A Modified Delphi Consensus Approach to Clinical Opinions on Tardive Dyskinesia

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INTRODUCTION

- With the increasing use of antipsychotic medications, particularly in mood disorder patients, the risk for tardive dyskinesia (TD) continues to be an ongoing safety concern[1,2]
- Despite substantial progress, many basic questions concerning the course and management of TD remain unresolved[3]
- In addition, the recent approval of two vesicular monoamine transporter 2 (VMAT2) inhibitors, valbenazine and deutetrabenazine, for the treatment of TD in adults,[4,5] has rekindled clinical interest in determining best practices for recognizing and managing TD
- A modified Delphi process was implemented to address gaps in clinical knowledge by identifying current best practices

METHODS

NOMINAL GROUP PROCESS

- A Steering Committee of 11 TD experts met in a Nominal Group meeting format, which was led by a facilitator to:
  - Discuss and prioritize questions to be addressed about TD
  - Reach agreement on criteria for potential survey panelists (e.g., publication history, clinical experience)
  - Identify experts in psychiatry and neurology to join a larger Delphi panel to respond on survey rounds

MODIFIED DELPHI ROUNDS

- Links to online surveys were sent to 60 individuals (including Steering Committee members); 29 agreed to participate as panelists (**Table 1**)
- Two survey rounds were conducted anonymously
- Reponses from panelists were collected, collated, and analyzed in the aggregate by the organizer (Xcenda)
- The following terms of response were defined a priori by the Steering Committee:
  - Unanimous agreement: 100% among survey respondents
  - Consensus agreement: 75-99% among survey respondents
  - Majority/most agreement: 50-74% among survey respondents
- For questions using a 5-point Likert scale, agreement was defined as a response ≥4
- Round 1 survey: included questions regarding TD screening, TD assessments and key diagnostic criteria, and treatment strategies and considerations
- Round 2 survey: included questions with 25-74% agreement, as those were deemed possible to achieve consensus; Round 2 excluded questions with < 25% agreement, as these were unlikely to achieve consensus

Table 1. Characteristics of Respondents (N=29)

	Delphi Panel Respondents
Primary area of practice, n (%)	
Psychiatry	23 (79)
Neurology	6 (21)
Geographic area of practice, n (%)*	
Northeast	14 (48)
West	8 (28)
South	8 (28)
Canada	2 (7)
Midwest	1 (3)
Practice setting, n (%)	
Academic institution	18 (62)
Community – office setting	6 (21)
Government – state hospital	2 (7)
Community – hospital	1 (3)
Government – federal hospital	1 (3)
Other	1 (3)
Median years in practice	29
Median number of patients currently or previously taking antipsychotic medication seen per year	100
Median number of patients presenting with TD symptoms seen per year	20

*Respondents could select all that apply.
TD, tardive dyskinesia.

RESULTS

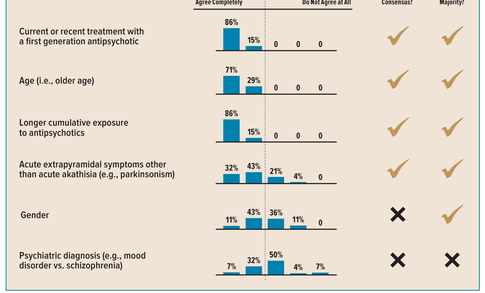
- Selected questions with consensus or majority agreement in either Round 1 or 2 are presented

TD SCREENING

- Respondents were unanimous (100%) that all patients currently taking dopamine receptor blocking agents (DRBAs; e.g., antipsychotics, metoclopramide) should be screened for TD
- Consensus reached on several attributes defining high TD risk patients (**Figure 1**)

Figure 1. Attributes of Patients at High Risk for TD

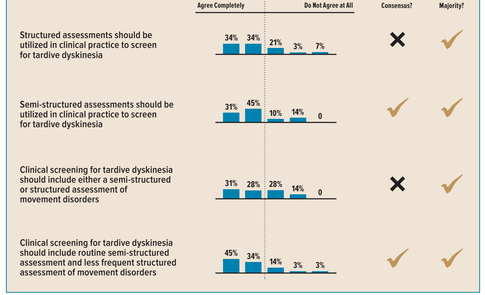
To what extent do you agree that each of the following patient or treatment attributes contribute to how high-risk for TD is identified? (N=28)



- The Abnormal Involuntary Movement Scale (AIMS) is the standard structured assessment for screening and monitoring for severity of TD (100%, unanimous)
- Consensus reached on 2 statements related to screening assessments (**Figure 2**)

Figure 2. Structured or Semi-Structured Assessments

How much do you agree with each of the following statements? (N=29)

