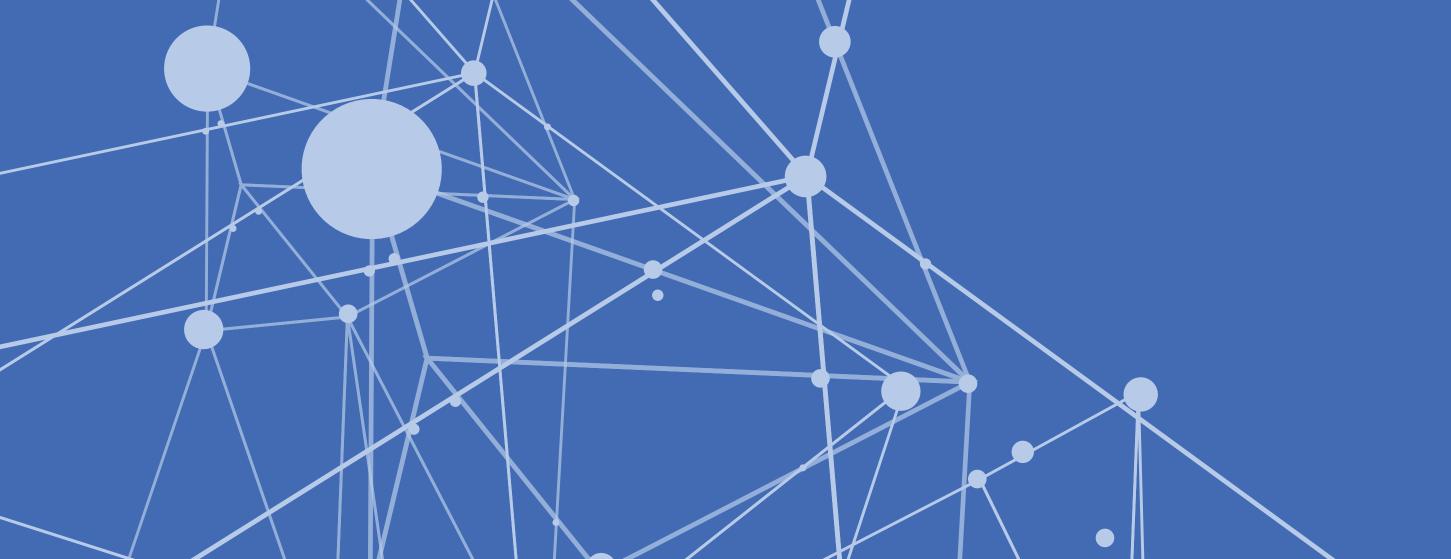
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Enclosure:

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A Prescription Digital Therapeutic, CT-152, for Treating Major Depressive Disorder: Effectiveness and Safety Results of the Mirai Randomized Controlled Trial

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Introduction

can access mental healthcare, antidepressa However, less than half of patients achieve remission with first-line antidepressant medication. 1-6

- some unmet needs, including increasing access via remote treatment and having a favorable side
- with MDD. CT-152 is comprised of 3 components: evidence-based cognitive-emotional training

exercises (Emotional Faces Memory Task [EFMT]); brief cognitive-behavioral therapy (CBT) based lessons and activities; and personalized

- EFMT is designed to enhance cognitive control over emotional information processing by targeting regions of the brain (ie, amygdala, dorsolateral prefrontal cortex) implicated
- the effectiveness and safety of CT-152 for people with MDD as an adjunct to antidepressant medication monotherapy (NCT04770285).
- Results from this study supported the recent clearance of CT-152 by the U.S. Food and Drug Administration (FDA) as a prescription DTx.

Methods

Participants and trial design

- adults aged 22-64 years with MDD and having an inadequate response to current antidepressant medication were enrolled in a pivotal phase 3 multicenter, randomized, blinded, sham-controlled, remote trial with a 6-week intervention period and 4-week extension (Figure 1).
- Inadequate response to antidepressant medication was defined as < 50% reduction in depression symptom severity, and an adequate trial was defined as ≥ 6 weeks at a minimum therapeutic dose [or higher], both evaluated per the Massachusetts General Hospital-Antidepressar
- Treatment Response Questionnaire. Eligible participants continued their current antidepressant medication and were randomly assigned 1:1 to CT-152 or the sham app, both
- delivered via smartphone apps. Participants and sites were blinded to treatmen assignment, and Montgomery-Åsberg Depression Rating Scale (MADRS) assessments were

