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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	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 15/09/2023	**Overall study status** Completed	
Last Edited 05/11/2024	**Condition category** Infections and Infestations	

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 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

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 x 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
-

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