

New drug combination found to be twice as effective for some ovarian cancer patients as next best treatment

June 5 2023



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A targeted drug combination for patients with a type of ovarian cancer could be nearly twice as effective as the next best treatment, according

to interim results from a phase II study.

Researchers hope these results, which are being presented at the [2023 American Society of Clinical Oncology \(ASCO\) Annual Meeting](#), will lead to a new option for patients with advanced low-grade serous ovarian cancer (LGSOC), a rare form of the disease that has a poor response rate to current treatments. The findings are published in a supplement to the *Journal of Clinical Oncology*.

The international RAMP-201 (ENGOTov60-National Cancer Research Institute (NCRI)/GOG3052) study, led by researchers from The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, London, and sponsored by Verastem Oncology, has tested avutometinib alone and in combination with defactinib in 29 patients with LGSOC. Both drugs are designed to block signals that encourage [cancer cells](#) to grow.

Approved treatment options available for patients with advanced LGSOC in the U.K. are currently limited to chemotherapy and hormone therapy, with response rates typically ranging from 0%–14%. Alongside standard treatment, LGSOC patients in England can access trametinib, a targeted treatment, via the Cancer Drugs Fund, which has a response rate of 26%.

Tumors shrink in half of patients

According to these results, nearly half (45%) of patients treated with avutometinib in combination with defactinib saw their tumors shrink significantly, suggesting the new combination could be almost twice as effective as the next best treatment.

Responses to the drug combination were particularly promising in those with a mutation in a gene called KRAS, with six in 10 (60%) patients

experiencing significant tumor shrinkage. However, nearly a third (29%) of patients without the mutation also had an encouraging response, which is also an improvement on [standard treatment](#).

Patients previously treated with other types of targeted therapies, including MEK inhibitors, also saw their tumors shrink following treatment with the drug combination.

Avutometinib is a dual RAF and MEK inhibitor, a type of targeted drug that blocks certain proteins that help control cancer growth and survival. Studies have shown the drug can become ineffective over time as tumors develop resistance to treatment.

However, when combined with defactinib—which is designed to combat a protein that encourages drug resistance—researchers believe avutometinib works more efficiently. This is confirmed by these results, which demonstrate that the drug combination is over four times more effective than avutometinib alone.

RAMP-201 follows the phase 1 FRAME trial, which tested avutometinib (then known as VS-6766) and defactinib on a slightly smaller cohort of patients with advanced LGSOC and was led by researchers from the ICR and The Royal Marsden. While survival data is not yet available from RAMP-201, results from FRAME indicate that this patient group lives an average of 23 months following treatment with this drug combination before their cancer progresses.

LGSOC accounts for about one in 10 cases of ovarian cancer, with around 700 women in the U.K. and 80,000 worldwide diagnosed each year. Compared with other forms of the disease, LGSOC tends to affect younger women.

Fantastic news

Global lead investigator of the study, Dr. Susana Banerjee, Consultant Medical Oncologist and Research Lead for The Royal Marsden NHS Foundation Trust Gynecology Unit and Team Leader in Women's Cancers at The Institute of Cancer Research, London, said, "These initial results could be fantastic news for women with low grade serous ovarian cancer, indicating a far more effective option than current treatments may be on the horizon.

"It's wonderful to see so many patients experience a meaningful response to this innovative drug combination and I'm so grateful to all who joined the trial, making this research possible. Low grade serous ovarian cancer does not respond well to currently approved treatments, so these results could represent a significant breakthrough in treating the disease.

"We are hopeful this drug combination will one day become a standard of care for women with low grade serous ovarian cancer."

'I felt relieved, amazed and so happy'

After being diagnosed with low grade [serous ovarian cancer](#) in 2009, Christine Cull, 71 from Coventry, found out the disease had returned in 2014. She was treated with chemotherapy and hormone therapy at her local hospital, which unfortunately didn't work, along with several surgeries. Christine joined the FRAME trial at The Royal Marsden in August 2020 and has been treated with this drug combination ever since. Her latest scan results showed no evidence of disease. She said,

"My lowest point throughout this experience was in 2019 when my local hospital said there was nothing more they could do for me—it was horrible. My cancer had completely resisted chemotherapy and [hormone therapy](#), and my team weren't able to operate again.

"Fortunately, my doctor referred me to The Royal Marsden who, as specialist cancer center, had the expertise to do another surgery. When the disease started growing again the next year, this trial had opened at the hospital, and I was chuffed to be able to join. I have scans every three months and each time we've seen the cancer getting smaller and smaller. After finding out recently that the [cancer](#) is currently not even visible on scans, I felt relieved, amazed and so happy to be able to pass this good news onto family and friends.

"The Royal Marsden means so much to me. The hospital gave me and my family hope when I thought my options were exhausted and, because of this trial, I'm able to live my life with my husband, three children and three grandchildren with barely any side effects."

More information: Susana N. Banerjee et al, Initial efficacy and safety results from ENGOT-ov60/GOG-3052/RAMP 201: A phase 2 study of avutometinib (VS-6766) ± defactinib in recurrent low-grade serous ovarian cancer (LGSOC)., *Journal of Clinical Oncology* (2023). [DOI: 10.1200/JCO.2023.41.16_suppl.5515](https://doi.org/10.1200/JCO.2023.41.16_suppl.5515)

Provided by Institute of Cancer Research

Citation: New drug combination found to be twice as effective for some ovarian cancer patients as next best treatment (2023, June 5) retrieved 15 May 2024 from <https://medicalxpress.com/news/2023-06-drug-combination-effective-ovarian-cancer.html>

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