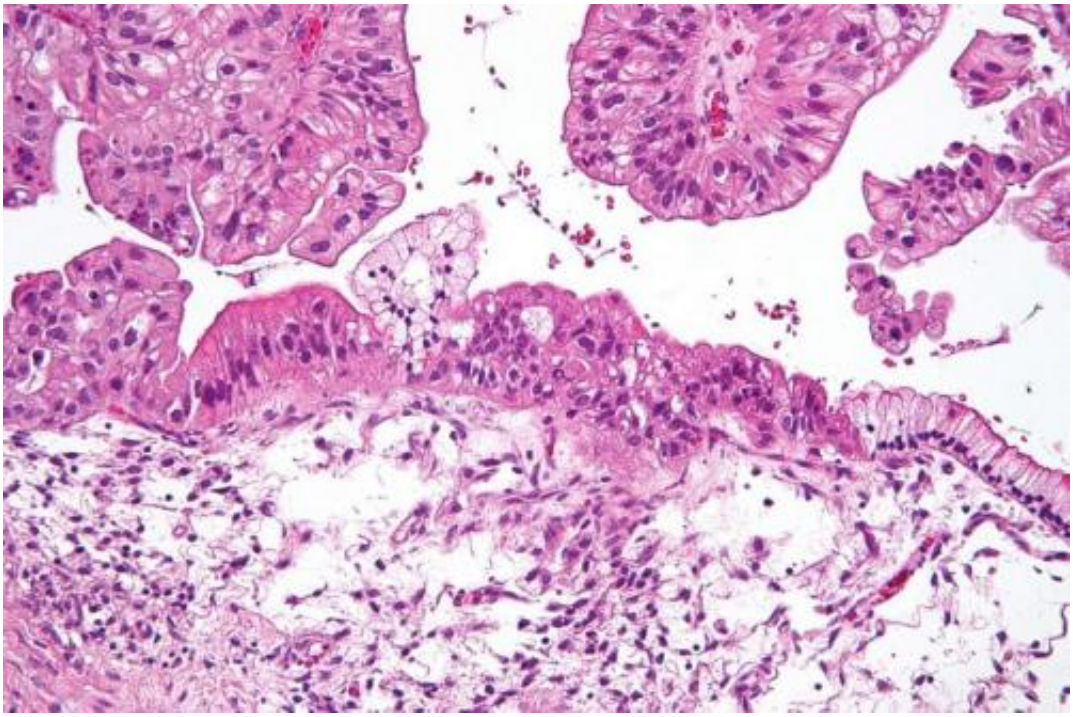
Drug combination shows promise in treatment-resistant advanced ovarian cancer

September 20 2021



Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. H&E stain. The micrograph shows: Simple mucinous epithelium (right) and mucinous epithelium that pseudo-stratifies (left - diagnostic of a LMP tumour). Epithelium in a frond-like architecture is seen at the top of image. Credit: Nephron /Wikipedia. CC BY-SA 3.0

A new combination of targeted drugs for a type of ovarian cancer has shown promising results in an early clinical trial—shrinking tumors in half of patients.

The combination of drugs—which both work by blocking signals cancer cells need to grow—could offer a new treatment option for women with an uncommon type of ovarian cancer that rarely responds to chemotherapy or hormone therapy.

Promising results

The phase I FRAME trial, led by a team at The Institute of Cancer Research, London and The Royal Marsden NHS Foundation Trust, tested the drugs—called VS-6766 and defactinib—in 25 patients with low-grade serous ovarian cancer.

Overall, nearly half (46 percent) of patients saw their tumors shrink significantly in response to the treatment.

Responses in patients who had a mutation in a gene called KRAS were even more promising. KRAS is one of the most commonly mutated genes in cancer, found in one quarter of all tumors. Until recently KRAS-driven tumors were extremely difficult to treat.

Nearly two-thirds of patients with a KRAS mutation (64 percent) saw their tumor shrink following treatment—suggesting that tumor profiling could be used to identify patients most likely to benefit from the new drug combination.

Targeted treatment

Participants lived an average of 23 months before their cancer progressed.

It is unusual to see such positive clinical responses in phase I clinical trials, which set out to determine the safety of the treatment, and

establish the dose that can be tolerated without unmanageable side effects.

