Potential Relevance of Rapid Viral Response for SVR and Optimisation of the Treatment of Hepatitis C (CHC) with Peginterferon alfa-2a (40KD) and Ribavirin

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INTRODUCTION

- In the last time rapid virological response (RVR; defined as undetectable viral load with qualitative PCR after 4 weeks of treatment) gains big interest as positive predictive value for sustained virological response (SVR).
- The "Association of German Independent Gastro-enterologists" (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 whether patients who achieve an RVR are overtreated with standard therapy (48 weeks in G1/4/5/6- and 24 weeks in G2/3-pts.) and would better be treated for a shorter duration.

METHODS

- This evaluation is part of a large ongoing German multi-centre, 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 treatment naive patients who initiated 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 31st, 2006, including queries solved.

RESULTS

Patients

- 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), in almost all cases plus ribavirin.
- Although there was no recommendation to measure viral load at week 4, this value was checked in 27.6% of the patients (N=1207/4377).
- Only 609/1207 patients (50.5%) were checked with a qualitative test (≤50 IU/ml):
  - Genotype 1/4/5/6 (N=379): 25.1% of these achieved RVR.
  - Genotype 2/3 (N=230): 63.0% of these achieved RVR.
- SVR data were available for 330 of patients with known RVR results. Data were evaluated in two groups:
  - RVR: N=122 patients with rapid virological response,
  - NON-RVR: N=208 RVR non-responders (see Figure 1).

Baseline data

- Baseline data were: male 56.1% vs. female 43.9%, mean age 42.0 years, mean weight 73.6 kg, mean BMI 24.9 kg/m² (Baseline data for RVR and NON-RVR see in Table 1).
- The mean duration of infection was 11.3 years with 2 years advantage for RVR.
- 16 patients (4.8%) had cirrhosis (15 Child A, 1 Child B), 4 of them had an RVR (see Figure 2).
- Genotype 1/4/5/6 was found in 197 patients, genotype 2/3 in 133 patients.

Rapid virological response (RVR)

- Rapid virological response (RVR; HCV RNA undetectable with qualitative test) was found in 122/330 patients (37.0%).
- Genotype 1/4/5/6: RVR was achieved in 18.8% (N=37/197) of the patients.
- Genotype 2/3: RVR was achieved in 63.9% (N=85/133) of the patients (see Figure 3)

Sustained virological response (SVR)

- Sustained virological response (SVR; HCV RNA undetectable after 24 weeks of follow-up) was found in 205/330 patients (62.1%).
- Genotype 1/4/5/6: SVR was achieved in 51.3% (N=101/197) of the patients.
- Genotype 2/3: SVR was achieved in 78.2% (N=104/133) of the patients (see Table 2).

SVR of RVR and Non-RVR patients against treatment withdrawals

- Genotype 1/4/5/6: SVR was achieved in 70.3% (N=26/37) of RVR-patients and in 46.9% (N=75/160) of NON-RVR-patients

Table 1: Baseline data

	RVR	NON-RVR	Total
N	N=122	N=208	N=330
Sex (male / female)	58% / 42%	55% / 45%	56% / 44%
Age (mean ± SD in years)	40.2 ± 11.8	43.1 ± 12.9	42.0 ± 12.6
Weight (mean ± SD in kg)	71.7 ± 13.9	74.7 ± 14.6	73.6 ± 14.4
BMI (mean ± SD in kg/m²)	24.0 ± 3.7	25.4 ± 4.4	24.9 ± 4.2
Duration of infection (years)	9.8 ± 7.7	12.3 ± 9.7	11.3 ± 9.0

Table 2: Virological response

	Genotype 1/4/5/6		Genotype 2/3	
	RVR	NON-RVR	RVR	NON-RVR
Percent (N/n)	18.8% (37/197)	81.2% (160/197)	63.9% (85/133)	36.1% (48/133)
SVR % (x/N)	70.3% (26/37)	46.9% (75/160)	89.4% (76/85)	58.3% (28/48)
SVR overall % (x/N)	51.3% (101/197)		78.2% (104/133)	

