# Targeted treatment plus chemotherapy could benefit women with ovarian cancer

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Conventional chemotherapy could further extend life in some women with ovarian cancer when used in tandem with a new type of targeted treatment, a new international study shows.

The research, published in the October issue of the journal *Clinical Cancer Research*, provides important evidence that PARP inhibitor drugs and chemotherapy can both be effective in the same patients, helping women live longer than they would if treated with chemotherapy alone.

The study, in women with mutations to BRCA genes – which increase the risk that ovarian cancer will relapse after treatment, as well as being linked to breast and other cancers – showed that ovarian cancers that have become resistant to PARP inhibitors often remain sensitive to conventional chemotherapy.

The study was led by researchers at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, and looked at follow-up data from patients who had previously taken part in clinical trials sponsored by pharmaceutical company AstraZeneca. The research was supported by grants from the Experimental Cancer Medicine Centre and a range of institutions including Cancer Research UK, the National Institute for Health Research and the Wellcome Trust.

The researchers monitored 89 patients with BRCA-mutated ovarian cancer at The Royal Marsden and other hospitals in the UK, Australia, Belgium, Israel and North America, all of whom received chemotherapy

following the development of resistance to a PARP inhibitor called olaparib.

Almost half (49 per cent) of olaparib-resistant patients showed a significant decrease in the size of their tumours when subsequently treated with platinum-based chemotherapy, a frequently-used treatment in ovarian cancer. The results show that a significant proportion of women with ovarian cancer could live longer if they received both treatments.

PARP inhibitors have the advantage of causing fewer and less toxic side-effects than traditional chemotherapy. They are being developed in clinical trials worldwide as a potential 'personalised' treatment for women with BRCA gene mutations, although some have also shown some benefit in patients with non-BRCA tumours.

The researchers also used high-tech new sequencing techniques to probe the precise genetic mechanisms responsible for drug resistance in ovarian tumours. Previously, tumours were thought to evolve resistance to both PARP inhibitors and platinum chemotherapy by acquiring new, secondary mutations to BRCA genes – transforming BRCA proteins from mutated, non-functioning forms back into working proteins.

However, in a small subset of six cases, the study found no sign of secondary BRCA mutations, suggesting that at least in these cases, cancer was developing resistance to PARP inhibitors and platinum-based chemotherapy in different ways.

Study leader Professor Stan Kaye, Cancer Research UK Professor of Medical Oncology at The Institute of Cancer Research, and Consultant at the Royal Marsden, said:

"Our study finds that for many women with ovarian cancer, it is not a

case of either/or chemotherapy or PARP inhibitors – there is a good chance that they may respond to both. Although some scientists were concerned that using PARP inhibitors would prevent chemotherapy from being effective, we've resolved that concern by showing that both drug types can work in the same patients.

"Ovarian cancer is a difficult disease to treat and our research does underline the complexity of cancer, and the many different routes it can use to become resistant to treatment. But it also presents us with an opportunity, by showing us that two different types of drug treatment given in sequence could potentially extend lives."

**More information:** 1. Although BRCA mutations are rare, affecting around one in every 500 women (in the USA), they dramatically increase the risk of developing cancers including breast and ovarian cancer and account for around 15 per cent of ovarian cancer cases. Source: National Cancer Institute factsheet BRCA1 and BRCA2: Cancer Risk and Genetic Testing: accessed online 30 August 2013.

Provided by Institute of Cancer Research