Researchers at the ICR and The Royal Marsden recently established that VS-6766 remains active in the body for extended periods and can be given in an unconventional, innovative, twice-weekly schedule to deliver its potent anti-tumor effects while minimizing side effects. Patients also received defactinib twice daily.

Phase II trial already in progress

The results were presented Sunday at the 2021 European Society for Medical Oncology Congress (ESMO).

A Verastem-sponsored phase II trial led globally by Dr. Susana Banerjee from the ICR and The Royal Marsden is now recruiting to further test the effectiveness of the combination.

Low-grade serous ovarian cancer is an uncommon form of cancer that tends to develop at an earlier age than other types of ovarian cancer. Less than 13 percent of patients respond to chemotherapy and less than 14 percent respond to hormone therapy.

Recent advances have shown that MEK inhibitors—which block part of cancer's RAS-RAF-MEK-ERK signaling growth pathway—can cause tumors to shrink in around one out of four people with this type of cancer, but they tend to stop working as tumors develop resistance to treatment.

A new treatment option

Researchers believe the resistance may be triggered by a molecule called

p-FAK which is also involved in growth pathways. The current study tested whether using VS-6766, a dual RAF/MEK inhibitor, in combination with defactinib, a FAK inhibitor, could offer a new treatment option for patients and avoid drug resistance.

The treatment continued to work in patients who had already received a MEK inhibitor prior to the study.

In the US the combination of VS6766 and defactinib has already received breakthrough therapy designation by regulators, which aims to accelerate the development and approval of highly promising drugs.

The phase I FRAME trial was led by the Investigator Initiated Trials team within the Drug Development Unit at the ICR and The Royal Marsden.

Unmet need

Dr. Susana Banerjee, Team Leader in Women's Cancers at The Institute of Cancer Research, London, and Consultant Medical Oncologist and Research Lead for The Royal Marsden NHS Foundation Trust Gynaecology Unit, said:

"If these findings are confirmed in larger trials, they'll represent a significant advance in low-grade serous ovarian cancer treatment. I am delighted that this drug combination has worked so well in a group of patients who are in urgent need of new treatments including those who have previously been treated with a MEK inhibitor.

"We're very hopeful that this could become the standard of care for women with low-grade serous ovarian cancer."

Significant progress

Professor Kristian Helin, Chief Executive of The Institute of Cancer Research, London said:

"Overcoming cancer's ability to evolve resistance to treatment is a huge challenge for cancer research. This study has turned a deep understanding of how cancer fuels its growth and develops resistance into a highly targeted treatment for patients who currently have few treatment options.

"Scientists have been working to develop treatments that can effectively target KRAS-driven cancers for decades. It's fantastic that early trials indicate this treatment is highly effective for this patient group, and that a phase II trial has already begun."

'FRAME has given me hope'

After experiencing groin pain in 2006, Ruth Joy (64 from West Sussex) was diagnosed with stage 3 low-grade serous ovarian cancer at her local hospital and was referred to The Royal Marsden for treatment, which included surgery and chemotherapy. However, in 2016 a routine scan showed that, unfortunately, the cancer had returned and spread.

Ruth was then treated with letrozole, a hormone therapy, for 18 months and, when the cancer progressed, took part in two clinical trials at the hospital. In May 2020, Ruth relapsed again, and joined the FRAME study two months later. Over a year on, Ruth's cancer has not worsened and she has seen some tumor shrinkage. She said:

"Each time my cancer has progressed, I'm so lucky to have been thrown another lifeline by The Royal Marsden. FRAME has given me hope and,

while there are some side effects like fatigue, none have been able to stop me living my life. I can't speak highly enough of the hospital as, because of them, I'm still here today and have had the chance to meet my nine beautiful grandchildren.

"My family including Keith, my husband of three years and partner of 28, have always been so supportive and celebrating our milestones is incredibly important to me. The next is the 18th birthday of my eldest grandchild in 2024, who was born the year I was originally diagnosed, and I'm determined to be around to plan it."

Provided by Institute of Cancer Research

Citation: Drug combination shows promise in treatment-resistant advanced ovarian cancer (2021, September 20) retrieved 24 May 2024 from https://medicalxpress.com/news/2021-09-drug-combination-treatment-resistant-advanced-ovarian.html