

LONG-TERM OUTCOME OF INTERFERON/RIBAVIRIN TREATMENT IN THE GERMAN REAL-LIFE SETTING: DURABLE SVR ASSOCIATED WITH LOW RATES OF LIVER-RELATED EVENTS

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Background

- The primary goal of treatment in patients with chronic hepatitis C virus (HCV) infection is to achieve a sustained virologic response (SVR).
- Long-term observational studies indicate that SVR has a profound impact on the natural course of chronic hepatitis C in relation to biochemical and histological remission of liver disease and improvement in quality of life
- An SVR achieved with conventional interferon alfa therapy has been shown to be durable
- However, limited data exist regarding the long-term durability of an SVR following peginterferon/ribavirin treatment for chronic hepatitis C
- In addition, limited data exist regarding long-term durability of SVR and incidence of liver-related morbidity after treatment with peginterferon-based therapies in the real-life setting

Objective

- To determine long-term durability of SVR and the long-term clinical outcome of chronic HCV infection after interferon-based treatments in the real-life setting

Methods

- Non-interventional follow-up survey in 45 German gastroenterological practices
- From May 2009 until October 2010 N=1372 patients were enrolled
- Data from patients ≥18 years with chronic hepatitis C who achieved SVR / Non-SVR after interferon or peginterferon-based treatment ≥3 years ago and who are still under routine medical observation were retrospectively documented
- Significant clinical events related to progression of liver disease such as liver transplantation, signs of decompensated liver disease [ascites, variceal bleeding, encephalopathy], and hepatic malignancy were recorded
- Patients with documented SVR after at least 6 months following termination of interferon/peginterferon-based therapy were assessed for durability of undetectable serum HCV-RNA
- From 1372 subjects enrolled 17 patients were excluded from the final analysis because of incomplete documentation or documentation errors
- From the remaining population of 1355 subjects 42 patients were firstly treated with conventional interferon alfa-2a or interferon alfa-2b while 1313 patients were firstly treated with pegylated interferon alfa-2a (N=432) or pegylated interferon alfa-2b (N=882). Overall, 1305 patients were treated with interferons together with ribavirin
- From 1355 subjects, 1105 patients received only one HCV treatment while 208 patients were re-treated with pegylated interferon alfa-2a (N=96), pegylated interferon alfa-2b (N=83) or non-pegylated interferons (N=29). Overall, 193 patients were re-treated with interferons together with ribavirin

Results

- Patients with chronic HCV infection enrolled in this non-interventional follow-up survey are summarized in Table 1
- 91.5% had HCV mono-infection while 8.5% were co-infected with HIV and HBV

Table 1: Patient and disease characteristics

	Evaluable Population (N=1355)
Age, years (mean ± SD)	49.2 + 11.5
Gender, % (N)	
- Female	42.0 (569)
- Male	58.0 (786)
Ethnicity, % (N)	
- Caucasian	94.2 (1277)
- Asian	2.1 (29)
- African	1.3 (17)
- Other/missing	4.1 (55)
Nationality, % (N)	
- German	68.6 (930)
- GUS	13.8 (187)
- Turkey	2.8 (38)
- Poland	2.7 (37)
- Italy	1.4 (19)
- Egypt	0.7 (10)
- Other/missing	10.0 (134)
Genotype, % (N)	
- 1	62.4 (845)
- 2	8.1 (110)
- 3	26.3 (357)
- 4	2.9 (39)
- 5	0.2 (3)
- 6	0.1 (1)
History of intravenous drug use, % (N)	33.4 (453)
- under stable substitution, % (N)	13.1 (178)
HIV co-infection, % (N)	6.1 (81)
HBV co-infection, % (N)	2.4 (32)
Clinical evidence for liver cirrhosis before first HCV therapy, % (N)	4.4 (59)

