



Supplementary Material

Article Title: A Randomized, Placebo-Controlled Study of the Efficacy and Safety of Fixed-Dose Brexpiprazole 2 mg/day as Adjunctive Treatment of Adults With Major Depressive Disorder

Author(s): Mary Hobart, PhD; Aleksandar Skuban, MD; Peter Zhang, PhD; Carole Augustine, MA; Claudette Brewer, BA; Nanco Hefting, MSc; Raymond Sanchez, MD; and Robert D. McQuade, PhD

DOI Number: <https://doi.org/10.4088/JCP.17m12058>

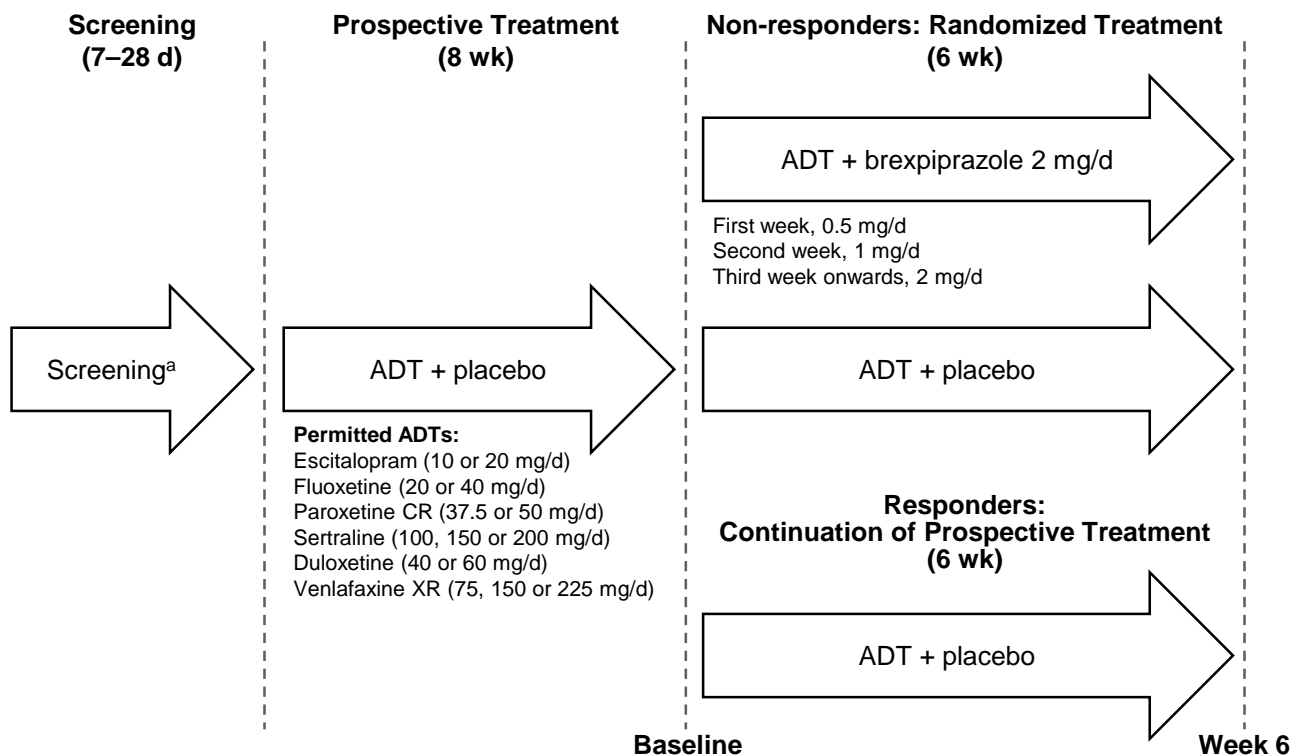
List of Supplementary Material for the article

1. [Figure 1](#) Study Design
2. [Table 1](#) Summary of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) Anxious Distress Specifier
3. [Table 2](#) Extrapyramidal Symptom Rating Scale Scores (Safety Population)
4. [Table 3](#) Laboratory Assessments (Safety Population)
5. [Table 4](#) Massachusetts General Hospital Sexual Functioning Questionnaire (MSFQ) Scores (Safety Population)

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Figure 1. Study Design



^aAnd washout of prohibited concomitant pharmacotherapy.

Patients received the same ADT for the duration of the study. ADT dose changes were permitted for the first 4 weeks of prospective treatment only.

During the prospective treatment phase patients visited the study center at weekly intervals for the first 4 weeks and then every 2 weeks; visits were at weekly intervals during the randomized treatment phase.

Abbreviations: ADT=antidepressant treatment, CR=controlled-release, XR=extended-release.

Supplementary Table 1. Summary of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) Anxious Distress Specifier

Anxious distress is defined as the presence of at least two of the following symptoms during the majority of days of a major depressive episode:

1. Feeling keyed up or tense.
 2. Feeling unusually restless.
 3. Difficulty concentrating because of worry.
 4. Fear that something awful may happen.
 5. Feeling that the individual might lose control of himself or herself.
-

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Arlington, VA: American Psychiatric Association; 2013.

