

Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy (CD PROBE): Treatment Patterns and Subject Disposition



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INTRODUCTION

- Cervical dystonia (CD) is a chronic condition characterized by involuntary muscular contraction, resulting in abnormal head, neck, and shoulder movements and/or postures; tremor; and pain¹
- Treatments for CD focus on the relief of symptoms, and botulinum toxin (BoNT) is the treatment of choice^{2,3}
 - The safety and efficacy of BoNT were established in randomized controlled clinical trials⁴
 - However, few studies have described current real-world BoNT treatment practices
- Thus, an observational, open-label multicenter, prospective registry (CD PROBE) was designed to assess the safety, effectiveness, and utilization patterns of onabotulinumtoxinA as a treatment for CD in clinical practice

OBJECTIVE

- To report the subject disposition and onabotulinumtoxinA treatment patterns from CD PROBE

METHODS

- CD PROBE was an open-label multicenter, prospective, observational registry designed to capture real-world practices and outcomes for onabotulinumtoxinA CD treatment in the US⁵
- Subjects diagnosed with CD and identified by the physician as candidates for onabotulinumtoxinA therapy were: new to principal physician's practice, new to BoNT therapy, or if previously participated in a BoNT clinical trial, must not have received BoNT for ≥16 weeks
- Subjects could receive 3 onabotulinumtoxinA treatment sessions
 - Dilution, dosing, use of injection guidance, and muscles injected with onabotulinumtoxinA were at the full discretion of the treating physician
 - Treatment intervals, and thus assessment intervals, were variable because the time to the next treatment session was determined by the physician
- Subject disposition as well as onabotulinumtoxinA treatment characteristics and paradigm will be presented here
- Adverse events (AEs) were assessed throughout the study

RESULTS

Subject disposition (Figure 1)

- Over 44 months, 1046 subjects were enrolled in CD PROBE
 - 1041 subjects received at least one onabotulinumtoxinA treatment
 - 636 (60.8%) subjects completed all 3 treatment sessions
 - 502 (48.0%) subjects completed all 3 treatment sessions and final assessment visit
- A total of 544 subjects withdrew over the course of the study
 - Approximately 20% of subjects withdrew after each treatment session
 - The most common reasons for withdrawal were lost to follow up (23.2%), withdrew consent (9.0%), lack of response (8.1%), AE (3.1%), and physician discretion (2.0%)
 - There were 4 deaths in the study, none of which were considered to be related to treatment

Baseline characteristics (Table 1)

- Mean age was 58.0 ± 14.7 y
- 74.4% of subjects were female
- Most predominant postures were torticollis (47.5%) and laterocollis (38.9%)
- Over half of subjects' CD (52.7%) was rated as moderate severity
- 63.5% of subjects were toxin naïve prior to treatment session 1

Treatment intervals

- The mean time between onabotulinumtoxinA treatment sessions 1 and 2 was 14.6 ± 4.1 weeks, with a range of 0.7–59.0 weeks
- The mean time between treatment sessions 2 and 3 was 15.1 ± 5.2 weeks, with a range of 7.3–81.9 weeks

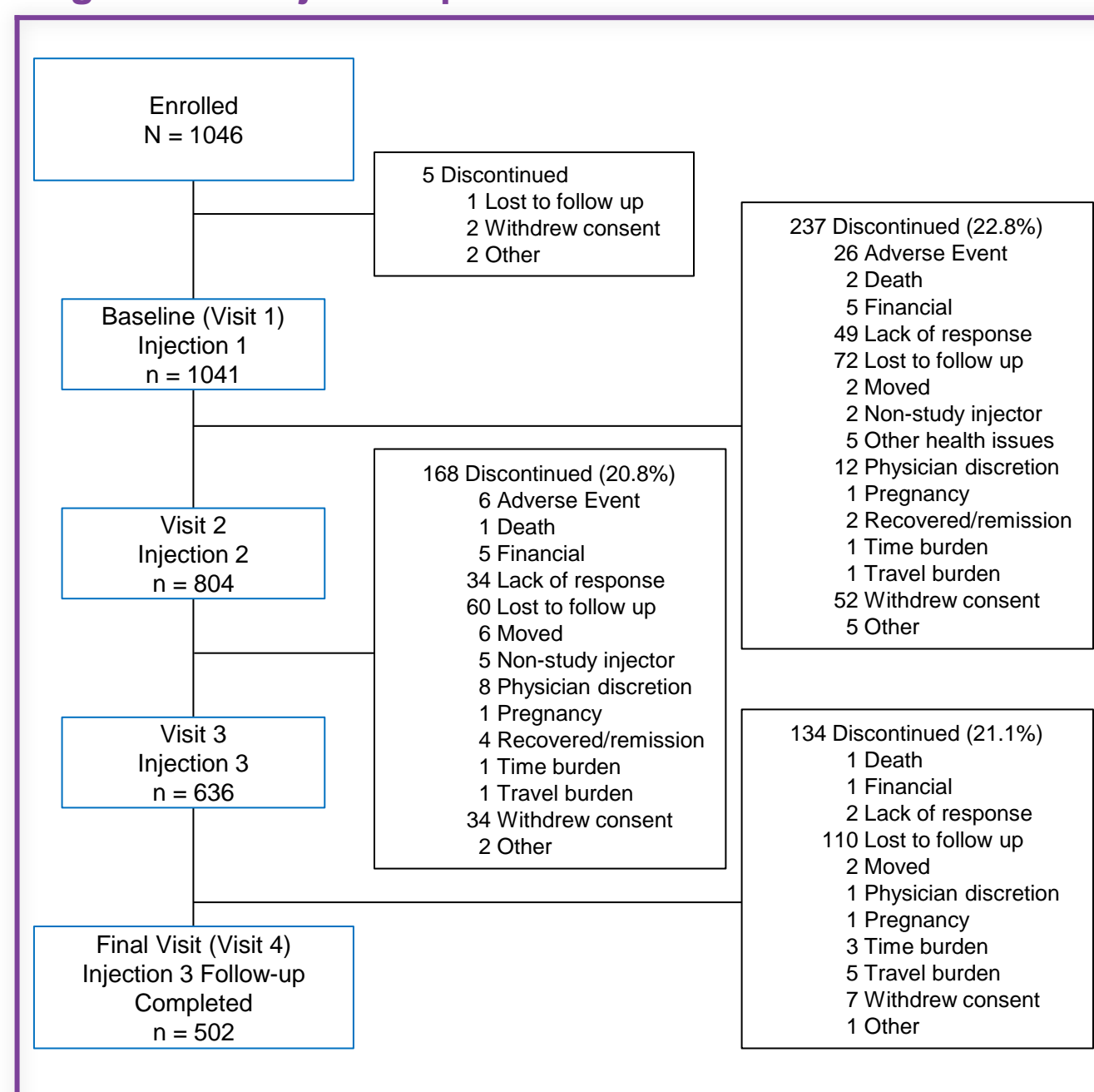
Treatment characteristics (Table 2)

- Data from almost 2500 onabotulinumtoxinA treatment sessions were captured in CD PROBE
- Overall, a mean of 9.3 ± 5.7 onabotulinumtoxinA injections were administered in a mean of 4.1 ± 1.4 muscles per treatment session
 - Mean number of total injections increased from sessions 1 to 3 (8.7 ± 5.2 to 10.0 ± 6.2)
- The mean total dose of onabotulinumtoxinA across all 3 treatment sessions was 189.8 ± 87.1
 - Mean doses increased over the treatment sessions, but dilution was consistent
- Electromyography (EMG) was the most commonly used injection guidance (73.3%) and was consistent across treatment sessions
- Overall, the most commonly injected muscles were the splenius capitis (86.1%), sternocleidomastoid (76.9%), levator scapulae (67.3%), and trapezius (63.6%) and were similar across all 3 sessions
- The least commonly injected muscles (<1%) were the pectoralis, masseter, procerus, and suboccipitalis

Treatment paradigm (Table 3)

- The majority of subjects (63.7%) received 101–200U onabotulinumtoxinA
 - 31.8% of subjects received a dose ≤100U
- Most subjects (56.2%) received 7-12 injections per treatment session, which most commonly involved 3-5 muscles (83.2%)
- Most subjects (77.9%) and treatment sessions (61.0%) had a treatment interval of >13 weeks
 - 25.7% of subjects had a treatment interval >16 weeks
 - Less than 5% of subjects and treatment sessions had a treatment interval of <11 weeks

Figure 1. Subject Disposition



The time between treatment sessions varied as determined by each clinician. The final visit occurred 4-6 weeks after the third treatment session.

Table 1. Baseline Demographics and Disease Characteristics

| Characteristic | N=1041 |
|--|-------------|
| Age, y | 58.0 ± 14.7 |
| Female gender, n (%) | 774 (74.4) |
| Race, n (%) | |
| White | 961 (92.3) |
| Non-white | 80 (7.7) |
| Body mass index ^a , kg/m ² | 26.6 ± 5.4 |
| Predominant Subtype ^a , n (%) | |
| Anterocollis | 59 (5.7) |
| Laterocollis | 404 (38.9) |
| Retrocollis | 55 (5.3) |
| Torticollis | 494 (47.5) |
| Other | 27 (2.6) |
| Severity ^a , n (%) | |
| Mild | 345 (33.2) |
| Moderate | 548 (52.7) |
| Severe | 146 (14.1) |
| Age at symptom onset, y | 49.0 ± 16.7 |
| Time from CD onset to diagnosis, y | 5.0 ± 8.1 |
| Time from diagnosis to treatment, y | 1.1 ± 4.5 |
| Prior treatment with botulinum toxin, n (%) | 380 (36.5) |

Data are presented as mean ± standard deviation unless otherwise indicated. ^aData were not available for 76 subjects. ^bData were not available for 2 subjects.

Table 2. Summary of Treatment Characteristics

| Characteristic | Treatment Session | | | Overall (N=2481) |
|---|-------------------|--------------|--------------|------------------|
| | 1 (n=1041) | 2 (n=804) | 3 (n=636) | |
| Total number of injections, n | | | | |
| Mean ± SD | 8.7 ± 5.2 | 9.5 ± 5.8 | 10.0 ± 6.2 | 9.3 ± 5.7 |
| Range | 1.0, 45.0 | 1.0, 41.0 | 0.0, 40.0 | 0.0, 45.0 |
| Total number of muscles injected, n | | | | |
| Mean ± SD | 4.0 ± 1.4 | 4.1 ± 1.5 | 4.3 ± 1.5 | 4.1 ± 1.4 |
| Range | 0.0, 11.0 | 1.0, 11.0 | 0.0, 13.0 | 0.0, 13.0 |
| Total dose ^a , U | | | | |
| Mean ± SD | 171.6 ± 78.9 | 199.6 ± 88.3 | 207.2 ± 93.0 | 189.8 ± 87.1 |
| Range | 15.0, 500.0 | 20.0, 517.7 | 25.0, 519.5 | 15.0, 519.5 |
| Dilution ^a , n (%) | | | | |
| 1 mL/100U vial | 681 (69.7) | 538 (71.3) | 424 (70.8) | 1643 (70.5) |
| 2 mL/100U vial | 257 (26.3) | 187 (24.8) | 146 (24.4) | 590 (25.3) |
| Other | 39 (4.0) | 30 (4.0) | 29 (4.8) | 98 (4.2) |
| Injection guidance ^b , n (%) | | | | |
| Anatomical ^c | 269 (25.8) | 217 (27.0) | 174 (27.4) | 660 (26.6) |
| Electromyography | 772 (74.2) | 585 (72.8) | 459 (72.4) | 1816 (73.3) |
| Ultrasound | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Other | 0 (0) | 2 (0.2) | 1 (0.2) | 3 (0.1) |
| Muscle injected ^d , n (%) | | | | |
| Splenius capitis | 901 (86.6) | 683 (85.0) | 551 (86.6) | 2135 (86.1) |
| Sternocleidomastoid | 788 (75.7) | 621 (77.2) | 499 (78.5) | 1908 (76.9) |
| Levator scapulae | 693 (66.6) | 543 (67.5) | 433 (68.1) | 1669 (67.3) |
| Trapezius | 654 (62.8) | 517 (64.3) | 407 (64.0) | 1578 (63.6) |
| Scalenes | 319 (30.6) | 268 (33.3) | 227 (35.7) | 814 (32.8) |
| Semispinalis | 299 (28.7) | 236 (29.4) | 199 (31.3) | 734 (29.6) |
| Longissimus | 188 (18.1) | 148 (18.4) | 128 (20.1) | 464 (18.7) |
| Splenius cervicis | 107 (10.3) | 80 (10.0) | 67 (10.5) | 254 (10.2) |
| Other ^e | 187 (18.0) | 230 (28.6) | 225 (35.4) | 642 (25.9) |

^aData were not available for 64, 49, and 37 subjects for treatment sessions 1, 2, and 3, respectively. ^bData were not available for 2 subjects for treatment session 3. ^cInspection and palpation. ^dIncludes muscles written in by physician (cervical paraspinal muscles, corrugator supercilii, frontalis, masseter, obliquus capitis inferior muscle, pectoralis, platismus, procerus, rhomboids, suboccipitalis, and temporalis); each was <10%.

Table 3. Treatment Paradigm

| Characteristic | Total Subjects (N=1041) | Total Treatment Sessions (N=2481) |
|------------------------|-------------------------|-----------------------------------|
| Dose ^a , U | | |
| ≤100 | 315 (31.8) | 486 (20.8) |
| 101-200 | 631 (63.7) | 1085 (46.5) |
| 201-300 | 344 (34.7) | 566 (24.3) |
| >300 | 108 (10.9) | 176 (7.6) |
| Injection sites | | |
| <7 | 510 (49.0) | 957 (38.6) |
| 7-12 | 585 (56.2) | 1032 (41.6) |
| >12 | 253 (24.3) | 492 (19.8) |
| Injected muscles | | |
| <3 | 176 (16.9) | 297 (12.0) |
| 3-5 | 866 (83.2) | 1839 (74.1) |
| >5 | 196 (18.8) | 345 (13.9) |
| Dosing interval, weeks | | |
| <11 | 39 (4.8) | 46 (3.2) |
| >13 | 627 (77.9) | 879 (61.0) |
| >16 | 207 (25.7) | 246 (17.1) |

Data are presented as n (%). ^aData were not available for 50 subjects and 150 treatment sessions.

Adverse events

- A total of 515 AEs were reported in 273 (26.2%) subjects, 46 serious AEs were reported in 33 (3.2%) subjects, and 315 treatment-related AEs were reported in 185 (17.8%) subjects
- More detailed safety data as well as effectiveness data are presented in poster P7.069, "Treatment Outcomes in Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy (CD PROBE)"

DISCUSSION & CONCLUSIONS

- CD PROBE is the largest registry of CD treatment experience, and defined subject demographics and disease characteristics
- We recognize that the frequency of discontinuations was relatively high compared with other CD clinical trials; however, this is not entirely unexpected given CD PROBE's registry design. Registries often enroll a broad subject population, have a long study duration, do not have protocol-defined treatment schedule.⁶ Also, registries do not provide study drug and so are limited by reimbursement and other financial challenges that may adversely impact retention.
- In summary, the mean onabotulinumtoxinA doses increased over the treatment sessions from 171.6U to 207.2U. The mean dose of 189.8 ± 87.1U is lower than maximum recommended dose,⁷ but is comparable to the mean dose of 187.0 ± 76.5U in another observational study,⁸ and is less than doses previously reported as typical in clinical practice.³ Furthermore, data shows that most physicians use EMG and >75% of subjects have a dosing interval of >13 weeks

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DISCLOSURES

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