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Enclosure:

• POSTER: Stamatis CA, Zhang Z, Cochran J, et al. Presented at Psych Congress, September 17-21, 2025; San Diego, CA, USA.

Evaluating Changes in Anxiety Symptoms With Rejoyn (CT-152) Among Participants With Major Depressive Disorder and Comorbid Anxiety

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Poster presented at the 38th Psych Congress 2025 September 17–21, San Diego, CA, USA



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Introduction

- Rejoyn® (CT-152) is the first US Food and Drug Administrationauthorized prescription digital therapeutic adjunct to antidepressant medication for patients with major depressive disorder (MDD).1
- Rejoyn is designed to promote emotional regulation and reduce perseverative thinking, symptomology that may be shared in MDD and anxiety disorders.^{1,2}
- Comorbid anxiety is common for those with MDD, with one study suggesting that 50–70% of depressed patients also have generalized anxiety disorder (GAD).²
- Although not specifically designed to treat anxiety disorders, the putative mechanism of action for Rejoyn targets the main brain regions implicated in both depression and anxiety that are responsible for cognitive control over emotions, the dorsolateral prefrontal cortex and amygdala.1,2
- These brain regions have also been implicated in repetitive negative thinking, a transdiagnostic process underlying worry in anxiety disorders and rumination in depression.^{3,4}

- In the pivotal Mirai trial (NCT04770285), Rejoyn showed benefit over the sham app on multiple clinical scales for MDD and comorbid anxiety symptoms.1
- Prior analysis supported improvements on the depressionspecific Montgomery-Asberg Depression Rating Scale (MADRS; between-group difference: -3.62, P=0.0099) and GAD 7-Item scale (GAD-7) total score (between-group difference: -2.17, P=0.0019) for those with baseline anxiety symptoms (GAD-7 ≥10).
- Post hoc analysis of participant subgroups with comorbid anxiety symptoms, as measured by the GAD-7, Hamilton Depression Rating Scale-Anxiety, and Hamilton Depression Rating Scale-Anxiety/Somatization, showed similar findings in change from baseline on the Patient Health Questionnaire 9-Item—favoring Rejoyn over sham in total score and respective line items.^{1,5,6}

Minimal anxiety GAD-7 total score: 1–4

Mild anxiety GAD-7 total score: 5–9

Moderate anxiety GAD-7 total score: 10–14

Severe anxiety GAD-7 total score: 15–21

Moderate-to-Severe anxiety (GAD-7 ≥10)

Objective

• This post hoc analysis assessed the efficacy of Rejoyn versus sham for line items on the GAD-7 for participants with comorbid symptoms of anxiety, defined as a baseline GAD-7 score ≥10.

Methods

- Adults aged 22–64 years with a primary diagnosis of MDD (based on the criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) and inadequate response to current antidepressant medication participated in the Phase 3 multicenter, randomized, blinded, sham-controlled, remote Mira study with a 6-week intervention period and 4-week extension.
- Participants were randomly assigned 1:1 to treatment with either Rejoyn or sham.⁷
- Delivered via a smartphone app, Rejoyn includes 3 components:⁷ 1. Cognitive-emotional training exercises (Emotional Faces Memory Task [EFMT])
- 2. Brief cognitive-behavioral therapy (CBT)-based lessons to reinforce and apply therapeutic skills
- 3. Personalized text messages

- The control group received a sham app that included a Shapes Memory Task, which is a working-memory task designed to match the EFMT for time, attention, and expectation of benefit, but which is not intended to be therapeutic and does not contain the CBT-based lessons.7

 All participants continued their current antidepressant medication, and both groups received supportive text messages to promote treatment engagement.^{1,7}

- To assess the effect of Rejoyn treatment on anxiety symptoms, we evaluated change from baseline on the GAD-7 line items for participants in Mirai that had elevated baseline anxiety symptoms, defined as baseline GAD-7 ≥10 (moderate-tosevere category, Figure 1).1,5,6
- GAD-7 is a 7-item scale commonly used in clinical practice to evaluate presence and frequency (in days) of anxiety symptoms. Each item ranges from 0 (not at all) to 3 (nearly every day), with higher scores indicating greater frequency of anxiety symptoms. The total score can then be used to categorize anxiety severity as "minimal anxiety," "mild anxiety," "moderate anxiety," or "severe anxiety" (Figure 1).
- Differences in GAD-7 line item change across groups were assessed via mixed-effects models for repeated measures, with the following terms: treatment, visit, treatment by visit, and baseline by visit interaction for Rejoyn versus sham groups.
- P values for post hoc analyses were not adjusted for multiplicity and not intended for hypothesis testing, and are provided to help interpret findings. Effect size is reported as Cohen's *d* (small: 0.20 to <0.50, medium: 0.50 to <0.80, large: ≥0.80).

