Clinical CHart Review to Assess the Real-World Impact of Sustained TreatMent in Adults with Tardive DyskinesiA: CHARISMA Study

NEUROCRINE® BIOSCIENCES

CHARISMA: Study Design[1,2]

- **Objective:** The CHARISMA study was a multi-center, retrospective, clinical chart review to assess the long-term outcomes of valbenazine in adults with tardive dyskinesia (TD) in real-world settings
  - Eight neurologic and psychiatric health professionals provided medical charts for 121 valbenazine-treated patients
- **Inclusion criteria:**
  - ≥18 years old
  - Clinical diagnosis of DRBA-induced TD
  - ≥6 consecutive months of valbenazine treatment
- **Data capture:** patient chart information was extracted and entered into a validated electronic data capture system, starting from baseline to abstraction date
  - **Baseline:** 1 month prior to initiation of valbenazine treatment; or, if applicable, last documented clinical visit prior to initial valbenazine prescription

DRBA, dopamine receptor blocking agent.

1. Morton RO, et al. AANP 2021. 2. Siegert S, et al. ASCP 2020.

CHARISMA: Assessments

- Baseline data included patient demographics, socioeconomic status, and psychiatric conditions
- Changes in TD and psychiatric status were assessed using simple descriptors per clinical judgement of the healthcare provider:
  - “improved”, “worsened”, and “no change”
- TD symptom severity was assessed using 2 different methods:
  - Descriptors based on clinical judgment: “mild”, “moderate”, and “severe”
  - Formal Abnormal Involuntary Movement Scale (AIMS) item scores for 7 different body regions (range, 0=none to 4=severe) and a total score (sum of items 1-7)
- All data were analyzed descriptively
- Cases with missing data were excluded from the analysis as missing data were not considered random*

*E.g., subjects with milder symptoms may have been less likely to visit the clinic than patients with more severe TD

Morton RO, et al. AANP 2021.

CHARISMA: Limitations

- These analyses were limited by missing data, a challenge that is often encountered in real-world TD studies[1]
  - In clinical practice, patients with milder symptoms may be less likely to visit their healthcare providers than patients with more severe symptoms
  - Physicians do not always complete surveys/questionnaires at every visit, which may be due to time constraints
- Despite the challenges of missing data, real-world studies play a crucial role in documenting the prevalence and impact of conditions such as TD, a disorder that continues to be underrecognized and misdiagnosed[1-3]

1. Morton RO, et al. AANP 2021. 2. Caroff SN, et al. *J Neurol Sci.* 2018;389:4-9. 3. Lockwood JT, et al. *Expert Opin Emerg Drugs*. 2015; 20(3):407-21.

CHARISMA: Patient Characteristics

- Eight physicians provided medical charts for 121 valbenazine-treated patients

Patient Demographics and Socioeconomic Status	All Patients (N=121)
Age, years, mean (SD)	56.4 (12.0)
Race, n (%)	
White	69 (57.0)
Black/African American	10 (8.3)
Asian	1 (0.8)
Other	1 (0.8)
Not specified/unknown	40 (33.1)
Marital status, n (%)	
Single	52 (43.0)
Married	25 (20.7)
Separated/divorced	9 (7.4)
Widowed	7 (5.8)
Living with a partner	1 (0.8)
Not specified/unknown	27 (22.3)

SD, standard deviation.

Morton RO, et al. AANP 2021.

