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Letters

Toremifene for Recurrent and Advanced Endometrial Carcinoma

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THE RESPONSE rates of recurrent endometrial cancer to therapy have generally been disappointing: less than 50% to cisplatin-based chemotherapy [1], and about 30% to progestogens and to tamoxifen [2, 3]. We present the effect of toremifene, another antioestrogen, in 18 postmenopausal women with recurrent and advanced endometrial cancer. In contrast to tamoxifen, which possibly may be associated with the development of endometrial cancer [4], and can at high daily doses cause liver damage [5], no carcinogenicity or liver toxicity has been observed with toremifene. Thus, toremifene can be safely given at high doses, up to at least 460 mg a day [6]. Toremifene has been shown to be effective in breast cancer, even after tamoxifen failure [7, 8]. In a preliminary study, endometrial cancer seemed to respond to toremifene [9].

Of the 18 patients, 17 had recurrent disease and 1 previously untreated, stage IV endometrial carcinoma. 13 of the tumours were adenocarcinomas, two adenocarcinomas, one serous adenocarcinoma, one carcinosarcoma and one undifferentiated carcinoma. In six instances, the oestrogen and progesterone receptor (ER, PR) content of the tumours was determined; of these, three were ER+/PR−, two were ER−/PR+, and one was ER−/PR−. The previously untreated carcinoma was one of the ER−/PR+ tumours; the specimen was taken from a vaginal metastasis. The receptor content in the remaining tumours was determined from the disease recurrence before toremifene therapy was instituted.

The mean age of the patients was 66 years (range 50–81 years). The patients had previously been treated by surgery with or without radiation, and in 12 patients, hormonal and/or cytotoxic therapy had also been used. Four of the recurrences were local, seven were distant and six were both local and distant. The patient who had not previously been treated had metastases in the lung and vagina.

Toremifene was given as a single oral dose of 200 mg daily for at least 12 weeks or until progression. The response to therapy was evaluated every 3 months. The responses were assessed as complete or partial response (CR, PR), no change (NC) and progressive disease (PD) according to UICC criteria [10].

Table 1. Response of endometrial cancer to toremifene 200 mg daily, and duration of the responses

Responses	*n*		Duration of response (months)
Complete response	2	22%	43+, 6
Partial response	2		9, 3
No change	4	22%	7, 6, 3, 3
Progressive disease	10	56%	
	18		

Toremifene did not cause any significant side-effects. The response to toremifene is shown in Table 1. The vaginal and lung metastases of the previously untreated patient disappeared almost completely for 9 months. Of the local recurrences, two responded, one stabilised and one progressed during toremifene treatment. The corresponding figures for the distant metastases were 0, 3 and 4, respectively. Of the combined recurrences, one responded and five progressed. 3 patients respoonded after having failed on hormonal therapy previously; 2 had received medroxyprogesterone acetate (MPA), and 1 MPA and tamoxifen. A stabilisation of the disease was achieved in 1 patient after previous tamoxifen therapy and in 1 after the combined hormonal therapy. Of the ER- and/or PR-positive tumours, two responded, one stabilised and two progressed. The receptor-negative tumour progressed.

In summary, 22% of the patients with endometrial cancer showed an objective response to toremifene at a daily dose of 200 mg, and altogether, 44% benefited from the treatment. 3 out of the 4 responders had previously failed on hormonal therapy.

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1. Edmonson JH, Krook JE, Hilton JF, *et al.* Randomized Phase II study of cisplatin and a combination of cyclophosphamide–doxorubicin–cisplatin (CAP) in patients with progestin-refractory advanced endometrial carcinoma. *Gynecol Oncol* 1987, **28**, 20–24.
2. Kauppila A. Progestin therapy of endometrial, breast and ovarian carcinoma. *Acta Obstet Gynecol Scand* 1984, **63**, 441–450.
3. Swenerton KD, Chrumka K, Paterson AHG, Jackson GC. Efficacy of tamoxifen in endometrial cancer. *Prog Cancer Res Ther* 1984, **31**, 417.
4. Gal D, Kopel S, Bashevkin M, Lebowicz J, Lev R, Tancer L. Oncogenic potential of tamoxifen on endometria of postmenopausal women with breast cancer—preliminary report. *Gynecol Oncol* 1991, **42**, 120–123.
5. Blackburn AM, Amiel SA, Millis RR, Rubens RD. Tamoxifen and liver damage. *BMJ* 1984, **289**, 288.
6. Kivinen S, Mäenpää J. Effect of toremifene on clinical chemistry, hematology and hormone levels at different doses in healthy postmenopausal volunteers: phase I study. *J Ster Biochem* 1990, **36**, 217–220.
7. Ebbs JR, Roberts JV, Baum M. Alternative mechanism of action of anti-oestrogens in breast cancer. *Lancet* 1987, **2**, 621.
8. Valavaara R, Pyrhönen S, Heikkinen M, *et al.* Toremifene, a new antiestrogenic compound for treatment of advanced breast cancer. Phase II study. *Eur J Cancer Clin Oncol* 1988, **24**, 785–790.
9. Horvath G, Stendahl U, Kalling M, Ferno M, Himmelmann A, Hajba A. Antiestrogenic treatment of advanced and recurrent carcinoma corporis uteri—a phase II study of toremifene. *Anticancer Res* 1990, **10**, 323–326.
10. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer* 1981, **47**, 207–214.