Supplementary Table 2. Extrapyramidal Symptom Rating Scale Scores (Safety Population)

Variable	ADT + Placebo (n=202)		ADT + Brexpiprazole 2 mg (n=190)			P Value
	Mean (SD) At Baseline	LS Mean (SD) Change ^a	Mean (SD) At Baseline	LS Mean (SD) Change ^a	LSMD From Placebo ^a (95% CL)	
SAS Total score	0.18 (0.51)	0.00 (0.63)	0.36 (0.89)	0.16 (1.11)	0.16 (0.00, 0.33)	.052
AIMS Movement rating score ^b	0.08 (0.49)	0.03 (0.63)	0.02 (0.15)	0.01 (0.35)	-0.02 (-0.12, 0.08)	.73
BARS Global score	0.21 (0.55)	-0.03 (0.55)	0.21 (0.53)	0.16 (0.76)	0.19 (0.07, 0.31)	.0018

^aChange from baseline to last visit.

^bn=198 for ADT + placebo, n=185 for ADT + brexpiprazole. AIMS Movement rating score was defined as the sum of items 1–7 (facial and oral, extremity, and trunk movements).

Abbreviations: ADT=antidepressant treatment, AIMS=Abnormal Involuntary Movement Scale, BARS=Barnes Akathisia Rating Scale, CL=confidence limits, LS=least squares, LSMD=least squares mean difference, SAS=Simpson–Angus Scale, SD=standard deviation.

Supplementary Table 3. Laboratory Assessments (Safety Population)

Parameter	ADT + Placebo	ADT + Brexpiprazole 2 mg
Glucose		
Fasting serum glucose (mg/dL), mean change ^a	1.42 (n=169)	-0.44 (n=160)
Fasting serum glucose normal to high (<100 mg/dL to ≥126 mg/dL), n/N (%) ^b	0/131 (0.0)	1/123 (0.8)
Fasting serum glucose impaired to high (≥100 and <126 mg/dL to ≥126 mg/dL), n/N (%) ^b	0/35 (0.0)	3/32 (9.4)
HbA1c (%), mean change ^a	0.03 (n=98)	0.05 (n=93)
Lipids (fasting)		
Total cholesterol (mg/dL), mean change ^a	3.03 (n=171)	1.68 (n=160)
HDL cholesterol (mg/dL), mean change ^a	0.31 (n=170)	1.97 (n=157)
LDL cholesterol (mg/dL), mean change ^a	1.89 (n=166)	-1.14 (n=153)
Triglycerides (mg/dL), mean change ^a	2.24 (n=171)	6.91 (n=160)
HDL cholesterol normal to low (≥40 mg/dL to <40 mg/dL), n/N (%) ^b	4/157 (2.5)	6/146 (4.1)
LDL cholesterol normal/borderline to high (<160 mg/dL to ≥160 mg/dL), n/N (%) ^b	11/140 (7.9)	7/124 (5.6)
Triglycerides normal to high (<150 mg/dL to ≥200 and <500 mg/dL), n/N (%) ^b	2/128 (1.6)	4/111 (3.6)
Triglycerides normal/borderline to high (<200 mg/dL to ≥200 and <500 mg/dL), n/N (%) ^b	7/151 (4.6)	10/132 (7.6)
Prolactin		
Serum prolactin (ng/mL), mean change ^a		
Female	0.0 (n=141)	7.2 (n=141)
Male	0.1 (n=55)	2.2 (n=44)
Prolactin >2x ULN, n/N (%) ^c		
Female	0/143 (0.0)	1/142 (0.7)
Male	0/57 (0.0)	0/44 (0.0)
Prolactin >3x ULN, n/N (%) ^c		
Female	0/143 (0.0)	0/142 (0.0)
Male	0/57 (0.0)	0/44 (0.0)

^aFrom baseline to last evaluable value.^bShift from baseline to any post-baseline visit.

^cAt any post-baseline visit (patients counted once, in the highest category that applies).

Abbreviations: ADT=antidepressant treatment, HDL=high-density lipoprotein, LDL=low-density lipoprotein, n/N=number of patients with potentially clinically relevant shift/total number of patients in category, ULN=upper limit of the normal range.

Supplementary Table 4. Massachusetts General Hospital Sexual Functioning Questionnaire (MSFQ) Scores (Safety Population)

Variable	ADT + Placebo (n=198)		ADT + Brexpiprazole 2 mg (n=184)			P Value
	Mean (SD) At Baseline	LS Mean (SD) Change ^a	Mean (SD) At Baseline	LS Mean (SD) Change ^a	LSMD From Placebo ^a (95% CL)	
Interest in sex	4.3 (1.4)	-0.11 (1.11)	4.4 (1.5)	-0.46 (1.25)	-0.35 (-0.58, -0.13)	.0023
Sexually aroused	4.3 (1.4)	-0.15 (0.94)	4.3 (1.5)	-0.42 (1.25)	-0.27 (-0.48, -0.06)	.012
Achieve orgasm	4.4 (1.4)	-0.18 (0.93)	4.6 (1.4)	-0.34 (1.34)	-0.16 (-0.38, 0.06)	.16
Maintain erection ^b	3.3 (1.2)	-0.12 (0.97)	3.8 (1.4)	-0.28 (1.06)	-0.16 (-0.60, 0.28)	.47
Overall sexual satisfaction	4.5 (1.5)	-0.25 (0.98)	4.6 (1.4)	-0.42 (1.18)	-0.17 (-0.39, 0.04)	.11

^aChange from baseline to last visit.

^bMen only: ADT + placebo, n=57; ADT + brexpiprazole 2 mg, n=44.

Abbreviations: ADT=antidepressant treatment, CL=confidence limits, LS=least squares, LSMD=least squares mean difference, SD=standard deviation.