

Tardive Dyskinesia by Body Region in Subjects with Schizophrenia/Schizoaffective Disorder or Mood Disorder: Findings from the KINECT 3 Study

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INTRODUCTION

- Antipsychotic medications are used to treat various psychiatric conditions, including schizophrenia, schizoaffective disorder, bipolar disorder, and treatment-resistant major depressive disorder
- However, prolonged exposure to antipsychotics has been associated with tardive dyskinesia (TD), a chronic disorder characterized by choreic or athetoid movements in the orofacial region, extremities, and/or trunk¹
- The Abnormal Involuntary Movement Scale (AIMS) is widely used to assess changes in severity (i.e., frequency and amplitude of abnormal movements) in TD clinical trials
- The first 7 items of the AIMS evaluate the severity of abnormal movements in different body regions, with the rating scale for these items ranging from 0 (none) to 4 (severe)
- In clinical trials of valbenazine (INGREZZA™), which is the first and only FDA-approved medication for the treatment of TD, efficacy was demonstrated based on mean changes in the AIMS dyskinesia total score (i.e., sum score of items 1-7)^{2,3}

OBJECTIVE

- To characterize TD in participants categorized by psychiatric diagnosis (schizophrenia/schizoaffective disorder or mood disorder) using AIMS item scores at baseline from the KINECT 3 study

METHODS

STUDY DESIGN AND PARTICIPANTS

- KINECT 3 was a 6-week, randomized, double-blind, fixed-dose, placebo-controlled trial in participants with schizophrenia, schizoaffective disorder, or mood disorder³
- The study included medically and psychiatrically stable men and women with moderate or severe TD, based on a qualitative assessment of screening videos by external AIMS reviewers
- Individuals with a comorbid movement disorder and those with significant risk for active suicidal ideation, suicidal behavior, or violent behavior were not allowed to participate
- Eligible participants were randomized 1:1:1 to once-daily placebo, valbenazine 40 mg, or valbenazine 80 mg
- Concomitant treatment with a stable antipsychotic regimen was allowed

ANALYSES

- Analyses were conducted by psychiatric diagnosis subgroup (schizophrenia/schizoaffective disorder, mood disorder)
- Analyses included:
 - Mean AIMS item scores at baseline
 - Mean regional scores at baseline, calculated by averaging mean scores for AIMS items as follows: orofacial (AIMS items 1-4), extremities (AIMS items 5-6), trunk (AIMS item 7)
 - Mean number of AIMS items with a score ≥ 2 , indicating mild or worse severity
 - Percentage of participants with an AIMS item score ≥ 2 at baseline, analyzed for each item
 - Percentage of participants with an AIMS score ≥ 1 at baseline in the orofacial region (AIMS items 1-4) or non-orofacial region (AIMS items 5-7)

RESULTS

PARTICIPANTS

- Demographics and baseline characteristics by psychiatric diagnosis are presented in **Table 1**

