Differences Between Genotype 1 Patients with SVR or Relapse after Treatment for Chronic Hepatitis C (CHC) with Peginterferon alfa-2a (40kd) (PEG) and Ribavirin (RBV)

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INTRODUCTION

- Although treatment with pegylated interferon and ribavirin have increased the Sustained Virological Response (SVR) substantially, there is still a relapse rate after End of Treatment Response (EOT) about 20-30%. It is unknown whether there are defined parameters at baseline or in the course of treatment, which are deciding for relapse.
- The "Association of German Independent Gastroenterologists" (bng, Berufsverband Niedergelassener Gastroenterologen Deutschlands e.V.) in cooperation with Roche, Germany, is conducting a nationwide observational study including screening and treatment phases to determine the quality of treatment for chronic hepatitis C in routine clinical practice.

OBJECTIVE

- The main aim of this evaluation of the ongoing study on the treatment of HCV patients is to find out parameters characterizing patients with relapse after EOT.

METHODS

- This evaluation is part of a large ongoing German multicentre, open-label observational study including anti-HCV-positive adults with detectable HCV RNA. The nature of this study allowed dosing and duration of both peginterferon alfa-2a (40KD) and RBV to be at the discretion of the physician.
- The study procedure includes a screening of all incoming patients with hepatitis C and, in case of treatment with peginterferon alfa-2a (40KD) (PEGASYS®) plus ribavirin, a documentation of the therapy.
- The screening data include age, sex, weight, height, duration and source of infection, prior antiviral treatment, clinical symptoms, histology, genotype, viral load, concomitant diseases and social status.
- The documented data should reflect the clinical routine as intended by the doctors in charge. Therefore, the statistical analysis remains descriptive.

- Due to the ongoing character of the study, the status of data was frozen on May 31st, 2006, including queries solved.
- The patient group being analysed in this evaluation is characterized by an End of Treatment Response (EOT), but failure to achieve a Sustained Virological Response (SVR).

RESULTS

Patients

- Between March 2003 and May 2006 data from 11700 patients have been documented at more than 500 centers.
- A total of 10326 treatment naive patient screenings have been completed and 4377 of these patients (42.4%) have been treated with peginterferon alfa-2a (40KD).
- From 648 treated patients with genotype 1 complete data with regard to EOT and SVR were available.
  - 517 patients (75.6%) with EOT achieved an SVR (group SVR),
  - 167 patients (24.4%) had a relapse (group REL).
- Demographic data for the 167 relapsers (REL) vs. 517 patients with SVR (SVR) were: mean age 46.8 years (REL) vs. 41.1years (SVR), whereas female relapsers were 51.9 years old. 58.7% (REL) vs. 56.3% (SVR) of the patients were male. The mean BMI was 25.8 (REL) vs. 24.7 (SVR) kg/m² (see Table 1).

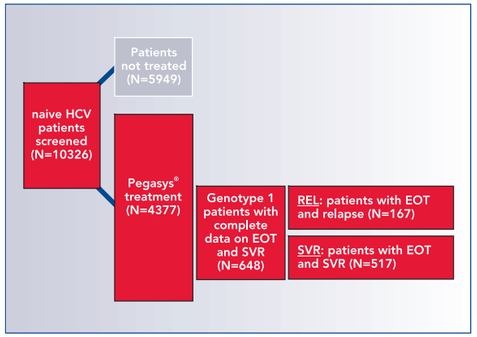

Figure 1. Study patients

Table 1: Baseline data

		REL	SVR
Patients	N	167	517
Gender	male	58.7%	56.3%
	female	41.3%	43.7%
Age*	years	46.8±12.5	41.1±12.0
Body Mass Index*	kg/m²	25.8±4.4	24.7±4.1
Duration of infection*	years	14.5±11.3	11.0±8.4

* Mean ± SD

Anamnesis

- The mean duration of HCV infection was 14.5 years for the patients with relapse (REL) and 11.0 years for the patients with SVR.
- Source of infection for REL/SVR: transfusion 24.0%/20.7%, iv drug abuse 27.0%/38.1%, medical action 11.4%/12.6%, unknown 30.5%/24.8% (more than one source possible; see Figure 2).

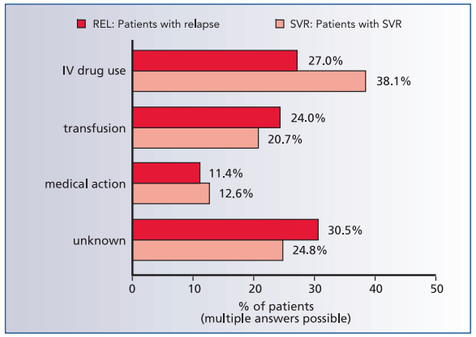

Figure 2. Source of infection

- Concomitant diseases were found in 56.3% of the relapsers (REL) and in 50.9% of the patients with SVR. The profile of concomitant diseases was not substantially different between both groups.
- Viral load: At baseline, 39.9% of the relapsers (REL) had low viral load (cut-off of 400.000 IU/ml) in contrast to 55.2% of the patients with SVR (see Figure 3).

Treatment

- The mean duration of treatment was 47.7 weeks for both groups, REL and SVR.
- No differences between REL and SVR were seen in the calculated mean cumulative dose of peginterferon alfa-2a (40KD): 95.9% (REL) and 96.3% (SVR).
- However, 28.0% of the relapsers (REL) received less than 80% of the cumulative Ribavirin dose compared to only 20.8% of the patients with SVR.

RVR and EVR

- Rapid Virological Response (RVR): One third of the patients (N=230/684) was checked for HCV-RNA in week 4 (RVR): only 10.8% of the relapsers (REL) achieved a RVR against 25.8% of the patients with a SVR.

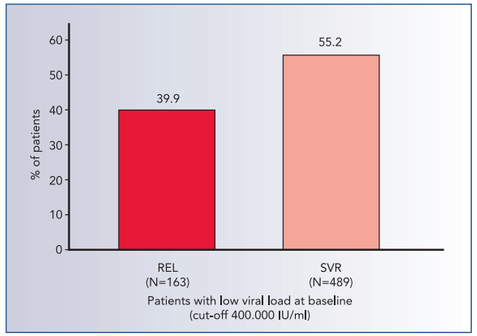

Figure 3. Viral load at baseline

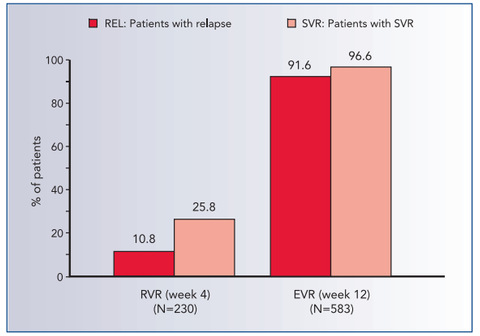

Figure 3. Virological response

- Early Virological Response (EVR): 85.2% of the patients were checked for an EVR at week 12 (≥2-$\log_{10}$ drop in HCV RNA or HCV RNA undetectable). The difference between relapsers and patients with SVR was smaller: 91.6% (REL) vs. 96.6% (SVR) (see Figure 4).

Adverse events

- The rate of Adverse Events (AE) was 57.5% in relapsers (REL) and 51.3% in patients with SVR.

CONCLUSIONS

- Concerning baseline predictive values besides age and duration of infection, there were no differences in host related parameters.
- Differences were given in the cumulative dose of RBV and virus determined factors like viral load and decay in viral load over treatment time. The latter leads to the assumption, that a decline in relapse rate is achievable through optimization of treatment duration.

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