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An fMRI study to assess the effects of INDV-2000 on brain activity in opioid-dependent participants taking methadone

Submission date
01/03/2024

Recruitment status
No longer recruiting

Registration date
07/05/2024

Overall study status
Completed

Last Edited
29/01/2026

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The study medicine (INDV-2000) is an experimental medicine for treating opioid use disorder (OUD). Severe OUD is a chronic disorder also referred to as opioid addiction. People with OUD may have physical dependence (where withdrawal can cause symptoms such as aches, pains, and nausea) and psychological dependence (where withdrawal can cause symptoms such as strong cravings for the opioid or affect behaviour and have difficulty thinking about anything else).

We hope INDV-2000 will help treat opioid addiction by binding to proteins in the brain called orexin-1 (OX1R) receptors, and reduce craving, relapse, and symptoms of withdrawal.

We aim to find out:
* if INDV-2000 affects the brain's response to heroin-related cues in participants with opioid addiction. To find out, we'll use a brain scan called a fMRI (functional magnetic resonance imaging) scan, which uses a strong magnetic field to take pictures of the brain
* the side effects and blood levels of INDV-2000 when taken with methadone;
* if INDV-2000 affects craving and anxiety.

Who can participate?
We'll test single doses of INDV-2000 in 36 opioid-dependent men and women (aged 18–65 years) who are taking a stable dose of methadone.

What does the study involve?
During the 4 weeks before the first study session, participants will have a screening visit. Participants will have 3 study sessions. Participants will take up to 3 weeks to finish the study and make up to 4 outpatient visits. Participants will take a single dose of INDV-2000 or placebo, by mouth. In each study session participants will come to the ward for an outpatient visit or stay on the ward for 1 night. Participants will have an fMRI scan in each study session.

What are the possible benefits and risks of participating?
The researchers don't expect the study participants to get any medical benefit from the study

medicine. The screening tests may be of benefit if an important medical problem is found, but they could reveal something people would prefer not to know about.

79 healthy participants have taken single doses of up to 720 mg of the study medicine, and 56 healthy participants have taken repeated doses of up to 400 mg of the study medicine for up to 28 days, so far. 16 participants with OUD have also taken 400 mg of the study medicine. There were no important side effects, but some people had sleepiness, headache, dizziness, back pain, tiredness, and dry mouth. The site research team will monitor participants closely during the study.

If a participant is withdrawn, the site research team ask them to complete a final follow up.

If a participant, or their partner, becomes pregnant during the study, the site research team ask to contact their GP about the pregnancy.

If the site research team finds any medically important problem at screening, the site physician will tell the participant in person, and pass on the results to the participant's GP.

The site research team contacts participants' GPs to inform them that their patient has volunteered to take part in a study, and provide the GP with a study summary. The site research team will ask the GP about the participants medical history to check if there's any medical problem that might compromise the volunteers' safety during the study. Participants consent to the researchers contacting their GP regarding their participation when they sign the ICF.

The Chief Investigator (CI) is a consultant addiction psychiatrist with over 20 years' experience. The research team includes experienced staff who can deal with any issues arising, and link with teams managing patients' clinical care. Patients will be engaged in specialist clinical services for their treatment and can access extra support if required. No treatment is withheld from participants. Some may find the long study days tiring. The site research team will take steps to ensure comfort and provide rest and sustenance during visits.

Participants will bring their usual prescription of daily methadone to the clinical site on dosing days, so, it may be taken at a later time than usual. From experience the site research team don't expect this to be a concern and lead to any withdrawal.

The cue reactivity task may trigger feelings of discomfort, craving and anxiety. The experienced team will be able to provide support and guidance.

Blood sample collection may cause discomfort, but the risk of pain, distress or infection is low. Bruising may occur at the sampling site.

Please refer to the informed consent form (ICF) for details on procedural risks, lifestyle and fasting restrictions, and contraception requirements.

