A multicentre study to assess safety and efficacy of COMP360 in patients with treatment-resistant depression following completion of COMP 001 and COMP 003 trials (P-TRD LTFU)

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Ethical review	Approved WMO
Status	Completed
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON55052

Source
ToetsingOnline

Brief title
COMP360 in Participants with Treatment Resistant Depression

Condition

- Mood disorders and disturbances NEC

Synonym
treatment resistant depression

Research involving
Human

Sponsors and support

Primary sponsor: COMPASS Pathfinder Ltd
Source(s) of monetary or material Support: Sponsor of the study COMPASS Pathfinder Inc.

Intervention

Keyword: COMP360, P-TRD, Treatment Resistant Depression

Outcome measures

Primary outcome

The primary endpoint of this long-term follow up study will be time to the first of any of the following depression-related events (from baseline ie one day prior to single dose COMP360 administration dosing in the prior study) in participants recruited from the COMP 001 study (presented for the 1 mg , 10 mg, and 25 mg COMP360 therapy groups):

• Initiation of new antidepressant treatment (first new antidepressant treatment in time period only)

• Hospitalization due to depression

• Suicide attempt, prevention of an imminent suicide attempt, or completed suicide

• Increased suicidality measured by worsening on MADRS item 10 i.e. either 1) a score of 5 or 6 on MADRS item 10; or 2) an increase of 2 points compared to Baseline in the prior study MADRS 10 score provided the score is >=3.

• Worsening in the MADRS clinician rated severity scale: i.e. a 5 point worsening compared to baseline score in the prior study at any timepoint post-baseline of the original study; or a worsening of >=5 points (providing the highest score is >=15) across two or more consecutive visits (in this case the

first date of the >=5 point increase will be classed as the event and at the final study visit the >=5 point worsening will qualify as an event without need for confirmation at a subsequent visit)

Secondary outcome

The secondary endpoints are:

• Change in MADRS total score from Baseline of the prior study to 12 , 16, 20, 24, 28. 40, and 52 weeks post COMP360

• The proportion of participants with a response (defined as a >= 50% improvement in MADRS total score from Baseline of the prior study) at Week 12 , 16, 20, 24, 28, 40, and 52 post COMP360

• The proportion of participants with remission (defined as a MADRS total score <= 10) at Week 12, 16, 20, 24, 28, 40, and 52 post COMP360

• The proportion of participants who have a sustained response at Week 12, 16, 20, 24, 28, 40 and 52. Sustained response is defined as the proportion of patients fulfilling response criteria at any visit up to and including Week 3 post-dosing (in the lead-in studies), that also fulfills response criteria at all subsequent visits up to and including Week 12, 16, 20, 24, 28, 40, and 52 post COMP360. Response is defined as >= 50% decrease in MADRS total score from Baseline of the prior study

• Longitudinal depression severity: the difference in the area under the curve between 1mg, 10 mg, and 25 mg COMP360 monotherapy and 25 mg COMP360 adjunctive therapy over 52 weeks post-baseline in QIDS-SR-16 total score

• Work and Social Adjustment (WSAS) score change from Baseline of the prior study to week 12, 18, 24, 30, 36, 42, 48

• Sheehan Disability Scale (SDS) score change from Baseline of the prior study

to week 12, 16, 20, 24, 28, 40, and 52 post COMP360

Study description

Background summary

A recent open label study of the effects of COMP360 in participants with treatment resistant depression (TRD) showed rapid, significant decrease of depressive symptoms after treatment with COMP360 coupled with psychological support. Over 40% of participants sustained response at 3 months. Given promising indications of efficacy, a phase IIb trial aiming to recruit 216 participants with TRD is currently underway: *The safety of COMP360 in participants with treatment-resistant depression* (P-TRD) study, also referred to as COMP 001. The aim of COMP 001 is to evaluate the efficacy and safety of COMP360 (25 mg or 10 mg) compared to 1 mg COMP360, administered under supportive conditions to adult participants with TRD over 12 weeks. In addition, there is an ongoing phase II, open-label study exploring the safety and efficacy of 25 mg COMP360 as an adjunctive therapy to ongoing selective serotonin reuptake inhibitors (SSRIs) in participants with TRD (referred to as COMP 003).
In this present study (COMP 004), the aim is to follow up participants from COMP 001 and COMP 003 in a long-term follow up study, with both remote and digital assessments, to explore the long term efficacy and safety of the three different doses of COMP360 (1 mg, 10 mg, and 25 mg) administered to patients with TRD as a monotherapy in COMP 001 and 25 mg COMP360 administered as an adjunct to an SSRI in COMP 003. Patients previously treated in COMP001 will be followed for approximately 40 weeks and patients previously treated in COMP003 will be followed for approximately 49 weeks giving a total follow up period of 52 weeks from COMP360 dosing.