- change from baseline to week 6.
- The primary outcome was MADRS total score Other outcomes included change in score from baseline for the Clinical Global Impression—Severity inadequate response scale (CGI-S), Patient Health Questionnaire-9 • HAM-D₁₇ score ≥ 18 (PHQ-9), and General Anxiety Disorder-7 scale (GAD-7), and week 6 MADRS response rates.
- Safety outcomes were assessed as the frequency and severity of treatment-emergent adverse

Statistical analysis

- The intent-to-treat (ITT) sample included all participants who were randomly assigned to a group; the modified ITT (mITT) sample included participants receiving ≥ 1 treatment session with a MADRS assessment at baseline and ≥ 1 MADRS assessment after baseline, and the safety sample included participants receiving ≥ 1 treatment session
- The primary efficacy endpoint was tested at a significance level of 0.049 (2-sided), and secondary and exploratory endpoints were tested at a nominal 0.05 level (2-sided) without adjusting

Other outcomes

Of 1034 adults screened, 386 were randomly

In the primary efficacy analysis (mITT sample) the

6-week mean MADRS score change from baseline

sham app group. The between-group difference in

6-week MADRS score change from baseline was

-1.78 (P = 0.0568), numerically favoring CT-152

In a supportive analysis (ITT sample), the

(P = 0.0211), favoring CT-152 (**Figure 3B**).

When compared with the sham app group at

week 6, the CT-152 group:

score change from baseline was -2.12

between-group difference in 6-week MADRS

had a higher percentage of participants who

(partial and full response defined as ≥ 30%

48.3%, respectively; *P* = 0.0485) (**Table 2**)

for the PHQ-9 (5.10 vs 6.68, respectively; P =

0.0029) and CGI-S (0.80 vs 1.06, respectively;

experienced improvements versus baseline

P = 0.0098) (Figure 4A, Figure 4B)

but < 50% reduction from baseline and ≥ 50%

was -9.03 in the CT-152 group and -7.25 in the

Patient characteristics

characteristics (Table 1).

