Estimating the Likelihood of Sustained Virological Response in Chronic Hepatitis C (CHC) Therapy

Mauss S[1], Hueppe D[2], John C[3], Goelz J[4], Meyer U[5], Heyne R[6], Moeller B[6], Link R[7], Teuber G[8], Sworszt S[9], Herrmann A[10], Spelter M[11], Wollschlaeger A[12], Steffens H[5], Baumgarten A[13], Simon K-G[14], Dikopoulos N[15], Witthoeft T[16]

[1]Center for HIV and Hepatogastroenterology, Duesseldorf; [2]Center of Gastroenterology, Herne; [3]Center of Gastroenterology, Berlin ; [4]Practice Centre Kaiserdamm, Berlin; [5]Center of Internal Medicine, Berlin ; [6]Center of Gastroenterology and Livercenter, Berlin; [7]Internal Medicine, St. Josef Clinic, Offenburg; [8]Johann Wolfgang Goethe University, Frankfurt/Main; [9]General Practice, Gelsenkirchen; [10]Friedrich Schiller University, Jena; [11]Center of Gastroenterology, Wuppertal; [12]Hospital Dresden Friedrichstadt, Dresden; [13]General Practice, Berlin; [14]Center of Gastroenterology, Leverkusen; [15]Department for Internal Medicine I, University of Ulm, Ulm; [16]Medical Department I, Div. of Gastroenterology, University Hospital Schleswig-Holstein Campus Luebeck, Luebeck; all Germany

INTRODUCTION

- For patients and physicians the likelihood of a treatment success is one of the most relevant factors for a decision to start or defer therapy of chronic hepatitis C (CHC). For this decision only baseline variables are important.
- The current evaluation is based on PRACTICE (Pegylated Interferons and Ribavirin: Analysis of CHC Treatment In Centres of Excellence), a nationwide retrospective observational study on routine clinical practice including centres with large expertise in the treatment of chronic hepatitis C (CHC).

OBJECTIVE

- Aim of this analysis is to identify predictive factors for the success of treatment of cHC-patients under real life conditions.

METHODS

- This evaluation is part of a large retrospective German multicentre, open-label observational study including anti-HCV-positive adults with detectable HCV RNA. According to the nature of this study, all treatment decisions concerning peginterferon and ribavirin (selection, dosing and treatment duration) were at the discretion of the physician.
- The data set includes patients who completed treatment with peginterferon alfa-2a or alfa-2b plus ribavirin. The data collection was performed via an e-CRF online via the internet.
- The documented data should reflect the clinical routine as intended by the physicians in charge. Therefore, the statistical analysis remains descriptive.

Treatment

- Patients were treated either with:
  - pegylated interferon alfa-2a (40KD) (Pegasys®) mostly plus ribavirin (Copegus®) or
  - pegylated interferon alfa-2b (PegIntron®) mostly plus ribavirin (Rebetol®).

Matched Pairs

- To achieve comparability regarding interferon therapy, patients were matched acc. to the following criteria:
  - age difference ≤3 years,
  - same HCV genotype (only main type),
  - same category of viral load: LVL or HVL (cut-off: ≤400.000 IU/ml),
  - BMI difference ≤2 kg/m²,
  - same anamnesis of hepatitis C incl. sub-categories (monotherapy, IFN-RBV-combination therapy, PEG-RBV-combination therapy, virological non-response, not adequate pretreatment),
  - presence of opioid maintenance (yes / no),
  - presence of HIV-coinfection (yes / no).

Baseline predictive factors

- In order to identify predictive factors for the response to treatment, the following factors were estimated:
  - gender,
  - age categories: <30, 30-<40, 40-<50, 50-<60, 60 or more years,
  - BMI: <22, 22-28, >28 kg/m²,
  - HCV genotype: 1, 2, 3 or 4,
  - HCV RNA: cut-off ≤400 000 IU/ml for High viral load (HVL) and Low viral load (LVL),
  - ALT: cut-off ULN,
  - GGT: cut-off ULN,
  - bilirubin: cut-off ≤1 mg/dl,
  - platelets (PLT): cut-off ≥150 000 /µl as surrogat marker for advanced fibrosis,
  - opioid maintenance: absence vs. presence,
  - treatment: PEG-IFN alfa-2a vs. -2b (plus ribavirin).

RESULTS

Patients

- 3470 patients treated with pegylated interferon plus ribavirin under real life conditions were documented between 2000 and 2007 from 23 large outpatient clinics.
- Matched data sets were available for 1204 pairs of patients (N=1204 PEG-IFN alfa-2a; N=1204 PEG-IFN alfa-2b).
- In order to evaluate only patients with chronic hepatitis C, patients with acute hepatitis C were excluded from the analysis.
- The resulting CHC-data set included 1189 matched pairs (N=1189 PEG-IFN alfa-2a; N=1189 PEG-IFN alfa-2b).
- The demographic data for the 2378 CHC-patients and the total group of 2408 patients are shown in Table 1.
- The following analysis is based on matched pairs of 2378 CHC-patients.

