Exploring Oral Skeletal Muscle Relaxant Therapy in Adult Poststroke Patients in the US

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TAKE-HOME MESSAGE

Patients may benefit from additional management strategies beyond oral skeletal muscle relaxants for the treatment of poststroke spasticity

BACKGROUND

- Stroke survivors often encounter long-term disabilities and complications, including motor and sensory impairments, such as spasticity[1]
- Poststroke spasticity (PSS) is associated with pain, stiffness, and joint contracture, all of which may lead to decreased quality of life, increased financial liability, and increased caregiver burden[2]
- PSS is estimated to occur in approximately 25% of stroke patients and 40% of stroke patients with paresis[3]
- Oral skeletal muscle relaxants (OSMRs) are recognized as a potentially beneficial intervention for PSS
  - Variability in patient response and adverse events may limit their efficacy[1]
  - Limited real-world evidence is available

OBJECTIVE

- To examine pharmacological treatment dynamics of OSMR therapy poststroke in adults following hospitalization over a 2-year period

CONCLUSIONS

- Patients with poststroke spasticity (PSS) treated with oral skeletal muscle relaxants (OSMRs) have low adherence and persistence to OSMR treatment along with a high incidence of polypharmacy at a great financial cost
- There is an unmet need for optimization of pharmacological PSS intervention and reduction of polypharmacy

METHODS

Study Design and Patients

- PRECEPT was a retrospective study utilizing claims from the Merative MarketScan® database of commercially insured members from October 1, 2015, to June 30, 2023
- Inclusion criteria:
  - ≥18 years of age
  - ≥1 inpatient hospitalization for treatment of stroke
    - Inpatient treatment for stroke was defined by primary ICD-10 diagnosis codes with a hospital as place of service
  - Continuous enrollment through the preindex, index, and postindex period
    - The index period was defined as the period of time for identifying the first stroke between October 1, 2016, and June 30, 2020
      - The index date, or index, was the date of the first stroke within the index period
    - The preindex period was defined as the date 1 year prior to the index
    - The postindex period was defined as 36 months after the index
  - Received ≥1 prescription for OSMR within 12 months of inpatient stroke event (OSMR-treated cohort only)
- Exclusion criteria:
  - Exposure to OSMR, intrathecal baclofen, or botulinum toxin (BoNT) during the preindex period
  - Exposure to intrathecal baclofen or BoNT prior to OSMR initiation during index period
  - Prior stroke or evidence of secondary stroke in the preindex period
  - Migraine, cerebral palsy, traumatic brain injury, silent cerebral infarction, multiple sclerosis, cervical dystonia, blepharospasm, or sialorrhea

Assessments and Endpoints

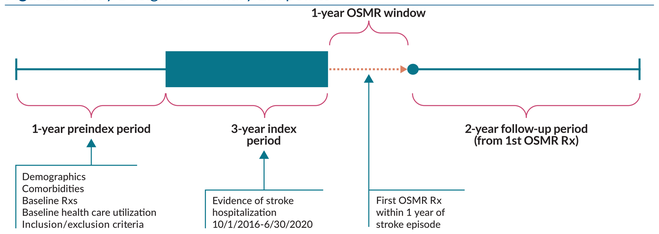
- For primary endpoints (Table 1), a 2-year postindex period followed the patient's first prescription for an OSMR (Figure 1)

Table 1. Study Endpoints

Type of Endpoint	Description
Primary (Figure 1)	Patient demographics at index
	OSMR persistency (time to discontinuation [nonpersistence*] from OSMR initiation)
	OSMR treatment patterns†
	Progression from OSMR therapy Progression from OSMR therapy included the addition of BoNT or intrathecal baclofen in the OSMR-treated cohort
Secondary (Figure 2)	HCRU and costs pre- and postindex among patients with OSMR vs no PSS treatment
Exploratory (Figure 2)	Predictors of initiation of OSMR therapy vs no PSS treatment
	Predictors of BoNT initiation within the OSMR-treated cohort

BoNT, botulinum toxin; HCRU, health care resource utilization; OSMR, oral skeletal muscle relaxant; PSS, poststroke spasticity.
*Nonpersistence is defined as no prescription refill within the days supply of the prescription, plus 1/2 days supply of that prescription as a "buffer."
†Restarters are defined as patients who discontinue but subsequently fill a prescription for an OSMR within the study period.