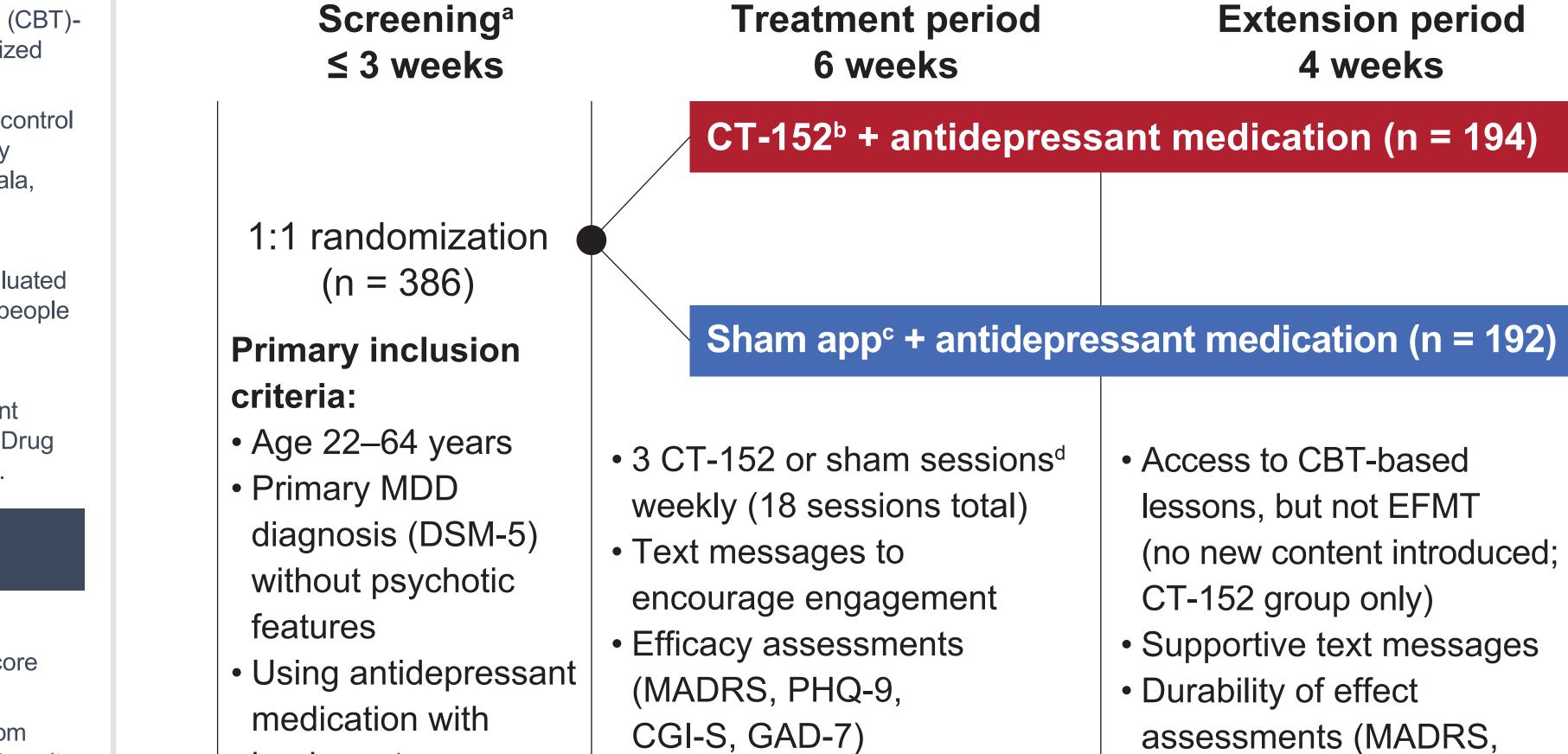
Efficacy outcomes

Results

- The mean MADRS score change from baseline assigned to CT-152 (n = 194) or the sham app to week 10 was -10.96 for the CT-152 group (n = 192) (**Figure 2**). compared with -9.93 for the sham app group (between-group difference −1.03), numerically Participants in both study arms had similar
 - Between-group differences in MADRS score change numerically favored CT-152 over the sham app among participants completing 18/18 treatment sessions at week 10, suggesting a durable treatment effect in the CT-152 group.
 - In participants with a baseline GAD-7 score ≥ 10 ("at least moderate anxiety"), the between-group differences in MADRS (Figure 5) and GAD-7 score change at week 6 favored CT-152 over the sham app group (P = 0.0099 and P = 0.0019, respectively).

- Overall, 20.6% of participants experienced TEAEs during the treatment period and 10.5% experienced TEAEs during the extension period with a numerically lower incidence in the CT-152 group (Table 3).
- experienced a partial or full MADRS response No TEAEs were assessed as being related
 - There were no participants with severe TEAEs, no participants who discontinued due to AEs,
 - TEAEs experienced by ≥ 2% of participants during the treatment period were upper respiratory tract infection, nasopharyngitis, and headache.
- had a numerically higher GAD-7 score All reported headaches were nonserious and change from baseline (-2.64 vs -3.41, occurred at a higher incidence in the CT-152 respectively; P = 0.0705). group (2.1%) than in the sham-app group (1.6%).

Figure 1. Mirai trial design



symptoms; and 3) personalized text messages to reinforce the lessons and encourage engagement; °The sham app used SMT, an emotionally neutral working memory task matched for time and attention to EFMT, along with text messaging; deach session of CT-152 included an EFMT exercise and a brief CBT-based lesson with an activity; each sham app session only included ar

Week 6

Safety assessments (AEs)

Week 10

Safety assessments (AEs)

AE, adverse event; CBT, cognitive-behavioral therapy; CGI-S, Clinical Global Impression—Severity scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; EFMT, Emotional Faces Memory Task; GAD-7, Generalized Anxiety Disorder-7; HAM-D₁₇, Hamilton Rating Scale for Depression, 17-item; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; PHQ-9, Patient Health Questionnaire-9; SMT, shapes memory task

Figure 2. Participant disposition flowchart (CONSORT)

