ISRCTN90678104 https://doi.org/10.1186/ISRCTN90678104

A phase Ib study of inhaled IN-006 (regdanvimab for nebulization) versus intravenous regdanvimab

Submission date
09/12/2022

Recruitment status
No longer recruiting

Registration date
17/05/2023

Overall study status
Completed

Last Edited
01/10/2024

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is mainly a respiratory illness caused by the virus SARS-COV-2. COVID-19 symptoms generally appear within 14 days of exposure and commonly include loss of taste or smell, cough, fever, and shortness of breath. Complications of severe COVID-19 in humans with late-stage infection include rapidly progressive lung disease shown by widespread inflammation in the lungs. The experimental study medication IN-006 (regdanvimab for nebulization) and intravenous regdanvimab are both monoclonal antibodies used to target the COVID-19 virus. An antibody is a protein produced by the body in response to harmful substances (for example bacteria, fungi, parasites and viruses). The antibody in IN-006 and intravenous regdanvimab is a fully human antibody. Regdanvimab has been found to be effective as a treatment for patients with mild to moderate symptoms of COVID-19 in a clinical trial sponsored by Celltrion. Currently, intravenous regdanvimab is approved for use in the European Union for the treatment of adults with COVID-19 who do not require supplemental oxygen, and who are at increased risk of progressing to severe COVID-19. The purpose of this research study is to determine whether the study drug, IN-006 (regdanvimab given by nebulization), is safe and well tolerated in healthy participants, and to compare the effects of regdanvimab given intravenously (medication is given in a vein in the arm) versus IN-006 given via nebulisation (medication is inhaled into the lungs).

Who can participate?
Healthy male and female volunteers aged 18-55 years old

What does the study involve?
The purpose of this research study is to determine whether the study drug, IN-006 (regdanvimab given by nebulization), is safe and well tolerated in healthy participants, and to compare the effects of regdanvimab given intravenously (medication is given in a vein in the arm) versus IN-006 given via nebulisation (medication is inhaled into the lungs). The study will evaluate two dose levels in three groups:

1. Group 1: A single intravenous dose of 40 mg/kg
2. Group 2: A single nebulization of 90 mg
3. Group 3: Five daily nebulizations of 90 mg

What are the possible benefits and risks of participating?
There is no anticipated benefit from taking part in this study. However, information from this study may help treat patients with COVID-19 in the future.

This study will be conducted by experienced investigators and well-trained medical, nursing and technical staff with ample experience in the conduct of early-phase clinical trials.
The main issues to consider for this study comprise:
1. Side effects of IN-006
2. Risk of pregnancy
3. Standard procedural risks

The individual participants in this study will not benefit from treatment. Inclusion and exclusion criteria have been chosen to enable a uniform trial sample of participants and to minimise possible risks due to the administration of IN-006. The trial is designed to closely monitor, treat and communicate potential expected adverse events as well as potential unexpected adverse events. To ensure the safety of the participants, adverse events, vital signs, physical examinations, electrocardiographic (ECG) variables, pregnancy testing, infusion site checks (if applicable), spirometry, oxygen saturation, diffusion capacity of the lung for carbon monoxide (DLCO), visual inspection of the large airways by bronchoscopy and laboratory parameters will be monitored. Immediately after dosing, volunteers are closely monitored for their safety.

All potential side effects of IN-006 and other possible risks or discomfort are listed in the patient information sheet (PIS) informed consent form (ICF).

Human Medicines Regulations (HMRs) Specific text:
If a participant is withdrawn, the site will ask them to consent to a final follow-up. The site will document their consent using an ICF, which has been approved by the HRA's Generic Review Committee (GRC; REC ref: 18/GR/0054). During their stay, participants must follow HMR's 'house rules'. An information leaflet is given to volunteers at screening and has been approved by the GRC (REC ref: 18/GR/0104). If a participant, or their partner, becomes pregnant during the study, the site asks to contact their GP about the pregnancy – site document that using a generic ICF that has been approved by the HRA's GRC (REC ref: 18/GR/0055 or 21/GR/16).
If the site 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, using a letter template, which has been approved by the GRC (REC ref: 18/GR/0101). Site contact participants' GPs to inform them that their patient has volunteered to take part in a study and provide the GP with a study summary. Site GP letter templates have been approved by the GRC (REC refs: 18/GR/0098 and 18/GR/0099); therefore, we have not attached copies of those letters to this application. Participants consent to site contacting their GP when they sign the ICF.

MEU Specific text:
MEU will not ask for subjects to consent to a final follow-up - we will follow protocol procedures for withdrawal only.

If a participant becomes pregnant MEU will ask them to sign ethics-approved pregnancy PIS/ICF and follow pregnancy accordingly.

Medically important information at screening - the physician will discuss the finding with the patient, they will then write their GP a letter using a GP letter template and ask the patient to follow up with GP themselves.

