Real World Experience with Novel VMAT2 Inhibitors

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OBJECTIVE

- To review the "real world" experience with novel vesicular monoamine transporter 2 (VMAT2) inhibitors, including tetrabenazine (Xenazine©, and generic; TBZ), deutetrabenazine (Austedo©; DTBZ), and valbenazine (Ingrezza©; VBZ) [1–4].

BACKGROUND

- VMAT2 inhibitors are FDA approved for the treatment of chorea in Huntington disease (HD; TBZ, 2008; DTBZ, 2017) and tardive dyskinesia (TD; DTBZ, 2017; VBZ, 2017) [5,6].
- Access to novel VMAT2 inhibitors may be limited by high cost and insurance denials [7].
- Lack of experience with the management of movement disorders using VMAT2 inhibitors, and differences in clinical efficacy and adverse event profile in a "real world" setting compared to clinical trials, may limit patient adherence.

METHODS

- The Institutional Review Board at Baylor College of Medicine approved this study and waiver of patient consent was obtained.
- Retrospective chart review (treatment indications, insurance approval/denial, and treatment outcomes) of all patients prescribed a VMAT2 inhibitor in our clinic for any indication between Jan. 1, 2017 and Aug. 30, 2018, supplemented with a questionnaire which was mailed to the patients.
- Measurement of treatment efficacy: 1-4 Likert scale (1=normal or mildly ill, 4=severely ill).
- Validated rating scales were generally not administered at the clinic visits.

RESULTS

- Patients (n) = 135 (78 male, 57.8%); 22 (16.3%) returned the survey (Table 1).
- Prescriptions (n) = 178 (TBZ, n=45, 25.3% [Figure 1-2]; DTBZ, n=104, 58.4% [Figure 3-4]; VBZ, n=29, 16.3% [Figure 5-6]) within the study period of 20 months.
- VMAT2 inhibitor prescription practice: FDA-approved indications: HD (n=25) and TD (n=28). Off-label indications (60.7% of all indications): Tourette syndrome (TS) (n=67), chorea (not HD; n=10), stereotypies (n=3), and other (n=2) (Figure 1-6).
- Insurance coverage: The rate of approval by patient's insurance was highest for FDA-approved conditions (98.2%) compared to off-label indications (59.0%). Approval rates (after appeals) for patients with TS: 100% for TBZ, 23.6% for DTBZ, and 72.7% for VBZ (Figure 1-6).
- Mean (range; SD) treatment durations and daily dosages (range; SD): TBZ (n=31) 5.1 months (1-19; 3.9) at 48.8 mg/day (12.5-112.5; 29.6); DTBZ (n=51) 8.0 months (0.25-16.5; 4.4) at 34.4 mg/day (6-96; 20.7); and VBZ (n=20) 6.0 months (0.1-16; 5.6) at 64 mg/day (40-160; 35.3).
- More than half of patients were still taking a VMAT2 inhibitor (TBZ, 64.5%; DTBZ, 78.8%; VBZ, 47.6%) at the end of the study period.
- Most patients experienced clinical improvement in their hyperkinetic movement disorder; the proportion of patients who had only mild symptoms was 60.9-71.9% while on treatment compared to 13.0-26.7% before starting treatment (Figure 7).
- Most common reason for discontinuation of VMAT2 inhibitor: Occurrence of adverse events (Table 2) out of proportion to clinical benefit (63.6-90.1%).

CONCLUSION

- Our retrospective chart review reveals a high approval rate of VMAT2 inhibitors for FDA-approved indications.
- DTBZ and VBZ were usually not covered by insurance for non-FDA approved conditions, while TBZ was covered most of the time.
- VMAT2 inhibitors were effective in the treatment of various hyperkinetic movement disorders with adverse event rates that are similar to those reported in clinical trials.
- A limitation of our retrospective study was the absence of a validated rating scale administered at each clinic visit.

DEMOGRAPHICS

	HD	TD	Chorea (not HD)	TS/tics	Stereotypies	Other
Patients, n	25	28	10	67	3	2
Gender, M | F	14 | 11	12 | 16	3 | 7	46 | 21	3 | 0	0 | 2
Age at symptom onset, years (range, SD)	47.6 (16-69, 13.9)	51.5 (13-78, 14.7)	35.8 (1-74, 29.1)	9.0 (1.5-34, 6.6)	20.0 (1-58, 28.9)	19.25 (0.5-38, 26.5)
Duration of symptoms, years (range, SD)	11 (3-35, 7.4)	6.8 (1-25, 5.5)	10.6 (1-47, 14.6)	18.6 (1-69, 14.4)	14.3 (3-27, 12.1)	19.8 (16-23.5, 5.3)

Table 1 (above). M = male, F = female, Other = any other movement disorder treated with a VMAT2 inhibitor (one patient with perioral dyskinetic movements and dystonia of unclear etiology and one patient with opsoclonus-myoclonus syndrome).

Table 2 (right). GI = gastrointestinal, RXN = reaction. Adverse event (AE) rates are not directly comparable due to differences in dosing between different VMAT2 inhibitors. For example, one patient in the VBZ group reported nine separate AEs out of a total of 17 AEs reported for the whole group.

