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Etoposide, Doxorubicin and Cisplatin in Advanced or Metastatic Gastric Cancer

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45–72% response rate of gastric cancer to combination chemotherapy with etoposide, doxorubicin and cisplatin (EAP) could really be a major advance in the treatment of this fatal disease [1–3]. In the light of such good results, high incidence of WHO grade 3 and 4 toxicities is sometimes negligible in the patients' recovery. However, it is disappointing when further trials cannot reproduce these results, achieving only 13–15% response rate and with intolerable toxic side-effects [4, 5].

Encouraged by the promising report of Preusser *et al.* [1], we initiated a trial using EAP in patients with metastatic and/or locally advanced or recurrent gastric cancer. The treatment schedule was 22–28 day cycles of doxorubicin 20 mg/m^2 on days 1 and 7, cisplatin 40 mg/m^2 on days 2 and 8 (or carboplatin 160 mg/m^2 when creatinine clearance fell below 50 ml/min), and intravenous etoposide 95 mg/m^2 on days 4–6. Patients, clinical data and treatment results to date are presented in Table 1.

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Our reponse rate was 0%. There was only 1 patient with disease stabilisation for 11 months, who had a partial response in levels of carcinoembryonic antigen. Toxicity, on the other hand, was severe. There was 2 treatment-related deaths and another 4 cases of severe leukopenia and infections. The patient with the minimal toxicity achieved the most favourable response in our group. All the patients had sites of disease reported to be resistant to EAP [1], and all of them had either poorly differentiated histology or signet ring cell carcinoma.

Our study to date far from concludes that EAP is a toxic rather than an effective regimen, as claimed by Taal *et al.* [5]. However, one would expect at least 1–2 positive responses in our small group, in view of the reported 51%–72% response rate [1–3].

A possible explanation for the difference in responses between the trials of Taal *et al.* [5], Sparano *et al.* [4] and our group, and those of Preusser *et al.* [1], Katz *et al.* [2] and Taguchi [3], may be due to (a) careful patient selection as regards histology and sites of disease and (b) the various disease courses and responsiveness in the different geographical areas and ethnic groups.

Further trials are, of course, needed in order to evaluate the real efficacy of EAP.

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2. Katz A, Gansl R, Simon S, *et al.* Phase II trial of VP-15 (V), adriamycin (A) and cisplatinum (C) in patients with advanced gastric cancer (AGC). *Proc Am Soc Clin Oncol* 1989, 8, 98.
3. Taguchi T. Combination chemotherapy with etoposide (E), adriamycin (A) and cisplatinum (P) for advanced gastric cancer. *Proc Am Soc Clin Oncol* 1989, 8, 108.
4. Sparano JA, Wiernik PH. Toxicity of etoposide, doxorubicin and cisplatin in gastric cancer. *J Clin Oncol* 1990, 5, 938–939.
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Table 1. Patients' clinical data and treatment results

Patient (sex/age)	KPS	Surgery	Sites	Courses	Response (overall /site)	Toxicity	Survival (wks)
1 (F/65)	70	Inoperable	Locally advanced, liver, nodes	1	-/-	Vomiting, pancytopenia (WBC=400/μl), sepsis, death	2
2 (M/32)	60	Subtotal gastrectomy	Bones, cord compression, pleural effusion	2	PD/PD	Leukopenia (1100/μl), follicular tonsillitis	10
3 (M/62)	70	Inoperable	Locally advanced, abdominal spread, pancreas	2	PD/PD	Vomiting, GIT bleeding, pancytopenia (WBC=300/μl), gram negative sepsis, death	8
4 (F/54)	90	Subtotal gastrectomy	Lymphangitic spread + lung metastases, CEA=17	2	PD/PD	Vomiting, fever, recurrent DVT	11
5 (F/68)	90	Inoperable	Locally advanced, CEA=16	4	SD/PR in CEA	Vomiting	50+
6 (M/65)	80	Inoperable	Locally advanced, nodes	1	PD/PD	Leukopenia (400/μl) sepsis	16
7 (M/64)	90	Oesophago-gastrectomy	Local recurrence, lung	1	PD/PD	Vomiting, leukopenia (1100/μl), fever	14
8 (F/65)	80	Inoperable	Locally advanced, abdominal spread, CEA=8	2	PD/PR in CEA	Vomiting, weakness, leukopenia (700/μl), fever	15+

Patients 2 and 4 had subtotal gastrectomy and 7 had oesophagogastrectomy; others were inoperable. Histology in patients 1, 2 and 6 was adenocarcinoma, G_3; others were signet ring. Patients 2 and 7 had disease-free periods of 56 and 4 months.
WBC = white blood cells, GIT = gastrointestinal, DVT = deep vein thrombosis, CEA = carcinosembryonic antigen, SD = stable disease, PR = partial response, PD = progressive disease.