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Phase II Trial of TCNU and Vindesine in Patients with Adenocarcinoma of the Lung

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VINDESINE (VDS) is among the most active single agents in adenocarcinoma of the lung (ACL) with a response rate of 20–25% [1]. In two phase I studies of TCNU (1-(2-chloroethyl)-3-[2-(dimethylaminosulfonyl)ethyl]-1-nitrosourea), a newer water soluble nitrosourea, impressive activity was observed [2, 3]; a subsequent phase II trial showed modest activity [4].

A phase II study of vindesine and TCNU has been carried out in patients with adenocarcinoma of the lung. Patient characteristics are shown in Table 1. Entry criteria were: non-resectable ACL (WHO), no previous chemotherapy or radiotherapy, measurable or evaluable disease, performance status ≤3 (ECOG scale), age ≤75 years, no previous or concurrent malignancies, no active uncontrolled infection, adequate haematological parameters, normal liver and renal function. Informed consent was obtained and the trial was approved by the regional ethical committee.

The dose for TCNU was 110 mg/m^2 p.o. every 4 weeks, and for vindesine 3 mg/m^2 i.v. for 8 weeks, then bi-weekly. Chemotherapy was postponed in the absence of full haematological recovery (i.e. WBC $<2{\cdot}5 \times 10^9$/l or platelets $<100 \times 10^9$/l), at the time of scheduled retreatment. Doses were adjusted according to the nadir values of WBC and platelets, and also according to neurotoxicity in the case of VDS. Treatment was discontinued where there was progressive disease after the first course. The duration of response was measured from the date the response was first observed, to the date of disease progression [5]. Patients were considered evaluable if they had received at least one treatment cycle. Patients with early death (death within 4 weeks) were considered as non-responders.

Table 1. Patient characteristics, response and survival

Total No. patients	64	
Not eligible	8	
Median age in years (range)	58 (38–73)	
Sex F/M	35/21	
Performance status (ECOG)		
PS 0–1	38 (68%)	
PS 2–3	18 (32%)	
Partial remission	11 patients	(20%)
Respone duration (range)	14 weeks	(2–49)
Median survival (range)	28 weeks	(0.5–86)

The response status of the 56 eligible patients is shown in Table 1. Toxicity was considerable, with dose reduction needed in 71% of the evaluable patients, either due to neurotoxicity (62%) or haematological toxicity (37%). Fifty-two per cent of the patients obtained WHO grade III and IV haematological toxicity. One death from sepsis was observed (WBC 0.2×10^9/l, platelets 21×10^9/l).

The response rate of 20% was comparable to either drug given alone. The doses employed in combination were lower than those used in single agent studies; however, it appears not to be possible to increase drug doses because the toxicity encountered was considerable. Treatment with TCNU and VDS in the present dose and schedule can not be recommended in patients with ACL.

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Phase II Trial of High Dose Recombinant Gamma-interferon in Advanced Hepatocellular Carcinoma

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THERE have been a few reported clinical trials of IFN-γ in human malignancies [1–3]. The results of low-dose IFN-γ for hepatocellular carcinoma (HCC) have been disappointing to date [4]. In a preliminary report from Japan [5], however, the tumour volume doubling time was reported to be prolonged in two of

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