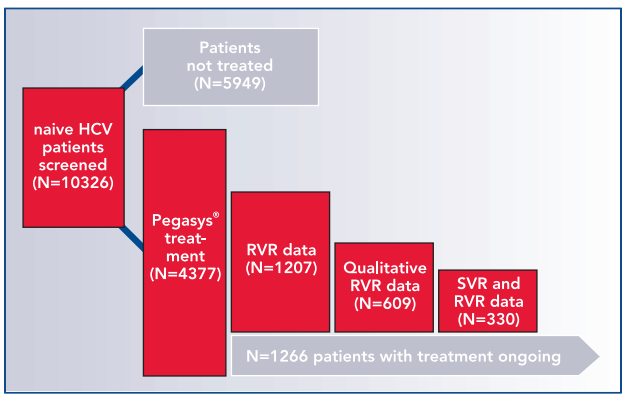

Figure 1. Study patients

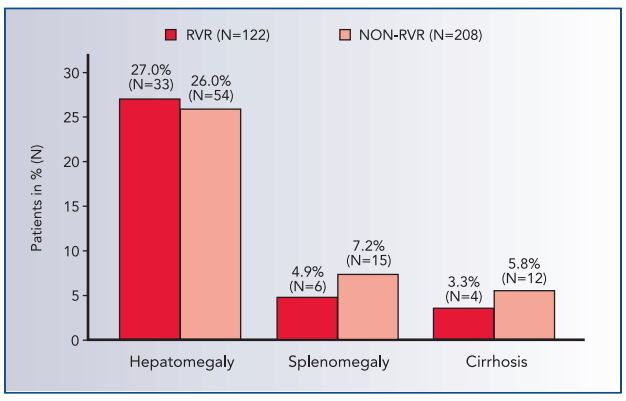

Figure 2. Clinical findings at baseline

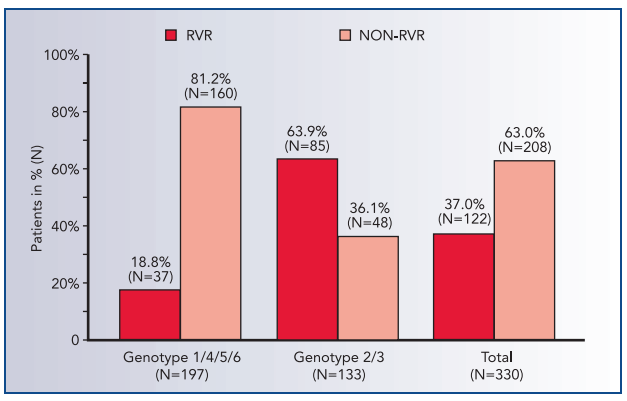

Figure 3. RVR

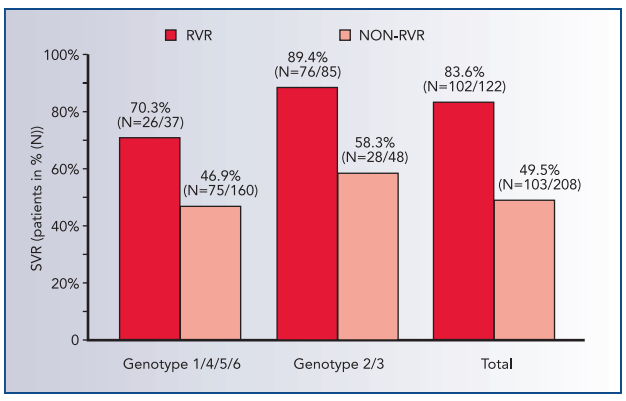

Figure 4. SVR in patients with RVR

(see Figure 4). Non-response due to discontinuation of therapy was documented in 16.2% and 29.4%, resp. (see Figure 5). In RVR-patients AEs and patients' requests were predominant factors of treatment discontinuation, in contrast in non-RVR patients lack of efficacy was the main reason of withdrawal.

- Genotype 2/3: SVR was achieved in 89.4% (N=76/85) of RVR-patients and in 58.3% (N=28/48) of NON-RVR-patients.

Duration of treatment

- In 16.2% of the GT 1/4/5/6-patients with RVR treatment duration was below 37 weeks compared to 31.9% of the Non-RVR patients (see Figure 6). In general, the results do not indicate an active controlled shortening or prolonging of standard treatment duration (48 weeks in GT 1/4/5/6- and 24 weeks in GT 2/3-patients).

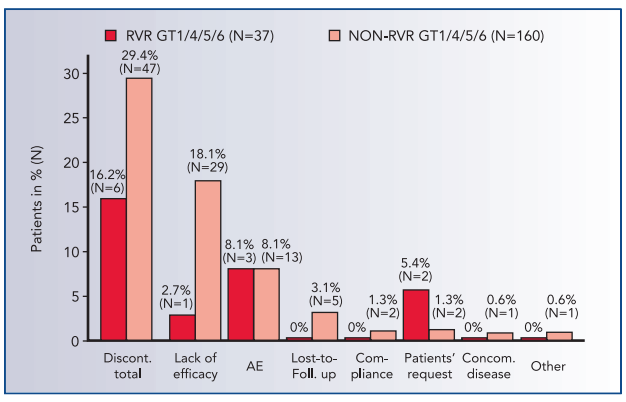

Figure 5. Discontinuations of therapy in GT 1/4/5/6-patients

CONCLUSIONS

- Rapid virological response (RVR) seems to be a good positive predictive value for sustained virological response (SVR).
- Treatment optimization through shorter courses of therapy (especially in G1/4/5/6) should only be attempted if other predictive factors apart from genotype and rapid response have carefully been assessed. Compliance and adherence should be excellent and use of a sensitive PCR is a must.
- Comparison of SVR and withdrawal rates indicate that shortening of treatment duration in RVR patients can be an advantage since there may be less non-virological reasons to stop therapy.

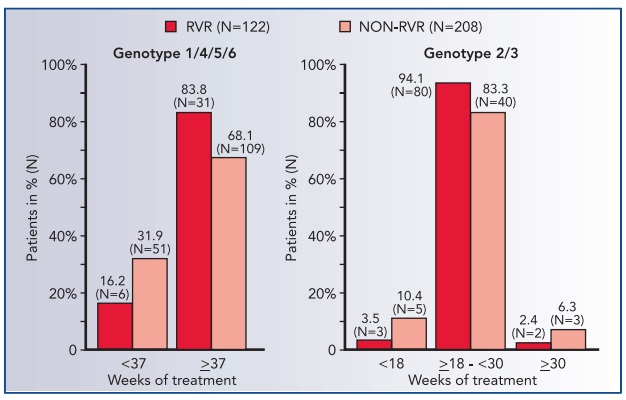

Figure 6. Duration of treatment

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