ELSEVIER

Journal of Hepatology 42 (2005) 323–328

Journal of Hepatology

www.elsevier.com/locate/jhep

Barriers to interferon-α therapy are higher in intravenous drug users than in other patients with acute hepatitis C☆

Barbara Broers[1], Beat Helbling[2], Anne François[1], Patrick Schmid[3], Christian Chuard[4], Antoine Hadengue[5], Francesco Negro[5,6,*], for the Swiss Association for the Study of the Liver (SASL 18)

[1]*Département de Médecine Communautaire, University Hospitals, Geneva, Switzerland*
[2]*Divisions of Gastroenterology and Hepatology, Kantonsspital, St Gallen, Switzerland*
[3]*Infectious Diseases, Kantonsspital, St Gallen, Switzerland*
[4]*Clinique de Médecine, Hôpital Cantonal, Fribourg, Switzerland*
[5]*Services de Gastroentérologie et d'Hépatologie et de, University Hospitals, Geneva, Switzerland*
[6]*Services de Pathologie Clinique, University Hospitals, Geneva, Switzerland*

See Editorial, pages 293–296

***Background/Aims*: Treatment with interferon-α (IFN-α) may eradicate HCV in most acute hepatitis C patients, thus preventing chronic hepatitis and avoiding less efficacious combination therapy.**

***Methods*: In a prospective study, we evaluated the impact of barriers to successful start and completion of treatment of acute and subacute (<12 months from infection) hepatitis C with pegylated IFN-α_{2b}, 1.5 μg/kg, QW, for 24 weeks.**

***Results*: Out of 27 patients (22 were active intravenous drug users [IVDU]), 5 cleared HCV spontaneously. Antiviral treatment was indicated in 22 patients: six refused therapy for fear of side effects, whereas two others were lost to observation. Eight patients completed the treatment or received >80% of the scheduled drug: seven (88%) were sustained virological responders 24 weeks after the end of treatment. Six patients (all IVDU) stopped prematurely due to side effects: only one had a sustained virological response. Based on an intent-to-treat analysis, and considering all 14 patients in whom at least one dose of drug was administered, only 8 (57%) became sustained virological responders.**

***Conclusions*: Treatment of acute hepatitis C with pegylated IFN-α is highly beneficial, but its effectiveness is affected by a poor rate of acceptance and/or adherence to currently available regimens, especially in IVDU and women.**

***Keywords*: Acute hepatitis C; Antiviral treatment; Interferon-α; Substance abuse; Compliance; Adherence**

1. Introduction

Acute hepatitis due to hepatitis C virus (HCV) is rarely severe and its clinical impact is essentially due to the significant propensity to evolve to chronicity [1–6]. Recent studies suggest that treatment of acute hepatitis C with interferon-α (IFN-α) is highly effective, since it may eradicate HCV in 80–100% of cases, thus preventing the development of chronic hepatitis and avoiding more expensive and less tolerated combination therapy [7–11]. Hence, antiviral therapy in this setting should be encouraged, and international guidelines support this attitude [3–6].

Intravenous drug users (IVDU) are a major risk group for infection with HCV [3,4]. In Switzerland, approximately 80% of newly acquired HCV infections are due to sharing of injection equipment among IVDU [12]. Treatment of IVDU with *chronic* hepatitis C has been generally discouraged, for

Received 16 September 2004; received in revised form 5 November 2004; accepted 15 November 2004; available online 24 November 2004

☆ The authors declare that they received funding from Essex Chemie AG, Lucerne in order to help them carry out the study.

* Corresponding author. Address: Services de Gastroentérologie et d'Hépatologie et de, Hôpital Cantonal Universitaire, 24 rue Micheli-du-Crest, CH-1211 Geneva 14, Switzerland. Tel.: +41 22 3729340; fax: +41 22 3729366.

E-mail address: negro-francesco@diogenes.hcuge.ch (F. Negro).

0168-8278/$30.00
doi:10.1016/j.jhep.2004.11.018

presumed non-adherence, increased risk and/or severity of side-effects (especially psychiatric), and risk of reinfection [12]. On the other hand, IVDU often share many factors of good response to therapy, such as young age, short duration of disease, and HCV genotype 3 infection. Moreover, different clinical studies suggest that IVDU can be treated successfully, also when active use of drugs has been withdrawn for only a short period of time [13–16]. Thus, more recent guidelines contain less restrictive recommendations [3,4].

As compared to their more tolerant attitude vis-à-vis chronically infected patients, physicians still seem very reluctant to treat active IVDU with *acute* hepatitis C. Recent studies on treatment of acute hepatitis C with IFN-α monotherapy have included only a minority of IVDU (10–25% of the total treated population) [7–11]. Whether this too cautious attitude should be maintained in the future, given the very high rate of success of treatment, remains to be proven.

The objective of our study was to evaluate the feasibility of pegylated IFN-α monotherapy in acute hepatitis C irrespectively of the risk factor for HCV acquisition.