Day 1

Screening

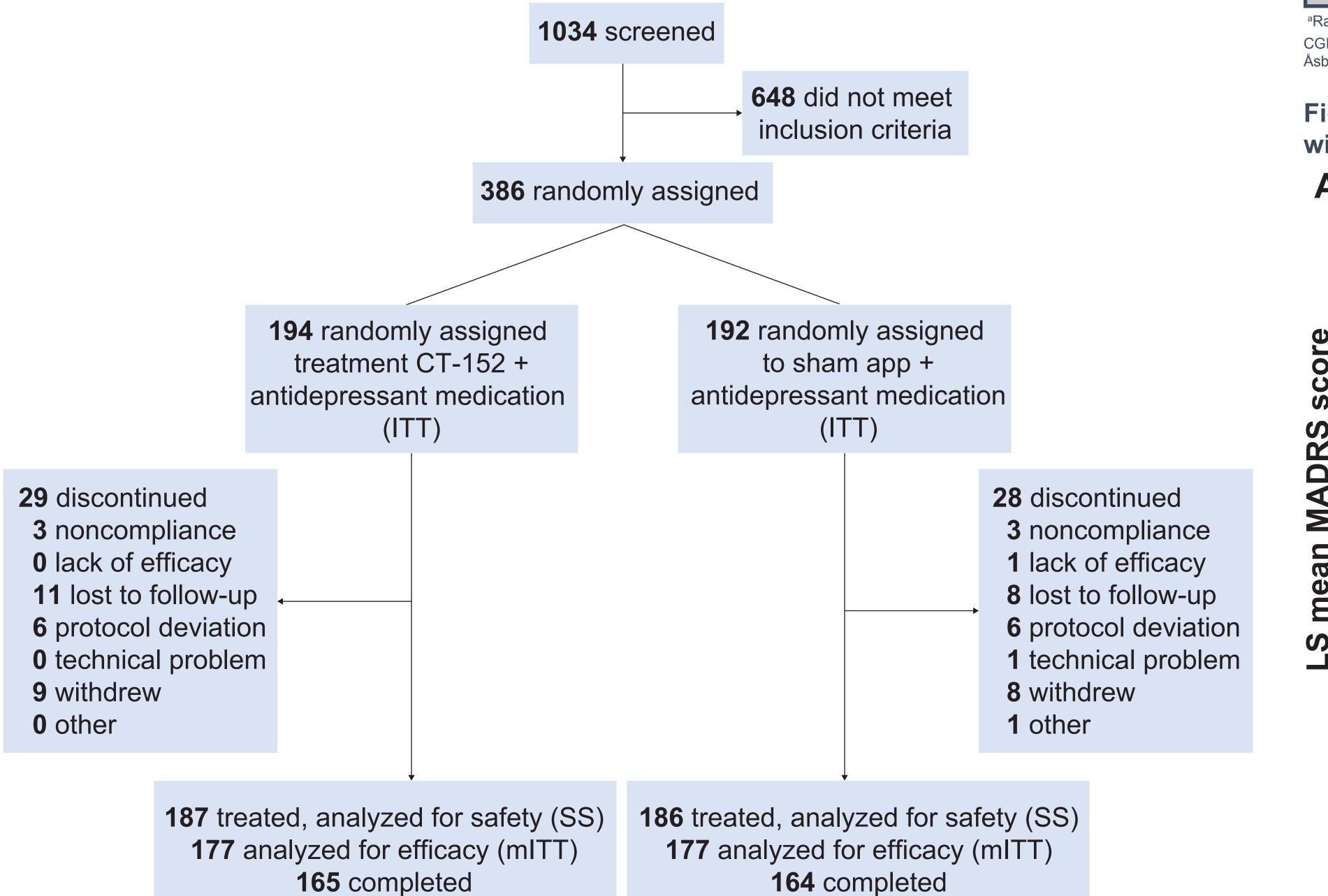
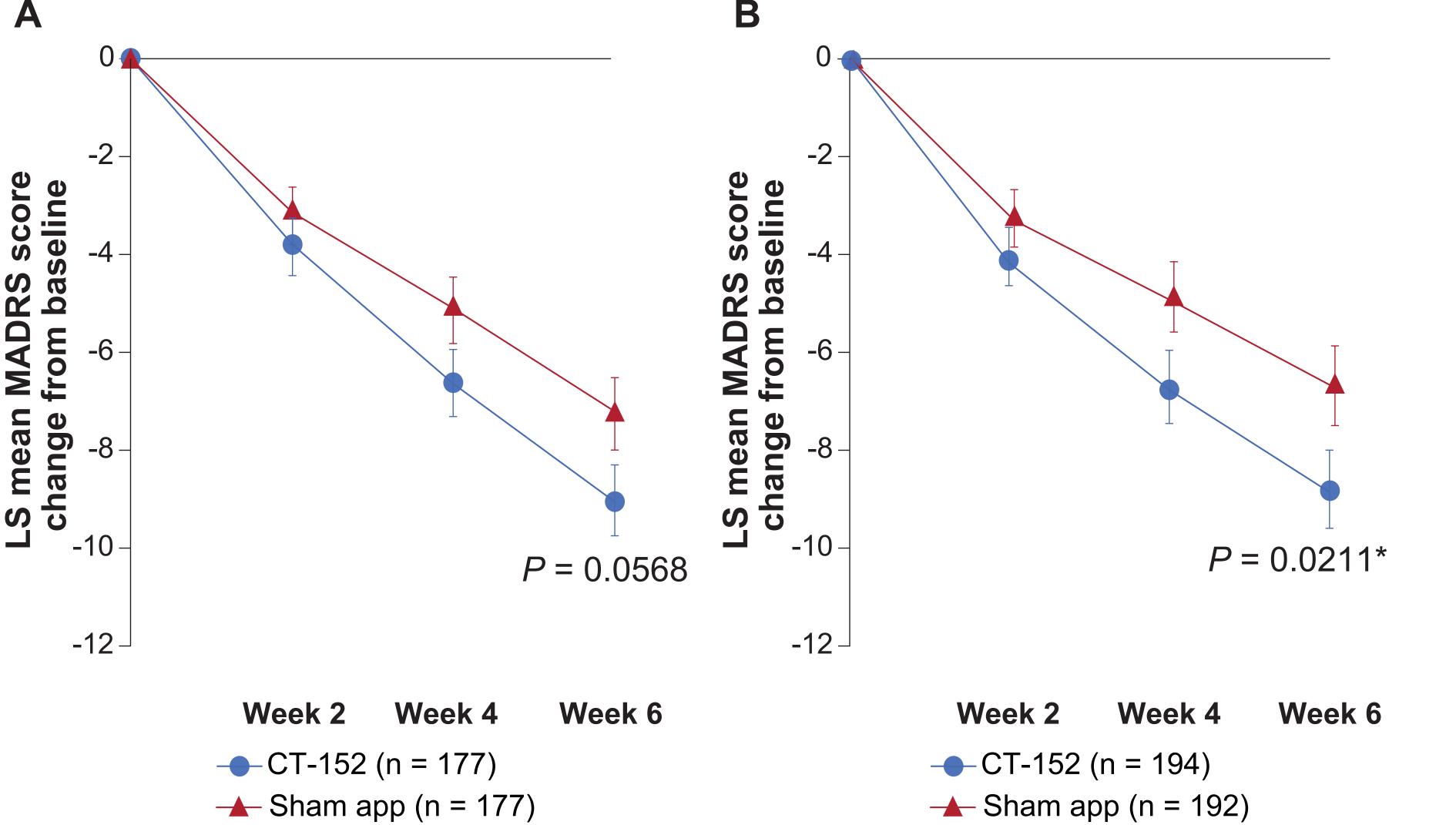