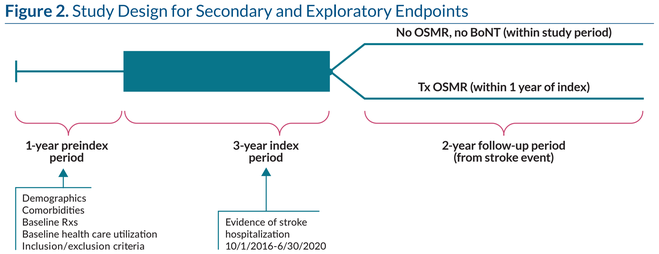
Figure 1. Study Design for Primary Endpoints



OSMR, oral skeletal muscle relaxant; Rx, prescription.

- For secondary and exploratory endpoints (Table 1), a 2-year postindex period followed OSMR initiation or index date if the patient did not initiate OSMR or BoNT therapy (Figure 2)

Figure 2. Study Design for Secondary and Exploratory Endpoints



BoNT, botulinum toxin; OSMR, oral skeletal muscle relaxant; Rx, prescription; Tx, treatment.

Data Analysis

- Patient demographics, time to OSMR following the index date, and OSMR treatment patterns were analyzed descriptively
- Elapsed days from OSMR initiation to nonpersistence were analyzed with Kaplan–Meier estimates
- Health care resource utilization (HCRU) and costs were analyzed descriptively
- A stepwise multivariate regression model was used to analyze the exploratory endpoints

RESULTS

Patient Demographics and Characteristics

- Overall, 13,306 patients fulfilled the study criteria (Table 2)
- Of these, 360 (2.7%) patients initiated OSMR treatment within 1 year of index

Table 2. Patient Demographics

Parameter	OSMR Cohort (n=360)	No PSS Treatment Cohort (n=12,946)
Age, mean (SD), y	59.2 (11.8)	65.9 (14.7)
Male, n (%)	206 (57.2)	7692 (59.4)
Etiology of spasticity, n (%)		
Hemorrhagic	36 (10.0)	879 (6.8)
Ischemic	311 (86.4)	11,644 (90.0)
Unspecified	13 (3.6)	423 (3.3)
Region, n (%)		
Northeast	45 (12.5)	2630 (20.3)
North Central	114 (31.7)	4505 (34.8)
South	180 (50.0)	4777 (36.9)
West	17 (4.7)	1017 (7.9)
Unknown	4 (1.1)	17 (0.2)
Payer, n (%)		
MS only	61 (16.9)	4302 (33.2)
MA only	6 (1.7)	292 (2.3)
Commercial only	244 (67.8)	6138 (47.4)
MA and MS	25 (6.9)	1748 (13.5)
MS and commercial	16 (4.4)	302 (2.3)
MA and commercial	3 (0.8)	59 (0.5)
MA, MS, and commercial	5 (1.4)	105 (0.8)
Index year, n (%)		
2016	39 (10.8)	1058 (8.2)
2017	128 (35.6)	3809 (29.4)
2018	69 (19.2)	3362 (26.0)
2019	65 (18.1)	3391 (26.2)
2020	59 (16.4)	1326 (10.2)

MA, Medicare Advantage; MS, Medicare Supplemental; OSMR, oral skeletal muscle relaxant; PSS, poststroke spasticity.

