

Table 1. Hospitalisation and cost (\$)

Cost*	G-CSF	Control	P value
Number of hospitalisations	18	19	NS*
Mean toxicity-related days of hospitalisation \pm S.E.	6.4 \pm 9.1	18.0 \pm 13.2	0.003†
Mean hospitalisation + G-CSF cost/cycle \pm S.E.	\$2282 (\pm 1345)	\$3232 (\pm 2283)	NS†

One day of hospitalisation is about \$450. * Fisher's test χ^2 . † Mann-Whitney test.

However, the mean duration of delays between cycles was reduced from 9 days in the control to 4 days in the G-CSF treated patients ($P = 0.01$). The overall response rates were similar, being 78% in the group treated with G-CSF and 88% in the control group.

As shown in Table 1, while the number of hospitalisations was similar in the two groups, there was a significant decrease in the mean duration of hospitalisation for toxicity per patient treated with G-CSF compared with the control group (6.4 ± 9.1 versus 18 ± 13.2 days; $P = 0.003$). Taking into consideration the cost of G-CSF and the cost of hospitalisation, the mean cost per cycle was $\$3232 \pm 2283$ in patients treated with chemotherapy without G-CSF compared to $\$2282 \pm 1345$ in patients treated with G-CSF. This difference was non-significant.

In conclusion, the prophylactic use of G-CSF in patients with HIV-related NHL receiving intensive chemotherapy is associated with a significant reduction of treatment-related myelosuppression, with a decrease of the overall cost of the treatment, although not at a statistically significant level. Further studies should be undertaken in order to evaluate whether G-CSF can be efficaciously given for a shorter period of time in order to further decrease the cost of the overall treatment. Finally, with the experience accumulated in these years, some patients with AIDS-related NHL can be safely treated with intensive chemotherapy regimens and G-CSF also in an outpatient setting.

1. Levine A, Wernz J, Kaplan L, *et al.* Low-dose chemotherapy with central nervous system prophylaxis and zidovudine maintenance in AIDS-related lymphoma. A prospective, multi-institutional trial. *JAMA* 1991, **266**, 84–88.
2. Levine A. Acquired immunodeficiency syndrome-related lymphoma. *Blood* 1992, **80**, 8–20.
3. Gianni A, Bregni M, Siena S, *et al.* Recombinant human granulocyte-macrophage colony-stimulating factor reduces hematologic toxicity and widens clinical applicability of high-dose cyclophosphamide treatment in breast cancer and non-Hodgkin's lymphoma. *J Clin Oncol* 1990, **8**, 768–778.
4. Coiffier B, Mandel U, Clause H, *et al.* Immunohistochemical expression of oncofetal fibronectin in benign and malignant lesions of the stomach. *JCO* 1989, **7**, 1018–1026.
5. Carde P, Meerwaldt H, van Glabbeke M, *et al.* Superiority of second over first generation chemotherapy in a randomized trial for stage III–IV intermediate and high-grade non-Hodgkin's lymphoma (NHL): the 1980–1985 EORTC trial. *Ann Oncol* 1991, **2**, 431–435.

Acknowledgements—This study was supported by grants of Istituto Superiore di Sanità and AIRC.

European Journal of Cancer Vol. 30A, No. 10, pp. 1590–1591, 1994.
Copyright © 1994 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0959-8049/94 \$7.00 + 0.00

Treatment of the Carcinoid Syndrome With a Depot Formulation of the Somatostatin Analogue Lanreotide

H. Scherübl, B. Wiedenmann, E.O. Riecken, F. Thomas, E. Böhme and U. Räh

SYMPTOMATIC CONTROL of the carcinoid syndrome can be achieved by somatostatin therapy in as many as 50–87% of all patients [1, 2]. In addition, in a small percentage (4.4%) of patients with neuroendocrine tumours of the gastroenteropancreatic system, partial regression, defined as tumour shrinkage by 30% or more, has been observed after 3 months of treatment with 200 μ g octreotide, subcutaneously (s.c.), every 8 h [3]. Due to the inconvenience of three daily s.c. injections of somatostatin analogues, such as octreotide or lanreotide, a depot formulation of lanreotide has been developed [4–6]. The purpose of this study was to evaluate the efficacy of fortnightly intramuscular (i.m.) injections of 30 mg of depot lanreotide in patients with carcinoid syndrome.

All patients included in the study were ambulatory, maintained a reasonable state of nutrition, had histologically-confirmed metastatic carcinoid tumour disease with elevated urinary 5-hydroxy-indolic acid excretion, and suffered from carcinoid syndrome. Moreover, all patients had measurable tumour masses to serve as objective indicators of response to therapy. All patients gave informed consent to participate in the study, which was approved by the ethics committee of Benjamin Franklin Medical Center. Patients' characteristics are shown in

Correspondence to H. Scherübl.

H. Scherübl, B. Wiedenmann and E.O. Riecken are at the Dept. of Internal Medicine/Gastroenterology, Klinikum Benjamin Franklin, Freie Universität Berlin, Hindenburgdamm 30, 12200 Berlin; E. Böhme and U. Räh are at the Dept. of Internal Medicine/Gastroenterology, Medizinische Universitätsklinik Heidelberg, Bergheimerstr. 58, 69115 Heidelberg, Germany; and F. Thomas is at Ipsen Biotech, 24 Rue Erlanger, 75781 Paris Cedex 16, France.

