Standard chemo works better against metastatic BRCA1/2 breast cancer than against sporadic tumors

April 17 2008

The first study to investigate the effects of chemotherapy on metastatic breast cancer in women with the BRCA1 or BRCA2 gene mutation has shown that standard chemotherapy works better in these patients than in women without the BRCA1/2 mutation.

The authors of a study presented today (Thursday) at the 6th European Breast Cancer Conference (EBCC-6) in Berlin found that women with BRCA2-associated breast cancer had a significantly higher response rate, a longer time without the disease progressing, and a longer overall survival when treated with anthracycline-based regimens than did women with sporadic breast cancers that were not associated with BRCA1/2.

Women with BRCA1-associated breast cancer also did better than women with sporadic breast cancer, but the rates were not statistically significant.

Researchers at the Daniel den Hoed Cancer Centre/Erasmus Medical Centre (Rotterdam, The Netherlands) conducted the study. They matched 112 women with BRCA1-associated metastatic cancer and 29 women with BRCA2-associated metastatic cancer with 141 women with sporadic breast cancers. The women had been treated with anthracycline-based or taxane-based regimens, CMF (cyclophosphamide, methotrexate and fluorouracil 5FU) or other chemotherapy regimens.

BRCA2 women had a higher response rate to chemotherapy (89% versus 50%), a longer progression-free survival (nearly a third better) and a longer overall survival (47% better) than did women with sporadic cancers. When the researchers looked more closely at the type of chemotherapy the women had received, they found that the improved progression-free survival mainly occurred in patients on anthracyclines and disappeared for those treated with CMF.

The lead author of the study, Dr Mieke Kriege, an epidemiologist and project researcher at the Rotterdam Family Cancer Clinic, said: “It is difficult to make firm conclusions about response to different treatments from our results so far, but it does seem that the higher sensitivity to treatment by BRCA2-associated patients is especially caused by the anthracycline regimen.”

The project leader, Professor Jan Klijn, medical oncologist and chairman of the Rotterdam Family Cancer Clinic, said: “Our findings show that various standard chemotherapy regimens are clinically effective in the treatment of metastatic BRCA1/2-associated breast cancer. The observation of the high efficacy of anthracycline-based regimens is especially reassuring. However, we would like to emphasise that larger, additional studies are urgently needed to investigate further newer regimens containing taxanes and platinum compounds.”

Dr Kriege said: “Currently, there are very few studies on the efficacy of chemotherapy in BRCA1/2-associated breast cancer – mainly a few, very small studies with less than 44 patients in the neo-adjuvant setting. Our study is the only one in metastatic disease and, with 141 BRCA1/2 gene mutation carriers included, it is by far the largest study in the world.”

The authors believe that an explanation of why chemotherapy seems to work better in BRCA1/2 breast cancers than in sporadic cancers is due

to the lack of a working BRCA1/2 protein. “Functional BRCA1 and BRCA2 proteins are involved in DNA repair,” said Dr Kriege. “Most chemotherapeutic agents are active by damaging DNA (especially anthracycline-based regimens). In BRCA1 and BRCA2 mutation carriers, who have no functional BRCA1 and BRCA2 proteins respectively, DNA repair after chemotherapy might be worse than in sporadic patients resulting in better treatment responses. Pre-clinical studies showed that BRCA1 and BRCA2 mutated cells are especially sensitive to chemotherapeutic agents that cause double-strand DNA breaks (such as anthracyclines and platinum).”

The researchers now plan to investigate the effects of adjuvant and neo-adjuvant treatments in women with BRCA1/2-associated breast cancers, and to evaluate taxane and platinum therapies further.

Source: ECCO-the European CanCer Organisation