



Comparative Prevalence of Suicidal Ideation and Self-Harm History: Rexulti vs Other Oral Atypical Antipsychotics

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BACKGROUND

Major depressive disorder (MDD) is a highly prevalent mental health condition affecting nearly 300 million people worldwide, with rates continuing to rise across populations.¹⁻³ Among the most serious complications of MDD is suicide, which ranks as the 11th-leading cause of death in the United States, with epidemiologic evidence indicating that ~15% of individuals with severe MDD die by suicide.^{4,5}

Selective serotonin reuptake inhibitors (SSRIs) are the most common first-line agents, yet nearly one-third of patients fail to achieve remission with monotherapy, especially those at higher risk, often requiring augmentation strategies.^{6,7} Atypical antipsychotics (AAPs) are increasingly used as adjunctive treatments to improve symptom reduction and functional recovery in MDD.⁷ Rexulti® (brexpiprazole), approved in 2015, is a newer AAP with a unique serotonin-dopamine activity modulating profile.⁸ Given its distinct pharmacology and growing use, the prevalence of suicidal ideation and self-harm history was examined for patients diagnosed with MDD who were treated with brexpiprazole vs other oral AAPs.

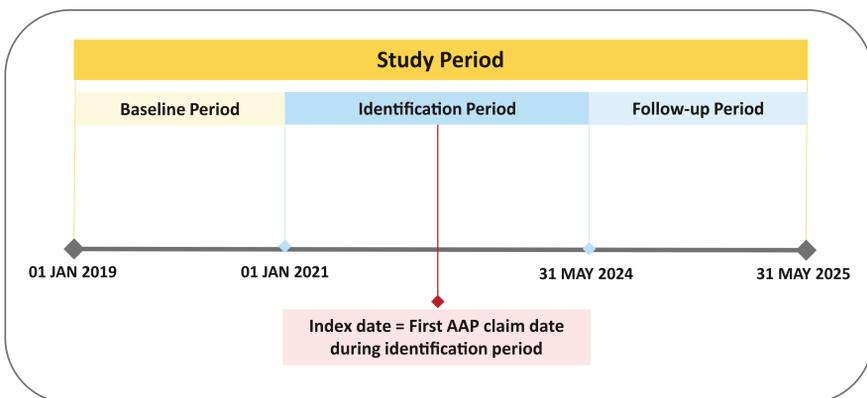
OBJECTIVES

This study compared the prevalence of suicidal ideation or personal history of self-harm among patients diagnosed with MDD who were treated with brexpiprazole use vs other AAPs.

METHODS

A retrospective cohort study was conducted using the Kythera Labs commercial database population from 01JAN2019-31MAY2025 (Figure 1).

Figure 1. Study Design



Inclusion criteria

- Initiated or re-initiated oral AAPs during identification period (01JAN2021-31MAY2024) following a ≥90-day washout period with no AAP use
- ≥2 MDD diagnoses during 2-year baseline period
- Continuous health plan enrollment 2 years pre- and 1 year post-index date
- ≥30 days of overlapping antidepressant and AAP use within 90 days post-index date to confirm adjunctive therapy

Exclusion criteria

- Diagnosed with serious mental illness, or
- Switched AAPs during follow-up period

Cohort Assignment

- Patients who augmented treatment with brexpiprazole
- Patients who augmented treatment with other oral AAPs (excluding brexpiprazole)

Baseline demographic and clinical characteristics were summarized descriptively for each cohort. Propensity score matching (PSM) was used to compare outcomes between the treatment cohorts.

RESULTS

After applying the inclusion and exclusion criteria, total 8,617 commercially-insured patients diagnosed with MDD who augmented treatment with brexpiprazole were compared to 115,388 patients who augmented treatment with other oral AAPs.

