Capivasertib-280: a Phase III study of capivasertib and docetaxel versus placebo and docetaxel in metastatic castration-resistant prostate cancer

Why are we performing this research?
- Capivasertib is a drug that blocks the activity of a protein called AKT, reducing the growth of cancer cells. Docetaxel is a type of chemotherapy used to treat prostate cancer that has spread from its original site (metastatic) and no longer responds to hormone therapy (castration-resistant prostate cancer).

How are we performing this research?
- Approximately 350 participants will be randomly assigned to one of two treatment groups: participants in the first group will be treated with capivasertib and docetaxel, and participants in the second group will receive placebo and docetaxel.

Who will participate in this study?
- Participants in this study must have metastatic castration-resistant prostate cancer.

Where can I access more information?
- This study is ongoing, and results are available. The study is expected to complete in 2026.

Key inclusion criteria:
- Adults at least 18 years of age with metastatic CRPC.
- No prior chemotherapy for metastatic CRPC.
- Prior ARTA (abiraterone, enzalutamide, or chemotherapy) for at least 3 months and evidence of disease progression (radiological or via clinical symptoms) at or after treatment.
- Serum testosterone level >450 ng/mL.
- Eligible for docetaxel treatment (investigator assessment).
- Ongoing ADT.

Key exclusion criteria:
- Radiotherapy to ≥20% of bone marrow within 4 weeks of the start of treatment.
- Major surgery within 4 weeks of the start of treatment.
- Brain metastases or spinal cord compression.
- Cardiac abnormalities.
- Clinically significant glucose metabolism abnormalities.
- Inflammatory or infiltrative disease involving bone.
- Inadequate bone marrow reserve or organ function.
- History of another primary malignancy except for non-melanoma skin cancer or a curable condition that has been in remission for ≥5 years.
- A bleeding disorder.
- Confirmed osteolytic bone metastases.
- Sickle cell disease.
- Uncontrolled hypertension.
- Impaired renal or hepatic function.
- Active infection.
- Cytopenia.

Study endpoints:
- Primary endpoint: OS defined as the time from randomization until the date of death due to any cause.

Rationale for combining capivasertib and docetaxel in treating patients with metastatic CRPC
- The PI3K/AKT signaling pathway plays a pivotal role in prostate cancer, with deregulation of this signaling pathway associated with the development of metastatic CRPC and resistance to chemotherapy.
- Capivasertib is a potent, selective inhibitor of all three AKT isoforms.
- This study is ongoing, and no results are available. The study is expected to complete in 2026.

Current treatment of metastatic CRPC and unmet need
- Docetaxel is the standard first-line chemotherapy for patients with metastatic CRPC, including those whose disease has progressed on an ARTA.
- However, most patients developing resistance to chemotherapy androgen-signaling inhibitors (ASIs) from the ProCAID trial using the same capivasertib dose and schedule.

Study background
- This is an ongoing, double-blind, placebo-controlled trial of capivasertib in combination with docetaxel compared with placebo and docetaxel in patients with metastatic CRPC who have not previously received chemotherapy for metastatic CRPC, but whose disease has progressed on treatment with an ARTA.

It is important to note that patients with newly diagnosed prostate cancer or those with asymptomatic disease within the past 5 years and of a low potential risk of recurrence are not eligible for this study.

For more information, please refer to the study's clinical trial registration number: NCT05348577.