- Clinical characteristics were generally well distributed between the cohorts during the preindex period (Table 3)
- A greater proportion of patients in the OSMR cohort had a Charlson Comorbidity Index score of 1-2 compared with the no PSS treatment cohort
- In the postindex period, a greater proportion of patients in the OSMR cohort compared with those in the no PSS treatment cohort were being treated with anticonvulsant, antidepressant, anxiolytic and sedative-hypnotic, nonsteroidal anti-inflammatory, or opioid medications

Table 3. Patient Clinical Characteristics During the Preindex and Postindex Periods

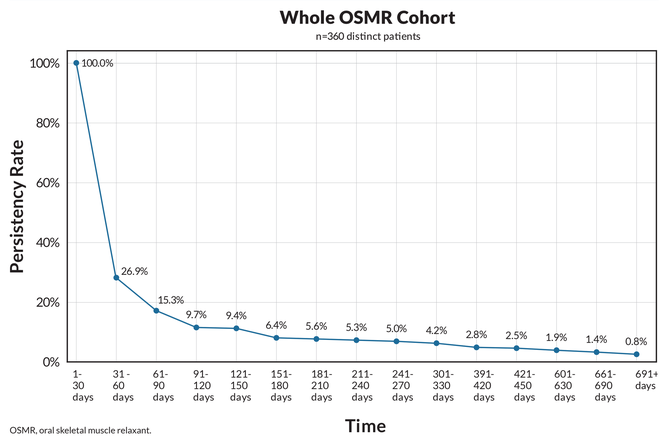
Parameter	OSMR Cohort (n=360)		No PSS Treatment Cohort (n=12,946)	
	Preindex	Postindex	Preindex	Postindex
Charlson Comorbidity Index, n (%)				
0	39 (10.8)	39 (10.8)	1031 (8.0)	1031 (8.0)
1-2	142 (39.4)	142 (39.4)	3917 (30.3)	3917 (30.3)
3-4	90 (25.0)	90 (25.0)	3836 (29.6)	3836 (29.6)
5-6	51 (14.2)	51 (14.2)	2290 (17.7)	2290 (17.7)
≥7	38 (10.6)	38 (10.6)	1872 (14.5)	1872 (14.5)
Comorbidities ≥5% incidence during the preindex period, n (%)				
Hypertension	219 (60.8)	319 (88.6)	7804 (60.3)	11,397 (88.0)
Diabetes	106 (29.4)	154 (42.8)	3906 (30.2)	5310 (41.0)
Coronary artery disease	60 (16.7)	135 (37.5)	2368 (18.3)	5070 (39.2)
Arrhythmia*	45 (12.5)	162 (45.0)	1705 (13.2)	5449 (42.1)
Anxiety	43 (11.9)	85 (23.6)	990 (7.6)	2214 (17.1)
Peripheral artery disease	38 (10.6)	110 (30.6)	1416 (10.9)	4009 (31.0)
Depression	32 (8.9)	89 (24.7)	912 (7.0)	2134 (16.5)
Heart failure	25 (6.9)	79 (21.9)	985 (7.6)	3059 (23.6)
Atrial fibrillation	24 (6.7)	85 (23.6)	1267 (9.8)	3520 (27.2)
Concomitant medications, n (%)				
Cardiovascular	213 (59.2)	303 (84.2)	7490 (57.9)	10,472 (80.9)
Antihypertensive	186 (51.7)	285 (79.2)	6730 (52.0)	9897 (76.4)
Antihyperlipidemia	126 (35.0)	279 (77.5)	5164 (39.9)	10,025 (77.4)
Beta blocker	112 (31.1)	208 (57.8)	4180 (32.3)	6853 (52.9)
ACE/ARB	99 (27.5)	139 (38.6)	3008 (23.2)	4402 (34.0)
Diabetes	80 (22.2)	123 (34.2)	2903 (22.4)	3837 (29.6)
Opiates	73 (20.3)	193 (53.6)	1767 (13.6)	3230 (24.9)
Calcium channel blocker	68 (18.9)	142 (39.4)	2859 (22.1)	5045 (39.0)
Antidepressant	66 (18.3)	147 (40.8)	1979 (15.3)	3233 (25.0)
NSAID	66 (18.3)	124 (34.4)	1524 (11.8)	1846 (14.3)
ASH	52 (14.4)	102 (28.3)	1234 (9.5)	1890 (14.6)
Anticoagulant	48 (13.3)	165 (45.8)	2100 (16.2)	6121 (47.3)
Anticonvulsant	29 (8.1)	107 (29.7)	1025 (7.9)	2025 (15.6)

ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASH, anxiolytic and sedative-hypnotic; NSAID, nonsteroidal anti-inflammatory drug; OSMR, oral skeletal muscle relaxant; PSS, poststroke spasticity.
*Other than atrial fibrillation.

