SUPPLEMENTARY MATERIAL

Safety of Deutetrabenazine for the Treatment of Tardive Dyskinesia and Chorea Associated With Huntington Disease

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Supplementary Table S1.

SMQ	Preferred terms included in the SMQ for this study
Depression	Activation syndrome, adjustment disorder with depressed mood, adjustment disorder with mixed anxiety and depressed mood, agitated depression, anhedonia, antidepressant therapy, childhood depression, decreased interest, depressed mood, depression, depression postoperative, depressive symptom, dysphoria, electroconvulsive therapy, feeling guilty, feeling of despair, feelings of worthlessness, helplessness, major depression, menopausal depression, poststroke depression, postictal depression, and postpartum depression
Suicidality/self-injury	Completed suicide, depression suicidal, intentional overdose, intentional self-injury, poisoning deliberate, self-injurious behavior, self-injurious ideation, suicidal behavior, suicidal ideation, and suicide attempt
Akathisia	Akathisia, extrapyramidal disorder, hyperkinesia, motor dysfunction, movement disorder, psychomotor hyperactivity, and restlessness
Parkinson-like events	Action tremor, akinesia, bradykinesia, bradyphrenia, cogwheel rigidity, drooling, dysphonia, extrapyramidal disorder, freezing phenomenon, gait disturbance, hypertonia, hypokinesia, masked facies, micrographia, mobility decreased, motor dysfunction, movement disorder, muscle rigidity, muscle tone disorder, musculoskeletal stiffness, on and off phenomenon, Parkinson's disease, Parkinson's disease psychosis, parkinsonian crisis, parkinsonian gait, parkinsonism rest tremor, parkinsonism, parkinsonism hyperpyrexia syndrome, postural reflex impairment, postural tremor, resting tremor, tremor, and walking disability
Torsades de pointes/QT prolongation	Cardiac arrest, cardiac death, cardiac fibrillation, cardio-respiratory arrest, electrocardiogram QT interval abnormal, electrocardiogram QT prolonged, electrocardiogram U-wave abnormality, electrocardiogram repolarization abnormality, long QT syndrome, long QT syndrome congenital, loss of consciousness, sudden cardiac death, sudden death, syncope, torsade de pointes, ventricular arrhythmia, ventricular fibrillation, ventricular flutter, ventricular tachyarrhythmia, and ventricular tachycardia
Somnolence and sedation	Sedation, somnolence, sopor, stupor, and lethargy

Supplementary Table S2. Assessments scales

	Purpose	**Range**	**Directionality**
C-SSRS	Assess presence of suicidal ideation or suicidal behavior	Binary response (yes/no) on 10 questions	Categorical
HADS – depression subscale	Assess presence of depression	0–21	Higher score reflects higher severity
UPDRS – motor score	Assess parkinsonism	0–108	Higher score reflects higher severity
UHDRS – parkinsonism subscale	Assess parkinsonism	0–40	Higher score reflects higher severity

C-SSRS Columbia Suicide Severity Rating Scale, *HADS* Hospital Anxiety and Depression Scale, *UPDRS* Unified Parkinson's Disease Rating Scale.

Supplementary Table S3. QTcF in the TD overall treatment period

QTcF category, *n* (%)	DTBZ 12 mg/day *n* = 72	DTBZ 24 mg/day *n* = 72	DTBZ 36 mg/day *n* = 72	Response-driven DTBZ *n* = 168	Placebo *n* = 130
>450 ms	9 (13)	4 (6)	4 (6)	12 (7)	12 (9)
>480 ms	2 (3)	0	1 (1)	1 (<1)	1 (<1)
>500 ms	1 (1)	0	0	0	1 (<1)
Change >30 ms	9 (13)	6 (8)	6 (8)	10 (6)	11 (8)
Change >60 ms	0	0	0	1 (<1)	1 (<1)

QTcF corrected Fridericia's QT interval, *TD* tardive dyskinesia, *DTBZ* deutetrabenazine, *ms* milliseconds.

Supplementary Table S4. Timing of Standardised MedDRA Queries of interest in the TD overall treatment period

SMQ	DTBZ *n* = 384	Placebo *n* = 130
Akathisia		
AEs, n	7	0
Distinct Patients, n (%)	7 (1.8)	0
Onset, mean day (IQR, range)	53 (19−83, 5−109)	N/A
Resolved, n	3	N/A
Resolved, mean duration, days (IQR, range)	53 (18−76, 6−122)	N/A
Depression		
AEs, n	12	1
Distinct Patients, n (%)	12 (3)	1 (<1)
Onset, mean day (IQR, range)	36 (12-55, 0-86)	N/A
Resolved, n	7	1
Resolved, mean duration, days (IQR, range)	33 (6-65, 2-83)	N/A
Parkinson-like events		
AEs, n	18	2
Distinct Patients, n (%)	17 (4.4)	2 (1.5)
Onset, mean day (IQR, range)	47 (29−56, 0−105)	35 (24−47)
Resolved, n	14	0
Resolved, mean duration, days (IQR, range)	75 (20−46, 4−532)	N/A
Somnolence and sedation		
AEs, n	29	11
Distinct Patients, n (%)	26 (6.8)	9 (6.9)
Onset, mean day (IQR, range)	27 (8−42, 1−85)	12 (6−16, 1−34)
Resolved, n	23	8
Resolved, mean duration, days (IQR, range)	62 (13−54, 3−549)	28 (8−40, 3−73)
Suicide/self-injury		

