Combination of new drug, CB-839, with everolimus stops advanced kidney tumors growing

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Munich, Germany: The first drug to target a key enzyme that cancer cells need to keep them alive has shown that it is effective in controlling disease in patients with advanced kidney cancer when it is used in combination with another anti-cancer drug, everolimus.

Dr Funda Meric-Bernstam told the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany, today (Wednesday) that out of 15 patients with clear cell and papillary renal cell cancer who had been given the new drug CB-839 together with everolimus in a phase I clinical trial and for whom data were available to analyse, 93% had their tumour controlled by the regimen: the tumour shrank by more than 30% in one patient (called a partial response), was stable in 13 other patients (stable disease), and grew by more than 20% in the last patient (called progressive disease).

Clear cell is the most common form of kidney cancer, accounting for 75% of cases, and in this study all the patients with this form of the disease (12) had their disease controlled. Papillary renal cell cancer is the next most common form of the disease and accounts for 10% of cases.

CB-839 targets glutaminase, an enzyme involved in the conversion of glutamine to glutamate, which is an important nutrient for cancer cells - without it they die. Dr Meric-Bernstam, who is chair of the Department of Investigational Cancer Therapeutics and Medical Director of the

Institute of Personalized Cancer Therapy at the University of Texas MD Anderson Cancer Centre (USA), said: "Glutaminase is a very interesting target and previous work in the lab has shown that CB-839 is effective at inhibiting it in renal cell cancers and that it enhances the anti-tumour efficacy of everolimus.

"To date, tumours in 93% of patients with clear cell and papillary renal cell cancers have had tumour control from the regimen, with a median [average] time without their cancer growing of 8.5 months. For more than half of these patients their time on this treatment has been longer than the time they remained on their prior treatment, which is considered to be a good sign."

The median number of previous treatments the patients had received was two, some of which included inhibitors of the mTOR cell signalling pathways, and checkpoint inhibitors that reactivate the body's immune system to attack the cancer. All had advanced or metastatic disease (cancer that has started to spread to other parts of the body). They were given CB-839 in oral doses that ranged from 400-800 mg twice a day in combination with a fixed oral dose of everolimus at 10 mg once a day. The patients tolerated the treatment well, with most adverse side effects being no more severe than was consistent with everolimus and advanced cancer.

"These results suggest that CB-839 is a very tolerable drug with significant potential in combination therapy for kidney cancer patients," said Dr Meric-Bernstam.

The researchers continue to enrol and treat patients in this trial, and they plan to evaluate CB-839 in combination with everolimus in a randomised controlled trial in the future. "In the current trial, we are also assessing the efficacy of CB-839 in kidney cancer in combination with another drug, cabozantinib. In another trial, we are evaluating the efficacy of

CB-839 in combination with immunotherapy in kidney cancer, lung cancer and melanoma patients," she concluded.

Chair of the scientific committee for the Symposium, Professor Jean Charles Soria from the Institut Gustave Roussy (France), commented: "Compounds able to modulate cancer metabolism represent a new and innovative area for cancer drug development."

Provided by ECCO-the European CanCer Organisation

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