Assessing real-world dosing patterns for vesicular monoamine transporter-2 inhibitors, valbenazine and deutetrabenazine, among persistent patients with tardive dyskinesia in a nationwide US claims database

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INTRODUCTION

- Tardive dyskinesia (TD) is a movement disorder characterized by involuntary and repetitive movements.[1] TD is associated with prolonged exposure to dopamine receptor-blocking agents, particularly antipsychotics, and can severely impact social, emotional, and physical functioning[1,2]
- Current United States (US) guidelines recommend vesicular monoamine transporter 2 (VMAT2) inhibitors, valbenazine (VBZ) and deutetrabenazine (dTBZ) for first-line treatment of TD[1,3-6]
- VBZ is administered once daily at an initial dose of 40 mg and dTBZ is administered as either a once-daily extended-release (XR) or twice-daily (BID) formulation, with initial recommended doses of 12 mg once daily and 6 mg twice daily, respectively[5,6]

OBJECTIVE

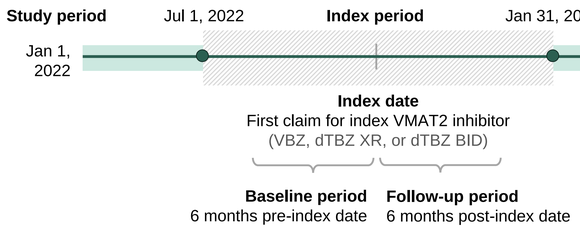
- To assess real-world dosing trends among patients with TD receiving at least 6 months of treatment with VBZ or dTBZ

METHODS

Study design

- We conducted a retrospective cohort study using linked data from IQVIA's US longitudinal prescription and professional fee claims databases. The study period ranged from 1/1/2022 to 7/31/2024 (Figure 1). Adult patients with TD were indexed at VMAT2 inhibitor initiation between 7/1/2022 and 1/31/2024. Patient characteristics were assessed during the 6-month baseline period and outcomes were assessed during the 6-month follow-up period
- Eligible patients had ≥1 pharmacy claim during both the 6-month baseline and follow-up periods, ≥1 claim for VBZ or dTBZ (either BID or XR) during the selection period, and ≥1 claim with a diagnosis of TD during the study period
- Patients were stratified into 3 separate cohorts: VBZ, dTBZ BID, or dTBZ XR. The full cohort was previously presented.[6] Persistent patients are reported here, defined as patients who remained on treatment for the full 6-month follow-up period without discontinuation (defined as a gap of >45 days) or switching agents
- Patients with a VMAT2 inhibitor claim during the baseline period, multiple VMAT2 inhibitor agents on the index date, or a diagnosis of Huntington's disease during the study period were excluded

Figure 1. Study design



Key: BID, twice daily; dTBZ, deutetrabenazine; XR, extended release; VBZ, valbenazine.

Outcomes

- Based on the minimum efficacious dose in phase 3 clinical trials,[8-10] therapeutic dosing thresholds were set at 40 mg/day for VBZ and 24 mg/day for dTBZ
- Outcomes were compared between VBZ and each dTBZ cohort, including monthly dosing trends, therapeutic dose attainment, and dose changes. Doses were rounded to the nearest available dosage form

Statistical analysis

- Results were analyzed descriptively, and pairwise comparisons were conducted using Chi-square tests for categorical variables, the Wilcoxon rank-sum test for continuous variables, and independent samples t-test for means. Statistical significance was indicated by a *P*-value <0.05

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RESULTS

- We identified 1,856 persistent patients taking VBZ, 1,007 taking dTBZ BID, and 126 taking dTBZ XR. Baseline characteristics were similar across cohorts (median age: 62-64 years; female: 65-72%) (**Table 1**)
- The most common baseline psychiatric conditions were anxiety disorders (44%-46%), depression (30%-35%), and bipolar disorder (29%-31%). Most patients were taking antipsychotic medications (62%-73% across cohorts)

