Psych Congress Network

TARDIVE DYSKINESIA 360

Practical Strategies for Patient Follow-Up and Long-Term VMAT2 Inhibitor Treatment

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Faculty Disclosure

- **Dr. Jain**: Advisory Board—Addrenex, Alkermes, Avanir, Forum, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka, Pamlab, Pfizer, Shionogi, Shire, Sunovion, Supernus, Takeda, Teva; Consultant—Addrenex, Allergan, Avanir, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka, Pamlab, Pfizer, Shionogi, Shire, Sunovion, Supernus, Takeda, Teva; Consultant (spouse)—Lilly, Otsuka, Pfizer, Sunovion; Grant/Research Support—Allergan, AstraZeneca, Lilly, Lundbeck, Otsuka, Pfizer, Shire, Takeda; Speakers Bureau—Addrenex, Alkermes, Allergan, Lilly, Lundbeck, Merck, Otsuka, Pamlab, Pfizer, Rhodes, Shionogi, Shire, Sunovion, Takeda, Tris Pharmaceuticals.

Disclosure

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
  - The off-label use of amantadine, clonazepam, baclofen, branched chain amino acid, botulinum toxin, deep brain stimulation, donepezil, Ginkgo biloba, tetrabenazine, valproic acid, and vitamins for the treatment of tardive dyskinesia will be discussed.
- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.
- This activity has been independently reviewed for balance.
- Video clips of patients were obtained with permission.

Learning Objectives

- Evaluate the available clinical trial data surrounding the long-term efficacy and tolerability of VMAT2 inhibitors for the treatment of tardive dyskinesia (TD)
- Develop comprehensive follow-up plans for patients with TD taking a VMAT2 inhibitor that incorporate individualized monitoring and dose adjustment for optimal efficacy and safety
- Apply practical strategies to overcome barriers to optimal VMAT2 inhibitor initiation and continuation when prescribed for the treatment of TD

Psych Congress Network

TARDIVE DYSKINESIA 360

- Latest information on TD
- Expert Review article
- Video patient interviews
- AIMS instructional videos
- Patient case quizzes

… and so much more!

You will receive monthly e-mails throughout the year to provide updated information and reinforce today's education.

www.TD-360.com

Definition of Tardive Dyskinesia

Tardive dyskinesia:

A type of dyskinesia that typically emerges after long-term use of antipsychotic drugs (DRBAs)

Tardive

Appearing or tending to appear late

Dyskinesia

Distortion or impairment of voluntary movement

Socially stigmatizing, functionally impairing, and probably irreversible medical condition

***DSM* Dx of Tardive Dyskinesia** (highlights)**:**

- Involuntary movements of the tongue, jaw, trunk, or extremities have developed in association with the use of neuroleptic medication
- The involuntary movements are present over a period of at least 4 weeks and occurring any of the following patterns: (1) choreiform movements (ie, rapid, jerky, nonrepetitive); (2) athetoid movements (ie, slow, sinuous, continual); (3) rhythmic movements (ie, stereotypies)

- Symptoms develop during exposure to a neuroleptic medication or within 4 weeks of withdrawal from an oral (or within 8 weeks of withdrawal from a depot) neuroleptic medication
- There has been exposure to neuroleptic medication for at least 3 months (1 month if age ≥ 60 years)

DRBA = dopamine receptor blocking agent.

Lerner PP, et al. *Psychiatry Clin Neurosci*. 2015;69(6):321-334. Dorland's Online Medical Dictionary. www.dorlands.com.

Patient Perspectives on Living with TD

Identifying TD in Our Practices: The AIMS

Abnormal Involuntary Movement Scale (AIMS) Preliminaries

The AIMS is a standardized objective rating scale administered via a well-defined examination procedure that is used to formally document the extent and severity of TD

Although the complete AIMS examination is useful for formally documenting the extent, course, and severity of TD every 3 months or less often depending on risk, patients should be questioned and visually observed *AT EVERY VISIT* for early signs of TD and other movement disorders

If a patient is < 50 years

- Every 6 months if on FGA
- Every 12 months if on SGA

If a patient is > 50 years OR has other risk factors

- Every 3 months (or less)

FGA = first-generation antipsychotic; SGA = second-generation antipsychotic.

Guy W. *ECDEU Assessment Manual for Psychopharmacology, Revised 1976*. Rockville, MD: U.S. Dept. of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976:534-537.

Abnormal Involuntary Movement Scale (AIMS) Preliminaries

- The chair to be used in the examination should be a hard, firm one without arms.
- Ask the patient whether there is anything in his or her mouth (such as gum or candy) and, if so, to remove it.
- Ask about the current condition of the patient's teeth. Ask if he or she wears dentures. Ask whether teeth or dentures bother the patient now.
- Ask whether the patient notices any movements in his or her mouth, face, hands, or feet. If yes, ask the patient to describe them and to indicate to what extent they currently bother the patient or interfere with activities.

Guy W. *ECDEU Assessment Manual for Psychopharmacology, Revised 1976*. Rockville, MD: U.S. Dept. of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976:534-537.

