Clinical trial results:
A multicentre study to assess safety and efficacy of psilocybin in patients with treatment-resistant depression following completion of COMP 001 and COMP 003 trials (P-TRD LTFU)

Summary

EudraCT number	2020-001348-25
Trial protocol	PT CZ DK NL DE
Global end of trial date	11 July 2022

Results information

Result version number	v1 (current)
This version publication date	20 March 2024
First version publication date	20 March 2024
Summary attachment (see zip file)	COMP 004 Efficacy Endpoints (COMP 004 Efficacy EPs3.pdf)

Trial information

Trial identification

Sponsor protocol code	COMP 004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	COMPASS Pathfinder Limited
Sponsor organisation address	3rd Floor, 1 Ashley Road, Altrincham, Cheshire, United Kingdom, WA14 2DT
Public contact	Guy Goodwin, COMPASS Pathways, Ltd, COMPASS Pathways, Ltd., 44 7443 136539, info@compasspathways.com
Scientific contact	Guy Goodwin, COMPASS Pathways, Ltd, COMPASS Pathways, Ltd., 44 7443 136539, info@compasspathways.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 July 2022
Global end of trial reached?	Yes
Global end of trial date	11 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the long-term efficacy of psilocybin with respect to use of new antidepressant treatment, hospitalisations for depression, suicidality, and depressive severity rated using the Montgomery and Asberg Depression Rating Scale (MADRS) over a total of 52 weeks (compared across the 1 mg, 10 mg and 25 mg psilocybin groups from COMP 001).

Protection of trial subjects:

All participants will be evaluated for safety and efficacy at enrollment, weeks 6, 9 & 12 (for participants from COMP 003 only) and at weeks 16, 20, 24, 28, 40 and 52. Participants' companions (friend or family member) will continue to be educated about the signs of worsening of depression and suicidality, and instructed on ways to contact the study team in case of significant worsening of depression. Rescue medications are allowed during the study as described in the protocol. Efficacy and safety assessments including Adverse Events are performed throughout the study up to the end of study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Netherlands: 50
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Ireland: 20
Country: Number of subjects enrolled	United States: 106
Worldwide total number of subjects	252
EEA total number of subjects	107

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	245
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects recruited into this study must have completed either the COMP 001 or COMP 003 study prior to entry into this long-term, observational follow up study.

Pre-assignment

Screening details:

At the Screening visit (V1), the following assessments will be performed and recorded: ICF, review of inclusion/exclusion criteria, loading the app on the participant's mobile phone if the participant opts to participate, set up subjects on the digital system for online assessments and for participants from COMP 001 they will be asked the TiC-P.

Period 1

Period 1 title	Originator Study Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	COMP360 25 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	COMP360
Investigational medicinal product code	
Other name	Psilocybin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

COMP360 25mg single dose treatment: 5 x 5 mg capsules

Arm title	COMP360 10 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	COMP360
Investigational medicinal product code	
Other name	Psilocybin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

COMP360 10mg single dose treatment: 2 × 5 mg capsules and 3 × placebo capsules

Arm title	COMP360 1 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	COMP360
Investigational medicinal product code	
Other name	Psilocybin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
COMP360 1 mg single dose treatment: 1 × 1 mg capsule and 4 × placebo capsules

Arm title	COMP360 25 mg + SSRI
Arm description: -	
Arm type	adjunctive therapy
Investigational medicinal product name	SSRI
Investigational medicinal product code	
Other name	SSRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Adjunctive therapy taken in the lead in study COMP 003.

Number of subjects in period 1	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg
Started	79	75	79
Completed	74	66	69
Not completed	5	9	10
Consent withdrawn by subject	2	6	6
Physician decision	-	-	1
Adverse event, non-fatal	2	2	-
Lost to follow-up	1	-	2
Lack of efficacy	-	1	1

Number of subjects in period 1	COMP360 25 mg + SSRI
Started	19
Completed	19
Not completed	0
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-
Lost to follow-up	-
Lack of efficacy	-

Period 2	
Period 2 title	Follow-up Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	COMP360 25 mg
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	COMP360 10 mg
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	COMP360 1 mg
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	COMP360 25 mg + SSRI
Arm description: -	
Arm type	adjunctive therapy
Investigational medicinal product name	SSRI
Investigational medicinal product code	
Other name	SSRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Adjunctive therapy taken in the lead in study COMP 003.

