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A study in healthy volunteers to assess how the body takes up different recipes of the test medicine (alectinib)

Submission date 06/12/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 16/12/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 05/04/2024	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Sponsor is investigating the development of new formulations of the test medicine, alectinib, as an oral formulation for the potential treatment of cancer in children. This healthy volunteer study is testing how four different formulations of the test medicine are taken up by the body over time (the pharmacokinetics) and the proportion of test medicine that enters the bloodstream (relative bioavailability). It is also looking to assess the safety and tolerability of the test medicine and assess its swallowability and the impact of food on the test medicine.

Who can participate?
Healthy male and non-pregnant, non-lactating female volunteers of non-childbearing potential aged 18 to 55 years.

What does the study involve?
The study consists of 2 parts, each consisting of 4 study periods, involving up to 32 healthy volunteers. In all study periods the volunteers receive a single oral 600 mg dose of test medicine, as either the reference Capsule or one of three prototype capsules. For each period, volunteers enter the clinical unit on Day -1 (the day before dosing) and are discharged on Day 4 (72 hours post dose). There is a minimum washout period of 10 days between each administration of study drug. There is also a follow up phone call 7 to 10 days following the final dose. Volunteer's blood and urine samples are collected throughout the study for analysis of the test medicine and for their safety. Volunteers are expected to be involved in this study for about up to approximately 10 weeks, from screening to the follow-up visit.

What are the potential benefits and risks of participating?
Participants get no medical benefit from taking part in this study. However, development of a cancer treatment for children may benefit the paediatric population as a whole. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. Full information on possible side effects is provided to volunteers in the Participant Information Sheet/Informed Consent Form. Volunteers are closely monitored during the study and safety assessments are performed regularly.

Where is the study run from?
Chugai (Japan)

When is the study starting and how long is it expected to run for?
October 2021 to March 2022.

Who is funding the study?
Chugai (Japan)

Who is the main contact?
regulatory@chugai-pharm.co.uk

Contact information

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Public

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Additional identifiers

EudraCT/CTIS number
2021-005346-14

IRAS number
306461

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
JP43291, IRAS 306461

Study information

Scientific Title
A two part, four way crossover, randomised, open-label study designed to evaluate the relative bioavailability of novel oral alectinib tablet formulations compared with oral reference alectinib capsule, in the fasted and fed state in healthy subjects

Study objectives
Primary objectives:
To determine the relative bioavailability of alectinib and its M4 metabolite following single oral doses of novel alectinib oral tablet prototype formulations in comparison with a reference alectinib capsule formulation in the fasted (Part 1) and fed (Part 2) state

Secondary objectives:
1. To determine the pharmacokinetics (PK) of alectinib and its M4 metabolite following single oral doses of alectinib oral tablet prototype formulations or reference alectinib capsule formulation in the fasted (Part 1) and fed (Part 2) state
2. To provide additional safety and tolerability information for alectinib oral tablet prototype formulations or reference alectinib capsule formulation in the fasted (Part 1) and fed (Part 2) state
3. To evaluate the swallowability of the alectinib oral tablet prototype formulations and alectinib capsule formulation

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 01/12/2021, HSC REC B (Unit 5, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, Co. Antrim, BT28 2RF, UK; +44 28 9536 1400; RECB@hscni.net), ref: 21/NI/0177

Study design
Single centre two-part open-label randomised 4-way cross-over trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a Participant information sheet

Health condition(s) or problem(s) studied
Cancer

Interventions
Participants will receive a single oral 600 mg dose of one of the following across four study periods each lasting 4 days with a minimum 10 day washout period in between each period:
1. Reference alectinib capsule in the fasted and fed state
2. Alectinib prototype 1 tablet in the fasted and fed state
3. Alectinib prototype 2 tablet in the fasted and fed state
4. Alectinib prototype 3 tablet in the fasted and fed state

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Alectinib

Primary outcome measure
Relative bioavailability (Frel) for Cmax, AUC(0-last) and AUC(0-inf) of alectinib and its M4 metabolite measured throughout the study period

Secondary outcome measures
Measured throughout the study period:
1. PK parameters, including but not limited to: Tlag, Tmax, Cmax, AUC(0-last), AUC(0-inf), Lambda-z, T1/2, CL/F, Vz/F, MRT, and metabolite parent ratios for alectinib and its M4 metabolite