AEs, n	3	1
Distinct Patients, n (%)	3 (<1)	1 (<1)
Onset, mean day (IQR, range)	20 (6−30, 2−48)	N/A
Resolved, n	3	1
Resolved, mean duration, days (IQR, range)	5 (4−6, 3−9)	N/A

AE adverse event, *DTBZ* deutetrabenazine, *IQR* interquartile range, *MedDRA* Medical Dictionary for Regulatory Activities, *SMQ* Standardised MedDRA Query.

Supplementary Table S5. Timing of Standardised MedDRA Queries of interest in the HD overall treatment period

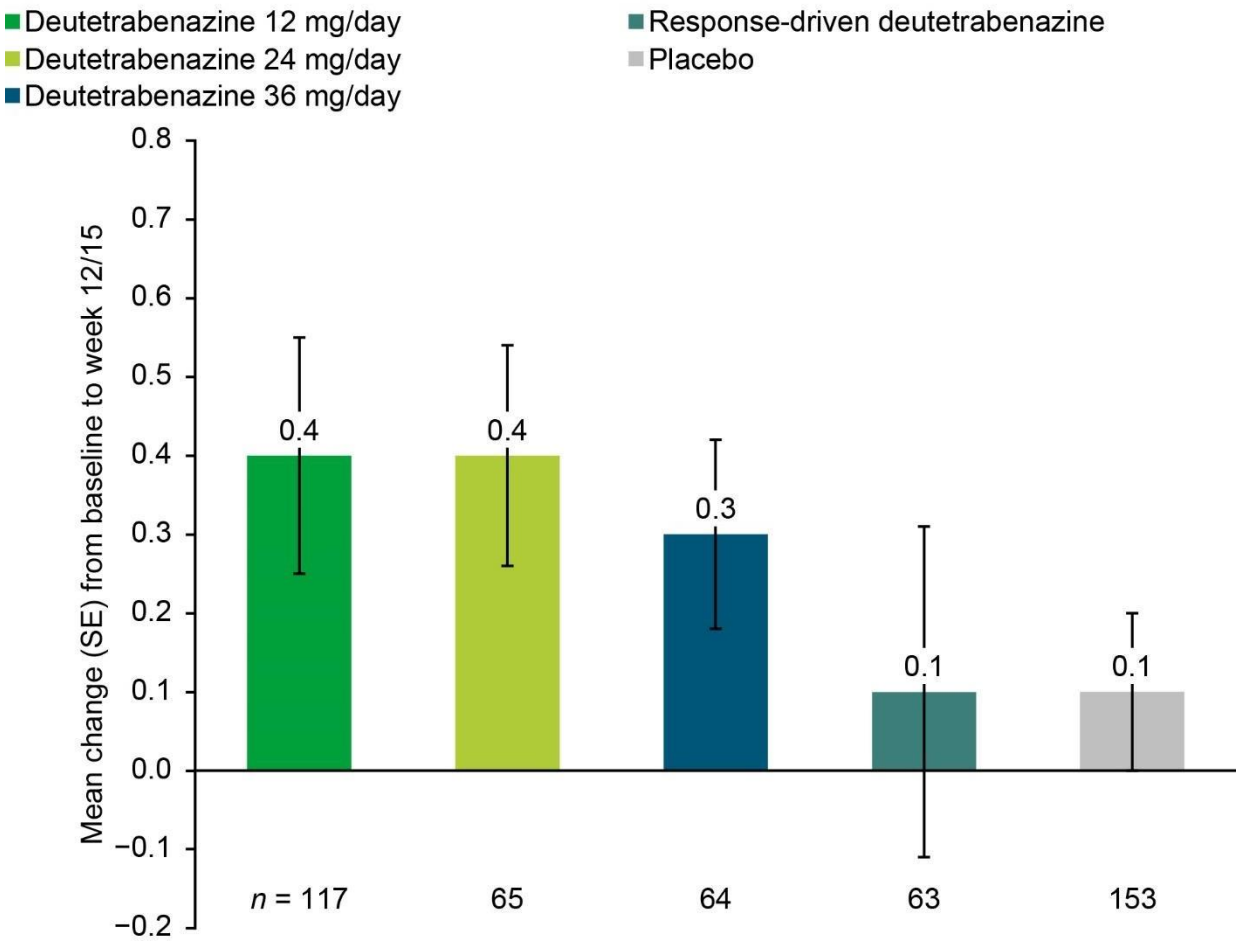
SMQ	DTBZ ***n*** = **84**	Placebo ***n*** = 45
Akathisia		
AEs, n	1	1
Distinct Patients, n (%)	1 (1.2)	1 (2.2)
Onset, mean day (IQR, range)	N/A	N/A
Resolved, n	1	1
Resolved, mean duration, days (IQR, range)	N/A	N/A
Depression		
AEs, n	5	3
Distinct Patients, n (%)	5 (6.0)	3 (6.7)
Onset, mean day (IQR, range)	49 (35−66, 23−74)	45 (26−60, 17−83)
Resolved, n	5	2
Resolved, mean duration, days (IQR, range)	26 (11−44, 7−47)	8 (7−10, 5−12)
Parkinson-like events		
AEs, n	6	0
Distinct Patients, n (%)	5 (6.0)	0
Onset, mean day (IQR, range)	46 (31−59, 23−77)	N/A
Resolved, n	1	N/A
1/Resolved, mean duration, days (IQR, range)	N/A	N/A
Somnolence and sedation		
AEs, n	11	2
Distinct Patients, n (%)	9 (10.7)	2 (4.4)
Onset, mean day (IQR, range)	26 (14−39, 2−52)	23 (13−33, 3−43)
Resolved, n	11	2
Resolved, mean duration, days (IQR, range)	51 (16−51, 2−255)	14 (14−15, 14−15)
Suicide/self-injury		
AEs, n	1	0

