Long-term outcome of chronic hepatitis C patients with sustained virological response to peginterferon plus ribavirin

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AIM: To assess the clinical, biochemical and virological long-term outcome in chronic hepatitis C (CHC) patients with a sustained virological response (SVR) after peginterferon (PEG-IFN) plus ribavirin combination therapy.

METHODS: One hundred and fifty-three patients with a SVR after treatment with PEG-IFN plus ribavirin were included in a 5-year follow-up study in a single Spanish center, based on standard clinical practice. Clinical anamnesis, biochemical analysis, hepatitis C virus RNA and alpha-fetoprotein measurement, ultrasonography and transient elastography were performed annually.

RESULTS: The mean follow-up period of the 153 patients was 76 ± 13 mo after they obtained a SVR. Five patients (3.26%) presented with cirrhosis before treatment and 116 (75.8%) had genotype 1. No patient showed evidence of hepatic decompensation. One patient (0.65%) developed a hepatocellular carcinoma at month 30 after achieving SVR. There were no virological relapses during this follow-up period. Persistently elevated alanine aminotransferase was found in only one patient (0.65%). At the end of the 5-year follow-up, the mean value of transient elastography was 7 ± 4.3 kPa (F1). There were no deaths and no other tumors.

CONCLUSION: The long-term outcome of 153 CHC patients with SVR to PEG-IFN plus ribavirin was good. No evidence of a virological relapse was seen. One patient (0.65%) developed a hepatocellular carcinoma.

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Key words: Chronic hepatitis C; Peginterferon; Ribavirin; Sustained virological response; Long-term effects

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Introduction

The combination of peginterferon (PEG-IFN) plus ribavirin is the current standard of care for naïve chronic hepatitis C (CHC) patients, achieving a high sustained virological response.
response (SVR) rate[1-4]. The long-term benefits of CHC combination therapy have been well established in several studies, but the results are limited by differing patient populations or treatment regimens and, importantly, a brief duration of follow-up[5]; in addition, occult hepatitis infection by hepatitis C virus (HCV) has been proposed[6]. The conclusions of long-term studies[7-14] may be compromised by the small number of patients, and most studies using IFN monotherapy or IFN combined with ribavirin, while only 4 studies used PEG-IFN plus ribavirin combination therapy[15-18].

We conducted an open-label cohort study in a single center in Spain from January 2000 to December 2009, and included patients with a SVR after antiviral combination therapy with PEG-IFN plus ribavirin achieved between 2000 and 2003, with a mean follow-up greater than 5 years. Our major aim was to assess the clinical, biochemical and virological outcomes, and the durability of the SVR.

MATERIALS AND METHODS

Study design
A total cohort of 303 CHC consecutive patients (18-65 years) treated with PEG-IFN plus ribavirin in 2000-2003 were included in this cohort study. All patients attended the Hepatology Unit, Hospital Universitario de La Princesa (a tertiary university care centre), CIBERehd, Madrid, Spain.

Patients
Eligible patients were those who achieved a SVR after PEG-IFN plus ribavirin for 24 or 48 wk (in genotypes 2/3 or genotypes 1/4, respectively), defined as negativization of HCV-RNA at the end of treatment and after 6 mo of follow-up. Criteria for exclusion were: alcohol or intravenous drug abuse; liver diseases not related to HCV infection (autoimmune, metabolic or toxicity by drugs); decompensated liver disease; coinfection with HBV or human immunodeficiency virus; and pregnancy.

All patients received the standard of care combination therapy: 60 (39%) patients had been treated with PEG-IFN α-2a (Pegasys, Roche) plus ribavirin (1-1.2 g/d) and 93 (61%) patients with PEG-IFN α-2b (Peginteron, Schering-Plough) plus ribavirin (1-1.2 g/d). Patients with genotypes 1 and 4 were treated for 48 wk and patients with genotypes 2 or 3 were treated for 24 wk[19].

Clinical, biochemical and virological evaluation
We obtained data on patients’ sex and age, treatment, virological data (genotype, baseline HCV-RNA), biochemical data (aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), α-fetoprotein (AFP)], and length of follow-up. Pre-treatment liver biopsy and transient elastography analysis during the follow-up was obtained in some patients taking into account that this study was performed as routine clinical practice.

