Genetic and clinical factors best to predict late recurrence in estrogen receptor POS breast cancer

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A new analysis has provided a comprehensive comparison of scores designed to predict which women with oestrogen-receptor positive breast cancer are at high risk of recurrence beyond five years after diagnosis, and may benefit from prolonged endocrine treatment.

The promising new findings will likely benefit the many women with oestrogen-receptor positive breast cancer whose cancer recurs more than five years after diagnosis, researchers told the 5th IMPAKT Breast Cancer Conference in Brussels, Belgium.

The IMPAKT meeting presents cutting edge, 'translational' breast cancer research that is beginning to have an impact for patients.

In oestrogen-receptor positive women, half of all recurrences of breast cancer will occur after the women finish the standard 5 years of hormonal treatment, explains lead author Dr Ivana Sestak from the Wolfson Institute of Preventive Medicine in London, UK.

"There is great interest in establishing which women are at adequate high risk of late recurrence after the initial hormonal treatment period, which is currently 5 years," Dr Sestak says.

At the meeting, researchers reported the findings of a comparison of five different scores designed to predict which women may be at

increased risk of developing a late recurrence of their cancer. This is the first time that all five scores have been compared within one dataset.

Knowing which women may be at increased risk of developing a late recurrence would enable doctors to identify those women who may be good candidates for extended hormonal therapy, she says.

The ATAC trial included nearly 10,000 women who were treated with surgery followed by five years of treatment with the drugs anastrozole, tamoxifen or a combination of both. Of these 1,125 from the monotherapy arms (tamoxifen, anastrozole) were included in the transATAC study.

The five scores being compared were the:

- Clinical Treatment Score, which includes information on the patient's disease and treatments so far;
- IHC4 score, which characterises the presence of cell surface markers on cancer cells;
- Three different gene expression scores—the Oncotype Dx Recurrence Score; the PAM50 Risk of Recurrence Score; and the Breast Cancer Index score.

The results showed that the clinical treatment score alone was the best for predicting late recurrence, the researchers report. The components of this score include some that are already widely used by doctors, such as whether the cancer has spread to sentinel lymph nodes, the tumour size and grade.

Among the other tests, the PAM50 risk of recurrence score and the Breast Cancer Index score added the most significant prognostic value between years 5 and 10 after diagnosis.

"The most promising new scores from this study are the PAM50 Risk of Recurrence score and the Breast Cancer Index score, both containing different genetic information that are not included in the clinical treatment score and at the moment not routinely measured in clinics," Dr Sestak says.

"Our further interest now lies in the investigation of which individual components of these scores attribute specifically to the prediction of late recurrence, since the Risk of Recurrence and Breast Cancer Index scores consist of several genes and other components. We are now undertaking these analyses and the results will hopefully tell us which genes specifically predict late recurrence. However, at this stage it is not possible to predict response to treatment."

Commenting on the results, Dr Peter Dubsky from the Medical University of Vienna, Austria, noted that oestrogen-receptor positive and Her2 negative breast cancers are prone to late recurrences.

"About half of all recurrences observed within 15 years of follow-up occur five years after diagnosis. Although there is a sustained benefit of adjuvant endocrine therapy beyond five years, we still see two-thirds of breast cancer deaths occurring after this time. Clearly, the identification of women that are at risk for these late types of recurrences is an important clinical research goal," said Dr Dubsky, who was not involved in the study.

"Sestak and colleagues provide highly relevant new data to meet this end: they have compared five different prognostic scores in order to predict outcome beyond the first five years of follow-up. Of note, none of these scores were primarily trained to specifically predict late recurrence. They show that a Clinical Treatment score (CTS) contained most of the prognostic information relevant to late distant metastases. Interestingly, only the Risk of Recurrence (ROR) score (PAM50) and the Breast

[Cancer](#) Index (BCI) score provided additional information to the CTS. This data will need further validation before actually being incorporated into clinical decision-making concerning adjuvant endocrine therapy beyond five years."

These findings are similar to those proposed by the Austrian Breast and Colorectal Cancer Study Group recently, Dr Dubsky said. "The Endopredict Score was able to add additional prognostic information to clinical variables concerning distant metastases occurring later than five years after diagnosis. Future research should further address which are the biologic motifs behind late recurrences. Furthermore, molecular tools specifically designed to predict late metastasis should be developed."

Provided by European Society for Medical Oncology

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