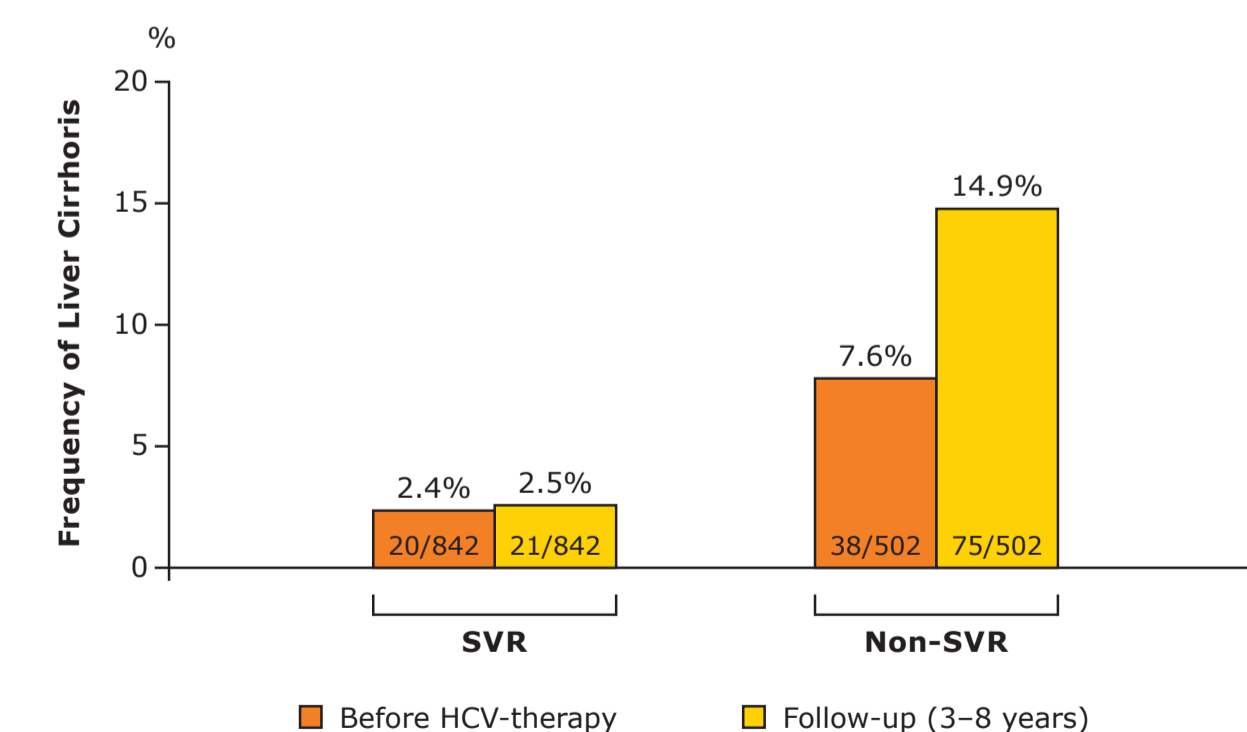
- After termination of first HCV-therapy, 55.7% of patients (755/1355) achieved SVR
- 208 of 596 patients who did not achieve SVR after first treatment were re-treated for HCV infection
- After re-treatment, SVR occurred in 87 of 208 subjects (42.3%)
- In total, 62.1% (842/1355) and 37.1% (502/1355) of patients achieved SVR and Non-SVR (missing data: N=11, 0.8%). Median follow-up of these patients was 4 years and ranged from 3 to 8 years as summarized in Table 2

Table 2: Duration of long-term follow-up after achieving SVR/Non-SVR

Years of follow-up after achieving SVR / Non-SVR	Proportion of patients with follow-up (N=1355) %, (N)
- 3 years	35.7 (484)
- 4 years	23.3 (316)
- 5 years	17.4 (236)
- 6 years	9.2 (125)
- 7 years	7.0 (95)
- 8 years	7.3 (99)

- As shown in Figure 1, a lower proportion of patients with SVR had clinical evidence for liver cirrhosis before first HCV treatment when compared with the group of patients who did not achieve SVR
- During follow-up, a 2-fold increase in the frequency of liver cirrhosis was observed in patients with treatment failure in contrast to a stable frequency in patients who achieved SVR

Figure 1: Frequency of liver cirrhosis before HCV-therapy and at the end of long-term follow-up