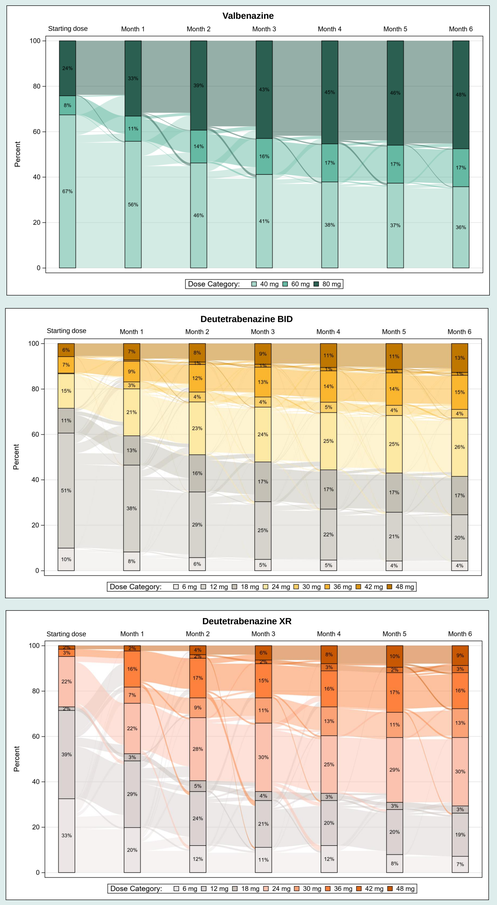
Table 1. Baseline demographic and clinical characteristics in persistent patients

Characteristic		VBZ cohort (N=1,856)	dTBZ BID cohort (N=1,007)	dTBZ XR cohort (N=126)
Age, years, mean (SD)		60.7 (13.0)	60.4 (13.4)	62.0 (12.2)
Gender, female, n (%)		1,314 (70.8)	726 (72.1)	82 (65.1)
CCI, mean (SD)		1.52 (2.36)	1.51 (2.28)	1.41 (2.12)
Payer type, n (%)	Medicare/Medicaid	1,341 (72.3)	731 (72.7)	84 (66.6)
	Commercial	511 (27.5)	272 (27)	42 (33.3)
	Other/unknown	4 (0.2)	4 (0.4)	0 (0.0)
Provider specialty,[a] n (%)	Neurology	416 (22.4)	256 (25.4)	31 (24.6)
	Geriatrics	6 (0.3)	3 (0.3)	1 (0.8)
	Primary care provider	113 (6.1)	51 (5.1)	5 (4.0)
	Nurse practitioner	668 (36.0)	360 (35.7)	48 (38.1)
	Physician assistant	152 (8.2)	68 (6.8)	15 (11.9)
	Psychiatry	462 (24.9)	242 (24.0)	26 (20.6)
	Other/unknown	39 (2.1)	27 (2.7)	0 (0.0)
Index year	2022	639 (34.4)	400 (39.8)	0 (0.0)
	2023	1,139 (61.4)	573 (56.9)	112 (89)
	2024	78 (4.2)	34 (3.4)	14 (11.1)
Psychiatric conditions of interest, n (%)	Serious mental illness	1,310 (70.6)	673 (66.8)	87 (69.0)
	Depression	657 (35.4)	303 (30.1)	42 (33.3)
	Schizophrenia	246 (13.3)	114 (11.3)	18 (14.3)
	Schizoaffective disorder	273 (14.7)	146 (14.5)	21 (16.7)
	Bipolar disorder	563 (30.3)	308 (30.6)	37 (29.4)
	Anxiety disorders[b]	850 (45.8)	440 (43.7)	57 (45.2)
Antipsychotic use, n (%)		**1,162 (62.6)**	**628 (62.4)**	**92 (73.0)**
FGA		150 (8.1)	73 (7.2)	8 (6.3)
SGA		1,106 (59.6)	597 (59.3)	90 (71.4)
Clozapine		40 (2.2)	13 (1.3)	2 (1.6)
Long-acting injectable		110 (5.9)	48 (4.8)	3 (2.4)

[a]Assessed on index date; If multiple specialties were identified, then a hierarchy was applied (Neurologist > Psychiatrist > Geriatrics > Primary care physician). [b]Anxiety disorders included phobia, panic disorder, obsessive-compulsive disorder, and post-traumatic stress disorder.

