

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.

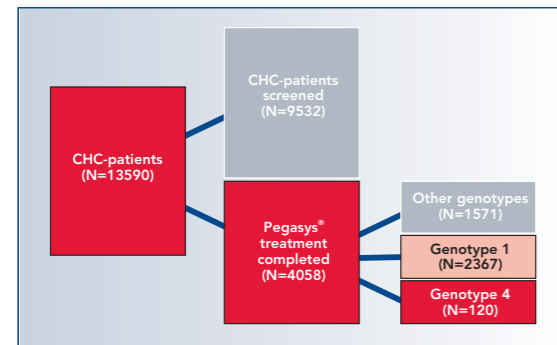


Figure 1. Study patients

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/m ²)	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

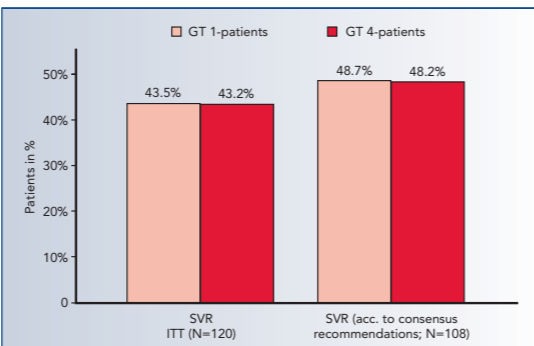


Figure 4. SVR

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.

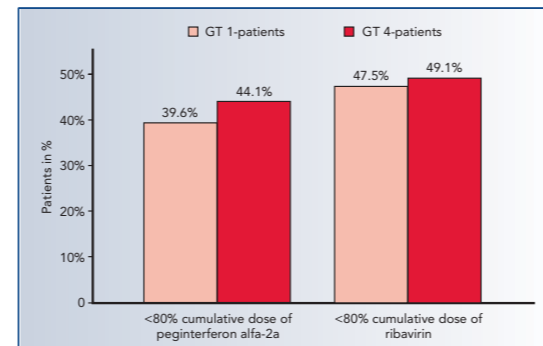


Figure 5. Cumulative doses

- ▶ 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-log₁₀ drop in HCV RNA and/or HCV RNA ≤50 IU/ml and/or HCV RNA qualitatively undetectable) (see Figure 3).

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).

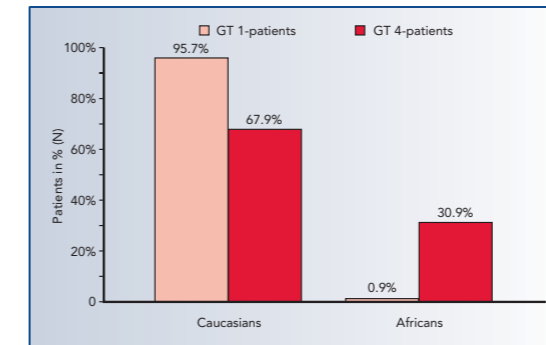


Figure 2. Ethnic groups

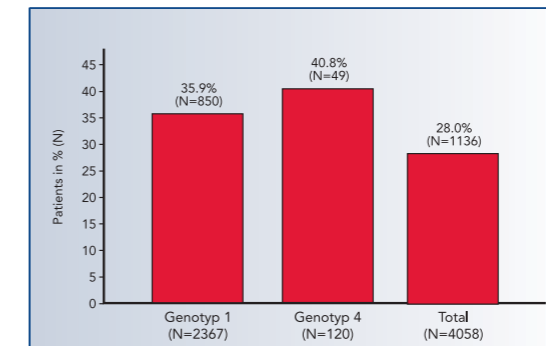


Figure 6. Discontinuation rates

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 a 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).

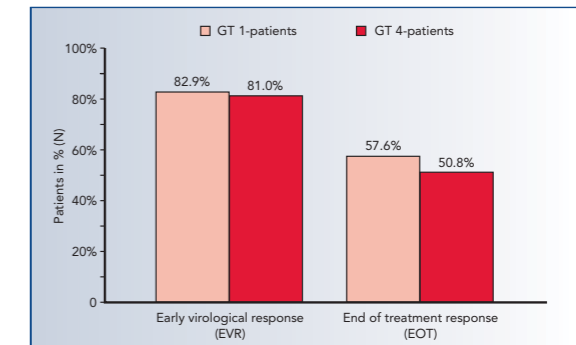


Figure 3. EVR and EOT

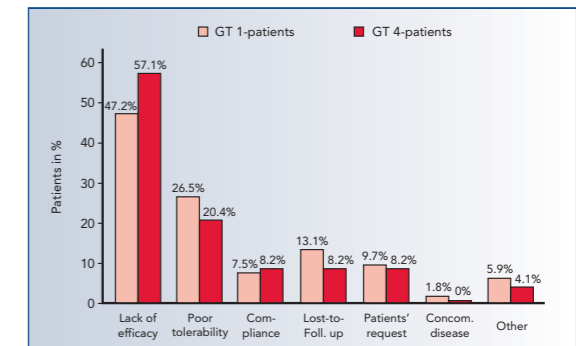


Figure 7. Reasons for discontinuation of therapy

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.

Presented at the Digestive Disease Week (DDW), May 17-22, 2008, San Diego, California, USA.
This research was supported by Roche Pharma AG, Grenzach-Wyhlen, Germany.