ADVERSE EVENTS

	TBZ n=23 (%)	DTBZ n=32 (%)	VBZ n=15 (%)
Drowsiness	9 (39.1)	3 (9.4)	6 (40.0)
Dry mouth	2 (8.7)	1 (3.1)	2 (13.3)
Depression	2 (8.7)	2 (6.3)	3 (20.0)
Anxiety	2 (8.7)	3 (9.4)	2 (13.3)
GI symptoms	1 (4.3)	0 (0)	0 (0)
Akathisia	1 (4.3)	1 (3.1)	1 (6.7)
Insomnia	1 (4.3)	3 (9.4)	0 (0)
Parkinsonism	1 (4.3)	4 (12.5)	1 (6.7)
Headache	1 (4.3)	1 (3.1)	0 (0)
Gait changes/falls	1 (4.3)	0 (0)	1 (6.7)
Acute dystonic RXN	0 (0)	2 (6.3)	0 (0)
Weight gain	0 (0)	1 (3.1)	0 (0)
Suicidal ideation	0 (0)	1 (3.1)	0 (0)
Drooling	0 (0)	2 (6.3)	0 (0)
Aggression	0 (0)	2 (6.3)	0 (0)
Allergy	0 (0)	0 (0)	1 (6.7)

Figure 1: TBZ - Prescription Characteristics

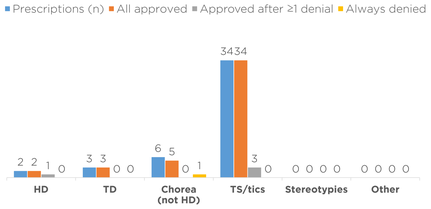


Figure 2: TBZ – Reason for Insurance Denial

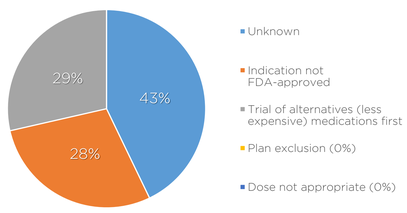


Figure 3: DTBZ - Prescription Characteristics

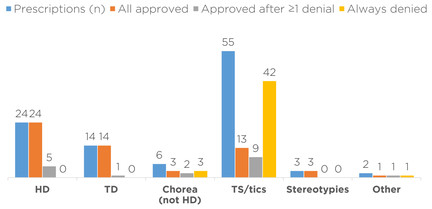


Figure 4: DTBZ – Reason for Insurance Denial

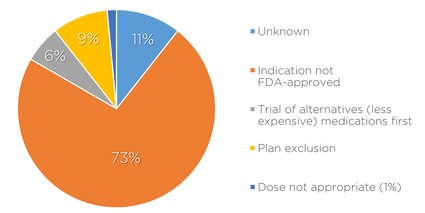


Figure 5: VBZ - Prescription Characteristics

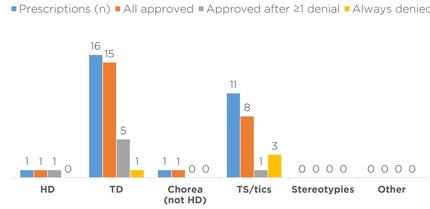


Figure 6: VBZ – Reason for Insurance Denial

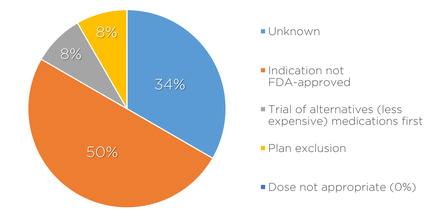
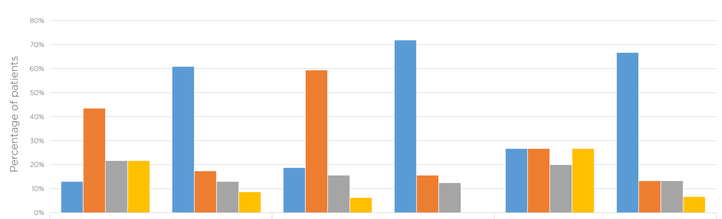


Figure 7: Clinical Response to VMAT2 Inhibitors



	Baseline	On treatment	Baseline	On treatment	Baseline	On treatment
	TBZ (n=23)		DTBZ (n=32)		VBZ (n=15)	
1 Mildly ill	13.0	60.9	18.8	71.9	26.7	66.7
2 Moderately ill	43.5	17.4	59.4	15.6	26.7	13.3
3 Markedly ill	21.7	13.0	15.6	12.5	20.0	13.3
4 Severely ill	21.7	8.7	6.3	0.0	26.7	6.7

REFERENCES

1. Kenney C, Hunter C, Mejia N, Jankovic J. Tetrabenazine in the treatment of Tourette syndrome. J Pediatr Neurol. 2007;5:9-13.
2. Jankovic J. Dopamine depleters in the treatment of hyperkinetic movement disorders. Expert Opin Pharmacother. 2016;17:2461-70.
3. Jankovic J, Jimenez-Shahed J, Budman C, Coffey B, Murphy T, Shprecher D, et al. Deutetrabenazine in tics associated with Tourette syndrome. Tremor Other Hyperkinetic Mov (NY). 2016;6:422.
4. Scorr LM, Factor SA. VMAT2 inhibitors for the treatment of tardive dyskinesia. J Neurol Sci. 2018;389:43-7.
5. Bashir H, Jankovic J. Treatment options for chorea. Expert Rev Neurother. 2018;18:51-63.
6. Niemann N, Jankovic J. Treatment of tardive dyskinesia: A general overview with focus on the vesicular monoamine transporter 2 inhibitors. Drugs. 2018;78:525-41.
7. Deutetrabenazine (Austedo) for Huntington's chorea and tardive dyskinesia. Med Lett Drugs Ther. 2018;60:65-8.

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