Distinct Patients, n (%)	1 (1.2)	0
Onset, mean day (IQR, range)	N/A	N/A
Resolved, n	1	N/A
Resolved, mean duration, days (IQR, range)	N/A	N/A

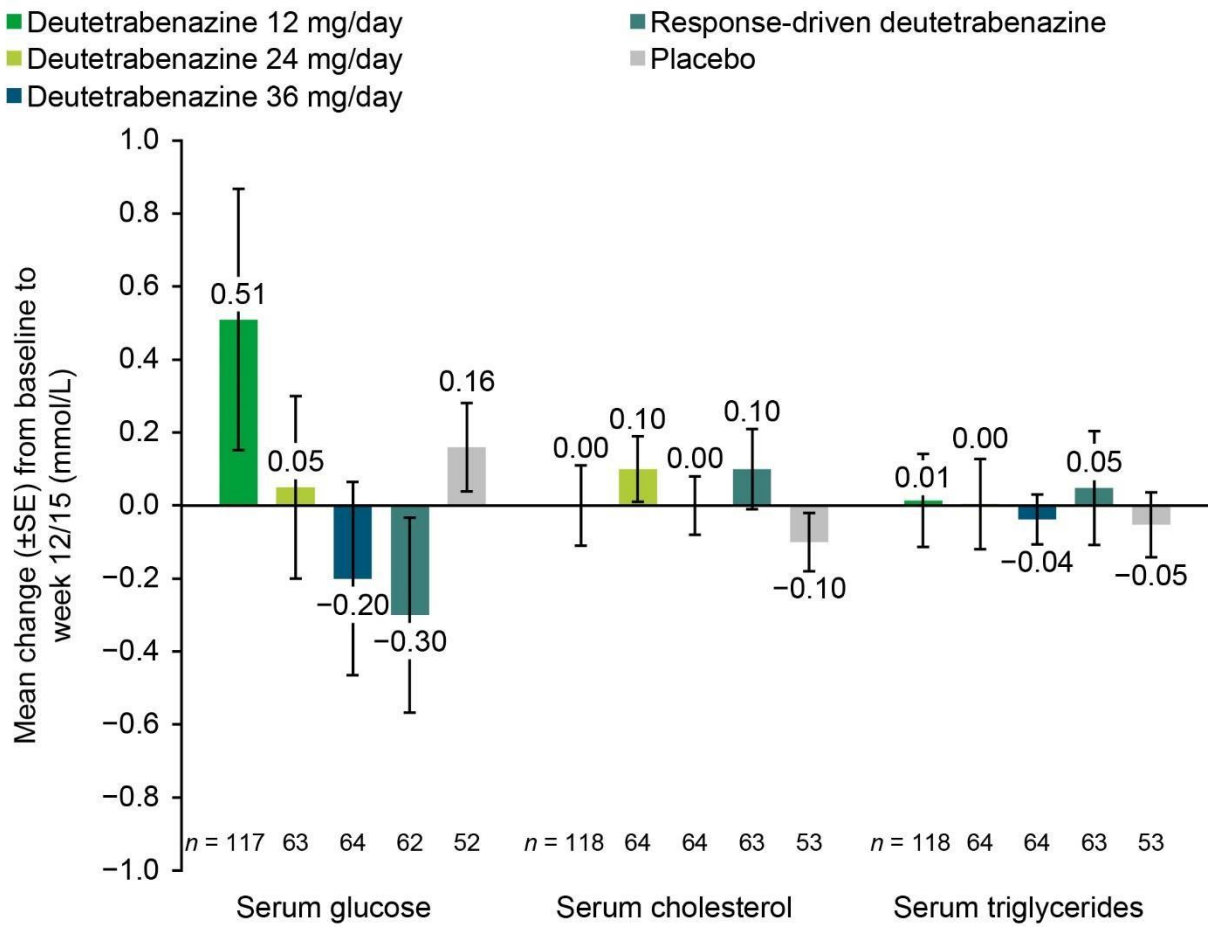
AE adverse event, *DTBZ* deutetrabenazine, *IQR* interquartile range, *MedDRA* Medical Dictionary for Regulatory Activities, *SMQ* Standardised MedDRA Query.

