Combination treatment with lapatinib and pazopanib doesn't improve outcomes for patients with IBC

June 1 2012

Inflammatory breast cancer is a very aggressive type of cancer associated with early metastasis and poor survival rates, and the prognosis is even worse for patients with tumors expressing the ErbB2 receptor. The ErbB2-inhibiting drug lapatinib can slow the spread of cancer cells in individuals with advanced breast cancer who have already tried other chemotherapy medications. Treating these patients with a combination of drugs has the potential to improve outcomes compared to treatment with lapatinib alone, but it has not been clear whether the additional benefits outweigh the risks. Now, researchers from Fox Chase Cancer Center and their international collaborators will present information at the 2012 Annual Meeting of the American Society of Clinical Oncology on Saturday, June 2 that will give clinicians the information needed to make that call.

Massimo Cristofanilli, M.D., F.A.C.P., professor of medicine at Fox Chase's department of medical oncology and lead investigator of the study, and colleagues, conducted a randomized, prospective phase II clinical study to test the effectiveness of combination therapy consisting of lapatinib and pazopanib—a drug already approved to treat advanced kidney cancer that works by inhibiting the growth of new blood vessels, which can also contribute to breast cancer progression. They found that combination therapy produces greater toxicity without significant clinical benefits in patients with inflammatory breast cancer, when compared with lapatinib treatment alone.

The multicenter trial consisted of patients with relapsed inflammatory breast cancer who had tumors expressing the ErbB2 receptor. In a group of 76 patients, individuals who received lapatinib and pazopanib had an overall response rate of 45 percent and median progression-free survival of about 14 weeks, compared with 29 percent and about 16 weeks, respectively, in patients who were treated with lapatinib alone. "But the differences in efficacy were not statistically significant," Cristofanilli says.

In addition, side effects such as diarrhea, vomiting and liver dysfunction occurred in patients undergoing combination therapy, but not in individuals who only took lapatinib. As a result, 21 percent of the patients undergoing combination therapy required dose reductions and 55 percent required dose interruptions, compared with only 3 percent and 11 percent, respectively, of patients who only took lapatinib.

Because of the side effects experienced by the first group of patients, Cristofanilli and his team used lower doses of lapatinib and pazopanib in a second group of 87 patients. Combination therapy resulted in an overall response rate of 58 percent and median progression-free survival of 16 weeks, compared with 47 percent and 16 weeks for lapatinib alone, and 31 percent and about 11 weeks for pazopanib alone. "Once again, the outcomes in patients who received combination therapy were not significantly better than those in patients who took lapatinib alone," Cristofanilli says.

Moreover, signs of liver dysfunction, diarrhea and fatigue were more common in patients who received combination therapy than in those who were treated with a single drug, and these side effects resulted in more frequent dose reductions and interruptions in patients undergoing combination therapy.

"The results demonstrate that combination therapy consisting of

lapatinib and pazopanib increases side effects, but does not significantly improve clinical outcomes, when compared with treatment with lapatinib as a single agent," Cristofanilli says. "Based on these findings, I don't recommend that this type of combination therapy be used to treat patients with inflammatory breast cancer, but we were able to confirm that lapatinib is an effective treatment for women with this disease."

To follow up on this research, Cristofanilli will continue to study how the growth of new blood vessels contributes to inflammatory breast cancer. "This particular type of disease requires more attention," he says. "We need to continue to investigate the biology of this disease and try to design better therapies for these patients."

Provided by Fox Chase Cancer Center