Sustained Efficacy and Tolerability of OnabotulinumtoxinA in Naive and Non-naive Patients with Cervical Dystonia: Preliminary Completer Analysis from CD-PROBE

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CONCLUSIONS

In this preliminary completer analysis, repeat treatments with onabotulinumtoxinA at consistent intervals attenuated disease severity, regardless of prior botulinum toxin exposure

OnabotulinumtoxinA was well tolerated in naive and non-naive patients

RESULTS

- In total, 350 patients were included in this analysis; 212 were naive and 138 non-naive to botulinum toxin treatment at baseline
- In general, baseline demographics and CD history were well balanced between naive and non-naive patients (**Table 1**)
- Overall, mean (standard deviation, SD) age was 57.3 (14.7) years, the majority of the completers in this study were female (74.9%), and most were white (94.6%)
- Time from disease onset to diagnosis was 5.1 ± 7.7 years
- Very few of the completers in this study had prior procedures or treatments for CD

Table 1. Baseline Demographics and Disease Characteristics

	Naive (n=212)	Non-naive (n=138)	Total (N=350)
Age, years, mean (SD)	57.8 (15.7)	56.7 (13.0)	57.3 (14.7)
Female, n (%)	155 (73.1)	107 (77.5)	262 (74.9)
Race/ethnicity, n (%)			
White	201 (94.8)	130 (94.2)	331 (94.6)
Hispanic	5 (2.4)	3 (2.2)	8 (2.3)
Asian	4 (1.9)	2 (1.4)	6 (1.7)
Black	2 (0.9)	3 (2.2)	5 (1.4)
Time from CD onset to CD diagnosis, years, mean (SD)	5.7 (8.1)	4.0 (7.0)	5.1 (7.7)
Past treatments, n (%)			
Muscle resection surgery	0	0	0
Phenol injection	0	0	0
Deep brain stimulation	0	2 (1.4)	2 (0.6)
Thalamotomy	0	0	0
Surgical denervation	1 (0.5)	5 (3.6)	6 (1.7)
None of the above	211 (99.5)	131 (94.9)	342 (97.7)

CD, cervical dystonia; SD, standard deviation

- Shifts in severity following each treatment with onabotulinumtoxinA were generally similar between naive and non-naive patients (**Table 2**)
- Following each injection most patients with mild or moderate symptoms maintained or improved their severity scores as determined by specific, validated assessments of CD
- Those patients with the highest severity scores, 30.0%–66.7%, shifted to a lower severity score across the 3 injection cycles; this was similar between naive and non-naive patients

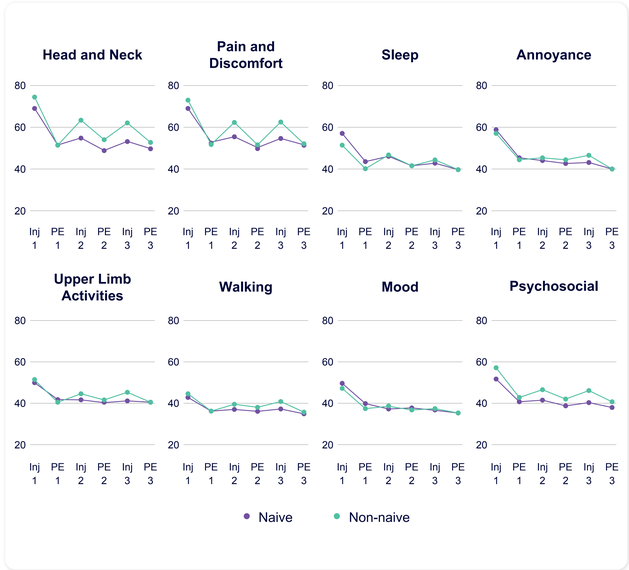
Table 2. Shift in CD Severity by Treatment Cycle

	Botulinum Toxin Naive n/n (%)				Botulinum Toxin Non-naive n/n (%)			
		Injection 2 CD Severity				Injection 2 CD Severity		
Injection 1 CD Severity	Total (n=212)	Mild (n=105)	Moderate (n=97)	Severe (n=10)	Total (n=138)	Mild (n=49)	Moderate (n=75)	Severe (n=14)
Mild	79/212 (37.3)	62/79 (78.5)	17/79 (21.5)	0/79 (0)	35/138 (25.4)	29/35 (82.9)	4/35 (11.4)	2/35 (5.7)
Moderate	111/212 (52.4)	38/111 (34.2)	71/111 (64.0)	2/111 (1.8)	79/138 (57.2)	20/79 (25.3)	55/79 (69.6)	4/79 (5.1)
Severe	22/212 (10.4)	5/22 (22.7)	9/22 (40.9)	8/22 (36.4)	24/138 (17.4)	0/24 (0)	16/24 (66.7)	8/24 (33.3)
		Injection 3 CD Severity				Injection 3 CD Severity		
Injection 2 CD Severity	Total (n=212)	Mild (n=110)	Moderate (n=89)	Severe (n=13)	Total (n=138)	Mild (n=58)	Moderate (n=66)	Severe (n=14)
Mild	105/212 (49.5)	85/105 (81.0)	20/105 (19.0)	0/105 (0)	49/138 (35.5)	42/49 (85.7)	7/49 (14.3)	0/49 (0)
Moderate	97/212 (45.8)	24/97 (24.7)	67/97 (69.1)	6/97 (6.2)	75/138 (54.3)	16/75 (21.3)	52/75 (69.3)	7/75 (9.3)
Severe	10/212 (4.7)	1/10 (10.0)	2/10 (20.0)	7/10 (70.0)	14/138 (10.1)	0/14 (0)	7/14 (50.0)	7/14 (50.0)
		Peak Effect Office Visit 3/ Exit CD Severity				Peak Effect Office Visit 3/ Exit CD Severity		
Injection 3 CD Severity	Total (n=212)	Mild (n=131)	Moderate (n=71)	Severe (n=10)	Total (n=138)	Mild (n=81)	Moderate (n=48)	Severe (n=9)
Mild	110/212 (51.9)	97/110 (88.2)	12/110 (10.9)	1/110 (0.9)	58/138 (42.0)	54/58 (93.1)	4/58 (6.9)	0/58 (0)
Moderate	89/212 (42.0)	34/89 (38.2)	54/89 (60.7)	1/89 (1.1)	66/138 (47.8)	25/66 (37.9)	40/66 (60.6)	1/66 (1.5)
Severe	13/212 (6.1)	0/13 (0)	5/13 (38.5)	8/13 (61.5)	14/138 (10.1)	2/14 (14.3)	4/14 (28.6)	8/14 (57.1)

