T-DM1 for residual, invasive, HER2-positive breast cancer

A new study has concluded that adjuvant trastuzumab emtansine (T-DM1) reduces the risk of recurrence or death in patients with HER2-positive breast cancer who have residual disease after neoadjuvant therapy and surgery.

In the phase 3, open-label trial, women with HER2-positive, early-stage breast cancer had received neoadjuvant therapy consisting of at least six cycles of chemotherapy, including a taxane, and trastuzumab for at least 9 weeks. Patients were randomly assigned to receive 14 cycles of either T-DM1 or trastuzumab (n=743 per group). The primary endpoint was invasive disease-free survival.

Median follow-up was 41·4 months (range 0·1–62·7) in the T-DM1 group and 40·9 months (0·1–62·6) in the trastuzumab group. 91 (12%) of 743 patients in the T-DM1 group and 165 (22%) of 743 patients in the trastuzumab group had recurrence or had died (hazard ratio [HR] 0.50; 95% CI 0·39–0·64; p<0·001). The risk of distant recurrence as the first invasive-disease event was also reduced by T-DM1 (HR 0·60; 0·45–0·79). 190 (26%) of 740 patients in the T-DM1 group had adverse events of grade 3 or higher, compared with 111 (15%) of 720 in the trastuzumab group. The most common grade 3 or worse adverse events in the T-DM1 group were decreased platelet count (42 [6%]) and hypertension (15 [2%]).

Co-author Charles Geyer (Virginia Commonwealth University Massey Cancer Centre, Richmond, VA, USA) noted that the common side-effects associated with T-DM1 were generally reversible. "The safety profile should not be problematic to manage, especially given the magnitude of the benefit with this therapy", he said.

Sara Tolaney (Dana Farber Cancer Institute, Boston, Massachusetts, USA) commented "This is a practice-changing trial". Subgroup analysis showed that T-DM1 was equally effective in patients who had received preoperative pertuzumab. "It means we can recommend T-DM1 for all HER2-positive patients who have residual disease after pre-operative chemotherapy", said Tolaney.

"We must not forget the patients who recurred after receiving T-DM1—we will still need to identify effective therapy for them", said Geyer. He added that the effectiveness of T-DM1 in patients with residual invasive cancer after neoadjuvant therapy could make it easier for researchers to investigate de-escalating systemic treatments for HER2-positive breast cancer.

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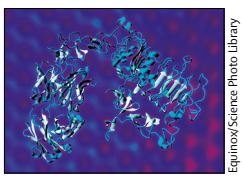

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For the **study by von Minckwitz and colleagues** see *N Engl J Med* 2018; published online Dec 5. DOI:10.1056/NEJMoa1814017