# Iniparib extends overall survival in metastatic triple-negative breast cancer

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Women with an aggressive subtype of metastatic breast cancer appear to live an average of almost five months longer when treated with iniparib plus chemotherapy, compared to chemotherapy alone, the results of a randomized Phase-II trial show.

At the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy, Joyce O'Shaughnessy, MD, lead investigator of the study and co-director of the Breast Cancer Research Program Baylor-Charles A. Sammons Cancer Center and Texas Oncology in Dallas, and US Oncology, reported the final efficacy and safety results from a trial which included 123 patients with metastatic triple-negative breast cancer (mTNBC).

Triple-negative tumors are clinically negative for expression of estrogen receptors, progesterone receptors or HER2. When metastatic, these tumors are associated with poor prognosis and short survival rates.

Women in the trial had mTNBC and had received up to 2 prior regimens for metastatic disease. They were randomly assigned to receive either gemcitabine-carboplatin chemotherapy, or chemotherapy plus iniparib. Iniparib is an investigational anti-tumor agent with PARP inhibitory activity. Inhibition of PARP1, a key DNA repair enzyme, may prevent cancer cells from repairing their DNA, therefore, enhancing the effectiveness of DNA-damaging chemotherapy.

"The treatment regimen significantly improved overall survival from 7.7

months with chemotherapy alone to 12.3 months with iniparib and chemotherapy, an improvement of almost 5 months," said Dr O'Shaughnessy. "That magnitude of the survival advantage is unusual in breast cancer and in metastatic tumors in general."

More than half of women (55.7 percent) in the iniparib arm experienced clinical benefit --defined as complete or partial response or stable disease for at least 6 months compared with 33.9 percent of patients in the chemotherapy-alone arm.

There was little or no increase in adverse events between the two groups, the researchers found.

"These data are promising and suggest that iniparib may provide a potential new treatment option for patients with metastatic triple-negative breast cancer, which currently has limited therapeutic options, " Dr O'Shaughnessy said.

"The data we've seen with iniparib demonstrate that it has the potential to extend progression free and overall survival in women with triple negative breast cancer, and may be the first therapy available specifically for these patients with few options," Dr O'Shaughnessy said. "In addition, based on this Phase-II study and other studies performed to date, iniparib seems to combine well with chemotherapy."

There are two Phase-III studies of iniparib ongoing, one in triple-negative breast cancer and another in squamous cell non-small cell lung cancer. Iniparib is also being studied in other difficult-to-treat cancers, including ovarian, pancreatic and brain cancers.

Commenting on the study, Dr Angelo Di Leo, head of Sandro Pitigliani Medical Oncology Unit at Hospital of Prato, Italy, said: "Triple-negative breast cancer accounts for about 15% of all breast cancer cases and there

is a desperate need to identify effective agents for these patients. "

"This trial suggests a clear superiority of the treatment combining chemotherapy with iniparib over chemotherapy alone. Such a clear superiority is not usually observed in a trial where only 120 patients have been recruited. This suggests that the drug might be very active."

"Questions that remain to be answered include whether the chemotherapy treatment tested in this trial is the best 'partner' for iniparib, Dr Di Leo said. "Pre-clinical data suggest that other agents such as cisplatin, cyclophospamide and anthracyclines might be very good chemotherapy drugs to be combined with iniparib. The issue of identifying the best chemotherapy treatment to be combined with iniparib is still an open question."

This and other questions are currently being investigated in ongoing trials, Dr Di Leo said.

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