CD, cervical dystonia

- These results were confirmed with sustained improvements seen in all CDIP-58 subscales that were generally similar between naive and non-naive patients (**Figure 1**)
- In non-naive patients, improvements in the "head and neck" and "pain and discomfort" subscales appeared to wane slightly at later timepoints, although still improved from baseline

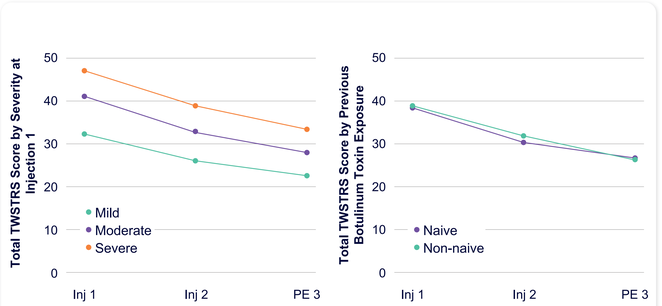
Figure 1. CDIP-58 Subscales Measured at Each Visit in Botulinum Toxin Naive and Non-naive Patients



CDIP-58, Cervical Dystonia Impact Profile; inj, injection; PE, peak effect

- Total TWSTRS scores improved regardless of severity and in both naive and non-naive patients (**Figure 2**)
- The median time interval between injections was similar between naive (93.0–98.0 days) and non-naive patients (96.0–97.0 days)
- Across the 3 treatments, onabotulinumtoxinA doses administered tended to be lower in naive (mean ± SD; 143 ± 64 to 181 ± 85U) than non-naive patients (223 ± 83 to 244 ± 93U)

Figure 2. Improvement in TWSTRS Scores



Inj, injection; PE, peak effect; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale

Safety

- The most common AEs (≥2% of patients) were muscular weakness, dysphagia, headache, and neck pain and were similar between naive and non-naive patients (**Table 3**)
- Two serious AEs of syncope were reported in the naive cohort and 2 of hip fracture in the non-naive cohort

Table 3. Most Common Adverse Events (≥2% of Patients)

Adverse Event, n (%)	Naive (n=212)	Non-naive (n=138)	Total (N=350)
Muscular Weakness			
All	16 (7.5)	13 (9.4)	29 (8.3)
Treatment-related	16 (7.5)	13 (9.4)	29 (8.3)
Dysphagia			
All	15 (7.1)	14 (10.1)	29 (8.3)
Treatment-related	14 (6.6)	14 (10.1)	28 (8.0)
Headache			
All	7 (3.3)	3 (2.2)	10 (2.9)
Treatment-related	6 (2.8)	2 (1.4)	8 (2.3)
Neck Pain			
All	7 (3.3)	2 (1.4)	9 (2.6)
Treatment-related	6 (2.8)	2 (1.4)	8 (2.3)

INTRODUCTION

- Cervical dystonia (CD) is the most common form of adult-onset focal dystonia[1]
- Treatment with botulinum toxin is the standard of care in this patient population
- Primary results from CD-PROBE (Cervical Dystonia – Patient Registry for Observation of BOTOX® Efficacy) demonstrated a robust improvement in clinical ratings in patients with CD after onabotulinumtoxinA treatment and that onabotulinumtoxinA was well tolerated in this patient population[2]

Aim

- This was a preliminary completer analysis of CD-PROBE designed to evaluate the sustained effectiveness and tolerability of onabotulinumtoxinA in patients who were naive or non-naive to botulinum toxin at enrollment

METHODS

- CD-PROBE was a multicenter, prospective, observational study of 3 treatments of onabotulinumtoxinA for CD
- Patients were stratified by prior exposure to any botulinum toxin (naive and non-naive)
- Time to next treatment was determined by standard of care at each physician's practice
- Follow-up: by telephone 4–6 weeks after the first and second treatments; office visit 4–6 weeks after the third treatment
- This analysis includes patients who completed all treatment cycles with data at each timepoint
- Assessments included shift in severity between injections, Cervical Dystonia Impact Profile (CDIP-58), total Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) scores, interval between injections, and total dose
- Adverse events (AEs) were also recorded

ADDL INFO

AUTHOR DISCLOSURES

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P Agarwal has served as a speaker/consultant for Acadia, Accorda, Adamas Pharmaceuticals, Amneal, Kyowa Kirin, Sunovion, and US WorldMeds.

M Schwartz is the founder of MS Biostatistics, LLC, and was formerly an employee of MedNet Solutions Inc., which was contracted by Allergan to provide biostatistical services for the study.

A Zuzek is an employee of AbbVie and may hold AbbVie stock.

A Patel has served as a consultant and speaker for Allergan, an AbbVie company, and Ipsen, and as a consultant for Revance. He has received research funding for clinical trials from Allergan, an AbbVie company, Ipsen, and Revance.

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