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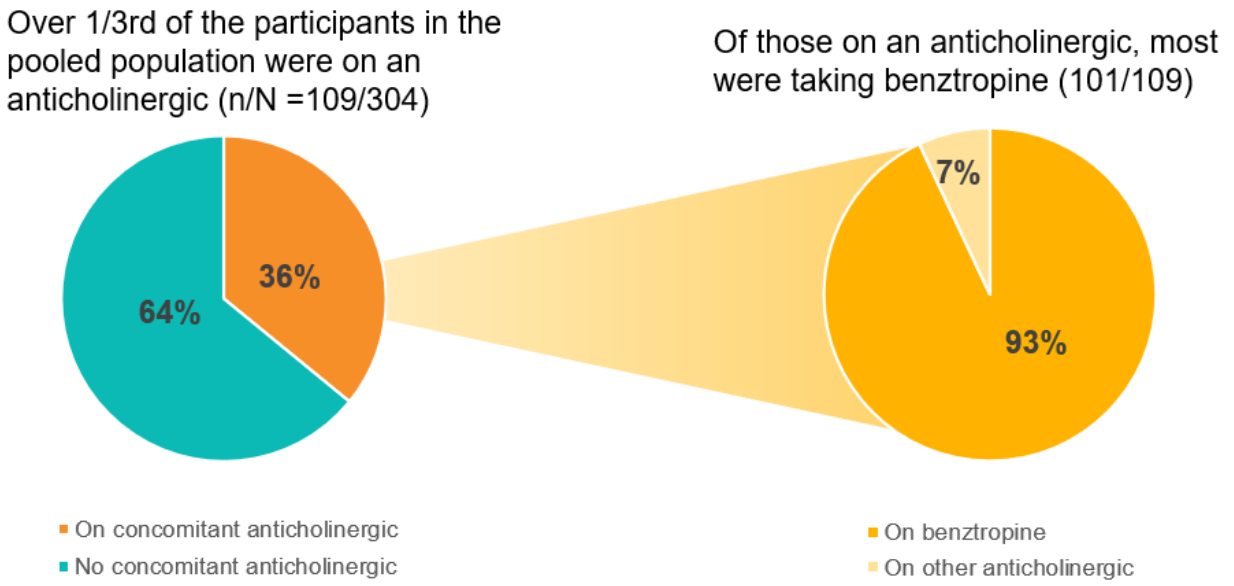
The Effects of Concomitant Anticholinergic Use in Patients Taking INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules with Tardive Dyskinesia

Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the effects of concomitant anticholinergic use on tardive dyskinesia (TD) outcomes in patients taking INGREZZA and INGREZZA SPRINKLE.

INGREZZA and INGREZZA SPRINKLE are vesicular monoamine transporter 2 (VMAT2) inhibitors indicated for the treatment of adults with tardive dyskinesia.[1]

Data were pooled from two long-term valbenazine clinical trials (2 Phase 3 studies: KINECT® 3 Long-term Extension [NCT02274558] and KINECT® 4 [NCT02405091]) to evaluate the effect of concomitant anticholinergic use with valbenazine on TD outcomes. During the study, participants were allowed to remain on stable doses of concomitant antipsychotic medications to treat psychiatric disorders. The mean change from baseline to Week 48 in the Abnormal Involuntary Movement Scale (AIMS) total score was used to evaluate TD improvement. The AIMS was scored by blinded central video raters in the KINECT 3 study and by site raters in the KINECT 4 study. Interpretation of this post-hoc analysis may be limited due to small sample size.[2]



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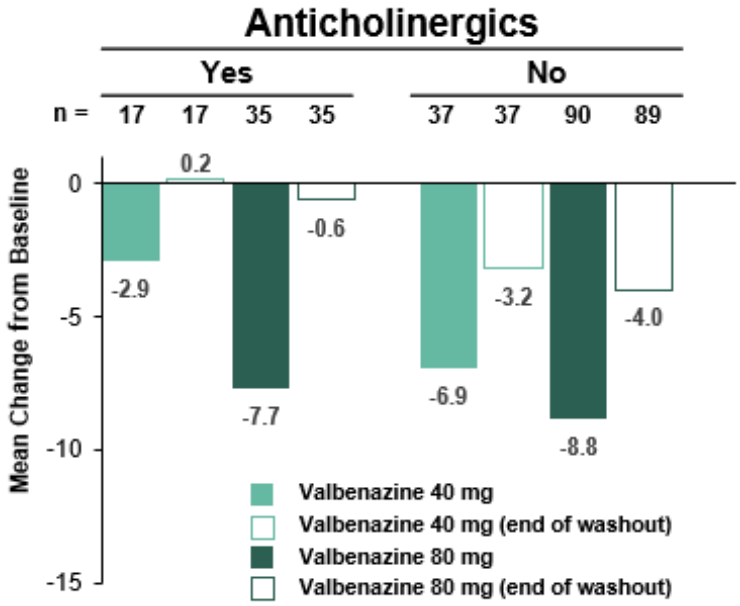
Sustained TD improvements were found at Week 48 in the pooled population, as indicated by mean AIMS change from baseline in both subgroups taking concomitant anticholinergics (**Figure 1**). At Week 52 (after 4-week washout), mean AIMS scores generally reverted towards baseline levels.[2]

Figure 1. AIMS Total Score Mean Changes from Baseline to Week 48 & Week 52



AIMS, Abnormal Involuntary Movement Scale

Adverse reactions that occurred in the three placebo-controlled studies of 6-week duration reported at an incidence of >2% and greater than placebo are presented in **Table 1**.[1]

Table 1. Adverse Reactions in 3 Placebo-Controlled Studies of 6-week Treatment Duration Reported at ≥2% and >Placebo

Adverse Reactions, %	Valbenazine (n=262)	Placebo (n=183)
Somnolence	10.9	4.2
Anticholinergic effects	5.4	4.9
Balance disorders/falls	4.1	2.2
Headache	3.4	2.7
Akathisia	2.7	0.5
Vomiting	2.6	0.6
Nausea	2.3	2.1
Arthralgia	2.3	0.5

For a more complete description of this analysis, please see attached data presentation from the 2019 Annual Meeting of the American Academy of Neurology by Comella C, et al.

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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. Comella C, et al. Effects of concomitant medication use on tardive dyskinesia outcomes in long-term valbenazine trials. Poster presented at the 2019 Annual Meeting of the American Academy of Neurology, Philadelphia, PA.

Enclosures:

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. INGREZZA [Important Safety Information]. San Diego, CA: Neurocrine Biosciences, Inc.
C. Comella C, et al. Effects of concomitant medication use on tardive dyskinesia outcomes in long-term valbenazine trials. Poster presented at the 2019 Annual Meeting of the American Academy of Neurology, Philadelphia, PA.