OSMR Persistence, Treatment Patterns, and Progression From Therapy

- The mean ± SD time to OSMR therapy initiation was 119.7 ± 106.6 days
- OSMR mean ± SD persistence was 53.4 ± 121.5 days (Figure 3)
  - Medication possession ratio was 54.9% ± 33.9%
  - Percentage of days covered was 52.6% ± 32.9%
- Following nonpersistence, 116 (32.2%) patients restarted OSMR therapy
- In the OSMR-treated cohort, 3 (0.8%) patients progressed to BoNT therapy, and no patients progressed to intrathecal baclofen therapy

Figure 3. OSMR Cohort Persistency



OSMR, oral skeletal muscle relaxant.

HCRU and Costs

- Median total costs for overall health care, physical therapy, and inpatient hospitalization increased from preindex to postindex in the OSMR and no PSS treatment cohorts (Table 4)

Table 4. Health Care Costs Per Patient From Preindex to Postindex

Median (IQR) Cost per Patient, $	OSMR Cohort (n=360)	No PSS Treatment Cohort (n=12,946)
Total overall health care cost		
Preindex	35,370.54 (61,408.27)	3,727.85 (10,175.50)
Postindex	65,105.58 (92,877.43)	43,197.42 (65,414.25)
Total physical therapy cost		
Preindex	134.00 (115.50)	140.00 (138.50)
Postindex	157.00 (254.00)	152.50 (200.00)
Total inpatient hospitalization cost		
Preindex	24,961.50 (49,757.00)	20,199.00 (29,048.50)
Postindex	36,283.00 (69,424.00)	26,838.00 (50,277.00)

OSMR, oral skeletal muscle relaxant; PSS, poststroke spasticity.

- Approximately 33% and 24% of patients in the OSMR and no PSS treatment cohorts, respectively, had ≥1 physical therapy visit during the postindex period
- The mean (SD) number of physical therapy visits per patient was 2.0 (2.0) for the OSMR cohort and 1.8 (2.0) for the no PSS treatment cohort
- All patients across both cohorts experienced ≥1 inpatient hospitalization
- Patients in the OSMR cohort were hospitalized for mean (SD) 79.6 (174.0) days compared with 58.7 (138.3) days in the no PSS treatment cohort
- Patients with nonsteroidal anti-inflammatory use at baseline were the most likely to initate BoNT therapy among those who previously initiated OSMR therapy (Table 5)
- Age and baseline Charlson Comorbidty Index were the least likely parameters to influence initiation of BoNT therapy

Table 5. Odds Ratio Estimates for the Initiation of BoNT Therapy Among Those Who Previously Initiated OSMR Therapy

Parameter	Point Estimate	95% Wald Confidence Limits	
Age	0.97	0.96	0.975
Charlson Comorbidity Index at baseline	1.06	1.01	1.11
NSAID use at baseline	1.56	1.18	2.052
ASH use at baseline	1.54	1.13	2.083
ACE use at baseline	1.32	1.04	1.682

ACE, angiotensin-converting enzyme inhibitor; ASH, anxiolytic and sedative-hypnotic; BoNT, botulinum toxin; NSAID, nonsteroidal anti-inflammatory drug; OSMR, oral skeletal muscle relaxant.

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Acknowledgments The authors thank Zoe McCord, PharmD, RPh, from The Curry Rockefeller Group, LLC, a Citrus Health Group, Inc., company (Chicago, IL), for providing medical writing support/editorial support, which was sponsored by Ipsen in accordance with Good Publication Practice guidelines.
Funding This study was funded by Ipsen (Cambridge, MA).
Disclosures **JB**, **SG**, and **AM** are employees of Ipsen.

Presented at ISPOR 2025, May 13-16, 2025; Montreal, Quebec, Canada