In conclusion, there are patients with Hodgkin's disease who develop tumour recurrence after a very long period of clinical complete remission. It is recommended that these cases are collected to learn more about the features of this disease.

1. Young RC, Bookman MA, Longo DL. Late complications of Hodgkin's disease management. *J Natl Cancer Inst Monog* 1990, **10**, 55–60.
2. Henry-Amar M, Somers R. Long term survival in early stages Hodgkin's disease: the EORTC experience. In Somers R, Henry-Amar M, Meerwaldt JK, Carde P, eds. *Treatment Strategy in Hodgkin's Disease*. Montrouge Editions John Libbey Eurotext 1990, 151–168.
3. Bodis S. Late relapse in early-stage Hodgkin's disease patients enrolled on European Organization for Research and Treatment of Cancer protocols. *J Clin Oncol* 1993, **11**, 225–232.
4. Henry-Amar M. Prognostic study of relapse-free survival by clinical stage. In Somers R, Henry-Amar M, Meerwaldt JK, Carde P, eds. *Treatment Strategy in Hodgkin's Disease*. Montrouge Editions John Libbey Eurotext 1990, 265–311.
5. Strum SB. The persistence of Hodgkin's disease in long-term survivors. *Am J Med* 1971, **51**, 222–240.
6. Urba JW, Longo DL. Hodgkin's disease. *New Engl J Med* 1992, **326**, 678–687.

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Phase II Study of Tauromustine in Disseminated Malignant Melanoma

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THE GLOBAL incidence of malignant melanoma (MM) is continuously increasing, most rapidly in Scandinavia with a 5% rise each year [1, 2]. The best response rates after chemotherapy or immunotherapy are 20–25%, with a median survival gain of only approximately 6 months [3, 4]. Tauromustine (TCNU) has been proven to have some antitumour effect on patients suffering from MM, and is well tolerated [5]. The objective of this study was to determine whether the response rate in patients with MM could be increased by employing a weekly dose schedule of TCNU [6].

Patients between 18 and 75 years of age, with histologically proven malignant melanoma, and with measurable and evaluable disease not amendable to curative surgery or radiotherapy, were included in this open phase II study. Other inclusion criteria were progressive disease, performance status of 2 or less, life expectancy of at least 3 months and normal liver, renal and bone marrow functions. All patients gave their informed consent to participate in the study, which was approved by the national board of health and the ethical committees. The dose of TCNU was 50 mg/m^2/week. Blood counts were monitored weekly. Patients were evaluated for response every 8 weeks, and the treatment was continued until progressive disease (PD) was observed. Dose reduction due to haematological toxicity was performed, as reported previously [6]. Response and toxicity were graded according to the WHO recommendations [7]. TCNU was supplied by Kabi Pharmacia Therapeutics AB (Helsingborg, Sweden) in tablets of 10, 20 and 50 mg.

Between October 1990 and October 1991, 56 patients entered the study. 2 patients were non-eligible (performance status 3). Among the 54 eligible patients, 2 left the trial after 2 and 3 weeks, respectively, due to concurrent disease. Thus, 52 patients (30 males and 22 females) were evaluable for response.

The median age was 60 years (range 24–72). Prior treatment comprised surgery (52 patients), regional perfusion with melphalan (1 patient) and radiotherapy (9 patients). Dominant sites of disease were visceral (28 patients), soft tissue (23 patients) and bone (1 patient). 34 patients had PD, including 2 early deaths, 11 had stable disease, 4 had a partial response and 3 had a complete response, yielding a response rate of 13.5%. Four of the responses occurred in patients with soft tissue disease, and 3 in patients with visceral disease. Median time to progression was 30 weeks (range 16–95) for responders, and 8 weeks (range 8–58) for non-responders. Median overall survival for all patients was 5.8 months (range 1–22). The median average dose tolerated was 37 mg/m^2/week over a median time of 9 weeks (range 8–67). Dose-limiting toxicities were thrombocytopenia and leucopenia. Non-haematological adverse effects and haematological toxicity did not differ from what was observed in the phase I study [6].

With this weekly schedule, the tolerable dose of TCNU was 37 mg/m^2/week. This corresponds to a 50% increase in the weekly dose compared with the 5-week schedule [5]. However, this did not translate into an increased response rate, which was 15% with the 5-week schedule [5] compared with 13.5% in the present study. The patient characteristics were not significantly different in the two studies in terms of age, sex, location of metastases or performance status, nor were they different from patients as such with MM [6, 8].

The median disease-free interval from diagnosis to start of TCNU medication was 1.9 months (range 0–13.8) for non-responders; for responders and patients with stable disease it was 2.2 months (range 0–21.8), a difference which is not statistically significant. The median survivals of these two groups were 4.0 and 9.7 months, respectively, indicating that TCNU in some patients may have reduced the progression rate of melanoma lesions.

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1. IARC. *Cancer Incidence in Five Continents*, vol. 5. IARC publ No. 88. Lyon, IARC, 1987.
2. La Vecchia C, Lucchini F, Negri E, *et al.* Trends of cancer mortality in Europe 1955–1989: II, respiratory tract, bone, connective and soft tissue, sarcomas, and skin. *Eur J Cancer* 1992, **28A**, 514–599.
3. Kleeberg UR. Clinical trials in disseminated malignant melanoma. *Anticancer Res* 1987, 7, 423–428.
4. Lakhani S, Selby P, Bliss JM, *et al.* Chemotherapy for malignant melanoma: combination and high doses produces more response without survival benefit. *Br J Cancer* 1990, **61**, 330–334.
5. Nolte H, Gjedde SB, Lindegaard Madsen E, *et al.* Phase I study of tauromustine in disseminated malignant melanoma. *Eur J Cancer Clin Oncol* 1989, **25**, 655–657.
6. Gjedde SB, Mouridsen HT, Lindegaard-Madsen E, *et al.* Phase I study of tauromustine administered in a weekly dose schedule. In press, 1993.
7. World Health Organization. *Handbook for Reporting Results of Cancer Treatment*. WHO offset Publication No 48. Geneva, World Health Organization, 1979.
8. Balch CM, Soong SJ, Murad TM, *et al.* A multifactorial analysis of melanoma. Prognostic factors in 200 melanoma patients with distant metastases (stage III). *J Clin Oncol* 1983, **1**, 128–134.