CHARISMA: Patient Characteristics

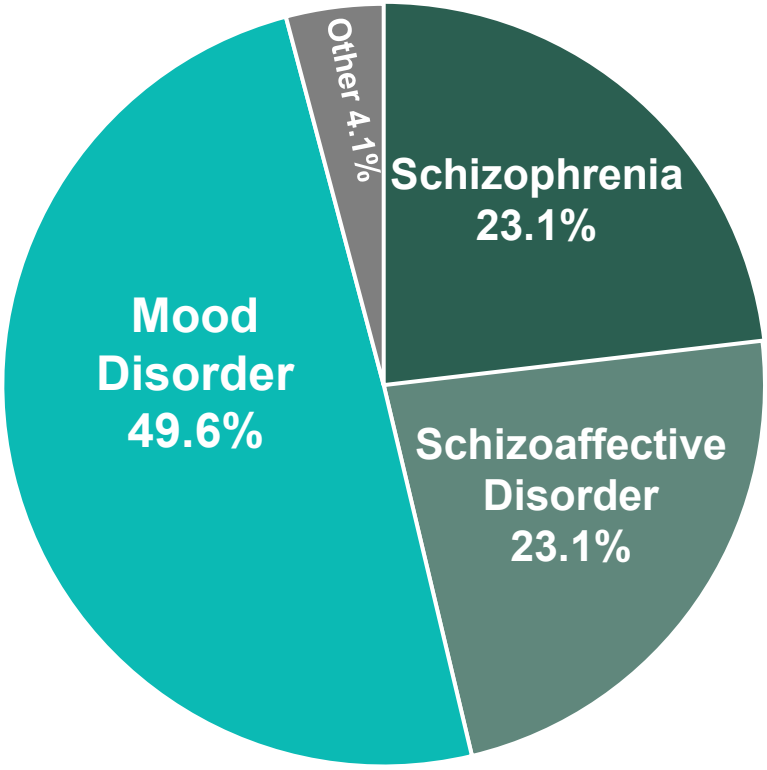
Patient Demographics and Socioeconomic Status	All Patients (N=121)
Education level, n (%)	
High school degree	32 (26.5)
Did not graduate from high school	20 (16.5)
College/undergraduate degree	17 (14.1)
Graduate degree	4 (3.3)
Not specified/unknown	48 (39.7)
Employment status, n (%)	
Unemployed	32 (26.5)
Retired	17 (14.1)
Employed full-time (≥30 hours/week)	9 (7.4)
Employed part-time (<30 hours/week)	7 (5.8)
On sick leave/unable to work	7 (5.8)
Homemaker	2 (1.7)
Not specified/unknown	47 (38.8)
Housing situation, n (%)	
Permanent residence	18 (14.9)
Nursing home	12 (9.9)
Assisted living	6 (5.0)
Other	26 (21.5)
Not specified/unknown	59 (48.8)

SD, standard deviation.

Morton RO, et al. AANP 2021.

CHARISMA: Psychiatric Conditions

- Mood disorder was the most common primary psychiatric condition at baseline



Morton RO, et al. AANP 2021.

CHARISMA: Concomitant Medications and Valbenazine Treatment

- Anticholinergics and antiseizure medications (e.g., benztropine, clonazepam) were commonly used despite a lack of supporting evidence for efficacy in TD[1-3]
- Despite the use of these medications, all patients in the CHARISMA study were prescribed valbenazine, suggesting that TD symptoms were not adequately managed by off-label use of any treatments[3]
- Median duration of valbenazine was 15.6 months (range, 5.6 to 36.6); mean duration was 16.9 months (standard deviation, 7.8) [3]
- Most patients were taking valbenazine 80 mg (56.2%) or 40 mg (41.3%) once daily at their most recent visit after baseline[3]

