CD PROBE

Cervical Dystonia Patient Registry for Observation of BOTOX® Efficacy

CD Impact on Quality of Life and Patient-Reported Outcome

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Background

- Cervical dystonia (CD), also referred to as spasmodic torticollis, 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 the abnormal head position and pain.[1]
- OnabotulinumtoxinA (BOTOX®, Allergan Inc.) was the first botulinum toxin formulation approved in the United States (1989); in 2000 it was approved for 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

- This presentation is an interim report on impact of onabotulinumtoxinA on quality of life and subject-reported outcomes after 2 injection cycles.

Methods

- Multi-center, prospective, observational study.
- Phone interviews completed 4–6 weeks after onabotulinumtoxinA Injections 1 (Peak 1) and 2 (Peak 2).
- Patient-reported Pain Numerical Rating Scale (NRS), Patient Global Impression of Change (PGIC), and Cervical Dystonia Impact Profile (CDIP-58).

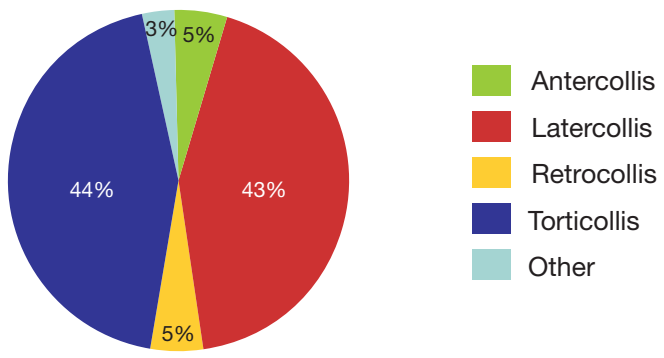
Subjects

- 373 subjects have enrolled as of April 21, 2010.
- Inclusion criteria:
  1. Diagnosis of CD and deemed by the physician to be a candidate for onabotulinumtoxinA therapy.
  2. Subject criteria:
     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 received must have been directed by the clinical trial protocol.
     d) May be included if they meet criteria A only, B only, or C only.
  3. Provide informed consent and written authorization for use and release of health and research observational study information (as applicable).
  4. Ability to follow study instructions and complete required study activities.
- Exclusion criteria:
  1. Subjects planning elective surgery during the observational study period.
  2. Females who are pregnant, nursing, or planning a 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

- The number of subjects who have received 1 or 2 injections are as follows:
  - 1 injection: 366
  - 2 injections: 201
- The mean (SD) time between Injection 1 and 2 is 99.6 (18.0) days.
- Torticollis and laterocollis were the predominant CD components at baseline (**Figure 1**).

Figure 1. Predominant CD Component at Baseline



- 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 2. Physician-Rated CD Severity

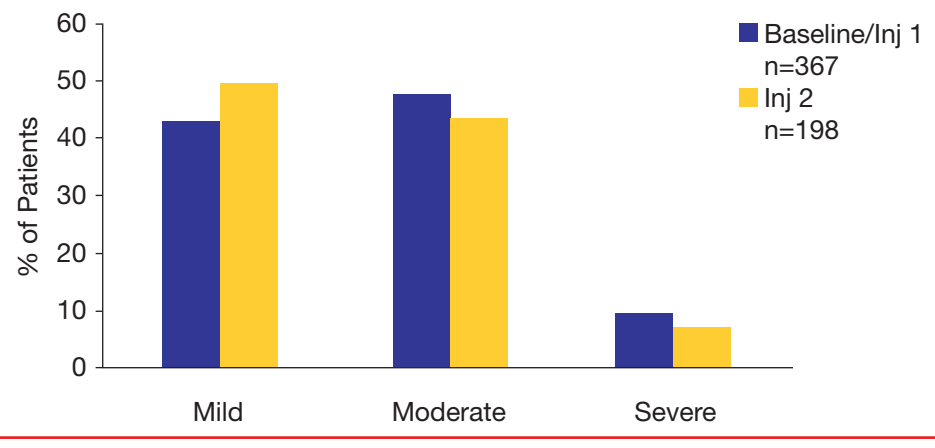


Table 1. Baseline demographics

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 Scale.

- Physician-rated CD severity correlated with CDIP-58 on the following subscales at baseline (**Table 2**):
  - Head and neck
  - Upper limb activities
  - Walking
  - Annoyance
  - Mood
  - Psychosocial

Table 2. Correlation of CDIP-58 and Physician-Rated CD Severity

CDIP-58 subscales	Mild (n=156)	Moderate (n=175)	Severe (n=35)
Head and Neck*	61.6 ± 16.4	72.5 ± 19.3	84.5 ± 15.5
Pain and Discomfort	70.3 ± 22.6	69.5 ± 23.0	73.0 ± 21.0
Upper Limb Activities*	47.1 ± 21.5	53.6 ± 22.4	64.1 ± 25.4
Walking*	37.4 ± 21.5	47.1 ± 24.9	58.3 ± 27.2
Sleep	57.2 ± 26.0	56.3 ± 28.1	63.0 ± 26.7
Annoyance*	52.5 ± 21.3	59.8 ± 20.6	66.3 ± 22.0
Mood*	44.7 ± 20.7	50.5 ± 22.1	54.7 ± 25.0
Psychosocial*	43.0 ± 21.6	54.2 ± 22.0	67.5 ± 24.0

Data presented as mean ± SD. Each subscale is scaled to a maximum of 100.
ANOVA = analysis of variance; CD = cervical dystonia; CDIP-58 = Cervical Dystonia Impact Profile; SD = standard deviation. * p<0.0005 (p-values by ANOVA F-test)

- Physician-rated CD severity correlated with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total and the following TWSTRS domains at baseline (**Table 3**):
  - Severity
  - Disability