Abnormal Involuntary Movement Scale (AIMS) Exam

Ratings

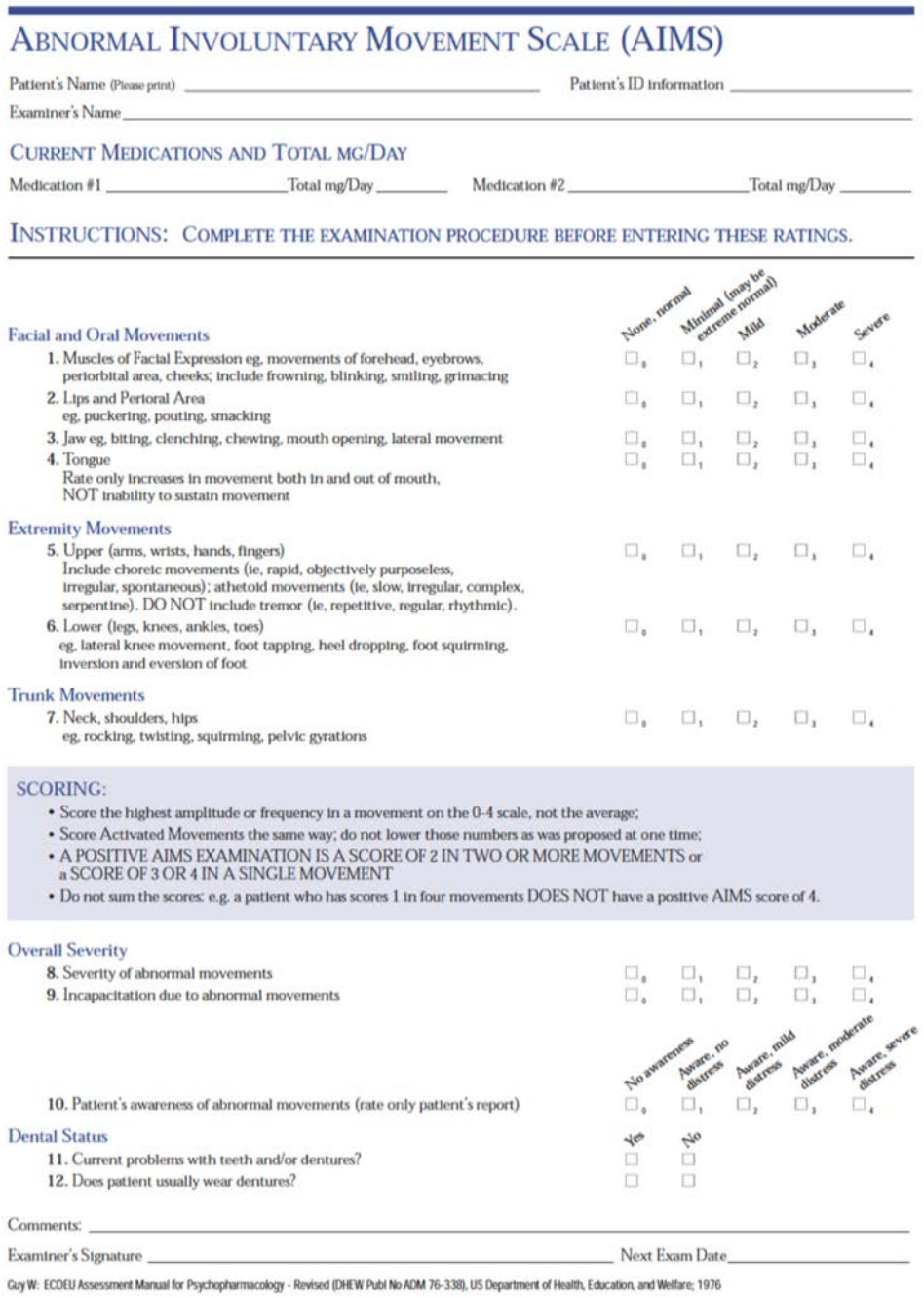
The scale is rated from

0 (none)
1 (minimal)
2 (mild)
3 (moderate)
4 (severe)

Positive AIMS

Score of 2 or more in **TWO** or more movements ***OR***

Score of 3 or 4 in a **SINGLE** movement



ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

Patient's Name (Please print) _____ Patient's ID information _____

Examiner's Name _____

CURRENT MEDICATIONS AND TOTAL MG/DAY

Medication #1 _____ Total mg/Day _____ Medication #2 _____ Total mg/Day _____

INSTRUCTIONS: COMPLETE THE EXAMINATION PROCEDURE BEFORE ENTERING THESE RATINGS.

	None, normal	Minimal (may be extreme normal)	Mild	Moderate	Severe
Facial and Oral Movements					
1. Muscles of Facial Expression eg, movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing	☐0	☐1	☐2	☐3	☐4
2. Lips and Perioral Area eg, puckering, pouting, smacking	☐0	☐1	☐2	☐3	☐4
3. Jaw eg, biting, clenching, chewing, mouth opening, lateral movement	☐0	☐1	☐2	☐3	☐4
4. Tongue Rate only increases in movement both in and out of mouth, NOT inability to sustain movement	☐0	☐1	☐2	☐3	☐4
Extremity Movements					
5. Upper (arms, wrists, hands, fingers) Include choreic movements (ie, rapid, objectively purposeless, irregular, spontaneous); athetoid movements (ie, slow, irregular, complex, serpentine). DO NOT include tremor (ie, repetitive, regular, rhythmic).	☐0	☐1	☐2	☐3	☐4
6. Lower (legs, knees, ankles, toes) eg, lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	☐0	☐1	☐2	☐3	☐4
Trunk Movements					
7. Neck, shoulders, hips eg, rocking, twisting, squirming, pelvic gyrations	☐0	☐1	☐2	☐3	☐4

SCORING:

- Score the highest amplitude or frequency in a movement on the 0-4 scale, not the average;
- Score Activated Movements the same way; do not lower those numbers as was proposed at one time;
- A POSITIVE AIMS EXAMINATION IS A SCORE OF 2 IN TWO OR MORE MOVEMENTS or a SCORE OF 3 OR 4 IN A SINGLE MOVEMENT
- Do not sum the scores: e.g. a patient who has scores 1 in four movements DOES NOT have a positive AIMS score of 4.

Overall Severity					
8. Severity of abnormal movements	☐0	☐1	☐2	☐3	☐4
9. Incapacitation due to abnormal movements	☐0	☐1	☐2	☐3	☐4
	No awareness	**Aware, no distress**	**Aware, mild distress**	**Aware, moderate distress**	**Aware, severe distress**
10. Patient's awareness of abnormal movements (rate only patient's report)	☐0	☐1	☐2	☐3	☐4
	Yes	**No**			
Dental Status					
11. Current problems with teeth and/or dentures?	☐	☐			
12. Does patient usually wear dentures?	☐	☐			

Comments: _____

Examiner's Signature _____ Next Exam Date _____

Guy W: ECDEU Assessment Manual for Psychopharmacology - Revised (DHEW Publ No ADM 76-338), US Department of Health, Education, and Welfare; 1976

Management of TD: *Historical and Contemporary Perspectives*

Historical Management of TD

- Prevention
- Removal of causative drug
  - Slow taper rather than sudden withdrawal
  - May precipitate worsening of psychosis or withdrawal dyskinesia
  - Change to atypical antipsychotic with low potency—quetiapine and clozapine
  - Restarting or increasing the dose of a causative DRBA or a similar agent can reduce TD, but this strategy should be avoided whenever possible and reserved only as an emergency solution
- Switch to a DRBA with less D_2 receptor occupancy
- Avoid medications that can worsen TD
  - Anticholinergics often worsen chorea and stereotypy, but may improve tardive dystonia
- GABA agonistic medications
  - Clonazepam, baclofen, valproic acid
- Other medications: amantadine, donepezil, branched chain amino acid, vitamins

Bhidayasiri R, et al. *Postgrad Med J*. 2011;87(1024):132-141. Waln O, et al. *Tremor Other Hyperkinet Mov*. 2013;3. pii: tre-03-161-4138-1. Caroff SN. *Current Psychiatry*. 2011;10(10):22-32.

Modern Management of TD

- Dopamine depleting drugs
  - Tetrabenazine (not FDA approved), Deutetrabenazine (FDA approved), Valbenazine (FDA approved)
- Amantadine (not FDA approved)
- Clonazepam (not FDA approved)
- Chemo-denervation with botulinum toxin injections (not FDA approved)
- Deep brain stimulation (not FDA approved)

Bhidayasiri R, et al. *Postgrad Med J*. 2011;87(1024):132-141. Waln O, et al. *Tremor Other Hyperkinet Mov*. 2013;3. pii: tre-03-161-4138-1. Caroff SN. *Current Psychiatry*. 2011;10(10):22-32.

Treatment of TD: Antidyskinetic Agents
American Academy of Neurology (AAN) Guidelines

Medication	Evidence Level	Recommendation
Clonazepam	Moderate	Probably effective for decreasing TD symptoms short-term (~3 months); may be considered for short-term treatment
Ginkgo biloba	Moderate	Probably useful in TD treatment, but data are limited to patients with schizophrenia
Amantadine	Weak	Amantadine with neuroleptics may be considered to treat TD for short-term use
Tetrabenazine	Weak	Possibly reduces TD symptoms; may be considered in treating TD

Previous reviews/meta-analyses and guidelines are limited in clinical application.

