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A study evaluating the interaction of the body with (pharmacokinetics) and safety of ipatasertib and darolutamide in patients with castration-resistant prostate cancer (CRPC)

Submission date
08/10/2020

Recruitment status
No longer recruiting

Registration date
06/11/2020

Overall study status
Completed

Last Edited
30/01/2026

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This is a study to assess the safety, tolerability, and the drug-drug interaction of the combined administration of two drugs (ipatasertib and darolutamide) in patients with prostate cancer. The primary purpose of this study is:
1: To evaluate the effect of darolutamide on the pharmacokinetics of ipatasertib and its primary metabolite M1 (G-037720)
2: To evaluate the effect of ipatasertib on the pharmacokinetics of darolutamide and its primary metabolite keto-darolutamide
(Pharmacokinetics investigates the uptake, distribution, turnover, and excretion of a drug. In this case, the investigation is aimed to see whether the pharmacokinetics of either ipatasertib or darolutamide is affected by the administration of the two drugs at the same time, which might result in an increase or a decrease of the ipatasertib/darolutamide concentrations in the body.)

Who can participate?
Males with castration-resistant prostate cancer will participate in this study

What does the study involve?
The study will comprise a screening period before the drug is taken and several treatment cycles thereafter. The screening period is 28 days prior to first administration of the study drug, and each cycle has 28 days. The total duration of the study depends on how many cycles the subject actually participates.

What are the possible benefits and risks of participating?
There is no guarantee that the patient will benefit from taking part in this clinical research study. It is possible if the patients are taking the study drugs that it may delay the growth of your cancer or extend your life. However, they may receive no medical benefit, and the study drugs may produce side effects and be harmful to the patient. The patient's cancer may not get better, or may even get worse while they are participating in this study. During the study some side

effects (unwanted effects or health problems) from the study drug or from the study procedures may be experienced. These side effects could vary from person to person.
The knowledge learned from this study may be helpful to other people with cancer in the future.

Where is the study run from?
1. Arensia Exploratory Medicine (Georgia)
2. Arensia Exploratory Medicine (Moldova)
3. Arensia Exploratory Medicine (Ukraine)

When is the study starting and how long is it expected to run for?
July 2020 to June 2024

Who is funding the study?
F. Hoffmann-La Roche Ltd. (Switzerland)

Who is the main contact?
global.trial_information@roche.com

Contact information

Type(s)
Scientific

Contact name
Dr Clinical Trials

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
GP42658

Study information

Scientific Title

An open-label, multicenter, 2-arm, phase Ib study to evaluate the pharmacokinetic drug- drug interaction between darolutamide and ipatasertib and the safety of the combination in castration-resistant prostate cancer

Study objectives
To assess the safety, tolerability, and the drug-drug interaction (DDI) of the combined administration of oral ipatasertib and oral darolutamide in CRPC patients

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 18/09/2020, Independent Local Ethics Committee (13a Tevdore Mgvdeli str, 3rd floor, 0112 Tbilisi, Georgia; +995 322342127; giasvan@gmail.com), ref: none provided
2. Approved 23/10/2020, Ethics Committee at Medical Center of Limited Liability Company “Harmoniya Krazy” (01135, Ukraine, Kyiv, Chornovola str., 12; +38 0442279432; no email provided), ref: none provided

Study design
Open-label multicenter 2-arm Phase Ib study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
This is a non-randomized, open-label, single sequence, crossover study. All subjects will receive both study drugs. There are 2 study arms (with approximately 15 subjects each) that will be executed sequentially. Whether Arm 2 will be executed will be determined after review of interim PK and safety data derived from patients in Arm 1. In addition, the dose of ipatasertib to be used in Arm 2 (i.e., 400 mg or 500 mg) will be selected based on this interim analysis.

Patients in Arm 1 will receive the following treatments:
Cycle 1:
Period 1: ipatasertib monotherapy (400 mg QD) from Day 1 to Day 10
Period 2: ipatasertib (400 mg QD) + darolutamide (600 mg twice daily [BID]) combination from Day 11 to Day 28
Cycle 2 and beyond:
Ipatasertib (400 mg QD) + darolutamide (600 mg BID) combination from Day 1 to Day 28 in each cycle

Patients in Arm 2 will receive the following treatments:
Cycle 1:
Period 1: darolutamide monotherapy (600 mg BID) from Day 1 to Day 10
Period 2: darolutamide (600 mg BID) + ipatasertib (400 mg or 500 mg QD) combination

from Day 11 to Day 28
Cycle 2 and beyond:
Darolutamide (600 mg BID) + ipatasertib (400 mg or 500 mg QD) combination from Day 1 to Day 28 in each cycle
Whether Arm 2 will be executed will be determined after review of interim PK and safety data derived from patients in Arm 1. In addition, the dose of ipatasertib to be used in Arm 2 (i.e., 400 mg or 500 mg) will be selected based on this interim analysis.

