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Interleukin-2 Therapy for Metastatic Uveal Melanoma

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METASTASES FROM uveal melanoma occurring in patients treated by surgery or radiotherapy [1] are usually first detected in the liver [2]. The median time to death after diagnosis of liver metastases ranges from 2 to 5 months [3]. Objective response rates up to 25% are commonly reported in patients with metastatic melanoma treated with regimens containing interleukin-2 (IL-2) alone or in association with lymphokine-activated killer cells or dacarbazine [4-7].

We initiated a phase II trial of IL-2 in patients with metastatic melanoma. All patients had adequate organ function, measurable metastatic disease and an anticipated survival of at least 4 months. Written informed consent was mandatory. Primary melanoma was cutaneous in 20 patients and uveal in 7 (all these 7 presented with liver metastases). IL-2 was administered by continuous intravenous infusion for 5 days at 18-20 Mu/m²/day. After a 9-day rest, a second induction cycle was administered at the same dose. Patients were then given maintenance therapy and received a 5-day cycle of IL-2 repeated every 3 weeks until major intolerance or disease progression occurred. In 10 of the 27 patients, dacarbazine (800 mg/m²) was given 3 days before starting IL-2.

Clinical toxicity was significant and consistent with previous reports [8]. All patients experienced fatigue, fever, gastrointestinal disorders and cutaneous toxicity; drowsiness and disorientation were less common. No life-threatening toxicity occurred. Haematological and liver enzyme modifications were common; a rise in creatinine serum with oliguria was observed in half the patients. Over all cycles, the average dose of IL-2 was 80% of that planned.

We observed 6 objective responses in 27 evaluable patients (2 complete and 4 partial). The site of response was lung, lymph nodes and subcutaneous tissue in 1, 2 and 3 patients, respectively. Response duration ranges from 4 to 42+ months. The six responses occurred in the patients with cutaneous primary tumour; all patients with liver metastases from uveal melanoma progressed and died 3 to 5 months after starting IL-2.

Our experience suggests that IL-2 provides no benefit in patients with metastases from uveal melanoma. The lack of efficacy could be linked to the nature of the primary tumour rather than to the liver metastatic site, as responses have been reported [9] in patients with liver metastases from cutaneous melanoma.

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1. Seddon JM, Egan KM, Gragoudas ES. Choroidal melanoma: prognosis. In Ryan SJ, ed. *Retina* Vol. 1: *Basic Science and Inherited Retinal Disease*. St. Louis, CV Mosby, 1989, 663-673.
2. Einhorn LH, Burgess MA, Gottlieb JA. Metastatic patterns of choroidal melanoma. *Cancer* 1974, **34**, 1001-1004.
3. Rajpal S, Moore R, Karakousis CP. Survival in metastatic ocular melanoma. *Cancer* 1983, **52**, 334-336.
4. West WH, Tauer KW, Yannelli JR, et al. Constant-infusion recombinant interleukin-2 in adoptive immunotherapy of advanced cancer. *N Engl J Med* 1987, **316**, 898-905.
5. Rosenberg SA, Lotze MT, Muul LM, et al. A progress report on the treatment of 157 patients with advanced cancer using lymphokine-activated killer cells and interleukin-2 or high-dose interleukin-2 alone. *N Engl J Med* 1987, **316**, 889-897.
6. Stoter G, Aamdal S, Rodenhuis S, et al. Sequential administration of recombinant human interleukin-2 and dacarbazine in metastatic melanoma: a multicenter phase II study. *J Clin Oncol* 1991, **9**, 1687-1691.
7. Dorval T, Mathiot C, Chosidow O, et al. IL-2 phase II trial in metastatic melanoma: analysis of clinical and immunological parameters. *Biutej* 1992, **3**, 63-79.
8. Spiegel JP, Puri RK. Interleukin-2 toxicity. *J Clin Oncol* 1991, **9**, 694-704.
9. Parkinson DR, Abrams JS, Wiernik PH, et al. Interleukin-2 therapy in patients with metastatic malignant melanoma: a phase II study. *J Clin Oncol* 1990, **10**, 1650-1656.