Dacarbazine (DTIC)-based chemotherapy or chemoimmunotherapy of patients with disseminated malignant melanoma

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Summary Combinations of dacarbazine (DTIC) and other cytotoxic agents or alpha-interferon were given to 136 patients in five different regimens. The total response rate was 32% (95% confidence interval 24–40%); 13% had a complete remission. Female patients had a significantly higher chance of response than male patients: 46% vs 25%. There was also a difference in complete response rate: 25% vs 9%. The overall survival was 6 months: 8% of patients had a response of more than 6 months and 2% of more than 2 years. Although response rates vary among the various regimens described in the literature, the complete response rates are quite similar and the long-term disease-free survival of these combinations may be similar to that of dacarbazine alone.

Patients with a histological diagnosis of malignant melanoma, who had not received previous chemotherapy, without clinical evidence of central nervous system involvement and without hyperbilirubinaemia were entered into the study. The age limit was set at 75. All patients had disease shown to be progressive within the last 6 months. Entry into these studies required evaluable or measurable disease.

Assessment of response and toxicity was done according to WHO criteria. Survival was measured from the start of chemotherapy. response duration from the moment response was diagnosed.

Results

One hundred and thirty-six patients were entered, 82 male and 54 female. Their median age was 47 years (range 17–74).

Patients entered into the five regimens and their characteristics are given in Table I. The complete and partial response rates, the number of patients responding for more than 6 months and the number of patients surviving disease free for more than 2 years are given in Table II, as well as the relation with sex.

The total number of responders is 44 or 32% (95% confidence interval 24–40%); of these 18 or 13% had a complete response. There is no significant difference between the various regimens. The response rate is, however, dependent on gender: the response rate in female patients is 25 out of 54 or 46% and in males is 23% (χ² = 7.96, P = 0.004). In complete responders this difference is also significant: 25% vs 9% in males (χ² = 3.97, P = 0.04). Responses are also much more common in the lung (39%) and lymph nodes (30%) than in the liver (2%) (Table III).

In the responding patients 11 responses lasted for more than 6 months (25%). Overall, in all patients treated, the chance of such a prolonged response is 8% (95% confidence

Patients and methods

Five different regimens were used consecutively:

Regimen I Dacarbazine 300 mg m⁻² on 4 consecutive days combined with continuous infusion of bleomycin 30 mg day⁻¹, followed on day 5 by vindelesine 3 mg m⁻² and actinomycin D 2 mg m⁻². Cycles were repeated every 4 weeks (Mulder et al., 1986).

Regimen II The same regimen without actinomycin D (Mulder et al., 1989).

Regimen III DTIC 750 mg m⁻² on day 1 and alpha-interferon 9 mU daily for 21 days, given for six cycles in responding patients (Mulder et al., 1990).

Regimen IV DTIC 750 mg m⁻² on day 1 and alpha-interferon 9 mU given for 28 days, on day 14 5-fluouracil (5-FU) 1.00 mg m⁻², six cycles (Mulder et al., 1992).

Regimen V DTIC 750–1,500 mg m⁻² on day 1 and alpha-interferon 9 mU for 21 days, repeated every 3 weeks, combined with daily granulocyte colony-stimulating factor (G-CSF) (Buter et al., 1994).

Table I Patient characteristics

| Regimen | Number of patients | Sex | Median age (range) (years) |
|---------|-------------------|-----|--------------------------|
| I       | 27                | 13  | 43 (24–59)               |
| II      | 31                | 21  | 47 (24–69)               |
| III     | 31                | 18  | 51 (17–74)               |
| IV      | 26                | 15  | 44 (15–57)               |
| V       | 21                | 14  | 47 (30–68)               |
| Total   | 136               | 82  | 47 (17–74)               |

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