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RESPONSE TO TOREMIFENE (Fc-1157a) THERAPY IN TAMOXIFEN FAILED PATIENTS WITH BREAST CANCER. PRELIMINARY COMMUNICATION

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Summary—Nine patients with measurable lesions of locally advanced or recurrent breast cancer have been treated with toremifene 200 mg daily. A response rate of 33% [complete remission (CR) + partial remission (PR)] or 78% [CR + PR + no change (NC)] has been achieved so far. As all our patients had previously relapsed on anti-oestrogen therapy (tamoxifen), we postulate that our response rate was achieved by a direct oncolytic effect.

INTRODUCTION

Clinical activity of the anti-oestrogen group of drugs does not correlate with their anti-oestrogenic activity. The most commonly used "anti-oestrogen", tamoxifen, has an incompletely understood mechanism of action which may, in part, be entirely independent of the oestrogen receptor [1].

Toremifene (Fc-1157a) is a new triphenylethylene anti-oestrogen which at low concentrations *in vitro* produces effects comparable with those of tamoxifen. At high doses *in vivo* toremifene exerts anti-tumor effects some of which are different from those of tamoxifen and are directed even against oestrogen-receptor negative tumours. The exact mechanism of these effects is unknown [2].

To determine whether this effect seen in an experimental cell line and in animal experiments is reproducible in man, we have used toremifene as a second line therapy in patients who have relapsed whilst receiving tamoxifen.

SUBJECTS AND METHODS

So far 9 breast cancer patients, age 72–86 yr, have been included in the trial. No patients had previously received any other therapy than tamoxifen 20 mg bd. When relapse occurred, the tamoxifen treatment was stopped and toremifene, 200 mg daily, was started immediately. This dose was used in order to replicate the high concentrations which produced the direct oncolytic effect in the experimental studies. Patients were evaluated according to UICC criteria in 6 weeks intervals.

Table 1. Results of high-dose toremifene treatment in tamoxifen relapsed patients

Patient	Age	Duration of therapy (months)	Result
1	72	8	PR
2	79	8	PR
3	79	8	PR
4	74	4	NC
5	79	4	NC
6	82	3	PD
7	82	3	NC
8	86	2	NC
9	76	2	PD

PR: Partial Remission; NC: No Change; PD: Progressive Disease.

RESULTS AND DISCUSSION

The treatment results are presented in Table 1. A response rate of 33% (CR + PR) or 78% (CR + PR + NC) has been reached so far. A single patient has reported minimal hair loss, no other side effects have been detected. In the patients treated for over 3 months, the ability of toremifene to produce a response (43% PR, 3/7 and 43% NC, 3/7) even after relapse on tamoxifen indicates that, as in cell culture and animal experiments, we may be witnessing an alternative pathway of action.

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