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# A study in healthy male volunteers to assess how the radiolabelled test medicine enters, is broken down and is removed from the body when given by mouth in the form of a tablet and liquid, and when given by short infusion into a vein

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| **Submission date**<br>22/02/2022 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[ ] Protocol<br>[ ] Statistical analysis plan<br>[ ] Results<br>[ ] Individual participant data<br>[ ] Record updated in last year |
| **Registration date**<br>07/04/2022 | **Overall study status**<br>Completed | |
| **Last Edited**<br>07/04/2022 | **Condition category**<br>Cancer | |

## Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, capivasertib, for the potential treatment of primary breast and prostate cancer. Cancer is a condition where cells in a specific part of the body grow and reproduce uncontrollably, causing a growth called a tumour. The cancerous cells can invade and destroy surrounding healthy tissue, including organs. The four most common types of cancer within the UK are breast, lung, prostate and bowel cancer. This two-part healthy volunteer study will try to identify the absolute bioavailability (amount of the test medicine that enters the bloodstream), mass balance recovery (how much radioactivity can be recovered from the urine and faeces) and the rates and routes of elimination of the test medicine. Two out of three recipes of the test medicine are radiolabelled with carbon-14. Radiolabelled means that the test medicine has a radioactive component (carbon-14) which helps us to track where the test medicine is in the body.

Who can participate?
Healthy male volunteers aged 30-65 years

What does the study involve?
In Part 1, volunteers will receive a single dose of two non-radiolabelled oral tablets in the fasted state followed by an intravenous infusion (solution into the vein) of radiolabelled test medicine 1 hour 15 mins minutes later. Volunteers will be discharged from the clinical unit on Day 5. In Part 2, volunteers will receive a single oral dose of a radiolabelled oral solution in the fasted state. Volunteers will be discharged on Day 8 but may be required to remain at the clinical unit until Day 10 if the mass balance criteria have not been met by Day 8. Volunteers will receive a follow-up phone call between Day 15 and Day 19. Volunteer's blood, urine and faeces will be

taken throughout the study for analysis of the test medicine, radiation and for safety. Volunteers are expected to be involved in this study for about 9 weeks from screening to the follow-up call.

What are the possible benefits and risks of participating?
Participants will get no medical benefit from taking part in this study. It is hoped that the development of a product to improve the treatment of primary breast and prostate cancer will be of benefit to patients with this condition. As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy volunteers. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation. Volunteers may experience side effects from the test medicine. Full information on possible side effects is provided to volunteers in the patient information sheet/informed consent form. When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals. Risks are further mitigated by ensuring that only volunteers who meet all inclusion/exclusion criteria are included and that if the safety of any volunteer represents a concern they will be withdrawn. There will be an extended period of overnight fasting for the volunteers taking part in this study. To ensure adequate fluid intake, the volunteers will be allowed fluids and will be monitored for signs of dehydration and fatigue. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not persist. One recipe of the test medicine will be administered via intravenous injection. Volunteers may experience some mild irritation at the site of injection, and they will be closely monitored to ensure any local irritation does not persist. By taking part in the study the volunteers will be exposed to a small amount of radiation.

Where is the study run from?
AstraZeneca (Sweden)

When is the study starting and how long is it expected to run for?
February 2022 to August 2022

Who is funding the study?
AstraZeneca (Sweden)

Who is the main contact?
Roberto Sommavilla
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# Contact information

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Scientific

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## Additional identifiers

### Clinical Trials Information System (CTIS)
2022-000277-59

### Integrated Research Application System (IRAS)
1005025

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
D3614C00007, IRAS 1005025

## Study information

### Scientific Title
A Phase I study to investigate the absolute bioavailability, absorption, metabolism, distribution and excretion of [14C]AZD5363 (capivasertib) in healthy male subjects

### Study objectives
Part 1:
1. To determine the absolute oral bioavailability of capivasertib
2. To determine the pharmacokinetics (PK) of capivasertib and [14C]AZD5363 (capivasertib) in plasma

Part 2:
1. To determine the PK of capivasertib in plasma and urine; and total radioactivity in plasma and whole blood
2. To determine the mass balance recovery after a single oral dose of [14C]AZD5363 (capivasertib)
3. To determine the routes and rates of elimination of [14C]AZD5363 (capivasertib)
4. To evaluate the extent of distribution of total radioactivity into blood cells

