Mitoxantrone Therapy of Advanced Adenocarcinoma of the Endometrium

A Phase II Trial

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Introduction Table 1. Patient characteristics

Characteristics Patients, n

Chemotherapy for advanced endometrial carcinoma remains ineffective. Only a minority of patients respond and the responses are generally partial and brief [1,2]. Further studies are required to identify new chemotherapeutic agents of untested chemical configuration and non-cross-resistance with commonly used drugs. Mitoxantrone, a synthetic aminoanthraquinone whose activity appears to be mediated by intercalation into the DNA double helix, was chosen for our phase II trial in patients with advanced or recurrent adenocarcinoma of the endometrium. Mitoxantrone showed a significant activity against animal tumors [3], it showed in vitro antitumor activity against human tumor colony-forming units [4, 5], and it has a very acceptable toxicity observed in phase I trials [6].

Patients and Methods

Eligible patients were required to have histologically confirmed recurrent or metastatic measurable disease, of FIGO-stage III and IV, performance status (Karnofsky > 50%), adequate hematologic function (granulocyte count > 3,000/mm³ and platelet count > 100,000/mm³), bilirubin < 1.5 mg/100 ml, SGOT < 50 IU and no former treatment with anthracyclines. Mitoxantrone was given at a dose of 12 mg/m², via a 5–10 min infusion (150 ml, NaCl 0.9%), and repeated every 21–28 days.

The dose was diminished for patients showing a granulocyte or platelet count toxicity detected in weekly blood cell counts (World Health Organization toxicity criteria), and for those with gastrointestinal toxicity [7].

Tumor responses were assessed using standard criteria for complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) [7]. Of 13 patients 9 were evaluable for response and toxicity. Six patients had adenocarcinoma, one had adenosquamous carcinoma, one had clear cell carcinoma, and one had endometrioid carcinoma. Patient characteristics are shown in table 1.

Results

A brief no-change status (3 months) was noted in a 64-year-old woman with upper abdominal metastasis which was followed by progression of disease under 2 further courses of therapy.

Toxicity was mild. The granulocyte count (cells/mm³) during

Patients, total n 13

Patients evaluable 9

Median age in years (range) 67 (61–75)

Grading

I (well) 0

II (medium, differentiated) 2

III (poorly) 7

Metastatic site

Pelvis only 1

Outside pelvis 8

Prior therapy

Surgery 7

Radiation therapy 4

Hormonal therapy 3

Chemotherapy 0

Doses of mitoxantrone

Total 20

Average 2.2 (1–5)

Results

Refusal of therapy 0

CR 0

PR 0

NC 1

PD 8

Median survival time

in months (range): 5.2 months (2.5–10)

Table 2. Mitoxantrone phase II trials
in adenocarcinoma of
the endometrium:

Patients Dosage

Results

(II)

CR (%) PR (%)

NC (%) PD (%)

Gynecologic Oncology Group study 1987 [9]

19 12 mg/m² - 1 (5) 4 (21) 14 (74)

Median survival time: 2.1 months

Southwest Oncology Group study 1985 [8]

15 12 mg/m² - 4 (27) 11 (73)

Median survival time: 4.0 months

Veenhof et al. 1987 [10]

14 14 mg/m² - - 1 (7) 13 (93)

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Short Communication/Kurzmitteilung

20 courses was once 500–1,000, 1,500–2,000 3 times, 2,000–2,500 twice, and 2,500–3,000 3 times; once the platelets count was < 100,000.

Mild nausea and vomiting occurred in 2 patients. No cardiac toxicity was observed. In this study, a no-change rate of 12% (1 response among 9 patients) and progression of disease in 88% of patients was observed. Our results are similar to those of the Southwest Oncology Group [8], where none of 15 patients with endometrial carcinoma responded, 9 having received prior doxorubicin (table 2). The results of Muss et al. [9] and Veenhof et al. [10] support these poor findings (table 2).

This indicates that mitoxantrone at this dosage is inactive as a single agent in the treatment of advanced or recurrent adeno-carcinoma of the endometrium.

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