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/paraaortic 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.

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European Journal of Cancer Vol. 30A, No. 10, pp. 1591–1592, 1994.

0959–8049/94 $7.00 + 0.00

Hepatitis C Virus Infection and B-cell Lymphomas

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

chronic hepatitis [1], various authors have suggested a possible role for this virus in different hepatic and extra-hepatic disorders; namely autoimmune liver diseases, porphyria cutanea tarda and mixed cryoglobulinaemia [2–6]. This latter condition is a benign lymphoproliferative disorder, which in some individuals can switch over to a malignant B-cell non-Hodgkin's lymphoma [6]. Recently, a clear-cut association between HCV infection and Waldenstrøm's macroglobulinemia, a B-lymphocyte neoplasia, has been reported [7]. In addition, HCV genomic sequences have been demonstrated in peripheral blood mononuclear cells of mixed cryoglobulinaemia [8] and HCV-related chronic hepatitis [9]. The HCV lymphotropism has reinforced the hypothesis of its pathogenetic role in chronic B-cell expansion underlying some lymphoprolifetive disorders. We preliminarily investigated the prevalence of HCV infection in patients with B-cell non-Hodgkin's lymphoma (NHL).

The study included 30 unselected patients with B-cell NHL (18 males, 12 females; mean age 60 ± 10 years, range 35–70 and mean disease duration 2 ± 3 years) followed at the Haematology Unit of the Clinica Medica I, University of Pisa, Italy. Patients were consecutively recruited during their routine ambulatory visits; in all cases, other neoplastic or chronic inflammatory disorders were excluded. Diagnosis of NHL was made by lymph node biopsy evaluated according to the Working Formulation classification [10], and by immunophenotypic analysis for surface T and B lymphocyte markers. All patients were Italian-born heterosexuals, and had no history of drug or alcohol abuse. In no case was interferon treatment employed during the previous follow-up and at the time of the study. Virological studies included serum HCV RNA detected by 'one-tube nested' polymerase chain reaction (PCR) assay, using primers corresponding to the well conserved 5′ non-coding region of the HCV genome, as described previously [8, 9]; antibodies against HCV (anti-HCV), evaluated by commercially available kits (Chiron ELISA HCV, Second Generation, and recombinant-based immunoblot assay, RIBA HCV, Second Generation; Chiron, Emeryville California, U.S.A.); and detection of hepatitis B antigens (HBsAg, HBeAg) and antibodies against HBV (anti-HBs, -HBc, -HBe) and human immunodeficiency virus (anti-HIV) (Hepanostika, Vironostika, Organon Teknica, Boxetel, The Netherlands). 23 patients with Hodgkin's lymphoma and 30 age-matched healthy subjects were used as control groups.

In over a third (37%) of our NHL patients (Table 1), both anti-HCV antibodies and HCV genomic sequences were present in the serum. Mild elevation of serum transaminases (4/30), presence of trace amount of circulating cryoglobulins (3/30), and previous exposure to blood products (4/24) were seldom recorded. HBV-related markers were present in 20% of our NHL series; this percentage was comparable to that found in an Italian population of healthy controls; in no cases were markers of active HBV infection (HBsAg, HBeAg, anti-HBc IgM) and anti-HIV found. Finally, HCV-related markers were never detected in either healthy subjects or control patients.

Table 1. HCV infection in B-cell non-Hodgkin's lymphomas

Disease	No. of patients	anti-HCV	HCV RNA (PCR+)
B-cell non-Hodgkin's lymphoma	30	37% (11/30)	37% (11/30)
Hodgkin's lymphoma	23	4% (1/23)	0%
Healthy subjects	30	7% (2/30)	0%

These preliminary data, showing the presence of HCV infection in a relevant number (37%) of NHL patients, are particularly significant if compared with the prevalence of HCV in an Italian population of healthy subjects (1.3%) and in our age-matched series of chronic diseases (2%), namely Sjøgren's syndrome, systemic lupus and rheumatoid arthritis [6], these latter characterised by frequent patient hospitalisation. Some lymphotropic viruses, i.e. Epstein–Barr virus and human herpes virus type 6, have been suggested as being the causative agents of malignant lymphomas [11, 12]. With the exception of Burkitt's [11] and HIV-related lymphomas [12], the aetiopathogenesis of lymphomas remains largely obscure. Non-Hodgkin's lymphomas are a heterogeneous group of lymphoproliferative neoplasias with variable grades of malignancy, and different aetiopathogenetic factors could be involved [11, 12]. Thus, the presence of HCV infection in a third of NHL suggests a possible role of this lymphotropic virus in such disorders. Hypothetically, in individuals with a peculiar genetic and immunological reactivity and in the presence of other unknown environmental factors, HCV can trigger a chronic B-cell proliferation with different clinical expressions, varying from 'benign' mixed cryoglubulinaemia to Waldenstrøm's macroglobulinaemia or to frank malignant lymphoma.

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Received 11 Apr. 1994; accepted 9 June 1994.

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