

BREAST CANCER

Progress from NOAH study comes in twos

There are many different subtypes of breast cancer, which are based largely on the expression levels of ER, PR and HER2 receptors. HER2-positive breast cancer is biologically heterogeneous and composed of the four intrinsic subtypes of breast cancer (luminal A, luminal B, HER2-enriched and basal-like). A gene-expression test, PAM50, that provides further prognostic value was introduced to the clinic in 2009.

Aleix Prat and colleagues have now carried out a gene-expression analysis with PAM50 in 156 pretreatment samples from women treated in the phase III NOAH study to see whether “HER2-positive tumours belonging to the HER2-enriched subtype might benefit the most from anti-HER2 therapies.” The researchers assessed women with newly diagnosed HER2-positive disease who were randomly assigned to trastuzumab treatment or to no treatment. They identified the four main intrinsic subtypes and looked for associations between these molecular entities and

treatment response and survival outcome. “We provide clinical evidence suggesting that advanced HER2-positive primary tumours belonging to the HER2-enriched subtype benefit the most from trastuzumab-based chemotherapy,” explains Prat. Moreover, they showed that the PAM50 assay identifies a cohort of HER2-positive patients with a high likelihood of achieving a pathological complete response and improved event-free survival after trastuzumab-based chemotherapy.

Prat comments, “these results suggest that clinically applicable gene expression-based tests, such as the PAM50 intrinsic subtype predictor, warrant further investigation in predicting response and survival during treatment with anti-HER2 agents with and without chemotherapy.”

In the future, the researchers plan to “test in a prospective trial if the HER2-enriched subtype can identify a group of patients with HER2-positive disease that can be cured with dual HER2 blockade without chemotherapy. This will be



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especially critical in the adjuvant setting, where the use of chemotherapy in small, node-negative HER2-positive tumours is still unclear.”

Lisa Hutchinson

Original article Prat, A. *et al.* Research-based PAM50 subtype predictor identifies higher responses and improved survival outcomes in HER2-positive breast cancer in the NOAH study. *Clin. Cancer Res.* **20**, 511–521 (2014)