Dose-Dense Chemotherapy in High-Risk Breast Cancer: Treatment Outcome and Toxicity

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Abstract

Purpose: To prospectively assess the treatment outcome of dose-dense adjuvant doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) in high risk breast cancer patients (dose-dense arm) and to compare it with the available treatment results of the conventionally scheduled fluorouracil, doxorubicin, and cyclophosphamide (FAC) used to treat high-risk patients (control arm). Study endpoints included relapse-free survival (RFS), overall survival (OS) and toxicity.

Patients and Methods: After mastectomy or breast conservative surgery, high-risk node-positive breast cancer 61 patients were assigned to receive adjuvant 4 cycles of doxorubicin/cyclophosphamide followed by 4 cycles of paclitaxel (AC/T) every 2 weeks. The treatment outcome of dose-dense AC/T was eventually compared with that of the conventionally treated high-risk patients using adjuvant 6 cycles of FAC combination chemotherapy scheduled every 3 weeks. The relevant data of 43 patients received FAC chemotherapy were obtained from the medical records. Both arms were balanced regarding age, menopausal status, number of positive axillary lymph nodes and hormonal status.

Results: At a median follow up of 37 months (range 12 – 48 months), the 3-year adjusted RFS rates for AC-T and FAC were 76% and 54.6%, respectively (P=0.042) and the mean disease-free interval was 40.6 ± 7.2 months (95% CI, 37.7 - 43.6) for dose-dense AC/T arm Vs 36.9 ± 6.9 months (95% CI, 32.3 - 41.5) for FAC arm, (P=0.040). The subgroup analysis revealed that dose-dense chemotherapy had a statistically significant positive effect on the 3-year RFS in premenopausal patients, patients with 10 or more (N3) positive axillary lymph nodes, positive ER status. There was no statistically significant difference in the 3-year OS between the two regimens. The dose-dense arm was associated with more grade 3-4 toxicity compared to FAC arm, mainly neuropathy (36%. vs 2.3%, P=0.002), anemia (49%. vs 13.9%, P=0.037) and granulocytopenia (57%. vs 213%, P=0.04). No toxicity-related mortality was observed in both arms.

Conclusion: Dose-dense AC/T significantly improved the relapse-free survival in patients with high-risk primary breast cancer and was less well tolerated compared with the conventionally scheduled FAC. The benefit was evident in premenopausal patients, extensive axillary nodal metastasis and positive ER status.