Aim: In locally advanced breast cancer pts (≥pN2), adjuvant iddETC resulted in superior disease-free (DFS) and overall survival (OS) compared to conventionally dosed EC > Tq3w (AGO-ETC; Möbus JCO 2010). In the GAIN trial, iddETC was compared to a 4-drug dose-dense regimen with capcetabine (iddEC > T,X). Using the GAIN data, here we want to confirm the iddETC-results of the AGO-ETC trial with regard to DFS, OS, and toxicity.

Methods: In the AGO-ETC trial (1998-2003) 681 of 1,284, and in GAIN (2004-2008) 1,498 of 3,023 pts were treated with iddETC. Pts were included in AGO-ETC if ≥pN2; median number of positive nodes was 8 and 5, respectively; all other inclusion criteria were comparable. Median follow-up was 62 and 74 months, respectively, in both trials early end point was DFS. iddETC consists of a sequence of 3 x E 150mg/m2, 3 x T 225 mg/m2, and 3 x C 2,5 g/m2 q2w, with primary G-CSF support. After 40% accrual in GAIN, a reduced dose of C (2,0 g/m2) and antibiotic prophylaxis was implemented. Pts were randomly assigned to anemia prophylaxis with ESF in AGO-ETC, and to adjuvant ibandronate in GAIN (von Minckwitz JCO 2013). Results: In the iddETC-arm of AGO-ETC, 5y- DFS was 70% (95% CI 68% - 75%) and 5y-OS was 82% (95% CI 79%to 85%). Comparing to conventional EC > Tq3w, HR for DFS was 0.69 (95% CI 0.57 - 0.84). In GAIN, 5y-DFS was 80% (95% CI 78% - 82%) and 5y-OS was 85%. iddEC > T,X was not superior to iddETC. Evaluating GAIN pts with ≥pN2 (n = 923) separately, in order to match with the AGO-ETC inclusion criteria, results were comparable: 5y-DFS was 75% (95% CI 72% - 78%) and 5y-OS was 85% (95% CI 83% - 88%). In AGO-ETC, 47 pts (7%) had at least one episode of febrile neutropenia during iddETC, no toxic death was observed. In GAIN, three pts (0.2%) died from therapy related septicemia during iddETC. In both trials, pacitaxel induced neuropathy was in the expected range, and no grade 3 congestive heart failure occurred. Treatment induced MDS/AML was rare in both, AGO-ETC (0,3%) and GAIN (0,3%).

Conclusions: We consistently show high efficacy of adjuvant iddETC for node-positive breast cancer pts (≥pN2), in two consecutive prospective trials: DFS and OS-results were superior to those with conventionally dosed therapy. In the reported studies, iddETC was feasible without excessive toxicity. We suggest to add iddETC to the group of preferred regimens in current guidelines.

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