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A study in healthy volunteers to assess the different formulations (recipes) of the drug product (alectinib)

Submission date
30/09/2022

Recruitment status
No longer recruiting

Registration date
07/10/2022

Overall study status
Completed

Last Edited
05/04/2024

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] 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 taste (palatability) 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 6 study periods involving up to 26 healthy volunteers. In all study periods, the volunteers receive a single oral 600 mg dose of test medicine, as either the reference capsule, powder for oral suspension, oral powder or minitablet. 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. Following both Period 3 and Period 5 there will be a minimum 14 day period to allow the data to be analysed. 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 41 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?

Who is funding the study?
Chugai (Japan)

Who is the main contact?
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003298-78

Integrated Research Application System (IRAS)
301567

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
JP43290, IRAS 301567

Study information

Scientific Title
Single part, open-label, phase 1 study designed to evaluate the relative bioavailability of oral alectinib formulations compared with an oral reference alectinib capsule, in healthy subjects

Study objectives
Primary objective:
To determine the relative bioavailability of alectinib and its M4 metabolite following single oral doses of alectinib powder for oral suspension, oral powder and minitablet oral formulations in comparison with a reference alectinib capsule formulation

Secondary objectives:
1.To determine the pharmacokinetics (PK) of alectinib and its M4 metabolite following single oral doses of alectinib capsule formulation, alectinib powder for oral suspension, oral powder and minitablet oral formulations
2. To provide additional safety and tolerability information for alectinib powder for oral suspension, oral powder and minitablet oral formulations
3. To evaluate the taste attributes (smell, sweetness, bitterness, flavour, mouthfeel/texture, grittiness and aftertaste) and overall palatability of the alectinib powder for oral suspension, oral powder and minitablet oral formulations

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 23/09/2021, Fast Track REC (2 Redman Place, Stratford, London. E20 1JQ, UK; no telephone number provided; fasttrack.rec@hra.nhs.uk), ref: 21/FT/0103

Study design
Single centre open label non-randomised trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Participants will receive a single oral 600 mg dose of one of the following across six study periods:
1. Reference alectinib capsule in the fasted state
2. Alectinib powder for oral suspension in the fed or fasted state
3. Alectinib oral powder in the fed or fasted state
4. Alectinib minitablet in the fed or fasted state

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. Following both Period 3 and Period 5 there will be a minimum 14 day period to allow the data to be analysed. 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 41 weeks, from screening to the follow-up visit.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Relative bioavailability (Frel) for Cmax, AUC(0-last) and AUC(0-inf) of alectinib and its M4 metabolite for alectinib powder for oral suspension, alectinib oral powder and alectinib minitablet formulations compared to a reference alectinib capsule formulation in plasma, measured using blood samples at pre-dose and multiple timepoints up to 72 h post-dose

Key secondary outcome(s))
1. Pharmacokinetic (PK) parameters, including but not limited to: Tlag, Tmax, Cmax, C24, AUC(0-last), AUC(0-inf), Lambda-z, T1/2, CL/F, Vz/F and metabolite parent ratios for alectinib and its M4

metabolite in plasma, measured using blood samples at pre-dose and multiple timepoints up to 72 h post-dose
2. Additional safety and tolerability information for alectinib collected by assessing adverse events (AEs), vital signs, electrocardiograms (ECGs), physical examinations and laboratory safety tests, from the time of signing the informed consent form up until the follow-up visit (up to 41 weeks)
3. Palatability, assessed using a 9-point rating scale immediately after dosing

Completion date
01/08/2022

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 defined in the protocol

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
26

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. Subjects who have previously had evidence of COVID-19 infection may be permitted to continue in future treatment periods, on a case by case basis, as per the judgement of the investigator and sponsors' medical monitor, provided the subject is asymptomatic, has recovered, a minimum of 14 days have passed since the initial

diagnosis, and the subject has a negative PCR or antigen test before admission to the clinical unit.
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. Clinically significant abnormal clinical chemistry, haematology or urinalysis at screening as judged by the investigator. Subjects will be excluded if they have ALT, aspartate aminotransferase 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 creatinine kinase 1.25 × the upper limit of the reference range without an alternative explanation (e.g. physical activity).
12. Confirmed positive drugs of abuse test result at screening or admission
13 Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) antibody results
14. Evidence of renal impairment at screening, as indicated by an eGFR of <80 ml/min/1.73 m2 using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula or any other evidence of renal impairment
15. 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
16. Subjects with a history of cholecystectomy or gall stones
17. Serious adverse reaction or serious hypersensitivity to any drug or the formulation excipients
18. Presence or history of clinically significant allergy requiring treatment, as judged by the investigator. Hay fever is allowed unless it is active
19. 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 or ventricular rate will take precedence over heart rate as measured by vital signs assessment if there is a discord)
20. Clinically significant findings on ECG including but not limited to prolonged QTcF, second degree heart block or greater
21. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
22. 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.

23. Failure to satisfy the investigator of fitness to participate for any other reason

Date of first enrolment
12/10/2021

Date of final enrolment
02/11/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
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Sponsor information

Organisation
Chugai Pharmaceutical Co., Ltd.

Funder(s)

Funder type
Not defined

Funder Name
Chugai Pharmaceutical Co., Ltd.

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 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes