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Long Term Psychiatric Stability in Patients Taking INGREZZA® (valbenazine) capsules with a Mood Disorder

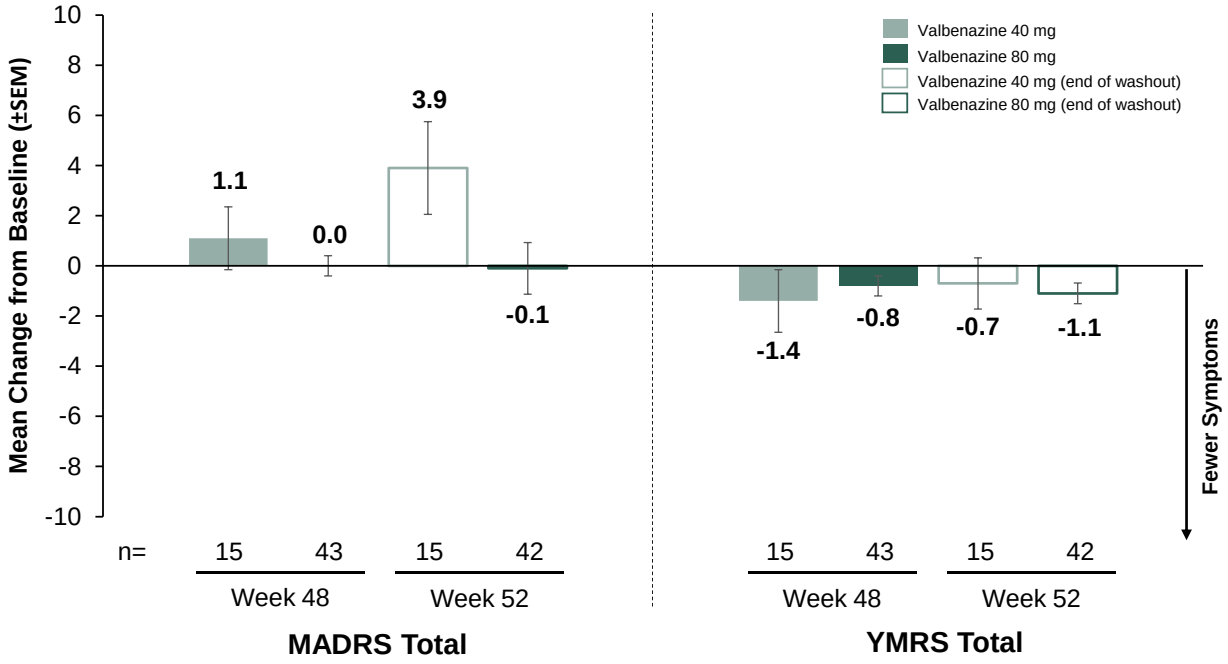
Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the long-term impact of INGREZZA on psychiatric stability in patients with mood disorder (e.g. bipolar disorder, major depressive disorder).

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

Pooled data from mood disorder participants in KINECT 3 [NCT02274558] and KINECT 4 [NCT02405091] were analyzed post hoc to evaluate psychiatric status during long-term valbenazine (VBZ) treatment. The Montgomery-Åsberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS) total scores and individual item scores were used to assess psychiatric stability of the mood disorder participants. The Columbia-Suicide Severity Rating Scale (C-SSRS) was also evaluated at baseline and throughout the long-term studies to measure suicidal ideation and behavior. All safety scales were analyzed descriptively.[2]

Baseline characteristics among the mood disorder participants (n=95) were generally similar between VBZ dose groups. The majority of participants (62.1%) had bipolar disorder and 33.7% had major depression. Most participants received concomitant antidepressants (84.2%) and/or antipsychotics (76.8%) during treatment. In the mood disorder participants (combined VBZ 40 mg and 80 mg dose groups) the mean MADRS and YMRS total score at baseline was 5.9 and 2.7, respectively.[2]
Mood symptoms remained generally stable during the studies, as indicated by minimal changes in mean total YMRS and MADRS scores (**Figure 1**). Changes in the individual items on the MADRS and YMRS scales were less than ± 0.2 in most participants at Weeks 48 and 52, indicating no clinically meaningful changes or worsening in specific mood symptoms or domains (**Table 1**).[2]