Where is the study run from?
Inhalon Biopharma Inc (USA)

When is the study starting and how long is it expected to run for?
December 2022 to August 2023

Who is funding the study?
U.S. Department of Defense (USA)

Who is the main contact?
Clinical Operations Inhalon, inhalonclinops@gmail.com

Contact information

Type(s)
Scientific

Contact name
Dr Clinical Operations

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Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number
2022-003470-23

IRAS number
1006745

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IN-006-02, IRAS 1006745

Study information

Scientific Title
A phase Ib, open-label, pharmacokinetics and safety study of IN-006 (regdanvimab for nebulization) versus intravenous regdanvimab in healthy volunteers

Study objectives
To assess the safety of the Study Drug after nebulization versus IV infusion.

To assess and characterize the respiratory and systemic pharmacokinetics and the immunogenicity of the Study Drug after administration by nebulization versus IV infusion.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/04/2023, South Central – Berkshire (Meeting held by video-conference via Zoom; +44 (0)207 104 8178, (0)207 104 8182; berkshire.rec@hra.nhs.uk), ref: 22/SC/0437

Study design
Unblinded open-label parallel-group-assignment study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Safety

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
SARS-COV-2

Interventions
The purpose of this research study is to determine whether the study drug, IN-006 (regdanvimab given by nebulization), is safe and well tolerated in healthy participants, and to compare the effects of regdanvimab given intravenously (medication is given in a vein in the arm) versus IN-006 given via nebulisation (medication is inhaled into the lungs). This is an unblinded open-label study without randomization. The study will evaluate two dose levels in three groups:
1. Group 1: A single intravenous dose of 40 mg/kg
2. Group 2: A single nebulization of 90 mg
3. Group 3: Five daily nebulizations of 90 mg
The study is designed to enroll approximately 48 (maximum of 52) normal healthy participants. Groups 1 and 2 will enroll approximately 18 participants each, Group 3 will enroll approximately 12 participants. Each group will be divided approximately equally between males and females. Groups may be enrolled in parallel.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
Regdanvimab (IN-006; Regkirona)

Primary outcome measure
Treatment-emergent adverse events measured using vital signs, visual assessment by bronchoscopy, ECG, forced expiratory volume/FEV1, oxygen saturation/SpO2, DLCO, and clinical laboratory tests from the signing of the informed consent form to participant exit from the study

Secondary outcome measures

The exploratory endpoints are:
1. Study Drug levels in airway fluids of the lower respiratory tract sampled via bronchial brushing and bronchoalveolar lavage measured using immunoassay at intervals after nebulization versus after intravenous infusion
2. Study Drug levels in nasal fluid sampled by mid-turbinate swabs measured using immunoassay at intervals after nebulization versus after intravenous infusion
3. Study Drug levels in serum measured using immunoassay sampled at intervals after nebulization versus after intravenous infusion
4. Anti-drug antibodies in serum measured using immunoassay

Measurements are taken at the following timepoints:
Group 1: Day -1, Day 1, 2, 4, 6, 8, 10, 15 and 22.
Group 2: Day -1, Day 1, 2, 3, 4, 5, 6, 8 and 10.
Group 3: Day -1, Day 1, 2, 4, 5, 6, 8, 10, 15 and 22.

Overall study start date
06/12/2022

Completion date
22/08/2023

Eligibility

Key inclusion criteria
1. Healthy male and female volunteers, aged 18-55 years, inclusive at the time of signing the informed consent
2. Non-smoker or light smoker (on average ≤10 cigarettes or ≤ 100 puffs from e-cigarettes per week as judged by the Investigator), and agrees to abstain during the in-patient period, and to use no more nicotine-containing products than the equivalent of smoking 10 cigarettes per week through study exit
3. In good health, as determined by the investigator after reviewing history, physical examination, vital signs, and laboratory tests within normal limits or deemed by the investigator to not be clinically significant
4. Negative serology for HBsAg, HCV antibodies, & HIV antibodies (however positive HCV serology is not an exclusion if negative for HCV RNA)
5. Willingness to comply with the protocol, including nasal swabs, bronchoscopy procedures, and follow-up visits
6. Able to successfully complete a trial saline nebulization treatment (Groups 2 and 3 only)
7. Women of childbearing potential, as defined in Clinical Trials Facilitation and Coordination Group 2020, must have a negative pregnancy test at Screening and agree to abstinence or the use of at least one highly effective form of contraception (with a failure rate of <1% per year when used consistently and correctly):
7.1. Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: Oral, Intravaginal, Transdermal
7.2. Progestogen-only hormonal contraception associated with inhibition of ovulation: Oral, Injectable, Implantable
7.3. Intrauterine device
7.4. Intrauterine hormone-releasing system
7.5. Bilateral tubal occlusion or tubal ligation
7.6. Vasectomized partner with confirmed azoospermia
Highly effective contraception or abstinence must be started at least 28 days before the first