Results

- Of the 386 participants randomly assigned to Rejoyn (n=194) or sham (n=192), 165 in the Rejoyn and 164 in the sham group completed the trial.
- Of these participants, 159 had GAD-7 total scores ≥10 at baseline (Rejoyn n=78; sham n=81), which corresponds to moderate-to-severe baseline anxiety symptoms.
- Baseline GAD-7 scores are presented in **Table 1**.
- Group differences favoring Rejoyn were observed for 5 of 7 GAD-7 line items, including "feeling nervous," "being restless" (both P < 0.01), "not able to stop worrying," "trouble relaxing," and "becoming easily annoyed" (each *P* < 0.05) (**Figure 2**).
- The remaining two items ("worrying too much about things" and "feeling as is if something awful will happen") also favored Rejoyn numerically (P < 0.1).
- Line items rated more severe at baseline showed the greatest improvements, including "feeling nervous," "not able to stop worrying," and "worrying too much about things" (Table 1; Figure 2).

GAD-7, Generalized Anxiety Disorder 7-Item scale.

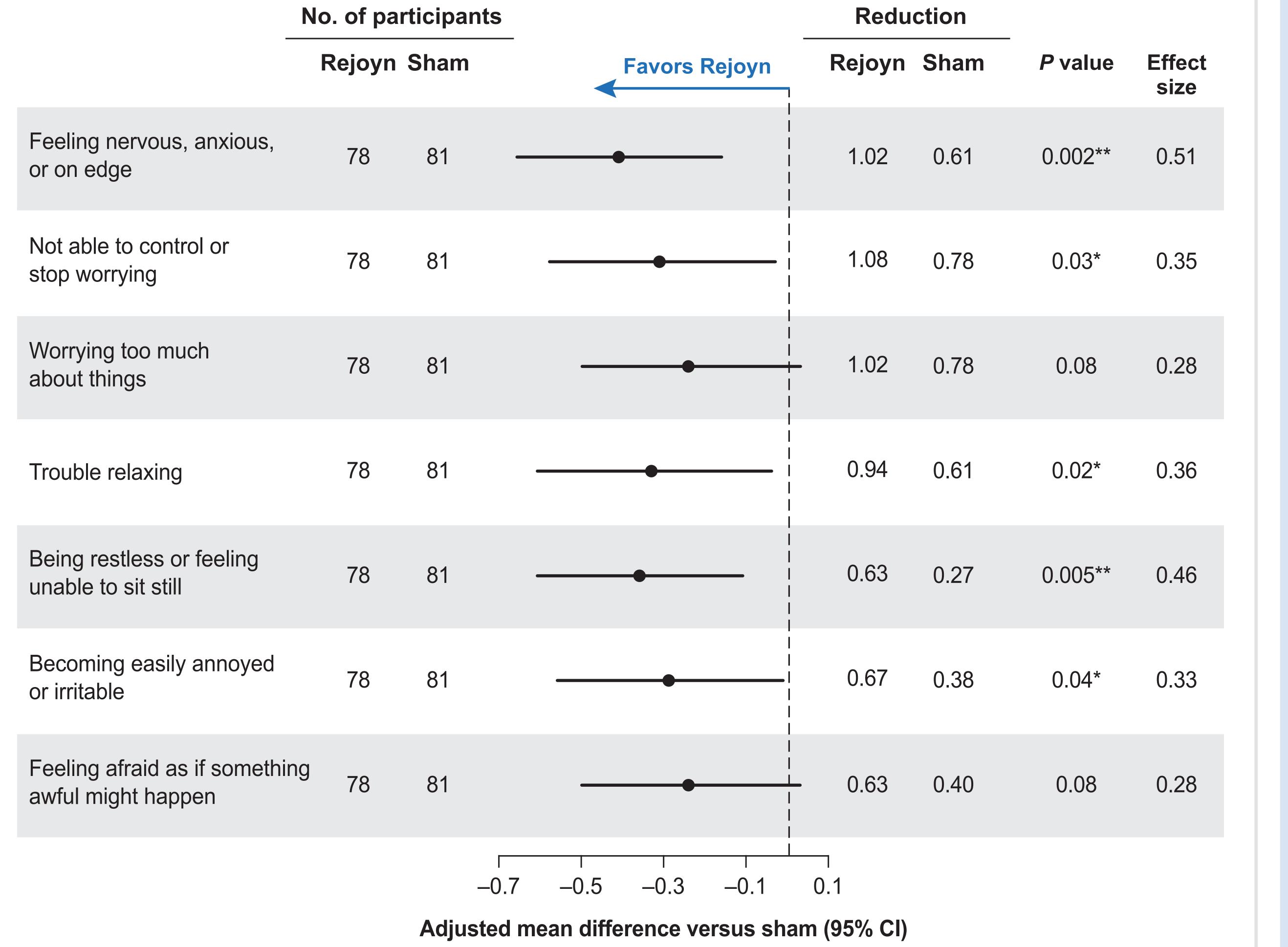
Figure 1. GAD-7 total score and corresponding anxiety severity categories

