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Pain Relief in Patients < 55 and ≥ 55 Years With Spasticity Treated With OnabotulinumtoxinA: Results From the ASPIRE Study

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OBJECTIVE

To assess the effect of onabotulinumtoxinA (onabotA) on pain relief in spasticity patients stratified by their median age <55 years and ≥55 years from the ASPIRE study

CONCLUSIONS

In this subanalysis of the ASPIRE study, onabotA treatment reduced pain in spasticity patients < 55 years and ≥ 55 years who had pain at baseline as measured by the NPRS and DAS pain subscale

Overall, most patients and physicians in both age groups were satisfied/extremely satisfied that onabotA helped the pain and would continue to use it to treat spasticity

This subanalysis of ASPIRE provides valuable real-world evidence on onabotA utilization and effectiveness on pain relief in spasticity patients regardless of age groups (< 55 years and ≥ 55 years), with no new safety signals observed

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INTRODUCTION

- Spasticity is a motor disorder characterized by muscle stiffness, tightness, and involuntary muscle contractions, which can lead to difficulties in movement and coordination and patients suffering from spasticity may also suffer from pain[1-2]
- OnabotulinumtoxinA (onabotA) is indicated for the treatment of upper limb (UL) and lower limb (LL) spasticity[3]
- Limited data exists to support the reduction of pain after onabotA treatment in patients with spasticity[4-6]; thus, a better understanding is needed on the effect of onabotA on pain in these patients
- OnabotA may be an effective treatment for spasticity patients with pain across age groups with any etiology

METHODS

Study Design and Patients

- The Adult Spasticity International Registry (ASPIRE) is an international, multicenter, prospective, observational study (NCT01930786), that examined onabotA utilization and effectiveness in treating adult patients with spasticity regardless of prior treatment with onabotA treatment
- Patients with spasticity across multiple etiologies were treated with onabotA at the clinician's discretion over 2 years
- Patients stratified based on statistical criteria as "< 55 years" and "≥ 55 years" of age and who received ≥ 1 onabotA treatment for spasticity and had pain (NPRS >0) at baseline are described in this subanalysis

Assessments

- OnabotA treatment utilization was evaluated over 8 treatment sessions
- Pain was assessed with the Numeric Pain Rating Scale (NPRS), changes in functional impairment was assessed by the Disability Assessment Scale (DAS) pain subscale for UL and LL, and patient and physician satisfaction was measured after each treatment session
- Safety was assessed throughout the 2-year study
- A mixed effects regression model was used to assess changes over time; p values and confidence intervals were adjusted for multiple comparisons using a multivariate t distribution

ASPIRE Data Collection

RESULTS

Baseline Characteristics

- Out of the 730 patients in ASPIRE who received ≥1 onabotulinumtoxinA (onabotA) treatment for spasticity, a total of 494 patients had pain (defined as NPRS > 0) at baseline
- The 494 spasticity patients with baseline NPRS >0 included in this subanalysis:
  - Were evenly distributed by age (< 55 years [n = 244, 49.3%] and ≥ 55 years [n = 250, 50.6%])
  - Were predominantly female (59% and 54%, respectively), largely White (71% and 81%, respectively), and 67.8% of patients from each age group received prior onabotA treatment for spasticity
  - Had stroke as the most frequently reported etiology (41% vs 70%, respectively)

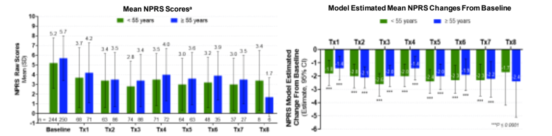
Total OnabotulinumtoxinA Dose by Treatment Session

