suggested by an increase in serum prostatic acid phosphatase and serum prostate-specific antigen from 6.4 to 24 ng/ml and from 96 to 180 ng/ml, respectively.

The accrual of 53% of the planned sample (10/19) yields a P value of 0.19 instead of the previously fixed 0.05. Interim analysis shows that any hypothesized response rate of 26% or more is rejected at the 0.05 one-sided level of significance [3]. With Hilsenbeck's method there will have been an 81% chance at the end of the completed study that the 95% confidence intervals for the true response rate would fail to include improvement rates of 30% or more [4]. Similar results were obtained by Dr C. Logothetis (personal communication).

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Treatment of Advanced Ovarian Cancer with Intraperitoneal Tumour Necrosis Factor

J. Hardy, A. Jones, M.E. Gore, C. Viner, P. Selby and E. Wiltshaw

TUMOUR NECROSIS FACTOR (TNF) is active *in vivo* when used intraperitoneally against human ovarian xenografts [1, 2]. Intraperitoneal administration of drugs in ovarian cancer is attractive for three reasons: patients have disease limited to the peritoneal cavity [3], there may be less systemic toxicity when drugs are given by this route and tumour cells may be exposed to higher concentrations of drug for longer. There is *in vitro* evidence that such prolonged exposure is required for TNF-induced cytoxicity [4]. We report our results of intraperitoneal TNF in ovarian cancer.

Patients with advanced epithelial ovarian cancer, refractory to cisplatin, were eligible if they had ascites, evaluable disease, projected survival greater than 2 months and had given informed consent. Exclusion criteria included leucopenia ($< 3.5 \times 10^9$/1), thrombocytopenia ($< 100 \times 10^9$/1), hepatic/renal dysfunction (unless due to metastases) and WHO performance status of 3–4. Patients had not received previous biological therapy and had not had chemotherapy for at least 2 weeks. Patients' details are shown in Table 1.

Abdominal paracentesis was done with a 14 G Abocath or dialysis catheter and the peritoneal cavity was drained to dryness. TNF (Asahi Chemical Co.) 2×10^5 U (89 μg)/m^2 was dissolved in 1 l normal saline and infused over 1 h via the paracentesis catheter. This was then clamped for 24 h after which any remaining ascites was drained and the catheter removed. Patients were rotated to ensure even distribution of TNF. Ketoprofen 100 mg was used prophylactically to reduce febrile reactions and established fevers were treated with paracetamol and pethidine. Treatment was repeated 4 weekly. Patients were assessed clinically once a week and by ultrasound or computerised axial tomography before each course.

Table 1. Patients' characteristics and toxicity and outcome of intraperitoneal TNF

	Patient			
	1	2	3	4
Age	45	59	49	38
Performance status	1	2	1	0
No. of courses	4	3	1	3
Acute toxicity (fever, etc.)	+	+	+	+
Abdominal pain/peritonism	+	+	+	+
Infection*	+	–	–	+
Response	PD	PD	PD	PD

*Cellulitis in case 1 and septicaemia in case 4.
PD = progressive disease.

The four patients received a total of eleven courses (Table 1). All patients developed pyrexia (temperature over 38°C), influenza-like symptoms and abdominal discomfort during infusion. Peritonism developed in six courses, one patient had gram negative septicaemia (*Escherichia coli*) not associated with leucopenia and one developed cellulitis of the abdominal wall due to leakage of infusate along the catheter tract. All patients had malaise for about 2 weeks. There were no objective responses.

The toxicity of intraperitoneal of TNF includes acute systemic symptoms similar to those reported after intravenous administration [5]. In addition, all patients complained of abdominal pain and peritonism was observed in over half the courses given. High doses of TNF can be given intraperitoneally to mice without clinical or histological evidence of peritonitis (A.J.). In man intraperitoneal TNF is not well tolerated even at doses well below the maximum tolerated intravenous dose (440 μg/m^2).

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Correspondence to: M.E. Gore.
J. Hardy, A. Jones, M.E. Gore, C. Viner, P. Selby and E. Wiltshaw are at the Department of Medicine, Royal Marsden Hospital, Fulham Road, London SW3 6JJ, U.K.