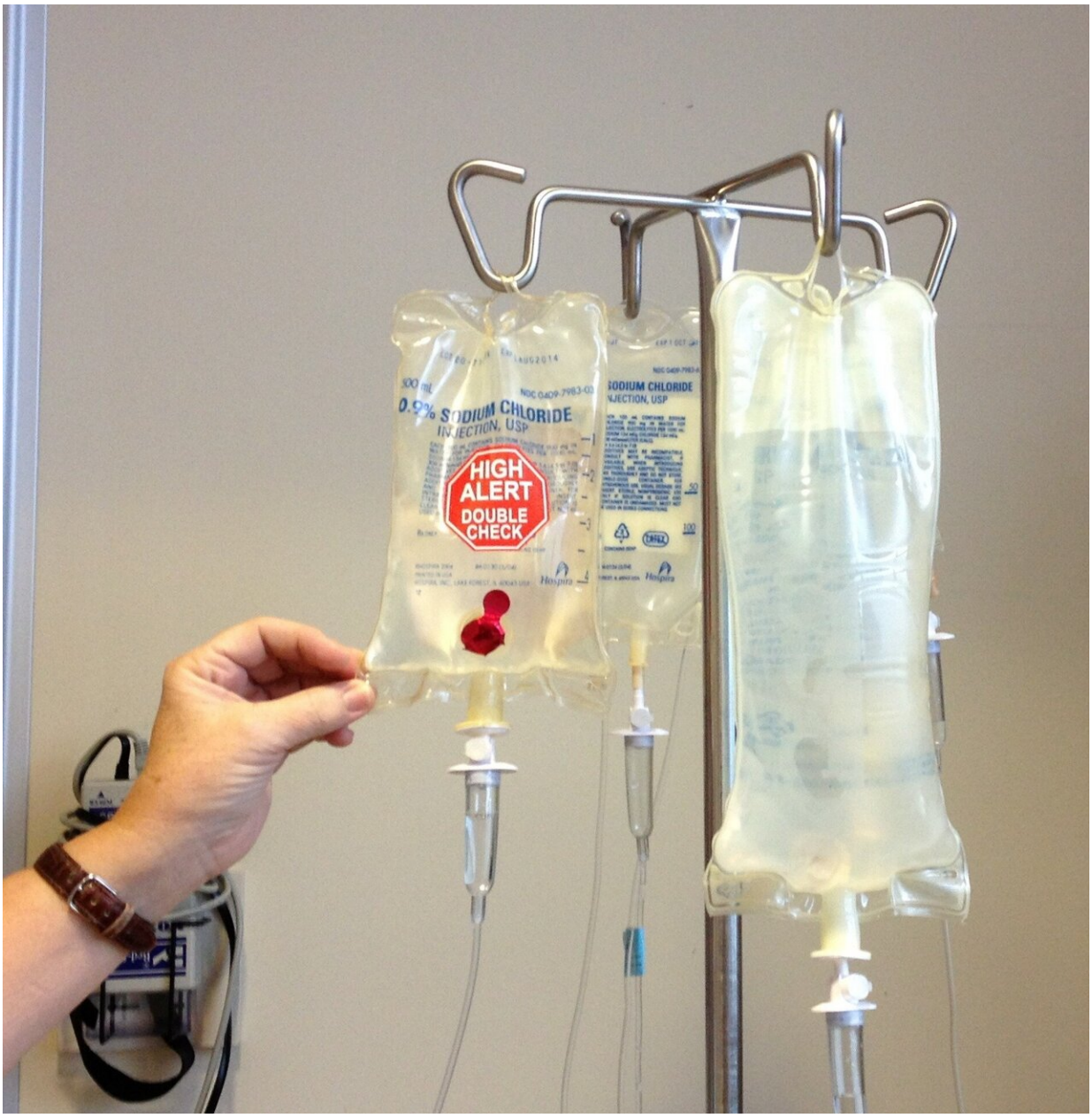
ESMO: PARP inhibitor plus immunotherapy lowers risk of endometrial cancer progression over chemotherapy alone

October 23 2023



Credit: Pixabay/CC0 Public Domain

Immunotherapy with the anti-PD-L1 monoclonal antibody durvalumab improved progression-free survival (PFS) in patients with newly diagnosed advanced or recurrent endometrial cancer compared with

chemotherapy alone, with further benefits gained from the addition of the PARP inhibitor olaparib in maintenance setting, according to researchers from The University of Texas MD Anderson Cancer Center.