Table 1. Baseline Demographics and Participant Characteristics^a

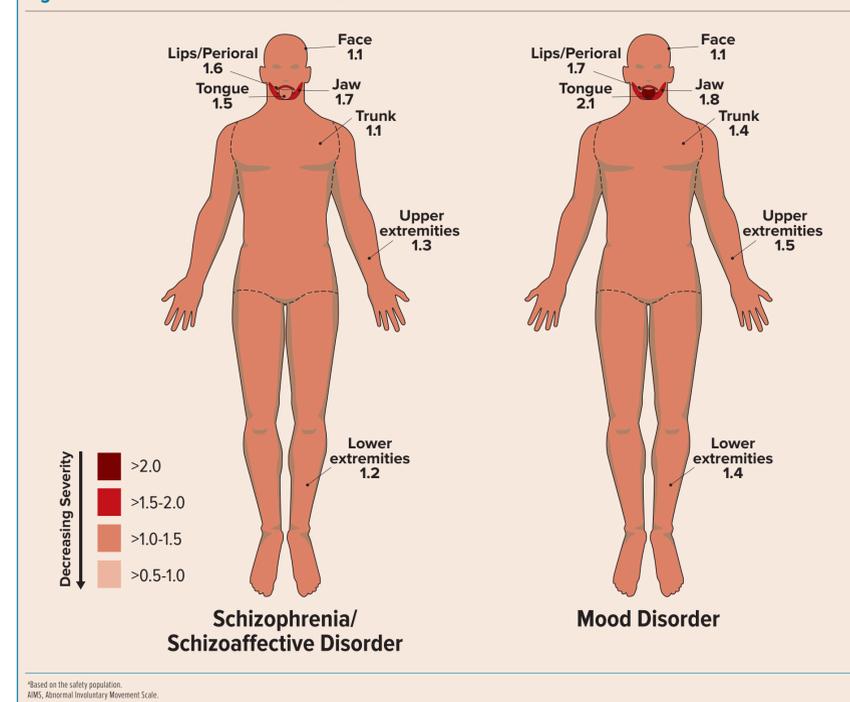
	Schizophrenia/Schizoaffective Disorder			Mood Disorder		
	Placebo (n=50)	Valbenazine 40 mg (n=48)	Valbenazine 80 mg (n=52)	Placebo (n=26)	Valbenazine 40 mg (n=24)	Valbenazine 80 mg (n=27)
Age, mean years	56.8	55.6	56.8	57.4	54.7	54.5
Men, %	68.0	64.6	64.6	30.8	45.8	37.0
White, %	40.0	47.9	51.9	88.5	75.0	63.0
Black, %	54.0	43.8	46.2	7.7	20.8	29.6
Mean age at TD diagnosis, years	47.7	47.2	47.6	51.6	48.7	47.6
Mean BPRS total score at screening	31.9	32.5	30.4	24.3	26.7	26.6
Mean AIMS total score at baseline	9.3	8.8	10.1	11.2	11.4	10.9

^aIn the safety population, defined as all participants who received ≥ 1 dose of study drug. AIMS, Abnormal Involuntary Movement Scale; BPRS, Brief Psychiatric Rating Scale; TD, tardive dyskinesia.

- In both diagnostic subgroups, AIMS items with the highest mean scores at baseline were jaw, lips, and tongue (**Figure 1**)

- Jaw had the highest mean score (1.7) in the schizophrenia/schizoaffective disorder subgroup
- Tongue had the highest mean score (2.1) in the mood disorder subgroup

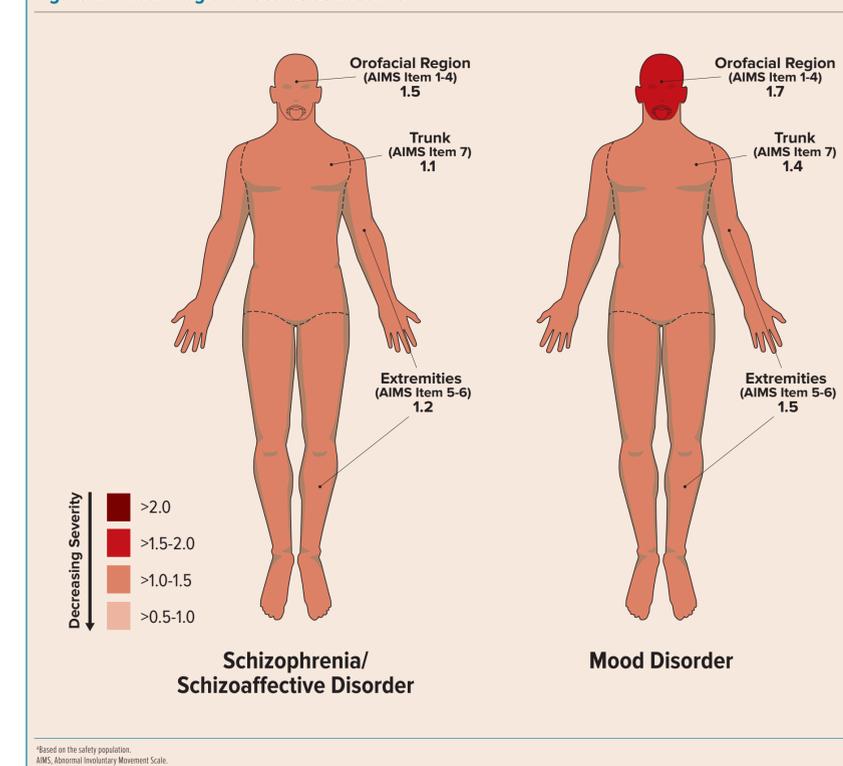
Figure 1. Mean AIMS Item Scores at Baseline^a



^aBased on the safety population. AIMS, Abnormal Involuntary Movement Scale.

