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Survival after neoadjuvant therapy with trastuzumab-lapatinib and chemotherapy in patients with HER2-positive early breast cancer: A meta-analysis of randomised trials

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Background

Studies testing addition of lapatinib (L) to neoadjuvant trastuzumab (T) plus chemotherapy reported an increase in pathologic complete response (pCR) rates but were discordant on the effect of treatment on survival, mainly due to suboptimal power. We here leverage the meta-analytic approach to resolve these inconsistencies.

Methods

We conducted a meta-analysis to combine findings from published or unpublished randomised phase 2 and 3 studies testing L in combination with neoadjuvant T plus chemotherapy for HER2+ early breast cancer. Pooled hazard ratios (HRs) were obtained for the effect of L plus T compared to T only, pCR compared to no pCR in the whole study populations, and pCR compared to no pCR in the hormone receptor-negative or positive cohorts.

Results

The meta-analysis included four studies (CALGB40601, CHER-LOB, NSABP-B41, NeoALTTO) for an overall population of 1410 patients. Patients received either T and L or T alone, in combination with paclitaxel or anthracyclines. Relapse-free survival (RFS) was higher with the combination of L plus T than with T only (HR 0.62, 95% CI 0.46-0.85). Dual blockade also led to improved overall survival (OS) (HR 0.65, 95% CI 0.43-0.98). For all treatments combined, patients achieving a pCR had better RFS and OS than those with residual disease at surgery (HR 0.45, 95% CI 0.34-0.60, and HR 0.34, 95% CI 0.23-0.51, for RFS and OS, respectively). In patients with hormone receptor-negative tumours, pCR was associated with a 65% reduction of risk of relapse (HR 0.35, 95% CI 0.23-0.53) and a 73% reduction of risk of death (HR 0.27, 95% CI 0.15-0.47). Patients with hormone receptor-positive tumours also had improved RFS if they achieved pCR (HR 0.60, 95% CI 0.37-0.97), but the benefit was smaller than in hormone receptor-negative disease.

Conclusions

These findings further validate the role of pCR as a strong predictor of outcome in patients with HER2+, especially in hormone receptor-negative disease. Moreover, we here provide robust evidence that dual blockade with L in combination with T and chemotherapy prolongs overall survival, suggesting that L could be repurposed in early settings.

Legal entity responsible for the study

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