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# Long-term Complete Remissions in Patients with Disseminated Melanoma Treated by Fotemustine and Dacarbazine

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FOTEMUSTINE IS a recent chloroethylnitrosourea, which has activity against disseminated malignant melanoma as a single agent [1–3] and in combination with dacarbazine (DTIC) [4, 5]. To confirm the activity of fotemustine–dacarbazine 14 patients were treated with the combination and 13 patients are evaluable for response. All patients had histologically confirmed malignant melanoma. There were 10 men and 3 women, the median age was 57 years (range 31–73), the median Karnofsky index was 90% (60–100) and the predominant metastatic sites were: cerebral (1), visceral (lung and liver, 7), non-visceral (eye, lymph nodes, skin, bones, 5). No patient had received prior chemotherapy or immunotherapy and only 1 had received radiotherapy. The treatment consisted of an induction cycle: fotemustine 100 mg/m$^2$ days 1 and 8, DTIC 500 mg/m$^2$ day 15 followed by 5 weeks rest, with maintenance cycles (fotemustine 100 mg/m$^2$ day 1, DTIC 500 mg/m$^2$ day 2 every 3 weeks) given to stable or responding patients until disease progression or occurrence of any unacceptable toxicity. Responses and toxicity were evaluated using WHO criteria. Patients were followed weekly during the induction cycle and with toxicity assessment before each maintenance cycle.

There were 4 complete responses, 3 stabilisations and 6 progressions. The response rate was 4/13 (30.8%). 3 of the complete responders had skin metastases, 1 had lung (Fig. 1) and bone lesions. Patients received a mean of four maintenance cycles (0–9) but the 4 complete responders each received nine maintenance courses. They all first became partial responders and went on responding until complete remission which occurred after the 4th, 7th or 8th maintenance cycle. The responses lasted 50, 80, 131+ and 142+ weeks from the first day of treatment and 25, 28, 90+ and 103+ weeks from the day the complete response was first assessed. 2 of the 4 responders are alive at 131 and 142 weeks and 2 died at 83 and 103 weeks. The median survival duration for all patients was 55 weeks (5–142+).

12 patients are evaluable for toxicity, which was mainly haematological, i.e. grade III–IV (neutropenia: 41.7% and thrombopenia: 16.7%). Other side-effects included a transient increase of transaminases in 2 patients and moderate nausea and vomiting (64% grade 0 and 36% grade I–II with fotemustine, 25.3% grade 0 and 72% grade I–II with DTIC).

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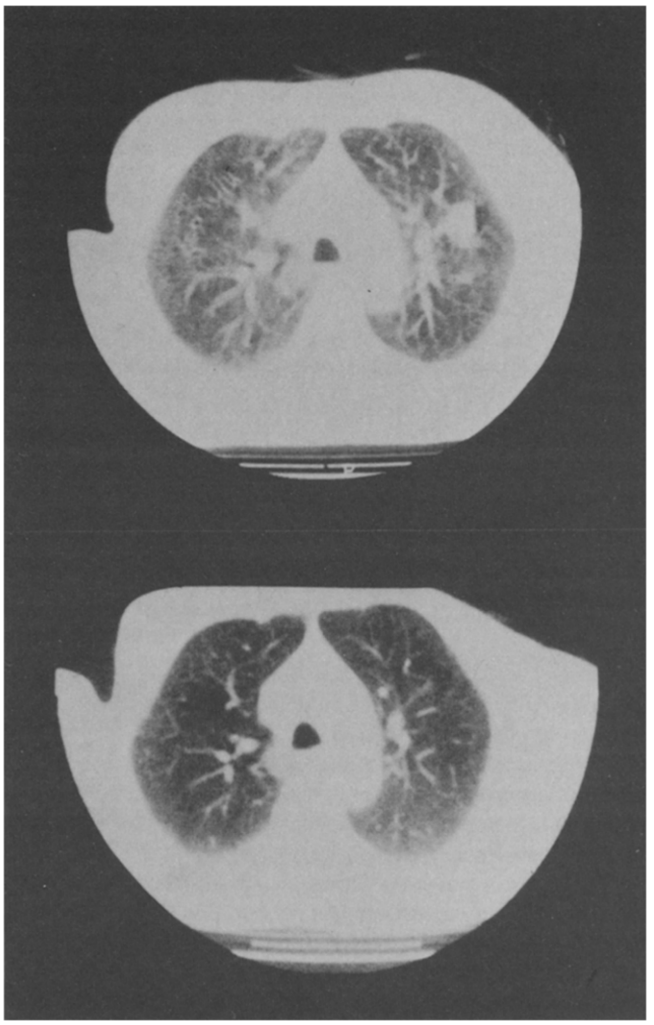

**Fig. 1. Pulmonary complete remission (CT scan before therapy and after the fourth maintenance cycle).**

Despite the small patient sample, the results are interesting in the view of the high complete response rate (30.8%) and of the long-term response and survival durations. The patients were not pretreated, had a good performance status and no major metastatic involvement, which may partially explain the complete response rate, especially on skin metastases. However, this is a well-tolerated regimen that can be easily performed on an out-patient basis for a long period, without cumulative toxicity.

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