Combination treatment shows significant reduction in disease growth in patients with advanced endometrial cancer

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In a study published in the *New England Journal of Medicine*, researchers at the UC San Diego School of Medicine and Moores Cancer Center at UC San Diego Health found the combination of immunotherapy and chemotherapy in patients with advanced endometrial cancer resulted in a significant reduction in disease growth when compared with chemotherapy alone. Credit: UC San Diego Health

In a study published in the March 27, 2023, online edition of the *New England Journal of Medicine*, researchers at the University of California San Diego School of Medicine and Moores Cancer Center at UC San Diego Health found the combination of immunotherapy (pembrolizumab) and chemotherapy in patients with advanced or recurrent/advanced endometrial cancer resulted in a significant reduction in disease growth when compared with chemotherapy alone.

Endometrial cancer, a type of cancer that begins in the lining of the uterus, is one of the few cancers with a rising incidence and death rate. Experts estimate that by 2040, it is projected to be the third most prevalent cancer and the fourth leading cause of cancer death among women.

In the past four decades, there have been limited advancements in treatment for patients with advanced endometrial cancer.

"These results may transform the way we care for patients with advanced stage or recurrent/advanced uterine cancer. Currently, chemotherapy alone is used in the first-line treatment for patients with this disease," said Ramez N. Eskander, MD, associate professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences at UC San Diego School of Medicine, principal investigator and lead author of the study.

"It is critical that we work to identify effective and innovative treatments and combination therapies, such as immunotherapy and chemotherapy, to attack this cancer and give patients more time to live their lives fully."

In the blinded, placebo-controlled, randomized Phase III trial, 816 people with Stage III or IV endometrial cancer were assigned to two groups: deficient mismatch repair (dMMR) and proficient mismatch repair (pMMR), and treated with either immunotherapy in combination

with chemotherapy or with chemotherapy alone.

In cancer, mismatch repair (MMR) proteins describe cells that have mutations in certain genes that are involved in correcting mistakes made when DNA is copied in a cell. pMMR is the "normal" state our cells are in, where the MMR pathway is active and functional. dMMR is the "mutant" state, where the MMR pathway is not working as usual.

At a follow up time of 12-months, the dMMR group showed a 70% reduction in the risk of disease growth in the participants who received immunotherapy in addition to chemotherapy. The pMMR group showed a 46% reduction in the risk of disease growth in the participants who received immunotherapy in addition to chemotherapy.

"These are exciting results that are both statistically significant and reflective of a clinically meaningful benefit," said Eskander, gynecologic oncologist at UC San Diego Health.

There are more than 60,000 cases of endometrial cancer diagnosed each year. Symptoms include vaginal bleeding/spotting, pelvic pain, bloating or change in bowel or bladder habits.

Eskander emphasizes that endometrial cancer is most common in post-menopausal women, and vaginal bleeding/spotting in this patient population can sometimes be overlooked.

"Anyone experiencing vaginal bleeding, even spotting, when post-menopausal should speak to their doctor. Early diagnosis often results in better outcomes."

Eskander adds next steps to further the study results are to receive approval from the Food & Drug Administration and implement the new treatment approach as a standard practice.

More information: Ramez N. Eskander et al, Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2302312. www.nejm.org/doi/10.1056/NEJMoa2302312