Poster #336

Treatment and Outcome of Genotype 4 Chronic Hepatitis C Patients With PegInterferon alfa 2b and Ribavirin in the Clinical Setting in Germany

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Abstract

Background: Pegylated interferon (PEG-IFN alfa) and ribavirin (RBV) are the standard of care for hepatitis C (HCV) treatment. Since there are no large controlled studies for genotype (GT) 4 patients (pts), available cohort data are of interest in order to better define response rates and suitable treatment strategies.

Methods: 285 sites (75 with GT 4 pts) have treated a total of 4130 HCV pts, of whom 126 were GT 4. The results of GT 4 pts who had reached an observational period beyond 72 weeks after baseline are described. Pts without available HCV-RNA data 24 weeks post therapy were counted as treatment failures. Data are analyzed using standard summary statistics.

Results: GT 4 pts had a mean age of 40.8 years, 61% (n=77) were male. 48% (n=61) were German, 6% (n=8) Italian, 12% (n=15) Egyptian, 4% (n=5) Ethiopian, and 5% (n=6) Turkish. 3% (n=4) of the pts showed cirrhosis and 6% (n=8) had HBV or HIV co-infection. 88% (111/126) of the pts received PEG-IFN and RBV as primary therapy, 12% (15/126) were retreated after unsuccessful IFN monotherapy. 38% (48/126) received standard PEG-IFN dose (1.5 µg/kg body weight), 35% (44/126) received lower and 25% (31/126) higher doses. 71% (90/126) received standard weight-dosed RBV (≥10.6 mg/kg body weight). Since the study is ongoing, only 83 pts have reached the end of therapy, yet 27% (22/83) were treated for less than 24 weeks, 6% (5/83) were treated 24 weeks, 48% (40/83) were treated >24 - ≤48 weeks and 19% (16/83) were treated for >48 weeks. As of yet, 58 pts have reached the 24 weeks follow-up after end of therapy. Normalization of ALT was seen in 55% (32/58) of the pts at follow-up. 47% (27/58) of the pts analyzed thus far showed sustained virologic response (SVR), 16% (9/58) relapsed, 22% (13/58) were nonresponders, and 16% (9/58) were lost to follow-up or missing. The BMI Index class ≥18< 25 showed the highest SVR rate with 64% (16/25) followed by ≥25< 30 with 47% (8/17) and the class ≥30 with 33% (1/3). In patients with baseline HCV-RNA <600,000 IU/ml (LVL) SVR rate was 67% (16/24) and 48% (10/21) in the HVL group (≥600,000 IU/mL). More nonresponders were seen in the HVL group (38.1%; 8/21) than in the LVL group (12.5%; 3/24). No differences in SVR were observed between different treatment durations ≥25 weeks ≤48 weeks (65%; 17/26) and >48 weeks (64%; 7/11), whereas in the group <25 weeks, only 25% (3/12) of the patients showed SVR.

Conclusion: Efficacy of PEG-IFN alfa-2b and RBV in GT 4 patients is comparable, but not superior to results in genotype 1 patients.

Background

- In clinical trials of patients with chronic hepatitis C, the highest overall rates of sustained virologic response (SVR) were attained using peginterferon (PEG-IFN) alfa plus ribavirin (RBV), the standard of care[1,2]
  - SVR rates of up to 82% were attained by patients infected with hepatitis C virus (HCV) genotype (G) 2 or 3[1]
  - Lower SVR rates were attained by patients infected with HCV G4, G5, G6 (50%), or G1 (42%)[1]
- Although treatment response rates among patients with HCV G1 or G2/3 infection are under investigation, there are few large controlled studies of treatment response among patients infected with HCV G4
- As part of a large investigation in Germany initiated in 2003, patients with chronic hepatitis C are being observed in a real-life setting in daily life conditions; patients infected with HCV G4 are included in this analysis

Aim

- To define treatment response rates and suitable treatment strategies for patients infected with HCV G4 who were treated with PEG-IFN alfa-2b (PegIntron®) plus RBV

