Low Dose Oral Cyclophosphamide-Methotrexate Maintenance May Benefit Receptor-Negative Breast Cancer Patients

CHICAGO – The use of low dose oral cyclophosphamide-methotrexate maintenance following adjuvant chemotherapy may benefit patients with hormone receptor-negative early breast cancer. The International Breast Cancer Study Group (IBCSG) presented the results of IBCSG Trial 22-00: Cyclophosphamide-Methotrexate Maintenance (CMM) today at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting.

Adding low dose oral cyclophosphamide-methotrexate maintenance (CMM) to adjuvant chemotherapy reduced the relative risk of developing breast cancer recurrence by 16% in women with hormone receptor-negative early breast cancer, when compared to treatment with adjuvant chemotherapy alone. This observed benefit was greater in women with triple-negative disease; CMM treatment following adjuvant chemotherapy reduced their relative risk of recurrence by 20%, and reduced the absolute risk of recurrence by 4.1%. Patients with triple negative and node positive disease experienced the largest benefit: a 7.9% reduction in their absolute risk of recurrence. These results are not statistically significant.

“Women with hormone receptor-negative breast cancer face a higher risk of early disease recurrence, and there is currently no targeted treatment available for patients with triple-negative breast cancer,” said study chair Marco Colleoni, M.D., Director, Division of Medical Senology, European Institute of Oncology, Italy. “This is the first trial to test the efficacy of adding a low dose oral cyclophosphamide-methotrexate maintenance component to adjuvant chemotherapy treatment for hormone receptor-negative breast cancer. While the disease-free survival benefits are not statistically significant, they are promising – especially for triple-negative patients.”

Researchers designed IBCSG Trial 22-00 (CMM) as a randomized, phase III clinical trial assessing the efficacy of a low dose cytotoxic chemotherapy regimen, hypothesized to have anti-angiogenic activity, following standard chemotherapy in patients with hormone receptor-negative tumors. Women with hormone receptor-negative early breast cancer of any nodal and HER-2 status were randomly assigned to treatment with adjuvant induction chemotherapy plus oral cyclophosphamide-methotrexate maintenance (cyclophosphamide 50 mg/day orally continuously and methotrexate 2.5 mg twice/day orally days 1 and 2 of every week) for 1 year, or adjuvant induction chemotherapy with no further treatment. The induction chemotherapy regimen was determined by physician-patient choice.

IBCSG Trial 22-00 (CMM) is one of largest trials ever conducted in patients with hormone receptor-negative disease. The treatment was generally well tolerated: only 13.5% of patients receiving at least one dose of the CMM regimen reported a grade 3 or 4 treatment-
related adverse event. The most frequently reported side effects were abnormal lab values including elevated hepatic SGPT levels and low white blood cell counts (leukopenia). Completing the entire year of CMM was difficult for some patients: one quarter of patients who started CMM did not complete the full year of treatment due to adverse events or patient/medical decision.

“Given the tolerability and low costs of an oral CMM regimen, we are optimistic about future treatment applications for hormone receptor-negative patients, in particular for patients at higher risk for recurrence” said Beat Thürlimann, M.D., Director of the Breast Center, Kantonsspital, St Gallen. “All patients consented to prospective tissue collection; translational studies, including multigene assays, are ongoing to further tailor treatment recommendations for this population.”

IBCSG Trial 22-00 (CMM) enrolled 1,086 women with hormone receptor-negative early stage breast cancer between January 2001 and December 2012. Trial treatment with low dose oral cyclophosphamide-methotrexate maintenance was assigned for 1 year; the women continue to be followed to assess long-term prognosis and side effects. The trial is led and supported by the International Breast Cancer Study Group, in partnership with 32 IBCSG centers worldwide.

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References: ASCO 2015 Abstract 1002

The International Breast Cancer Study Group (IBCSG) is a Swiss nonprofit cooperative breast cancer research organization that has conducted clinical research in adjuvant endocrine therapy and chemotherapy, timing and duration of adjuvant therapies, and quality of life for over 35 years.