right-side excess (right/left=1.25), which is in contrast with the significant left-side excess reported elsewhere [5], but consistent with the series described in some populations [6].

During the same period, there were nine deaths in the male resident population due to breast cancer. The age-adjusted (world standard) mortality rate was 0.14 × 100 000 (S.E.=0.1).

The observed survival, according to Kaplan and Meier [7], was 75.0% (95% C.I. 56.2–86.6) for the first year and 62.5% (95% C.I. 43.5–76.7) 5 years after diagnosis. The 5-year relative survival was 79%. Both crude and relative 5-year survival rates were quite high compared with other wider population-based series [8].

As far as the treatment is concerned, 1 case refused treatment and 24 (75%) underwent surgical intervention. There were 14 modified radical mastectomies or Halsted mastectomies and eight simple mastectomies or limited excisions. For 23 cases (71.9%), the histology was available and, as expected [9,10], the great majority were epithelial tumours (87% ductal carcinomas, one solid carcinoma and one not otherwise specified carcinoma); moreover, there was one myxoid liposarcoma. As regards the stage as defined by the registry, 8 (25%) patients had a localised cancer, 10 (31%) had local diffusion and 3 (9%) had distant metastases; the stage was quite advanced compared to other wider reports [8]. For 15 cases, the pathological T of TNM was available: there were 8 TI, 3 T2 and 4 T4 patients; for 15 cases, partially overlapping with the previous ones, N was known with 10 N0 and 5 N1 patients. 3 cases had distant metastases at the time of diagnosis.

In comparison with breast cancers occurring in the female population in the same area, males were of older age at onset and with a more advanced stage at the time of diagnosis ([10] and Barchielli, personal communication). Among these cases, probably the oldest case (94 years old at the time of the diagnosis) ever reported is registered [5].

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European Journal of Cancer Vol. 30A, No. 11, pp. 1733–1734, 1994.
Elsevier Science Ltd
Printed in Great Britain
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0959-8049(94)00298-3

FLEP (5-Fluorouracil, Leucovorin, Etoposide, Cisplatin) in Advanced Gastric Cancer

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Gastric cancer is the most chemosensitive adenocarcinoma among digestive systems neoplasms. Recent schemes have attempted to take advantage of drug synergism and the modulation of 5-fluorouracil (5-FU) by several agents. Such strategies resulted in a response rate ranging between 40 and 70% [1–4].

Table 1. Patients' characteristics

	No. of patients
Total no. of patients	46
Median age, years (range)	55 (21–72)
Male/female	24/22
Pretreatment ECOG	
0–1	7
2	32
3	7
% of weight loss	
None	12
0–10%	15
> 10%	19
Locoregional/metastatic	6/40
Sites of metastatic disease	
Distant lymph nodes	15
Liver	20
Lung	4
Peritoneum	11
Others	11
Number of metastatic locations	
0	6
1	28
2	8
3	4

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Revised 13 May 1994; accepted 12 July 1994.

The modulation of 5-FU with leucovorin (LV) and the potential synergism of 5-FU, etoposide and cisplatin make the combination of these four drugs (FLEP) an appealing one. In a preliminary report in 1989, Preusser and associates obtained a 57% response rate with this scheme in a series of 14 patients [5], so we decided to assess its efficacy.

From May 1989 to December 1992, 46 consecutive, previously untreated patients with unresectable measurable gastric carcinoma were treated with LV 300 mg/m^2, etoposide 100 mg/m^2, 5-FU 500 mg/m^2 and cisplatinum 30 mg/m^2 on days 1, 2 and 3 every 28 days. All courses were administered on an outpatient basis. All the patients were less than 70 years old, had a life expectancy of > 3 months and histologically confirmed gastric cancer. Table 1 shows the patients' characteristics.

A total of 169 cycles were administered to the 46 patients (median 3.6 per patient, range 1–6). 18 out of 46 patients (39%) obtained an objective response (95% confidence interval, 25–54%) and 2 a complete response (4%). The median duration of response was 5 months. The main side-effects were haematological and gastrointestinal; grade 3–4 toxicity was as follows: leucopenia in 9.5% of courses, anaemia in 3%, thrombocytopenia in 3%, nausea/vomiting in 4%, and diarrhoea in 5%. Hospitalisation, due to fever and neutropenia, was required in 5 patients, 3 of whom died of sepsis.

Our results indicate that the FLEP combination shows moderate activity, although with high toxicity. It should be noted that some of our patients' characteristics, such as the high percentage of a bad performance status (ECOG 2–3 in 85%) or distant metastases (87%) are adverse prognostic factors for response and survival [6, 7]. However, our results coincide with those of Preusser and colleagues who, after studying 29 patients, reported a lower response rate of 38% and high toxicity (one toxic death) [8].

The currently available data with the FLEP combination do not permit its recommendations for treatment of gastric carcinoma.

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European Journal of Cancer Vol. 30A, No. 11, pp. 1734–1736, 1994.
Elsevier Science Ltd
Printed in Great Britain
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0959-8049(94)00264-9

Escalating Doses of Mitoxantrone With Granulocyte Colony-stimulating Factor (G-CSF) Rescue Plus 5-Fluorouracil and High-dose Levofolinic Acid in Metastatic Breast Cancer

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The combination of mitoxantrone (DHAD) plus levofolinic acid (1-FA) and 5-fluorouracil (5-FU) has been reported to be highly active (47.3% mean overall response rate) in metastatic breast carcinoma (MBC) with an excellent tolerance, as recently reviewed by Hainsworth [1]. In this paper, we report the results of a dose-finding study in which DHAD dosage, in combination with 1-FA/5-FU and granulocyte colony-stimulating factor (G-CSF) rescue, has been progressively increased up to the identification of the dose-limiting toxicity (DTL) and the maximum tolerated dose (MTD) in a series of patients with MBC. Analysis of dose intensity (DI) and objective response is also presented.

Standard eligibility criteria have been described elsewhere [2,3]. Chemotherapy consisted of 1-FA 100 mg/m^2 intravenous (i.v.) bolus and 5-FU 400 mg/m^2 over 15 min on days 1–3, plus DHAD on day 3 starting from 14 mg/m^2 cycle for the first group of 3 patients. DHAD dosage was then escalated by 2 mg/m^2 for subsequent groups of 3 patients until unacceptable toxicity was recorded. G-CSF 5 μg/kg/day was given subcutaneously (s.c.) for 10 days, starting at least 48 h after DHAD administration. WHO criteria were employed for definitions of both objective responses and toxicity. DLT was represented by any of the following side-effects occurring in at least 2 of the 3 patients entered at any given dose level: nadir absolute neutrophil count (ANC) <500/mm^3 for ≥5 days; grade 4 thrombocytopenia for ≥5 days; fever lasting >5 days requiring antibiotics; grade 3–4 extrahaematological toxicity; decrease in left ventricular efection fraction (LVEF) >15% from basal level; toxicity-related delay >8 days. The MTD of DHAD was established as the level below the dose at which DLT was seen.

There were 22 patients with a mean age of 54.4 years (range 36–68), and a mean Karnofsky index of 85 (range 70–100). There were 20 ductal infiltrating (91%), one lobular and one mixed ductal/lobular carcinomas; 12 patients (55%) were premenopausal, and 10 (45%) postmenopausal; basal oestrogen receptor (ER) status was positive in 8 patients (36%), negative

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Revised 10 June 1994; accepted 24 June 1994.