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A study to investigate the effects of IOA-244 in healthy volunteers, including assessment of food effect

Submission date	Recruitment status	[_] Prospectively registered
30/05/2024	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/08/2024	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
31/07/2025	Cancer	

Plain English summary of protocol

Background and study Aims
The purpose of this study is to investigate IOA-244 (also known as roginolisib). The main objectives are as follows:
- To investigate the effect of food on the concentration of IOA-244 in the blood following administration of IOA-244 in both a fasted state (without food) and fed state (following a high-fat, high-calorie meal) at two different dose strengths.
- To evaluate the effect of IOA-244 on the body (known as pharmacodynamics) by analysing the levels of specific biomarkers in the body (markers within the body such as a gene, molecule or characteristic which can be used to identify the presence of a particular biological process occurring in the body or a particular disease).
- To investigate the concentration of IOA-244 in the blood, how this changes over a period of time and to measure if and how this concentration differs when IOA-244 is administered at two different dose strengths.
- To determine the safety and tolerability (degree to which side effects of the study drug can be tolerated) of IOA-244 when it is administered at two different dose strengths and following administration in a fasted state (without food) and fed state (following a high-fat, high-calorie meal).

Who can participate?
A total of up to 32 participants are needed to fully complete this study. Participants must be healthy adult males and females with a minimum age of 18.

What does the study involve?
The study will consist of up to 32 participants with each participant required to complete both treatment periods. Across the two treatment periods, each participant will receive:
- a single dose of IOA-244 (40 or 80 milligrams (mg)) in the form of oral capsules in a fasted state,
- a single dose of IOA-244 (40 or 80 mg) in the form of oral capsules following a high-fat, high calorie meal.
The study will consist of a screening visit (between 35 and 1 day prior to first dose), 2 treatment periods (consisting of a maximum of 13 days with 12 overnight stays for both treatment periods

combined – Day -1 of treatment period 1 – Day 6 of treatment period 2) and a post-study follow-up visit approximately 6-10 days following the last dose of IOA-244 in treatment period 2. Each dose in each treatment period will be separated by a washout period of at least 6 days. Blood, urine and stool samples will be taken in order to measure the levels of IOA-244 and specific markers associated with the study drug. We will analyse the results from each of the treatment periods and combine this information in order to better understand how IOA-244 works in the body.

What are the possible benefits and risks of participating?
Taking part in this study is not expected to provide participants with any direct medical benefit. However, the information we get from this study may help improve the treatment of different types of cancer.
Possible risks include the following:
Blood Sampling: The procedure for blood collection either by direct venepuncture or indwelling cannula may cause mild pain and bruising at the collection site. Placement of an indwelling catheter is proposed in order to minimise these effects for rapid PK sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time.
Blood pressure and pulse rate: The participants blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated.
ECG: Small sticky pads will be placed on the participants' upper body before the ECG and an ECG machine will measure the electrical activity of the participants' heart. Before the pads are applied, the skin needs to be cleaned. Trained staff may need to shave/clip small patches of the participants hair in these areas. Like Elastoplast® these sticky pads may be uncomfortable to remove.
COVID-19 Risks: Participants should also be aware of the risks of exposure to COVID-19. When participants attend the clinical unit at each visit, they may be asked to complete a self-declaration form and temperature check to confirm that they are not showing any early signs of COVID-19 infection and that they have not had any contact with individuals who are currently self-isolating or have tested positive (dependent on risk mitigation measures employed at the clinical unit at the time of clinical conduct).
Participants may also be required to have a negative COVID-19 test prior to admission to the clinical unit for any overnight stays as defined within the study protocol. This procedure may cause some mild discomfort in the nose or throat when the swab is being taken but this should resolve after the procedure has been completed. Additionally, at the clinical unit, participants may be asked to wear a facemask during procedures where clinical staff cannot maintain a 2 m distance. It is noted that if participants have a medical exemption from wearing a face mask, they will not be required to do so. In any circumstance, to prevent risk of transmission between staff and participants, all staff will be wearing appropriate personal protective equipment i.e., face masks, face shields etc during the course of the study (as appropriate for the level of risk mitigation measures in place at the clinical unit at the time of conduct).
Stool Sampling: There is no discomfort/risk expected with this procedure. However, participants may find the provision of the sample itself to be unpleasant in nature.
Harm to the unborn child: The treatment might harm the unborn child; therefore, volunteers who are pregnant, breastfeeding or who intend to become pregnant during the study and up to 3 months following the last dose will not be eligible to take part. For male participants and female participants (of childbearing potential), they will be required to use a highly effective form of contraception, in addition to a male condom from Day 1 of treatment period 1 (first dose) until at least 3 months following the last dose of IOA-244 in treatment period 2. In addition, for female participants (of childbearing potential) a negative pregnancy result must be obtained prior the start of the study.

