwide for more than 20 years.
- Physicians differ in the care of patients and in the application of neurotoxin injection for CD.
- CD-PROBE (Cervical Dystonia Patient Registry for Observation of BOTOX® Efficacy) is a multicenter, prospective, standard-of-care, observational registry designed to capture data on patients' clinical presentation, dosing of onabotulinumtoxinA, and treatment outcomes.

OBJECTIVE

- To report an interim analysis of pain-related outcomes in subjects receiving injections of onabotulinumtoxinA as part of the ongoing CD-PROBE clinical registry.

METHODS

- CD-PROBE is a prospective, open label, multi-center, clinical registry for subjects treated for CD (ClinicalTrials.gov Identifier NCT00836017).
- Subjects were administered 3 injections separated by >90 days. The dose and treatment intervals were based on standard of care for the physician's practice.
- Assessments made at baseline (injection 1) and 4-6 weeks after each injection (peak effect).
- Pain measures included the Pain Numeric Rating Scale (P-NRS), Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) pain subscale, and Cervical Dystonia Impact Profile (CDIP-58).
- Inclusion criteria:
  1. Subjects with CD appropriate for neurotoxin therapy
  2. Subjects are at least one of the following:
     a) New to the treating physician
     b) Not previously treated with neurotoxin
     c) If previously treated, have not received neurotoxin for ≥16 weeks
  3. Available to understand and participate in study procedures
  4. Provided informed consent and release of health information related to the study
- Exclusion criteria:
  1. A planned surgical procedure during the study
  2. Pregnancy or nursing, or a planned pregnancy during the study
  3. Poor compliance with past treatment plans
  4. Medical condition that could place the subject at risk if they participated in the study.

RESULTS

Table. Baseline Demographic and Disease Characteristics

Enrollment as of October 11, 2010, N	499
Sex, n (%)	
Females	384 (77.0)
Males	115 (23.0)
Race/ethnicity, n (%)	
Asian	10 (2.0)
Black	6 (1.2)
Hispanic	13 (2.6)
Native American	1 (0.2)
Other	1 (0.2)
White	468 (93.8)
Age, y, mean ± SD	57.5 ± 14.3
Height, in, mean ± SD	65.8 ± 7.7
Weight, lbs, mean ± SD	160.8 ± 38.6
BMI, kg/m^2, mean ± SD	26.3 ± 5.5
Age at symptom onset, y, mean ± SD	48.2 ± 16.1
Time to CD treatment after diagnosis, y, mean ± SD	1.0 ± 3.7
TWSTRS scores, mean ± SD	n=131
Severity	18.1 ± 5.0
Disability	11.5 ± 6.8
Pain	10.9 ± 5.3
Total	40.5 ± 13.2

CD = cervical dystonia; SD = standard deviation; TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale.

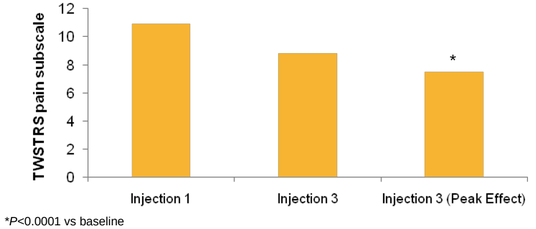
OnabotulinumtoxinA dosage

- The mean ± SD dose at injection 1 (baseline) was 175.6 ± 104.9 U.
- The mean ± SD time interval between injections 1 and 2 was 100.4 ± 22.9 days and 100.0 ± 22.3 days between injections 2 and 3.
- At the time of this interim analysis, 495 patients received 1 injection, 312 received 2 injections, and 194 received 3 injections

Summary of pain improvement

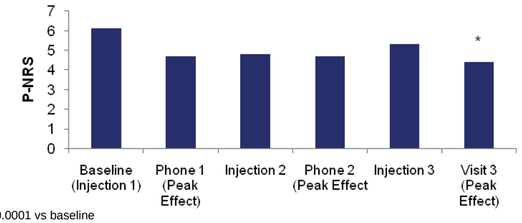
- 89.6% (440/491) of subjects reported pain at baseline.
- Pain measured by the TWSTRS pain subscale significantly improved from 10.9 ± 5.3 at baseline to 7.5 ± 5.5 (*P*<0.0001) **(Figure 1).**
- Pain measured by P-NRS significantly improved from 6.1 ± 2.2 to 4.4 ± 2.7 (*P*<0.0001) **(Figure 2).**
- All domains for CDIP-58 improved significantly, including the pain subscale, which improved from 70.6 ± 24.7 to 52.0 ± 24.2 (*P*<0.0001) **(Figure 3).**

Figure 1. Toronto Western Spasmodic Torticollis Scores (TWSTRS), pain subscale (n=131)



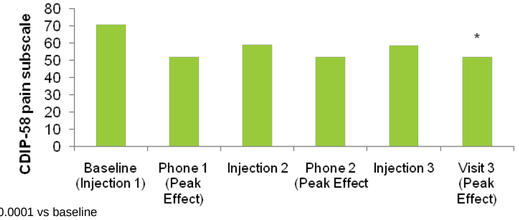
*P<0.0001 vs baseline

Figure 2. Pain numeric rating scale (P-NRS) (n=84)



*P<0.0001 vs baseline

Figure 3. Cervical Dystonia Impact Profile (CDIP-58) (n=111)



*P<0.0001 vs baseline

Correlations of pain measures

- The TWSTRS pain subscale correlated with the CDIP-58 pain subscale at baseline (r=0.61; *P*≤0.0001).
- The TWSTRS pain subscale also correlated with the P-NRS at baseline (r=0.78; *P*≤0.0001).
- The CDIP-58 pain subscale correlated with the P-NRS at baseline (r=0.56; *P*≤0.0001).

CONCLUSIONS

- The majority of subjects with CD reported pain.
- The pain associated with CD improved significantly following onabotulinumtoxinA injection, as measured on 3 separate scales.
- There was a significant correlation of 3 measures used to assess pain at baseline: TWSTRS pain subscale, P-NRS, and CDIP-58 pain subscale.
- Additional information concerning the improvement of CD-associated pain relief following neurotoxin injection will become available as more subjects enroll in CD-PROBE.

References

1. Simpson DM, Blitzer A, Brashear A, et al. *Neurology*. 2008;70(19):1699-1706.
2. BOTOX® Prescribing Information. Irvine, CA: Allergan, Inc.; 2010.

CD PROBE Study Group

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DISCLOSURE
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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.
*Dr Boo was employed at Allergan Inc at the time that this study was initiated. She is currently employed at Biosense Webster, Diamond Bar, CA.

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