The findings, published today in the *Journal of Clinical Oncology*, were also presented at the 2023 European Society for Medical Oncology (ESMO) Congress.

Results of the Phase III DUO-E trial demonstrated that durvalumab plus chemotherapy followed by durvalumab plus olaparib reduced the risk of disease progression or death by 45% while adding durvalumab alone to chemotherapy achieved a 29% reduction compared to chemotherapy alone. Exploratory subgroup analyzes by mismatch repair (MMR) status showed PFS benefits in both MMR-deficient (dMMR) and MMR-proficient (pMMR) disease.

"In cases of advanced or recurrent endometrial cancer, treatment choices are limited, as the cancer is typically unresponsive to hormonal therapy and requires chemotherapy," said global lead investigator Shannon Westin, M.D., professor of Gynecologic Oncology and Reproductive Medicine. "These findings showcase, for the first time, the potential of combining immunotherapy with a PARP inhibitor to deliver significant clinical improvements for these patients."

According to the American Cancer Society, endometrial cancer is the most common cancer of the female reproductive organs and, contrary to many other cancer types, incidence is on the rise. The five-year survival rate for advanced endometrial cancer is 20%, highlighting the need for treatment alternatives after current therapies are exhausted.

The DUO-E trial (GOG-3041/ENGOT-EN10) was conducted in 253 study locations across 22 countries, including the United States and locations across Europe, South America and Asia.

The trial randomized 718 patients with newly diagnosed stage III-IV or recurrent endometrial cancer to three treatment arms. In the control arm, patients received chemotherapy alone followed by a placebo. In arm two, patients received chemotherapy with durvalumab, followed by durvalumab maintenance and placebo. In arm three, patients received chemotherapy, durvalumab and olaparib maintenance. The primary endpoint was PFS.

The MMR status in endometrial cancer indicates if the normal DNA mismatch repair system is functioning correctly. MMR deficiency occurs in 20-40% of endometrial cancers and can influence treatment decisions and prognosis. Combining immunotherapy and chemotherapy has been effective in treating some patients with endometrial cancer, with more significant advantages observed in dMMR cases compared to those with pMMR.

Prespecified exploratory subgroup analyzes by MMR status showed a PFS benefit of 58% in patients with dMMR disease in the durvalumab arm and 59% for those in the durvalumab plus olaparib arm, compared to the control arm. In the pMMR subgroups, PFS was improved by 23% in the durvalumab arm and 43% in the durvalumab plus olaparib arm compared to the control arm. An additional clinical benefit was observed when olaparib maintenance was added to durvalumab following durvalumab plus chemotherapy in the pMMR subgroup.

The safety profiles of the experimental arms were consistent with the known safety profiles of the individual agents. The trial analyzes are ongoing. Although the overall survival data are not yet mature, a positive trend was observed.

"These findings may offer oncologists novel avenues to enhance outcomes for endometrial cancer patients," Westin said. "We are encouraged by these responses and look forward to reviewing the long-

term data from this trial and others."

The trial was supported by AstraZeneca. Westin reports research support and consulting fees from AstraZeneca. A complete list of collaborating authors and disclosures can be found in the abstract here.

More information: Shannon N. Westin et al, Durvalumab Plus Carboplatin/Paclitaxel Followed by Maintenance Durvalumab With or Without Olaparib as First-Line Treatment for Advanced Endometrial Cancer: The Phase III DUO-E Trial, *Journal of Clinical Oncology* (2023). DOI: 10.1200/JCO.23.02132

Provided by University of Texas M. D. Anderson Cancer Center