Table 1. Participant baseline characteristics

	mITT sample			ITT sample			
Participant characteristics	CT-152	Sham app	Total	CT-152	Sham app	Total	
	(n = 177)	(n = 177)	(n = 354)	(n = 194)	(n = 192)	(N = 386)	
Demographics							
Mean age in years (SD)	42.6 (11.9)	42.1 (12.2)	42.4 (12.1)	43.0 (12.1)	42.2 (12.1)	42.6 (12.1)	
Sex, n (%) Female Male	151 (85.3)	155 (87.6)	306 (86.4)	165 (85.1)	167 (87.0)	332 (86.0)	
	26 (14.7)	22 (12.4)	48 (13.6)	29 (14.9)	25 (13.0)	54 (14.0)	
Race ^a , n (%) American Indian or Alaska Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Other	5 (2.8)	1 (0.6)	6 (1.7)	5 (2.6)	1 (0.5)	6 (1.6)	
	5 (2.8)	4 (2.3)	9 (2.5)	5 (2.6)	4 (2.1)	9 (2.3)	
	31 (17.5)	23 (13.0)	54 (15.3)	36 (18.6)	25 (13.0)	61 (15.8)	
	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	129 (72.9)	147 (83.1)	276 (78.0)	141 (72.7)	160 (83.3)	301 (78.0)	
	7 (4.0)	2 (1.1)	9 (2.5)	7 (3.6)	2 (1.0)	9 (2.3)	
Ethnicity ^a , n (%) Hispanic or Latino Not Hispanic or Latino Unknown	20 (11.3)	16 (9.0)	36 (10.2)	20 (10.3)	16 (8.3)	36 (9.3)	
	156 (88.1)	159 (89.8)	315 (89.0)	173 (89.2)	174 (90.6)	347 (89.9)	
	1 (0.6)	2 (1.1)	3 (0.8)	1 (0.5)	2 (1.0)	3 (0.8)	
Baseline psychiatric evalua	tion scores, n	nean (SD)					
MADRS	28.4 (6.0)	28.5 (6.0)	28.5 (6.0)	28.4 (6.0)	28.4 (6.0)	28.4 (6.0)	
	n = 177	n = 177	n = 354	n = 189	n = 186	n = 375	
PHQ-9	15.4 (4.7)	15.1 (4.7)	15.2 (4.7)	15.4 (4.7)	15.2 (4.7)	15.3 (4.7)	
	n = 175	n = 175	n = 350	n = 192	n = 189	n = 381	
GAD-7	9.6 (4.5)	9.6 (4.9)	9.6 (4.7)	9.5 (4.5)	9.7 (4.8)	9.6 (4.7)	
	n = 171	n = 171	n = 342	n = 185	n = 184	n = 369	
CGI-S	4.3 (0.6)	4.3 (0.5)	4.3 (0.5)	4.3 (0.5)	4.3 (0.5)	4.3 (0.5)	
	n = 177	n = 176	n = 353	n = 194	n = 191	n = 385	
HAM-D ₁₇	22.8 (3.4)	22.3 (3.1)	22.6 (3.2)	22.7 (3.3)	22.4 (3.1)	22.5 (3.2)	
	n = 177	n = 177	n = 354	n = 187	n = 186	n = 373	