- Treatments studied have limited evidence, based on small trials that are often underpowered, uncontrolled, unblinded, from single sites, or unreplicated – *Absence of evidence is not evidence of absence!!!*
- Focus is on design and statistical validity but less so on tolerability, reliability, and availability of products.
- Antipsychotics and antimuscarinics are analyzed equally with specific antidyskinetics, apart from psychiatric necessity.
- Recent RCTs of novel VMAT2 inhibitors are not included and far exceed previous levels of evidence.

RCT = randomized controlled trial.

Bhidayasiri R, et al.; American Academy of Neurology. *Neurology*. 2013;81(5):463-469.

Overview of VMAT2 Inhibitors

Tetrabenazine –

- FDA approved for the treatment of chorea in Huntington's disease
- Clinical trials in TD (off-label)

Valbenazine –

- FDA approved for the treatment of TD

Deutetrabenazine

- FDA approved for the treatment of chorea associated with Huntington's disease
- FDA approved for the treatment of TD

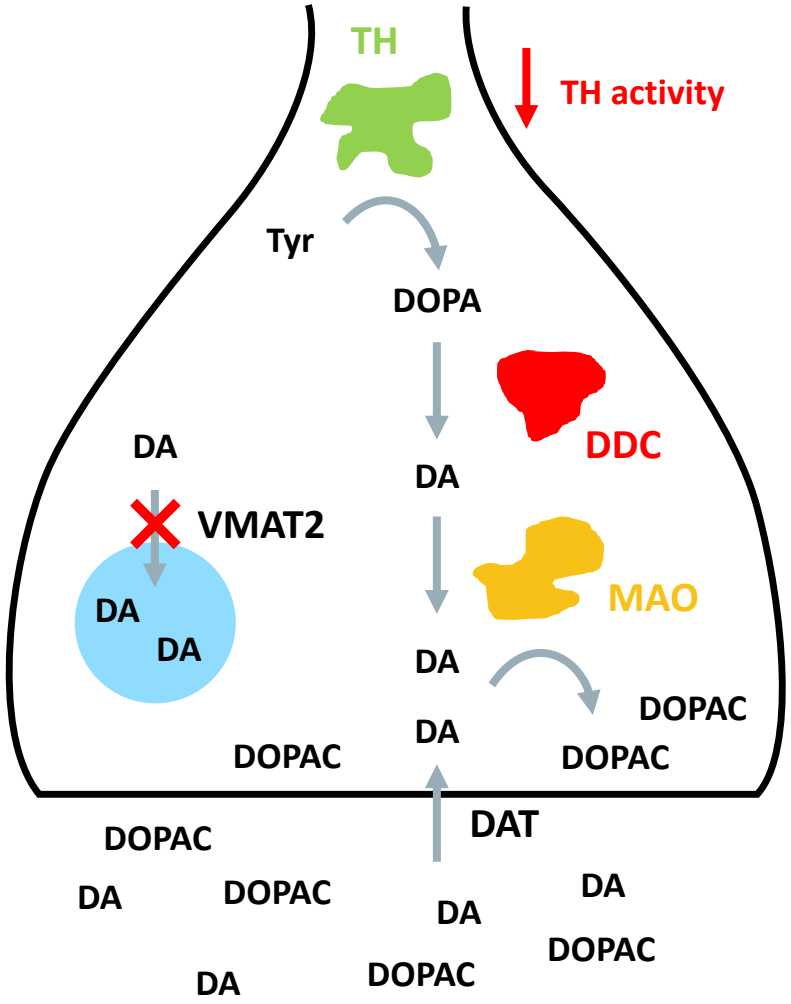
Dopamine Depletion:
The Birth of a New Mechanism to Treat TD

VMAT1 is not widely distributed in the human brain

VMAT2 is extensively distributed in the human cortex, striatum, and basal ganglia

