European Journal of Cancer Vol. 30A, No. 3, p. 420, 1994.

0959-8049/94 $6.00 + 0.00

Treatment of Patients with Metastatic Melanoma with a One Day Regimen of Dacarbazine, Vincristine, Bleomycin and Lomustine plus Interferon-α

M. Vuoristo, P. Gröhn, E. Kumpulainen and M. Korpela

PREVIOUS STUDIES on interferon-α-2b (IFN-α2b) combined with chemotherapy have reported response rates of 23–53% in metastatic melanoma [1, 2].

We carried out a phase II study of metastatic melanoma with four-drug chemotherapy plus recombinant IFN-α in 1990–1991. The treatment consisted of dacarbazine 700 mg/m^2 intravenously (i.v.), vincristine 2 mg i.v., bleomycin 30 mg i.v. and lomustine 80 mg orally (DOBC) every 28 days plus IFN-α2b 3×10^6 U (Intron-A®, Schering-Plough) subcutaneously three times weekly. 9 patients (5 males and 4 females, aged 28–67 years, median 58 years) with measurable metastatic melanoma were enrolled for the study. The metastatic sites were the lung (5 patients), the lymph nodes (3 patients), the liver (3 patients) and the skin (2 patients). 5 patients had multiple metastatic sites. The response and adverse effects were evaluated according to the WHO criteria [3].

All patients were evaluable for toxicity and 8 patients for response. The response rate was low: only 1 patient achieved partial response in lung metastases lasting for 5 months and another had stable disease lasting for 3 months. The overall survival of the responding patient was 12 months. The median survival of all patients was 5 months (range 2 weeks–32+ months). The treatment was moderately toxic. The flu-like syndrome attributable to IFN was controlled by non-steroidal anti-inflammatory drugs. The most common adverse reactions of chemotherapy were cytopenia, gastrointestinal symptoms and alopecia (Table 1). There was one treatment-related death caused by haematotoxicity. It was concluded that the present regimen offers no benefit for patients with melanoma.

Table 1. Toxicity of the treatment (DOBC plus IFN-α2b)

	WHO grade	
Adverse event	1–2	3–4
Haematological	3	3
Gastrointestinal	7	1
Alopecia	4	0
Neurological	2	0
Stomatitis	1	0

Values expressed are numbers of patients.

Correspondence to M. Vuoristo at the Department of Oncology, University of Tampere and Tampere University Hospital, 36280 Pikonlinna, Finland.
P. Gröhn is at the Deaconess Hospital in Helsinki, Alppikatu 2, 00530 Helsinki; E. Kumpulainen is at the Department of Radiotherapy and Oncology, Kuopio University Hospital, 70210 Kuopio; and M. Korpela is at the Department of Radiotherapy and Oncology, Oulu University Central Hospital, 90220 Oulu, Finland.
Revised 8 July 1993; accepted 13 Sept. 1993.

1. Falkson CI, Falkson G, Falkson HC. Improved results with the addition of interferon alfa 2b to dacarbazine in the treatment of patients with metastatic malignant melanoma. *J Clin Oncol* 1991, **9**, 1403–1408.
2. Gröhn P, Kumpulainen E, Nuortio L, *et al.* A phase II study of metastatic melanoma treated with a combination of interferon alpha-2b, dacarbazine and nimustine. *Eur J Cancer* 1992, **28A**, 441–443.
3. Miller AB, Hoosgstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer* 1981, **47**, 207–214.

Acknowledgements—We wish to thank the Cancer Society of Pirkanmaa for supporting this study.

European Journal of Cancer Vol. 30A, No. 3, pp. 420–421, 1994.

0959-8049/94 $6.00 + 0.00

Bioavailability of Oral Etoposide in Gastric Cancer

B.G. Taal, J.H. Beijnen, F.G.M. Teller, W.W. ten Bokkel Huinink, R. Dubbelman and H. Boot

IN THEIR recent report, Pinkerton *et al.* [1] described a 48% bioavailability of etoposide in children, and they advised a twice daily administration based on the short half-life of the drug. In adults, recent pharmocokinetic studies showed similar data with wide variations, and found better resorption at the lower dosages: 76% ± 22 bioavailability at an oral dose of 100 mg, and 48% ± 18 with a 400 mg dose [2]. As knowledge of the specific mechanism of this topoisomerase II inhibitor is increasing, there is a growing interest in the oral application [3]. The oral route seems to be simple and safe, as well as effective. Experience in small cell lung cancer suggests that long-term oral administration of etoposide is superior to short-term intravenous administration, which is reflected in much improved response rates [2]. In developing drug schedules with protracted oral etoposide, especially in combination with other cytostatic drugs, the dose-dependent variation in bioavailability is very important. We would like to report on another possible problem in bioavailability.

Recently, we performed a phase II trial in gastric cancer using the ELF regimen (etoposide, high dose leucovorin and 5-fluorouracil), as described previously by Preusser [5]. To improve results, we modified the regimen using oral doses of etoposide. However, in patients with gastric carcinoma the stomach is often either pathologically or surgically removed, and one might assume that this would interfere with the bioavailability of orally administered agents. Therefore, a pharmacoki-

Correspondence to B.G. Taal.
B.G. Taal, F.G.M. Teller and H. Boot are at the Department of Gastroenterology; W.W. ten Bokkel Huinink and R. Dubbelman are at the Department of Medical Oncology; and J.H. Beijnen is at the Department of Pharmacology, Netherlands Cancer Institute/Antoni van Leeuwenhoekhuis, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands.
Received 17 Aug. 1993; accepted 6 Sep. 1993.