Drug matched to patients according to tumour gene testing shows signs of being effective

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Dublin, Ireland: Treatment with capivasertib, a drug designed to work against a particular gene mutation found in some tumours, shows signs of being effective in a trial of 35 patients presented today (Tuesday) at the 30th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Dublin, Ireland.

The phase 2 trial (EAY131-Y) is part of a larger USA study, called NCI-MATCH (EAY131), that aims to determine whether cancer patients can be treated successfully by selecting therapies that target gene abnormalities found in their tumours, rather than by cancer type.

Researchers say their results provide further evidence that the approach of tailoring treatment according to tumour genes could offer more effective treatments for individual patients in the future. The more traditional approach is to treat patients based on what has worked in the past for other patients with the same type of cancer.

The research was presented by Dr. Kevin Kalinsky, Assistant Professor of Medicine, New York Presbyterian-Columbia University Irving Medical Centre, USA. He explained: "Capivasertib can be taken by mouth and it's a type of drug called an AKT inhibitor. This means it binds to a molecule called AKT that has mutated a change that plays a role in helping cancer cells grow. In a prior phase 2 study, capivasertib has shown potential in treating an aggressive form of breast cancer.

"In this trial, we wanted to see if capivasertib could be used in patients with any type of cancer whose tumours have the mutation that leads the AKT molecule to become over-active and make the cancer grow."

Patients were selected by having the cells from their tumours tested. Each of the 35 patients in the trial was carrying the AKT mutation in the cells of their tumour. Although this mutation occurs in several different types of cancer, overall it is rare. Researchers found the mutation in 1.3% of patients (70 of 5548) tested centrally in the NCI-MATCH trial.

In all patients on the EAY131-Y study, the cancer had spread to other parts of the body, and most had already received three or more previous treatments. The patients were treated with capivasertib, taken by mouth twice a day, in weekly cycles of four days with treatment and three days without treatment.

Patients' tumours were measured by imaging, such as CT scans, before and after treatment. In the best confirmed responses, the tumour reduced in size in eight patients (23%), and in 16 patients (46%) the tumour did not grow but did not shrink either. In three patients (9%), the tumour grew.

Researchers observed the following side effects from the drug, saying that physicians should carefully manage these in patients being treated with capivasertib: high blood sugar, fatigue, diarrhoea, nausea, vomiting, and skin rash.

Dr. Kalinsky said: "Overall, 23% of the patients in our trial experienced a positive response, which was defined as tumour shrinkage from before they started capivasertib. We determined in advance that if 16% of patients experienced this response from the treatment, it would be a signal to move the drug on to a larger trial. This is a positive finding in a trial with patients whose cancers continued to grow despite previous

treatments."

Researchers estimate that, six months after the treatment, the percentage of patients alive and without their tumours growing was 52%.

"This study is a limited but important piece of evidence. More trials are needed to learn the benefit in each tumour type and to understand why some patients did not have a response while others had a prolonged time without tumour growth," Dr. Kalinsky added.

Professor Charles Swanton of the Francis Crick Institute, London, UK, is scientific co-chair of the EORTC-NCI-AACR Symposium and was not involved in the research. He said: "Although we understand more than ever about the role of genes in different cancers, there is still a lack of evidence on using this knowledge to guide treatments and improve patient survival. Outside of a trial setting, this approach is not widely available.

"This study is a small but important piece of evidence and it's part of a larger study that will help us move towards more personalised cancer treatments.

"This trial approach is particularly important for those with rarer cancers where we know less about which treatments are most effective and conducting patient trials is difficult."

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