Table 1. Toxicity (maximal toxicity per patient)

	Group 1 (60 mg/m²) n = 27				Group 2 (90 × 3 mg/m² then 60 mg/m²) n = 27			
WHO Grade	1	2	3	4	1	2	3	4
Leucocytes (10^9/l)	6	6	—	—	7	7	3 (11%)	1 (3.7%)
Neutrophils (10^9/l)	6	3	2 (7.4%)	—	5	4	4 (14.8%)	2 (7.4%)
Platelets (10^9/l)	3	2	1 (3.7%)	1 (3.7%)	3	4	5 (18.5%)	2 (7.4%)
Nausea/vomiting	5	6	1 (3.7%)	—	8	2	3 (11%)	—
Diarrhoea	1	—	—	—	2	—	—	—
Fever	—	—	—	—	—	1	—	—
Haemorrhage	—	—	—	—	1	1	—	—
Infection	1	—	—	—	—	—	—	—
Neurotoxicity	2	—	—	—	—	—	—	—
Hypotension	1	—	—	—	—	—	—	—
Asthaenia	1	—	—	—	1	3	—	—
Alopecia	1	—	—	—	—	1	—	—
Hot flushes	—	—	—	—	2	—	—	—

n = number of patients.

× 10^9/l; range: 0.07–9.59). For 31 cycles (12.1%) of a total of 256 cycles in the two groups, the dosage and schedule of treatment were modified according to the protocol. Haemoglobin nadir grade 3–4 was observed only in 5 patients of group 2 (median: 6.2 mmol/l; range: 2.7–8.8).

In conclusion, the present study reveals that the new nitrosourea cystemustine, scheduled either for 60 mg/m² or 90 × 3 mg/m² then 60 mg/m² every 2 weeks, has minimal activity in advanced renal cancer with only 1 response amongst 54 eligible patients. The drug is less toxic than other nitrosoureas (lomustine, fotemustine) with minor clinical side-effects, and acceptable myelotoxicity, but with the same mild antitumour efficacy. Thus cystemustine cannot be recommended for further use in renal cancer at these schedules of administration.

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European Journal of Cancer Vol. 31A, No. 1, pp. 131–132, 1995

0959–8049/95 $9.50+0.00

0959-8049(94)00410-2

Cladribine and Tumour Lysis Syndrome

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CLADRIBINE (2-CHLORODEOXYADENOSINE, 2-CDA) is an adenosine analogue with a broad spectrum of activity among lymphoproliferative disorders [1]. Recent reports on the occurrence of tumour lysis syndrome after treatment with cladribine [2,3] drew our attention to a similar case which further cautions against its use.

A 29-year old Caucasian man presented with a 10-year history of cutaneous T-cell lymphoma treated elsewhere with chemotherapy, alpha interferon, radiotherapy, phototherapy and plasmapheresis. He was ill and pyrexic at 39°C with pachydermia, itching erythema, lymph oedema, generalised lymphadenopathy, liver and spleen enlargement. White blood cells were 13 × 10^9/l with 73% lymphocytes CD3 and CD4 positive. Platelets were 395× 10^9/l. The LDH was 953 U/l. Bone marrow and skin biopsies showed massive infiltration by abnormal CD3 positive lymphocytes. Ultrasound revealed retroperitoneal lymphadenopathy, hepatosplenomegaly, kidney infiltration and ascites. Electrolyte and creatinine were within normal limits.

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Received 7 Jul. 1994; accepted 28 Sep. 1994.

Subcutaneous bolus injection of 0.1 mg/kg/day of cladribine for 5 days was started according to our current protocol. Itching and pyrexia disappeared on day 11. However, vomiting, profuse diarrhoea and oliguria developed. Blood glucose was 2.5 mmol/l, potassium 5.6 mmol/l, urea 30.6 mmol/l, creatinine 348 μmol/l, uric acid 941 mmol/l, LDH 6624 U/l, phosphate 2.84 mmol/l, and calcium 1.59 mmol/l. Acute renal failure with tumour lysis syndrome was diagnosed. Hydration, allopurinol and antibiotics were given. On day 20, the white cell count was 11.2×10^9/l with 3% of lymphocytes and creatinine was 143 μmol/l. After transient normalisation the potassium concentration rose to 5.8 mmol/l. Cardiac failure developed with pulmonary oedema requiring oxygen, diuretics, dobutamine and dopamine. Methicillin-resistant Staphylococcus aureus septicaemia and disseminated candidosis were diagnosed and were concurrent with the patient's death despite an almost complete response to the treatment with cladribine. This was confirmed at autopsy which showed normalisation of the skin and the kidneys, but persistence of lymphomatous infiltration of the heart, lungs, liver, spleen, bone marrow and retroperitoneal lymph nodes.

This case is another example of the potency of cladribine in lymphoproliferative disorders. Indeed, apart from serious infections [4] and severe myelotoxicity [5], this agent can also induce fatal tumour lysis syndrome. In this case, the dose of cladribine was not in the range previously reported as being nephrotoxic and this is probably not a concomitant factor [6]. The clinical course was characterised by initial good control with hydration and allopurinol despite the high tumour burden. However, tumour lysis lasted longer than was expected, leading to additional complications with multiple organ failure and death. This may reflect some of the particular mechanisms of action of cladribine-induced apoptosis, and we would strongly advise against early withdrawal of intensive supportive measures once tumour lysis has started.

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