Number of subjects in period 2[1]	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg
Started	22	19	17
Completed	16	14	15
Not completed	6	5	2
Consent withdrawn by subject	-	4	2
Non-compliance	3	-	-
Participant no longer wants to continue in study	-	-	-
Lost to follow-up	3	1	-

Number of subjects in period 2[1]	COMP360 25 mg + SSRI
Started	8

Completed	3
Not completed	5
Consent withdrawn by subject	1
Non-compliance	2
Participant no longer wants to continue in study	1
Lost to follow-up	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants continued from the COMP 001 and COMP 003 lead-in studies into the COMP 004 follow-up study as not all participants had the opportunity to enroll due to delayed study set-up. For those that did have the opportunity to enroll, participation was optional.

Baseline characteristics

Reporting groups	
Reporting group title	COMP360 25 mg
Reporting group description: -	
Reporting group title	COMP360 10 mg
Reporting group description: -	
Reporting group title	COMP360 1 mg
Reporting group description: -	
Reporting group title	COMP360 25 mg + SSRI
Reporting group description: -	

Reporting group values	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg
Number of subjects	79	75	79
Age categorical Units: Subjects			
18 to 34 Years	24	29	31
35 to 64 Years	52	44	46
65 to 84 Years	3	2	2
>84 Years	0	0	0
Age continuous Units: years			
arithmetic mean	40.2	40.6	38.7
standard deviation	± 12.19	± 12.76	± 11.71
Gender categorical Units: Subjects			
Female	44	41	36
Male	35	34	43
Race Units: Subjects			
White	70	72	73
Black or African American	4	0	1
Asian	4	3	5
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	1	0	0
Prior Psilocybin Experience Units: Subjects			
Yes	5	5	4
No	74	70	75
Not Recorded	0	0	0
Number of Failed Treatments for the Current Episode Units: Subjects			
One (1)	0	1	1
Two (2)	66	62	63
Three (3)	8	9	11
Four (4)	4	2	3

Unknown	1	1	1
HAM-D-17 Baseline Severity Categories Units: Subjects			
Moderate (18-23)	57	49	59
Severe (≥ 24)	22	26	20
MGH-ATRQ Units: Subjects			
<25% Improved	55	47	46
25 - 49% Improved	24	26	32
50 - 75% Improved	0	2	1
>75% Improved	0	0	0
Length of Current Depressive Episode Units: Subjects			
< 1 year	12	10	10
≥ 1 year and < 2 years	33	28	33
≥ 2 years	34	37	36
Weight at Screening Units: kilogram(s)			
arithmetic mean	79.877	83.363	83.102
standard deviation	± 19.4131	± 25.7905	± 23.3533
Height at Screening Units: centimeters			
arithmetic mean	173.401	173.186	173.773
standard deviation	± 10.3295	± 11.3620	± 9.8703
Body Mass Index Units: kilograms/meters^2			
arithmetic mean	26.52	28.26	27.26
standard deviation	± 6.134	± 8.203	± 6.025
HAM-D-17 Total Score Units: Points			
arithmetic mean	21.8	22.4	22.2
standard deviation	± 3.04	± 2.77	± 2.93
MSI-BPD Total Score Units: Points			
arithmetic mean	2.1	2.1	1.8
standard deviation	± 1.64	± 1.55	± 1.62
Length of Current Depressive Episode Units: Months			
arithmetic mean	42.41	42.09	38.34
standard deviation	± 48.930	± 39.934	± 43.727

Reporting group values	COMP360 25 mg + SSRI	Total	
Number of subjects	19	252	
Age categorical Units: Subjects			
18 to 34 Years	4	88	
35 to 64 Years	15	157	
65 to 84 Years	0	7	
>84 Years	0	0	

Age continuous Units: years			
arithmetic mean	42.2		
standard deviation	± 10.8	-	
Gender categorical Units: Subjects			
Female	13	134	
Male	6	118	
Race Units: Subjects			
White	15	230	
Black or African American	2	7	
Asian	0	12	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Other	2	3	
Prior Psilocybin Experience Units: Subjects			
Yes	0	14	
No	0	219	
Not Recorded	19	19	
Number of Failed Treatments for the Current Episode Units: Subjects			
One (1)	0	2	
Two (2)	12	203	
Three (3)	6	34	
Four (4)	1	10	
Unknown	0	3	
HAM-D-17 Baseline Severity Categories Units: Subjects			
Moderate (18-23)	17	182	
Severe (≥ 24)	2	70	
MGH-ATRQ Units: Subjects			
<25% Improved	13	161	
25 - 49% Improved	6	88	
50 - 75% Improved	0	3	
>75% Improved	0	0	
Length of Current Depressive Episode Units: Subjects			
< 1 year	3	35	
≥ 1 year and < 2 years	13	107	
≥ 2 years	3	110	
Weight at Screening Units: kilogram(s)			
arithmetic mean	75.420		
standard deviation	± 19.3330	-	
Height at Screening Units: centimeters			
arithmetic mean	169.4		

