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De-escalated neoadjuvant T-DM1 with or without endocrine therapy (ET) vs trastuzumab+ET in early HR+/HER2+ breast cancer (BC): ADAPT-TP survival results

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Background

HR+/HER2+ BC is a distinct entity associated with different molecular and therapeutic features compared to HR-/HER2+ BC. The HER2 antibody drug conjugate T-DM1 is highly effective in metastatic and early HER2+ BC. So far, no survival data for de-escalated T-DM1-based (neo)adjuvant regimens without systemic chemotherapy (CT) are available. Here, we present first survival data from ADAPT-TP.

Methods

The prospective WSG-ADAPT-TP phase II-trial is part of the ADAPT-umbrella protocol (NCT NCT01779206): 375 patients (pts) with HR+/HER2+ BC were randomized to 12 weeks of T-DM1 +/- standard ET and trastuzumab+ET q3w (ratio 1:1:1). Primary endpoint was pCR (ypT0/is/ypN0) (previously published: T-DM1/T-DM1+ET/T+ET: 41%/42%/15%). Secondary endpoints: safety, 5-y DFS, OS, translational research. Omission of further CT was allowed in all pts with pCR after 12-weeks study therapy.

Results

After median follow-up of 5 years, no significant differences between study arms were observed regarding DFS (T-DM1/T-DM1+ET/T+ET 5-y rate: 88.9%, 85.3%, and 84.6%) and OS (97.2%, 96.4% and 96.3%). pCR (vs. non-pCR) after the 12-week study treatment was strongly associated with improved DFS (5y DFS 92.7% vs. 82.7, HR=0.40, 95% CI 0.18-0.85). Among 117 pts with pCR, no further CT was given in 41 pts (35%). Significant differences between CT-treated vs. non-treated pCR pts regarding baseline characteristics were only observed for age (median 50y vs. 56y, p=0.005); similar 5y DFS was observed in both groups (92.1% (95%-CI: 78-97%) vs. 93% (84-97%)). Only 3 deaths occurred in pts with pCR.

Conclusions

Early pCR after 12 weeks of therapy was strongly associated with improved outcome in ADAPT TP and may serve as a predictive marker for CT treatment (de)-escalation. Despite substantially higher pCR rates, T-DM1 +/- ET was not associated with different DFS or OS vs. T+ET, most likely due to standard CT, given to all non-pCR pts and most pCR pts or small sample size of study. Excellent 93% 5y DFS in pts with pCR after only 12 weeks of T-DM1 +/- ET (even w/o further CT) is promising and may serve as a basis for further prospective trials addressing omission of CT overtreatment in carefully selected patients with HER2+ early BC.

Clinical trial identification

NCT01779206.

Legal entity responsible for the study

West German Study Group.

Funding

Roche.

Disclosure

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