Asberg Depression Rating Scale; mITT, modified intent-to-treat; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

Figure 3. Depression symptom changes from baseline with use of CT-152 versus sham app for adults with MDD in the mITT (A) and ITT (B) samples



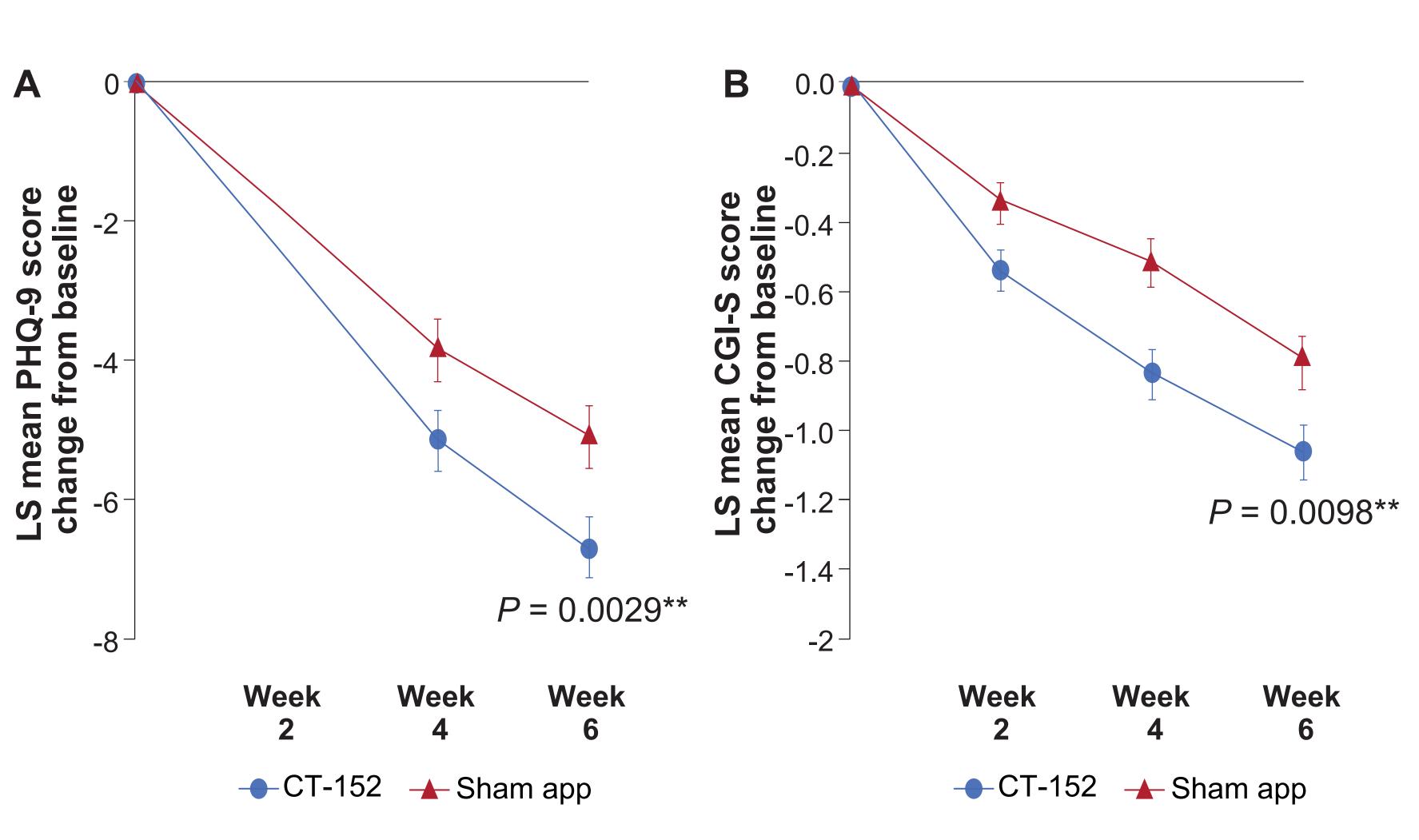
*P < 0.05; error bars are LS means ± 1 standard error. app, application; ITT, intent-to-treat; LS, least squares; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; mITT, modified intent-to-treat.

