RE-AKT

Can a new drug combination (Capivasertib and Enzalutamide) be an effective treatment for metastatic castration resistant prostate cancer?

Capivasertib in combination with enzalutamide for metastatic castration resistant prostate cancer: results from the RE-AKT trial.

Who carried out the study?

The RE-AKT trial was funded by AstraZeneca and Astellas, who provided the drugs. The Chief Investigator is Professor Johann de Bono of The Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research. RE-AKT is coordinated by the Clinical Trials and Statistics Unit at The Institute of Cancer Research (ICR-CTSU).

What was the aim of the study?

The RE-AKT clinical trial is a study for men who have had treatment for prostate cancer and whose cancer continues to grow. The main aim of the RE-AKT trial was to:

- Find out if a drug called Enzalutamide given in combination with a newer drug called capivasertib could stop the cancer from progressing;
- know more about the sides effects of having the two drugs together;
- Identify the genetic markers that may make the treatment more effective in some people.

Why was the research needed?

Doctors usually treat advanced prostate cancer with hormone therapy and chemotherapy. These can work well for a period of time, but the cancer can start to grow again.

Enzalutamide is a type of hormone therapy that is used for men with advanced prostate cancer who have already had other types of hormone therapy and a type of chemotherapy called docetaxel. Capivasertib is a newer drug which stops signals that cancer cells use to divide and grow. Researchers wanted to see if the combination of the two drugs would help control the growth of the cancer for longer.

Who participated in the study and what treatment did they receive?

In the main part of the study, 137 men previously treated with Abiraterone volunteered to take part from 15 hospitals in the UK between July 2016 and September 2019. 100 were well enough to take part. They were randomly allocated to receive either enzalutamide and capiversatib or enzalutamide

and a dummy tablet (placebo). Neither patients nor clinicians knew which treatment was given to make the study more robust.

A further 31 patients who had previously been treated with Enzalutamide alone also volunteered to take part from 5 hospitals in the UK between September 2016 and April 2018. 13 patients in this group were all given the drug combination.

What happened during the study?

Capivasertib (or placebo) was taken twice a day for 4 days with a 3 day break for a 28-day cycle. 160mg Enzalutamide was taken once a day every day without a break.

The effect of the drugs on the cancer was measured by blood tests as well as by CT scans and bone scans. The research team were looking whether the prostate cancer was stable or it "responded" to treatment.

What did the trial show?

In the group of patients who had received enzalutamide before joining the study, only one of the thirteen patients receiving the combination treatment had a cancer that responded . The combination treatment did not seem to be effective in this group and this part of the study was stopped early on the recommendation of the independent committees monitoring the trial.

In the main part of the study, for those patients on treatment where response could be measured 12 weeks after start of treatment:

- 9 out of 47 patients (19.1%) were considered to have had a response to treatment in the enzalutamide/capivasertib group vs 9 out of 48 patients (18.8%) enzalutamide/placebo group.

In the main part of the study, the results were also analysed by the presence (or not) of a specific marker (PTEN loss) in the genetic make-up of their tumour. 26 patients had tumours that had the PTEN loss genetic marker, and 62 patients had tumours that did not (the tumours were what is called PTEN normal). Regardless of the treatment received:

- 1 out of 26 (3.8%) patients whose tumour carried the PTEN loss marker experienced a response. 7 .
- 17 out of 62 (27.4%) patients whose tumour was PTEN normal experienced a response.

Did the treatments have side effects?

- The most common side effects reported for the combination treatment were fatigue (6 out of 10 patients), diarrhoea (7 out of 10 patients) , decreased appetite (4 out of 10 patients) and nausea (4 out of 10 patients)
- Those side effects were generally mild and the symptoms could usually be relieved.

What do these results mean?

Although the combination treatment was shown to be safe and tolerable, treatment with Enzalutamide and Capivasertib did not perform better than enzalutamide alone for patients with advanced prostate cancer. The trial however did confirm that the PTEN loss biomarker was helpful in predicting patients whose prognosis was worse and whose tumour did not respond well to the treatment. This will lead to targeted further research into this specific patient group to understand the reasons for this and identify effective treatments.

Where can you learn more about this study?

For further information, please visit the RE-AKT trial page on the Institute of Cancer Research Clinical Trials and Statistics Unit's website: https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/our-research/clinical-trials/re-akt

Would you like to help influence cancer research in the future?

We are recruiting trial participants to become patient advocates to help us to develop and deliver our research. You can find out more about our work at the Institute of Cancer Research Clinical Trials and Statistics Unit on our website: https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit

If you would like to help us, then please contact us via email on ppi-icrctsu@icr.ac.uk and we will send you further details.