Patients were evaluated as outpatients at sequential annual clinical visits (1, 2, 3, 4, 5 years after the completion of antiviral therapy and 6 mo of follow-up). Blood tests with hematological, biochemical and virological assays were performed at the basal visit and thereafter. Serum HCV-RNA levels (IU/mL) were determined with Cobas Amplicor Hepatitis C Monitor Test (v2.0 Roche Diagnostics) and reverse transcription-polymerase chain reaction (RT-PCR), with a limit of detection < 50-100 IU/mL. HCV genotyping was performed by a reverse-hybridization line probe assay (INNO-LiPA HCV; Innogenetics, Zwijndrecht, Belgium).

Liver decompensation or failure was defined if a patient showed any of these findings: bleeding varices, hepatic encephalopathy, jaundice, or ascites. Patients were classified pretreatment by liver biopsy, and the establishment of cirrhosis was done using the META VIR score for fibrosis stage. In addition, transient elastography was performed during follow-up after achieving the SVR. Hepatocellular carcinoma (HCC) was diagnosed if 2 coincident imaging techniques [ultrasonography, computed tomography (CT) or magnetic resonance imaging] showed a focal lesion larger than 2 cm with arterial hypervascularization or if one imaging technique showed a focal lesion larger than 2 cm with arterial hypervascularization in the presence of an AFP level > 400 ng/mL.

Statistical analysis
Quantitative variables are expressed as mean ± SD. Qualitative variables are expressed as percentage with range. The Student t-test with Welch’s and Fisher’s correction, the chi-squared test, the Mann-Whitney U test and the Kruskal Wallis test were used for continuous or discrete variables as appropriate. Logistic regression was used to analyze if baseline factors could be associated with SVR. The Kaplan-Meier method was used to determine the rate of HCC occurrence. A value of P < 0.05 was considered to be statistically significant. Statistical analyses were performed using SPSS version 15.0.

RESULTS

Characteristics of patients
Among the 303 CHC patients, a total of 150 were excluded as they did not achieve a SVR. Those 153 patients with a SVR after treatment with PEG-IFN plus ribavirin (weight based) were included, with a mean age of 49 ± 9 years. There were 82 males (53.6%). Genotypes of HCV were distributed as follows: 116 genotype 1 (75.8%), one genotype 2 (0.6%), 32 genotype 3 (21%) and 4 patients with genotype 4 (2.6%). The baseline characteristics of patients with a SVR are shown in Table 1. One hundred and thirty patients (85%) were followed up for 5 or more after SVR. The median duration of follow-up was 76 ± 13 mo (range, 54-90) after the end of treatment, i.e., after achievement of a SVR was established.

Clinical outcomes
At the end of the follow-up, all patients were alive. Of 153 sustained responders, 5 patients had cirrhosis (F4) and 8 patients had F3 stage fibrosis before the start of the treatment, as determined by the META VIR score. No
patient with a SVR developed signs of liver failure during the follow-up. These patients were hepatitis B surface antigen negative and HCV-RNA negative, and no other risk factors for liver disease were reported.

One patient, with cirrhosis on pre-treatment biopsy and genotype 1b, developed a HCC at 30 mo of follow-up. It was assessed by ultrasonography, AFP level and CT scan, was 3.5 cm in size and located sub-diaphragmatically at segment VIII. The patient was still negative for serum HCV-RNA at the time of HCC diagnosis, and at last follow-up, HCV-RNA remained undetectable. The patient received an orthotopic liver transplant. Given that 5 patients had cirrhosis pre-treatment and one developed HCC, this represents a 20% risk of HCC after SVR in patients with pre-treatment cirrhosis. The incidence of HCC in this cohort of 153 SVR patients after a mean of 4-5 years of follow-up was 7 ± 4.3 kPa. One patient (0.8%) had a decrease in fibrosis stage from liver biopsy F3 to F1 per se, but the majority analyzed patients treated with recombinant IFN as monotherapy or in combination with ribavirin. At present, only 4 studies have enrolled patients treated with Peg-IFN plus ribavirin as shown in Table 3: in the study by Veldt et al[18], 83 patients were analyzed; Chavalitdhamrong et al[14] recently published the results of a long-term study of SVR patients including only 4 patients (3%) treated with Peg-IFN plus ribavirin; and Giannini et al[19] included 231 patients treated with Peg-IFN plus ribavirin, but only 33.3% were genotype 1.

### DISCUSSION

We assessed the long-term clinical, biochemical and virological outcomes of 153 patients with CHC who achieved a SVR after Peg-IFN plus ribavirin combination therapy. This study showed that a SVR is associated with permanent undetectable HCV-RNA in serum during a long-term follow-up. Nevertheless, it is difficult to say whether the treatment per se is important or whether a SVR is important because no controls were included. A late relapse of at least 0.8% after 4-5 years of follow-up has been reported[7-11,15-27]; however, introduction of more sensitive PCR methods may contribute to reduce this late-relapse rate.

There are some studies of the long-term clinical outcome of CHC patients with a SVR[15,16,20-27] but the majority analyzed patients treated with recombinant IFN as monotherapy or in combination with ribavirin. At present, only 4 studies have enrolled patients treated with Peg-IFN plus ribavirin as shown in Table 3: in the study by Veldt et al[18], 83 patients were analyzed; Chavalitdhamrong et al[14] studied 78 patients; George et al[19] recently published the results of a long-term study of SVR patients including only 4 patients (3%) treated with Peg-IFN plus ribavirin; and Giannini et al[19] included 231 patients treated with Peg-IFN plus ribavirin, but only 33.3% were genotype 1.
It is noteworthy that we included only patients treated with PEG-IFN plus ribavirin with a high proportion being genotype 1 (75.8%), in contrast to other studies (Chavalitdhamrong et al., where genotype 3 represented 62%; George et al., genotype 1 represented 47%; and Giannini et al. genotype 1 represented 66.6%).

Overall, our study showed that clinical events were rare in this population, indicating that SVR patients have an excellent prognosis, similar to previous studies[^8,9,11,14-16,20,21,25-29]. No patient developed decompensated liver disease. There were 5 (4.2%) patients with cirrhosis pre-treatment in this study. None of the patients with advanced fibrosis (F3) pre-treatment progressed to cirrhosis. Similar findings have been reported with PEG-IFN[^10,14,22]. In contrast, Pradat et al.[^23] found that cirrhosis developed in 2 of 87 patients who were followed for at least 5 years after a SVR.

One patient with pre-treatment cirrhosis developed a HCC that represented a rate of 0.8%. This patient had no other risk factors such as obesity, alcohol intake or diabetes. This is a similar rate of HCC as reported in other studies[^11,13,20,21,25,29]. Veldt et al.[^24] reported that 3/142 patients (2%) with a SVR and F3-F4 stage pre-treatment developed HCC during follow-up. Nevertheless, Japanese authors[^15,32] have reported a HCC rate of 0.02%-0.5% per year, slightly lower than our study. These data confirm that the risk of late development of HCC after a SVR is a real problem, and we must continue the follow-up of these patients for a long time. It is also important to take into account that HCV-RNA remains undetectable when HCC appears. Scientists speculate about the possibility of hepatocarcinogenesis, despite null replication of HCV, by other pathways[^29,33,34].

It is well-known that most patients with a SVR normalize their serum ALT, AST and total bilirubin, unless another liver disease is present[^8,9,11,24]. We found the same results in our study: 99% of patients had normal AST and ALT levels during the entire period of follow-up. The patient with HCC had persistently normal serum ALT values. Only one patient had elevated ALT and AST levels during follow-up period: a woman with fibromyalgia and relevant consumption of non-steroidal anti-inflammatory drugs. Nevertheless, ALP values were increased after treatment, but remained within the normal range (< 100 U/L).

There is no explanation for this finding.

Limitations of our study are that not all patients had a period of follow-up greater than 5 years and, importantly, that analysis of outcomes of fibrosis (stability, improvement or progression) are of limited value as no paired pre-treatment and post-treatment biopsies were analyzed from each patient. However, a large European study[^25] clearly demonstrated that the 5-year survival rate of patients achieving a SVR was similar to the overall population and that a SVR was associated with a decrease in fibrosis score; the authors speculated that excellent prognosis of sustained virological responders “is likely to hold true in the era of PEG-IFN and ribavirin”. Our data confirm this important prognostic assumption. Moreover, extensive recent histological analyses have shown that most virological responders without cirrhosis had normalization of liver histology[^13]; that is, up to 82% had improved fibrosis scores[^4] and in addition to fibrosis stability/improvement in 88%, in 64% of patients (9 of 14) regression of cirrhosis was observed[^15]. Taken all together[^13,14,21,35], these data question the indication for a second liver biopsy in CHC patients with a SVR after antiviral combination therapy.

The long-term clinical outcome of patients with a SVR to PEG-IFN plus ribavirin is favorable. However, a risk of HCC development still remains, although it is very low, so we must clinically monitor SVR patients for a long time, even with undetectable HCV-RNA, normal ultrasoundography, and normal aminotransferase and AFP levels after PEG-IFN plus ribavirin therapy.

**COMMENTS**

**Background**

The combination treatment of peginterferon (PEG-IFN) α plus ribavirin improved the sustained virological response (SVR) rate in chronic hepatitis C (CHC) patients. The long-term benefits of CHC combination therapy have been well established in several studies, but the results are limited by differing patient populations or treatment regimens and, importantly, a brief duration of follow-up.

**Research frontiers**

Occult hepatitis infection by hepatitis C virus (HCV) has been proposed and some cases of delayed relapses have been published.

**Innovations and breakthroughs**

The conclusions of long-term studies may be compromised by the small number of patients, and the fact that most studies used IFN monotherapy or IFN combined with ribavirin, with only 4 studies using PEG-IFN plus ribavirin combination therapy. This study analyzed patients with a SVR after antiviral combination therapy of PEG-IFN plus ribavirin with a mean follow-up greater than 5 years.

**Applications**

The study demonstrated that the long-term outcome of CHC patients who were sustained virological responders was good. It is important that evidence of a virological relapse must be assessed for a long time, as well as screening for hepatocellular carcinoma.

**Terminology**

A SVR is comparable with “clinical cure” in CHC patients. However, a minimal
percentage of patients present an activation of HCV replication, and are consid-
ered as "relapsers".

Peer review
The study has been well conducted and includes a large number of patients. Results have been described in a lucid and informative manner and are of clinical relevance.

REFERENCES
1. Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, Goodman ZD, Koury K, Ling M, Albrecht JK. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet 2001; 358: 958-965
2. Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Gonçalves FL Jr, Häussinger D, Diago M, Carosi G, Dhmeaux D, Craxi A, Lin A, Hoffmann J, Yu J. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med 2002; 347: 975-982
3. McHutchison JG, Gordon SC, Schiff ER, Shiffman ML, Lee WM, Rustgi VK, Goodman ZD, Ling MH, Cort S, Albrecht JK. Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. Hepatitis Interferon Interventinal Therapy. N Engl J Med 1998; 339: 1485-1492
4. Hadziyannis SJ, Sette H Jr, Morgan TR, Balan V, Diago M, Marcellin P, Ramadori G, Bodenheimer H Jr, Bernstein DJ, Rizzetto M, Zeuzem S, Pockros PJ, Lin A, Ackrill AM. Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and duration of virological response. Ann Intern Med 2004; 140: 346-355
5. Moreno-Otero R. Desperately seeking hepatitis C virus. World J Gastroenterol 2008; 14: 2946-2947
6. Carreño V. Occult hepatitis C virus infection: a new form of hepatitis C. World J Gastroenterol 2006; 12: 6922-6925
7. Saracco G, Rosina F, Abate ML, Chiandussi L, Gallo V, Ce-rettì E, Di Napoli A, Solinas A, Deplano A, Tocco A. Long-term follow-up of patients with chronic hepatitis C treated with different doses of interferon-alfa 2b. Hepatology 1993; 18: 1300-1305
8. Marcellin P, Boyer N, Gervais A, Martinot M, Pouteau M, Castelnau C, Kilani A, Areias J, Auperin A, Benhamou JP, Degott C, Erlinger S. Long-term histologic improvement and loss of detectable intrahepatic HCV RNA in patients with chronic hepatitis C and sustained response to interferon-alfa monotherapy. Ann Intern Med 1997; 127: 875-881
9. Lau DT, Kleiner DE, Ghaney MG, Park Y, Schmid P, Hoof-nagle JH. 10-Year follow-up after interferon-alfa therapy for chronic hepatitis C. Hepatology 1998; 28: 1121-1127
10. Cammà C, Di Marco V, Lo Iacono O, Almasio P, Giunta M, Fuschetti P, Vaccaro A, Fabiano C, Magrini S, Di Stefano R, Bonura C, Faglione L, Craxi A. Long-term course of interferon-treated chronic hepatitis C. J Hepatol 1998; 29: 531-537
11. Reichard O, Glaumann H, Frydén A, Norkrans G, Wejstål R, Weiland O. Long-term follow-up of chronic hepatitis C patients with sustained virological response to alpha-interferon. J Hepatol 1999; 30: 783-787
12. Yoshida H, Shiratori Y, Moriyama M, Arakawa Y, Ide T, Sata M, Inoue O, Yano M, Tanaka M, Fujiyama S, Nishiguchi S, Kuroki T, Imazeki F, Yokosuka O, Kino yama S, Yamada G, Omata M. Interferon therapy reduces the risk for hepatocellular carcinoma in patients with sustained virological response to interferon monotherapy. J Clin Gastroenterol 2005; 36: 53-520
13. Giannini EG, Basso M, Savarino V, Picciotto A. Sustained virological response to pegylated interferon and ribavirin is maintained during long-term follow-up of chronic hepatitis C patients. Aliment Pharmacol Ther 2010; 31: 502-508
14. National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C. 2002–June 10-12, 2002. Hepatology 2003; 36: 53-520
15. Veldt BJ, Heathcote EJ, Wedemeyer H, Reichen J, Hofmann WP, Zeuzem S, Manns MP, Hansen BE, Schalm SW, Janssen HL. Sustained vireologic response and clinical outcomes in patients with chronic hepatitis C and advanced fibrosis. Ann Intern Med 2007; 147: 677-684
16. Chavalitdamrong D, Tanwandeep T. Long-term outcomes of chronic hepatitis C patients with sustained virological response at 6 months after the end of treatment. World J Gastroenterol 2006; 12: 5532-5535
17. Aronsohn A, Reau N. Long-term outcomes after treatment with interferon and ribavirin in HCV patients. J Clin Gastroenterol 2009; 43: 661-671
18. Giannini EG, Basso M, Savarino V, Picciotto A. Sustained virological response to pegylated interferon and ribavirin is maintained during long-term follow-up of chronic hepatitis C patients. Aliment Pharmacol Ther 2010; 31: 502-508
19. National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C. 2002–June 10-12, 2002. Hepatology 2003; 36: 53-520
20. Imazeki F, Yokosuka O, Fukai K, Saisho H. Favorable prog-nosis of chronic hepatitis C after interferon therapy by long-term cohort study. Hepatology 2003; 38: 493-502
21. Veldt BJ, Saracco G, Boyer N, Cammà C, Bellobuono A, Hofp U, Castillo I, Weiland O, Nevens F, Hansen BE, Schalm SW. Long term clinical outcome of chronic hepatitis C patients with sustained virological response to interferon monotherapy. Gut 2004; 53: 1504-1508
22. Schvarcz R, Glaumann H, Reichard O, Weiland O. Histological and virological long-term outcome in patients treated with interferon-alpha2b and ribavirin for chronic hepatitis C. J Viral Hepat 1999; 6: 237-242
23. Okanoue T, Itoh Y, Minami M, Sakamoto S, Yasui K, Saka-moto M, Nishiiori K, Murakami Y, Kashima K. Interferon therapy lowers the rate of progression to hepatocellular carcinoma in chronic hepatitis C but not significantly in an advanced stage: a retrospective study in 1148 patients. Viral Hepatitis Therapy Study Group. J Hepatol 1999; 30: 653-659
24. Shiratori Y, Imazeki F, Moriyama M, Yano M, Arakawa Y, Yokosuka O, Kuroki T, Nishiguchi S, Sata M, Yamada G, Fujiyama S, Yoshida H, Omata M. Histologic improvement of fibrosis in patients with hepatitis C who have sustained response to interferon therapy. Ann Intern Med 2000; 132: 517-524
25. Poynard T, McHutchison J, Manns M, Scharf M, Lindsay K, Goodman Z, Ling MH, Albrecht J. Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C. Gastroenterology 2002; 122: 1303-1313
26. Akuta N, Suzuki F, Suzuki Y, Szekai H, Hosaka T, Someya T, Kobayashi M, Saioth S, Arase Y, Ikeda K, Kobayashi M, Kumada H. Long-term follow-up of interferon monotherapy in 454 consecutive naïve patients infected with hepatitis C virus: multi-course interferon therapy may reduce the risk for hepatocellular carcinoma and increase survival. Scand J Gastroenterol 2005; 40: 688-696
27. Pradat P, Tillmann HL, Sauleda S, Braconnier JH, Saracco G, Thursz M, Goldin R, Winkler R, Alberiti A, Esteban JL, Hadziyannis S, Rizzetto M, Thomas H, Manns MP, Trepo C. Long-term follow-up of the hepatitis C HENCORE cohort: Interferon Statement: Management of hepatitis C: 2002--June 10-12, 2002. Hepatology 2003; 36: 53-520
28. Arthur MJ. Reversibility of liver fibrosis and cirrhosis fol-lowing treatment for hepatitis C. Gastroenterology 2002; 122: 1525-1528
29. Ikeda M, Fujiyama S, Tanaka M, Sata M, Ide T, Tsuchahashi H, Watanabe H. Risk factors for development of hepatocellular carcinoma in patients with chronic hepatitis C after sus-tained response to interferon. J Hepatol 2005; 40: 148-156
30. Sanešuji K, Kayashima H, Iuchi T, Sugimachi K, Yamashita Y, Yoshizumi T, Soejima Y, Nishizaki T, Taketomi A, Mae-
hara Y. Characterization of hepatocellular carcinoma developed after achieving sustained virological response to interferon therapy for hepatitis C. J Surg Oncol 2009; 99: 32-37

31 Kasahara A, Hayashi N, Mochizuki K, Takayanagi M, Yoshioka K, Kakumu S, Iijima A, Uruishihara A, Kiyosawa K, Okuda M, Hino K, Okita K. Risk factors for hepatocellular carcinoma and its incidence after interferon treatment in patients with chronic hepatitis C. Osaka Liver Disease Study Group. Hepatology 1998; 27: 1394-1402

32 Imai Y, Kawata S, Tamura S, Yabuuchi I, Noda S, Inada M, Maeda Y, Shirai Y, Fukuzaki T, Kaji I, Ishikawa H, Matsuda Y, Nishikawa M, Seki K, Matsuzawa Y. Relation of interferon therapy and hepatocellular carcinoma in patients with chronic hepatitis C. Osaka Hepatocellular Carcinoma Prevention Study Group. Ann Intern Med 1998; 129: 94-99

33 Koike K. Steatosis, liver injury, and hepatocarcinogenesis in hepatitis C viral infection. J Gastroenterol 2009; 44 Suppl 19: 82-88

34 Chang ML, Chen TH, Chang MY, Yeh CT. Cell cycle perturbation in the hepatocytes of HCV core transgenic mice following common bile duct ligation is associated with enhanced p21 expression. J Med Virol 2009; 81: 467-472

35 Maylin S, Martinot-Peignoux M, Moucari R, Boyer N, Ripault MP, Cazals-Hatem D, Giuly N, Castelnau C, Cardoso AC, Asselah T, Féray C, Nicolas-Chanoine MH, Bedossa P, Marcellin P. Eradication of hepatitis C virus in patients successfully treated for chronic hepatitis C. Gastroenterology 2008; 135: 821-829