Virological response

- Over all, a Sustained virological response (SVR) was achieved in 1377 of 2378 patients (57.9%).

Univariate analyses

- In univariate analyses SVR was significantly associated with genotype (p≤.0001; see Figure 1), pegylated interferon (p≤.05; see Figure 2), viral load (p≤.0001), age (p≤.0001; see Figure 3), BMI (p≤.0001), GGT (p≤.0001; see Figure 4) and platelets (p≤.0001).
- No association was observed with gender, ALT and opioid maintenance.

Multivariate analysis

- Positive predictive factors being significantly associated with SVR in multivariate logistic regression (MLR) are (see Figure 5):
  - genotype 2 (p≤.0001; OR=5.214; 95% CI: 3.252-8.358),
  - genotype 3 (p≤.0001; OR=2.871; 95% CI: 2.276-3.621),
  - LVL (p≤.0001; OR=1.710; 95% CI: 1.397-2.093),
  - PEG-IFN alfa-2a (p≤.05; OR=1.276; 95% CI: 1.051-1.550).
- Negative predictive factors being significantly associated with SVR in multivariate logistic regression (MLR) are (see Figure 5):
  - age 40-<50 yrs (p≤.0001; OR=.550; 95% CI: .397-.762),
  - age 50-<60 yrs (p≤.001; OR=.521; 95% CI: .359-.756),
  - age ≥60 yrs (p≤.0001; OR=.349; 95% CI: .220-.552),
  - increased GGT (p≤.0001; OR=.428; 95% CI: .349-.526),
  - decreased platelets (p≤.0001; OR=.571; 95% CI: .434-.752).
- The BMI was not significantly associated with SVR (data not shown).

CONCLUSIONS

- Genotype 2, genotype 3, low viral load and treatment with Peginterferon alfa-2a were identified as positive predictive factors for treatment success in this well controlled large cohort.
- Higher age (≥ 40 years), elevated GGT and platelets <150 000 /µl were identified as negative predictors for treatment success.

Table 1: Baseline data

	Acute and chronic hepatitis C	Only chronic hepatitis C
N	N=2408	N=2378
Sex (male / female)	57.8% / 42.2%	57.3% / 42.7%
Age (mean ± SD in years)	42.2 ± 11.3	42.2 ± 11.4
BMI (mean ± SD in kg/m²)	24.7 ± 3.6	24.7 ± 3.6
Duration of infection (years)	13.8 ± 9.0	13.9 ± 9.0
Genotype 1	61.9	61.6
2	6.6	6.6
3	30.2	30.4
4	1.3	1.3

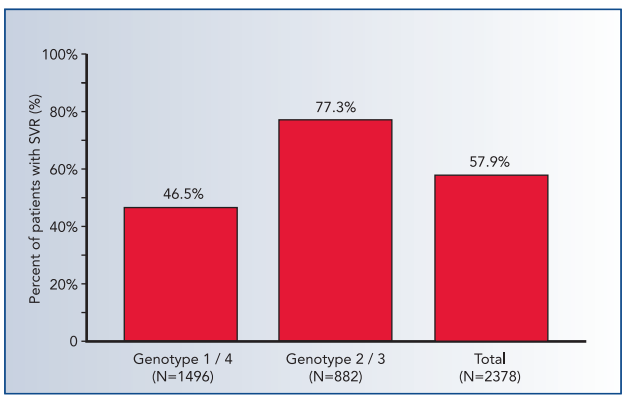

Figure 1. Sustained virological response (SVR)