Throughout the study the health of the participants will be regularly monitored and appropriate treatment for any medical condition will be provided if required. All doctors employed by Simbec-Orion are trained and certified in Advanced Life Support Procedures in order to deal with a medical emergency. Nurses and other clinical staff are also trained in emergency procedures. Simbec-Orion also has an agreement with Prince Charles Hospital for referral of participants if required following a medical emergency.

Where is the study run from?
The study will be conducted at Simbec-Orion Clinical Pharmacology Unit, an MHRA Phase 1 accredited CRO based in South Wales.

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

Who is funding the study?
This study is funded and sponsored by a pharmaceutical company called iOnctura SA, based and headquartered in Geneva, Switzerland.

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
1008779

Protocol serial number
IOA-244-102

Study information

Scientific Title
A randomised, open-label, two-period, parallel group design, phase I study to assess the effect of food, pharmacokinetics and pharmacodynamics of roginolisib (IOA-244) in healthy subjects

Study objectives
The primary objective of this study is:
To determine the effect of food on the PK of IOA-244 following a single dose administration with and without a meal.

The secondary objectives of this study are:
1. To characterise the plasma concentration time profile of the IOA-244 capsule formulation following single dosing at both 40 and 80 mg QD in fasted conditions.
2. To compare the effect of IOA-244 on CD63 expression in blood at 40 and 80 mg dose levels following single dosing.
3. To assess the safety and tolerability of IOA-244 in healthy subjects.
4. To conduct a preliminary assessment of excretion and metabolism of IOA-244 following single dosing at both 40 and 80 mg dose levels.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 08/07/2024, Wales Research Ethics Committee 1 (WREC1) (Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 292 2940931; Wales.REC1@wales.nhs.uk), ref: 24/WA/0151

Primary study design
Interventional

Study design
Interventional double-blind randomized parallel-group trial

Study type(s)
Safety

Health condition(s) or problem(s) studied
B Cell, Solid Tumour & Haematologic Malignancies

Interventions

This is a randomised, open label, parallel group design, Phase I study to assess the pharmacokinetics, pharmacodynamics and effect of food on IOA-244 in healthy subjects in 2 periods. Up to thirty-two (32) adult males and females aged 18 years and above are planned to participate in this study. In each of the 2 dosing periods a subject will receive a single dose of IOA-244 in either the fed or fasted state. There will be a minimum of a 6-day washout between doses in each treatment period.

A sufficient number of subjects (up to 32) will be enrolled to ensure 24 subjects complete the study (a maximum of 8 and a minimum of 6 participants per group). Subjects will be randomised to one of 4 groups and receive the following:
Group 1a – Period 1 - 40 mg as a single dose (in a fasted state) & Period 2 - 40 mg as a single dose (after a meal)
Group 1b - Period 1 - 40 mg as a single dose (after a meal) & Period 2 - 40 mg as a single dose (in a fasted state)
Group 2a - Period 1 - 80 mg as a single dose (in a fasted state) & Period 2 - 80 mg as a single dose (after a meal)
Group 2b - Period 1 - 80 mg as a single dose (after a meal) & Period 2 - 80 mg as a single dose (in a fasted state)

The clinical phase is anticipated to take place between Q2 2024 and Q3 2024. The conclusion of the study is defined as last participant last visit.

The study will take place in the Clinical Unit of Simbec-Orion Clinical Pharmacology (Clinical Unit) under full medical and nursing supervision.

Screening (Day-35 to Day-2): Screening assessments will be carried out within 35 days before the first administration of IOA-244. Eligible participants will be asked to return for the treatment period, and continued eligibility will be confirmed on Day-1 of treatment period 1.