Received 28 Mar. 1994; accepted 17 May 1994.

Table 1. Patients' characteristics and therapeutic response

	No. of patients
No. of patients entered	18*
No. of patients evaluable for response (at 12 months)	12
Female/male	4/8
Median age, years (range)	58 (31–84)
ECOG performance score	
1	10
2	2
Symptoms	
Flushing	7
Diarrhoea	12
Abdominal pain	6
Median pretreatment chromogranin A level (ng/ml) (range)	389(78–34 000)
Median post-treatment chromogranin A level (ng/ml) (range)	265(18–100 000)
Site of primary	
Stomach	1
Pancreas	1
Ileum	7
Appendix	1
Unknown	2
Site(s) of secondaries	
Liver	8
Mesenteric/para-aortic lymph nodes	4
Peritoneal carcinosis	3
Tumour response (UICC)	
Objective tumour regression	0
Stable disease	7
Progressive disease	5
Symptomatic control/improvement	
Flushing	6/7
Diarrhoea	5/12
Abdominal pain	3/6
Toxicity	
Local pain (at injection site)	9
Gall stones	2

*There were 4 "drop-outs" after 7 days ($n = 2$) or after 1 month ($n = 2$) because of severe pain at the injection site ($n = 2$), severe pancreatic insufficiency ($n = 1$) or loss of libido ($n = 1$). In 2 other patients, lanreotide treatment was stopped after 3 or 6 months due to tumour progression.

Table 1. Tumour growth was evaluated at 3, 6, 9 and 12 months by abdominal computed tomography, abdominal ultrasound scans and chest X-rays. Serum chromogranin A levels were also determined at 3-month intervals. An objective response was declared if bidimensionally measurable lesions decreased by at least 50% in the product of largest perpendicular diameters. Stable disease was assumed if less than a 25% increase or less than a 50% decrease in tumour size was seen. Progressive disease was defined as an increase in tumour size by more than 25% or new tumour lesions.

In case of progressive disease, lanreotide therapy was stopped. In 1 patient injection intervals were shortened from 14 to 10 days, and in another to 7 days, in order to control symptoms. Of the 18 patients who entered the study, there were 4 "drop-outs": 2 patients discontinued the study after 7 days due to loss of libido

or severe pain at the injection site, respectively. 2 other patients discontinued the therapy after 1 month due to severe local pain and severe exocrine pancreatic insufficiency, respectively. In 2 patients, lanreotide therapy was stopped after 3 and 6 months due to tumour progression.

Therapeutic response and toxicity data are shown in Table 1. Among the 12 patients treated for 12 months, flushing was abolished or reduced in 6/7 (85.7%), and diarrhoea in 5/12 patients (41.7%). Abdominal pain was alleviated in 3/6 patients (50%). There were no objective responses in terms of tumour shrinkage. Nevertheless, stable disease was observed in 7 patients. Progressive disease was seen in the other 5. Since lanreotide therapy had to be discontinued due to tumour progression in 2 other patients, 3 and 6 months after starting therapy, the total number with progressive disease was 7/14 (50%) patients treated for longer than 1 month.

Toxicity mainly consisted of local reactions and of transient (the first 2 days after injection) diarrhoea or steatorrhoea. In 2/18 patients who entered the study, lanreotide therapy had to be discontinued due to severe local pain after 7 days and 1 month of therapy, respectively. Formation of gall stones was encountered in 2 patients.

Thus, somatostatin therapy with the depot formulation of lanreotide given i.m. every 7 to 14 days is an attractive and effective treatment modality for the symptomatic control of the carcinoid syndrome.

1. Kvols LK. Therapy of the malignant carcinoid syndrome. *Endocrinol Metab Clin North Am* 1989; **18**, 557–568.
2. Öberg K. Chemotherapy and biotherapy in neuroendocrine tumors. *Current Opinion Oncol* 1993; **5**, 110–120.
3. Arnold R, Benning R, Neuhaus C, Rolwage M, Trautmann ME and the German Sandostatin Study Group. Gastroenteropancreatic endocrine tumours: effect of Sandostatin on tumour growth. *Digestion* 1993; **54** (suppl. 1), 72–75.
4. Heron I, Thomas F, Dero M, *et al.* Pharmacokinetics and efficacy of a long-acting formulation of the new somatostatin analog BIM 23014 in patients with acromegaly. *J Clin Endocrinol Metab* 1993; **76**, 721–727.
5. Anthony L, Johnson D, Hande K, *et al.* Somatostatin analogue phase I trials in neuroendocrine neoplasms. *Acta Oncol* 1993; **32**, 217–223.
6. Scherübl H, Räh U, Riecken EO, Kommerell B, Wiedenmann B. Treatment of carcinoid tumor disease with the somatostatin analogue lanreotide. *Gastroenterology* 1993; **104**, A447.

European Journal of Cancer Vol. 30A, No. 10, pp. 1591–1592, 1994.
Copyright © 1994 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0959-8049/94 \$7.00 + 0.00

Hepatitis C Virus Infection and B-cell Lymphomas

C. Ferri, F. Caracciolo, L. La Civita,
M. Monti, G. Longobardo, F. Greco and
A.L. Zignego

AFTER THE identification of hepatitis C virus (HCV) as the major causative agent of post-transfusion and sporadic non-A, non-B