Baseline Patient Characteristics

Patients diagnosed with MDD who augmented treatment with brexpiprazole were:

- Younger on average (mean age 46.96 vs 49.61 years; $p < 0.0001$)
- More likely to be female (74.70% vs 68.37%; $p < 0.0001$)
- Had a lower mean Charlson Comorbidity Index (CCI) score (0.77 vs 0.96; $p < 0.0001$)
- Slightly more likely to reside in the Midwest (27.02% vs 25.82%; $p = 0.0261$) and South US regions (41.74% vs 37.74%; $p < 0.0001$; Table 1)

RESULTS

Table 1. Baseline Descriptive Characteristics of Patients with MDD and Treatment Augmentation with Brexpiprazole vs Other Oral AAPs

	Brexpiprazole Cohort (N=8,617)		Oral AAP Cohort (N=115,388)		P-Value
	Mean	SD	Mean	SD	
Age					
Mean Age	46.96	14.72	49.61	17.7	<0.0001
Age Groups	N	%	N	%	
18-34 years	1,638	22.77%	20,009	23.67%	0.0834
35-54 years	3,070	42.67%	28,743	34.00%	<.0001
55-64 years	1,715	23.84%	18,779	22.21%	0.0015
65+ years	772	10.73%	17,007	20.12%	<0.0001
Sex	N	%	N	%	
Male	1,820	25.30%	26,736	31.63%	<0.0001
Female	5,375	74.70%	57,802	68.37%	<0.0001
US Region	N	%	N	%	
Midwest	1,944	27.02%	21,829	25.82%	0.0261
Northeast	1,058	14.70%	13,435	15.89%	0.008
South	3,003	41.74%	31,906	37.74%	<0.0001
West	895	12.44%	14,627	17.30%	<0.0001
Comorbidity Index Score	Mean	SD	Mean	SD	
Charlson Comorbidity Index Score	0.77	1.31	0.96	1.54	<0.0001

AAP: atypical antipsychotic; MDD: major depressive disorder; SD: standard deviation

In the unmatched analysis, patients who augmented treatment with brexpiprazole showed a significantly lower prevalence of suicidal ideation and self-harm history vs other oral AAPs (suicidal ideation: 0.94% vs 2.76%; self-harm history: 0.42% vs 1.84%; either measure: 1.24% vs 3.88%, $p < 0.0001$ for all; Table 2).

Table 2. Unadjusted Prevalence of Suicidal Ideation and History of Self-harm among Patients Diagnosed with MDD and Augmented Treatment with Brexpiprazole vs Other Oral AAPs

	Brexpiprazole Cohort (N=8,617)	Oral AAP Cohort (N=115,388)	P-Value
(1) Suicidal ideation	81 (0.94%)	3,186 (2.76%)	<0.0001
(2) Personal history of self-harm	36 (0.42%)	2,125 (1.84%)	<0.0001
Any of (1) or (2)	107 (1.24%)	4,474 (3.88%)	<0.0001

AAP: atypical antipsychotic; MDD: major depressive disorder

In a matched analysis, a total of 8,617 patients in each cohort were evaluated following 1:1 PSM, adjusting for index medication year, age, CCI score, and other comorbid conditions.

After PSM, the prevalence of suicidal ideation/self-harm was significantly lower among patients who augmented treatment with brexpiprazole vs other AAPs (either measure: 1.24% vs 3.38%, $p < 0.0001$; Table 3).

Table 3. Risk-adjusted Prevalence of Suicidal Ideation and History of Self-harm among Patients Diagnosed with MDD and Augmented Treatment with Brexpiprazole vs Other Oral AAPs

	Brexpiprazole Cohort (N=8,617)	Oral AAP Cohort (N=8,617)	P-Value
(1) Suicidal ideation	81 (0.94%)	215 (2.50%)	<0.0001
(2) Personal history of self-harm	36 (0.42%)	134 (1.56%)	<0.0001
Any of (1) or (2)	107 (1.24%)	291 (3.38%)	<0.0001

AAP: atypical antipsychotic; MDD: major depressive disorder

CONCLUSION

Patients diagnosed with MDD who augmented treatment with brexpiprazole vs other oral AAPs were found to have a lower prevalence of suicidal ideation and personal history of self-harm, were generally younger, and more likely to be female. These associations remained statistically significant even after applying PSM to control for baseline confounders.

Although additional studies are needed to understand the underlying mechanisms and validate these findings across broader populations, the results offer important guidance for clinicians selecting antipsychotic treatments for patients diagnosed with MDD.

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