Methods

Patient Selection

- In total, 285 sites (hospitals, medical practices, and medical practices that are members of the Association of German Independent Gastroenterologists [bng, Berufsverband Niedergelassener Gastroenterologen Deutschlands e.V.]) treated 4130 patients with chronic hepatitis C
- Patients infected with HCV G4 who reached an observational period beyond 72 weeks after baseline were included in this analysis

Treatment

- PEG-IFN alfa-2b (1.4 µg/kg/wk, ≥1.4 to <1.6 µg/kg/wk, or ≥1.6 to <4.0 µg/kg/wk) plus RBV 600-1200 mg/d for 48 weeks as primary therapy or as retreatment after unsuccessful management with IFN alfa monotherapy

Assessments

- The primary end point was SVR, defined as undetectable HCV RNA 24 weeks after the end of treatment
  - Relapse was defined as undetectable HCV RNA at the end of treatment but detectable HCV RNA during the 24 weeks of follow-up
  - A nonresponder was defined as a patient with detectable HCV RNA at the end of treatment and during follow-up
- Patients without available HCV RNA data at follow-up were defined as treatment failures
- Data were analyzed using standard summary statistics

Results

Baseline Patient Demographics and Characteristics

- Of the 285 sites, 75 treated a total of 126 patients infected with HCV G4
- Patients infected with HCV G4 were 20-67 years of age (mean age, 41 years); 61% (77/126) were men; and 74% (93/126) were Caucasian (**Table 1**)
- A small percentage of patients with HCV G4 infection had cirrhosis (3%, 4/126), and 5% (6/126) and 2% (2/126) were coinfected with HIV or hepatitis B virus, respectively

Table 1. Baseline Patient Demographics and Characteristics

	G4 Population (n = 126)
Sex, n (%)	
Male	77 (61)
Female	47 (37)
Missing data	2 (2)
Age, y	
Mean	41
Range	20-67
Weight,[a] kg	
Mean	75
Range	44-120
Race, n (%)	
Caucasian	93 (74)
Black	12 (10)
Asian	4 (3)
Other	16 (13)
Missing data	1 (1)
Ethnicity, n (%)	
German	61 (48)
Italian	8 (6)
Egyptian	15 (12)
Ethiopian	5 (4)
Turkish	6 (5)
Other	22 (18)
Unknown	8 (6)
Missing data	1 (1)
Comorbidity, n (%)	
Cirrhosis	4 (3)
HIV coinfection	6 (5)
Hepatitis B virus coinfection	2 (2)

[a]n = 123.
G4 = genotype 4.

Baseline Treatment

- Most patients (88%, 111/126) were treatment naive; the remainder (12%, 15/126) were being retreated with PEG-IFN alfa-2b plus RBV after unsuccessful management using IFN alfa monotherapy
- Patients were treated with 1 of 3 dosages of PEG-IFN alfa-2b (**Table 2**)
  - 38% (48/126) received the standard dosage of 1.5 µg/kg/wk
- Most patients (71%, 90/126) received weight-based dosing of RBV, at least 10.6 mg/kg/d

Table 2. Baseline Dosages of PEG-IFN alfa-2b and RBV

	G4 Population (n = 126)
PEG-IFN alfa-2b, n (%)	
<1.4 µg/kg/wk	44 (35)
≥1.4 to <1.6 µg/kg/wk	48 (38)
≥1.6 to <4.0 µg/kg/wk	31 (25)
Unknown	3 (2)
RBV, n (%)	
1200 mg/d (capsules; 3 morning, 3 night)	30 (24)
1000 mg/d (capsules; 3 morning, 2 night)	61 (48)
800 mg/d (capsules; 2 morning, 2 night)	31 (25)
600 mg/d (capsules; 1 morning, 2 night)	1 (1)
Other	3 (2)

G4 = genotype 4; PEG-IFN = pegylated interferon; RBV = ribavirin.

