

## TARGETED THERAPIES

## TH3RESA trial, overcoming hurdles in breast cancer

HER2 is overexpressed in about 20% of breast cancers. Although overexpression of HER2 is associated with poor outcome, the design of trastuzumab (a humanized monoclonal antibody targeting the extracellular domain of HER2) has rendered this disease subset treatable, becoming the cornerstone of targeted therapy in breast cancer. However, despite the benefits in progression-free survival (PFS) and overall survival obtained with trastuzumab—especially

when administered in combination with chemotherapy—disease progresses within 18 months in most patients, who then switch to treatment with lapatinib (another inhibitor of HER2) plus capecitabine, or to dual HER2 inhibition with a combination of trastuzumab and lapatinib.

Trastuzumab emtansine is an antibody–drug conjugate of trastuzumab and the cytotoxic emtansine. This compound was initially developed to overcome resistance to trastuzumab and, after the EMILIA trial that showed improved PFS and overall survival when compared with lapatinib plus capecitabine, has been approved in patients pretreated with taxanes plus trastuzumab.

Now, Ian E. Krop and colleagues have reported the results of the TH3RESA trial, a randomized phase III trial that compared trastuzumab emtansine with physicians' treatment of choice in 602 patients with HER2-positive metastatic breast cancer pretreated with two or more lines. Patients receiving trastuzumab emtansine ( $n = 404$ ) had a

PFS of 6.2 months compared with a PFS of 3.3 months in patients in the control group ( $n = 198$ ). Interim overall survival analysis also showed a trend in favour of trastuzumab emtansine (overall survival not reached in the trastuzumab emtansine group compared with 14.9 months in the control group). Importantly, grade 3 or worse adverse events were more common in the physician's choice group than in the trastuzumab emtansine group.

The findings from the TH3RESA study, together with those from the EMILIA trial, suggest that trastuzumab emtansine could be considered a new standard option for patients with heavily pretreated HER2-positive advanced-stage breast cancer.

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**Original article** Krop, I. E. *et al.* Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): a randomised, open-label, phase 3 trial. *Lancet Oncol.* **15**, 689–699 (2014)



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