CD PROBE

Cervical Dystonia Patient Registry for Observation of BOTOX® Efficacy
Preliminary Safety Data

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Background

- Cervical dystonia (CD) is one of the most common forms of adult-onset focal dystonia.
- Treatment of CD with injections of botulinum toxin has become the standard of care to provide relief from abnormal head position and pain.[1]
- OnabotulinumtoxinA (BOTOX® Allergan Inc.) was the first botulinum toxin formulation approved in the United States (1989), and in 2000 it was approved for the treatment of CD.[2]
- After 2 decades of experience, many unanswered questions remain about CD, such as how best to treat this chronic, disabling neurological condition.

Objective

- To report interim safety data related to onabotulinumtoxinA injections for CD.

Methods

- Multi-center, prospective, observational study.
- Spontaneous adverse event reporting over 2 onabotulinumtoxinA injection cycles
- Adverse events are coded to the Preferred Term using MedDRA Version 11.1.

Subjects

- Inclusion criteria:
  1. Diagnosis of CD and deemed by the physician to be a candidate for onabotulinumtoxinA therapy.
  2. Subject must be:
     a) New to principle physician's practice
     b) New to botulinum toxin therapy
     c) If previously participated in a botulinum toxin clinical trial, must not have received botulinum toxin for ≥16 weeks, and the last injection must have been directed by the clinical trial protocol.
  3. Provide informed consent and written authorization for use and release of health and research observational study information.
  4. Ability to follow study instructions and complete required study activities.
- Exclusion criteria:
  1. Planning elective surgery during the observational study period.
  2. Females who are pregnant, nursing, or planning pregnancy.
  3. History of poor cooperation or noncompliance with medical treatment.
  4. Any condition or situation which, in the physician's opinion, places the subject at significant risk, could confound the registry data, or may interfere with the subject's participation, such as unstable medical conditions.

Results

Study Participants

- 373 subjects enrolled as of April 21, 2010
- Subjects receiving 1 or 2 injections:
  - 1 injection: 366
  - 2 injections: 201
- The mean (SD) time between Injection 1 and 2 is 99.6 (18.0) days.
- Baseline demographic characteristics are summarized in **Table 1**.

Table 1. Baseline demographics

Subjects enrolled as of April 21, 2010[a]	N=373
Female (%)	291 (78.4)
Male (%)	80 (21.6)
Caucasian (%)	350 (94.3)
Age (yrs)	57.5 ± 14.7 (20–90)
Height, median inch, IQR	65 (63–68)
Weight, median lbs, IQR	156 (132–180)
BMI, median M^2, IQR	25.6 (23–29)
Age at symptoms onset, yrs	48.4 ± 16.5 (0–89)
Time from symptom onset to CD diagnosis, yrs	5.4 ± 8.7 (0–53)
Time to CD treatment after diagnosis, yrs	1.0 ± 3.4 (0–31)
TWSTRS[b], Total (range)	38.3 ± 13.6 (4–77)
Severity (range)	17.0 ± 5.4 (2–32)
Disability (range)	10.6 ± 6.6 (0–30)
Pain (range)	10.6 ± 5.2 (0–20)

[a] N for each baseline variables may vary due to missing data.
[b] Maximum scores: Severity=35, Disability=30, Pain=20, Total=85
Data presented as mean ± SD (range) unless otherwise specified
BMI = body mass index; CD = cervical dystonia; IQR: Inter-quartile range; TWSTRS = Toronto Western Spasmodic Torticollis Rating Score.

- Torticollis and laterocollis were the predominant CD components at baseline (**Figure 1**).
- The majority of CD symptoms were rated by the physician to be moderate in severity at baseline and mild at Injection 2 (**Figure 2**).

Figure 1. Predominant CD Component at Baseline

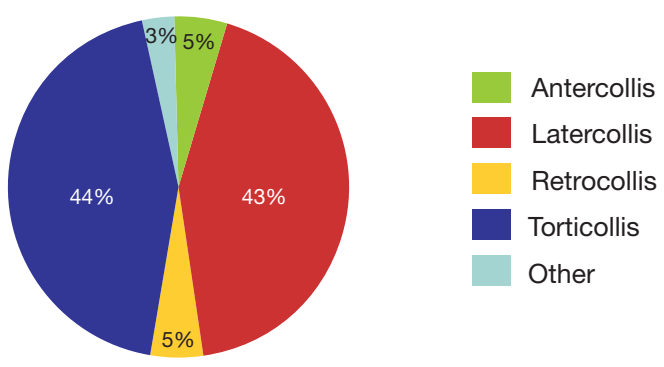
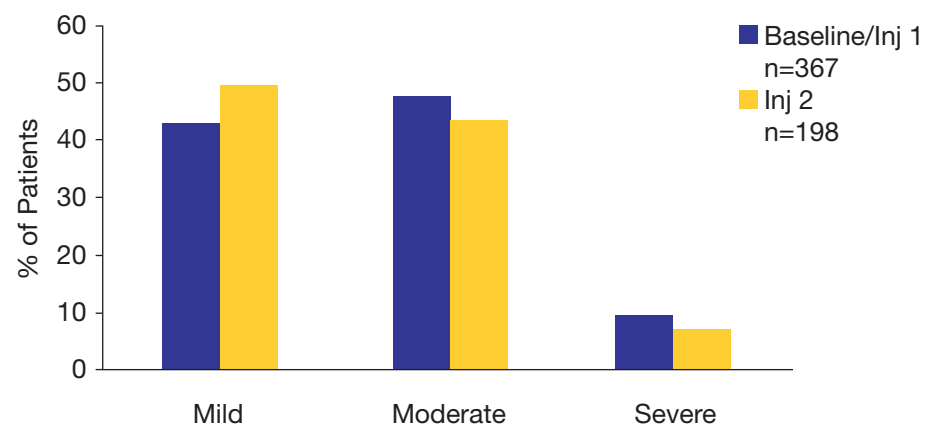


