with a goal of ~3000 pts. The success of enrollment demonstrates the feasibility of conducting an adjuvant trial in pts remote from their primary BC diagnosis.

| Characteristic | Randomized population (N = 2103) |
|---|---|
| Mean age, yr (range) | 51.9 (24−87) |
| Postmenopausal, % | 66 |
| Ethnicity, % | |
| European | 72 |
| East Asian | 16 |
| American Indian/Alaskan | 5 |
| African | 3 |
| Other | 4 |
| Stage at diagnosis, % | |
| I | 19 |
| II | 56 |
| III | 24 |
| Time from diagnosis $\leqslant$4 yr, % | 73 |
| Hormone receptor ER/PR positive, % | 57 |
| Axillary lymph node positive, % | 57 |

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**Neoadjuvant docetaxel (DOC 75) followed by fluorouracil, epirubicin, cyclophosphamide (FEC 100) in primary operable breast cancer: results of a multicenter phase II trial**

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**Background:** Combination regimens of an anthracycline and a taxane have been widely used as preoperative systemic therapy in patients with operable breast cancer. Our previous study (JBCRG01: FEC 100 followed by DOC 75, Toi et al, SABCS 2006 #1037), showed most tumors responded to docetaxel despite non response to FEC. However, due to the toxicity of FEC, completion rate of DOC was only 80%. To resolve issues from the JBCRG01 trial, we evaluated the efficacy and safety of neoadjuvant therapy with the reverse regimen DOC 75 followed by FEC 100 (JBCRG03).

**Material and Methods:** Eligible women had T1c−3N0M0, T1−3N1M0 operable breast cancer. Chemotherapy consisted of 4 cycles of DOC (75 mg/m$^2$) every 3 weeks followed by 4 cycles of FEC (F: 500 mg/m$^2$, E: 100 mg/m$^2$, C: 500 mg/m$^2$) every 3 weeks. The primary endpoint was pathologic response rate; secondary endpoints were safety, efficacy and a subset analysis of biomarkers.

**Results:** From October 2005 to October 2006, 137 women were enrolled and 135 were evaluable. The median age was 46 (range, 24−62) with 70% being premenopausal. All patients had ECOG Performance Status of 0 and 54% were node positive. 73% of patients had tumor stage T2, 9% T1, and 18% T3. Hormone status was: ER positive 64%, PgR positive 47%, both negative 33%. HER2 (IHC) status: positive (3+) 23%, negative 77%. Patient characteristics were similar to JBCRG01. 6 patients stopped chemotherapy because of progressive disease during DOC treatment. In DOC–FEC treatment, completion rates of DOC and FEC were 85% and 79%, respectively. The overall response rate was 79% with 21% CR. Addition of FEC improved overall response rate from 64% to 79%. Grade 3−4 hematological toxicity included leucopenia 58%, neutropenia 69%, and febrile neutropenia 15%. Grade 3 non-hematological toxicity included nausea 2%, vomiting 2%, fatigue 2%, anorexia 2%, diarrhea 1%, and weight loss 1%. There were no reports of grade 4 non-hematological toxicity.

**Conclusions:** The regimen of DOC 75 followed by FEC 100 as primary therapy for early stage breast cancer was an active regimen with an acceptable rate of severe toxicity. Further analyses including translational research are needed to evaluate the benefit of taxane first administration in the neoadjuvant setting.

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**Optimal timing and duration of the use of an aromatase inhibitor (AI) in the adjuvant treatment of postmenopausal hormone receptor-positive (HR+) breast cancer (BC)**

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**Introduction:** It is clear that AIs have a central role to play in the adjuvant treatment of postmenopausal HR+ BC. They are more effective than tamoxifen (TAM) and generally have a better side-effect profile. However uncertainty exists as to whether they should be offered as the initial adjuvant treatment, or whether they are more effective after an initial "priming" period with TAM, where relative benefits appear to be larger. There is uncertainty between the efficacy of the different AIs and the timing of treatment.

**Methods:** Models are presented, based on published data from 8 trials, to evaluate the use of an AI upfront compared with sequencing it after varying periods of initial treatment with TAM. We model recurrence rates for the first 10 and 20 years of follow-up using only the reported hazard ratios. Historically, carryover effect had only been demonstrated with TAM as documented in the EBCTCG overview; however, it is now reported to be significantly greater with AIs [1].

**Results:** These models indicate that initial or early treatment always dominates a strategy of using TAM for 5 years initially. Using current data to estimate hazard ratios suggests that starting with an AI dominates a 2-year initial use of TAM followed by 3 years of an AI, even though the reduction in hazard ratios after switching may be larger after the switch has taken place. Based on data from the extended treatment studies of 5 years of an AI after 5 years of TAM, and the ATLAS study of 5 vs 10 years of TAM, we also model a range of 10-year treatment plans.

**Conclusions:** While it is clear that the current evidence suggesting use of an AI upfront, in the first 5 years of adjuvant treatment, is the best strategy, additional clinical trials results (ie, BIG 1-98 comparing upfront vs sequencing) will provide additional information regarding the optimal time to introduce an AI. Available evidence also supports continued treatment beyond 5 years in some patients, but no data exist on the optimal duration of treatment with an AI.

**References**

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**Long-term results and comparative analysis of normo fractionated (NF) and hypo fractionated (HF) adjuvant radiotherapy after breast conserving surgery in elderly**

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**Purpose:** To evaluate the results of elderly breast cancer (BC) patients (pts) treated with adjuvant once-weekly HF radiotherapy (RT).

**Patients and Methods:** Between 1995 and 1999, 401 patients older than 70 yrs were treated with conservative surgery and then adjuvant RT at the Institut Curie for non-metastatic BC. The surgery consisted of lumpectomy and lymph node dissection (LND) followed by NF RT, delivered to the total dose (TD) of 50 Gy in 25 fractions (fr.) to the breast +/− boost or HF: once weekly in five fr. of 6.5 Gy to a TD of 32.5 Gy to the breast. The regional LN were irradiated in NF group. Pts are regularly followed up and toxicity is evaluated. Hormonal treatment (HT) was delivered to all RH positive pts.

**Results:** There were 347 pts in the NF RT and 54 pts in HF RT group. The median follow-up was 92 months (9–143). In NF 36% of pts were older than 80 yrs vs 87% in HF group. The cause specific survival at 5 and 10 yrs was as follows: 96% and 89% for NF vs 93% and 85% for HF (p 0.3). HT was mostly neoadjuvant in HF pts (35%) and adjuvant in 91% in NF group. There was no significant difference in the local control between 2 groups with p 0.65, at 5 and 10 yrs, as follows: 95% and 89% for NF and 94% and 91% for HF. No metastatic disease was found at 5 and 10 yrs: 94% and 90% in NF and 93% and 91% in HF. The treatment tolerance and cosmetic results were comparable also between the 2 groups of patients.

**Conclusions:** The HF RT scheme resulted to providing excellent long-term local control, in mild early reactions and acceptable late toxicity. This treatment represents a good alternative in elderly with equal results in term of cause specific survival, local control, and metastatic rates, compared to NF RT. Large prospective randomised trials are needed to confirm these results.