It is found in presynaptic neurons

VMAT2 Controls Dopamine in Presynaptic Vesicles

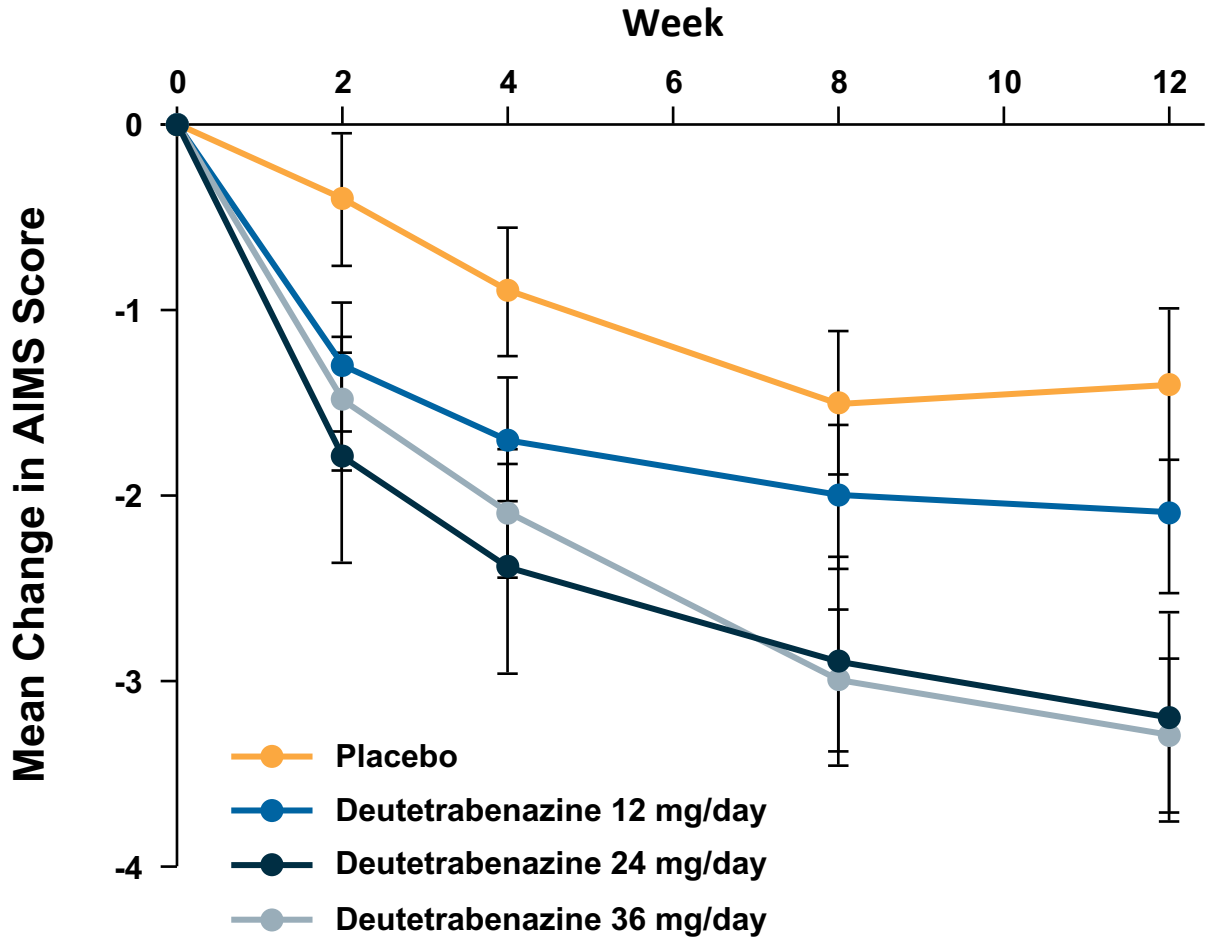


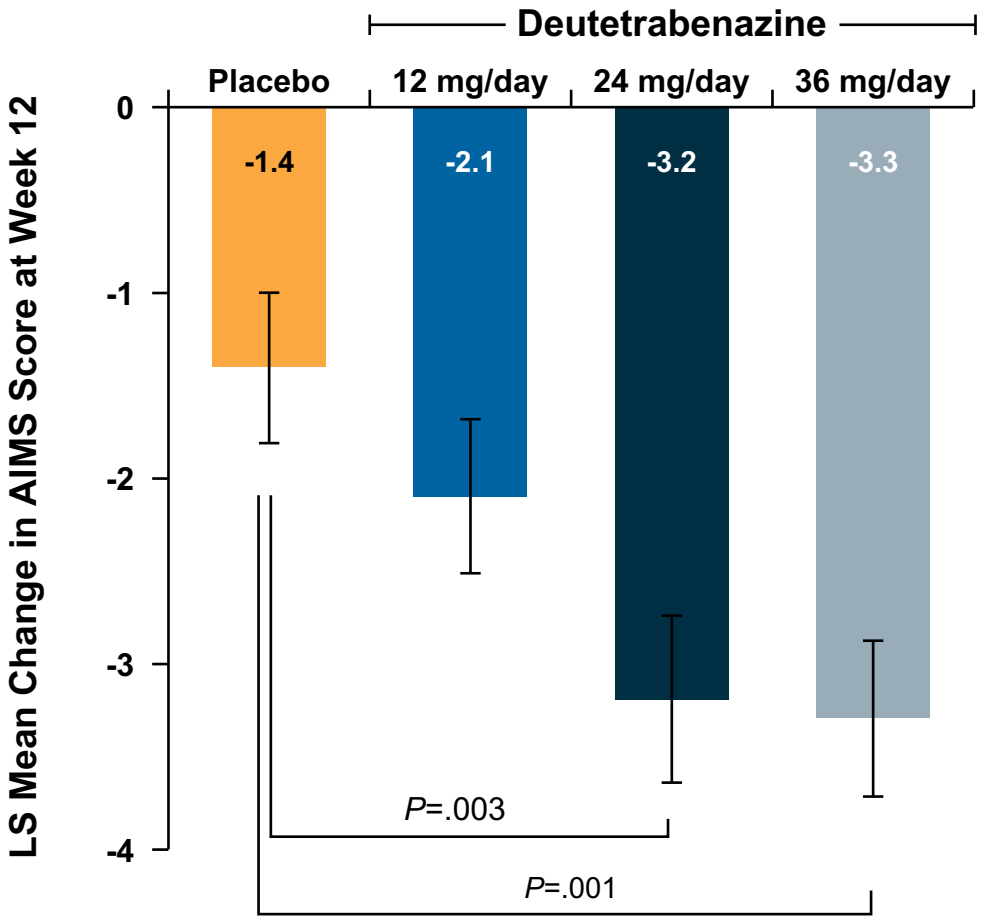
DAT = dopamine transporter; DOPA = dihydroxyphenylalanine; DOPAC = dihydroxyphenylacetic acid; DDC = dihydroxyphenylalanine decarboxylase; MAO = monoamine oxidase; TH = tyrosine hydroxylase; Tyr = tyrosine; VMAT = vesicular monoamine transporter.

Meyer AC, et al. *J Neurochem*. 2013;127(2):187-198.

Recent Clinical Trials of VMAT2 Inhibitors for Treatment of TD

Deutetrabenazine (AIM-TD): Mean Change in AIMS Score (Fixed-Dose Study Design)





Anderson KE, et al. *Lancet Psychiatry*. 2017;4(8):595-604.

Deutetrabenazine Safety and Tolerability Profile in Placebo-Controlled TD Studies

Placebo-Controlled TD Studies: Adverse Reactions Reported in ≥ 2% of Patients Treated with Deutetrabenazine

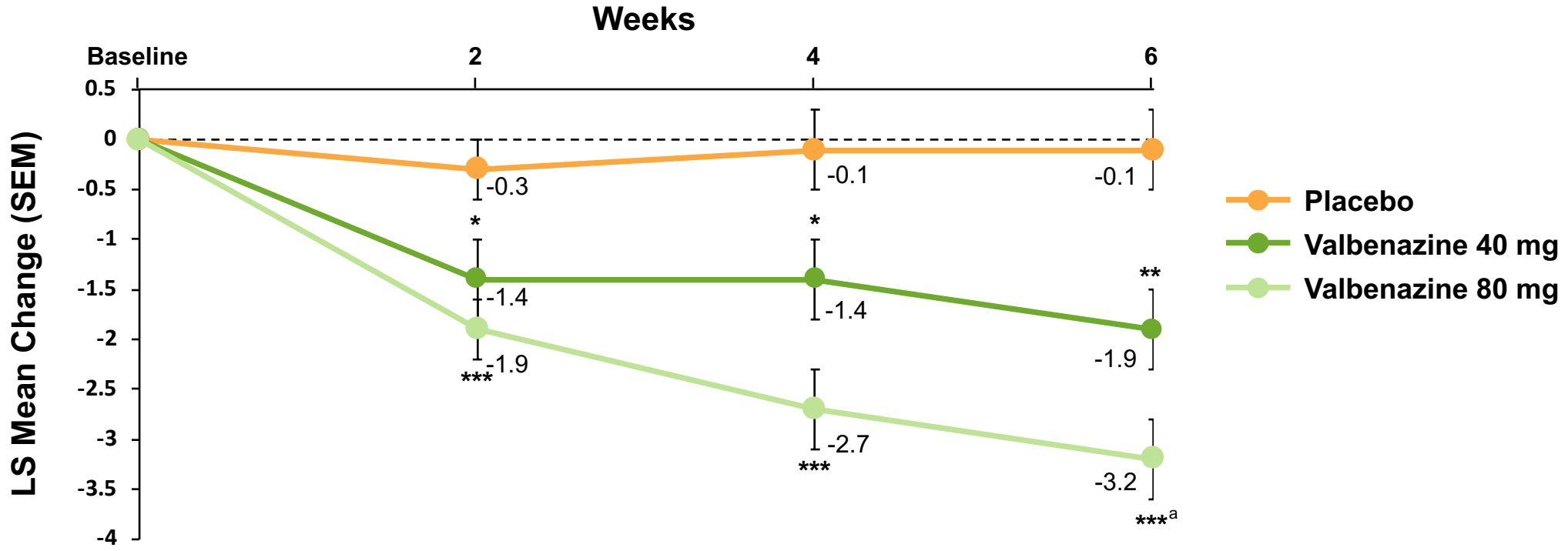
Adverse Reaction	Deutetrabenazine (n=279)	Placebo (n=131)
Headache	5%	8%
Somnolence	4%	7%
Diarrhea	4%	4%
Nasopharyngitis	4%	2%
Fatigue	4%	5%
Insomnia	4%	1%
Anxiety	4%	5%
Upper respiratory tract infection	3%	4%
Dry mouth	3%	5%
Nausea	2%	7%
Weight increased	2%	3%
Urinary tract infection	2%	2%
Depression/dysthymic disorder	2%	1%
Akathisia/Agitation/Restlessness	2%	1%

4% of patients required dose reduction of deutetrabenazine due to AEs vs 2% of patients taking placebo

AE = adverse effect.

