These results indicate that precystectomy intra-arterial cisplatin for advanced squamous cell carcinoma of the urinary bladder is ineffective, and unduly delays cystectomy, which is currently the only effective known treatment for this disease.

1. Kubota Y, Kakizaki H, Humasawa K, *et al.* Preoperative intra-arterial infusion chemotherapy for patients with bladder cancer. *Eur Urol* 1989, **16**, 189–194.
2. Maatman TJ, Montie JE, Bukowski RM, *et al.* Intra-arterial chemotherapy as an adjuvant to surgery in transitional cell carcinoma of the bladder. *J Urol* 1986, **153**, 256–260.
3. Mitsuhata N, Seki M, Matsumura Y, *et al.* Intra-arterial infusion chemotherapy in combination with angiotensin II for advanced bladder cancer. *J Urol* 1986, **136**, 580–585.

Eur J Cancer, Vol. 28, No. 2/3, p. 613, 1992.
Printed in Great Britain
0964-1947/92 $5.00 + 0.00

Treatment of Recurrent Gynaecologic Malignancies with a New Camptothecin Derivative

H. Mori, N. Itoh, H. Kondoh and T. Tamaya

THE ANTITUMOUR activity of camptothecin, a plant alkaloid isolated from *Camptotheca acuminata*, was studied in the 1970s. However, this compound has been a disappointment because of its low response rate in clinical trials and significant myelotoxicity. The demonstration that DNA topoisomerase I is the main target of camptothecin [1] has revived interest in research on camptothecin analogues as antitumour agents. A new derivative of camptothecin, 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxy camptothecin (CPT-11) has been synthesised in Japan [2]. We report our preliminary experience of CPT-11 treatment for gynaecological malignancies.

Patients with recurrent gynaecologic malignancies were eligible if they had evaluable disease, projected survival greater than 2 months and had given informed consent. Exclusion criteria included leukopenia (cells < 3000/μl), thrombocytopenia (platelets < 80000/μl) and WHO performance status of 4. Patients had not received chemotherapy for at least 4 weeks. The characteristics of 4 patients entered in this study are shown in Table 1. All the patients had evaluable pulmonary metastases, which of patients 2, 3 and 4 had been refractory to prior chemotherapy. CPT-11 (150 mg/m^2; Yakult Co. Ltd., Tokyo, Japan) was dissolved in 200 ml normal saline and infused intravenously over 30 min. CPT-11 was administered by single injections every 3 weeks. The scheduled course was delayed when haematological recovery was incomplete. Response and toxicity were assessed according to the UICC-WHO criteria.

Table 1. Clinical features of 4 patients and response to CPT-11 therapy

	Patient			
	1	2	3	4
Age	59	61	45	26
Primary focus	Cervix	Cervix	Corpus	Ovary
Histology	Squamous cell carcinoma	Squamous cell carcinoma	Chorio-carcinoma	Serous cyst-adeno-carcinoma
Clinical stage	IIb	IIIb	III	IV
Initial therapy	*	†	‡	§
Prior chemotherapy	—	‖	¶	**
Performance status	1	3	1	1
Number of pulmonary metastatic nodules	4	3	10	3
Total no. of courses	6	11	4	3
Response	CR	CR	PR	PD
No. of courses required to achieve response	6	2	1	
Duration of response (weeks)	20+††	4	20+	
Curent status	Alive(−)‡‡	Alive(+)§§	Alive(+)	Alive(+)

* Radical hysterectomy plus bilateral lymphadenectomy. † Whole pelvic irradiation. ‡ Supravaginal hysterectomy. § Total anterior hysterectomy plus bilateral salpingo-oophorectomy. ‖ [platin/peplomycin/etoposide] × 1 course. ¶[Methotrexate/actinomycin D] × 3 courses. **[platin/-doxorubicin/cyclophosphamide] × 5 courses. CR = complete response; PR = partial response; PD = progressive disease. †† (+), still responding. ‡‡ (−), with no evidence of disease. §§ (+), with disease.

As shown in Table 1, 2 complete responses (patients 1 and 2), 1 partial response (patient 3) and 1 progressive disease (patient 4) were observed. The principal toxicity was myelosuppression. Patients 1 and 2 developed leukopenia grade III and II, respectively. In these patients, the nadir was observed on day 7 after each course, resolving 2 to 4 weeks later. Patients 3 and 4 had grade I leukopenia. However, no patients developed neutropenic fever. Grade II alopecia was also noted in all patients. No renal, hepatic or cardiac toxicity was encountered.

Although the number of patients studied was small, the clinical impression was that CPT-11 was especially effective against pulmonary metastasis. CPT-11 is a unique drug that interferes with the function of DNA topoisomerase I and is notable for its non renal toxicity. CPT-11 may have significant clinical advantages for patients unable to receive cisplatin.

Correspondence to H. Mori.
The authors are at the Department of Obstetrics and Gynaecology, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu 500, Japan.
Received 2 Sep. 1991; accepted 18 Oct. 1991.

1. Hsiang Y-H, Hertzberg R, Hecht S, Liu LF. Camptothecin induces protein-linked DNA breaks via mammalian DNA topoisomerase I. *J Biol Chem* 1985, **260**, 14873–14878.
2. Kunimoto T, Nitta K, Tanaka T, *et al.* Antitumor activity of 7-ethyl-10-[4-(piperidino)-1-piperidino]carbonyloxy camptothecin, a novel water-soluble derivative of camptothecin, against murine tumors. *Cancer Res* 1987, **47**, 5944–5947.