	Tx 1	Tx 2	Tx 3	Tx 4	Tx 5	Tx 6	Tx 7	Tx 8
Total Dose (U) in < 55 years	n = 244	n = 209	n = 173	n = 148	n = 112	n = 89	n = 57	n = 16
Mean (SD)	351.8 (200.8)	352.8 (198.6)	355.3 (197.3)	372.3 (209.0)	395.7 (209.8)	371.1 (194.4)	381.0 (187.8)	447.2 (243.3)
Min, Max	40.0, 1000.0	50.0, 1125.0	60.0, 1100.0	50.0, 1200.0	100.0, 1200.0	62.0, 1225.0	100.0, 1200.0	160.0, 1200.0
Total Dose (U) in ≥ 55 years	n = 250	n = 209	n = 176	n = 146	n = 111	n = 72	n = 47	n = 12
Mean (SD)	337.9 (191.9)	347.9 (173.1)	365.3 (165.7)	363.6 (169.4)	384.5 (154.5)	375.1 (149.9)	387.0 (138.3)	485.4 (131.0)
Min, Max	30.0, 1100.0	45.0, 930.0	50.0, 830.0	50.0, 800.0	50.0, 800.0	50.0, 650.0	50.0, 600.0	300.0, 710.0

n, number of patients in each treatment session by age group category; SD, standard deviation; Tx, treatment session; U, units

- The mean onabotA dose over the 8 treatment sessions ranged from 351.8 U to 447.2 U in patients < 55 years compared to 337.9 U to 485.4 U in patients ≥ 55 years

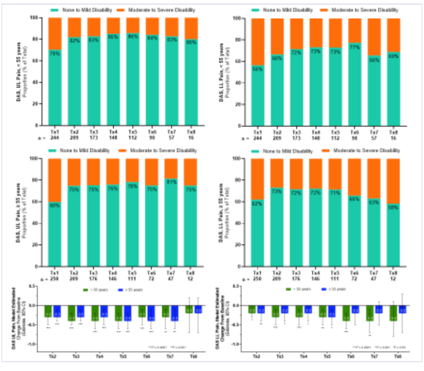
Patients in Both Age Groups Had Improvements in Pain From Baseline After OnabotulinumtoxinA Treatment as Assessed by the Numeric Pain Rating Scale (NPRS)



NPRS, numeric pain rating scale; n, number of patients; Tx, treatment session. [a]NPRS rates the level of pain experienced in the last 24 hours from 0 (no pain) to 10 (highest pain imaginable). The baseline NPRS was evaluated at office visit 1; response to treatments (Tx) 2 - 8 were collected by phone or web after each treatment. The baseline NPRS reflects the initial measurements available for the cohort patients treated at any subsequent time point. Missing or ambiguous responses resulted in variation in the number of n's for each graph. A multivariate t distribution method is used to adjust confidence intervals and p values for multiple comparisons. *Indicates statistically significant differences between txs.

- Patients with spasticity in both age groups had improvements in pain from baseline
  - Mean NPRS scores for pain decreased from 5.2 at baseline to 3.4 at Tx 8 in patients < 55 years
  - Mean NPRS scores for pain decreased from 5.7 at baseline to 1.7 at Tx 8 in patients ≥ 55 years
- Model estimated NPRS was significantly reduced from baseline after Tx 1 - 7 for both age groups

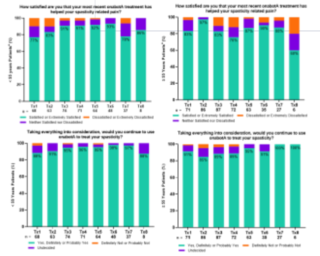
Disability Assessment Scale (DAS)a Pain Subscale for UL and LL Spasticity Improved Relative to Baseline Across all Treatment Sessions



DAS, disability assessment scale; n, number of patients; onabotA, onabotulinumtoxinA, UL, upper limb; LL, lower limb; Tx, treatment sessions. [a]DAS objectively evaluates functional impairment, such as pain, resulting from spasticity. DAS uses a 4-point rating scale, with 0 as no disability; 1, mild disability; 2, moderate disability; 3, severe disability; baseline DAS measurement was taken prior to injection with onabotulinumtoxinA at the first treatment visit (Tx 1), thus, Tx 1 represents the baseline level of disability. DAS for treatments (Tx) 2 – 8 reflects response to the prior treatment (ie, Tx 2 reflects the response to Tx 1). Missing or ambiguous responses resulted in variation in the number of n's for each panel. A multivariate t distribution method is used to adjust confidence intervals and p values for multiple comparisons. *Indicates statistically significant differences between treatments.