Fernandez HH, et al. *Neurology*. 2017;88(21):2003-2010.
Anderson KE, et al. *Lancet Psychiatry*. 2017;4(8):595-604.

Valbenazine (KINECT 3): AIMS Change from Baseline by Study Visit (Fixed-Dose Study Design)



	n:				
Placebo		76	76	73	69
Valbenazine 40 mg		70	70	64	63
Valbenazine 80 mg		79	77	73	70

Intent-to-Treat Population: Included all randomized participants who had at least one post-randomization AIMS value.
***P*<.05. ****P*<.01. *****P*≤.001 for valbenazine vs placebo. [a]Dose that was statistically significantly different from placebo after adjusting for multiplicity.**

Hauser RA, et al. *Am J Psychiatry*. 2017;174(5):476-484.

Adverse Reactions in 3 Placebo-Controlled Studies of Valbenazine 6-Week Treatment Duration Reported at ≥ 2% and > Placebo

Adverse Reaction[a]	Valbenazine (n=262) (%)	Placebo (n=183) (%)
General Disorders		
Somnolence (somnolence, fatigue, sedation)	10.9%	4.2%
Nervous System Disorders		
Anticholinergic effects (dry mouth, constipation, disturbance in attention, vision blurred, urinary retention)	5.4%	4.9%
Balance disorders/fall (fall, gait disturbance, dizziness, balance disorder)	4.1%	2.2%
Headache	3.4%	2.7%
Akathisia (akathisia, restlessness)	2.7%	0.5%
Gastrointestinal Disorders		
Vomiting	2.6%	0.6%
Nausea	2.3%	2.1%
Musculoskeletal Disorders		
Arthralgia	2.3%	0.5%

[a]Within each adverse reaction category, the observed adverse reactions are listed in order of decreasing frequency.

US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. www.accessdata.fda.gov/scripts/cder/daf/index.cfm.

Additional Information: VMAT2 Inhibitors for TD

- Deutetrabenazine and valbenazine can reduce abnormal movements of TD that often cause substantial physical, social, and psychological impairment
  - Effective
  - Well-tolerated
- Patients can remain on antipsychotic therapy
  - Reduced risk of psychiatric decompensation
- Treatment goal = to reduce the severity and impact of TD
  - It is not necessary to eliminate all signs of TD
  - Attempting to completely suppress all TD will likely result in overtreatment and a greater potential for adverse effects

Margolius A, et al. *Parkinsonism Relat Disord*. 2018 Dec 19;[Epub ahead of print]. Citrome L. *J Neurol Sci*. 2018;389:61-66. Niemann N, et al. *Drugs*. 2018;78(5):525-541.

Additional Information: VMAT2 Inhibitors for TD (cont'd)

- There are no head-to-head studies of deutetrabenazine and valbenazine
- Customize therapy for patients in choosing drug
  - Consider adherence (valbenazine is once daily)
  - Consider need to fine-tune dosing regimen (greater dose flexibility with deutetrabenazine)
  - Consider side-effect profile

- Tolerability and efficacy between the 2 drugs may differ from patient to patient

Margolius A, et al. *Parkinsonism Relat Disord*. 2018 Dec 19:[Epub ahead of print]. Citrome L. *J Neurol Sci*. 2018;389:61-66. Niemann N, et al. *Drugs*. 2018;78(5):525-541.

Critical Issues to Remember with Both VMAT2 Therapies

- There is no need to discontinue or reduce or change antipsychotic therapy
- If patient is already on mood stabilizers and / or antidepressants – OK to continue therapy
- Both VMAT2 medications are effective in TD irrespective of their diagnosis (schizophrenia or mood disorder)
- Neither VMAT2-based FDA approved medications destabilize depression, mania, psychosis, or induce suicidality

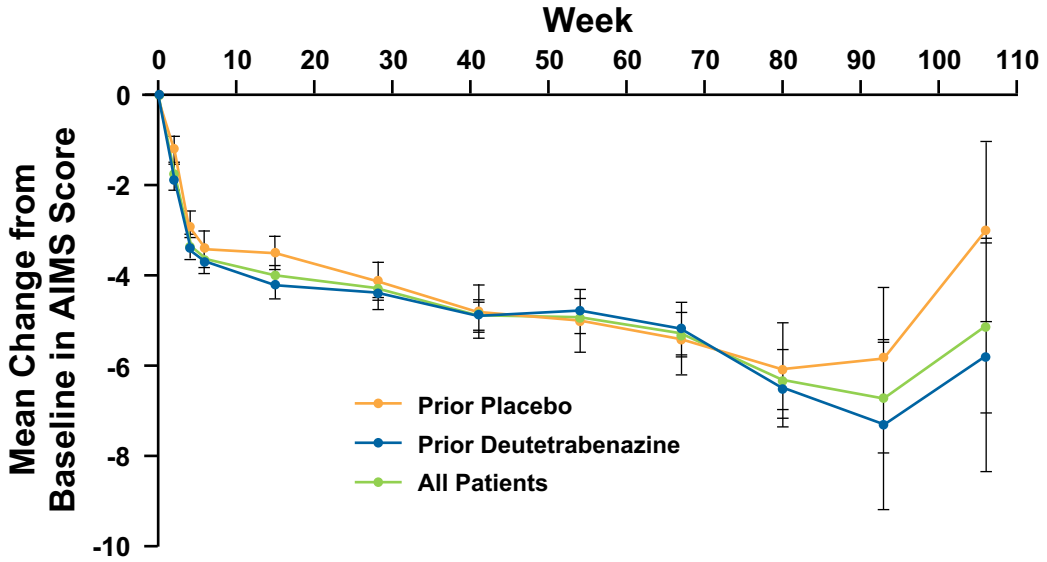
Margolius A, et al. *Parkinsonism Relat Disord*. 2018 Dec 19:[Epub ahead of print]. Citrome L. *J Neurol Sci*. 2018;389:61-66. Niemann N, et al. *Drugs*. 2018;78(5):525-541.

