Drug–Drug Interactions With Vesicular Monoamine Transporter 2 Inhibitors: Population Estimate of Patients With Tardive Dyskinesia at Risk in Real-World Clinical Practice

Poster 30

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Introduction

- Valbenazine (VBZ) and deutetrabenazine (DTBZ), vesicular monoamine transporter 2 (VMAT2) inhibitors are approved in the United States for treatment of adults with tardive dyskinesia (TD)[1]
- VBZ labeling recommends dose adjustment to the lowest available dose (40 mg/day) when taking strong CYP3A4 or CYP2D6 inhibitors and avoidance of strong CYP3A4 inducers and monoamine oxidase inhibitors (MAOIs) because of potential drug–drug interactions (DDIs)[2]
- DTBZ labeling recommends dose adjustment to ≤36 mg/day when taking strong CYP2D6 inhibitors and avoidance of MAOIs[3]
- Drugs with potential for DDIs with VMAT2 inhibitors include antidepressants and antipsychotics (APs) commonly taken by patients with TD, as well as a number of other important medications (**Table 1**)[4]

Table 1. Drugs With Potential Drug-Drug Interactions With VMAT2 inhibitors

Strong CYP3A4 inhibitors	Strong CYP2D6 inhibitors	Strong CYP3A4 inducers	MAOIs
• Antidepressants – Nefazodone • Antibiotics – Clarithromycin – Telithromycin – Troleandomycin • Antifungals – Itraconazole – Ketoconazole – Posaconazole – Voriconazole • Antiretrovirals – Cobicistat – Ritonavir – Nelfinavir • Antineoplastics – Ceritinib – Idelalisib	• Antidepressants – Bupropion – Fluoxetine – Paroxetine • Antifungals – Terbinafine • Antiarrhythmics – Quinidine	• Antibiotics – Rifampin • Anticonvulsants – Carbamazepine – Phenytoin • Androgen receptor inhibitors – Apalutamide – Enzalutamide – Lumacaftor • Antineoplastics – Ivosidenib – Mitotane	• Antidepressants – Selegiline – Isocarboxzaid – Phenelzine – Tranylcypromine

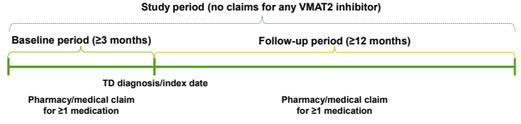
Objective

- To estimate the proportion of patients with newly diagnosed TD not currently taking a VMAT2 inhibitor at risk of DDIs with VBZ and DTBZ use in real-world practice

Methods

- Patients (aged ≥18 years) with first diagnosis of TD (index date) between July 2019 and June 2022 were identified from the Symphony Health Sciences database, a US-based medical, hospital, and pharmacy claims database using the following inclusion criteria:
  - ≥1 claim for APs at any time
  - No VBZ or DTBZ claims within ≥3 months prior and ≥12 months after their index date
  - Continuous enrollment for ≥3 months pre- and ≥12 months post-index identified by ≥1 medical/pharmacy claim(s) ≥3 months prior and ≥12 months after index date (**Figure 1**)

Figure 1. Study Timeline



Study Design

- Included patients were divided into groups based on claims made for medication that have potential DDI risk with VBZ or DTBZ
  - Risk of DDI with VBZ >40 mg (includes claims for strong CYP3A4 inducers and inhibitors, strong CYP2D6 inhibitors, or MAOIs)
  - Risk of DDI with VBZ 40 mg (strong CYP3A4 inducers or MAOIs) or DTBZ ≤36 mg (MAOIs)
  - Risk of DDI with DTBZ >36 mg (strong CYP2D6 inhibitors or MAOIs)
- Proportions of patients meeting VBZ/DTBZ concomitant medication labeling restrictions were summarized descriptively

Results

- Among 66,046 patients with TD identified in the database, 14,264 met inclusion criteria and were included in the analysis (**Table 2**)
- Most of the population were female (63.2%), from the South (37.4%) and Midwest regions (28.7%) of the US with a mean age of 57.4 years and commercial insurance (48.1%) (**Table 3**)
- 62.1% of patients were taking APs and diagnosed with an underlying mood disorder (57.1%), and 73.2% had an outpatient visit during the baseline period (**Table 3**)