The study treatment will be given to the patients beyond Cycle 2 (each cycle will last 28 days) until disease progression, intolerable toxicity, withdrawal of consent, the decision of the Investigator, or study termination.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Darolutamide, ipatasertib

Primary outcome(s)
The safety, tolerability, and the DDI of study drugs assessed through pharmacokinetic analysis measured using:
Arm 1: Plasma samples will be collected on Day 10 and Day 28 of Cycle 1, where ipatasertib and M1 (G-037720) levels will be measured on Day 10 and Day 28 of Cycle 1 and darolutamide and keto-darolutamide will be measured only on Day 28 of Cycle 1
Arm 2: Plasma samples will be collected on Day 10 and Day 28 of Cycle 1, where darolutamide and keto-darolutamide levels will be measured on Day 10 and Day 28 of Cycle1 and ipatasertib and M1 (G-037720) will be measured only on Day 28 of Cycle 1

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
01/06/2024

Eligibility

Key inclusion criteria
General Inclusion Criteria:
1. Age ≥18 years
2. Eastern Collaborative Oncology Group performance status of 0 or 1 at screening
3. Adequate hematologic and organ function
4. Ability to comply with the study protocol, per Investigator judgment
5. Life expectancy of at least 6 months
6. Agreement to remain abstinent or use contraceptive measures, and agreement to refrain from donating sperm

Disease-Specific Inclusion Criteria:
7. Histologically confirmed prostate adenocarcinoma without neuroendocrine differentiation or

small-cell features and has progressed during treatment of at least one hormonal therapy
8.Asymptomatic or mildly symptomatic form of prostate cancer
9. Progressive disease before initiating study treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
Male

Total final enrolment
15

Key exclusion criteria
General Exclusion Criteria:
1. History of malabsorption syndrome or other condition that would interfere with enteral absorption or other impairment of gastrointestinal (GI) function
2. Liver cirrhosis, current alcohol abuse, or current known active infection with hepatitis B virus (HBV) or hepatitis C virus (HCV), or other clinically significant history of liver disease
3. Need of more than 10 mg/day of prednisone or an equivalent dose of other corticosteroids as a current systemic corticosteroid therapy to treat a chronic disease
4. History of another malignancy within 5 years prior, unless the patient has undergone potentially curative therapy with no evidence of disease and are deemed by the treating physician to have a recurrence rate of < 5% at 5 years
5. Any other diseases; cardiovascular, pulmonary, or metabolic dysfunction; physical examination finding; or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or renders the patients at high risk from treatment complications

Disease-Specific Exclusion Criteria:
6. Pathologic findings consistent with small-cell or neuroendocrine carcinoma of the prostate
7. Any therapy including chemotherapy or biological therapy for the treatment of CRPC In the case of hormone-sensitive prostate cancer, chemotherapy is permitted provided that it is initiated within 6 months from the time of first castration
8. Known untreated or active central nervous system (CNS) metastases
9. Use of any medications (only for the first 12 days of Arm 1) that may have the potential to affect heart rate or QTc Interval

Darolutamide-Specific Exclusion Criteria:
10. Uncontrolled hypertension, recent stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, congestive heart failure New York Heart Association (NYHA) Class III or IV
11. Gastrointestinal disorder or procedure which expects to interfere significantly with absorption of darolutamide
12. Known hypersensitivity to darolutamide or any of its ingredients

Ipatasertib-Specific Exclusion Criteria:
13. Type 1 or Type 2 diabetes mellitus requiring insulin at study entry
14. History of inflammatory bowel disease
15. Any ongoing cardiac arrhythmias (including uncontrolled atrial fibrillation) that require medical therapy
16. Uncontrolled or untreated hypercholesterolemia or hypertriglyceridemia
17. Lung disease

Date of first enrolment
17/11/2020

Date of final enrolment
23/03/2021

Locations

Countries of recruitment
Georgia

Moldova

Ukraine

Study participating centre
Arensia Exploratory Medicine
13a Tevdore Mgvdeli st.
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Study participating centre
Arensia Exploratory Medicine
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Moldova
2025

Study participating centre
Arensia Exploratory Medicine
31 Blyzhnya St.
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Sponsor information

Organisation
Roche (United States) (Genentech, Inc)

ROR
https://ror.org/011qkaj49

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, Inc., Genentech USA, Inc., Genentech USA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		30/09/2022	30/01/2026	Yes	No