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Breast and ovarian cancer drug outperforms targeted hormone therapy in some men

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A drug used for breast and ovarian cancer is more effective than modern targeted hormone treatments at slowing progression and improving survival in some men with advanced prostate cancer, phase III clinical trial findings reveal.

The PROfound trial compared the genetically targeted cancer drug olaparib—already licensed for women with breast and ovarian cancer who have BRCA mutations—with the modern hormone treatments abiraterone and enzalutamide in patients who had advanced prostate cancer and faulty DNA repair genes.

The study, led by researchers at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, and Northwestern University, Chicago, USA, showed that treatment with olaparib in men withfaulty DNA repair genes significantly delayed disease progression by about four months compared with enzalutamide and abiraterone. Treatment with olaparib resulted in a 66 per cent greater delay in disease progression.

The trial selected men who had been unsuccessfully treated with a modern hormone therapy and whose tumours had defects in at least one of 15 pre-selected DNA repair genes, including BRCA1 and BRCA2. The research follows on from an earlier trial, led by The Institute of Cancer Research (ICR) and The Royal Marsden, which found that around 80 per cent of men whose tumours had faults in the BRCA genes responded to olaparib.

For patients with genetic alterations in BRCA1, BRCA2 or ATM, the PROfound trial showed that the median length of time before the cancer got worse, known as progression-free survival, was 7.4 months with olaparib, compared to 3.6 months with targeted hormonal treatment. Additionally, median overall survival was 18.5 months with olaparib compared with 15 months with targeted hormonal treatment. However, researchers pointed out that the patients on the study needed longer follow-up to show a survival improvement conclusively.

The results were presented at the European Society for Medical Oncology (ESMO) Congress 2019 and demonstrate the efficacy of olaparib in men with advanced prostate cancer and gene defects involved in a cell's ability to repair its DNA.

The PROfound findings also showed that, like breast and lung cancers, prostate cancer has different disease sub-types. As a consequence, this phase III trial is the first to highlight the importance of genomic testing in prostate cancer patients, and the need to identify different patient groups and tailor treatment for them.

The researchers did find that adverse effects were more common with olaparib than with abiraterone or enzalutamide—16.4 per cent of patients discontinued olaparib because of adverse events, compared with 8.5 per cent with the modern hormone-based drugs. However, the duration of treatment with olaparib was twice as long.

The ICR discovered how to genetically target olaparib and worked with The Royal Marsden to develop the drug in clinical trials. The ICR also discovered, and developed with The Royal Marsden, abiraterone—which has transformed treatment for men with prostate cancer.

Professor Johann de Bono, Regius Professor of Cancer Research at The Institute of Cancer Research, London, and Consultant Medical

Oncologist at The Royal Marsden NHS Foundation Trust, who co-led the PROfound trial, said:

"Our clinical trial shows that olaparib, a pill without the side-effects of chemotherapy, is able to target an Achilles' heel in cancer cells. Olaparib is able to kill cancer cells with faulty DNA repair genes while sparing normal cells.

"This study is a powerful demonstration of the potential of precision medicine to transform the landscape for patients with the commonest of male cancers. I hope that within the next couple of years, olaparib will become the first precision medicine to become available as a standard treatment for men with prostate cancer.

"Our findings also have wider implications—in showing that prostate cancer, like many other cancer types, is really a range of sub-types of disease identifiable by their different arrays of genetic faults. It's essential that we become smarter in the way we treat prostate cancer, so that every man gets the treatment that will be of greatest benefit for them."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"It was scientists at the ICR who first discovered how to target olaparib at cancer's genetic weaknesses.Olaparib has already improved and extended the lives of women with ovarian and breast cancer and it's hugely positive to now see the results of this trial paving the way for olaparib to become an innovative new treatment for prostate cancer.

"It's only through discovering innovative treatments like olaparib that we're going to give doctors the treatment options they need to combat cancer's ability to evolve resistance and evade treatment. Our new Centre

for Cancer Drug Discovery, which we hope to finish next year, will help us discover the drugs needed to overcome cancer evolution and turn cancer into a long-term manageable disease."

Provided by Institute of Cancer Research