

Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy (CD PROBE): Study Design of a Prospective Observational Registry

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INTRODUCTION

- Cervical dystonia (CD), or spasmodic torticollis, is a chronic condition characterized by sustained, involuntary muscle contractions that result in abnormal postures of the head, neck, and shoulders; tremor; and pain.^{1,2}
- CD is the most common form of adult-onset focal dystonia.²
- As there is no known cure for CD, treatments have focused on relief of symptoms. The treatment of choice is botulinum toxin, which is supported by evidence from multiple clinical trials.³
- Despite years of use in CD, questions remain on the optimal treatment regimen of onabotulinumtoxinA for CD.
- Thus, CD PROBE (Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy) was designed to capture data on patients' clinical presentation, physician practices, and patient-reported treatment outcomes.

OBJECTIVE

- To describe the study design and baseline patient and disease characteristics from CD PROBE, a registry designed to capture real-world data on physician practices and patient-reported outcomes for the use of onabotulinumtoxinA in CD.

METHODS

CD PROBE is a multicenter, national, prospective, standard-of-care, observational registry of subjects with CD treated with onabotulinumtoxinA (NCT00836017).

Primary Objectives

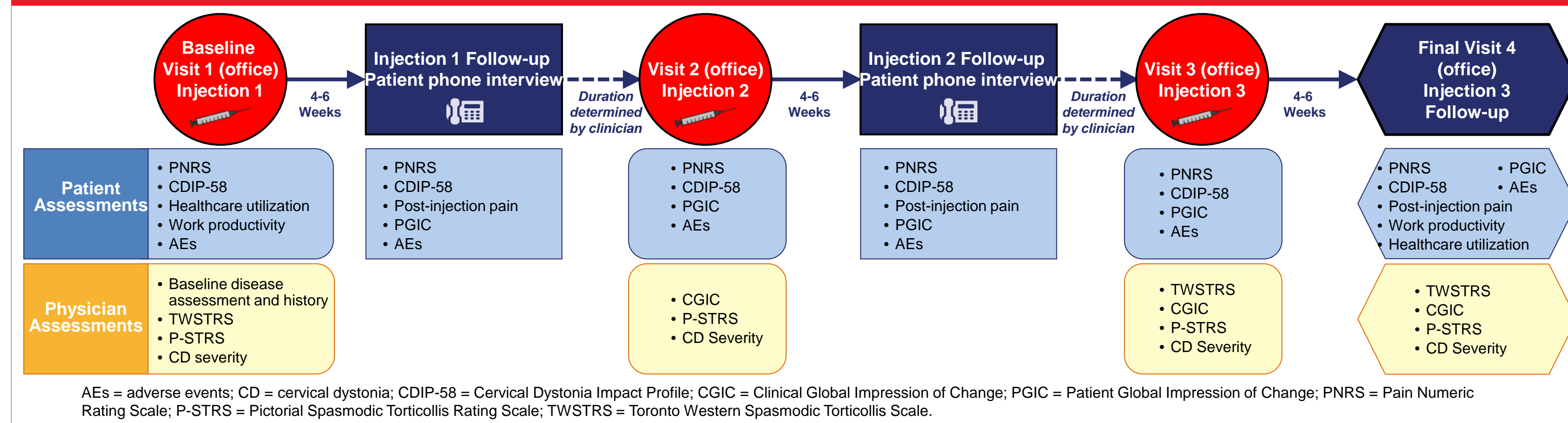
The primary objectives for CD PROBE, as predefined by the CD-PROBE Charter Committee (JJ, CA, PDC, CC, and MS) are to determine if:

- presentation of anatomical subtypes of CD correlates with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) scores and global assessment of severity rating;
- specific presentations of CD driven treatment choices
- there are clinically definable severity subtypes that correlate with CD scales/questionnaires;
- the impact of disease and treatment affects quality of life;
- there are potential predictors of outcomes.

Study Design

- The study design is presented in **Figure 1**. The study consisted of 3 injection cycles of onabotulinumtoxinA, with dosing and injection schema customary of physicians' practices.
- Patients were evaluated for safety and efficacy at each injection and at peak effect 4 to 6 weeks after injection.
- Information on physician specialties, practices, and experience with botulinum toxin for CD was collected to examine real-world treatment practices.

Figure 1. CD PROBE Study Design



Patient-Reported Outcomes

Patient Global Impression of Change (PGIC)	Post-Injection Pain Questionnaire	Work Productivity Questionnaire	Pain Numeric Rating Scale (PNRS)	Cervical Dystonia Impact Profile (CDIP-58)	Healthcare Utilization Questionnaire
<ul style="list-style-type: none"> General questionnaire that assesses the patient's perspective in the change in his/her health status on a 7-point scale Scale ranges from "very much improved" to "very much worse" 	<ul style="list-style-type: none"> 2-item questionnaire that assesses neck pain relief after onabotulinumtoxinA injection and if so, the number of days post-injection prior to pain relief 	<ul style="list-style-type: none"> Prospectively elicits information on <ul style="list-style-type: none"> Employment status Effect of CD on employment and productivity Impact of treatment with onabotulinumtoxinA injections in restoring employment status 	<ul style="list-style-type: none"> Single-item questionnaire in which the patient assesses his/her current level of pain from 0-10 	<ul style="list-style-type: none"> Validated, disease-specific 58-item questionnaire Composed of 8 subscales: <ul style="list-style-type: none"> Head and neck Pain and discomfort Upper limb activities Walking Sleep Annoyance Mood Psychological More sensitive than comparable subscales of the SF-36 and TWSTRS⁴ 	<ul style="list-style-type: none"> Developed for this study Assesses patient's use of doctor and allied healthcare visits, emergency room visits, and hospitalizations for treatment of CD symptoms

