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Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Device:

PEAR-004 is an investigational medical device, which is a prescription digital therapeutic app.

Trial Indication(s)

schizophrenia

Protocol Number

CPEA001A12201

Protocol Title

A Randomized, Sham-Controlled Study of PEAR-004 as an adjunct to standard-of-care treatment for schizophrenia

Clinical Trial Phase

Phase 2

Phase of Program Development

Phase II

Study Start/End Dates

Study Start Date: December 2018 (Actual)
Primary Completion Date: September 2019 (Actual)
Study Completion Date: September 2019 (Actual)

Study Design/Methodology

This was a randomized, sham-controlled, rater-blinded, parallel group trial in subjects with schizophrenia, receiving clinician-directed standard-of-care treatment. The study consisted of a 28-day screening period, 85 days treatment period (4 visits), and a follow-up visit at Week 16 (Day 115).

Centers

United States(6)

Objectives:

The Primary objectives were:

To assess the efficacy of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to reduce symptoms of schizophrenia

To evaluate retention to assigned study Treatment

The secondary objectives were:

To evaluate the efficacy of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to reduce positive symptoms of schizophrenia

To evaluate the efficacy of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to reduce negative symptoms of schizophrenia

To assess safety and tolerability of PEAR-004

To evaluate the efficacy of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to improve psychosocial functioning in subjects with schizophrenia

To evaluate the efficacy of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to reduce depression symptoms in subjects with schizophrenia

To evaluate the magnitude of the effect of PEAR-004 as an adjunct to existing clinician-directed pharmacotherapy to reduce symptoms of schizophrenia

To evaluate the response to treatment

To evaluate subject adherence to antipsychotic medication

Test Product (s), Dose(s), and Mode(s) of Administration

No investigational medicinal product was provided in this study; subjects continued on their prescribed clinician-directed pharmacotherapy.

PEAR-004 is an investigational medical device, which is a prescription digital therapeutic app.

The duration of treatment of 12 weeks with PEAR-004 or sham was selected based on the standard treatment duration for antipsychotic drug trials in schizophrenia to assess short-term benefit.

Statistical Methods

The change from baseline in total PANSS score was analyzed using the mixed-effects model for repeated measures (MMRM), including the fixed, categorical effects of treatment, visit (i.e., Day 1, 29, 57, 85), and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline score, baseline score-by-visit interaction, and disease duration at baseline. An unstructured (UN) covariance structure was used to model the within-subject errors. The Kenward-Roger (KR) method was used to adjust the estimated covariance of the mean difference and the degrees of freedom.

The primary hypothesis tested was that mean change from baseline in PANSS was greater with PEAR-004 than with sham at Day 85 or last visit. The primary comparison was the contrast between treatments on Day 85. The significance test was carried out using 1-sided α=0.05.

Data from subjects who had a protocol deviation regarding stable concomitant medication were regarded as missing from time of concomitant medication change onwards.

In addition, two-sided 90% confidence intervals (CI) for the treatment mean differences, as well as individual treatment mean change from baseline values at each study visit were constructed.

The secondary efficacy endpoints were analyzed separately using an MMRM analysis. The change from baseline to each post-baseline visit was the dependent variable. The model included the fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline score, baseline score-by-visit interaction, and disease duration at baseline (in years).

A total of 112 subjects were randomized in a 1:1 ratio to one of two treatment groups: PEAR-004 and Sham. This sample size would provide 80% power to detect a statistically significant difference between the two groups at a 1-sided alpha=0.05 when the true mean difference is 8 points assuming SD =16 (common to the two groups). This difference is equivalent to a standardized effect size of 0.5, which is considered a moderate effect size, and is consistent with prior randomized controlled trials (RCTs) of cognitive behavioral therapy (CBT) in schizophrenia.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:
- Signed informed consent must be obtained prior to participation in the study.
- Healthy male and female subjects 18 to 65 years of age, inclusive, and in good health as determined by medical history, physical examination, and vital signs at screening
- SCID-based DSM-5 diagnosis of schizophrenia and a total PANSS score > 60
- Proficient in English at 5th grade reading level or higher, in the judgement of the investigator
- Capable of using a mobile device (compatible with PEAR-004) and using common applications, in the judgement of the investigator

Key Exclusion Criteria:
- Major change in primary antipsychotic medication in the prior 4 weeks before screening (e.g., switching to a new agent or a dose adjustment within two weeks of randomization)
- Planning to move out of the geographic area within 3 months
- Unable to use English to participate in the consent process, the interventions or assessments
- Inability to comply with study procedures, due to severe medical conditions or otherwise
- Meet DSM-5 diagnosis for a current episode of major depression, mania, or hypomania in the past month
- Meet DSM-5 diagnosis for a current moderate or severe alcohol or cannabis use disorder in the past 2 months
- Meet DSM-5 diagnosis for a current substance use disorder (other than alcohol or cannabis) in the past 2 months
- Considered high risk for suicidal behavior based on ISST-Plus score at screening, or in the judgement of the investigator
- Previously participated in a clinical study involving PEAR-004

Participant Flow Table

Overall Study

	PEAR-004	Sham	Total
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as	

	and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.	
Started	56	56	112
Full Analysis Set (FAS)	54	55	109
Safety Set (SAF)	55	55	110
Completed	48	44	92
Not Completed	8	12	20
Adverse Event	0	1	1
Lost to Follow-up	3	5	8
Physician Decision	0	2	2
Protocol Violation	0	2	2
Withdrawal by Subject	5	2	7

Baseline Characteristics

	PEAR-004	Sham	Total
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.	
Number of Participants [units: participants]	55	55	110
Age Continuous (units: Years) Mean ± Standard Deviation			
	43.7±10.99	45.7±11.60	44.7±11.29

Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	19	19	38
Male	36	36	72
Race/Ethnicity, Customized (units: Participants)			
American Indian or Alaska Native	3	0	3
Asian	3	4	7
Black or African American	28	25	53
Native Hawaiian or other Pacific Islander	0	1	1
White	18	25	43
Other	3	0	3
Disease duration at baseline[1] (units: Years) Mean ± Standard Deviation			
	16.2±11.40	18.2±11.56	17.2±11.47
Total Positive and Negative Syndrome Scale (PANSS) score at baseline[2] (units: Score) Mean ± Standard Deviation			
	73.5±10.25	72.7±10.10	73.1±10.14

[1] Disease Duration at baseline: Duration (in Years) from informed consent to date of diagnosis. Date of diagnosis corresponds to date where subjects reported schizophrenia diagnosis in medical history at screening visit.
[2] The Positive and Negative Syndrome Scale (PANSS) assesses: positive (hallucinations, delusions, thought disorder), negative (blunted affect, abstract thinking and general symptomatology. The positive and negative subscale each consist of 7 items rated from 1(absent) - 7(extreme) with a minimum score = 7, maximum score = 49. The general subscale consists of 16 items with a minimum score = 16, maximum score = 112. A Total PANSS score (positive+ negative + general scores) has a minimum of 30 and maximum of 210. Higher scores represent more severity in symptoms.

Primary Outcome Result(s)

Change from Baseline in total Positive and Negative Syndrome Scale (PANSS) score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55

Change from Baseline in total Positive and Negative Syndrome Scale (PANSS) score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-1.6 ± 0.86	-2.2 ± 0.84
Day 57 (n=49,47)	-2.5 ± 0.9	-3.3 ± 0.9
Day 85 (n=48,49)	-2.6 ± 1.14	-5.3 ± 1.13

Statistical Analysis

Groups	PEAR-004, Sham	Day 29
Other Comparison of adjusted least square mean	0.61	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	1.200	
90 % Confidence Interval 2-Sided	-1.4 to 2.6	

Statistical Analysis

Groups	PEAR-004, Sham	Day 57
Other Comparison of adjusted least square mean	0.80	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit

		and baseline * visit interaction effects.
Standard Error of the mean	1.279	
90 % Confidence Interval 2-Sided	-1.3 to 2.9	

Statistical Analysis

Groups	PEAR-004, Sham	Day 85
P Value	0.0931	
Method	t-test, 2 sided	
Other Comparison of adjusted least square mean	2.73	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	1.611	
90 % Confidence Interval 2-Sided	0.1 to 5.4	

Percent of dropout

(Time Frame: Day 115)

	PEAR-004	**Sham**
Arm/Group Description	Eligible participants were to access PEAR-	Eligible participants were to access a

	004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	56	56
Percent of dropout (units: Participants) Count of Participants (Not Applicable)		
	8 (14.29%)	12 (21.43%)

Secondary Outcome Result(s)

Change from Baseline in the positive PANSS score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the positive PANSS score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-0.2 ± 0.36	-0.4 ± 0.35
Day 57 (n=49,47)	-0.8 ± 0.38	-1.4 ± 0.38
Day 85 (n=48,49)	-1.0 ± 0.46	-1.8 ± 0.45

Statistical Analysis

Groups	PEAR-004, Sham	Day 29
Other Comparison of adjusted least square mean	0.21	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.501	
90 % Confidence Interval 2-Sided	-0.6 to 1	

Statistical Analysis

Groups	PEAR-004, Sham	Day 57
Other Comparison of adjusted least square mean	0.61	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.538	
90 % Confidence Interval 2-Sided	-0.3 to 1.5	

Statistical Analysis

Groups	PEAR-004, Sham	Day 85
P Value	0.2069	
Method	t-test, 2 sided	
Other Comparison of adjusted least square mean	0.82	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.648	
90 % Confidence Interval 2-Sided	-0.3 to 1.9	

Change from Baseline in the General Psychopathology PANSS score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the

	suggestions about coping strategies to overcome difficulties in daily life.	participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the General Psychopathology PANSS score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-0.8 ± 0.61	-1.4 ± 0.59
Day 57 (n=49,47)	-1.4 ± 0.63	-1.5 ± 0.63
Day 85 (n=48,49)	-1.2 ± 0.76	-2.8 ± 0.75

Statistical Analysis

Groups	PEAR-004, Sham	Day 29
Other Comparison of adjusted least square mean	0.51	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.849	

90 % Confidence Interval 2-Sided	-0.9 to 1.9

Statistical Analysis

Groups	PEAR-004, Sham	Day 57
Other Comparison of adjusted least square mean	0.12	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.890	
90 % Confidence Interval 2-Sided	-1.4 to 1.6	

Statistical Analysis

Groups	PEAR-004, Sham	Day 85
P Value	0.1368	
Method	t-test, 2 sided	
Other Comparison of adjusted least square mean	1.61	
Standard Error of the mean	1.071	
90 % Confidence Interval 2-Sided	-0.2 to 3.4	

Change from Baseline in the Negative PANSS score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the Negative PANSS score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-0.5 ± 0.31	-0.4 ± 0.3
Day 57 (n=49,47)	-0.3 ± 0.32	-0.5 ± 0.32

Day 85 (n=48,49)	-0.4 ± 0.41	-0.9 ± 0.41

Statistical Analysis

Groups	PEAR-004, Sham	Day 29
Other Comparison of adjusted least square mean	-0.13	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.430	
90 % Confidence Interval 2-Sided	-0.8 to 0.6	

Statistical Analysis

Groups	PEAR-004, Sham	Day 57
Other Comparison of adjusted least square mean	0.15	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.453	
90 % Confidence Interval 2-Sided	-0.6 to 0.9	

Statistical Analysis

Groups	PEAR-004, Sham	
P Value	0.3798	
Method	t-test, 2 sided	
Other Comparison of adjusted least square mean	0.51	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.581	
90 % Confidence Interval 2-Sided	-0.5 to 1.5	

Change from Baseline in the Motivation and Pleasure Self-report (MAP-SR) score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications

	receive suggestions about coping strategies to overcome difficulties in daily life.	prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the Motivation and Pleasure Self-report (MAP-SR) score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=51,54)	0.8 ± 1.05	1.6 ± 1.02
Day 57 (n=49,47)	-0.5 ± 1.41	1.1 ± 1.43
Day 851.43 (n=48,49)	-1.2 ± 1.26	2.8 ± 1.25

Statistical Analysis

Groups	PEAR-004, Sham	Day 29
Other Comparison of adjusted least square mean	-0.79	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.