2. Incidence of adverse events (AEs), physical examinations and change from baseline for vital signs, electrocardiograms (ECGs), physical examinations and laboratory safety tests
3. Swallowability questionnaire utilising a 5-point rating scale

Overall study start date
27/10/2021

Completion date
22/03/2022

Eligibility

Key inclusion criteria
1. Healthy males or non-pregnant, non-lactating healthy females of non-childbearing potential
2. Aged 18 to 55 years inclusive at the time of signing informed consent
3. Body mass index (BMI) of 18.0 to 32.0 kg/m² as measured at screening
4. Must be willing and able to communicate and participate in the whole study
5. Must provide written informed consent
6. Must agree to adhere to the contraception requirements

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
32

Total final enrolment
29

Key exclusion criteria
1. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1
2. Subjects who are, or are immediate family members of, a study site or sponsor employee
3. Evidence of current SARS-CoV-2 infection
4. History of any drug or alcohol abuse in the past 2 years
5. Regular alcohol consumption in males >21 units per week and females >14 units per week (1 unit = ½ pint beer, or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type)
6. A confirmed positive alcohol breath test at screening or admission
7. Current smokers and those who have smoked within the last 12 months. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or admission

8. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
9. Females of childbearing potential including those who are pregnant or lactating (all female subjects must have a negative highly sensitive serum pregnancy test at screening and urine at all other time points). A woman is considered of childbearing potential unless she is permanently sterile (hysterectomy, bilateral salpingectomy, and bilateral oophorectomy) or is postmenopausal (had no menses for 12 months without an alternative medical cause and a serum follicle stimulating hormone [FSH] concentration ≥40 IU/L)
10. Male subjects with pregnant or lactating partners
11. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
12. Clinically significant abnormal clinical chemistry, haematology or urinalysis at screening as judged by the investigator. Subjects will be excluded if they have ALT, AST or total bilirubin above the upper limit of the reference range or haemoglobin less than the lower limit of the reference range, neutrophil or lymphocyte count below the lower limit of normal or creatine kinase 1.25 × the upper limit of the reference range without an alternative explanation (e.g. physical activity)
13. Confirmed positive drugs of abuse test result at screening or admission
14. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) antibody results
15. Evidence of renal impairment at screening, as indicated by an estimated glomerular filtration rate (eGFR) of <80 mL/min/1.73m² using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula or any other evidence of renal impairment
16. History of clinically significant cardiovascular, renal, hepatic, dermatological, chronic respiratory or gastrointestinal disease, neurological or psychiatric disorder, as judged by the investigator or history of visual disturbances (e.g. blurred vision, vitreous floaters, visual impairment, reduced visual acuity, asthenopia, and diplopia) unless determined to be clinically not significant by agreement between the investigator and the sponsor's medical monitor
17. Subjects with a history of cholecystectomy or gall stones
18. Subjects with known deglutition/oesophageal pathology which can affect transit of food /drink, or who have any swallowing difficulties/evidence of swallowing impairment
19. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
20. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
21. Subjects with a resting heart rate of <50 beats per min as determined by ECG or vital signs measurement at screening or as a mean of triplicate ECG at baseline measurement on pre-dose Day 1 of Period 1 (mean of triplicate ECG observation for ventricular rate will take precedence over heart rate as measured by vital signs assessment if there is a discord)
22. Clinically significant findings on ECG including but not limited to prolonged QTcF, second degree heart block or greater
23. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
24. Subjects who are taking, or have taken, any prescribed or over-the-counter drug or herbal remedies (other than up to 4 g of paracetamol per day and HRT) in the 14 days before first IMP administration. COVID-19 vaccines are accepted concomitant medications. Exceptions may apply on a case by case basis, if considered not to interfere with the objectives of the study, as determined by the investigator.
25. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
31/12/2021

Date of final enrolment
06/02/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Quotient Sciences Limited
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Sponsor type
Industry

Website
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Funder(s)

Funder type
Industry

Funder Name
Chugai Pharmaceutical Co., Ltd.

Results and Publications

Publication and dissemination plan
1. Internal report
2. Submission to regulatory authorities

Intention to publish date
22/03/2023

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 their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

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			28/06/2023	No	No