VMAT2 Therapy: Long-Term Data

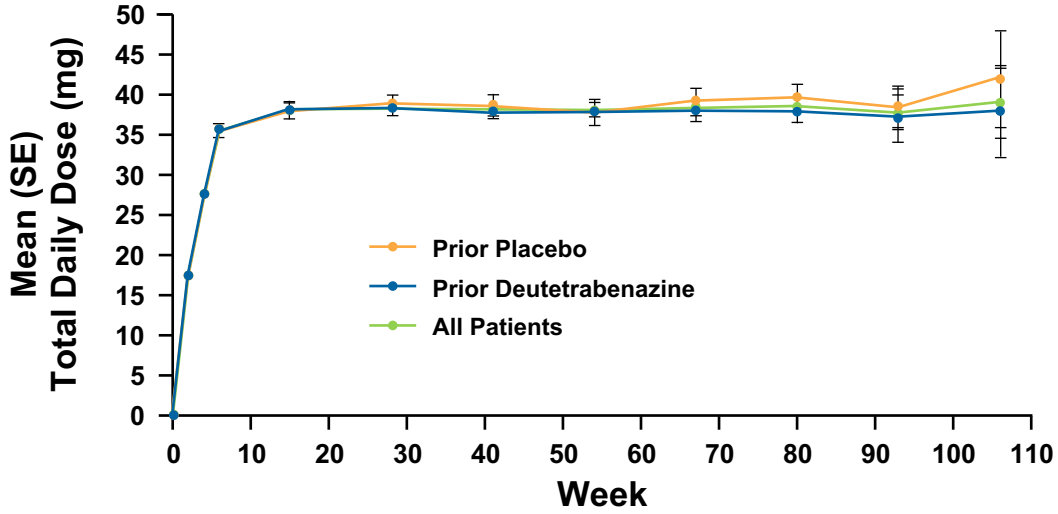
Deutetrabenazine
Valbenazine

Deutetrabenazine: Long-Term Data is Reassuring

2-year (Week 106) open-label response rates are reported in this interim analysis. Of 343 patients enrolled in the extension study, 232 previously received deutetrabenazine and 111 previously received placebo.



Week	0	2	4	6	15	28	41	54	67	80	93	106
Prior Placebo (n)	111	111	108	104	101	83	65	50	34	27	10	2
Prior Deutetrabenazine (n)	232	230	229	223	208	168	137	96	69	39	13	6
All Patients (n)	343	341	337	327	309	251	202	146	103	66	23	8



Week	0	2	4	6	15	28	41	54	67	80	93	106
Prior Placebo (n)	111	111	108	104	95	78	62	47	32	27	10	2
Prior Deutetrabenazine (n)	232	228	226	220	204	160	132	94	67	39	13	6
All Patients (n)	343	339	334	324	299	238	194	141	99	66	23	8

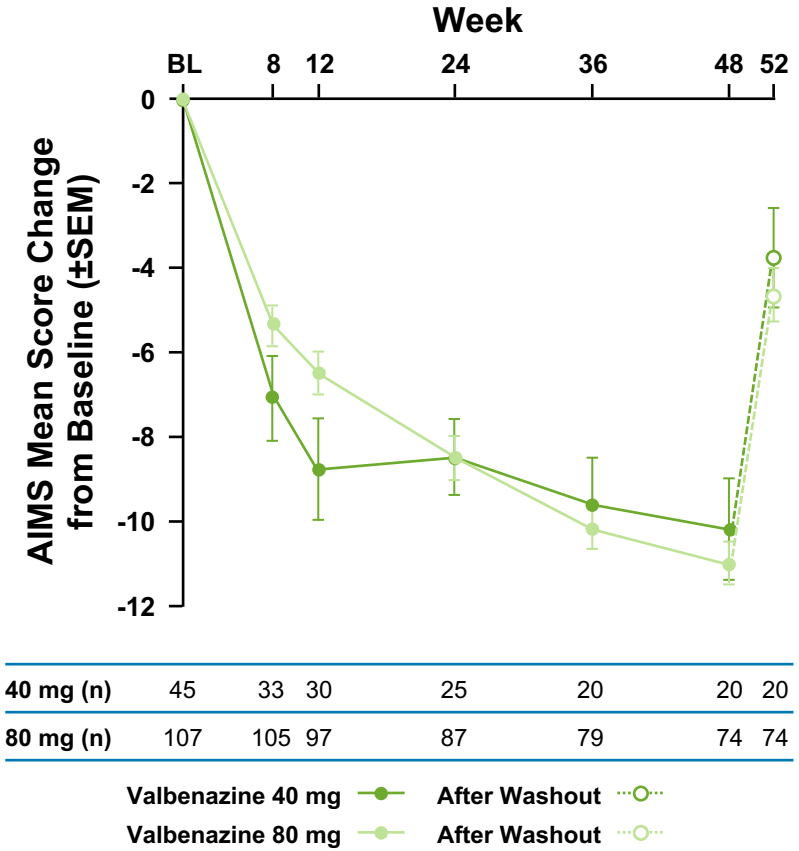
The mean total daily dose of deutetrabenazine at Week 80 was 38.6 (1.13) mg for all patients

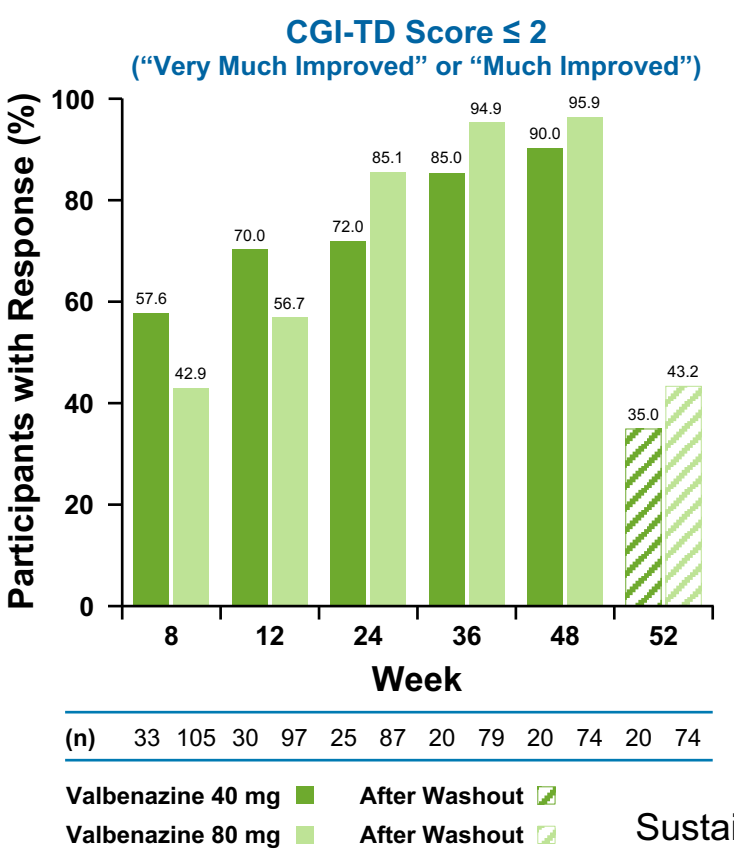
No new safety signals or concerns emerged in this long-term study