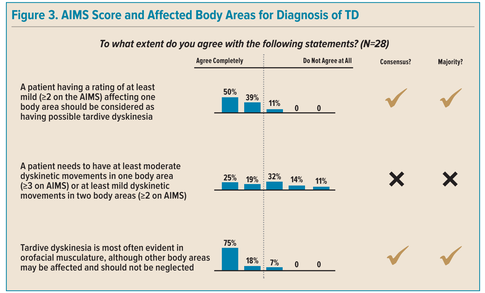


TD DIAGNOSIS

- Consensus reached (89%) that a patient having a rating of at least mild (>2 on the AIMS) affecting one body area should be considered as having possible tardive dyskinesia (**Figure 3**)
- Consensus reached (93%) that TD was most often evident in orofacial musculature, although other body areas may be affected and should not be neglected

Figure 3. AIMS Score and Affected Body Areas for Diagnosis of TD

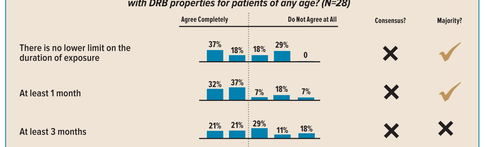
To what extent do you agree with the following statements? (N=28)



- Consensus not reached regarding minimum cumulative duration of exposure to antipsychotics or other drugs with DRB properties as a diagnostic criterion for TD
- Most respondents (69%) reported minimum cumulative exposure of 1 month may be sufficient for a diagnosis of TD (**Figure 4**)

Figure 4. Minimum Duration of Cumulative Exposure to Antipsychotic Medication to Meet Diagnostic Criteria for TD

To what extent would you agree that diagnostic criteria for TD should include the following minimum durations of cumulative exposure to antipsychotics or other drugs with DRB properties for patients of any age? (N=28)

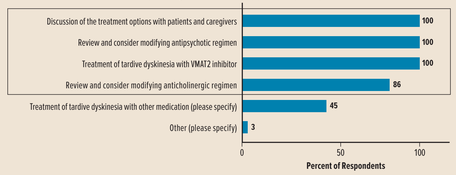


TD TREATMENT

- Consensus reached on 4 strategies to consider when treating TD (**Figure 5**)

Figure 5. Approaches to TD Treatment

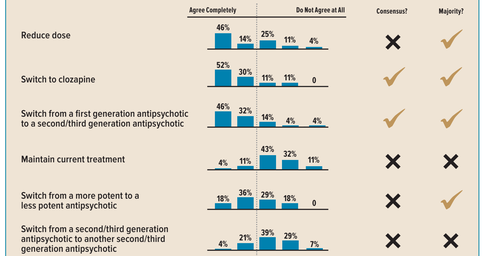
After a patient is diagnosed with TD, which of the following do you consider as part of your treatment approach? (N=29)



- Consensus reached on 2 strategies for antipsychotic changes (**Figure 6**)

Figure 6. Options for Antipsychotic Changes

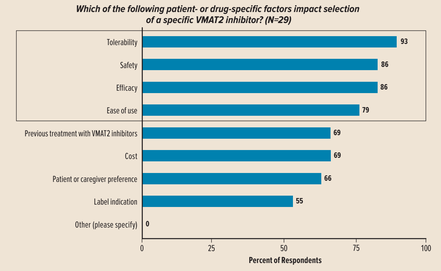
To what extent do you agree that each of the following should be considered as a possible option or modification to antipsychotic treatment for patients with TD who are unable to be withdrawn from antipsychotic therapy? (N=28)



- Consensus reached that tolerability, efficacy, safety, and ease of use are factors that impact selection of a specific VMAT2 inhibitor (**Figure 7**)

Figure 7. Factors in Selecting Specific VMAT2 Inhibitors

Which of the following patient- or drug-specific factors impact selection of a specific VMAT2 inhibitor? (N=29)



CONCLUSIONS

- Recent evidence, including the approval of 2 novel VMAT2 inhibitors for TD treatment,[4,5] suggests that new guidelines are required to advance best practices in the treatment of TD
- Given continued need for research in several areas of management, a standardized consensus process may offer an expedient method to facilitate updated management guidelines
- Using a Nominal Group and modified Delphi process, consensus was reached rapidly (within 1 or 2 rounds) regarding several key aspects of TD screening, diagnosis and treatment; additional areas requiring further study were also identified

REFERENCES

1. Correll CU, Kane JM, Citrome LL. *J Clin Psychiatry.* 2018;78(8):1136-47.
2. Meyer JM. *CNS Spectr.* 2016;21(S1):13-24.
3. Caroff SN, Unguvari GS, Cunningham Owen DG. *J Neurol Sci.* 2018;389:4-9.
4. INGREZZA® (valbenazine) prescribing information. San Diego, CA: Neurocrine Biosciences, Inc., 2017.
5. AUSTEDO® (deutetrabenazine) prescribing information. North Wales, PA: Teva Pharmaceuticals USA, Inc., 2017.

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