Table 1. Baseline GAD-7 line items for participants with moderate-to-severe anxiety (GAD-7 ≥10)

Parameter	Rejoyn	Sham
Feeling nervous, anxious, or on edge n Mean (SD) Median	78 2.22 (0.7) 2	81 2.42 (0.63) 2
Not able to control or stop worrying n Mean (SD) Median	78 2.22 (0.75) 2	81 2.16 (0.75) 2
Worrying too much about things n Mean (SD) Median	78 2.33 (0.62) 2	81 2.20 (0.71) 2
Trouble relaxing n Mean (SD) Median	78 2.31 (0.74) 2	81 2.26 (0.74) 2
Being restless or feeling unable to sit still n Mean (SD) Median	78 1.33 (0.91) 1	81 1.49 (0.95) 1
Becoming easily annoyed or irritable n Mean (SD) Median	78 1.88 (0.84) 2	81 1.94 (0.95) 2
Feeling afraid as if something awful might happen n Mean (SD) Median	78 1.37 (0.98) 1	81 1.32 (0.86) 1

GAD-7, Generalized Anxiety Disorder 7-Item scale; Max, maximum; Min, minimum; N, number of participants; SD, standard deviation.

Figure 2. Change from baseline in GAD-7 line items for participants with baseline anxiety (GAD-7 ≥10)



P* <0.05; *P* <0.01.

CI, confidence interval; GAD-7, Generalized Anxiety Disorder 7-Item scale; No, number.

CONCLUSIONS

Findings from this post hoc analysis support the efficacy of Rejoyn for anxiety symptoms among participants with MDD and comorbid anxiety.

The GAD-7 line item analysis is consistent with the Mirai primary and prior supporting post hoc analyses, which suggested clinical symptom improvements for those with comorbid anxiety. 1,5,6

Although not designed for anxiety symptoms, these findings may support that Rejoyn targets the transdiagnostic processes of emotion regulation and repetitive negative thinking, which are shared across depression and anxiety disorders.3,4

References

1. Rothman B et al. J Affect Disord. 2025;388:119409.

2. Renna ME et al. Front Psychol. 2017;8:98.

3. Ehring T and Watkins ER. Int J Cogn Ther. 2008;1(3):192–205. 4. Puccetti NA et al. Cogn Affect Behav. 2025;25(2):488–500.

5. Ash J et al. Presented at the APA 2025 Annual Meeting; Los Angeles, CA, USA. Abstract 4233.

6. Zhang Z et al. Presented at the Psych Congress Elevate 2025; Las Vegas, NV, USA. Abstract 14.

7. Rothman B et al. *JMIR Res Protoc*. 2024;13:356960.

Funding

This study was funded by Otsuka Pharmaceutical Development & Commercialization, Inc. Click Therapeutics, Inc. was a co-development collaborator.

Acknowledgments

Medical writing support was provided by George Pellegrino, MD, PhD, of Oxford PharmaGenesis Inc., Wilmington, DE, USA, and was funded by Otsuka Pharmaceutical Development & Commercialization, Inc.

At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

Disclosures

CAS, ZZ, JC, JA, BR, TC, CM, and AF employees: Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA. DC employee: Otsuka Precision Health, Inc., Princeton, NJ, USA. SEL employee: Click Therapeutics, Inc., New York, NY, USA.