Study objective

The primary objective of this study is to assess the long-term efficacy of COMP360 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 COMP360 groups from COMP 001).
The secondary objectives are:
• To assess response, sustained response, remission and change in depression severity (compared across all treatment groups - 1 mg, 10 mg and 25 mg COMP360 in COMP 001 and 25 mg as an adjunct to SSRIs in COMP 003) over a total of 52 weeks

• To evaluate the effect of COMP360 on functioning and associated disability compared across the groups over a total of 52 weeks
The safety objective is:
• To evaluate the safety of COMP360 in participants with TRD based on adverse events (AEs) reported over the full follow-up period (a total of 52 weeks) since COMP360 administration
The exploratory objectives are:
• To evaluate the effects of COMP360n on quality of life, self reported depression and anxiety, and healthcare utilization and productivity losses compared across the groups over a total of 52 weeks
• To assess the long-term efficacy of COMP360 with respect to use of new antidepressant treatment, hospitalizations for depression, suicidality, and depressive severity rated using the Montgomery and Asberg Depression Rating Scale (MADRS) over a total of 52 weeks in participants recruited from COMP 003
• To assess the long-term efficacy of COMP360 with respect to use of new antidepressant treatment, hospitalizations for depression, suicidality, and depressive severity rated using the self-report Quick Inventory of Depressive Symptomatology - 16 item over a total of 52 weeks (compared across the 1 mg, 10 mg and 25 mg COMP360 groups from COMP 001) and separately in participants recruited from COMP 003
• To assess the feasibility of conducting a long-term follow up study in participants who received COMP360 therapy for TRD
• To evaluate the impact of different COMP360 doses on real life functional activity estimated from passive data streams collected on a mobile app on participants* mobile phones

Study design

This is a long-term follow up study of participants who have previously taken part in the dose ranging phase 2b, international, multicenter, randomized, fixed dose double blind COMP 001 trial or the open-label COMP 003 trial delivering 25 mg COMP360 therapy open label as an adjunct to SSRIs in TRD patients. The study populations for COMP 001 and COMP 003 includes adult men and women, 18 years of age and older, with TRD. Participants will be enrolled into this long-term follow up study once they have completed their final study visit in the COMP 001 or COMP 003 trial, ie this will be a non-probability sample.
This long-term follow up study will continue to observe participants who took part in both the COMP 001 and COMP 003 studies up to a total of 52 weeks post COMP360 administration. All weeks referenced in this protocol relate to the time from COMP360 administration in the lead in studies. Participants in COMP 001 are followed up for a total of 12 weeks and participants in COMP 003 are followed up for a total of 3 weeks in these clinical trials and therefore participants recruited into this study from COMP 003 will participate in this follow up study for 9 weeks longer than COMP 001 participants should they consent to take part. Thus patients previously treated in COMP001 will be followed for 40 weeks and patients previously treated in COMP003 will be