standard deviation	± 9.94	-	
Body Mass Index Units: kilograms/meters^2			
arithmetic mean	26.26		
standard deviation	± 6.521	-	
HAM-D-17 Total Score Units: Points			
arithmetic mean	20.3		
standard deviation	± 2.75	-	
MSI-BPD Total Score Units: Points			
arithmetic mean	1.6		
standard deviation	± 1.50	-	
Length of Current Depressive Episode Units: Months			
arithmetic mean	23.5		
standard deviation	± 22.06	-	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) consists of all enrolled participants in COMP 004 that complete at least one efficacy assessment.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all enrolled participants in COMP 004.

Subject analysis set title	Modified Full Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified Full Analysis Set (mFAS) consists of all enrolled participants in COMP 001/ COMP 003 that complete at least one efficacy assessment, which was 252. This analysis set also includes patients that were not enrolled in the COMP 004 study. 66 of these patients were enrolled into this study.

Reporting group values	Full Analysis Set	Safety Analysis Set	Modified Full Analysis Set
Number of subjects	66	66	252
Age categorical Units: Subjects			
18 to 34 Years	23	23	88
35 to 64 Years	40	40	157
65 to 84 Years	3	3	7
>84 Years	0	0	0
Age continuous Units: years			
arithmetic mean	41.1	41.1	
standard deviation	± 12.04	± 12.04	±
Gender categorical Units: Subjects			
Female	32	32	134
Male	34	34	118

Race Units: Subjects			
White	62	62	230
Black or African American	2	2	7
Asian	0	0	12
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	2	2	3
Prior Psilocybin Experience Units: Subjects			
Yes	3	3	14
No	55	55	219
Not Recorded	8	8	19
Number of Failed Treatments for the Current Episode Units: Subjects			
One (1)	0	0	2
Two (2)	53	53	203
Three (3)	10	10	34
Four (4)	3	3	10
Unknown	0	0	3
HAM-D-17 Baseline Severity Categories Units: Subjects			
Moderate (18-23)	50	50	182
Severe (≥ 24)	16	16	70
MGH-ATRQ Units: Subjects			
<25% Improved	42	42	161
25 - 49% Improved	22	22	88
50 - 75% Improved	2	2	3
>75% Improved	0	0	0
Length of Current Depressive Episode Units: Subjects			
< 1 year	11	11	35
≥ 1 year and < 2 years	21	21	107
≥ 2 years	34	34	110
Weight at Screening Units: kilogram(s)			
arithmetic mean	84.948	84.948	
standard deviation	± 21.6662	± 21.6662	±
Height at Screening Units: centimeters			
arithmetic mean	173.739	173.739	
standard deviation	± 11.9752	± 11.9752	±
Body Mass Index Units: kilograms/meters^2			
arithmetic mean	28.35	28.35	
standard deviation	± 7.389	± 7.389	±
HAM-D-17 Total Score Units: Points			
arithmetic mean	21.5	21.5	

standard deviation	± 2.78	± 2.78	±
MSI-BPD Total Score			
Units: Points			
arithmetic mean	1.9	1.9	
standard deviation	± 1.49	± 1.49	±
Length of Current Depressive Episode			
Units: Months			
arithmetic mean	40.34	40.34	
standard deviation	± 40.760	± 40.760	±

End points

End points reporting groups

Reporting group title	COMP360 25 mg
Reporting group description: -	
Reporting group title	COMP360 10 mg
Reporting group description: -	
Reporting group title	COMP360 1 mg
Reporting group description: -	
Reporting group title	COMP360 25 mg + SSRI
Reporting group description: -	
Reporting group title	COMP360 25 mg
Reporting group description: -	
Reporting group title	COMP360 10 mg
Reporting group description: -	
Reporting group title	COMP360 1 mg
Reporting group description: -	
Reporting group title	COMP360 25 mg + SSRI
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) consists of all enrolled participants in COMP 004 that complete at least one efficacy assessment.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set consists of all enrolled participants in COMP 004.

Subject analysis set title	Modified Full Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified Full Analysis Set (mFAS) consists of all enrolled participants in COMP 001/ COMP 003 that complete at least one efficacy assessment, which was 252. This analysis set also includes patients that were not enrolled in the COMP 004 study. 66 of these patients were enrolled into this study.

Primary: Time to Depressive Event

End point title	Time to Depressive Event[1][2]

End point description:

Time to the first depressive event (from COMP360 dose in the prior study) in participants recruited from the COMP 001 study. A participant withdrawing from the study for reported lack of efficacy that did not experience any of the relevant depressive events will be considered as having the event at the time of discontinuation

End point type	Primary

End point timeframe:

Whole Study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data are summarised for this endpoint as detailed in SAP amendment

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For the primary endpoint the COMP360 25mg + SSRI arm was not of interest and thus was not analysed.

