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Letter to the Editor

VP-16 in Advanced Soft Tissue Sarcoma: A Phase II Study of the EORTC Soft Tissue and Bone Sarcoma Group

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VP-16 HAS high antitumour activity in small cell carcinoma, acute leukaemia, malignant lymphoma, testicular cancer and childhood tumours, while the efficiency in soft tissue sarcoma is uncertain due to the limited number of patients treated [1]. We here report a phase II study of VP-16 in patients with advanced soft tissue sarcoma, resistant to standard treatment.

Patients with histologically proven, progressive, measurable, advanced soft tissue sarcoma, with age between 15 and 75 years, performance status ≤ 2, WBC count $\geq 3 \times 10^9/l$, platelet count $\geq 100 \times 10^9/l$ and adequate kidney and liver function were entered. Patients with CNS metastases, secondary malignancies, radiotherapy to the indicator lesion or treatment with chemotherapy in the previous 4 weeks were ineligible.

VP-16 was administered at a dose of 130 mg/m^2 orally once daily for 5 days every 3 weeks. Treatment was delayed by 1 week when the WBC were $< 3.0 \times 10^9/l$ or the platelets were $< 100 \times 10^9/l$ at the time scheduled for the next cycle. The initial dose was reduced by 25% if the WBC nadir was < 1.5 or the platelet nadir $< 50 \times 10^9/l$. If treatment was delayed for 2 consecutive courses due to haematologic toxicity, the subsequent dose was reduced by 25%. The dose was escalated to 125% if the WBC nadir was ≥ 2.5 and platelet nadir $\geq 100 \times 10^9/l$ in the previous course.

Patients were required, unless rapid progression or unacceptable toxicity occurred, to receive a minimum of 2 courses. Patients showing a response or disease stabilization remained on study until progression occurred.

The evaluation of response and toxicity was performed according to WHO criteria.

The patient's informed consent was obtained according to local regulations.

Of the 33 patients entered 2 were ineligible. Of the 31 eligible patients 5 were not evaluable for tumour response. These included 2 early deaths due to malignant disease, 1 early toxic death, 1 patient was lost to follow-up, and 1 patient refused treatment.

Of the 26 evaluable patients 16 were males with median age of 47 years (range 17–72). Median performance status was 1 (range 0–2).

Twenty-four patients had received previous chemotherapy. The median number of prior drugs was 4 (range 1–6). All previously treated patients had received anthracyclines.

One patient (4%) had a PR (95% confidence limits 0–11) of 19 months duration.

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Other participants included J.H. Mulder, Rotterdamsch Radiotherapeutisch Instituut, Rotterdam, Holland.

The median number of treatment courses was 2 (range 1–25) and a total of 99 treatment cycles were given.

VP-16 was well tolerated. Reduction of the drug dose had to be done in 5 patients, while drug escalation was performed in 12.

WBC nadirs below 3.0, 2.0 and 1.0×10^9/l during the first 2 courses were observed in 48, 22 and 13%, respectively. In 17% of the patients the platelet counts were below 100×10^9/l and in 13% below 50×10^9/l.

Alopecia occurred in 5 patients and moderate nausea, vomiting or diarrhoea in 4 patients.

Welt *et al.* also recently tested VP-16 in patients with advanced soft tissue sarcoma [2]. The dose was 120 mg/m^2 i.v. every other day for 3 days every 3 weeks. Among 26 patients, no complete or partial responses were observed. The toxicity also was generally mild and consisted mainly of myelosuppression.

In conclusion VP-16 has no significant antitumour activity in pretreated adult patients with soft tissue sarcoma.

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