Treatment Periods 1 and 2 (Day-1 to Day 6): Eligible participants will receive a single dose of either 40 mg or 80 mg in a fed or fasted state as per the randomisation schedule on Day 1. Participants will be admitted to the unit on Day-1 of treatment period 1 and will remain in the unit until 120 h post dose of treatment period 2 (discharge on treatment period 2 Day 6) after all measurements are completed and there are no medical concerns. For treatment periods 1 and 2 PK and PD samples will be taken pre-dose and up to 120 h post-dose (Day 1-6). Treatment period 1 and 2 will be 13 days in duration from Day-1 of treatment period 1 to discharge on Day 6 of treatment period 2. There will be a minimum of a 6-day washout between dosing in each treatment period.

Post Study Follow Up: Post-study assessments will be performed 6-10 days after the last dose of IOA-244.

The study end is defined as last subject last visit.

The study will take place in the Clinical Unit of Simbec-Orion Clinical Pharmacology (Clinical Unit) under full medical and nursing supervision.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
IOA-244 20 mg Oral Capsules [Roginolisib hemi fumarate (proposed)]

Primary outcome(s)
The primary endpoints for this study are pharmacokinetic parameters derived from analysis of plasma samples for concentrations of IOA-244.
PK endpoints are defined as follows:
Cmax, tmax, Clast, tlast, λz, t1/2, AUC0-24, AUC0-t, AUC0-inf, AUC%extrap, CL/F, Vz/F, RCmax, fed:fasted, RAUC,fed:fasted.
Plasma samples will be obtained at the following timepoints:
Day 1 pre dose and 30 minutes, 1, 2, 4, 6, 8, 12, 18, 24, 36, 48, 72, 96 and 120 h post dose in each treatment period (treatment period 1 & treatment period 2).

Key secondary outcome(s)
The secondary endpoints for this study are secondary PK endpoints, safety and PD endpoints:
1. PK endpoints - Cmax, tmax, Clast, tlast, AUC0-t, AUC0-24, AUC0-inf, λz, t1/2, CL/F, Vz/F, AUC% extrap. Blood PK parameters will be derived for both parent drug and metabolites where meaningful.
2. Free Drug Concentration - albumin, AAG, free and total IOA-244 parameters
3. CD63 Expression - % inhibition of CD63 expression and change from baseline
4. Safety - Adverse Events, Physical Examination, Laboratory Safety Testing (Biochemistry & Haematology), ECG, Vital Signs
5. Excretion & Metabolism - Urine: Cumulative amount (Ae) and fraction (fe) of drug excreted in urine and renal clearance (CLR), Faeces: Ae and fe of drug excreted in faeces
6. PD Samples
Day 1 pre dose and 1, 2, 4. 6, 8, 24, 48 and 72h post dose (TP1 & TP2)
7. Adverse Events
AEs recorded from informed consent up to post-study follow up visit.
8. Physical Exam
Screening & post-study follow up visit.
9. Laboratory Safety Testing
Screening, Day -1, Day 2 & Day 6 (TP1 & TP2) & post-study follow up visit.
10. 12-Lead Triplicate ECGs
Screening, Day 1 pre dose and 30 mins, 1, 2, 4, 6, 8, 12, 18, 24 and 36 h post dose & post-study follow up visit (single).
11. Vital Signs
Screening, Day 1 pre dose and 4, 8 and 24 h post dose & post-study follow up visit.
12. Urine PK
Day 1: 0-4, 4-8, 8-12, 12-24, 24-48, 48-72, 72-96 and 96-120 h post dose (TP1 & TP2)
13. Faecal PK
Day 1: 0-24, 24-48, 48-72, 72-96 and 96-120 h post dose (TP1 & TP2).