2. Methods

Patients with acute (<6 months from the estimated date of infection) or subacute (>6 but <12 months from the estimated date of infection) hepatitis C were enrolled in a multicenter prospective trial if they had (1) a documented seroconversion for HCV or (2) a clinical picture compatible with acute hepatitis (symptoms including jaundice and/or fatigue together with serum ALT ≥20 the upper level of the normal, i.e. 50 U/l for males and 42 U/l for females) and a suspected exposure to HCV. Pegylated IFN-α_{2b} monotherapy (PEG-Intron™, Essex Chemie AG, Lucerne, Switzerland), 1.5 μg/kg, QW, for 24 weeks was offered to (1) all symptomatic patients with persisting HCV viral load for at least 5 weeks from onset of symptoms [9,11], and to (2) all asymptomatic patients [8]. All patients were fully informed of the benefits of the treatment and of its potential adverse effects, and simultaneously followed by experienced hepatologists and specialists in substance abuse (albeit at different units). Psychiatric counselling was guaranteed if indicated. Patients had access to a telephone hot line for support.

Clinical and laboratory data were gathered on standardized study forms. The primary endpoint was a sustained virological response at the end of a 24 weeks period of follow up after the end of treatment, and was defined by undetectable levels of HCV RNA in serum by a qualitative PCR (Roche Amplicor Monitor™, Roche Diagnostics, Rotkreuz, Switzerland). Additional data were collected on factors that could potentially influence acceptance of antiviral therapy and/or its completion (age, gender, active IVDU at the time of enrolment, presence of symptoms, ongoing psychiatric therapy, hospitalisation at a psychiatric institution during the 6 months preceding therapy, ongoing methadone therapy, as well as housing, household and professional status). The time from diagnosis to start of therapy was also considered, as well as the number of missed appointments during treatment. HCV RNA was measured by quantitative PCR (Amplicor Monitor, Roche Diagnostics, Rotkreuz, Switzerland). HCV genotyping was performed with a second-generation reverse-hybridisation line probe assay (Inno-Lipa HCV II, Innogenetics, Zwijndrecht, Belgium). Differences between groups were evaluated by the Fisher's exact test.

This study was sponsored by the Swiss Association for the Study of the Liver (SASL 18). It was approved by all local Ethical Committees and conducted in conformity with the Helsinki declaration. All patients consented to participate.

3. Results

Between May 2002 and September 2003, 27 cases (20 males) fulfilling the criteria for acute ($n=24$) or subacute ($n=3$) hepatitis C were referred. A total of 26 patients had a documented seroconversion against HCV, whereas only one patient had anti-HCV already at presentation, together with a recent acute post-transfusion hepatitis contracted in a developing country, and no prior history of liver disease.

Risk factors for HCV infection were active IVDU (22 cases, or 81.5%), accidental needle-stick with HCV-containing blood (two cases, both healthcare workers [HCW]), sexual contact with an HCV-infected partner (1 case), transfusion with HCV-contaminated blood (1 case) whereas for one patient, in spite of a documented seroconversion against HCV, no overt risk factors for HCV infection were identified.

The date of exposure to HCV was estimated based on the self-reported date of risk behaviour (for IVDU) or on the exact date of exposure in case of accidental needle-stick, sexual intercourse or blood transfusion. For the patient in whom no risk factors were identified—but for whom a HCV-negative serology was available 6 months before seroconversion—we estimated that he had been infected with HCV 3 months before seroconversion. HCV genotype was assessed in 21 cases and was 1a in 5 cases, 1b in 4, 2 in one, and 3a in 11.

Sixteen patients (59.3%) had symptomatic acute hepatitis, the most prevailing symptoms being jaundice (in 7 cases) and fatigue (all 16 patients). Symptoms occurred 64±46 days from the estimated date of infection.

Of the 27 patients, five (three symptomatic) presented spontaneous HCV clearance upon HCV RNA retesting and had no indication for further treatment (Fig. 1). Patients with spontaneous HCV clearance were comparable to the remaining patients in terms of serum HCV RNA levels at presentation (400,830±894,000 IU/ml vs. 3,560,000±8,740,000 IU/ml, P=NS), peak ALT levels (1316±1143 U/l vs. 661±635 U/l, $P=0.09$), occurrence of symptoms (3/5 vs. 13/22, P=NS), and HCV genotype distribution (1/2 vs. 10/18 with genotype 3a, P=NS).

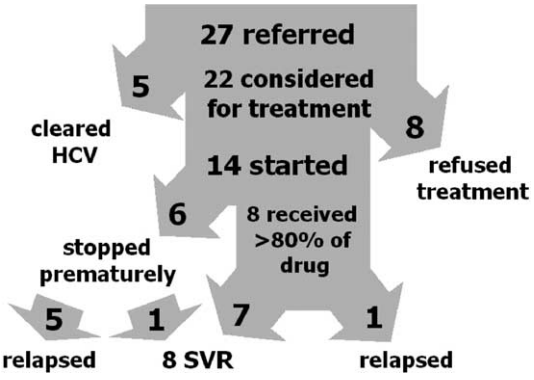

Fig. 1. Schematic representation of the outcome of 27 acute hepatitis C patients considered in the present study.