Physician Assessments

Toronto Western Spasmodic Torticollis Scale (TWSTRS)	Clinical Global Impression of Change	Pictorial Spasmodic Torticollis Rating Scale (P-STRS)	CD Severity Rating
<ul style="list-style-type: none"> Validated, disease-specific scale Scored from 0-85 Composed of 3 subscales: <ul style="list-style-type: none"> Severity (0-35) Disability (0-30) Pain (0-20) 	<ul style="list-style-type: none"> General questionnaire used to determine whether change in patient's health is clinically meaningful Captures physician's assessment of change in patient's health compared with baseline using a 7-point scale 	<ul style="list-style-type: none"> New, disease-specific tool that uses pictorial representation of anatomical position to assess CD severity Based on TWSTRS severity subscale Preliminary assessments indicate that P-STRS is valid, reliable, and sensitive to change in patient symptoms with treatment⁶ 	<ul style="list-style-type: none"> Clinician's assessment of severity (mild, moderate, severe)

Disclosure

This study and its analysis were sponsored by Allergan, Inc., Irvine, CA. Assistance for poster development was provided by Jennifer Gial, 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 Stacy received compensation from Allergan, Inc, Boehringer-Ingelheim Inc, General Electric, Novartis, Osmotica, Synosia, Schering-Plough, GlaxoSmithKline, Teva, Biogen, and Neurologix for consulting, speaker bureau, protocol steering committee, and/or safety monitoring boards; he received royalties from Informa Press and research support from Ceregene, IMPAX, Michael J. Fox Foundation, Neurotrax, Novartis, Parkinson Study Group, and Schering-Plough. Dr Charles receives income from Allergan, Inc, Ipsen, Medtronic, Pfizer, and Teva for education or consulting services. Vanderbilt University receives income from grants and contracts with Allergan, Inc, Ipsen, and Medtronic for research lead by Dr Charles. Dr Adler received consulting fees from Eli Lilly, Ipsen, Medtronic, and Merck Serono. 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, for which she was a Principal Investigator. 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.

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 to or converted into units of any other botulinum toxin products assessed with any other specific assay method.

Presented at the 15th International Congress of Parkinson's Disease and Movement Disorders, June 5-9, 2011, Toronto, Ontario, Canada

RESULTS

Baseline Results

- As of February 4, 2011, 77 investigators across the United States have participated in CD PROBE (**Figure 2**).
 - Neurologists: 68
 - Physical medicine and rehabilitation specialists: 8
 - Pain specialist: 1
- Baseline demographic and baseline disease characteristics of subjects enrolled as of February 4, 2011 are presented in **Table 1**.
 - Disease characteristics indicate that the population in this study is representative of CD patients.
- The disabling nature of CD is supported by effects on employment status, missed work, decreased productivity, and disability status at baseline (**Table 2**).

Figure 2. Map of CD PROBE Patient Enrollment



Table 2. Work Productivity Assessment of Patients at Baseline

Work Productivity Assessment	No. of Patients	Response
Employed at baseline	575	Yes: 262 (45.6)
Employed when CD symptoms began	313	Yes: 161 (51.4)
Stopped working due to CD	161	Yes: 59 (36.6)
Employment status affected by CD	262	<ul style="list-style-type: none"> Different job with less responsibility or pay: 14 (5.3) Same job, reduced hours or responsibility: 50 (19.1) No change: 198 (75.6)
Missed work in past month due to CD	261	Yes: 74 (28.4)
Number of missed work days in past month	74	5.7 ± 11.6
Decreased productivity due to CD	261	Yes: 150 (57.5)
Estimated decrease in work productivity (%)	150	72.1 ± 20.5
Have received disability benefits due to CD	262	Yes: 12 (4.6)
Duration of disability benefits (months)	12	33.2 ± 60.8

CD = cervical dystonia. Data are presented as n (%) or mean ± SD unless otherwise noted.

CONCLUSIONS

- CD PROBE is the largest observational study of CD treatment.
- Baseline demographics indicate that this cohort is representative of the general CD patient population.
- Work productivity assessment at baseline demonstrated that CD affected employment status, led to missed work days, and was associated with decreased productivity.
- This registry will provide clinical data on current treatment practices as well as physician and patient assessments of treatment with onabotulinumtoxinA, with the ultimate goal of improving treatment outcomes.

References

- Jankovic J. *Lancet Neurol*. 2006;5:864-872.
- Stacy M. *Neural Clin*. 2008;26(suppl 1):23-42.
- Simpson DM, Blitzer A, Brashear A, et al. *Neurology*. 2008;70:1699-1706.
- Cano SJ, Hobart JC, Edwards M, et al. *Neurology*. 2006;67:2230-2232.
- Papapetropoulos S, Rosa K, Comella C, Boo LM, Brin M. *Neurology*. 2011;76(suppl 4):A587.

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