followed for 49 weeks.
Only participants who complete the final study visit of COMP 001 and COMP 003 will be recruited into this study.
After signing the informed consent form (ICF) and when the participant has been determined as eligible for this study by the investigator, participants will be given access to an online electronic patient-reported outcome (ePRO) system to complete self-report questionnaires. Automatic reminders for questionnaire completion will be sent to participants and the study team will demonstrate the system to participants in this first screening visit.
Participants will complete self-report assessments every 2 weeks (with a visit window of ± 3 days). As participants recruited from COMP 003 will be recruited into COMP 004 three weeks after baseline in the previous study (COMP003) compared with COMP 001 participants who will be recruited 12 weeks after Baseline, participants from COMP 003 will complete the same assessment schedule as COMP 001 participants up to week 12 using the following measures: the MADRS, Work and Social Adjustment Scale (WSAS), Generalized Anxiety Disorder - 7 item scale (GAD-7), EuroQol- 5 Dimension - 3 level scale (EQ-5D-3L), QIDS-SR-16, Sheehan Disability Scale (SDS) - interviewer administered version, and reporting of AEs and concomitant medications/therapies.
Therefore, participants from COMP 003 will be asked to complete the QIDS-SR-16 and MADRS (assessed by a blinded rater) at weeks 6, 9, and 12. They will also be asked questions regarding concomitant medication/therapy received since their last study visit, and questions regarding AEs experienced since the participant*s last assessment by a study investigator at these three timepoints (week 6, 9, and 12). Additionally, they will be asked to complete the WSAS, GAD-7, SDS and EQ-5D-3L at week 12 after baseline in COMP 003.
From week 14 onwards, participants recruited from both COMP 001 and COMP 003 will be asked to complete two questionnaires every 2 weeks. The QIDS-SR-16 will be asked every two weeks and an additional three questionnaires will be rotated ie asked at every third timepoint in a staggered manner ie assessed every six weeks rather than every two weeks like the QIDS-SR-16. These three questionnaires are the EQ-5D-3L, GAD-7, and WSAS. The EQ-5D-3L will be asked at week 14 (post baseline in the original studies), GAD-7 at week 16 (post baseline in the original studies), and WSAS at week 18 (post baseline in the original studies), and this order will be repeated up to and including week 52 post baseline in COMP 001/003.
At 12 weeks (±2 weeks) post the baseline in COMP 001 and COMP 003, all COMP 004 participants will be asked to complete a healthcare utilization measure - the Treatment Inventory Costs in Patients with psychiatric disorders (TiC-P). The TiC-P measures medical costs and productivity losses (including absenteeism, presenteeism, and informal care costs). Participants will be asked this questionnaire every eight weeks throughout the study ie at 12, 20, 28, 36, 44, and 52 weeks.
Participants recruited from both COMP 001 and COMP 003 will have remote assessments with study investigators (the option of an in-person visit will be provided at the investigator*s discretion) at 16, 20, 24, 28, weeks (all ± 1 week), 40 weeks (± 2 weeks) and 52 weeks (± 2 weeks) post COMP360

administration (ie Day 0 in either the COMP 001 or COMP 003 studies). Assessments will include the MADRS (conducted by a blinded assessor), Sheehan Disability Scale (SDS) - interviewer administered version, questions regarding concomitant medication/therapy the participants has received since their last study visit, and questions regarding AEs experienced since the participant*s last assessment with a study investigator.
At the end of the present study (52 weeks post-IP administration in COMP 001 or COMP 003), participants will be asked to complete an study feedback survey remotely with a few short questions about how they found the methodology and frequency of assessments in this long-term follow up study.
The main purpose of this study is to explore the long term safety and efficacy of COMP360 therapy in patients with treatment-resistant depression. This study will be a study. No treatments are specified in this protocol and participants will be treated as per standard clinical practice by their existing clinicians. No medications or therapies will be prohibited in this study.
Blinding will be maintained from the COMP 001 phase IIb trial for both site investigators and participants ie they will not be informed of their treatment allocation prior to or whilst this long-term follow up trial is ongoing. COMP 003 is an open-label trial and therefore site investigators and patients will not be blind to treatment allocation. For all participants the MADRS will be conducted by a blinded, independent rater.

Study burden and risks

N/A

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1)Signed ICF
2)Each participant having completed the final study visit of either COMP 001 or COMP 003
3)Ability to complete all protocol required assessment tools (including having access to the internet in order to complete the digital assessments) without any assistance or alteration to the copyrighted assessments, and to comply with all study visits

Exclusion criteria

1)Subject has any condition, for which in the opinion of the investigator, participation would not be in the interest of the subject eg participation could compromise the wellbeing of the participant or prevent, limit, or confound the protocol-specified assessments

Study design

Design

Study phase:	2
Study type:	Observational non invasive
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-06-2021
Enrollment:	23
Type:	Actual

Ethics review

Approved WMO Date:	02-07-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-12-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	16-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-001348-25-NL
CCMO	NL73761.042.20

Study results

Date completed:	11-07-2022
Results posted:	10-10-2023
Actual enrolment:	3

First publication
16-08-2023