Figure 1. MADRS and YMRS Total Scores Changes (Mood Disorder Participants)



MADRS, Montgomery-Åsberg Depression Rating Scale; SEM, standard error of the mean; YMRS, Young Mania Rating Scale

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Table 1. MADRS and YMRS Item Score Changes (Mood Disorder Participants)

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	Week 48		Week 52	
Mean Score Change (SEM)	Valbenazine 40 mg n=15	Valbenazine 80 mg n=43	Valbenazine 40 mg n=15	Valbenazine 80 mg n=42
MADRS items				
Reported sadness	-0.1 (0.2)	0.0 (0.2)	0.1 (0.3)	-0.1 (0.2)
Apparent sadness	0.2 (0.2)	0.1 (0.2)	0.7 (0.3)	-0.0 (0.2)
Inner tension	-0.1 (0.3)	0.1 (0.2)	0.3 (0.2)	-0.0 (0.2)
Reduced sleep	0.5 (0.5)	-0.3 (0.3)	0.4 (0.5)	-0.3 (0.2)
Reduced appetite	0.2 (0.3)	-0.0 (0.1)	0.4 (0.3)	-0.0 (0.1)
Concentration difficulties	0.2 (0.3)	-0.1 (0.2)	0.3 (0.3)	0.0 (0.2)
Lassitude	0.3 (0.3)	0.1 (0.2)	0.8 (0.3)	0.0 (0.2)
Inability to feel	-0.2 (0.2)	0.1 (0.1)	0.5 (0.3)	0.0 (0.1)
Pessimistic thoughts	-0.1 (0.1)	0.2 (0.1)	0.5 (0.3)	0.1 (0.2)
Suicidal thoughts	0.1 (0.1)	0.0 (0.1)	0.0 (0.0)	0.1 (0.1)
YMRS items				
Elevated mood	-0.1 (0.1)	-0.0 (0.1)	-0.1 (0.1)	-0.1 (0.1)
Increased motor activity/energy	-0.2 (0.1)	-0.1 (0.1)	-0.1 (0.2)	-0.0 (0.1)
Sexual interest	0.0 (0.1)	0.0 (0.0)	0.1 (0.2)	-0.0 (0.0)
Sleep	-0.1 (0.2)	-0.3 (0.2)	0.1 (0.3)	-0.3 (0.1)
Irritability	-0.1 (0.2)	0.2 (0.1)	-0.1 (0.3)	0.1 (0.1)
Speech (rate and amount)	-0.3 (0.2)	-0.2 (0.2)	-0.4 (0.2)	-0.2 (0.1)
Language/thought disorder	-0.1 (0.2)	-0.1 (0.1)	-0.1 (0.2)	-0.1 (0.1)
Content	-0.3 (0.2)	-0.3 (0.2)	-0.4 (0.2)	-0.3 (0.2)
Disruptive/aggressive behavior	-0.2 (0.1)	0.0 (0.1)	0.3 (0.4)	-0.0 (0.0)
Appearance	-0.1 (0.1)	0.0 (0.1)	0.1 (0.1)	0.0 (0.1)
Insight	0.1 (0.1)	-0.1 (0.1)	0.0 (0.0)	-0.1 (0.1)

MADRS, Montgomery-Åsberg Depression Rating Scale; SEM, standard error of the mean; YMRS, Young Mania Rating Scale

Based on available C-SSRS data, most mood disorder participants had no suicidal ideation at baseline (97.9% [n=93/94]). Of these participants, 93.5% (n=87/93) had no emergence of C-SSRS suicidal ideation at any time during the long-term studies. In the 1 participant who had suicidal ideation at baseline ("wish to be dead"), no worsening in C-SSRS score was found at any time during the study.[2]

For a more complete description of this analysis, please see attached data presentation from the 2018 Annual US Psychiatric and Mental Health Congress by McIntyre et al.[2]

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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. McIntyre RS, et al. Effects of long-term valbenazine on psychiatric status in patients with tardive dyskinesia and a primary mood disorder. Presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.

Enclosures

A. INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.
B. McIntyre RS, et al. Effects of long-term valbenazine on psychiatric status in patients with tardive dyskinesia and a primary mood disorder. Presented at the US Psychiatric and Mental Health Congress; October 25-28, 2018; Orlando, FL.