Standard Error of the mean	-0.79	
90 % Confidence Interval 2-Sided	-3.2 to 1.6	

Statistical Analysis

Groups	PEAR-004, Sham	Day 57
Other Comparison of adjusted least square mean	-1.60	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	2.006	
90 % Confidence Interval 2-Sided	-4.9 to 1.7	

Statistical Analysis

Groups	PEAR-004, Sham	Day 85
P Value	0.0245	
Method	t-test, 2 sided	
Other Comparison of adjusted least square mean	-4.07	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit

		and baseline * visit interaction effects.
Standard Error of the mean	1.780	
90 % Confidence Interval 2-Sided	-7.0 to -1.1	

Change from Baseline in the World Health Organization Quality of Life (WHOQOL-BREF) scale

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.

Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the World Health Organization Quality of Life (WHOQOL-BREF) scale (units: Score) Least Squares Mean ± Standard Error		
Day 29-Domain 1 (n=52,54)	-0.1 ± 0.37	0.1 ± 0.36
Day 57-Domain 1 (n=49,47)	-0.3 ± 0.44	-0.3 ± 0.45
Day 85-Domain 1 (n=48,49)	0.2 ± 0.45	0.1 ± 0.45
Day 29-Domain 2 (n=52,54)	-0.6 ± 0.4	-0.1 ± 0.39
Day 57-Domain 2 (n=49,47)	-0.7 ± 0.37	-0.6 ± 0.38
Day 85-Domain 2 (n=48,49)	-0.5 ± 0.43	0.1 ± 0.42
Day 29-Domain 3 (n=52,54)	-0.3 ± 0.28	0.1 ± 0.27
Day 57-Domain 3 (n=49,47)	-0.3 ± 0.33	0.1 ± 0.33
Day 85-Domain 3 (n=54,55)	0.5 ± 0.33	0.3 ± 0.33
Day 29-Domain 4 (n=52,54)	-0.2 ± 0.61	-0.9 ± 0.6
Day 57-Domain 4 (n=49,47)	-0.5 ± 0.61	-0.7 ± 0.61
Day 85-Domain 4 (n=54,55)	-0.1 ± 0.69	1.1 ± 0.68

Statistical Analysis

Groups	PEAR-004, Sham	Day 29-Domain 1
Other Comparison of adjusted least square mean	-0.18	mixed effects model with treatment, visit as fixed effects, baseline and disease duration at baseline as continuous covariates, treatment * visit and baseline * visit interaction effects.
Standard Error of the mean	0.516	
90 % Confidence Interval 2-Sided	-1.0 to 0.7	

Change from Baseline in the Beck Depression Inventory, Second Ed. (BDI-II) total score

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app,

	overcome difficulties in daily life.	and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Change from Baseline in the Beck Depression Inventory, Second Ed. (BDI-II) total score (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-1.0 ± 1.13	-0.1 ± 1.11
Day 57 (n=49,47)	-4.8 ± 1.14	-1.5 ± 1.15
Day 85 (n=48,49)	-3.4 ± 1.32	-3.2 ± 1.3

Percentage change from Baseline in total PANSS score (within assigned treatment group)

(Time Frame: Baseline, Day 29, Day 57, Day 85)

	PEAR-004	**Sham**
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications

	receive suggestions about coping strategies to overcome difficulties in daily life.	prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Percentage change from Baseline in total PANSS score (within assigned treatment group) (units: Score) Least Squares Mean ± Standard Error		
Day 29 (n=52,54)	-2.0 ± 1.21	-3.0 ± 1.18
Day 57v (n=49,47)	-3.6 ± 1.28	-4.4 ± 1.29
Day 85 (n=48,49)	-3.7 ± 1.57	-7.1 ± 1.55

