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Update on CAPItello-280 Phase III trial of *Truqap* in metastatic castration-resistant prostate cancer

AstraZeneca is discontinuing the CAPItello-280 Phase III trial evaluating the efficacy and safety of *Truqap* (capivasertib) in combination with docetaxel and androgen-deprivation therapy (ADT) compared to docetaxel and ADT with placebo in patients with metastatic castration-resistant prostate cancer (mCRPC).

This decision is based on the recommendation of the Independent Data Monitoring Committee (IDMC) following their review of data from a pre-specified interim analysis, which concluded that the *Truqap* combination was unlikely to meet the dual primary endpoints of radiographic progression-free survival (rPFS) and overall survival (OS) versus the comparator arm upon trial completion. The safety profile for *Truqap* was consistent with previous trials.

The Company will work with investigators to ensure the necessary follow up with patients. Data from the trial will inform ongoing research.

Notes

Prostate cancer
Prostate cancer is the second most prevalent cancer in men and the fifth leading cause of male cancer death globally, with an incidence of more than 1.4 million and over 397,000 deaths in 2022.[1]

Metastatic prostate cancer is associated with a significant mortality rate, with only one third of patients surviving five years after diagnosis.[2] Development of prostate cancer is often driven by male sex hormones called androgens, including testosterone.[3]

Metastatic castration-resistant prostate cancer
Approximately 10-20% of men with advanced prostate cancer will develop castration-resistant prostate cancer within five years.[4] In patients with mCRPC, their prostate cancer grows and spreads to other parts of the body despite the use of androgen-deprivation therapy to block the action of male sex hormones.[3] At least 84% of these men will have metastases at the time of CRPC diagnosis and, of those patients with no metastases at CRPC diagnosis, 33% are likely to develop metastases within two years.[4] Approximately half of patients with mCRPC may receive only one line of active treatment, and those that go on to receive further treatment often have diminishing benefit of subsequent therapies.[5-6]

Despite the advances in mCRPC treatment with taxane and new hormonal agent treatments, there is high unmet need in this population.[4,7,8]

CAPItello-280
CAPItello-280 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of *Truqap* in combination with docetaxel and ADT compared to docetaxel and ADT in combination with placebo in patients with mCRPC.

The global trial enrolled 1,033 adult patients with histologically confirmed prostate adenocarcinoma with evidence of mCRPC with progression of disease despite ADT. The dual primary endpoints of the CAPItello-280 trial are rPFS as assessed by investigator and OS in the overall trial population. Key secondary endpoints include OS and rPFS as assessed by investigator in patients with mCRPC and PTEN-deficient tumours, OS and rPFS as assessed by investigator in patients with mCRPC and PTEN-proficient tumours, time to pain progression (TTPP) in the overall trial population and time to first symptomatic skeletal-related event (SSRE) in the overall trial population.

Truqap
Truqap is a first-in-class, potent, adenosine triphosphate (ATP)-competitive inhibitor of all three AKT isoforms (AKT1/2/3). *Truqap* 400mg is administered twice daily according to an intermittent dosing schedule of four days on and three days off. This was chosen in early phase trials based on tolerability and the degree of target inhibition.

Truqap in combination with *Faslodex* (fulvestrant) is approved in the US, EU, Japan, China and several other countries for the treatment of adult patients with HR-positive (or estrogen receptor-positive), HER2-negative locally advanced or metastatic breast cancer with one or more biomarker alterations (*PIK3CA*, *AKT1* or *PTEN*) following recurrence or progression on or after an endocrine-based regimen based on the results from the CAPItello-291 trial. *Truqap* is also approved in Australia for the treatment of adult patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer following recurrence or progression on or after an endocrine based regimen based on these trial results.

Truqap is being evaluated in ongoing Phase III trials for the treatment of breast and prostate cancers.

Truqap was discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics (and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited).

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

Contacts
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here

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