Completion date
07/11/2024

Eligibility

Key inclusion criteria
1. Healthy Male or Female participant, 18 years of age and over, inclusive.
2. Female participant of childbearing potential willing to use a highly effective method of

contraception, if applicable (unless of non childbearing potential or where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the participant) from the first dose until 3 months after the last dose of IMP.
3. Female participant of non-childbearing potential. For the purposes of this study, this is defined as the participant being amenorrhoeic for at least 12 consecutive months or at least 4 months post-surgical sterilisation (including bilateral salpingectomy or bilateral oophorectomy with or without hysterectomy).
4. Female participant with a negative pregnancy test at Screening.
5. Female participant of menopausal status confirmed by demonstrating at Screening that the serum level of the follicle stimulating hormone (FSH) falls within the respective pathology reference range.
6. Male participant (and partner of childbearing potential) willing to use a highly effective method of contraception, if applicable (unless anatomically sterile or where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the participant) from first dose until 3 months after last dose of IMP.
7. Participant with a body mass index (BMI) of 18-32 kg/m².
8. No clinically significant history of previous allergy / sensitivity to IOA-244 or any of the excipients contained within the IMP.
9. No clinically significant abnormal test results for serum biochemistry, haematology and/or urine analyses within 35 days before the first dose administration of the IMP. Participant with a negative urinary drugs of abuse (DOA) screen (including alcohol) test results, determined within 35 days before the first dose administration of the IMP (N.B.: A positive test result may be repeated at the Investigator's discretion).
10. Participant with negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg)) and hepatitis C virus antibody (HCV Ab) test results at Screening.
11. No clinically significant abnormalities in 12-lead electrocardiogram (ECG) determined within 35 days before first dose of IMP including a PR interval ≤ 220ms, QT interval corrected using Fredericia's formula QTcF ≤450ms for males and <470 for females, or any clinically significant abnormality in the resting ECG, as judged by the Investigator.
12. No clinically significant abnormalities in vital signs (e.g., blood pressure/heart rate) determined within 35 days before first dose of IMP. Supine Systolic BP ≤150 or >90 mmHg /Diastolic BP≤ 90 or >50 mmHg after resting for ≥3 minutes. Supine heart rate, after resting for ≥3 minutes, outside the range of 40 to 100 bpm. The Sponsor may allow exceptions if they are not deemed clinically significant.
13. Participant must be available to complete the study (including all follow-up visits).
14. Participant must satisfy an Investigator about his/her fitness to participate in the study.
15. Participant must provide written informed consent to participate in the study.
16. Participants with a negative COVID-19 test on admission (if required).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
32

Key exclusion criteria
1. A clinically significant history of gastrointestinal disorder likely to influence IMP absorption.
2. Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements within 14 days and antibiotics within 35 days or 5 half-lives (whichever is longer) prior to the first dose of IMP.
3. Evidence of renal, hepatic, central nervous system, respiratory, cardiovascular or metabolic dysfunction.
4. A clinically significant history of drug or alcohol abuse (defined as the consumption of more than 14 units [for male and female participants] of alcohol a week) within the past two years.
5. Inability to communicate well with the Investigators (i.e., language problem, poor mental development or impaired cerebral function).
6. Participation in a New Chemical Entity (NCE) clinical study within the previous 3 months or five half-lives, whichever is longer, or a marketed drug clinical study within the 30 days or five half-lives, whichever is longer, before the first dose of IMP. (Washout period between studies is defined as the period of time elapsed between the last dose of the previous study and the first dose of the next study).
7. Donation of 450 mL or more blood within the 35 days before the first dose of IMP.
8. Vegans, vegetarians or other dietary restrictions (e.g., restrictions for medical, religious or cultural reasons, etc) which would preclude a participant from consuming a standardised high-fat breakfast.
9. Consumption of alcohol and/or food and beverages containing methylxanthines, grapefruit, grapefruit juice, Seville oranges, or Seville orange juice within 72 hours prior to dosing.
10. Users of nicotine products i.e., current smokers or ex-smokers who have smoked within the 6 months prior to Screening or users of cigarette replacements (i.e., e-cigarettes, nicotine patches or gums).
11. Female participants who are pregnant, breastfeeding or lactating.
12. Participants with veins unsuitable for venepuncture and cannulation.
13. Participants with a haemoglobin value less than the lower limit of normal at screening or initial admission.

Date of first enrolment
23/07/2024

Date of final enrolment
07/10/2024

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec-Orion Clinical Pharmacology (AKA Simbec Research Ltd)
Simbec-Orion Clinical Pharmacology, Merthyr Tydfil Industrial Park, Cardiff Road
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Sponsor information

Organisation
iOnctura SA

Funder(s)

Funder type
Industry

Funder Name
iOnctura SA

Results and Publications

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 reasons of commercial confidentiality and sensitivity

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	31/07/2025	31/07/2025	No	No