BMC Cancer. 2014 Jul 15;14:515. doi: 10.1186/1471-2407-14-515.

Dose-dense sequential adjuvant chemotherapy followed, as indicated, by trastuzumab for one year in patients with early breast cancer: first report at 5-year median follow-up of a Hellenic Cooperative Oncology Group randomized phase III trial.

Fountzilas G[1], Dafni U, Papadimitriou C, Timotheadou E, Gogas H, Eleftheraki AG, Xanthakis I, Christodoulou C, Koutras A, Papandreou CN, Papakostas P, Miliaras S, Markopoulos C, Dimitrakakis C, Korantzopoulos P, Karanikiotis C, Bafaloukos D, Kosmidis P, Samantas E, Varthalitis I, Pavlidis N, Pectasides D, Dimopoulos MA.

Abstract

BACKGROUND:

Dose-dense sequential chemotherapy including anthracyclines and taxanes has been established in the adjuvant setting of high-risk operable breast cancer. However, the preferable taxane and optimal schedule of administration in a dose-dense regimen have not been defined yet.

METHODS:

From July 2005 to November 2008, 1001 patients (990 eligible) were randomized to receive, every 2 weeks, 3 cycles of epirubicin 110 mg/m2 followed by 3 cycles of paclitaxel 200 mg/m2 followed by 3 cycles of intensified CMF (Arm A; 333 patients), or 3 cycles of epirubicin followed by 3 cycles of CMF, as in Arm A, followed 3 weeks later by 9 weekly cycles of docetaxel 35 mg/m2 (Arm B; 331), or 9 weekly cycles of paclitaxel 80 mg/m2 (Arm C; 326). Trastuzumab was administered for one year to HER2-positive patients post-radiation.

RESULTS:

At a median follow-up of 60.5 months, the 3-year disease-free survival (DFS) rate was 86%, 90% and 88%, for Arms A, B and C, respectively, while the 3-year overall survival (OS) rate was 96% in all arms. No differences were found in DFS or OS between the combined B and C Arms versus Arm A (DFS: HR = 0.81, 95% CI: 0.59-1.11, P = 0.20; OS: HR = 0.84, 95% CI: 0.55-1.30, P = 0.43). Among the 255 patients who received trastuzumab, 189 patients (74%) completed 1 year of treatment uneventfully. In all arms, the most frequently reported severe adverse events were neutropenia (30% vs. 27% vs. 26%) and leucopenia (12% vs. 13% vs. 12%), while febrile neutropenia occurred in fifty-one patients (6% vs. 4% vs. 5%). Patients in Arm A experienced more often severe pain (P = 0.002), neurological complications (P = 0.004) and allergic reactions (P = 0.004), while patients in Arm B suffered more often from severe skin reactions (P = 0.020).

CONCLUSIONS:

No significant differences in survival between the regimens were found in the present phase III trial. Taxane scheduling influenced the type of severe toxicities. HER2-positive patients demonstrated comparable 3-year DFS and OS rates with those reported in other similar studies.