Figure 2. Physician-Rated CD Severity



Adverse Events

- Overall adverse event profile is listed in **Table 2**.
  - 48 of 373 subjects (12.9%) reported 70 adverse events.
  - 29 subjects (7.8%) reported 40 adverse events that were determined by investigators to be possibly, probably, or highly probably related to onabotulinumtoxinA (**Tables 2** and **3**).
  - 20 (5.3%) subjects reported 30 adverse events that were unlikely or not related to onabotulinumtoxinA.
  - 5 (1.3%) subjects reported serious adverse events that were unrelated or unlikely related to onabotulinumtoxinA as assessed by investigators.
- Of the treatment-related adverse events, all but 9 subjects recovered at time of analysis: 4 reported adverse events improved and 5 remained unchanged.
- 7 subjects (1.9%) withdrew due to adverse events.

Table 2. Overall Adverse Event Profile

	% Patients (N=373)	No. of Events
Total number of AEs	12.9	70
Treatment-related AEs	7.8	40
Serious AEs	1.3	5

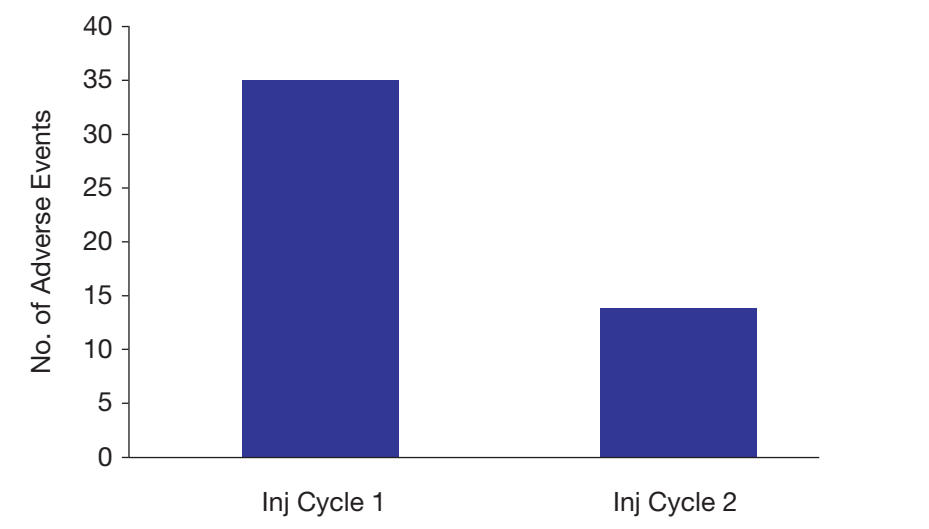
AE = adverse event.

Table 3. Treatment-Related Adverse Events Reported by >1% of Subjects

Adverse Events	% Patients (N=373)	No. of Events
Gastrointestinal disorders		
Dysphagia	2.1	8
Musculoskeletal and connective tissue disorders		
Muscle weakness (neck)	3.2	12
Neck pain	1.1	4

- The number of adverse events decreased over treatment cycles for subjects who have received 2 onabotulinumtoxinA injections (**Figure 3**).

Figure 3. Number of Adverse Events Over 2 Treatment Cycles



Conclusions

- Adverse events reported in this observational registry are consistent with the known adverse events related to onabotulinumtoxinA injection for CD.
- Additional safety information will become available as more subjects enroll.

References

1. Simpson DM, et al. Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;70:1699-706
2. BOTOX® Prescribing Information. Allergan Inc. 2010.

CD PROBE Study Group

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- Dr Comella has served as a consultant for Merz Pharmaceuticals, Jazz Pharmaceuticals, Valeant, Cephalon, Allergan Inc., UCB, Eisai, Boehringer-Ingelheim Inc., and Ipsen Limited; she has received research grants from Allergan Inc., Ipsen Limited, Boehringer-Ingelheim Inc., Merz Pharmaceuticals, Parkinson Study Group, National Institutes of Health (NIH), and Dystonia Study Group.
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- Dr Kurth receives personal compensation from Allergan Inc. for consulting services.
- Dr Brin and Dr Boo are employees of Allergan Inc. Dr Brin receives stock and stock options from Allergan Inc.

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