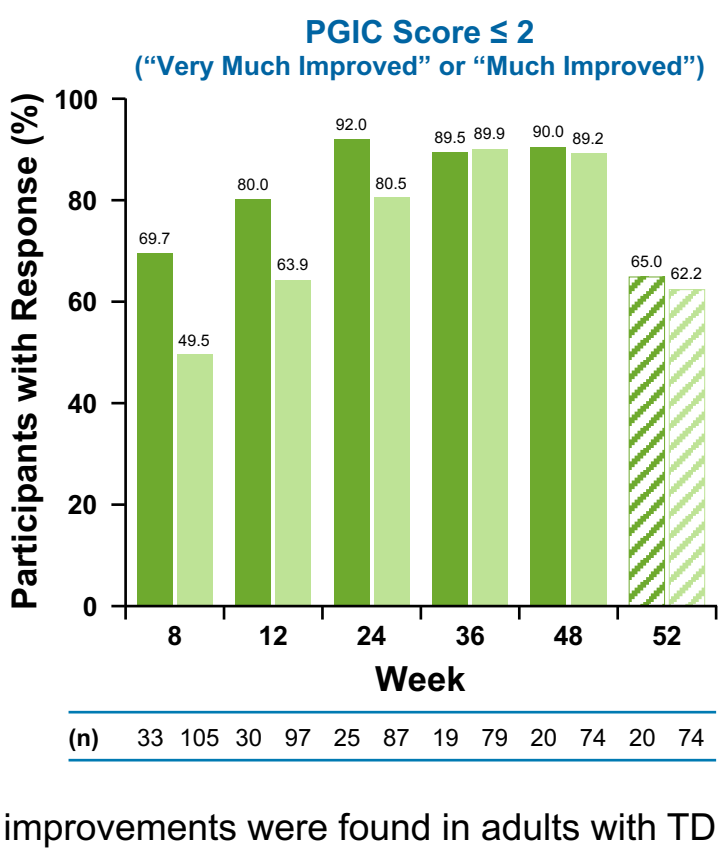
Hauser RA, et al. Long-Term Treatment With Deutetrabenazine Is Associated With Continued Improvement in Tardive Dyskinesia (TD): Results From an Open-Label Extension Study. Presented at: 70th Annual Meeting of the American Academy of Neurology; April 21–27, 2018; Los Angeles, CA.

Valbenazine: Long-Term Data is Reassuring

Of the 163 participants included in the analyses,149 completed the Week 8 visit and 103 completed Week 48







No new safety signals or concerns emerged in this long-term study

Sustained improvements were found in adults with TD who received once-daily valbenazine for up to 48 weeks, based on clinician- and patient-rated measures

Factor SA, et al. Effects of Long-Term Valbenazine on Tardive Dyskinesia and Patient-Reported Outcomes: Results from the KINECT 4 Study. Presented at: 70th Annual Meeting of the American Academy of Neurology; April 21–27, 2018; Los Angeles, CA.

Long-Term Side Effects

- ✓ Good news. In long-term studies in TD with both the VMAT2 therapies (deutetrabenazine and valbenazine), no new or unexpected side effects emerged

- ✓ This is very reassuring. However, monitoring and vigilance for emergent side effects is prudent on part of every clinician

Fernandez HH, et al. Confirmed Safety of Deutetrabenazine for Tardive Dyskinesia in a 2-Year Open-Label Extension Study. Presented at: 31st Annual Psych Congress; October 25–28, 2018; Orlando, FL. Marder SR, et al. Long-Term Safety and Tolerability of Once-Daily Valbenazine in Patients with Tardive Dyskinesia. Presented at: 31st Annual Psych Congress; October 25–28, 2018; Orlando, FL.

After the Diagnosis: *8 Steps to Ensure Long-Term Success*

After the Diagnosis:
8 Steps for Ensuring Success

1. **Solicit and answer** all patient's and family's questions

2. **Share** educational resources with patient and family to educate and support the TD diagnosis

After the Diagnosis:
8 Steps for Ensuring Success (cont'd)

3. Determine whether antipsychotic therapy can be withdrawn, reduced, or changed to lower affinity D_2 blocker to prevent long-term worsening of TD (often not possible)

4. Offer patient an FDA approved TD treatment option. If dystonia is a significant component of movements, consider movement disorder neurology evaluation for botulinum toxin injections

After the Diagnosis:
8 Steps for Ensuring Success (cont'd)

5. **Discuss** access issues, side effects, and set the correct expectations

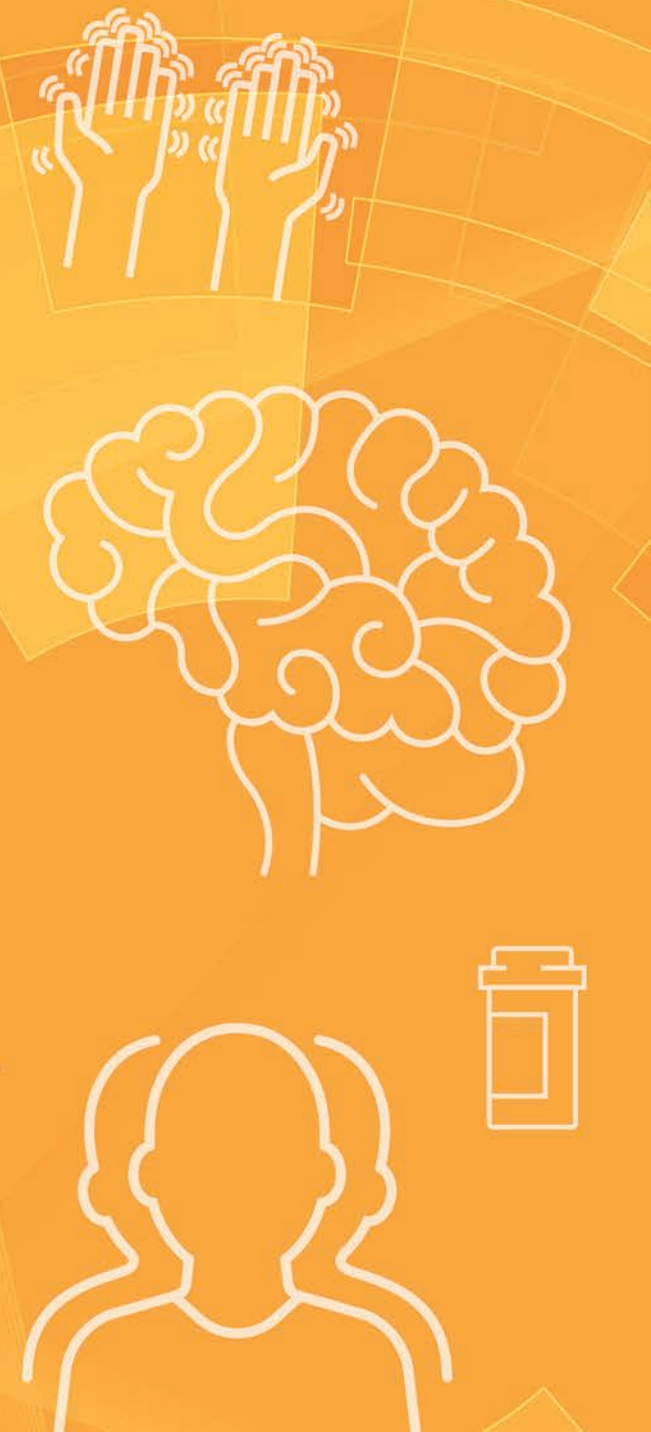
6. **Have patient call clinic** in a week to ensure tolerability