Where is the study run from?
Imperial College Research Facility (ICRF) within Imperial College Healthcare NHS Trust and Invicro (UK)

When is the study starting and how long is it expected to run for?
February 2024 to December 2025

Who is funding the study?
Indivior (UK)

Who is the main contact?
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Contact information

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1009658

Protocol serial number
INDV-2000-106, IRAS 1009658

Study information

Scientific Title
Randomised, placebo-controlled functional evaluation of INDV-2000 effects on cue reactivity in opiate dependence: An fMRI study.

Study objectives
1. To explore the effects of INDV-2000 on the brain's response to drug related cues in participants with opioid use disorder.
2. To explore safety and tolerability of INDV-2000 when administered in combination with methadone
3. To explore the effect of INDV-2000 on patient-reported outcomes for craving and anxiety before and after exposure to salient drug cues

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 15/04/2024, Wales REC 1 (Castlebridge 4, 15-19 Cowbridge Rd E, Cardiff, CF11 9AB, United Kingdom; +44 2922 940912; Wales.REC1@wales.nhs.uk), ref: 24/WA/0044

Study design
Interventional double blind randomized cross over placebo controlled trial

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Opioid use disorder

Interventions
Participants will have 3 study sessions. In each study session, they'll take their prescribed dose of methadone, and then either a low dose (100 mg) or high dose (600 mg) of study medicine, or placebo by mouth. Up to 36 participants will be enrolled.
In each study session, participants will have an fMRI scan about 1.5 h after their dose of study medicine or placebo.
In each study session participants will come to the ward for an outpatient visit or stay on the ward for 1 night. They will have a final follow-up about a week after their last dose.
A computer program will decide randomly when a participant takes the low dose and high dose of the study medicine, and placebo.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
INDV-2000

Primary outcome(s)
Pharmacodynamic parameters including the mean blood oxygenation level dependent (BOLD) signal of the (cue minus neutral) contrast across the voxels in the region of interest (ROI). For each voxel in ROI, the BOLD signal of the (cue minus neutral) contrast is an averaged difference between cue and neutral in arbitrary unit (a beta value) over the time when the participants viewing cue images vs neutral images in a single CR task run.

Responses will be measured using MRI scans (BOLD signal) and cue administration tasks on days 1,8, and 15

Key secondary outcome(s))
1. Safety and tolerability will be assessed by measuring the adverse events (including incidence, severity, and relatedness of treatment emergent adverse effects (TEAEs), serious adverse events (SAEs), and events leading to discontinuation or death) reported during placebo and individual INDV-2000 dosage treatment period.
2. Effect of INDV-2000 on patient-reported outcomes for craving before and after exposure to salient drug cues will be measured using in-scan difference in opioid craving numerical rating scale (NRS) assessed before and after cue reactive task.
3. Safety and tolerability will be assessed before dosing, at regular intervals up after each dose, and at the subject's final follow-up visit.
4. Cue administration tasks and craving and anxiety NRS will be performed on day 1,8, and 15.

Completion date
17/12/2025

Eligibility

Key inclusion criteria
1. Males or females with a diagnosis of OUD who are clinically stable with no new signs or symptoms for at least 1 month on take-home methadone treatment with no dose increase in the last 10 days prior to screening;
2. Agreed 18 – 65 years of age, inclusive;
3. BMI of 18.0 to 35.0 kg/m², inclusive (minimum weight of at least 50.0 kg at Screening);
4. Males who are sexually active with individuals who are of childbearing potential, and females who are of childbearing potential, must agree to use at least one medically acceptable form of contraception;
5. Females of childbearing potential must not be pregnant as confirmed by a negative serum and/ or urine hCG test at screening;
6. Females of childbearing potential must not be lactating; and
7. Participants must be able to give written consent (including verbalise understanding of the consent form); be willing and likely to complete all study procedures; be able to comply with the protocol requirements and site procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Take over 120 mg/day of prescribed methadone;
2. Have a medical history of clinically significant neurological, cardiovascular, renal, hepatic, chronic respiratory or gastrointestinal disease, or psychiatric disorder (current severe mental health disorder excluding opiate dependence) as judged by an Investigator
3. Use regular prescription medications which in the opinion of the investigators will interfere with participant safety or study integrity. Regular use of psychotropic medication will be permitted e.g., antidepressants, provided the participant is compliant with administration and the investigators concur that they will not interfere with participant safety or study integrity
4. Have clinically significant abnormal biochemistry, haematology or urinalysis results
5. Have a history of narcolepsy, cataplexy or obstructive or central sleep apnoea
6. Have disorders that may interfere with drug ADME processes
7. Tests positive for HIV-1/HIV-2 antibodies, and/or has serological evidence of active Hepatitis B or Hepatitis C infection
8. Have serious cardiac illness or other cardiac assessments including, but not limited to:
8.1. Uncontrolled arrhythmias
8.2. History of congestive heart failure (CHF)
8.3. Myocardial infarction in the last 6 months
8.4. Uncontrolled symptomatic angina
8.5. QTcF > 460 ms for males and >480 ms for females or history of prolonged QT syndrome
9. Have current active hepatic or biliary disease, including participants with cholecystectomy <90 days prior screening
10. Have received concurrent treatment or treatment with an investigational drug, or participation in any other clinical study within 30 days prior to screening
11. Have received drugs that are moderate or strong inhibitors/inducers of CYP3A4 or CYP2C19, including St. John’s Wort, within 30 days prior to first dose of IMP
12. Have a history of suicidal ideation within 30 days prior to providing written informed consent as evidenced by answering "yes” to questions 4 or 5 on the suicidal ideation portion of the C-SSRS completed at the Screening Visit or history of a suicide attempt (per the C-SSRS) in the 6 months prior to informed consent.
13. Have known allergy or hypersensitivity to IMP or its excipients
14. Are affiliated with, or a family member of, site staff directly involved in the study, or anyone with a financial interest in the outcome of the study
15. Currently have severe substance dependence disorder for any other substance except for opiates and nicotine. Lifetime history of dependence on other substances will be allowed given very high incidence of co-dependence.
16. Are regular on-top user of heroin or other opiates or other illicit substances in combination with methadone, which in the opinion of the investigators will interfere with participant safety

or study integrity
17. Have a blood pressure reading outside of the following range: Systolic 159 mmHg; Diastolic 99 mmHg
18. Have any combination of the following at screening:
18.1 TBL ≥1.5x ULN (with direct bilirubin >1.3 mg/dL)
18.2 ALT ≥3x ULN
18.3 AST ≥3x ULN
18.4 serum creatinine >2x ULN
18.5 or INR >1.2x ULN
19. Have received any prior treatment with a buprenorphine injection at least 1 year prior to randomisation
20. Currently incarcerated or pending incarceration/legal action that could prevent participation or compliance in the study
21. Contraindication to MRI based on the standard MRI screening questionnaire. Contraindications include, but not limited to, certain ferromagnetic foreign bodies (e.g., shrapnel, ferromagnetic fragments in the orbital area), certain implanted medical devices (e.g., aneurysm clips, cardiac pacemakers), or claustrophobia.
22. Have any condition that, in the opinion of an investigator or medically responsible physician, would interfere with evaluation of the IMP or interpretation of participant safety or study results.

Date of first enrolment
17/07/2024

Date of final enrolment
17/12/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College Research Facility (ICRF) within Imperial College Healthcare NHS Trust
160 Du Cane Road
London
England
W12 0HS

Study participating centre
Invicro
Burlington Danes Building, Imperial College London, Du Cane Road
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Sponsor information

Organisation
Indivior Inc.

Funder(s)

Funder type
Industry

Funder Name
Indivior UK Limited

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available