P7.062

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

David Charles[1], Joseph Jankovic[2], Cynthia Comella[3], Mark Stacy[4], Marc Schwartz[5], Aubrey Manack[6], Mitchell F. Brin[6,7]

[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]Baylor College of Medicine, Houston, TX, USA; [3]Rush University Medical Center, Chicago, IL, USA; [4]Duke University Medical Center, Durham, NC, USA; [5]MedNet Solutions, Minnetonka, MN, USA; [6]Allergan, Inc., Irvine, CA, USA; [7]University of California, Irvine, CA, USA

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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 pain[1]
- 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 trials[4]
  - 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 US[5]
- 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

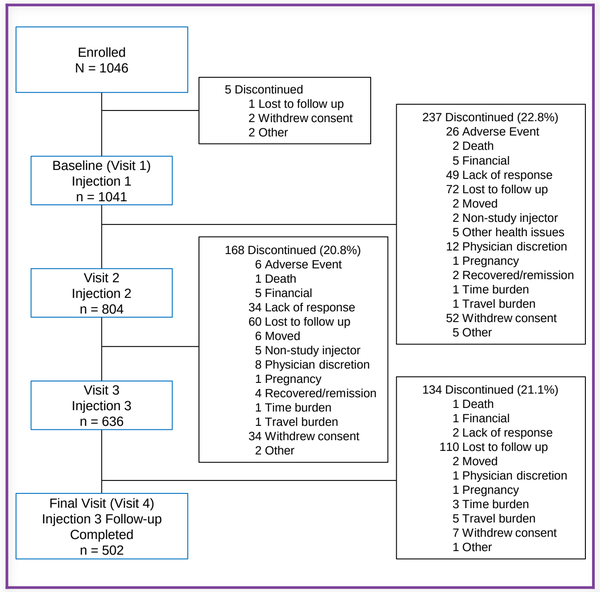
Treatment characteristics (Table 2)

- 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[b], n (%)	
Anterocollis	59 (5.7)
Laterocollis	404 (38.9)
Retrocollis	55 (5.3)
Torticollis	494 (47.5)
Other	27 (2.6)
Severity[b], 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. [a]Data were not available for 76 subjects. [b]Data were not available for 2 subjects.

Table 2. Summary of Treatment Characteristics

Characteristic	Treatment Session 1 (n=1041)	Treatment Session 2 (n=804)	Treatment Session 3 (n=636)	Overall (N=2481)
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 capitus	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[†]	187 (18.0)	230 (28.6)	225 (35.4)	642 (25.9)

[a]Data were not available for 64, 49, and 37 subjects for treatment sessions 1, 2, and 3, respectively. [b]Data were not available for 2 subjects for treatment session 3. [c]Inspection and palpation. [d]Includes 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 (%). [a]Data 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

REFERENCES

1. Albanese A, et al. *Mov Disord.* 2013;28:863-873. 2. Simpson DM, et al. *Neurology.* 2008;70:1699-1706. 3. Ramirez-Castaneda J and Jankovic J. *Toxins* (Basel). 2013;5:249-266. 4. Charles D, et al. *Clin Neuropharmacol.* 2012;35:208-214. 5. Jankovic J, et al. *BMC Neurol.* 2011;11:140. 6. Manack A, et al. In: Lunet N, ed. *Epidemiology - Current Perspectives on Research and Practice*: Intech, 2012. 7. BOTOX® Summary of Product Characteristics. Marlow, UK: Allergan Ltd.; 2013. 8. Brin MF, et al. *Mov Disord.* 2008;23:1353–1360.

DISCLOSURES

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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.

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