Part 1:
1. To provide additional safety and tolerability information for capivasertib

Part 2:
1. To identify the chemical structure of each metabolite accounting for more than 10% of circulating total radioactivity or accounting for 10% or more of the dose in excreta
2. To provide additional safety and tolerability information for capivasertib

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 11/03/2022, Fast Track REC (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8012; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0039

## Study design
Non-randomized study

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Breast and prostate cancer

## Interventions
This is a study in healthy male volunteers to assess how the radiolabelled test medicine, [14C] AZD5363 (capivasertib), enters, is broken down and is removed from the body when given by mouth in the form of a tablet, an oral solution, and when given by short infusion into a vein. This study is not a randomised trial.

This study consists of two parts involving up to 8 healthy male participants in a single group. All participants will take part in both parts of the study to receive three different doses of test medicine. There is no placebo. In Part 1, on Day 1, participants will receive a single dose of 400 mg capivasertib (2 x 200 mg non-radiolabelled oral tablets) in the fasted state followed by an intravenous infusion (solution into the vein) of radiolabelled test medicine containing 100 µg [14C]AZD5363 (capivasertib), 1 hour 15 min minutes later. Participants will be discharged from the clinical unit on Day 5. In Part 2, on Day 1, following a minimum washout period of 14 days, participants who completed part 1 will receive a single oral dose of a radiolabelled oral solution containing 400 mg [14C]AZD5363 (capivasertib), in the fasted state. Participants will be

discharged on Day 8, however, they may be required to remain at the clinical unit until Day 10 if the mass balance criteria have not been met. Participants will receive a follow-up phone call on Day 15 to Day 19, after they have left the ward, to check on their wellbeing.

Blood, urine and faeces will be taken throughout the study for analysis of the test medicine, its breakdown products, radiation and for safety.

Participants will be involved in the study for approximately 9 weeks from screening to the follow-up call. Participants will visit the ward to be screened before they take part, to check that they are healthy.

### Intervention Type
Drug

### Phase
Phase I

### Drug/device/biological/vaccine name(s)
Capivasertib

### Primary outcome(s)
Part 1:
Levels of drug and metabolites in blood assessed using high-performance liquid chromatography (HPLC) analysis of blood samples taken at 22 timepoints between Day 1 and Day 5

Part 2:
Absorption, distribution, metabolism, and excretion (ADME) characteristics calculated from levels of drug and metabolites in blood, faeces, urine and saliva assessed using HPLC analysis of samples collected throughout the trial between day 1 and (up to) day 10

### Key secondary outcome(s))
Part 1:
1. Other safety measures (including physical examinations, vital signs, ECGs and laboratory safety tests) will be assessed by standard phase 1 unit monitoring at screening, from Day -1 to discharge from the ward on Day 5

Part 2:
1. Chemical structure identification of breakdown products of the test medicine accounting for more than 10% of circulating total radioactivity or accounting for 10% or more of the dose in excreta, assessed by high-resolution mass spectrometry and HPLC analysis of samples collected throughout the trial between Day 1 and (up to) Day 10
2. Other safety measures (including physical examinations, vital signs, ECGs and laboratory safety tests) assessed by standard phase 1 unit monitoring, at screening, from Day -1 to discharge from the ward on Day 10

### Completion date
01/08/2022

## Eligibility

### Key inclusion criteria

1. Provision of signed and dated, written informed consent prior to any study-specific procedures
2. Must be willing and able to communicate and participate in the whole study
3. Healthy males aged 30 to 65 years inclusive at the time of signing the informed consent
4. Must be vasectomised (at least 6 months prior to screening) and must agree to adhere to the contraception requirements
5. Body mass index (BMI) of 18.0 to 32.0 kg/m², weigh at least 50 kg and no more than 100 kg inclusive as measured at screening
6. Must have regular bowel movements (i.e. average stool production of ≥1 and ≤3 stools per day)
7. Provision of signed, written and dated informed consent for optional genetic research. If a subject declines to participate in the genetic component of the study, there will be no penalty or loss of benefit to the subject. The subject will not be excluded from other aspects of the study described in this protocol.

