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Multi-gene test identifies early breast cancer patients who can be spared chemo

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Researchers have shown for the first time that it is possible to use a multi-gene test to identify patients with early breast cancer who can be spared chemotherapy and who will still be alive and well five years after diagnosis.

New results from the West German Study Group (WSG) phase III PlanB trial, presented at the 10th European Breast Cancer Conference (EBCC-10) today (Friday), showed that 94% of women who had been assessed as at low risk of a recurrence of their disease by the 21-gene Recurrence Score (Oncotype DX) test were disease-free after five years.

The trial is the first study worldwide using the 21-gene Recurrence Score (RS) to report five-year survival data in patients with node negative or node positive early breast cancer (cancer that has not spread to the lymph nodes, or has spread to between 1-3 nodes), and who have hormone receptor positive (HR+) or HER2 negative disease (where cancer cells do not have high numbers of human epidermal growth factor receptors on their surfaces, meaning they will be unresponsive to targeted HER2 therapies such a trastuzumab, brand name Herceptin).

Between 2009 and 2011, the trial enrolled 3198 patients with an average (median) age of 56. The 21-gene RS is a test that analyses a group of 21 genes that can affect how a cancer is likely to behave and respond to treatment. It ranges form 0-100 and, for this trial, patients who had a score of 11 or less, were assessed as being at low risk of recurrence, even though other clinical factors such as nodal status, grade, tumour size or

age suggested they could be at high risk.

For 348 patients (15.3%) with an RS of 11 or less, adjuvant chemotherapy was omitted and they were treated with anti-hormonal therapy only. All other patients with an RS of more than 11 or with more than four involved lymph nodes or hormone-receptor negative disease were assessed as being at intermediate or high risk and were randomised to receive one of two types of chemotherapy: six cycles of docetaxel/cyclophosphamide or four cycles of epirubicin/cyclophosphamide followed by four cycles of docetaxel.

After a median 55 months follow-up, 94% of the genomic low-risk patients, who were treated with anti-hormonal therapy alone, were still alive and disease-free at five years. Among the intermediate-risk patients who were treated with adjuvant chemotherapy, five-year disease-free survival was also 94%, and it was 84% among the high-risk patients (RS of more than 25) who had also received chemotherapy.

Dr Oleg Gluz, one of the two scientific coordinators of the West German Study Group, based in Mönchengladbach, Germany, told EBCC-10: "In this prospective trial for patients who had a clinically-determined intermediate or high risk of recurrence and who had 0-3 lymph nodes involved, we have been able identify about 15% who were assessed by the 21-gene RS as being at low genomic risk. We were thus able to treat them by anti-hormonal therapy alone and to spare them chemotherapy. The 94% disease-free survival rate that we observe after five years without adjuvant chemotherapy is an excellent result."

Further analysis of other prognostic factors, such as nodal status, tumour size, grade and Ki67 protein (an indicator of cell proliferation), showed that the 21-gene RS was a better independent predictor of disease recurrence than the clinical factors alone or Ki67, whether it was used on its own or in combination with them.

"The RS provided additional and independent prognostic information beyond that of established and important clinical prognostic markers such as nodal status, tumour grade and size," said Dr Gluz. "These are the first five-year data for a prospectively planned comparison between an independent review of the tumour pathology, including Ki67, versus 21-gene RS. Our data clearly reveal a stronger prognostic impact of RS compared to immunohistochemical tools, such as Ki67 and hormone receptor expression, and thus support the incorporation of the RS test, in combination with nodal status, grade and tumour size, into routine clinical practice for making treatment decisions for these patients."

The 21-gene RS test takes about 8-10 days to complete, as the tumour tissue is sent to a central laboratory for analysis. "Implementation of the test is easy, but so far, the costs are not yet covered in all countries. Several studies have shown that it is cost efficient because it enables a more personalised and less frequent use of chemotherapy," he said.

Professor Nadia Harbeck, scientific lead of the WSG and head of the breast centre at the University of Munich, Germany, commented: "Based on our results, we now have stronger evidence for the use of the 21-gene RS test and its implementation into clinical guidelines. We are also awaiting further long-term data for another test (i.e. Mammaprint) from a prospective trial in the next few months. We would hope that reimbursement for prospectively evaluated genomic assays would now be possible in most, if not all, European countries.

"The use of multi-gene tests such as this one also seems reasonable for selecting patients in the future who may benefit from novel targeted therapies, since patients in the genomic high-risk group do have a relatively poor outcome despite the use of chemotherapy."

The researchers will be extending the follow-up of the patients in the trial up to ten years. In addition, the follow-up trial, WSG-ADAPT, has

already enrolled more than 4000 patients to look at combining the RS with the assessment of early response to short-term preoperative anti-hormonal therapy as indicated by a decrease in Ki67. "The combination of both tools may help to omit adjuvant chemotherapy in about 50-60% of early breast cancer patients," said Dr Gluz. "Final survival results of this study will be available in 2021."

Chair of EBCC-10, Professor Fatima Cardoso, who is Director of the Breast Unit at the Champalimaud Clinical Centre, Lisbon, Portugal, said: "This very important trial adds to the evidence from the low-risk arm of the TAILORx study, and to a wealth of other retrospective studies, supporting the use of genomic testing to help accurately select early breast cancer patients who can safely be spared chemotherapy. Many cost-effectiveness studies have provided additional support for this strategy. Hopefully, very soon these type of tests will become reimbursed and hence accessible to breast cancer patients in Europe."

More information: Abstract no: 8 LBA. "Prospective WSG Phase III PlanB trial: Clinical outcome at 5-year follow up and impact of 21 Gene Recurrence Score result, central/local-pathological review of grade, ER, PR and Ki67 in HR+/HER2- high risk node-negative and -positive breast cancer", Friday, Plenary session: oral and late breaking abstracts, 09.45-11.15 hrs, Elicium.

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