Efficacy and Tolerability of Peginterferon alfa-2a (40KD) and Ribavirin in Genotype 4-Patients with Chronic Hepatitis C (CHC) under Real Life Conditions

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INTRODUCTION

- Since Genotype 4 has a low prevalence in European patients infected with chronic hepatitis C (cHC), only few data, mostly cross sectional analyses with small numbers of treated patients have been described.
- 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 (CHC) in routine clinical practice.

OBJECTIVE

- Aim of this analysis is to evaluate the treatment of cHC-patients with genotype 4 under real life conditions.

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 ribavirin to be at the discretion of the physician.
- 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.
- This data set includes patients who completed treatment with peginterferon alfa-2a (40KD) plus ribavirin. The data collection was performed online via the internet.
- 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 15th, 2007, including queries solved.

RESULTS

Patients

- Until May 2007 the online data documentation has been completed for a total of 13590 cHC patients including:
  - 9532 patients with screening data and
  - 4058 patients with completed treatment with peginterferon alfa-2a (40KD) in almost all cases plus ribavirin.
- A genotype 4 was found in 388 of the 13590 patients (2.86%).
- A complete treatment documentation is available for 120 of the 4058 treated cHC patients (2.96%; see Figure 1).

Baseline data

- Baseline data for treated GT4-patients were: male 73.3% vs. female 26.7%, mean age 41.6 years, mean BMI 26.2 kg/m² (Baseline data for patients with GT1, GT4 and all patients see in Table 1).
- The mean duration of infection was 10.9 years for GT4-patients.
- Sources of infection for GT4-patients were: i.v. drug abuse (31.7%), transfusion (10.8%), sexual contacts (10.8%), medical action (8.3%), unknown (39.2%) (multiple answers possible).
- 30.9% of the GT4-patients were Africans, 67.9% Caucasians reflecting a higher proportion of Africans compared to all other patients (see Figure 2). For 44.7% of the patients German was specified as mother language.
- 90.8% of the GT4-patients were treatment naïve, 9.2% were relapsers (GT1: 89.5% naïve, 10.3 relapsers, 0.3% nonresponders).

Early virological response (EVR)

- 68 of 84 GT4-patients (81.0%) and 82.9% of the GT1-patients achieved Early virological responses (≥2-$\log_{10}$ drop in HCV RNA and/or HCV RNA ≤50 IU/ml and/or HCV RNA qualitatively undetectable) (see Figure 3).

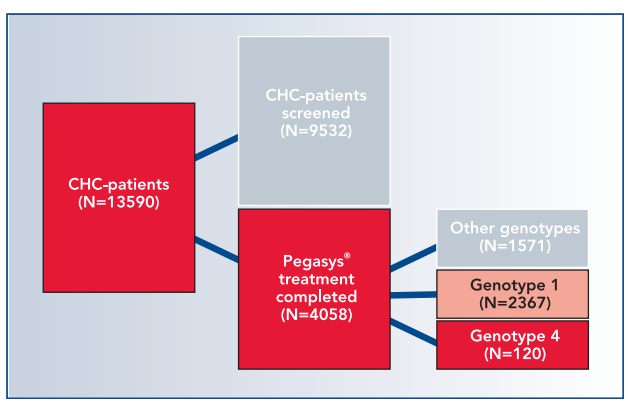

Figure 1. Study patients

Table 1: Baseline data of patients with completed treatment

	Genotype 1	Genotype 4	Total
N	N=2367	N=120	N=4058
Sex (male / female)	58.5% / 41.5%	73.3% / 26.7%	60.4% / 39.6%
Age (mean ± SD in years)	44.6 ± 12.6	41.6 ± 9.8	42.1 ± 12.2
Weight (mean ± SD in kg)	75.2 ± 14.2	79.2 ± 14.1	74.7 ± 14.4
BMI (mean ± SD in kg/m²)	25.2 ± 4.3	26.2 ± 4.1	25.0 ± 4.2
Duration of infection (years)	13.0 ± 9.5	10.9 ± 8.5	11.8 ± 8.9

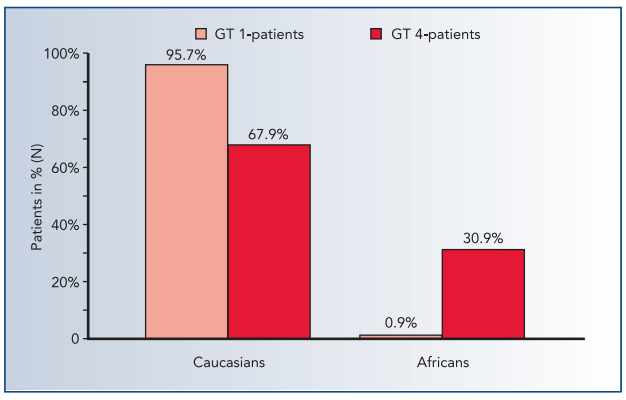

Figure 2. Ethnic groups

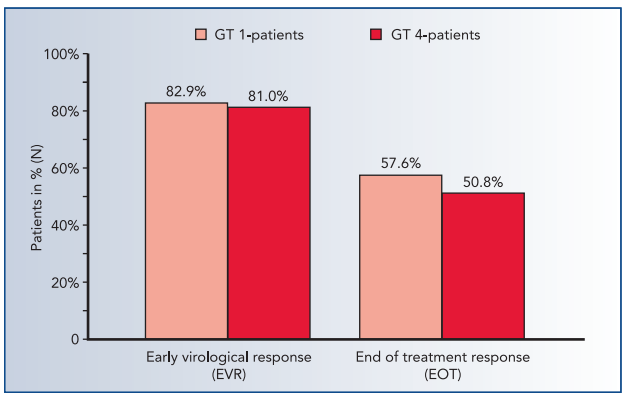

Figure 3. EVR and EOT

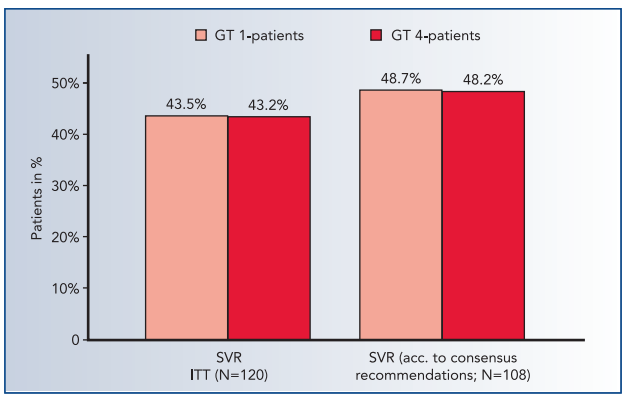

Figure 4. SVR

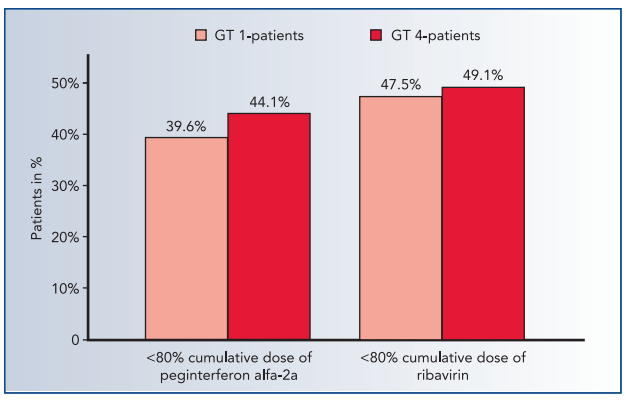

Figure 5. Cumulative doses

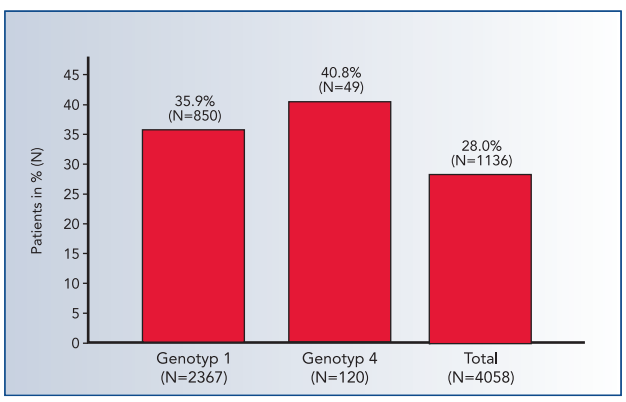

Figure 6. Discontinuation rates

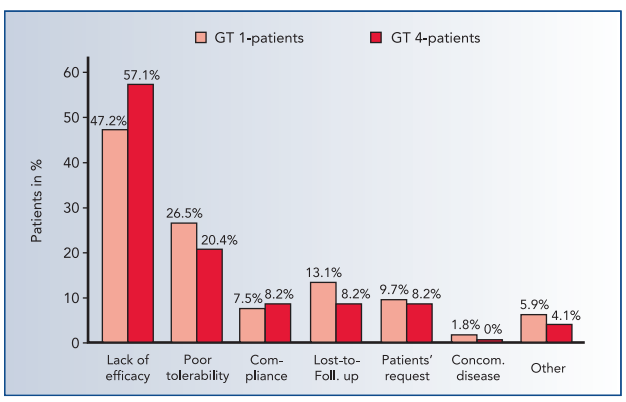

Figure 7. Reasons for discontinuation of therapy

End of treatment response (EOT)

- End of treatment response (EOT) was achieved in 50.8% of the GT4-patients and in 57.6% of the GT1-patients (HCV RNA ≤50 IU/ml and/or HCV RNA qualitatively undetectable) (see Figure 3).

Sustained virological response (SVR)

- For the GT4-patients the Sustained virological response rate (HCV RNA ≤50 IU/ml and/or HCV RNA undetectable after 24 weeks of follow-up) was 43.3% according to an ITT analysis (N=120) with an relapse rate of 14.8%. The respective SVR for GT1-patients was 43.5%.
- From 108 patients, who were treated according to consensus recommendations (i.e. treatment finished as intended or discontinuation due to nonresponse or poor tolerability), 52 achieved SVR (48.2%). The respective SVR for GT1-patients was 48.7% (see Figure 4).

Treatment

- The mean duration of therapy was 35.6 weeks for the GT4- and 37.7 weeks for the GT1-patients.
