New small molecule inhibitor could be a safe and first-line treatment for metastatic breast cancer

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Previous research has shown that a family of genes, proteins and enzymes called the uPA system (for urokinase plasminogen activator) plays an active role in different facets of cancer's biology, including tumor cell invasion, the spread of metastases, and the growth of a primary tumor. Mesupron® is a new small molecule inhibitor, taken as a pill, that inhibits the uPA system. The results from a recent phase II clinical study suggest that the drug could be a safe and first-line treatment that extends progression-free survival for metastatic breast cancer patients, when combined with the chemotherapeutic drug Capecitabine. Results will be presented by Lori J. Goldstein, MD, Director of the Breast Evaluation Center at Fox Chase Cancer Center, at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium on Friday, December 7, 2012.

The trial was designed based on the results of a Phase I study completed at Fox Chase, led by Dr. Goldstein, showing both the safety of the combination drug and some evidence of the drug's benefit.

The study included 132 patients with metastatic breast cancer from 20 centers in five countries. In the trial, patients who took Mesupron combined with Capecitabine went without the return of disease for a median 8.3 months after the therapy. Patients who only took Capecitabine had a progression-free survival of 7.5 months.

"The combination of oral agents was convenient for and well tolerated by the patients," says Goldstein. "Plans for future studies are ongoing"

The drug was developed by WILEX, a German pharmaceutical company that focuses on the development of small molecule inhibitors and other new targeted cancer drugs designed to give patients treatment options with fewer side effects than traditional chemotherapy. In the Phase II study, Goldstein and her collaborators also investigated the safety and efficacy of the drug, as well as the objective response rate—the patient population who had no sign of disease after a specific amount of time.

Nine percent of the patients who received only Capecitabine had a complete objective response after 24 weeks. The objective response rate among the patients taking the combination therapy was nearly twice that, at 17 percent.

The researchers also looked at different subgroups of participants to try to identify which patients might receive the most benefit from a combination therapy involving Mesupron. Among 109 Caucasian patients, the progression free survival was 7.5 months for patients who received Capecitabine alone, and 9.1 months for those who also received Mesupron.

The drug also showed a significant improvement for patients who had previously received treatment—before their disease became metastatic. In the subgroup of patients (n=95) who received adjuvant chemotherapy following the primary diagnosis of breast cancer, progression free survival improved from 4.3 months in the Capecitabine alone group to 8.3 months in the Mesupron combination group.

The drug has shown similar results in pancreatic cancer, extending progression free survival and boosting the objective response rate. "The data confirm the results of the pancreatic cancer trial reported in 2012.

This proof of concept study shows the Mesupron may be of benefit in breast cancer as well as pancreatic cancer. Because the uPA system has been implicated in a range of solid tumors, the drug could well find application in a variety of indications," says Paul Bevan, PhD, Head of R&D and Member of the Executive Management Board of WILEX.

Provided by Fox Chase Cancer Center