Table 2. MADRS response rates in the mITT sample

	CT-152 (n = 177)	Sham app (n = 177)	Relative risk	P value
MADRS response rates				
Full or partial response	48.3%	37.5%	1.27	0.0485*
Full response	28.4%	20.4%	1.38	0.0884
Partial response	19.9%	17.0%	1.15	0.5342
Remission	17.0%	13.6%	1.24	0.3901

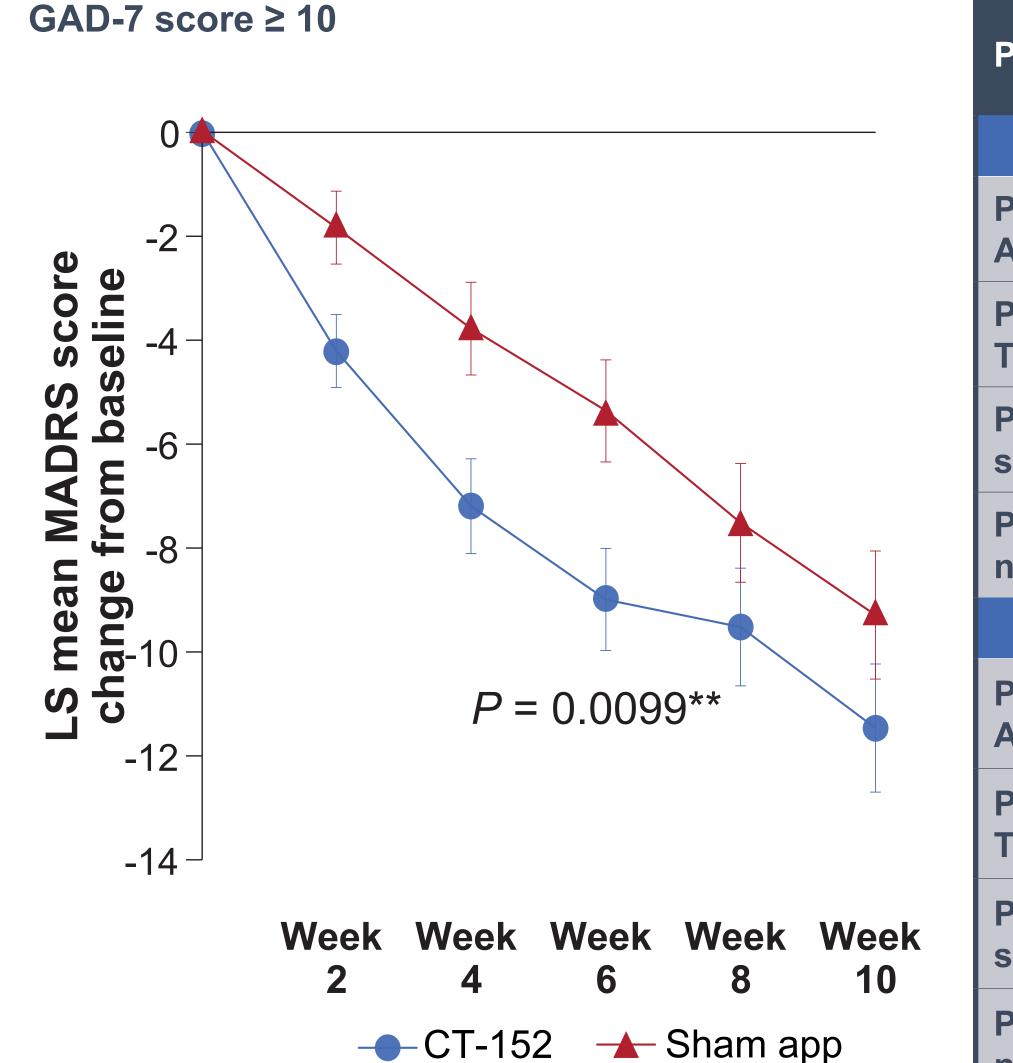
Response definitions: partial response rate defined as ≥ 30% but < 50% reduction from baseline; full response rate defined as ≥ 50% reduction from baseline; and remission defined as ≥ 50% reduction from baseline; and remission defined as ≥ 50% reduction from baseline. reduction from baseline and MADRS score ≤ 10.

