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New cancer drug Olaparib 'shows promise'

Researchers say a new type of cancer treatment has produced highly promising results in preliminary drug trials.

Olaparib was given to 19 patients with inherited forms of advanced breast, ovarian and prostate cancers caused by mutations of the BRCA1 and BRCA2 genes.

In 12 of the patients - none of whom had responded to other therapies - tumours shrank or stabilised.

The study, led by the Institute of Cancer Research, features in the New England Journal of Medicine.

CASE STUDY
Julian Lewis
Julian Lewis, 62, was treated with olaparib after being diagnosed with advanced prostate cancer.

Within a month or two levels of a key chemical marker of cancer went down to a low level, and have now stayed low for more than two years.

In addition, secondary tumours in his bones have almost disappeared.

He has experienced minor side-effects, such as stomach discomfort and mild nausea, but he said: "I hope to carry on with this for as long as possible.

Partly the aim is the obvious one of keeping my cancer cells in check, but there's a broader goal too: to help find out how long this drug can be used safely in other people."

One of the first patients to be given the treatment is still in remission after two years.

Olaparib - a member of a new class of drug called PARP inhibitors - targets cancer cells, but leaves healthy cells relatively unscathed.

The researchers, working with the pharmaceutical company AstraZeneca, found that patients experienced very few side-effects, and some reported the treatment was "much easier than chemotherapy".

Researcher Dr Johann de Bono said the drug should now be tested in larger trials.

He said: "This drug showed very impressive results in shrinking patients' tumours.

"It's giving patients who have already tried many conventional treatments long periods of remission, free from the symptoms of cancer or major side-effects."

Olaparib is the first successful example of a new type of personalised medicine using a technique called "synthetic lethality" - a subtle way of exploiting the body's own molecular weaknesses for positive effect.

In this case the drug takes advantage of the fact that while normal cells have several different ways of repairing damage to their DNA, one of these pathways is disabled by the BRCA mutations in tumour cells.

Olaparib blocks one of the repair pathways by shutting down a key enzyme called PARP.

BRCA MUTATIONS
BRCA1 or BRCA2 mutations weaken the cells' ability to repair DNA damage
They are thought to be responsible for about 5% of breast and ovarian cancers, and about 1-2% of early onset prostate cancers
Women with a BRCA mutation have a risk of up to 85% on breast cancer, and up to 60% on ovarian cancer
Men with a BRCA mutation have a risk of up to 15% on prostate cancer

This does not affect normal cells because they can call on an alternative repair mechanism, controlled by their healthy BRCA genes.

But in tumours cells, where the BRCA pathway is disabled by genetic mutation, there is no alternative repair mechanism, and the cells die.

Cancer cells with the BRCA1 or BRCA2 mutations are the first to be shown to be sensitive to PARP inhibitors.

But there is evidence that olaparib will also be effective in other cancers with different defects in the repair of DNA.

Professor Stan Kaye, who also worked on the study, said: "The next step is to test this drug on other more common types of ovarian and breast cancers where we hope it will be just as effective."

The researchers say the process of drug evaluation and registration may have to be revamped to take consideration of the fact that new generation cancer drugs target specific molecular defects, rather than types of cancer.

Dr Peter Sneddon, of the charity Cancer Research UK, said: "It is very encouraging to see the development of 'personalised treatment', tailored to the requirements of the individual patient, becoming a reality as it offers the opportunity to design new drugs that are truly selective.

"Although development of this drug is in its early stages, it is very exciting to see that it has the potential to work when other treatment options have failed."