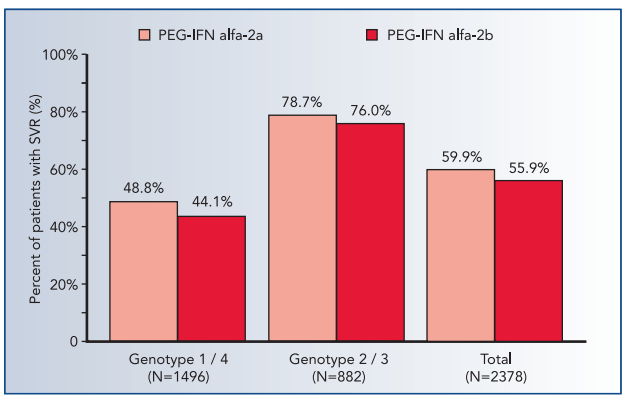

Figure 2. SVR and peginterferon treatment

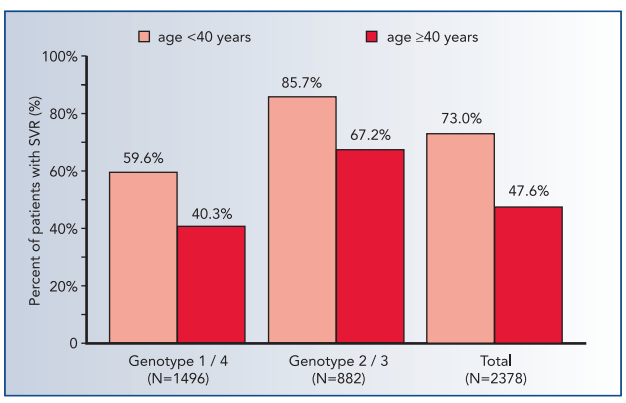

Figure 3. SVR and age

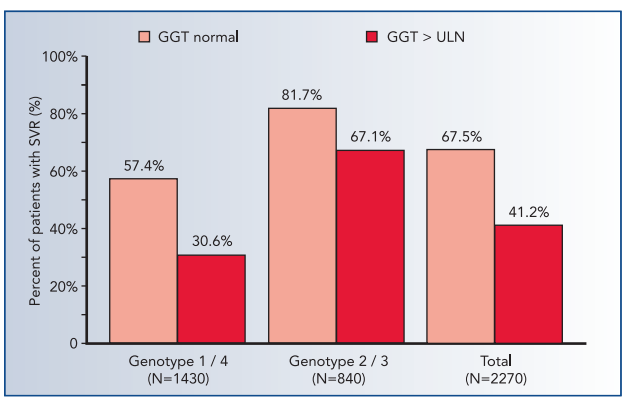

Figure 4. SVR and GGT

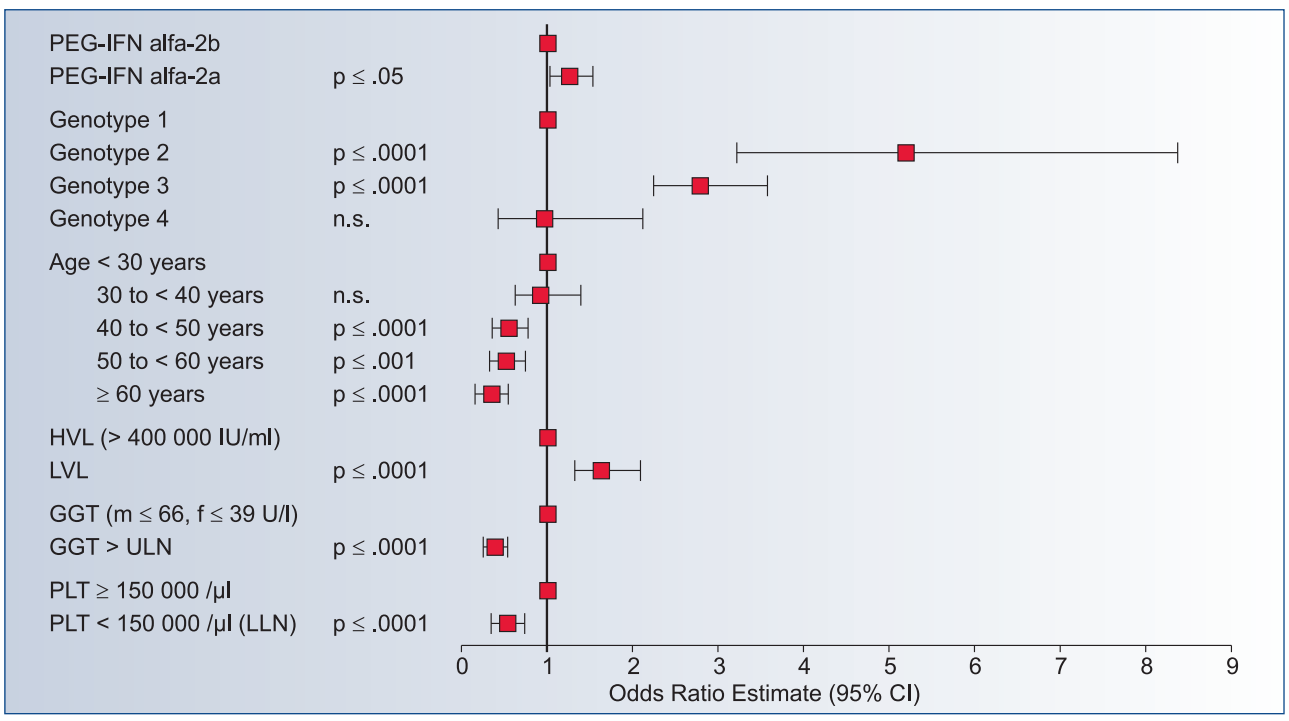

Figure 5. Multivariate logistic regression (references were PEG-IFN alfa-2b, genotype 1, age <30 years, HVL (>400 000 IU/ml), GGT (m≤66, f≤39 U/l), PLT ≥150 000 µ/l)

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