PARP Inhibitors as New Standard of Care for More Ovarian Cancers

Olaparib (Lynparza) may become standard follow-up therapy for women with newly diagnosed ovarian cancer that has a *BRCA* mutation.

February 8, 2019 By Dana-Farber Cancer Institute

On the strength of the results of a major international clinical trial, there is now a new standard of care for patients with an advanced form of ovarian cancer who have responded to initial chemotherapy. The trial, dubbed SOLO-1, found that these patients — newly diagnosed with ovarian cancer that carries a mutation in the genes BRCA1 or BRCA2 — had a 70 percent lower risk of dying or having their disease worsen if they received the drug olaparib rather than a placebo after completing their chemotherapy. Olaparib (trade name: Lynparza) is a PARP inhibitor, which works by interfering with cancer cells' ability to repair damage to their DNA. In tumor cells whose ability to repair DNA damage is already impaired because of BRCA mutations, olaparib can cause so much genomic damage to build up that the cells self-destruct.

The trial, led by investigators in the United States and on three continents, involved 391 patients who were newly diagnosed with advanced high-grade serous or endometrioid ovarian cancer, primary peritoneal cancer, or fallopian-tube cancer that tested positive for a BRCA mutation and had shrunk after treatment with surgery and platinum-based chemotherapy. Two hundred sixty of the participants were randomly assigned to receive olaparib and 131 received a placebo. After a median period of 41 months, not only was the risk of death or disease progression 70 percent lower in the olaparib group, but also researchers estimate that median progression-free survival – the time in which patients are alive without the disease worsening – was approximately three years longer in the olaparib group.

The most common adverse side effects of the treatment were nausea, fatigue, vomiting, anemia, and diarrhea. Results of the trial were announced this fall at the European Society for Medical Oncology 2018 Congress in Munich and in a paper in the New England Journal of Medicine.

Olaparib has previously received U.S. Food and Drug Administration (FDA) approval as a "maintenance" therapy — used to prevent a worsening or recurrence of cancer following front-line treatment — for patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who respond to platinum-based chemotherapy regardless of whether the cancer tests BRCA-positive or -negative.

Based on the results of SOLO-1, olaparib was approved by the FDA in December 2018 as “maintenance therapy” for women with newly diagnosed advanced ovarian cancer that tests positive for a BRCA mutation and whose cancers have responded to their initial platinum-based chemotherapy.

“This is a major and exciting advance in our treatment of BRCA-related ovarian cancer. Upcoming trials should provide additional insight into whether PARP inhibitors, either by themselves or in combination with other therapies, can also benefit women whose ovarian cancers do not have a BRCA mutation,” says Joyce Liu, MD, MPH, director of Clinical Research in the Division of Gynecologic Oncology at Dana-Farber and a co-author of the New England Journal paper.

This article was originally published on January 25, 2019, by Dana-Farber Cancer Institute. It is republished with permission.