End point values	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	75	79	
Units: Days				
median (confidence interval 95%)	92 (42 to 199)	83 (39 to 142)	62 (28 to 9999.99)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Full study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	COMP360 25 mg
Reporting group description: -	
Reporting group title	COMP360 10 mg
Reporting group description: -	
Reporting group title	COMP360 1 mg
Reporting group description: -	
Reporting group title	COMP360 25 mg + SSRI
Reporting group description: -	

Serious adverse events	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	1 / 19 (5.26%)	2 / 17 (11.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Therapy change			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 22 (9.09%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intentional self-injury			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal behaviour			
subjects affected / exposed	1 / 22 (4.55%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	COMP360 25 mg + SSRI		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Therapy change			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intentional self-injury			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal behaviour			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	COMP360 25 mg	COMP360 10 mg	COMP360 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 22 (77.27%)	15 / 19 (78.95%)	15 / 17 (88.24%)
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 22 (9.09%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	2	2	1
Feeling abnormal			
subjects affected / exposed	2 / 22 (9.09%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	2	2	1
Chills			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Feeling hot			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Hangover			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Crying			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Feeling jittery			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Feeling of relaxation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Uterine spasm			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Hypopnoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 22 (4.55%)	2 / 19 (10.53%)	3 / 17 (17.65%)
occurrences (all)	1	2	4
Insomnia			
subjects affected / exposed	2 / 22 (9.09%)	2 / 19 (10.53%)	3 / 17 (17.65%)
occurrences (all)	2	2	3
Suicidal ideation			
subjects affected / exposed	2 / 22 (9.09%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	2	2	2
Depression			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1

Euphoric mood			
subjects affected / exposed	1 / 22 (4.55%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Time perception altered			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
Affect lability			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Depressive symptom			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Hallucination, visual			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Mood altered			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Panic attack			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Abnormal dreams			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Depersonalisation/derealisation disorder			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Emotional disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Feeling of despair			

subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hallucination, auditory			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hallucinations, mixed			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Illusion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Inappropriate affect			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Libido decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Thinking abnormal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Liver function test increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 22 (36.36%)	5 / 19 (26.32%)	5 / 17 (29.41%)
occurrences (all)	9	6	7
Dizziness			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Dreamy state			
subjects affected / exposed	0 / 22 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Sensory disturbance			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Aphasia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypersomnia			

subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Mental impairment			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 22 (18.18%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences (all)	4	0	2
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Abdominal discomfort			
subjects affected / exposed	2 / 22 (9.09%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Dry mouth			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Pancreatic cyst			

subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Limb discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Muscle tightness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 22 (18.18%)	2 / 19 (10.53%)	3 / 17 (17.65%)
occurrences (all)	4	2	3
Urinary tract infection			
subjects affected / exposed	1 / 22 (4.55%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	2	1	1

Cystitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 22 (9.09%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Increased appetite			
subjects affected / exposed	0 / 22 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Non-serious adverse events	COMP360 25 mg + SSRI		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)		
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Feeling abnormal			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hangover			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Crying			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Feeling jittery			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Feeling of relaxation			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Uterine spasm			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypopnoea			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Suicidal ideation			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Euphoric mood			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Time perception altered			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Affect lability			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Depressive symptom			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hallucination, visual			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Mood altered			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

Panic attack				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Abnormal dreams				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Depersonalisation/derealisation disorder				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Depressed mood				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Emotional disorder				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Feeling of despair				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Hallucination, auditory				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Hallucinations, mixed				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Illusion				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Inappropriate affect				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Irritability				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences (all)	0			
Libido decreased				

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Thinking abnormal			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Liver function test increased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		

Dizziness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dreamy state subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Sensory disturbance subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Aphasia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Hypersomnia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Mental impairment subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Paraesthesia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Somnolence subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Eye disorders Eye pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Vision blurred subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Dry mouth subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Pancreatic cyst subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		

Arthralgia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Limb discomfort subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Muscle tightness subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Cystitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Increased appetite subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Hypercholesterolaemia			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2020	Amendment 1 (V2) dated 20 Nov 2020 changes: -The mobile phone application used for passive data collection was changed from the Mindstrong application to the Measure Health application as the Mindstrong application had become unavailable. Section 7.3 of the protocol was updated to replace the wording for the Mindstrong application with wording for the Measure Health application. -Other minor edits to the protocol to clarify methodology.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported