697 PUBLICATION

Toxicity data of a multicenter, randomized study of standard FEC (FEC60) vs FEC With double epirubicin (EPI) (FEC120) plus G-CSF in metastatic breast cancer (MBC)

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Purpose: Is feasible increasing EPI dosage into FEC in a multicenter trial?

Methods: Pts <70 yrs with MBC were randomly treated with 6 courses (every 21 days) of FEC60 (mg/mq: 5-FU 600, EPI 60, CTX 600) or of FEC120 (as FEC60, but with EPI 120) + G-CSF (from day 4 to 13).

Results: Between V. 95 and VII. 96, 46 of 71 recruited pts (23 treated with 114 courses of FEC60 and 21 treated with 108 courses FEC120) completed the treatment. Non hematological toxicity was similar. Hematological toxicity was somewhat, but not significantly greater in FEC120. For all pts and courses, median nadir, day of nadir and % and days of toxicity.

	WBC nadir (day)	WBC G3–4% (days)	Platelet nadir (day)	Platelet G3–4% (days)	Hb nadir (day)	Hb G3–4% (days)
FEC60	2.5 (11)	15 (7)	174 (10)	0 (4)	11.2 (10)	15 (11)
FEC120	5.0 (7)	32 (4)	103 (10)	35 (4)	9 4 (10)	32 (11)

Conclusion: Administering 6 courses of FEC120 with G-CSF is feasible in multicenter trial.

698 PUBLICATION

Paclitaxel (P) Taxol® plus epirubicin (E) as first-line therapy in patients (pts) with advanced breast cancer (ABC) a preliminary analysis

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Introduction: Since the confirmation of the single agent activity of P in breast cancer several studies to develop a synergistic combination began P plus Doxorubicin is a highly active combination with response rates ranging between 63% to 94%. Epirubicin is an equieffective but less cardiotoxic analogue of Doxorubicin. We report a phase II study to evaluate the efficacy and safety of the combination of P plus E as first-line therapy in patients with ABC.

Material and Methods: From January 1996 to January 1997 – 18 patients with bidimensionally measurable untreated ABC were treated with Epirubicin 70 mg/m^2 infused over 30 minutes followed by Paclitaxel 200 mg/m^2 administered as a 3 hours intravenous infusion. All patients were premedicated with Dexamethasone 16 mg. Diphenhydramine 50 mg and Ranitidine 50 mg infused 1 hour before the P administration. Courses were repeated every 21 days.

Patient characteristic: Median age: 54 years, Range (36 to 70) *ECOG performance status:* 0 = 8 pts (44.44%); 1 = 7 pts (38.89%); 2–3 pts (16.67%) *Estrogen receptor status;* (+) = 10 pts (55.56%); (–) = 6 pts (33.33%); unknown = 2 pts (11.11%) *Menopausal status:* Pre = 5 pts (27.78%); Post = 13 pts (72.22%). *Dominant disease site:* Bone: 7 pts (38.89%); Viscera: 5 pts (27.78%); Soft tissue: 6 pts (33.33%). *N° of metastatic disease sites:* 1 = 13 pts (72.22%); 2 = 4 pts (22.22%); >2 = 1 pts (5.56%). 13 pts (72.22%) had previously received adjuvant chemoterapy (6 pts (33.33%) with Anthracycline containing regimen); 5 pts (27.78%) had received adjuvant hormonal therapy and 11 pts (61.11%) had received chest radiotherapy. The media basal LVEF (Left ventricular ejection fraction) was 57% (LVEF) was monitored every second cycle to assess for cardiotoxicity.

Results: A total of 82 cycles (4.5 p/pts) were administered. All pts were evaluable for toxicity. No hypersensitivity reactions were observed: No pts showed clinical cardiac toxicity, ECG was normal and only 4 pts (22.22%) experienced a symptomatic LVEF decrease of 10%. Grade 3 alopecia was universal.

Neutropenia	G1 5 pts (27.78%)	G2 8 pts (44.44%)	G3: 5 pts (27 78%)
Mucositis	G1· 9 pts (50.00%)	G2 4 pts (22.22%)	G3 0 pts (00.00%)
Diarrhea	G1· 5 pts (27.78%)	G2: 3 pts (16.67%)	G3. 0 pts (00.00%)
Myalgia/Arthralgia	G1 7 pts (38.89%)	G2: 3 pts (16 67%)	G3· 0 pts (00 00%)
Nausea/Vomiting	G1: 0 pts (33.33%)	G2· 2 pts (11.11%)	G3: 0 pts (00 00%)
Peripheral neuropathy	G1: 5 pts (27.78%)	G2: 3 pts (16.67%)	G3: 0 pts (00.00%)
16/18 pts were evaluable for response:	CR: 1 pts (6.25%)	PR· 10 pts (62.5%)	SD: 3 pts (18.75%)
	PD: 2 pts (15.50%)	CR + PR: 68.75%	

Conclusions: In our experience the combination of P plus E is a safe schedule for the outpatient setting. Is an active regimen with a response rate of 68.75%; does not produce cardiac toxicity and the main toxicity has been neutropenia.

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Combination of paclitaxel with mitoxantrone in patients with advanced breast cancer

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Purpose: The encouraging results of phase II studies for the possible synergistic and additive effects of paclitaxel in combination with other drugs known to be active in breast cancer, such as doxorubicin and the lesser cardiotoxicity of mitoxantrone led us to evaluate the efficacy and safety of the combination paclitaxel with mitoxantrone for the treatment of initially extensive or relapsing breast cancer.

Methods: From May 1995 to December 1996, 42 patients with state IV or relapsing breast cancer were treated with paclitaxel and mitoxantrone Paclitaxel was given as 3-hour infusion of 200 mg/m^2 with premedication, followed by intravenous bolus of mitoxantrone 14 mg/m^2 on day 1. Courses were repeated every 3 weeks for six courses. G-CSF 5 μg/Kg/day was given subcutaneously for 10 days starting at least 5 days after drug administration.

Results: There were 7 complete responses and 18 partial responses for an overall response rate of 65.78% (95% CI, 48.65%–80.37%). The most significant observed toxicity associated with the administration of paclitaxel/mitoxantrone has been peripheral neuropathy, primarily WHO grade I–II.

Conclusions: Paclitaxel and mitoxantrone supported by G-CSF can be administered safely enhancing the median performance status of the patients and achieving high response rate. These factors are of crucial importance considering the palliative nature of salvage chemotherapy in relapsing breast cancer patients. Also our results indicate that this combination might be an effective first-line treatment for patients with advanced breast cancer.

700 PUBLICATION

Advanced breast cancer: High dose toremifene in tamoxifen-refractory patients

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Purpose: Postmenopausal women with advanced breast cancer often receive tamoxifen as first-line hormonal treatment of their disease. After failure of the first-line treatment a second-line hormonal treatment may benefit for some patients. Toremifene (Fareston®) is a novel antiestrogen which is well tolerated at high doses. The purpose of study is to evaluate efficacy and safety of toremifene after tamoxifen failure. Predictive factors for effective treatment are evaluated.

Methods: 96 patients received toremifene 200–240 mg/day until disease progression. Response and toxicity evaluation was based on WHO criteria. Data of 5 individual prospective clinical trials are overviewed.

Results: 2 CRs, 5 PRs and 21 SDs (disease stabilization ≥5 months) were observed with an overall objective response rate of 29.2%. Time to treatment failure of those patients with described response ranged from 5 to 27+ months. The most frequent adverse drug reactions were sweating/hot flashes and nausea of WHO grade I. Deep venous thrombosis was detected in two patients. No dose reductions due to clinical toxicity were necessary. The data suggests that patients with ER positive primary tumors who had previously responded to tamoxifen are most likely to respond again to other hormonal treatment.

Conclusions: Efficacy and safety of high dose toremifene after failure of previous tamoxifen treatment in postmenopausal patients with advanced breast cancer is similar to that seen with other hormonal treatments including MPA and aromatase inhibitors.