- When calculated as 3 overall body regions, the mood disorder subgroup had higher mean scores (i.e., more severe) at baseline than the schizophrenia/schizoaffective disorder subgroup (**Figure 2**)

Figure 2. Mean Regional Scores at Baseline^a



^aBased on the safety population. AIMS, Abnormal Involuntary Movement Scale.

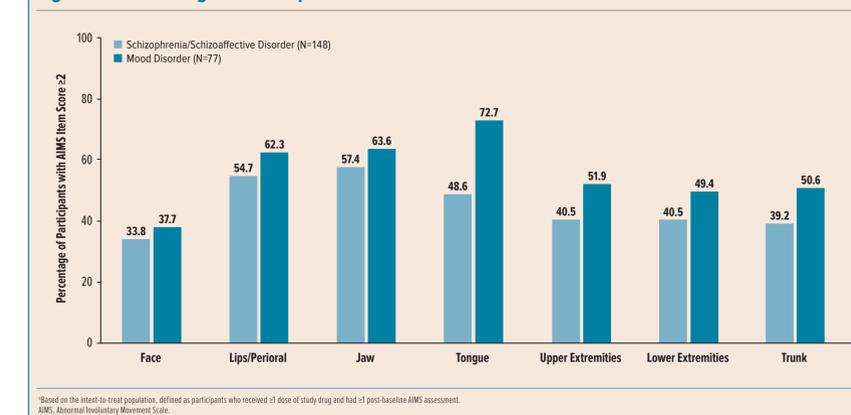
- The mood disorder subgroup had more AIMS items with a score ≥ 2 at baseline than the schizophrenia/schizoaffective disorder subgroup

- Mean number of items (standard deviation): mood disorder, 3.9 (1.5); schizophrenia/schizoaffective disorder, 3.1 (1.8)
- Median number of items (minimum, maximum): mood disorder, 4 (0, 7); schizophrenia/schizoaffective disorder, 3 (0, 7)

- For each AIMS item, the percentage of participants with a baseline score ≥ 2 was higher in the mood disorder subgroup than in the schizophrenia/schizoaffective disorder subgroup (**Figure 3**)

- In the mood disorder subgroup, the most common regions with mild or worse severity were the tongue (72.7%), jaw (63.6%), and lips/perioral (62.3%)
- In the schizophrenia/schizoaffective disorder subgroup, the most common regions with mild or worse severity were the jaw (57.4%), lips/perioral (54.7%), and tongue (48.6%)
- In both subgroups, all AIMS items had $>30\%$ of participants with a score ≥ 2

Figure 3. Percentage of Participants with an AIMS Item Score ≥ 2 at Baseline^a



^aBased on the intent-to-treat population, defined as participants who received ≥ 1 dose of study drug and had ≥ 1 post-baseline AIMS assessment. AIMS, Abnormal Involuntary Movement Scale.

- In both diagnostic subgroups, most participants had some dyskinesia (AIMS item score ≥ 1) in both orofacial and non-orofacial regions: schizophrenia/schizoaffective disorder, 94.6%; mood disorder, 96.1%
- However, 2 participants with schizophrenia/schizoaffective disorder only had an AIMS item score ≥ 1 in a non-orofacial region

CONCLUSIONS

- Among participants in the KINECT 3 study, regions with the highest AIMS item scores were tongue, jaw, and lips
- The phenomenological pattern of TD was generally similar between diagnostic subgroups, but dyskinesic movements appeared to be somewhat more severe in participants with mood disorder as compared to those with schizophrenia/schizoaffective disorder
- The most marked difference between subgroups was in the tongue region
 - The mean score at baseline was higher (i.e., more severe) in the mood disorder subgroup than in the schizophrenia/schizoaffective disorder subgroup (2.1 and 1.5, respectively)
 - The percentage of participants with a score ≥ 2 for the tongue item was also higher in the mood disorder subgroup than in the schizophrenia/schizoaffective disorder subgroup (72.7% and 48.6%, respectively)
- Approximately 95% of participants in both diagnostic subgroups also had dyskinesia in an orofacial region and a non-orofacial region, reinforcing the recommendation that TD screening should include all regions of the body
- However, a more condensed version of the AIMS exam may be possible based on 3 overall regions: orofacial, extremities, trunk
- Further characterization of the phenomenology (e.g., chorea, dystonia, etc.) is warranted

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