Individualized treatment duration with peginterferon alfa-2b and ribavirin for 24, 30 or 36 weeks in HCV genotype 1-infected patients with undetectable HCV-RNA early during therapy (INDIV-2 study)

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1. INTRODUCTION

Shortening of treatment duration with peginterferon and ribavirin to 24 weeks in patients with chronic hepatitis C virus (HCV) genotype 1 infection and low baseline viral load ($<6–8\times10^5$ IU/ml) in addition to a rapid virologic response (RVR) is approved in Europe.

Currently, it is unknown whether patients with high baseline viral load and RVR really need 48 weeks of therapy. Furthermore, it is conceivable that also in patients with undetectable HCV-RNA at week 6 shortening of treatment duration is possible.

2. METHODS

398 treatment-naïve HCV genotype-1 patients were enrolled in a multicenter, randomized trial for individualization of duration of treatment with peginterferon alfa-2b and ribavirin. (Figure 1)

Here we report an interim analysis of patients with shortened treatment to 24, 30 or 36 weeks according to low-viral load (LVL) or high-viral load (HVL) (cut-off 800.000 IU/ml by Versant HCV Quantitative bDNA 3.0 assay) and undetectable HCV-RNA at week 4 (RVR) or 6 by a highly sensitive assay (Versant HCV Qualitative TMA assay, cut-off 5–10 IU/ml).

Sustained virologic response (SVR) rates were compared to a historical control group of 224 patients treated for 48 weeks (INDIV-1-study)[1] based on identical HCV-RNA assays (bDNA3.0 and TMA). (Figure 2 and 3)

1 Berg et al., Individualized treatment strategy according to early viral kinetics in hepatitis C virus type 1-infected patients. Hepatology 2009 in press.

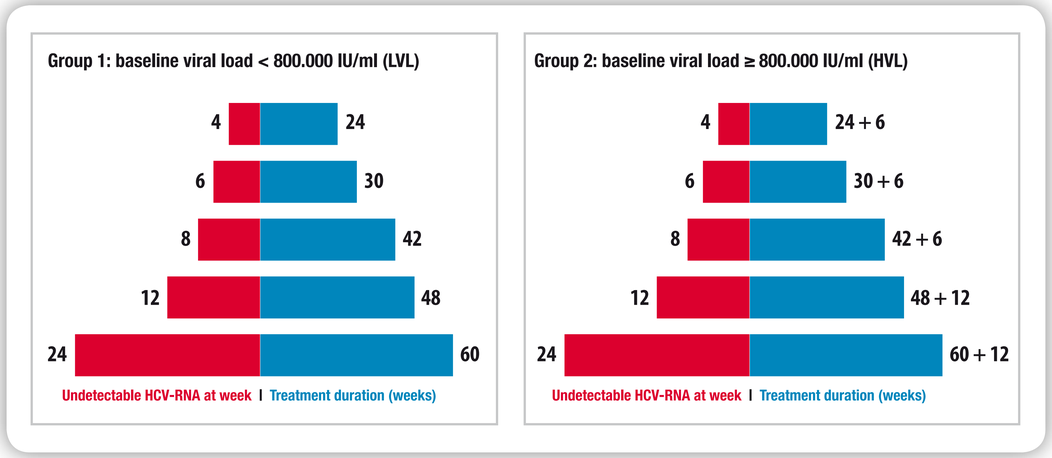

Figure 1. INDIV-2 study design:
398 therapy-naïve HCV genotype-1 patients were enrolled in a multicenter, randomized trial for individualization of duration of treatment with peginterferon alfa-2b and ribavirin.

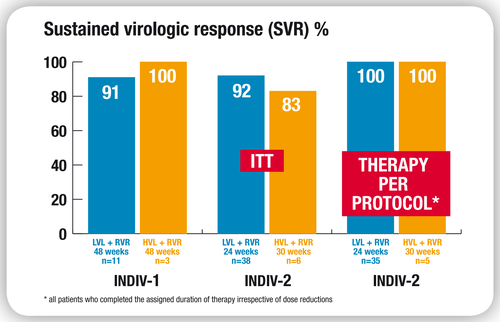

Figure 2. Interim analysis of patients with shortened treatment to 24 or 30 weeks according to LVL or HVL (cut-off 800.000 IU/ml bDNA3.0) and undetectable HCV-RNA at week 4 (RVR) by a highly sensitive assay (TMA). Sustained virologic response (SVR) rates were compared to a historical control group of 224 patients treated for 48 weeks (INDIV-1-study)[1] based on identical HCV-RNA assays (bDNA3.0 and TMA).

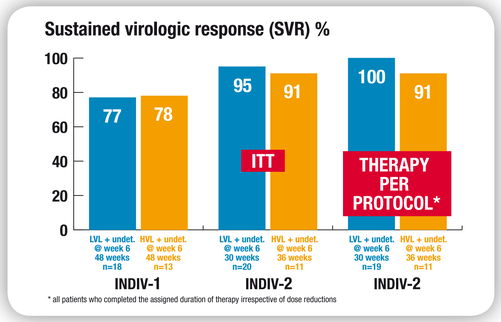

Figure 3. Interim analysis of patients with shortened treatment to 30 or 36 weeks according to LVL or HVL (cut-off 800.000 IU/ml bDNA3.0) and undetectable HCV-RNA at week 6 by a highly sensitive assay (TMA). Sustained virologic response (SVR) rates were compared to a historical control group of 224 patients treated for 48 weeks (INDIV-1-study)[1] based on identical HCV-RNA assays (bDNA3.0 and TMA).

DISCLOSURE INFORMATION

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3. RESULTS

Thirty-eight patients with RVR and LVL were treated for 24 weeks. One discontinued therapy and one was lost to follow-up. Six patients with RVR and a HVL were treated for 30 weeks. One discontinued treatment at week 13 followed by a relapse. Twenty patients with undetectable HCV-RNA at week 6 and LVL were treated for 30 weeks. One patient experienced a relapse. Eleven patients with undetectable HCV RNA at week 6 and a HVL received 36 weeks of therapy. One of these patients had a relapse. SVR rates for individualized treated patients in comparison with the control group are given in Table 1. The remaining patients are currently still under therapy.

	Individualized treatment duration (INDIV-2)		Control group (INDIV-1)	
	Treatment duration	SVR**	Treatment duration	SVR**
RVR + low bl. VL ($<8\times10^5$ IU/ml)	24 weeks (n=38)	92%	48 weeks (n=11)	91%
RVR + high bl. VL ($\geq8\times10^5$ IU/ml)	30 weeks (n=6)	83%	48 weeks (n=3)	100%
Week 6 HCV-RNA undetectable + low bl. VL ($<8\times10^5$ IU/ml)	30 weeks (n=20)	95%	48 weeks (n=18)*	77%
Week 6 HCV-RNA undetectable + high bl. VL ($\geq8\times10^5$ IU/ml)	36 weeks (n=11)	91%	48 weeks (n=13)*	78%

bl. = baseline; VL = viral load
* includes patients with HCV-RNA undetectable for the first time at week 5, 6 or 7
** intent to treat (ITT) analysis

Table 1

4. CONCLUSION

Based on differentiation between low and high baseline viral load together with virologic response to treatment at week 4 and 6 further individualization of treatment duration to 24, 30 and 36 weeks seems possible.

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