dose, continue for the duration of the study, and for at least 90 days after the last dose of the study drug.
All females will be considered of childbearing potential unless they are postmenopausal or have been permanently sterilized surgically (e.g., hysterectomy, bilateral salpingectomy, bilateral oophorectomy).
8. Males who are sexually active with women of childbearing potential who have not had a vasectomy must agree to use a barrier method of birth control during the study and for at least 90 days after the last dose of the study drug. Males must also refrain from sperm donations during this time period. Males who are abstinent will not be required to use a contraceptive method unless they become sexually active. Males who have undergone a vasectomy are not required to use a contraceptive method if at least 16 weeks post-procedure.
9. Body mass index (BMI) 18.0 – 32.0 (kg/m2) at the screening visit
10. Forced expiratory volume in 1 second (FEV1) ≥ 80% of predicted at the screening visit and Day -1
11. Electrocardiogram without clinically relevant abnormalities at Screening
12. Clinical laboratory test results within normal limits or judged by the investigator to be not clinically significant within 7 days of or upon admission
13. Total neutrophil count within normal limits or considered to be non-clinically significant (repeat test is allowed if out of range) within 7 days of or upon admission
14. Negative for SARS-CoV-2 on RT-PCR or lateral flow test by nasal swab on Day -1 prior to admission to the inpatient unit
15. Has not received a COVID-19 vaccination or booster for 2 weeks prior to dosing on Day 1 and willing to defer receipt of a COVID-19 vaccination for 2 weeks after the last study drug dose
16. Willing to forego the use of any of the following prohibited medications within 7 days or 5 half-lives (whichever is longer) prior to enrollment through study exit:
16.1. Prescription or nonprescription small molecule medications (excluding hormonal birth control and medications indicated during or following the study bronchoscopy procedure), OTC drugs, vitamins, recreational drugs, dietary supplements or herbal remedies unless approved by the Sponsor's Medical Monitor. Paracetamol/Acetaminophen at doses of < 2 grams/day and multi-vitamins are permitted for use at any time before or during the study
16.2. Any vaccinations unless deemed medically necessary by the Investigator (however, COVID-19 vaccination is permitted as described in Inclusion Criteria #15)
17. Willingness to give written consent to have data entered into The Over-Volunteering Prevention System (TOPS).
18. Agrees not to donate blood or blood products during the study and for at least 3 months after the final dose of the Study Drug.
19. Has not received any other investigational drug for 90 days or five half-lives (whichever is longer) prior to dosing and is willing to forgo these drugs through study exit
20. Has not received a monoclonal antibody or other biologic for 6 months or five antibody half-lives, whichever is longer, prior to dosing and is willing to forgo these drugs through study exit

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit

55 Years

Sex
Both

Target number of participants
48

Total final enrolment
48

Key exclusion criteria
1. Known or suspected symptomatic viral infection within 14 days of dosing initiation
2. Signs of active pulmonary infection or pulmonary inflammatory condition within 14 days of dosing
3. Loss of more than 400 mL of blood within 90 days of first dose, e.g., as a blood donor
4. History of hypersensitivity or allergies to a biologic drug or a constituent of the study drug
5. History of airway hyperresponsiveness (however, a history of resolved childhood asthma is not an exclusion)
6. History of angioedema or anaphylaxis
7. Currently active allergic rhinitis requiring inhaled medication or allergic dermatitis currently requiring medication
8. A positive alcohol breathalyzer or urine test and/or a positive blood or urine drug screen for substances of abuse at screening or upon
admission to the clinical research unit

Date of first enrolment
07/06/2023

Date of final enrolment
26/07/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Medicines Evaluation Unit Limited
The Langley Building
Southmoor Road
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Study participating centre
Hammersmith Medicines Research Limited
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Sponsor information

Organisation
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Sponsor type
Industry

Funder(s)

Funder type
Government

Funder Name
U.S. Department of Defense

Alternative Name(s)
United States Department of Defense, Department of Defense, U.S. Dept of Defense, US Department of Defense, DOD, USDOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Submission to regulatory authorities

At this stage in the development of the study medicine, the study data are highly commercially confidential. They will be shared with others only as the sponsor sees fit.
The sponsor, PPD, part of Thermo Fisher Scientific and regulatory authorities will be granted direct access to medical records for verification of study procedures and data without violating the confidentiality of the records to the extent permitted by the applicable laws and regulations. Before data transfer, all identifiable information will be replaced by a code. The sponsor shall ensure that necessary measures are taken to protect and maintain the confidentiality of data when transferred outside of the UK and EEA.

Intention to publish date

31/10/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to accordance with the common practice of Pharmaceutical Sponsors.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Basic results			01/10/2024	No	No