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Truqap combination in PTEN-deficient metastatic hormone-sensitive prostate cancer demonstrated statistically significant and clinically meaningful improvement in radiographic progression-free survival in CAPItello-281 Phase III trial

First and only AKT inhibitor combination to demonstrate benefit in this specific subtype of prostate cancer

Positive high-level results from the CAPItello-281 Phase III trial showed that AstraZeneca's *Truqap* (capivasertib) in combination with abiraterone and androgen deprivation therapy (ADT) demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of radiographic progression-free survival (rPFS) versus abiraterone and ADT with placebo in patients with PTEN-deficient *de novo* metastatic hormone-sensitive prostate cancer (mHSPC).

Overall survival (OS) data were immature at the time of this analysis; however, the *Truqap* combination showed an early trend towards an OS improvement versus abiraterone and ADT with placebo. The trial will continue as planned to further assess OS as a key secondary endpoint.

Prostate cancer is the second most prevalent cancer in men and the fifth leading cause of male cancer death globally.[1] Only one third of patients with metastatic prostate cancer survive five years after diagnosis.[2] Newly diagnosed mHSPC is an aggressive form of the disease associated with poor outcomes and survival.[3,4] Approximately 200,000 patients are diagnosed with mHSPC each year, and one in four have PTEN-deficient tumours.[5] Patients with a tumour biomarker of PTEN deficiency have a particularly poor prognosis.[6]

Karim Fizazi, MD, PhD, Institut Gustave Roussy, and University of Paris Saclay in Villejuif, France, and principal investigator for the trial said: "Patients with this aggressive form of prostate cancer with tumour PTEN deficiency currently face a particularly poor prognosis, and there is an urgent need for new treatments that improve upon current therapies. The results seen with capivasertib in combination with abiraterone-prednisone and androgen deprivation therapy in the CAPItello-281 trial represent a step forward for these patients."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "These results show for the first time, that adding an AKT inhibitor to a standard-of-care therapy can provide benefit to patients with a biomarker of PTEN-deficient metastatic hormone-sensitive prostate cancer. By targeting a key driver of the disease, we have been able to improve upon current therapies and demonstrate the potential role of this combination in an area of critical unmet need. It will be important to see greater maturity in key secondary endpoints including overall survival."

The safety profile of *Truqap* in combination with abiraterone and ADT in CAPItello-281 was broadly consistent with the known profile of each medicine.

Data will be presented at a forthcoming medical meeting and shared with global regulatory authorities.

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 approximately 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.[7]

Metastatic hormone-sensitive prostate cancer
In patients with mHSPC, also known as metastatic castration-sensitive prostate cancer (mCSPC), prostate cancer cells need high levels of androgens to drive cancer growth.[4,7] Hormone therapies, such as ADT, are widely used to block the action of male sex hormones and lower the levels of androgens in the body.[4,8] However, resistance to these therapies is common and there is a need to extend their use to delay disease progression and castration resistance, where the prostate cancer grows and spreads to other parts of the body despite the use of these therapies.[3,4,8]

In patients with *de novo* mHSPC, the cancer has spread to distant parts of the body at the time of first diagnosis.[9]

PTEN-loss or deficiency fuels the growth of cancer cells, leading to dysregulation of the PI3K/AKT pathway, and is associated with poor outcomes in patients with prostate cancer.[6,10]

CAPItello-281
CAPItello-281 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of *Truqap* in combination with abiraterone and ADT versus abiraterone and ADT in combination with placebo in the treatment of patients with PTEN-deficient *de novo* mHSPC.

The global trial enrolled 1,012 adult patients with histologically confirmed *de novo* hormone-sensitive prostate adenocarcinoma and PTEN deficiency as confirmed by central testing. The primary endpoint of the CAPItello-281 trial is rPFS as assessed by investigator, with OS as a secondary endpoint.

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 is approved in the US, EU, Japan and several other countries for the treatment of adult patients with HR-positive (or ER-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 currently being evaluated in Phase III trials for the treatment of breast cancer (CAPItello-292) and prostate cancer (CAPItello-280 and CAPItello-281) in combination with established treatments.

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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Adrian Kemp
Company Secretary
AstraZeneca PLC