Table 2. Sample Attrition

	Total
Patients with ≥1 medical/pharmacy claim for TD July 2019–June 2022 (study period)	66,046
Patients with ≥1 medical/pharmacy claim ≥3 months prior to TD diagnosis (baseline period)	54,946
Patients with ≥1 medical/pharmacy claim ≥12 months post TD diagnosis (follow-up period)	29,132
Patients aged ≥18 years at diagnosis	28,739
Patients with ≥1 AP claim at any time	16,564
Patients with no VMAT2 inhibitor claims ≥3 months prior to and ≥12 months after diagnosis	14,264

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Disclosures
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Abbreviations
AP = antipsychotic, DDI = drug-drug interactions, DTBZ = deutetrabenazine, MAOI = monoamine oxidase inhibitor, TD = tardive dyskinesia, VBZ = valbenazine, VMAT2 = vesicular monoamine transporter 2

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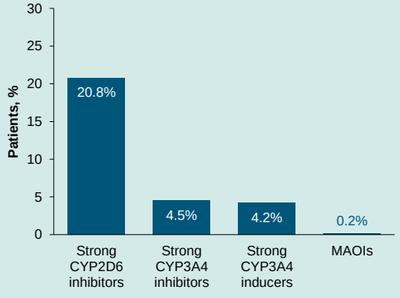
Key Results

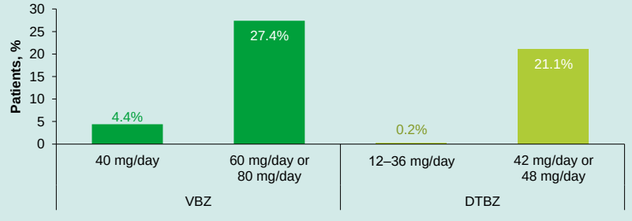
- Proportion of patients at potential risk of DDIs shown below (**Figure 2**)

Figure 2. Proportion of Patients at Risk of DDIs by Concomitant Medication



- Proportion of patients at potential risk of DDIs were lower if DTBZ 12–36 mg/day (0.2%) were prescribed versus VBZ 40 mg/day (4.4%) (**Figure 3**)
- Proportion of patients at potential risk of DDIs were also lower if DTBZ 42 mg/day or 48 mg/day (21.1%) were prescribed versus VBZ 60 mg/day or 80 mg/day (27.4%) (**Figure 3**)

Figure 3. Proportion of Patients at Risk of DDIs With VBZ and DTBZ



- Similar results were observed when patients with ≥1 VBZ/DTBZ claim following TD diagnosis were included in the analysis

Table 3. Patient Characteristics at Baseline

		Total n=14,264
Female, n (%)		9014 (63.2)
Age (years), mean (SD)		57.4 (14.4)
US region, n (%)	South	5328 (37.4)
	Midwest	4089 (28.7)
	Northeast	2616 (18.3)
	West	2158 (15.1)
	Unknown	73 (0.5)
Payer type, n (%)	Commercial	6860 (48.1)
	Medicare	2738 (19.2)
	Medicaid	1603 (11.2)
	Self/Other	3063 (21.5)
Underlying psychiatric disorder, n (%)	Mood disorder (MD)	8146 (57.1)
	Bipolar disorder (BD)	4727 (33.1)
	Schizophrenia (SCZ)	3486 (24.4)
	Major depressive disorder (MDD)	2275 (15.9)
Antipsychotic use, n (%)		8864 (62.1)
Healthcare resource utilization, n (%)	Outpatient visit	10,436 (73.2)
	Emergency department visit	3694 (25.9)
	Hospitalization	2316 (16.2)

Discussion

- This study evaluated the proportions of patients newly diagnosed with TD potentially at risk of DDIs with VMAT2 inhibitors based on the medications they were receiving at the time of their diagnosis. The analysis did not include any observations of DDIs
- The primary analysis included patients who were not taking VMAT2 inhibitors during the study period, and therefore, characterized a real-world population of patients with TD who clinicians could consider for potential treatment with VMAT2 inhibitors
- The database contained a larger proportion of commercially-insured patients (versus Medicare/Medicaid) than the general population. This may limit the generalizability of the study results
- Based on a separate real-world study (START study),[6] for the 83% of patients who achieved an optimal DTBZ dose, the dose was between 24 mg/day and 36 mg/day, for which the predicted risk of DDIs is low based on the analyses shown here

Conclusions

- **Based on analysis of real-world data, it was observed that the proportion of patients with TD at risk for DDIs was lower for DTBZ than with VBZ**
- **These data will be useful for healthcare professionals in selecting the most appropriate VMAT2 inhibitor for the treatment of TD after considering other concomitant medications that individual patients may be using**