

WHOLE BODY HYPERTHERMIA COMBINED WITH IFOSFAMIDE AND CARBOPLATIN IN RECURRENT OVARIAN CARCINOMA. A PHASE I-II STUDY

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Recurrent ovarian carcinoma regularly demonstrates chemosensitivity. Prognosis is nevertheless poor. In an effort to increase response to systemic treatment, a procedure for whole body hyper-thermia (WBH) was established and combined with i.v. ifosfamide and carboplatin. Fifteen patients with incurable relapse or metastases after primary treatment with surgery and chemotherapy (carboplatin and paclitaxel), have so far been treated.

The patients started treatment in the period January -02 to November -04. All patients had disease evaluable by radiology and/or clinical investigation. The first three patients were treated in a pilot study to establish the method. In the following phase, a six month interval between primary treatment and recurrence was added as an inclusion criterion. So far twelve patients have completed treatment in that study.

The treatment plan consisted of three courses of chemotherapy/WBH every fourth week, followed by evaluation. Responding patients got three additional courses before observation without further treatment. The WBH procedure was performed with continuous infusion of propofol (10mg/ml) and alfentanil (0.01mg/ml) with varying infusion rate. Lidocaine 3 mg/kg/h was given as arrhythmia prophylaxis. Heating was achieved in DMT 2000 hot water circulated chamber with 100% relative humidity, with a heating period lasting on average 120 min. (110-150 min.), a 60 min. plateau phase at 41.8 °C, and a return to normal body temperature during the following 60-90 minutes. During the heating up period, ifosfamide (3g/m² in the pilot study, 4 g/m² in the phase I-II study) was infused. In the first part (20 min.) of the plateau phase, carboplatin was given (300 mg/m² in the pilot, 250 mg/m² in the phase I-II). Patients were observed in the hyperthermia unit until they were awake, thereafter observed at an ordinary bed ward at least overnight. All patients were given G-CSF as filgrastim (300 microgr./day) as bone marrow support from day five.

Toxicity/Complications

There were no serious acute anesthesiological complications during or after the 72 WBH sessions. One patient developed ileus after the first WBH. At surgery large abdominal tumour masses made restoration of gastrointestinal function impossible, and she died two weeks after the first WBH. In a second patient, an ileostomy had to be performed, but the patient continued treatment. In one patient a pulmonary embolus was diagnosed three weeks after the first treatment. No further WBH was possible.

The two most common toxicities were reduced well-being the first 3-6 days after each treatment, and thrombocytopenia, requiring dose reduction in the later courses in most patients. Thrombocytopenia limited the number of courses to 5 (2 patients), and 4 (one patient). One patient only got two treatments due to renal toxicity. The remaining nine patients got the planned six treatments.

Response

Two patients receiving only one course were not evaluated for response. There was 1 CR and 9 PR. One patient had stabilization during 4 courses, but rapid progression thereafter. One had a mixed response (ascites og pain gone, but increase in one measurable lesion). One pa-

tient with disease progression 6 months after adjuvant carboplatin/paclitaxel is still progression free at 26+ months. Survival from treatment start was 1, 7, 9, 10, 15, 17, 19, 21, 16+, 20+, 26+, 27+, 34+, 39+, and 48+ months.

Conclusion

We have demonstrated in patients with recurrent ovarian carcinoma that WBH can be combined with carboplatin and ifosfamide with acceptable toxicity. Response rate in this limited study is good. Although response duration in many patients is short, there are patients with a protracted response. It thus seems possible to increase chemosensitivity by WBH in some patients previously exposed to standard chemotherapy for ovarian carcinoma.