ASPEN-1: A Phase 3 Trial Evaluating the Efficacy, Duration of Effect, and Safety of DaxibotulinumtoxinA for Injection in the Treatment of Cervical Dystonia

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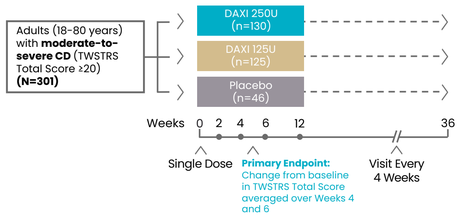
Introduction and Methods

- DaxibotulinumtoxinA for Injection (DAXI) is a novel, long-acting formulation of botulinum toxin type A in development for the treatment of cervical dystonia (CD)
- ASPEN-1 was a Phase 3, single-dose, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of 2 doses of DAXI for the treatment of CD over 36 weeks across 60 sites in the US, Canada, and the EU



TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

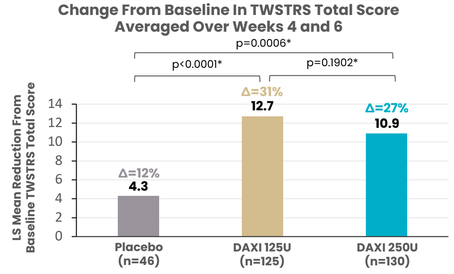
Results

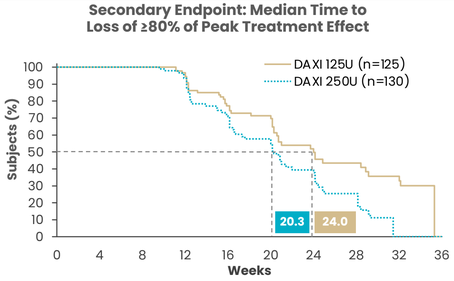
Demographics and Baseline Characteristics

	Placebo (n=46)	DAXI 125U (n=125)	DAXI 250U (n=130)	All Subjects (n=301)
Sex, female, n (%)	29 (63.0)	87 (69.6)	79 (60.8)	195 (64.8)
Age, years				
Mean (SD)	56.5 (11.8)	57.2 (13.4)	58.6 (10.6)	57.7 (12.0)
Range, min-max	29-80	18-80	30-79	18-80
Race, n (%)				
White	43 (93.5)	119 (95.2)	125 (96.2)	287 (95.3)
Black/African American	2 (4.3)	2 (1.6)	2 (1.5)	6 (2.0)
Other*	1 (2.2)	4 (3.2)	3 (2.3)	8 (2.7)
Baseline TWSTRS				
Mean (SD)	45.3 (10.5)	43.1 (9.4)	42.6 (8.6)	43.3 (9.3)
Range, min-max	25.5-71.3	20.3-66.0	27.0-72.0	20.3-72.0
CD duration years, mean (SD)	11.3 (9.5)	10.8 (8.8)	10.5 (9.6)	10.8 (9.2)
Prior BoNT for CD, n (%)	37 (80.4)	108 (86.4)	109 (83.8)	254 (84.4)

*Other includes Asian (3), American Indian or Alaska Native (1), Native Hawaiian or Other Pacific Islander (1), and Other (3).
BoNT, botulinum toxin; CD, cervical dystonia; DAXI, DaxibotulinumtoxinA for Injection; SD, standard deviation; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

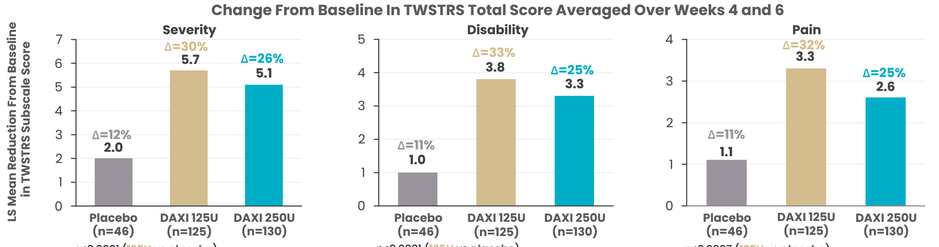
Primary Endpoint Met for Both the 125U and 250U Doses





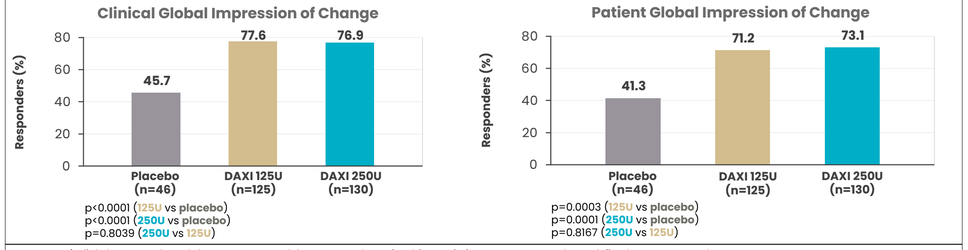
*Analysis of covariance. Δ, % change from baseline.
DAXI, DaxibotulinumtoxinA for Injection; LS, least squares; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

TWSTRS Subscales Consistent With the Primary Endpoint



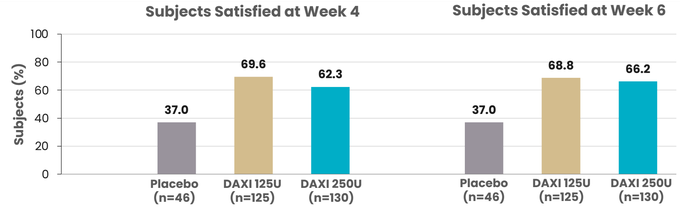
Δ, % change from baseline.
DAXI, DaxibotulinumtoxinA for Injection; LS, least squares; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

Clinical and Patient Global Impression of Change Consistent at Week 4 or 6



Response of a little better, moderately better, or very much better at Week 4 or 6. Subjects missing response on study are defined as non-responders.
DAXI, DaxibotulinumtoxinA for Injection.

Treatment Satisfaction at Week 4 and Week 6



Response of "very satisfied", "satisfied", or "somewhat satisfied" on the Treatment Satisfaction Questionnaire at Week 4 and Week 6.
DAXI, DaxibotulinumtoxinA for Injection.

DAXI Was Generally Safe and Well Tolerated at Both Doses Through Week 36

	Placebo (n=46)	DAXI 125U (n=125)	DAXI 250U (n=130)	All Subjects (n=301)
Subjects with TEAEs, n (%) # of events				
Any TEAEs	18 (39.1) 34	74 (59.2) 148	64 (49.2) 134	156 (51.8) 316
Any serious TEAEs*	0	5 (4.0) 5	3 (2.3) 4	8 (2.7) 9
Any treatment-related TEAEs	8 (17.4) 11	37 (29.6) 54	31 (23.8) 49	76 (25.2) 114
Injection site pain	2 (4.3)	10 (8.0)	6 (4.6)	18 (6.0)
Headache	1 (2.2)	6 (4.8)	6 (4.6)	13 (4.3)
Injection site erythema	1 (2.2)	6 (4.8)	3 (2.3)	10 (3.3)
Muscular weakness	0	6 (4.8)	3 (2.3)	9 (3.0)
Musculoskeletal pain	0	3 (2.4)	4 (3.1)	7 (2.3)
Dysphagia	0	2 (1.6)	5 (3.8)	7 (2.3)

Note: Single case of neck pain reported as severe (onset at Day 10, duration of 2 days). *No serious TEAEs were treatment related; there was 1 unrelated death.
DAXI, DaxibotulinumtoxinA for Injection; TEAE, treatment-emergent adverse event.

Conclusions

- DAXI, at either 125U or 250U, was an effective, well-tolerated, long-lasting treatment for reducing the signs and symptoms of CD
- Highly statistically significant results achieved on TWSTRS total score primary endpoint at Weeks 4 and 6 (p<0.0001, 125U vs placebo; p=0.0006, 250U vs placebo)
- Median duration of effect (time to loss of ≥80% peak treatment effect) was 24 weeks for the 125U dose and 20 weeks for the 250U dose
- Most DAXI-treated subjects were somewhat satisfied to very satisfied at Week 4 (DAXI 125U, 69.6%; DAXI 250U, 62.3%) and Week 6 (DAXI 125U, 68.8%; DAXI 250U, 66.2%), consistent with the primary endpoint
- DAXI appeared to be generally safe and well tolerated, with adverse event rates similar to, or lower than, other botulinum toxin products for the treatment of CD
  - Incidences of dysphagia and muscular weakness were low

The **positive results** reinforce the findings from the previous studies with DAXI as a **highly differentiated neuromodulator**

The ASPEN-1 pivotal trial demonstrates the scientific validity and clinical benefit of a **long-acting neuromodulator**

CD, cervical dystonia; DAXI, DaxibotulinumtoxinA for Injection; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

Disclosures
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