

Standard of Medical Care for Patients with Chronic Hepatitis C (cHC) and Liver Cirrhosis in Germany

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INTRODUCTION

- The "Association of German Gastroenterologists in Private Practice" (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.
- Patients with chronic hepatitis C (cHC), who already have developed a cirrhosis of the liver, are in urgent need of treatment, in particular due to an increased risk of liver associated diseases or a hepatocellular carcinoma (HCC).

- 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.

RESULTS

Patients

- The present analysis includes 10,326 screenings of treatment naive cHC patients being completed in more than 500 centres.

Cirrhosis

- Sonography:** In 8,464 patients a sonography was performed. In 459 of these patients (5.4%) a cirrhosis was found.
- Histology:** In 2,234 patients a histology was performed. In 81 of these patients (3.6%) a cirrhosis (F4, Desmet Scheuer) was found.
- Clinical examination:** In 310 of the 10,326 patients (3.0%) a cirrhosis was clinically found and classified according to Child Pugh: A 86.5%, B 10.0%, C 3.5% (see Fig. 1).

OBJECTIVE

- The main aim of this ongoing study on the treatment of HCV patients with liver cirrhosis is to perform an evaluation of clinical routine treatment in everyday practice beyond controlled studies which may contribute to an optimization of clinical care for these patients.

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.

Table 1: Demographic and Baseline Data

	Cirrhosis	Total
N	459	10,326
Age (yrs)	58.2	43.4
Gender male	60.6%	58.8%
BMI (kg/m ²)	26.3	24.7
Duration of infection (yrs)	19.2	12.1
Platelets (/µl)	137,989	221,099
Genotype 1	75.0%	61.7%
2 / 3	21.1%	34.9%
4 / 5 / 6	3.1%	3.4%

Patient Characteristics

- The 459 patients with liver cirrhosis confirmed by sonography showed the following patient characteristics:
- Demography:** The mean age was 58.2 years. 60.6% of the patients were male. The mean BMI was 26.3 kg/m² (see Table 1). 22.8% of the patients were employed. 77.8% were not employed, in most cases pensioners (61.9% of the patients not employed). In total, 17.2% of these patients were unemployed.
- Concomitant diseases** were reported in 76.5% of patients with cirrhosis. The 5 most frequent concomitant diseases referred to the cardiovascular system (29.3%), abuse of drugs/alcohol (23.9%), diabetes mellitus (23.6%), liver disorder (21.9%) and thrombocytopenia (18.2%).

- The mean duration of infection was 19.2 years.
- Source of infection:** The following sources of infection were specified (multiple answers possible): 31.4% blood products, 23.7% i.v. drug abuse, 8.7% medical intervention, 35.3% unknown (see Fig. 2).
- Platelets:** The mean of platelets at screening was 137,989 /µl.
- Alcohol abuse:** In 12.2% of the patients a current alcohol abuse was specified.
- Distribution of genotypes (GT):** 75.3% of the patients with GT 1, 21.1% with GT 2/3 and 3.1% with GT 4 (see Fig. 3).

Treatment of cHC

- A treatment of cHC with peginterferon alfa-2a (40KD) (PEGASYS[®]) was initiated (see Fig. 4):
 - in 144 patients with cirrhosis in sonography (31.4%).
 - in 61 patients with cirrhosis in histology (75.3%).
 - in 132 patients with clinically found cirrhosis (42.6%).

Reasons for Decline of Therapy

- If a cHC therapy with peginterferon alfa-2a (40KD) (PEGASYS[®]) was not initiated, the reasons should be specified. In 315 patients with cirrhosis in sonography (68.6%) reasons for decline of therapy were:
 - decompensated disease (33.6%),
 - concomitant disease / continued drug abuse (25.7%),
 - patient's desire (22.2%),
 - other therapy (10.2%) and
 - age of the patient (8.3%; see Fig. 5).

- If the decline of therapy was accompanied by continued drug abuse, in 75.0% of the patients at least alcohol abuse was specified.
- In case of patient's desire, this was mostly fear of therapy (58.7%) or missing understanding of the urgency of therapy (46.0%; these data were included since April 2005).
- As far as age was specified in patients with decline of therapy, the mean age was 75.4 years.

Virological Response

- An Early Virological Response (EVR) was observed in 80/104 patients (76.9%).
- An End-of-Treatment Response (EOT) was observed in 54/103 patients (52.4%).
- In 75 of the 459 patients with cirrhosis in sonography end-of-follow-up data were available until the cut-off day: A SVR was observed in 28 of the 75 patients (37.3%; see Fig. 6).

Discontinuations of Treatment

- A discontinuation of therapy was specified in 29.2% of the patients. The mean reasons were virological non-response (50.0%) and lacking safety (42.9%).

Adverse Drug Reactions

- Adverse drug reactions were specified in 54.2% of the patients. The most frequent reports were fatigue (18.1%), depression, head ache and thrombocytopenia (7.6%, each).

