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New combination therapy fails to delay progression of advanced breast cancer

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Adding the antibody therapy ramucirumab to the chemotherapy drug docetaxel did not delay disease progression for patients with HER2-negative, advanced breast cancer, according to results of a placebo-controlled, randomized, phase III clinical trial presented here at the 2013 San Antonio Breast Cancer Symposium, held Dec. 10-14.

"Patients with metastatic or recurrent breast cancer, as well as those with locally advanced disease that cannot be surgically removed, have no curative options," said John R. Mackey, M.D., professor of oncology at the University of Alberta in Edmonton. "Standard cytotoxic chemotherapy is an option, but the efficacy of current treatments is modest and patients experience many adverse side effects.

"We had hoped that ramucirumab would give patients a new option for metastatic breast cancer. The outcome is disappointing, especially for the patients who participated on the trial and the many others suffering with this disease," added Mackey, who is also director of Translational Research in Oncology (TRIO). "Antiangiogenic agents have been successful in prolonging survival in a number of solid tumor types, including colon cancer and gastric cancer, but unfortunately, for reasons that we don't understand, they have not yet been shown to work for breast cancer."

"But we must work with the results that we have, and there were some patients on the trial who responded to treatment with ramucirumab," continued Mackey. "As a result, we will be conducting biomarker

analyses to see if we can identify a subgroup of patients for whom the antibody therapy might be beneficial, but it will be a while before we have results."

For tumors to thrive, they need a good blood supply, and many tumors release factors that trigger nearby blood vessels to grow, a process called angiogenesis. Ramucirumab blocks angiogenesis by attaching to the protein on blood vessels that is key to the new blood vessel growth, vascular endothelial growth factor receptor 2 (VEGFR2). According to Mackey, other antiangiogenic therapies have not yielded great success in breast cancer but it had been hoped that ramucirumab would benefit patients because it is the only antiangiogenic antibody therapy to directly target VEGFR2.

Between August 2008 and December 2011, Mackey and colleagues enrolled 1,144 patients in the placebo-controlled, randomized, multinational, phase III clinical trial called the ramucirumab overall survival evaluation (ROSE) trial or the TRIO-12 trial. Patients were randomly assigned 1:2 to docetaxel plus placebo or docetaxel plus ramucirumab. To be eligible for the trial, patients had to have HER2-negative breast cancer that could not be removed surgically or HER2-negative, locally recurrent or metastatic breast cancer.

After a median follow-up of 16.2 months, progression-free survival was 9.5 months in the ramucirumab arm and 8.2 months in the control arm.

"The biggest positive that we can take from the trial is that we showed that a global academic group, TRIO, can successfully partner with industry to run a large, late-stage cancer clinical trial," said Mackey.

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