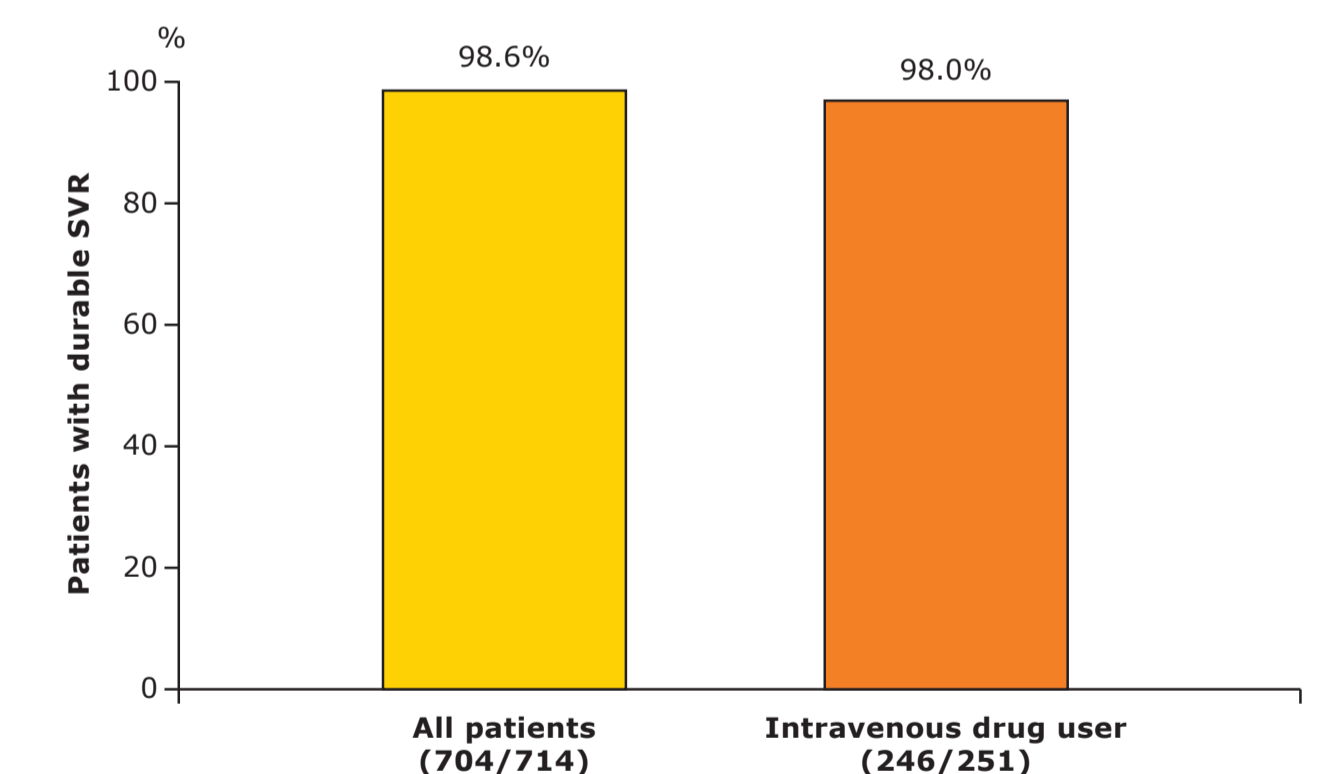
- Interestingly, only 3 patients (0.4%) with SVR and preexisting cirrhosis developed a liver-related clinical event in contrast to 33 events (6.6%) in patients who did not achieve SVR
- In addition only one patient with SVR received liver transplantation (LTX) while another patient was prepared for LTX in contrast to 6 and 13 patients in the treatment failure group (Table 3)

Table 3: Liver-related events and liver transplantation during follow-up of patients with/without SVR

	Pts who achieved SVR %, (n/N)	Pts who did not achieve SVR %, (n/N)
Ascites	0 (0)	1.8 (9/502)
Esophageal varices	0.4 (3/842)	3.8 (19/502)
Hepatocellular Carcinoma	0 (0)	1.0 (5/502)
Liver transplantation (LTX)	0.1 (1/842)	1.2 (6/502)
Preparation for LTX	0.1 (1/842)	2.6 (13/502)

- Most patients who achieved SVR after first HCV treatment continued to have undetectable HCV-RNA after a mean follow-up of 2.4±1.5 years (Figure 2)
- Similar results were obtained in the subgroup of intravenous drug user after a mean follow-up of 2.5 years. Only 5 patients became HCV-RNA detectable after a mean of 1.8 yrs (range 1 to 3 years)

Figure 2: Patients negative for HCV-RNA at last follow-up visit



Conclusions

- SVR following treatment with conventional / pegylated interferon ± ribavirin is durable in the real-life setting, in particular also for the majority of patients with previous intravenous drug use or opioid maintenance
- In addition, SVR almost completely eliminates morbidity by liver-related clinical events suggesting cure of chronic hepatitis C
- Liver-related clinical events after achieving SVR occurred exclusively in patients with preexisting cirrhosis