

PARP inhibitor plus chemotherapy improves progression-free survival for advanced ovarian cancer patients

September 28 2019

Researchers from The University of Texas MD Anderson Cancer Center reported study results showing that initial treatment with the PARP inhibitor veliparib in combination with chemotherapy significantly increased progression-free survival (PFS) for patients with newly diagnosed, metastatic high-grade serous ovarian cancer, according to the results of the VELIA trial.

The Phase III randomized study, was led by GOG Foundation investigators and was conducted at 202 sites in 10 countries. The [trial results](#) published today in the *New England Journal of Medicine* and will be presented at the European Society for Medical Oncology (ESMO) Congress 2019.

Among patients with BRCA mutations, those receiving the [combination therapy](#) followed by veliparib maintenance therapy had a median PFS of 34.7 months, compared to 22 months in the control arm of [chemotherapy](#) plus placebo followed by placebo maintenance. Similarly, PFS was 31.9 months on combination therapy compared to 20.5 months on control therapy for patients with any [homologous recombination](#) (HR) deficiency.

Across all trial participants, combination therapy achieved a PFS of 23.5 months, compared to 17.3 months for the control arm.

"This is the first clinical trial to use a PARP inhibitor combined with chemotherapy for newly diagnosed [ovarian cancer patients](#)," said lead investigator Robert L. Coleman, M.D., professor of Gynecologic Oncology and Reproductive Medicine. "These results further validate the role of this class of drug in the treatment of patients with ovarian [cancer](#) and offer a new therapeutic asset that can be initiated with the start of their adjuvant chemotherapy treatment."

According to the American Cancer Society, ovarian cancer accounts for more deaths than any other cancer of the female reproductive system. About 22,530 women will receive a new diagnosis of ovarian cancer in 2019. Although there have been treatment advances, more than 75% of patients develop progressive disease within three years.

Approximately 20% of ovarian cancer tumors exhibit BRCA mutations and an additional 30% more have

HR deficiencies, all of which lead to disruptions in normal DNA damage repair. These mutations make tumors vulnerable to PARP inhibitors, which target a compensatory DNA repair pathway. Although results were strongest in patients with tumors harboring a BRCA mutation, the trial also confirmed the benefit of a PARP inhibitor for patients without a BRCA mutation.

Patients were newly diagnosed with high-grade ovarian, fallopian tube or primary peritoneal carcinoma. Blood and tissue samples were analyzed to determine BRCA status and homologous recombination status.

From July 2015 to July 2017, 1140 patients were randomized to either chemotherapy/placebo followed by placebo maintenance (control arm); chemotherapy/veliparib followed by placebo maintenance (veliparib-combination only arm); or chemotherapy/veliparib followed by veliparib maintenance (veliparib-throughout arm).

The combination was generally well tolerated with no unexpected toxicities. Adverse events with veliparib were increased anemia and thrombocytopenia when combined with chemotherapy, as well as nausea, and fatigue overall.

"The patient population enrolled in the trial were reflective of those we see in clinic every day as it allowed for both stage III and stage IV patients and those getting primary surgery or those undergoing neoadjuvant chemotherapy before surgery," said Coleman. "These results are encouraging and apply for a majority of newly diagnosed [ovarian cancer](#) patients."

Future studies will look at combinations, predominately in maintenance setting including anti-angiogenesis agents, immunotherapy or both. Bevacizumab also can be administered with full dose chemotherapy and would be a next step for a primary therapy, or concomitant chemotherapy strategy with veliparib.

This study was supported by The GOG Foundation and sponsored by AbbVie.

A full list of collaborating researchers and their disclosures are included in the paper.

More information: *New England Journal of Medicine* (2019).
www.nejm.org/doi/full/10.1056/NEJMoa1909707

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

Citation: PARP inhibitor plus chemotherapy improves progression-free survival for advanced ovarian cancer patients (2019, September 28) retrieved 7 May 2024 from

<https://medicalxpress.com/news/2019-09-parp-inhibitor-chemotherapy-progression-free-survival.html>

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