

Olaparib slows growth of BRCA-related metastatic breast cancer

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Findings from a phase III clinical trial of about 300 women may introduce PARP inhibitors as a new type of treatment for breast cancer. Compared to standard chemotherapy, the oral targeted medicine olaparib (Lynparza) reduced the chance of progression of advanced, BRCA-related breast cancer by 42%, delaying progression by about 3 months.

These data will be presented in ASCO's Plenary Session, which features four abstracts deemed to have the greatest potential to impact patient care, out of the more than 5,000 abstracts featured as part of the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

"This is the first demonstration of improved outcomes with a PARP inhibitor compared to standard treatment in women with BRCA mutation-associated [breast](#) cancer," said lead study author Mark E. Robson, MD, Clinic Director of the Clinical Genetics Service and medical oncologist at Memorial Sloan Kettering Cancer Center in New York. "It is especially encouraging to see that olaparib was effective against triple negative breast cancers that arise in women with inherited, germline BRCA mutations. This type of breast cancer is particularly difficult to treat and often affects younger women."

Up to 3% of all breast cancers occur in people with inherited changes in genes BRCA1 and BRCA2. These changes lower the cell's ability to repair damaged DNA. Olaparib blocks other key players in the cell's DNA repair machinery, PARP1 and PARP2. Because of their underlying defect in DNA repair, cancer cells with BRCA mutations are

particularly vulnerable to treatments that target PARP. Olaparib is already FDA approved for use in women with BRCA-related ovarian cancer.

"This study is proof of the principle that breast cancers with defects in a specific DNA damage repair pathway are sensitive to a targeted therapy designed to exploit that defect," said Dr. Robson.

About the Study

The study enrolled [patients](#) with inherited BRCA mutations who had metastatic breast cancer that was either hormone receptor-positive or triple negative (estrogen receptor-negative, progesterone-receptor negative, and HER2-negative). Women with HER2-positive breast cancer were not included in this study because there are already very effective targeted treatments for this group. All patients had up to two prior rounds of chemotherapy for metastatic breast cancer, and those with hormone receptor-positive cancer had received hormonal therapy.

The researchers randomly assigned 302 patients to receive olaparib tablets or standard chemotherapy (either capecitabine, vinorelbine, or eribulin) until the cancer worsened or the patient developed severe side effects.

Key Findings

Tumors shrank in about 60% of patients who received olaparib, compared with 29% of those who received chemotherapy. At a median follow-up of about 14 months, patients who received olaparib had a 42% lower chance of cancer progression than those who received chemotherapy. The median time to progression was 7 months with olaparib and 4.2 months with chemotherapy.

After progression, the researchers kept track of patients to see how long it would be before the [cancer](#) worsened again. The time to second progression was also longer in patients receiving olaparib, indicating that the cancers did not return in a more aggressive way once olaparib stopped working. The study is insufficiently mature to permit a determination if the benefits provided by olaparib translate into prolongation of overall survival at this time.

The most common side effects in the olaparib group were nausea and anemia, whereas low white blood cell counts, anemia, fatigue, and rash on hands and feet were most common in the chemotherapy group. Severe side effects were less common with olaparib, occurring in 37% of patients compared to 50% of those treated with chemotherapy. Only 5% of patients needed to stop olaparib due to side effects. Health-related quality of life was significantly better in the olaparib group.

"Olaparib will probably be best used early in the course of [metastatic breast cancer](#). It helps preserve patient quality of life, offers the chance to postpone the need for I.V. chemotherapy, and avoids side effects like hair loss and low white blood cell counts," said Dr. Robson.

Next Steps

Given the relatively small size of the study, it is difficult to tell which subset of patients would benefit the most from olaparib.

This is the first of four ongoing phase III clinical trials of PARP inhibitors in [breast cancer](#) to report findings. More research is needed to determine how well olaparib works in cancers that worsen despite [platinum-based chemotherapy](#), a standard regimen not included in this study, and whether platinum-based [chemotherapy](#) would be useful after cancers worsen despite olaparib.

Provided by American Society of Clinical Oncology

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