Figure 4. Change from baseline in PHQ-9 (A) and CGI-S (B) scores for participants in the mITT sample



**P < 0.01: error bars are LS means ± 1 standard erro

Figure 5. Change from baseline MADRS scores for participants in the mITT sample with a baseline



**P < 0.01; error bars are least-squares mean ± 1 standard error.

app, application; LS, least squares; MADRS, Montgomery-Asberg Depression Rating Scale.

Table 3. Summary of safety outcomes in the safety sample

Participants, n (%)ª	CT-152 (n = 187)	Sham app (n = 186)	Total (n = 373)	
	Treatment Period			
Participants with AEs	33 (17.6)	52 (28.0)	85 (22.8)	
Participants with TEAEs ^b	28 (15.0)	49 (26.3)	77 (20.6)	
Participants with serious TEAEs	0 (0.0)	0 (0.0)	0 (0.0)	
Participants with nonserious TEAEs	28 (15.0)	49 (26.3)	77 (20.6)	
	Extension Period			
Participants with AEs	26 (13.9)	38 (20.4)	64 (17.2)	
Participants with TEAEs ^b	16 (8.6)	23 (12.4)	39 (10.5)	
Participants with serious TEAEs	1 (0.5)	0 (0.0)	1 (0.3)°	
Participants with nonserious TEAEs	15 (8.0)	23 (12.4)	38 (10.2)	

^aPercentages are based on the number of treated participants; ^bNo TEAEs were assessed as being related to CT-152; cOnly 1 serious TEAE was reported: a transient ischemic attack of moderate severity, which resolved and was deemed unrelated to CT-152.

AE, adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

The findings from this study support the effectiveness and safety of CT-152 as an adjunctive treatment to antidepressant medication monotherapy for adults with MDD.

 There is convergent validity in these results, as scales scored by independent raters, healthcare providers (CGI-S), and participants (PHQ-9) all indicated that CT-152 provided benefits to participants.

Participants in the CT-152 group with moderate to severe anxiety at baseline a group that is challenging to treat showed improvement in both MDD and anxiety symptoms.

CT-152 has a demonstrated safety profile. In this study, no TEAEs were assessed as related to CT-152, there were no severe TEAEs, there were no discontinuations due to TEAEs, and no deaths occurred.

This study is an example of how to conduct a robust trial of a DTx with multiple gold standard measures, and a rigorous sham app control that allowed for blinding of participants, sites, and raters.

- HHS Publication No. PEP23-07-01-006, NSDUH Series
- 6. Gartlehner G et al. Ann Intern Med. 2011;155: 772-785.

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8. Dang A et al. J Family Med Prim Care. 2020;9:2207-221

12. Hoch MM et al. Chronic Stress (Thousand Oaks)

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

BR. MS. EL. MF. D. Chen, and AF are employees of Otsuka Pharmaceutical Development & Commercialization, Inc., and D. Carpenter is an employee of Otsuka Precision Health, Inc. AS and SEL are employees of Click Therapeutics, Inc. MHT is a consultant for Otsuka Pharmaceutical Development & Commercialization, Inc.

app, application; ITT, intent-to-treat; MADRS, Montgomery-Asberg Depression Rating Scale; MDD, major depressive disorder; mITT, modified intent-to-treat; SS, safety sample.