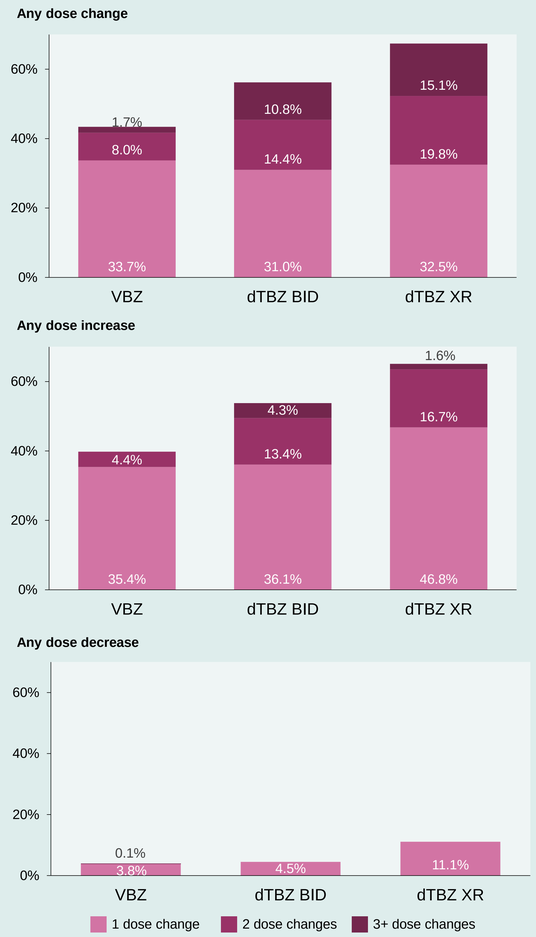
Key: BID, twice daily; CCI, Charlson Comorbidity Index; dTBZ, deutetrabenazine; FGA, first-generation antipsychotics; SD – standard deviation; SGA, second-generation antipsychotics; VBZ, valbenazine; XR, extended release.

Figure 2. Dosing patterns in persistent patients over the follow-up period by cohort



Key: BID, twice daily; XR, extended release.

Figure 3. Dose changes during the follow-up period by cohort



Key: BID, twice daily; dTBZ, deutetrabenazine; VBZ, valbenazine; XR, extended release.

Therapeutic dose attainment

- All VBZ patients (n=1,856) reached a therapeutic dose as the starting dosage strength of VBZ is clinically effective
- Significantly fewer dTBZ patients met the therapeutic threshold of ≥24 mg/day within 6 months (BID: 62% [n=627]; XR: 73% [n=92]; both *P*<0.001)

Dosing trends (Figure 2)

- Significantly more VBZ patients remained on their starting dose (57% [n=1,050] vs 44% [BID; n=441] and 33% [XR; n=41]; both P<0.001) and significantly fewer experienced any dose increase (40% [n=738] vs 54% [BID; n=542] and 65% [XR; n=82]; both *P*<0.001) compared to dTBZ cohorts (**Figure 3**)
  - 30% (n=564) of VBZ patients started on 40 mg daily and remained on 40 mg
  - 38% (n=379) of dTBZ BID and 27% (n=34) of dTBZ XR patients started and remained on doses under 24 mg total daily
- Experiencing multiple dose increases with dTBZ was roughly four times more common (BID: 18% [n=178], XR: 18% [n=23]) compared to VBZ (4%; n=81) (**Figure 3**)
  - 29% (n=532) of VBZ patients, 44% (n=439) of dTBZ BID patients, and 44% (n=56) of dTBZ XR patients experienced any dose increase after Month 1 (both *P*<0.01 compared to VBZ). 19% (n=347), 31% (n=308), and 31% (n=39) experienced any dose increase after Month 2, respectively (both *P*<0.01 compared to VBZ)

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LIMITATIONS

- This study used open (unadjudicated) claims data from participating plans, which may have incomplete data capture for patients receiving care outside of participating plans
- Drug samples are not captured in claims data, which may limit the understanding of the use and impact of titration packs

CONCLUSIONS

- **To our knowledge, this is the first study to compare real-world VMAT2 inhibitor dosing patterns in the context of TD trial results. These specific results focus on patients persistent for 6 months**
- **Approximately one-third of dTBZ XR patients started below the recommended starting dose**
- **Over one-quarter of dTBZ patients on either formulation did not attain therapeutic dosing**
- **Persistent patients taking VBZ experienced fewer dose changes than dTBZ patients, representing a simpler treatment regimen**
- **The burden of dose changes and subtherapeutic dosing of VMAT2 inhibitors may be explored in future research**

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