- 44.1% of the GT4-patients compared to 39.6% of the GT1-patients received less than 80% of the cumulative dose of peginterferon alfa-2a for 48 weeks (see Figure 5).
- 49.1% of the GT4-patients and 47.5% of the GT1-patients received less than 80% of the cumulative dose of ribavirin for 48 weeks (see Figure 5).

Treatment discontinuations

- 40.8% of the GT4-patients and 35.9% of the GT1-patients discontinued therapy before end of treatment (see Figure 6). Main reasons for withdrawal were (multiple answers possible):
  - virological nonresponse (GT4 57.1%; GT1 47.2%),
  - poor tolerability (GT4 20.4%; GT1 26.5%),
  - personal reasons, non-compliance or lost to follow-up (see Figure 7).

CONCLUSIONS

- The results of this observational study show that the outcome of peginterferon alfa-2a/ribavirin therapy in GT 4-patients is comparable with treatment of GT 1-patients under real life conditions.
- In clinical trials it seems that GT 4 is not so difficult to treat compared to GT 1. Reasons for the described results could be verbal miscommunication and second a large proportion of non-compliant patients who did not achieve EOT and subsequent SVR due to insufficient medication effected by shorter duration of treatment and lower cumulative doses of peginterferon alfa-2a and ribavirin.

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