Table 3. Correlation of TWSTRS and Physician-Rated CD Severity

TWSTRS	Mild (n=157)	Moderate (n=174)	Severe (n=35)
Total*	31.6 ± 11.7	41.9 ± 11.9	51.1 ±13.7
Severity*	13.5 ± 4.5	18.9 ± 4.3	23.5 ± 5.0
Disability*	8.0 ± 5.7	11.9 ± 6.3	16.5 ± 6.8
Pain	10.2 ± 5.2	11.0 ± 5.0	11.1 ± 5.7

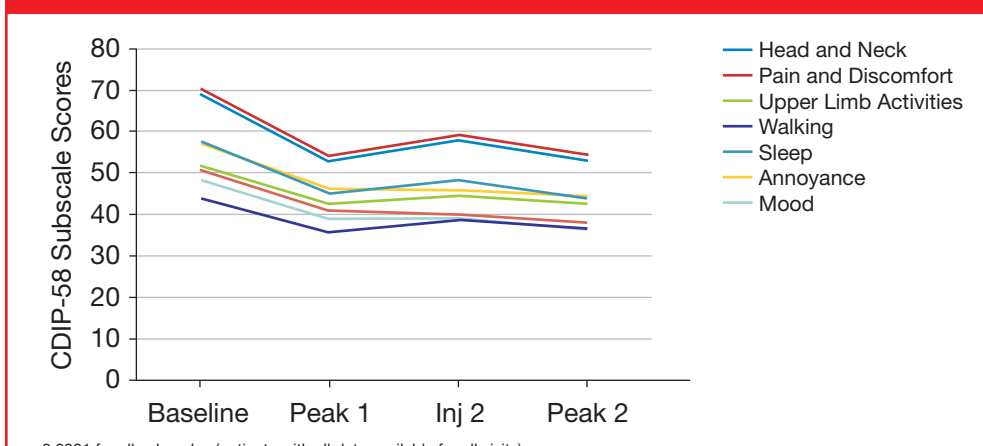
Data presented as mean ± SD.
Maximum scores: Severity=35, Disability=30, Pain=20, Total=85.
ANOVA = analysis of variance; CD = cervical dystonia; SD = standard deviation; TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale.
* p<0.0001 (p-values by ANOVA F-test)

- PGIC and all CDIP-58 subscales continued to improve over 2 treatment cycles (**Table 4, Figure 3**).

Table 4. Patient-Rated Global Impression of Change

PGIC	Peak 1 (n=322)	Inj 2 (n=199)	Peak 2 (n=164)
Very much improved	12.7	13.1	17.7
Much improved	31.7	34.7	31.7
Minimally improved	32.6	34.7	36.0
No change	13.4	14.1	10.4
Minimally worse	4.7	3.5	1.8
Much worse	3.4	0	1.8
Very much worse	1.6	0	0.6

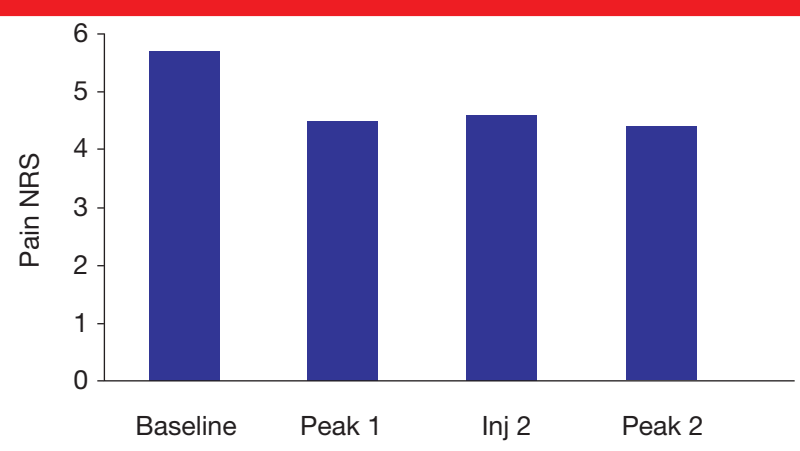
Figure 3. CDIP-58



p<0.0001 for all subscales (patients with all data available for all visits)

- 90.4% of subjects reported some pain due to CD at baseline.
- For subjects who reported pain at baseline and where data are available:
  - Pain NRS continued to decrease from baseline to Peak 2 after 2 onabotulinumtoxinA injections (**Figure 4**).
  - The median days to pain relief reported by subjects were 7 days (range 4–10) after first injection and 6 days (range 4–10) after second injection.
- The correlations between Pain NRS–TWSTRS Pain (r=0.77), Pain NRS–CDIP-58 Pain (r=0.55), and TWSTRS Pain–CDIP-58 Pain (r=0.63) are high at baseline (p<0.0001 for all 3).

Figure 4. Pain NRS



p<0.0001 by repeated measures analysis of variance

Conclusions

- Subjects treated with repeated onabotulinumtoxinA injections for CD reported sustained reduction in neck pain and improvement in quality of life as measured by CDIP-58.
- A majority of subjects reported CD conditions improved as assessed by PGIC after 2 onabotulinumtoxinA injections.
- Physician-rated CD severity correlated with most CDIP-58 subscales and TWSTRS domains.
- Patterns of response will become more apparent as additional patients enter this large study.

References

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2. BOTOX® Prescribing Information. Allergan Inc. 2010.

CD PROBE Study Group

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- Dr Charles receives personal compensation from Allergan Inc. and Medtronic for speaking, consulting, or serving on scientific advisory boards; Vanderbilt University receives income from Allergan Inc. and Medtronic for research led by Dr Charles.
- 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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