## Participant type(s)
Healthy volunteer

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 years

## Sex
Male

## Key exclusion criteria
1. History of any clinically significant disease or disorder which, in the opinion of the investigator, may either put the volunteer at risk because of participation in the study, or influence the results or the volunteer's ability to participate in the study
2. History of any clinically significant disease or disorder (e.g. cardiovascular, pulmonary, GI (including but not limited to refractory nausea and vomiting, malabsorption syndrome, chronic GI diseases, previous cholecystectomy, inability to swallow the formulated product or previous significant bowel resection, or other condition that would preclude adequate absorption of capivasertib), liver, renal, neurological, musculoskeletal, endocrine, metabolic, malignant, psychiatric, major physical impairment, skin abnormalities and glucose metabolism abnormalities) which, in the opinion of the investigator, may either put the subject at risk because of participation in the study, or influence the ADME of drugs.
3. History of latent or chronic infections (e.g. tuberculosis, recurrent sinusitis, genital herpes, urinary tract infections) or at risk of infection (surgery, trauma or significant infection within previous 90 days, history of skin abscesses within previous 90 days)
4. Any clinically significant illness, medical/surgical procedure, or trauma within 4 weeks of the first administration of IMP
5. History of severe allergy/hypersensitivity or ongoing allergy/hypersensitivity, as judged by the investigator or history of hypersensitivity to drugs with a similar chemical structure or class to capivasertib. Hay fever is allowed unless it is active.
6. Any known or suspected hypersensitivity or contraindication to the components of the study drug, capivasertib, judged to be clinically relevant by the investigator

7. History of severe COVID-19 (e.g. hospitalisation, extracorporeal membrane oxygenation, mechanically ventilated) in the last 6 months
8. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the investigator or delegate at screening
9. Any clinically significant abnormal findings in vital signs, at screening or pre-dose, as judged by the investigator
10. QTcF >450 msec or QT >500 msec or other clinically significant ECG abnormality, as judged by the investigator, at screening or pre-dose, or a history of additional risk factors for Torsades de Points (e.g. heart failure, hypokalaemia, family history of long QT syndrome), which in the opinion of the Investigator may put the volunteer at risk.
11. Evidence of current SARS-CoV-2 infection within 2 weeks of first IMP administration
12. Any clinically significant abnormalities in clinical chemistry, haematology, or urinalysis results, as judged by the investigator
13. Total bilirubin (TBL) ≤1.5 × ULN or ≤3 × ULN in the presence of documented Gilbert's syndrome (unconjugated hyperbilirubinemia)
14. Clinically significant abnormal fasting blood glucose or triglycerides at screening
15. Any positive result on screening for serum hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (HCV Ab), and human immunodeficiency virus (HIV) 1 and 2 antibody
16. Evidence of renal impairment at screening, as indicated by an estimated CLcr of <70 ml/min using the Cockcroft-Gault equation
17. Has received another new chemical entity (defined as a compound which has not been approved for marketing) within the 90 days prior to Day 1, or less than 5 elimination half-lives prior to Day 1, whichever is longer. Note: subjects consented and screened, but not randomised in this study or a previous Phase I study, are not excluded.
18. Subjects who report having previously received capivasertib
19. Radiation exposure, including that from the present study, excluding background radiation but including diagnostic x-rays and other medical exposures, exceeding 5 mSv in the last 12 months or 10 mSv in the last 5 years. No occupationally exposed worker, as defined in the Ionising Radiation Regulations 2017, shall participate in the study.
20. Subjects who have been administered IMP in an ADME study in the last 12 months
21. Plasma donation within 1 month of screening or any donation or loss (e.g. due to trauma or surgery) of >500 mL blood within the previous 3 months or 1350 ml of blood in 12 months prior to the current study

To see the remaining exclusion criteria please refer to the clinical protocol.

### Date of first enrolment
11/04/2022

### Date of final enrolment
25/04/2022

## Locations

### Countries of recruitment
United Kingdom

England

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

# Sponsor information

**Organisation**
AstraZeneca (Sweden)

**ROR**
https://ror.org/04wwrrg31

# Funder(s)

**Funder type**
Industry

**Funder Name**
AstraZeneca

**Alternative Name(s)**
AstraZeneca PLC, Pearl Therapeutics, AZ

**Funding Body Type**
Government organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
United Kingdom

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated during and/or analysed during the current study are/will be available upon request via https://vivli.org/

## IPD sharing plan summary

Available on request

## 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 |