CONCLUSIONS

- In 3-5% of the screened patients a cirrhosis was found. Compared to the average, these patients were older and the duration of infection was prolonged. The source of infection was medical intervention in most cases.
- There is consent that the development of a manifest cirrhosis (Desmet-Scheuer) in general can be assessed even without histology on the one hand and is an indication for therapy on the other hand. Although, a high rate of therapy initiation was found only following histology, not following clinical or sonographical findings. Compared to other observational studies, this rate of biopsies is rather high. The confirmation of the cirrhosis by histology seems to provide more certainty on the decision for therapy, compared to patients with low fibrosis score and better baseline factors, as in this group a biopsy is performed only in approx. 20% of the patients (see Hüppe et al., DGVS 2005).
- Although treatment is urgent in patients with liver cirrhosis and cHC, more than 20% of the patients cannot be convinced of the indication. The main reasons for a decline of therapy with interferon/ribavirin are fear of therapy and missing understanding of the urgency of treatment.
- Despite worse baseline data (higher age, low platelets, more concomitant diseases) and clearly worse safety compared to other patient groups, the SVR of 37% is a relatively high success rate under everyday conditions.
- Unfortunately in case of decompensation and other concomitant diseases, help by interferon therapy is not longer possible for many patients with cirrhosis.

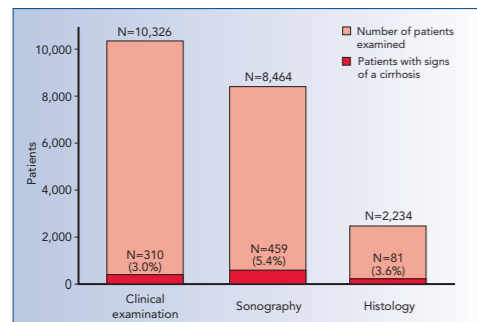


Fig. 1. Patients with signs of a cirrhosis using different diagnostic procedures

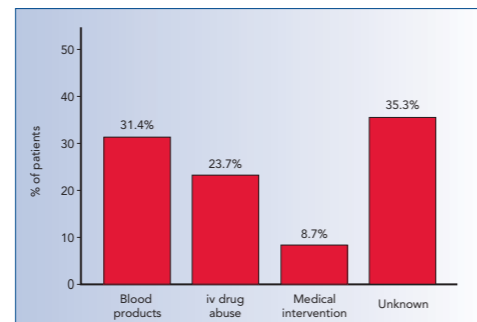


Fig. 2. Source of infection

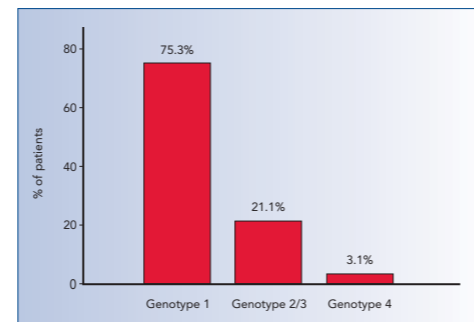


Fig. 3. Distribution of genotypes

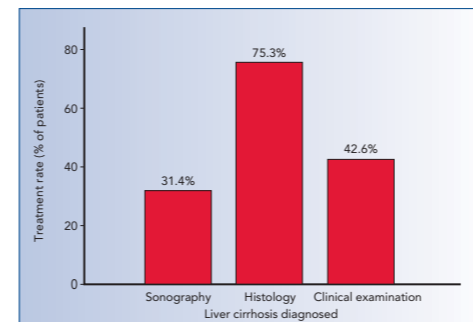


Fig. 4. Rate of treated patients

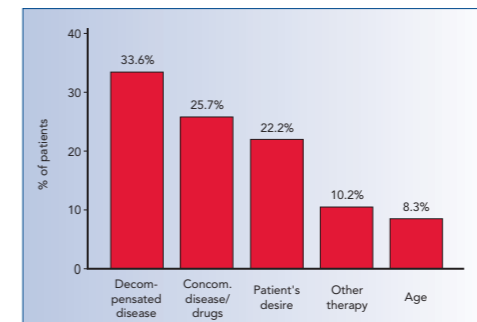


Fig. 5. Reasons for a decline of therapy

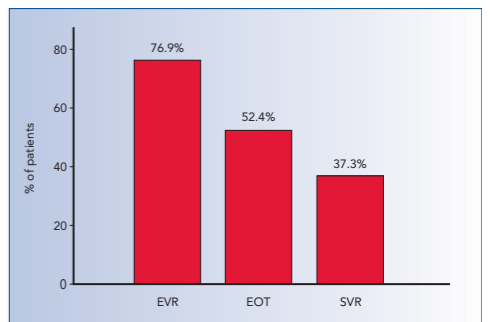


Fig. 6. Virological result of the treatment with Peginterferon alfa-2a (40KD) (Pegasis[®])