Supplementary Fig. S1. Change in (A) BMI and (B) metabolic parameters in the TD overall treatment period

a

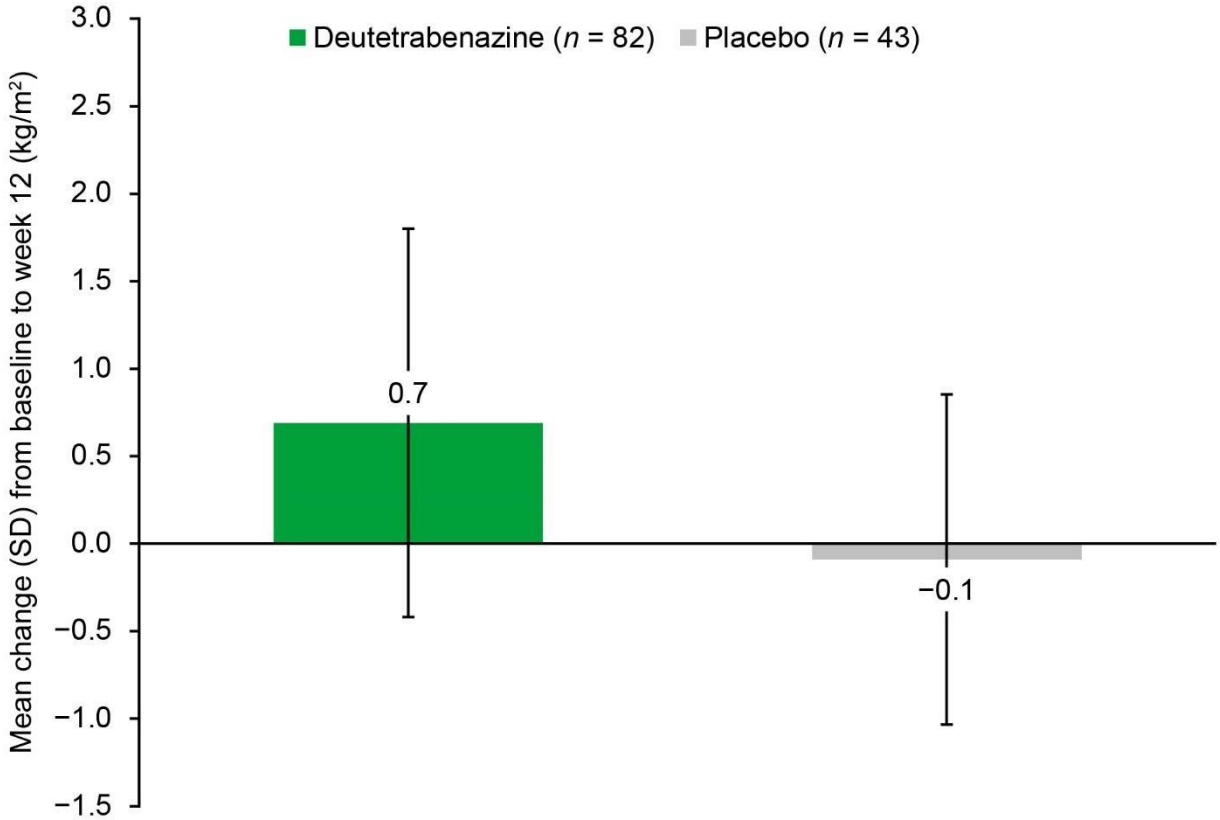


b



BMI body mass index, *TD* tardive dyskinesia.

Supplementary Fig. S2. Change in BMI in the HD overall treatment period



BMI body mass index, *HD* Huntington disease.