ISRCTN40852430 https://doi.org/10.1186/ISRCTN40852430

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

Submission date 23/12/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 03/01/2023	**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 developing a new oral formulation of the test medicine, alectinib, for the treatment of certain types of cancer, namely metastatic (cancer that has spread in the body from where it started) non-small cell lung cancer. The aim of this healthy volunteer study is to compare a new tablet formulation of the test medicine against the approved existing capsule formulation. This study is comparing how the two different formulations of the test medicine are taken up by the body (the pharmacokinetics) in the fed and fasted (empty stomach) states. The study is also looking at the safety and tolerability of 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 two parts, each consisting of two study periods, involving up to 32 healthy volunteers. In Part 1 of the study the volunteers receive a single oral 600 mg dose of test medicine, as either the reference capsule or tablet in the fed state on two separate occasions. In Part 2 of the study the volunteers receive a single oral 600 mg dose of test medicine, as either the reference capsule or tablet in the fasted state on two separate occasions. 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 visit 7 to 10 days following the final dose. Volunteer's blood samples are collected throughout the study for analysis of the test medicine and for their safety alongside urine samples for their safety. Volunteers are expected to be involved in this study for up to approximately 8 weeks, from screening to the follow-up visit.

What are the possible risks and benefits of participating?
Participants get no medical benefit from taking part in this study. However, development of a treatment for cancer may benefit the 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?
November 2022 to March 2023

Who is funding the study?
Chugai (Japan)

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

Contact information

Type(s)
Public

Contact name
Mr William Davidson

Contact details
Mulliner House
Flanders Road
London
United Kingdom
W4 1NN
+44 (0)20 8987 5632
Regulatory@chugai-pharm.co.uk

Type(s)
Principal investigator

Contact name
Dr Somasekhara Menakuru

Contact details
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 3031000
recruitment@weneedyou.co.uk

Type(s)
Scientific

Contact name
Ms Miki Nomura

Contact details
2-1-1 Nihonbashi-Muromachi
Chuo-Ku, Tokyo
Japan
103-8324
+81 (0)3 3281 6611
JP44468@mail.chugai-pharm.co.jp

Additional identifiers

Integrated Research Application System (IRAS)
1006569

Protocol serial number
Quotient Code: QSC300271, Protocol Number: JP44468

Study information

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

Study objectives
The trial will meet the following primary and secondary objectives:

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

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

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 11/01/2023, London - Surrey Borders REC (London HRA Centre, 2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8104, +44 (0)207 104 8143, +44

(0)207 104 8057; surreyborders.rec@hra.nhs.uk); ref: 22/LO/0834
2. Approved 11/01/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 17122/0009/001-0001
The HRA has approved deferral of publication of trial details.

Primary study design
Interventional

Study design
Single centre two-part two-way crossover randomized open-label relative bioavailability study

Study type(s)
Other

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

Interventions
Part 1
Across two study periods, each lasting 4 days with a minimum 10 day washout period in between the periods, participants will receive a single oral 600 mg dose of one of the following in the fed state in each period:
1. Reference alectinib capsule
2. Alectinib tablet

Part 2
Across two study periods, each lasting 4 days with a minimum 10 day washout period in between the periods, participants will receive a single oral 600 mg dose of one of the following in the fasted state in each period:
1. Reference alectinib capsule
2. Alectinib tablet

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, its M4 metabolite and total exposure (alectinib + M4) in plasma, measured using blood samples at pre-dose and multiple timepoints up to 72 h post-dose

Key secondary outcome(s)
1. PK parameters where appropriate, including but not limited to: Tmax, Cmax, AUC(0-last), AUC (0-inf), T1/2 and metabolite parent ratios for alectinib, its M4 metabolite and total exposure (alectinib + M4) in plasma, measured using blood samples at pre-dose and multiple timepoints up to 72 h post-dose

2. Incidence of adverse events (AEs) and change from baseline for 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 (7 to 10 days post-final dose)

Completion date
17/03/2023

Eligibility

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

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
32

Key exclusion criteria
1. Serious adverse reaction or serious hypersensitivity to any drug or formulation excipients
2. Presence or history of clinically significant allergy requiring treatment, as judged by the Investigator. Hay fever is allowed unless it is active
3. 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
4. Subjects with a history of cholecystectomy or gall stones
5. Subjects with known deglutition/oesophageal pathology which can affect transit of food /drink, or who have any swallowing difficulties/evidence of swallowing impairment

6. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or delegate at screening
7. Evidence of current SARS-CoV-2 infection
8. Clinically significant abnormal clinical chemistry, haematology or urinalysis 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)
9. Positive hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab) or human immunodeficiency virus (HIV) 1 and 2 antibody results
10. 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; 2009) equation or any other evidence of renal impairment
11. Subjects with a resting heart rate of <50 beats per min as determined by a mean of triplicate 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 for each study part (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)
12. Clinically significant findings on ECG including but not limited to prolonged QTcF, second degree heart block or greater
13. 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)
14. Subjects who have received any IMP in a clinical research study within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer
15. Donation of blood or plasma within the previous 3 months or loss of greater than 400 mL of blood
16. 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, HRT or hormonal contraception) in the 14 days before first IMP administration. COVID-19 vaccines are accepted concomitant medications. Exceptions may apply, as determined by the Investigator, if each of the following criteria are met: medication with a short half-life if the washout is such that no pharmacodynamic activity is expected by the time of dosing with IMP; and if the use of medication does not jeopardise the safety of the trial subject; and if the use of medication is not considered to interfere with the objectives of the study
17. History of any drug or alcohol abuse in the past 2 years
18. Regular alcohol consumption in males >21 units per week and in 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)
19. A confirmed positive alcohol breath test at screening or each admission
20. Current smokers and those who have smoked within the last 12 months
21. A confirmed breath carbon monoxide reading of greater than 10 ppm at screening or each admission
22. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 12 months
23. Confirmed positive drugs of abuse test result at screening or each admission
24. Male subjects with pregnant or lactating partners
25. Subjects who are, or are immediate family members of, a study site or sponsor employee
26. Failure to satisfy the Investigator of fitness to participate for any other reason

Date of first enrolment
13/01/2023

Date of final enrolment
17/03/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Chugai Pharmaceutical Co., Ltd.

Funder(s)

Funder type
Industry

Funder Name
Chugai Pharmaceutical Co., Ltd.

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study are not expected to be made available because of 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