- The majority of spasticity patients in both groups (≥ 70% patients in the < 55 years group and ≥ 60% patients in the ≥ 55 years group) reported none to mild disability for UL
- A lower proportion of patients reported none to mild disability for LL compared to UL (≥ 56% patients in the <55 years and ≥ 58% patients in the ≥ 55 years groups)
- Model estimated DAS for UL spasticity on pain subscale was significantly reduced after onabotA treatment compared to baseline across most treatment sessions (Tx 2 – 7) regardless of age group
- Model estimated DAS for LL spasticity on pain subscale showed significant reduction in pain compared to baseline across most treatment sessions regardless of age group

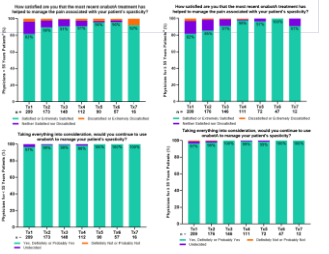
Increased Patient Satisfaction After OnabotulinumtoxinA Treatments Across Age Groups



n, number of respondents; N/A, not applicable; onabotA, onabotulinumtoxinA; Tx, treatment session. [a]Not applicable (N/A) responses to this question (the only question for which N/A could have been selected) are not included in bars but are included in the total number of respondents below each treatment. Patient-reported outcomes were collected at baseline and approximately five weeks after each treatment; a follow-up interview was conducted 12 weeks after the final treatment. Missing or ambiguous responses resulted in variation in the number of n's for each panel.

- OnabotA treatment resulted in overall high patient satisfaction across age groups
  - After each treatment session, ≥ 77% of spasticity patients in the < 55 years group and ≥ 60% in the ≥ 55 years group were satisfied that onabotA treatment helped their pain
  - After each treatment session, comparable proportion of patients in both age groups (≥ 88% of patients in the < 55 years and ≥ 85% in the ≥ 55 years) considered continuing using onabotA to treat their spasticity

Increased Physician Satisfaction After OnabotulinumtoxinA Treatments Across Age Groups



n, number of respondents; N/A, not applicable; Tx, treatment session. [a]Not applicable (N/A) responses to this question (the only question for which N/A could have been selected) are not included in bars but are included in the total number of respondents below each treatment. Physician-reported outcomes for treatments (Tx) 1 - 7 were collected at each office visit subsequent to treatment. Study requirements did not stipulate a final follow-up visit; thus, clinician-reported outcomes for Tx 8 were not evaluated. Missing or ambiguous responses resulted in variation in the number of n's for each panel.

- OnabotA treatment resulted in overall high physician satisfaction to treat their patient's spasticity across age groups
  - After each treatment session, ≥ 82% of physicians of spasticity patients in in both age groups were satisfied that the onabotA treatment helped their patient's pain
  - After each treatment session, ≥ 97% of physicians of spasticity patients in both age groups indicated they would continue to use onabotA to treat their patient's spasticity

Safety

- Overall, 230 nonserious adverse events (AEs) were reported in 86/244 patients (35.2%) in the < 55 years age group; 234 nonserious AEs were reported in 86/250 patients (34.4%) in the ≥ 55 years age group
  - 10 nonserious AEs in 10/244 patients (4.1%) in the < 55 years age group were considered treatment-related; the most common treatment-related AE was muscular weakness (3 events in 3/244 patients, 1.2%)
  - 7 nonserious AEs in 5/250 (2.0%) in the ≥ 55 years age group were considered treatment-related; the most common treatment-related AE was muscular weakness (3 events in 3/250 patients, 1.2%)
- Overall, no serious AEs were reported in patients in the < 55 years age group; 3 serious AEs were reported in 2/250 (0.8%) patients in the ≥ 55 years age group and were considered treatment related: muscular weakness, dysphagia, and slow speech

Study Limitations

- Given the observational nature of the study, the generality of this analysis is limited
- Low sample sizes for some outcomes an treatment sessions (due to missing or ambiguous responses resulting in variation in the number of n's for each treatment session)
- DAS has been validated for UL spasticity only; however, it has also been used to evaluate LL spasticity

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