

An open-label, two-part study to investigate the drug-drug interaction potential of INE963 and KAE609 administered together, and the effect of food on pharmacokinetics and safety of INE963 in healthy participants.

Submission date 04/04/2023	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 15/09/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 05/11/2024	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

This is an open-label study in about 30 healthy male and female subjects (18 to 55 years, 15 per study part), at a single centre.

The main purpose is to assess the pharmacokinetics between single oral doses of INE963 and KAE609 (Part A) and to assess the effect of food on the pharmacokinetics of a single oral dose of INE963 (Part B). Pharmacokinetics refers to how the study medicine is taken up into and distributed throughout the body; broken down and finally removed from the body.

Furthermore, the safety and tolerability following single oral dose of KAE609 and/or INE963 alone, and in combination (Part A) and of INE963 in fasted and fed conditions (Part B), will be evaluated.

Who can participate?

Healthy volunteers aged 18 – 55 years.

What does the study involve?

Both study parts consist of a screening period of up to 28 days, 3 or 2 treatment periods (including wash-out periods after dosing) of approximately 66 days in Part A and 57 days in Part B, an ambulatory End-of-Study visit 22 days after last dosing and a safety follow-up call 30 days after dosing.

What are the possible benefits and risks of participating?

Benefits:

Not provided at time of registration

Risks:

INE963 and KAE609 are being developed by Novartis for a combination treatment for malaria. INE963 and KAE609 have not been approved by health authorities for the treatment of patients.

One first in human study with INE963 has been completed and 9 clinical studies with KAE609. INE963 and KAE609 are co-administered for the first time in this study.

COVID-19

A throat swab for COVID-19 is performed with a cotton swab via nose and/or mouth. Possible risks and discomforts regarding the throat swab are retching, nose throat pain and mucosal damage. The risk of participants being exposed to COVID-19 (transmission and infection) in relation to site visits is overall considered to be low. To minimise the risk as much as possible, the following measures have been taken: Testing for COVID 19 infection by laboratory assessment (RT-PCR) and adhering to current national laws and local recommendations for prevention of pandemic. In addition, physical distancing and person-to-person contact restrictions will be applied during site visits and in-house confinement. Where physical distancing is not possible personal protective equipment (PPE) will be used by the participant and staff (for example but not limited to masks, gloves, protectors, medical suits) if deemed appropriate by the investigators and site staff and guided by local requirements. Participants who receive a COVID-19 vaccine within 2 weeks before first dosing will be excluded from the trial.

Where is the study run from?

Novartis Pharmaceuticals UK Limited

When is the study starting and how long is it expected to run for?

March 2023 to September 2024

Who is funding the study?

Novartis Pharmaceuticals UK Limited

Who is the main contact?

Pablo.Fortesoto@parexel.com

Contact information

Type(s)

Scientific

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Additional identifiers**Clinical Trials Information System (CTIS)**

2023-000047-23

Integrated Research Application System (IRAS)

1007303

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

CINE963A02102, IRAS 1007303

Study information**Scientific Title**

A Phase I, open-label, two-part, fixed sequence, three period crossover study to investigate the drug-drug interaction potential of INE963 and KAE609 (Part A) administered together, and a two period crossover study to investigate the effect of food on pharmacokinetics and safety of INE963 (Part B), in healthy participants.

Study objectives

Primary objectives:

Part A: To assess the PK interaction between single oral doses of INE963 and KAE609 in healthy

participants.

Part B: To assess the effect of food on the PK of a single oral dose of INE963 in healthy participants

Secondary objectives:

Part A: To assess the safety and tolerability following single oral dose of KAE609 and/or INE963 alone, and in combination in healthy participants

Part B: To assess the safety and tolerability following single oral dose of INE963 in fasted and fed conditions.

