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The Effect of Patient Characteristics on Tardive Dyskinesia Outcomes

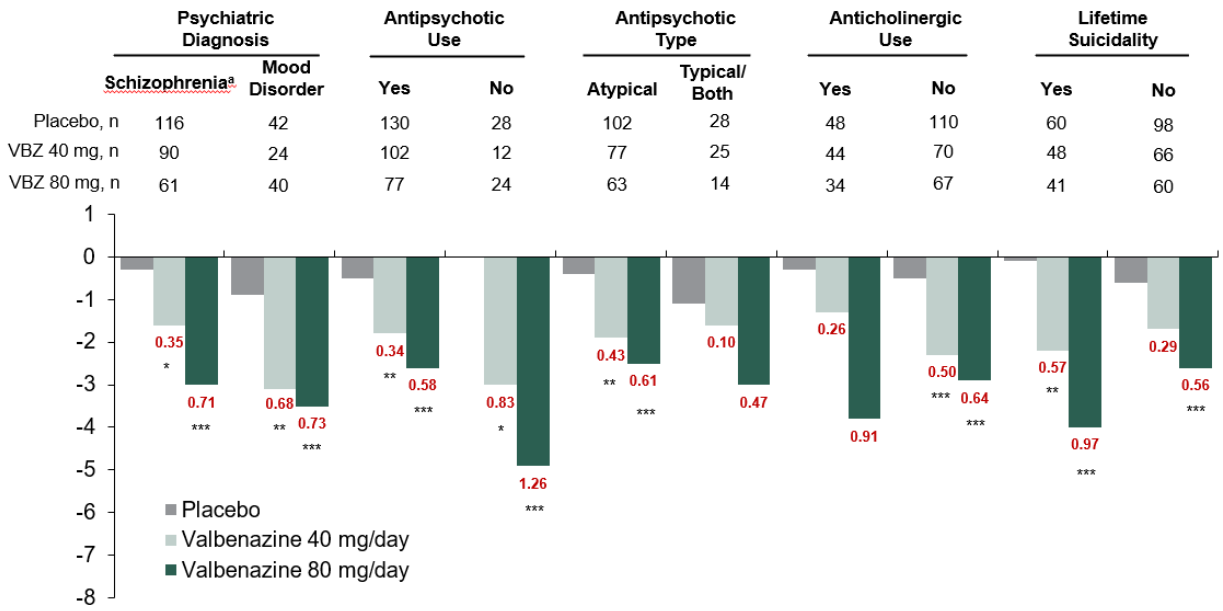
Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding INGREZZA® (valbenazine) capsules and the effect of patient characteristics on tardive dyskinesia (TD) outcomes.

INGREZZA is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia.[1]

Data were pooled from three 6-week, randomized, double-blind, placebo-controlled trials of once-daily valbenazine in adults with TD (2 Phase 2 and 1 Phase 3): KINECT (NCT01688037), KINECT 2 (NCT01733121), and KINECT 3 (NCT02274558), respectively. The population subgroups analyses included: age, sex, psychiatric diagnosis, TD duration, antipsychotic/anticholinergic medication use at baseline, antipsychotic medication category, lifetime history of suicidality, CYP 2D6 genotype and body mass index (BMI). The mean change from baseline to week 6 in the Abnormal Involuntary Movement Scale (AIMS) total score was used to evaluate TD improvement in all subgroups. The clinical relevance for AIMS mean score change was evaluated using Cohen's d effect size. Interpretation of these post-hoc analyses may be limited for some subgroups, due to relatively small sample size.[2]

The pooled analyses included 373 participants (valbenazine 80 mg, n=101; valbenazine 40 mg, n=114; placebo, n=158). Baseline characteristics were generally similar across treatment groups, with the mean baseline AIMS total scores ranging from 8 to 12. In all subgroups, mean changes in AIMS total score from baseline to Week 6 indicated greater reductions with valbenazine relative to placebo (**Figure 1A** and **1B**). A significant difference between valbenazine 80 mg and placebo (P<0.05) was found in all subgroups except participants who were taking a typical antipsychotic or a combination of typical/atypical antipsychotics (i.e., typical/both subgroup). Subgroups with the largest effect sizes (d ≥0.8) for valbenazine 80 mg were: age ≥55 years, men, TD duration <7 years, no concomitant antipsychotic use (also 40 mg), concomitant anticholinergic use, history of lifetime suicidality, CYP2D6 PM genotype, BMI 25 to <30 kg/m^2.[2]

Figure 1A. AIMS Total Score Mean Changes from Baseline to Week 6 by Subgroup



[a]Includes schizophrenia or schizoaffective disorder.
*P ≤0.05, ** P ≤0.01, ***P ≤0.001 vs placebo. Cohen's d effect sizes are indicated in red.
PM, poor metabolizer; TD, tardive dyskinesia; VBZ, valbenazine.

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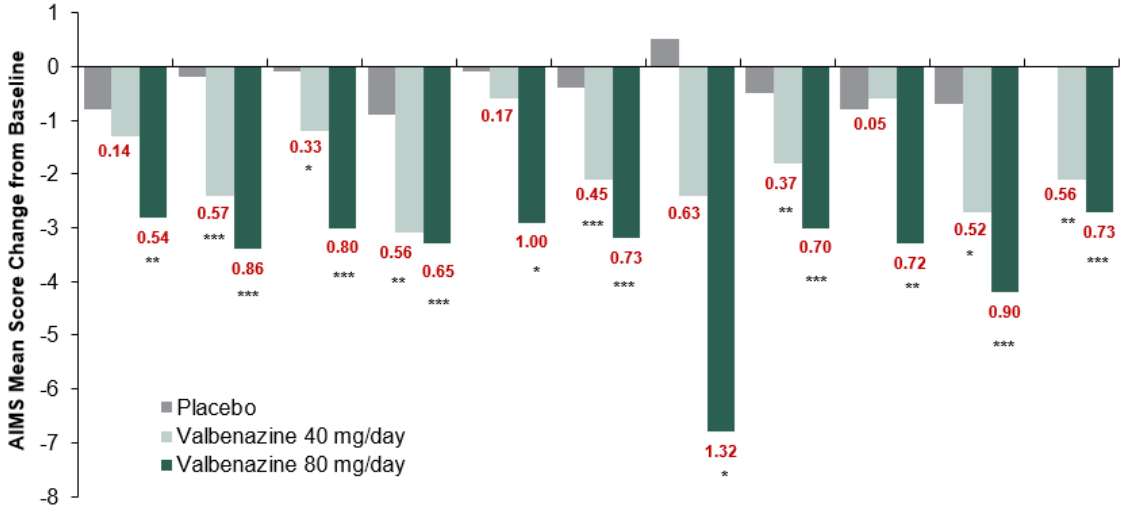
Figure 1B. AIMS Total Score Mean Changes from Baseline to Week 6 by Subgroup

	Age		Sex		TD Duration		CYP2D6 Genotype		Body Mass Index kg/m²		
	<55 yr	≥55 yr	Male	Female	<7 yr	≥7 yr	PM	Non-PM	18.5 to <25	25 to <30	≥30
Placebo, n	65	93	89	69	11	133	6	152	42	51	63
VBZ 40 mg, n	51	63	72	42	11	94	7	106	28	38	47
VBZ 80 mg, n	38	63	55	46	10	79	4	96	30	26	40



*$P \leq 0.05$, ** $P \leq 0.01$, ***$P \leq 0.001$ vs placebo. Cohen's *d* effect sizes are indicated in red.
PM, poor metabolizer; TD, tardive dyskinesia; VBZ, valbenazine.

Adverse reactions in the three placebo-controlled studies of 6-week duration reported at an incidence of ≥2% and greater than placebo were somnolence (10.9% and 4.2%), anticholinergic effects (5.4% and 4.9%), balance disorders/falls (4.1% and 2.2%), headache (3.4% and 2.7%), akathisia (2.7% and 0.5%), vomiting (2.6% and 0.6%), nausea (2.3% and 2.1%) and arthralgia (2.3% and 0.5%), for valbenazine and placebo respectively.[1]

For a more complete description of this analysis, please see attached data presentation from the 2017 Neuroscience Educational Institute Annual Congress presented by Meyer et al.

This letter and the enclosed material are provided in response to your unsolicited medical information inquiry. Please feel free to contact Neurocrine Medical Information at (877) 641-3461 or medinfo@neurocrine.com if you would like to request additional information.

References:

1. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
2. Meyer J, et al. Effects of valbenazine on tardive dyskinesia: subgroup analyses of 3 randomized, double-blind, placebo-controlled trials. Poster presented at the 2017 Neuroscience Education Institute; November 8-12, 2017; Colorado Springs, CO.

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. Meyer J, et al. Effects of valbenazine on tardive dyskinesia: subgroup analyses of 3 randomized, double-blind, placebo-controlled trials. Poster presented at the 2017 Neuroscience Education Institute; November 8-12, 2017; Colorado Springs, CO.