J. steroid Biochem. Vol. 36, No. 3, pp. 227–228, 1990
Printed in Great Britain.

0022-4731/90 $3.00 + 0.00

TREATMENT OF ADVANCED BREAST CANCER WITH 20 mg TOREMIFENE, A PHASE II STUDY. PRELIMINARY COMMUNICATION

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Summary—Fourteen postmenopausal women with estrogen-receptor positive advanced breast cancer and no prior cytostatic treatment received 20 mg toremifene daily as a single dose after a loading dose (120→60→60 mg) for the first 3 days. All were evaluable and had undergone at least 6 weeks' treatment. Results were: no complete remissions (CR), 3 partial remissions (PR), 8 no change (NC) and 3 cases of progressive disease (PD). Three patients had mild side effects: nausea, insomnia, sweating and arm pain.

INTRODUCTION

Our previous phase II study with 60 mg daily dose has shown that toremifene is an effective drug in advanced estrogen-receptor positive breast cancer [1]. Since the optimal dose level is not yet known, we initiated a study using a single 20 mg daily dose. Preliminary results are reported here.

PATIENTS AND TREATMENT

Patients entering the study were postmenopausal women with histologically verified inoperable primary, metastatic or recurrent mammary cancer with at least one measurable or evaluable lesion. Limit of estrogen receptor content positivity in the primary or metastatic lesion was 10 fmol/mg cytosol protein. No previous chemotherapy or hormonal therapy was accepted and any adjuvant tamoxifen therapy had to be stopped at least 6 months before initiation of toremifene treatment. The characteristics of the patients and metastatic sites are indicated in Table 1.

The treatment consisted of 20 mg toremifene as a single dose every morning. To obtain the putative therapeutic drug concentration rapidly, a loading dose of 60 mg was administered on the first three mornings of treatment and on the first evening of treatment.

The patients were evaluated at 6-week intervals. The responses, duration of responses and side effects were classified according to UICC criteria [2]. In cases of disease progression at any time or when disease was still stable at 18 weeks, the daily toremifene dose was increased to 60 mg.

RESULTS AND DISCUSSION

Responses

So far 14 patients have entered the study and all of them have been treated for at least 6 weeks. Their responses to the treatment are shown in Table 2. Only 3 out of 14 patients (21%) showed a partial response compared to 46% (18 patients) during the first 18

Table 1. Patient characteristics and location of metastases

Number of patients	14
Karnofsky	
Mean	80
Range	60–100
Age	
Mean	63.6
Range	45–73
Postmenopausal years	
Mean	17
Range	7–33
ER (fmol/mg protein)	
Mean	223
Range	12–973
PgR (fmol/mg protein)	
Mean	62
Range	0–316
Soft tissue	6
Visceral	4
Skeletal	1
Multiple sites (all with skeletal involvement)	3

Proceedings of the Toremifene Satellite Symposium held at the *UICC World Cancer Congress*, Budapest, Hungary, 1986.

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Table 2. Treatment results in evaluable patients

Response	No. of patients	%
Complete	0	0
Partial	3	21
Stabilized disease	8	58
Progressive disease	3	21

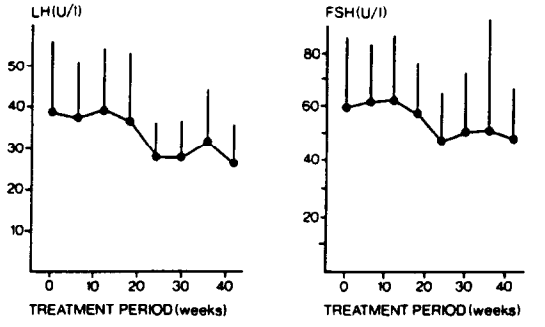

Fig. 1. Decrease of serum LH and FSH levels during the toremifene treatment. The decrease was most remarkable after 18 months when most of the treated patients had 60 mg daily dose.

weeks of a 60 mg daily study [1]. In this latter study 3 patients also had a complete response during this time. In a patient with pleural and lung metastases who had disease progression with the 20 mg daily dose within the first 6 weeks of treatment, relief of dyspnea and decrease in pleural effusion as well as lung infiltration was obtained by increasing the daily dose to 60 mg. Her condition has been stable for more than 12 months now.

Side effects

All symptoms and side effects were actively questioned. The following symptoms which might be associated with the treatment were reported: sweating or hot flushes (4 patients), nausea (1 patient), insomnia (1 patient), pain in the arm (1 patient). All reported symptoms were mild and no patient interrupted the treatment due to side effects.

Laboratory variables

A decrease of mean erythrocyte sedimentation rate from 46 to 35 during the first 6 weeks was noted. No changes in hematological blood counts, serum calcium and creatinine levels or in liver enzymes (except in cases with liver metastases) were observed. During the follow-up there was a decrease in LH and FSH serum levels (Fig. 1).

The number of patients is still too small and the follow-up too short to conclude.

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