Percentage of Responders as assessed by the Brief Medication Questionnaire (BMQ)

(Time Frame: Day 29, Day 57, and Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android

	device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Percentage of Responders as assessed by the Brief Medication Questionnaire (BMQ) (units: Participants) Count of Participants (Not Applicable)		
Day 1	53 (98.15%)	54 (98.18%)
Day 29	52 (96.3%)	53 (96.36%)
Day 57	49 (90.74%)	46 (83.64%)
Day 85	48 (88.89%)	48 (87.27%)
Day 115 / End of Study	54 (100%)	52 (94.55%)

Percentage of Responders as assessed by the total PANSS score

(Time Frame: Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	55
Percentage of Responders as assessed by the total PANSS score (units: Participants) Count of Participants (Not Applicable)		
	2 (3.7%)	9 (16.36%)

Number of Patients with Adverse events

(Time Frame: Day 115)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.
Number of Participants Analyzed [units: participants]	55	55
Number of Patients with Adverse events (units: Participants) Count of Participants (Not Applicable)		
Participants with at least one AE	12 (21.82%)	10 (18.18%)

Study drug-related AEs	1 (1.82%)	0 (%)
Participants with at least one SAE	0 (%)	1 (1.82%)
AEs leading to discontinuation of study treatment	0 (%)	0 (%)
Study-drug related AEs leading to treatment disc.	0 (%)	0 (%)

Number of Patients with Vital Sign measurements

(Time Frame: Day 85)

	PEAR-004	Sham
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of

		app availability.
Number of Participants Analyzed [units: participants]	55	55
Number of Patients with Vital Sign measurements (units: Number of participants)		
	55	55

InterSePT Scale for Suicidal Thinking-Plus (ISST-Plus) Score

(Time Frame: Baseline, Day 29, 57, 85, and 115)

	PEAR-004	**Sham**
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the

		remaining duration of app availability.
Number of Participants Analyzed [units: participants]	54	53
InterSePT Scale for Suicidal Thinking-Plus (ISST-Plus) Score (units: scores on a scale) Mean ± Standard Deviation		
Baseline (n=52,50)	0.0 ± 0.00	0.1 ± 0.24
Day 1 (n=50,52)	0.1 ± 0.31	0.0 ± 0.14
Day 29 (n=51,53)	0.0 ± 0.28	0.1 ± 0.41
Day 57 (n=47,46)	0.1 ± 0.44	0.0 ± 0.00
Day 85 (n=48,49)	0.1 ± 0.45	0.1 ± 0.32
Day 115 / End Of Study (n=54,53)	0.1 ± 0.43	0.1 ± 0.45

Safety Results

All-Cause Mortality

	PEAR-004 N = 55	**Sham N = 55**	**Total N = 110**
Arm/Group Description	Eligible participants	Eligible participants	Total

	were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.	
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 119 days.
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment

	PEAR-004 N = 55	Sham N = 55	Total N = 110
Arm/Group Description	Eligible participants were to access PEAR-004 (an investigational digital therapeutic) on a mobile device (iOS and Android based) as needed to receive suggestions about coping strategies to overcome difficulties in daily life.	Eligible participants were to access a sham control downloaded on a mobile device (iOS and Android based) as needed to delivering notifications prompting the participant to open the sham app, and then display a prescription timer for the remaining duration of app availability.	Total
Total participants affected	0 (0.00%)	1 (1.82%)	1 (0.91%)
Psychiatric disorders			
Suicidal ideation	0 (0.00%)	1 (1.82%)	1 (0.91%)

Conclusion:

In this study, PEAR-004 was not effective in the primary outcome of total PANSS scores compared with sham. The secondary and exploratory results also failed to find any notable benefits, except for possible temporary improvement in depressive symptoms.

Date of Clinical Trial Report

19 Mar 2020