Clinical Trial

Optimal duration of adjuvant chemotherapy for high-risk node-negative (N—) breast cancer patients: 6-year results of the prospective randomised multicentre phase III UNICANCER-PACS 05 trial (UCBG-0106)

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Abstract  Purpose: Optimal duration of adjuvant chemotherapy in the treatment of early-stage breast cancer remained to be investigated rigorously for the standard regimens in widespread use in North America (doxorubicin/cyclophosphamide, AC) and Europe (5-fluorouracil/epirubicin/cyclophosphamide, FEC). Whether six cycles of FEC 100 present an advantage, or not, compared with only four cycles was tested directly in a phase III prospective multicentre trial.

Patients and methods: Between 2002 and 2006, 1515 women between 18 and 65 years of age, with node negative N0 high-risk early-stage breast cancer, were included in the study following breast surgery and axillary lymph node dissection or procedure by sentinel node technique. Inclusion in the study required tumour size T2 cm and at least one of the high-risk factors: T > 2 cm, negative oestrogen receptor/progesterone receptor (ER and PR), Scarff-Bloom-Richardson (SBR) grade II or III and age > 35 years. Patients were randomly assigned to either six FEC 100 (Arm A) or four FEC 100 (Arm B). The trial was powered to detect an absolute difference ≥6% in disease-free survival (DFS) at 5 years.

Results: At 6.1 years median follow-up, with 91 (12%) events recorded in Arm A versus 106 (14%) in Arm B, no statistically significant risk increase was associated with four versus six FEC 100: DFS (hazard ratio (HR) = 1.18; CI 95% [0.89–1.56], P = .24) and overall survival (OS) (HR = 1.39; CI 95% [0.91–2.13], P = .12).

Conclusion: Differences in chemotherapy duration did not induce notably different outcomes in our cohort of high-risk patients.

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1. Introduction

Many prospective randomised trials and several meta-analyses conducted by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) have established the benefit of adjuvant polychemotherapy in the treatment of early-stage breast cancer as it significantly reduces the rate of distant relapse and death [1–3]. However, the number and types of cytotoxic drugs that are combined together, as well as their administration schedule, dosage, dose intensity and duration has varied according to each particular institution and country. Several anthracycline-based standard treatment protocols (4 AC (doxorubicin/cyclophosphamide), 4 EC (epirubicin/cyclophosphamide), 6 FAC (5-fluorouracil/doxorubicin/cyclophosphamide), 6 FEC) with supposedly comparable efficacy existing between North America and Europe [3]. In France, six cycles of the 3-weekly FEC 100 (5-fluorouracil/epirubicin/cyclophosphamide) regimen constitute the standard chemotherapy protocol since superiority over 6 FEC 50 was demonstrated in 2005 [11].

Consensus conferences have confirmed the benefit of adjuvant chemotherapy in all patients irrespective of the number of lymph nodes involved, especially for those considered at high risk of recurrence [12–15]. Four main indicators of poor prognosis were identified for the group of node-negative patients N(−): tumour size, Scarff-Bloom-Richardson (SBR) histological grade, hormone receptor status and the patient’s age [16–20]. Optimal duration of adjuvant chemotherapy was estimated within a window of 3–6 months with no definite consensus [21,22]. This question has however remained of relevance for anthracycline dose-intense regimens (FEC 100) for which haematological toxicity and cardiac risk are linked to cumulative dose [7,8,23].

2. Patients and methods

2.1. Patient selection

From 18-year-old to 65-year-old women were eligible for inclusion in the study when presenting a N(−) non-metastatic operated breast cancer with complete tumour
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