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## *Letter to the Editor*

# Phase II Trial of Triglycidylurazol (TGU) in Advanced Malignant Melanoma

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1,2,4-TRIGLYCIDYLURAXOL (TGU) is a triepoxide alkylating anticancer agent. The activity of TGU was investigated by Atassi and Dumont [1] in a series of murine tumours. It was found to be active against L1210, L5222 and P388 leukemia as well as s.c. implanted colon 38 tumour and $B_{16}$ melanoma. In the $B_{16}$ melanoma they found a 98% increase in life span of mice innoculated with $2 \times 10^{16}$ cells i.p. on day 0 and treated with 15.5 mg/kg i.p. daily on days 1–9. Phase I clinical trial was undertaken by Early Clinical Trials Group of EORTC [2] using either single dose schedule q 3–4 weeks or the daily × 5 q 3–4 weeks schedule. Dose-limiting toxicity at MTD of 1000 mg was hematologic with leucopenia and thrombocytopenia occurring with nadir 10–12 days after drug administration, and recovery usually within 4 weeks. Further toxicity noted included local phlebitis and skin rash.

In a phase II study patients with histologically confirmed progressive malignant melanoma with previously non-irradiated measurable or evaluable lesions were treated. None of the patients had received chemotherapy previously. Eligibility criteria included performance status (WHO) $< 3$, life expectancy $\geq 3$ months, age $\leq 75$ years, white blood cell counts (WBC) $\geq 4000\ mm^3$, platelet counts $\geq 100{,}000\ mm^3$, serum bilirubin level $\leq 2$ mg/dl and serum creatinine level $\leq 1.5$ mg/dl.

TGU was given as an i.v. bolus injection in 5–10 min at a dose of 800 mg/m$^2$ repeated every 4 weeks. Drug administration was postponed by 1 week if there was no full hematologic recovery at scheduled retreatment. Dosage adjustments were planned for each course according to the WBC and platelet nadirs in the previous course. The dose was increased by 20% with WBC $\geq 4000\ mm^3$ and platelets $\geq 150{,}000\ mm^3$. The dose was reduced by 25% with WBC between 1000 and 1999 mm$^3$ or platelets between 50,000 and 74,999 mm$^3$, or 50% for respective values $< 1000/mm^3$ and $< 50{,}000\ mm^3$.

A minimum of two courses was necessary for treatment assessment. The criteria for response were those recommended by UICC.

Of 20 eligible patients 2 received only one course of therapy, 1 due to early death and 1 due to early progressive disease. One patient received an inadequate dosage.

The remaining 17 fully-evaluable patients had had no previous exposure to chemotherapy, while 2 had received radiotherapy at other sites than indicator lesions. Nine patients received 2 courses, 7 patients received 3 courses and 1 patient 4 courses. Four patients had dose reductions due to leukopenia grade 3–4, while the rest received full doses. No dose escalations were undertaken. No responses were seen. Four patients had stable disease. The remaining 13 patients had progressive disease.

The median WBC and platelet nadirs were 2300 mm$^3$ (900–6500) and 108,000/mm$^3$ (17,000–327,000) after the first course. Through all courses the respective values were 2000/mm$^3$ (900–2400) and 106,000/mm$^3$ (12,000–327,000). Phlebitis WHO grade 2 was seen in 3 patients and grade 3 in 1, while the rest did not experience phlebitis.

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Nausea and vomiting WHO grade 1 was seen in 7, grade 2 in 7 and grade 3 in 3 patients. Diarrhoea grade 2 was experienced in 1 patient, alopecia in 1 and toxic death due to gastrointestinal haemorrhage was seen in 1 patient with nadir platelet count 9000/mm$^3$.

It is concluded that TGU has no or minimal activity in advanced malignant melanoma.

## REFERENCES

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