Part A and Part B: To assess additional PK parameters following single oral dose of INE963 and /or KAE609, administered alone or in combination

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 14/09/2023, South Central – Berkshire B Research Ethics Committee (Manchester HRA, 3rd Floor Barlow House, Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 207 104 8276; berkshireb.rec@hra.nhs.uk), ref: (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0) 207 104 8276; berkshireb.rec@hra.nhs.uk), ref: 23/SC/0097

Study design

Interventional non randomized

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Malaria

Interventions

This study is in 2 parts i.e. a drug – drug interaction part (Part A) and then a food effect part (Part B). Part A will look at the effect of taking the 2 study medicines (INE963 and KAE609) together, and Part B will look at the effect of food on how the study medicine INE963 works, as well as assessing the safety of INE963. The study medicine will be administered by the study staff and both the volunteer and the Study Doctor will know what study medicine the volunteer is getting in both Part A and Part B.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

INE963, KAE609

Primary outcome(s)

Primary plasma PK parameters (AUClast, AUCinf and Cmax) for INE963 and KAE609

Primary plasma PK parameters (Cmax, AUClast, AUCinf and Tmax) for INE963

Part A Period 1: 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24 h, 48 h, 72 h, 120 h, 168 h, 264 h, 360 h, and 504 h postdose of INE963

Part A Period 2: 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24 h, 48 h, 72 h, 120 h, 168 h postdose of KAE609

Part A Period 3: 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24 h, 48 h, 72 h, 120 h, 168 h, 264 h, 360 h, and 504 h postdose of INE963

Part B Day 1 Period 1: 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24 h, 48 h, 72 h, 120 h, 168 h, 264 h, 360 h, and 504 h postdose of INE963

Part B Day 1 Period 2: 0 h, 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24 h, 48 h, 72 h, 120 h, 168 h, 264 h, 360 h, and 504 h postdose of INE963

Key secondary outcome(s)

1. Adverse events, physical examination findings, vital signs, ECG findings, safety laboratory assessments including chemistry, hematology, and urinalysis results.
2. Additional PK parameters of INE963 and KAE609 including but not limited to: Tmax, CL/F, Vz/F and T1/2.

Completion date

03/09/2024

Eligibility

Key inclusion criteria

1. Signed informed consent
2. Healthy male and female* participants of non-childbearing potential * aged 18 to 55 years (inclusive)
3. In good health as determined by medical history, physical examination, vital signs, ECG, and laboratory test at Screening or Baseline
4. Vital signs (systolic and diastolic blood pressure and pulse rate) will be assessed at Screening or Baseline in the supine position after at least five minutes rest in a quiet environment. Supine vital signs must be within the following ranges:
 - oral body temperature between 35.0°C and 37.5°C
 - systolic blood pressure between 90 mmHg and 140 mmHg
 - diastolic blood pressure between 50 mmHg and 90 mmHg
 - pulse rate between 45 bpm and 90 bpm
5. Participants must weigh at least 50 kg with a body mass index (BMI) within the range of 18.0 kg /m²- 29.9 kg/m². BMI = Body weight (kg) / [Height (m)]², inclusive.

Participant type(s)

Healthy volunteer

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

55 years

Sex

All

Total final enrolment

48

Key exclusion criteria

1. Significant illness which has not resolved within two (2) weeks prior to initial dosing.
2. A history of clinically significant ECG abnormalities, or any other ECG abnormalities considered clinically significant by the Investigator at Screening and/or Baseline, including but not limited to:
 - QTcF > 450 msec (males)
 - QTcF > 460 msec (females)
3. Any clinically significant hematology parameters outside normal ranges as defined by the local laboratory at Screening and/or Baseline. Participants with neutrophils $<1.5 \times 10^9/L$ should be excluded.
4. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism, or excretion of drugs, or which may jeopardize the participant in case of participation in the study. The Investigator should make this determination in consideration of the participant's medical history and/or clinical or laboratory evidence including but not restricted to any of the following at Screening or Baseline:
 - 4.1. Use of any prescription drugs, over-the-counter (OTC) medication, herbal supplements, prescribed medicinal use of cannabis/marijuana, within four weeks prior to initial dosing, with the exception of coronavirus disease 2019 (COVID-19) vaccine which will be restricted within 2 weeks prior to first dosing.

Date of first enrolment

06/10/2023

Date of final enrolment

23/02/2024

Locations**Countries of recruitment**

United Kingdom

Study participating centre

-

United Kingdom

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Sponsor information

Organisation

Novartis Pharmaceuticals UK Limited

Funder(s)

Funder type

Industry

Funder Name

Novartis Pharmaceuticals UK Limited

Alternative Name(s)

Novartis UK, NOVARTIS UK LIMITED

Funding Body Type

Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be included as part of the Clinical Study Report once the study has been completed.

IPD sharing plan summary

Published as a supplement to the results publication