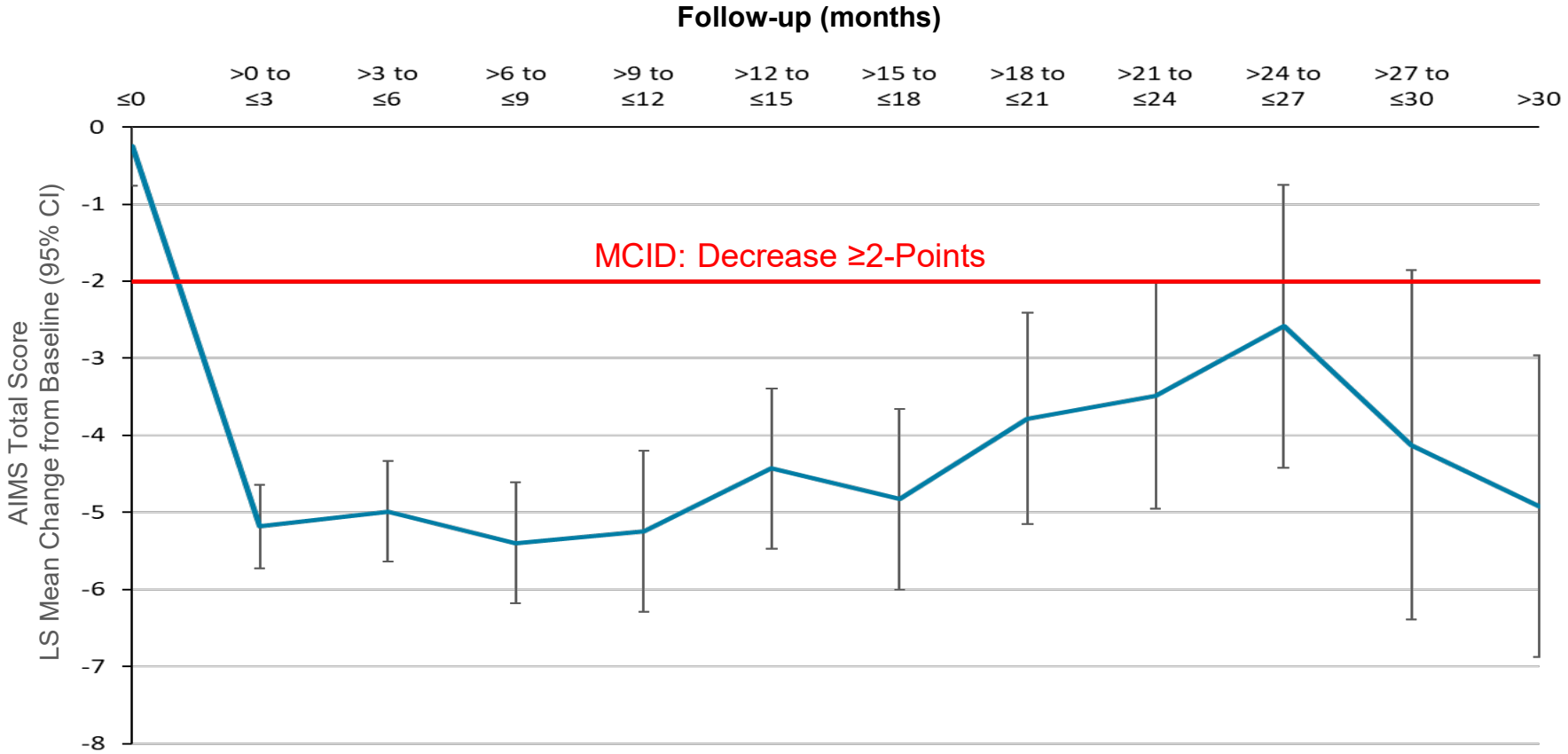
	All Patients (N=121)
n (%)	
Quetiapine	41 (33.9)
Aripiprazole	34 (28.1)
Clonazepam	25 (20.7)
Clozapine	25 (20.7)
Benztropine	24 (19.8)
Valproic acid	24 (19.8)
Lorazepam	22 (18.2)
Escitalopram	20 (16.5)
Mirtazapine	19 (15.7)
Trazodone	19 (15.7)
Olanzapine	18 (14.9)
Risperidone	14 (11.6)
Vortioxetine	14 (11.6)
Bupropion	13 (10.7)
Lurasidone	13 (10.7)
Sertraline	13 (10.7)

Concomitant medications used in >10% of patients are presented.

1. APA Practice Guideline for Treatment of Patients with Schizophrenia. Accessed on August 6, 2021. https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines. 2. Bhidayasiri R. et al. *J Neurol Sci.* 2018;389:67-75. 3. Morton RO, et al. AANP 2021.

CHARISMA: Improvements in AIMS Total Score with Valbenazine[1]

- Mean changes from study baseline in AIMS total score met the minimal clinically important difference (MCID) for AIMS total score (≥2-point reduction)2 within 3 months of valbenazine treatment and through 30+ months[1]



Results are limited by the challenges of missing data often seen in real-world studies; AIMS, Abnormal Involuntary Movement Scale; CI, confidence interval; LS, least-squares; MCID, minimal clinically important difference.

1. Morton RO, et al. AANP 2021. 2. Stacy M, et al. et al. *Mov Disord.* 2019;34(8):1203-9.

CHARISMA: AIMS Item Scores by Body Region

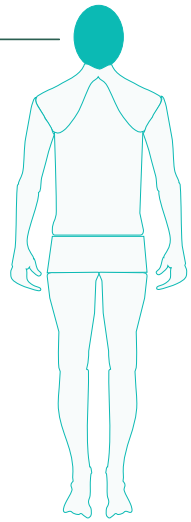
- AIMS item scores were generally ≤2 (“mild”) throughout the follow-up period (1 to 30+ months) in all 7 body regions, with mean score ranges as follows[1]:

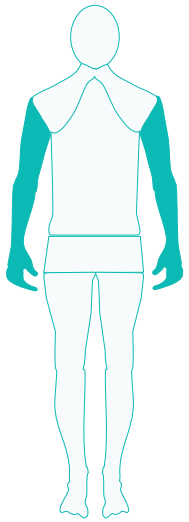
Face
0.0 – 1.0

Lips
0.0 – 2.0

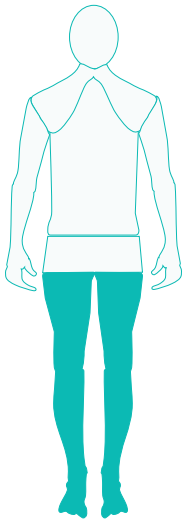
Jaw
0.3 – 2.0

Tongue
0.0 – 1.5

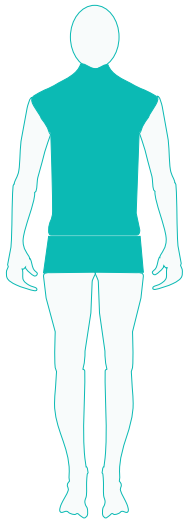




Upper extremities
0.0 – 2.0



Lower extremities
0.0 – 1.0



Neck/ trunk
0.0 – 0.7

Morton RO, et al. AANP 2021.

CHARISMA: Summary

- This multicenter retrospective chart review aimed to characterize the TD patient population in adults receiving long-term valbenazine treatment[1]
- Mood disorder was the most common primary psychiatric condition at baseline (49.6%)[1]
- Although non-approved TD treatments (e.g., anticholinergics) were frequently used (benztropine: 19.8%), all CHARISMA patients were treated with valbenazine (approved for TD), suggesting that these off-label medications had little effect on TD[1]:
  - Most patients were taking valbenazine 80 mg (56.2%) or 40 mg (41.3%) once daily at their most recent visit after baseline
- AIMS item scores were generally ≤2 (“mild”) throughout the follow-up period (1 to 30+ months) in all 7 body regions[1]
- Mean changes from study baseline in AIMS total score met the minimal clinically important difference (MCID) for AIMS total score (≥2-point reduction)[2] within 3 months of valbenazine treatment and through 30+ months[1]

1. Morton RO, et al. AANP 2021. 2. Stacy M, et al. et al. *Mov Disord.* 2019;34(8):1203-9.