After the Diagnosis:
8 Steps for Ensuring Success (cont'd)

7. Titrate appropriately

8. Schedule 4-week follow-up appointment: Evaluate for efficacy and tolerability and need for further titration

6 *Potential Challenges* with VMAT2 Therapy and *Potential Solutions*



6 Common Issues

- Sleepiness / Sedation
- Akathisia / EPS
- Depression
- Cost / Access
- Forgetfulness / Adherence
- Lack of Insight

Patient Vignettes

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Sleepiness and Sedation

- Both VMAT2 therapies can cause sedation
- It can be a threat to adherence
- It can lead to medication discontinuation

- Rates are relatively low for both options; most cases are mild to moderate, and in most it is time limited
- Caution patient before starting therapy
- Reduce the dose – don't increase until sedation disappears or is manageable
- If needed, off-label recommendation is to offer valbenazine 40 mg every other day until sedation is improved. Later challenge with approved doses
- If needed, off-label recommendation is to offer deutetrabenazine nighttime dose only. Temporarily skip AM dosing until sedation is manageable. Later challenge with approved doses

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Akathisia / EPS

- Both VMAT2 therapies can cause akathisia / EPS
- It can be a threat to adherence
- It can lead to medication discontinuation

- Rates are relatively low for both options; most cases are mild to moderate, and in most it is time limited
- Caution patient before starting therapy
- Reduce the dose – don't increase until akathisia or EPS disappear or are manageable
- If EPS presents, ask yourself, "Did I uncover disease?"
- If needed, off-label recommendation is to offer valbenazine 40 mg every other day until akathisia/EPS is improved. Later, challenge with approved doses
- If needed, off-label recommendation is to offer deutetrabenazine nighttime dose only. Temporarily skip AM dosing until akathisia/EPS is manageable. Later, challenge with approved doses

Akathisia / EPS (cont'd)

- Both VMAT2 therapies can cause akathisia / EPS
- It can be a threat to adherence
- It can lead to medication discontinuation

- If your patient has both Parkinson's disease and TD – consult with a movement disorder neurologist. Patient may need both VMAT2 and Parkinson's therapy
- Beta-blockers may be temporarily used for akathisia management
- An anticholinergic agent, such as benztropine, can be used for short-term management of any emerging EPS symptoms
- If your patient has been taking long-term anticholinergic agent, it's prudent to not change its dose as the VMAT2 therapy is being titrated. Changes in anticholinergic therapy should be delayed until a later suitable time

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Affect Blunting / Depression

- Both VMAT2 therapies can cause or worsen depression
- It can be a threat to adherence
- It can lead to medication discontinuation

- Rates are relatively low for both options; most cases are mild to moderate, and in most it is time limited
- Caution patient before starting therapy
- Reduce the dose – don't increase until depression disappears or is manageable
- If your patient has an earlier diagnosis of MDD, consider restarting antidepressant therapy
- If your patient is currently on antidepressant therapy, consider optimization of treatment
- If depression is significant, difficult to manage, or suicidal ideations emerge – stop therapy and re-evaluate for any underlying mood disorder. Consider at a later point a trial of the other VMAT2 treatment option

MDD = major depressive disorder.

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Cost / Access

- Both VMAT2 therapies are expensive
- It can be a threat to adherence
- It can lead to medication discontinuation

- Many, if not most, insurance carriers cover VMAT2 therapy around the nation
- Good documentation of need for VMAT2 therapy is critical
- Both VMAT2 therapies have robust access / patient assistance programs

Cost / Access (cont'd)

- Document need for VMAT2 therapy in the preauthorization paperwork well. Document the following:
  - The location and severity of abnormal movements
  - That the patient has a diagnosis of TD
  - Document the bio-psycho-social impairment caused by TD
  - Document why therapy with benztropine, clozapine, or clonazepam are inappropriate for this patient
  - Proactively document all 4 of the above. This reduces the chance of rejection of request for VMAT2 therapy

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Forgetfulness / Adherence

- Both early and later in treatment with VMAT2 therapies, forgetfulness is common
- It can be a threat to adherence
- It can lead to medication discontinuation

- Forgetfulness with chronic medication therapy is common in both psychiatric and non-psychiatric disorders (eg, diabetes, hypertension, etc.)
- Forgetfulness is particularly problematic in psychotic and mood disorders – the 2 most common disorders associated with TD
- It's best to address this issue at the very first opportunity—at the start of VMAT2 therapy

Forgetfulness / Adherence (cont'd)

- Some suggestions:
  - Using a smartphone to set regular daily or twice a day alarms (depending on which VMAT2 therapy is utilized)
  - Consider using a calendar with check off with each dose taken
  - Using a support system to alert or remind to take the medication
  - Leaving the medication in a place where the patient lays eyes on the medication bottle
  - Customizing an adherence plan that best fits the patient

Patient Vignettes

Sedation

Akathisia / EPS

Depression

Cost / Access

Forgetfulness / Adherence

Lack of Insight

Lack of Insight

"I don't have a problem" / "It doesn't bother me"

- Lack of self awareness, and/or lack of insight, are both prevalent in some patients afflicted with TD

- We should appreciate that many psychiatric disorders, particularly psychotic disorders, are often accompanied by lack of awareness and lack of insight
- Sometimes, a patient is concerned, a clinicians might "change my medications and mess things up." They may therefore minimize TD symptoms and minimize impairments resulting from it
- Assuring such patients that the addition of a VMAT2 therapy does not mean you have to reduce or change other current medications automatically. This often reassures the patient and they are more open to discussing

Lack of Insight

"*I don't have a problem*" / "*It doesn't bother me*" (cont'd)

- Lack of self awareness, and/or lack of insight, are both prevalent in some patients afflicted with TD

- Regarding impairments, many patients have to be gently prompted to discuss any or all impairments caused by TD, eg, social shame and stigma, trouble eating, swallowing, dropping things, stumbling, falling, etc.
- Sometimes this question asked of a patient is highly helpful:

"I know you don't see anything abnormal, or you aren't bothered by them, but is ANYONE else telling you they notice any movement changes or problems caused by these unusual movements in your body?"

In Conclusion:
What have we learned together today?

- TD is often forgotten as a problem in this age of atypical antipsychotics, but it is still a very real challenge
- Our understanding of the risks and characteristics of TD have evolved, and more data and knowledge have accumulated, but more work needs to be done …
- The consequences of TD on human life are considerable

In Conclusion:
What have we learned together today? (cont'd)

- Screening proactively, routinely, and systematically for TD in patients on atypical and typical antipsychotics is a mandate for all clinicians
- Innovative alterations of tetrabenazine (ie, deutetrabenazine and valbenazine) are expected to better serve patient's needs
- Significant, promising research is occurring including activity on control of TD symptoms with multiple VMAT2 inhibitors. It behooves us clinicians to keep abreast of important new developments in this field