Assessment of Therapy

- To date, 83 patients have completed therapy
  - 33% (27/38) were treated for ≤24 weeks
  - 48% (40/83) were treated for >24 and ≤48 weeks
  - 19% (16/83) were treated for >48 weeks
- 58 patients have completed treatment and 24 weeks of follow-up and are included in this analysis
  - In more than half (55%, 32/58), alanine transaminase levels (ALT) were normalized at follow-up
  - Almost half (47%, 27/58) attained SVR (**Table 3**)
- A greater percentage of patients with a body mass index (BMI) ≥18.5 kg/m^2 to <25 kg/m^2 attained SVR (53%,16/30) than did those with a BMI ≥25 kg/m^2 (**Table 3**)

Table 3. SVR, Relapse, and Nonresponder Rates at Follow-Up by BMI

			BMI, kg/m^2			
	Overall (n = 58)	Missing (n = 3)	<18.5 (n = 1)	≥18.5 to <25 (n = 30)	≥25 to <30 (n = 19)	≥30 (n = 5)
SVR, n (%)	27 (47)	1 (33)	1 (100)	16 (53)	8 (42)	1 (20)
Relapse, n (%)	9 (16)	1 (33)	0	2 (7)	5 (26)	1 (20)
Nonresponder, n (%)	13 (22)	1 (33)	0	7 (23)	4 (21)	1 (20)
Other,[a] n (%)	7/1/1 (16)	0/0/0 (0)	0/0/0 (0)	4/1/0 (17)	2/0/0 (11)	1/0/1 (40)

[a]Lost to follow-up/missing data/or discontinued.
BMI = body mass index; SVR = sustained virologic response.

- SVR rates were 67% (16/24) and 48% (10/21) in patients with low baseline viral load (HCV RNA <600,000 IU/mL) and in patients with high baseline viral load (≥600,000 IU/mL), respectively (**Table 4**)
- There were more nonresponders in the group of patients with high baseline viral load (38%, 8/21) than in the group with low baseline viral load (13%, 3/24) (**Table 4**)
- SVR rates were higher for patients treated for ≥24 weeks to ≤48 weeks (65%, 17/26) or for >48 weeks (64%, 7/11)
  - Among patients who were treated for ≤24 weeks, only 25% (3/12) attained SVR

Table 4. Effects of Baseline Viral Load and Duration of Therapy on SVR

	HCV RNA at Baseline, IU/mL		Duration of Therapy, weeks		
	<600,000 (n = 24)	≥600,000 (n = 21)	≤24 (n = 12)	>24 to ≤48 (n = 26)	>48 (n = 11)
SVR, n (%)	16 (67)	10 (48)	3 (25)	17 (65)	7 (64)
Relapse, n (%)	5 (21)	3 (14)	1 (8)	5 (19)	3 (27)
Nonresponder, n (%)	3 (13)	8 (38)	8 (67)	4 (15)	1 (9)

HCV = hepatitis C virus; SVR = sustained virologic response.

Summary

- For patients infected with HCV G4 who were treated with PEG-IFN alfa-2b plus RBV
  - Nearly half (47%) attained SVR
  - ALT levels normalized in more than half
  - More patients with BMI in the normal range attained SVR than did those in the overweight or the obese range
  - More patients with low baseline viral load attained SVR than those with high baseline viral load
  - Higher SVR rates were attained by patients who were treated for ≥25 weeks than those treated for <25 weeks
- SVR rates within the G4 population were similar to SVR rates attained in patients infected with HCV G1 in the same study (47% vs 40%; data not shown)
- Because of small patient numbers in some subgroups, results of this study should be interpreted with caution

Conclusion

- Efficacy of PEG-IFN alfa-2b plus RBV in patients with HCV G4 infection is comparable, but not superior, to results in patients with HCV G1 infection within this German cohort of patients

References

1. Manns MP et al. *Lancet.* 2001;358:958-965.
2. Fried MW et al. *N Engl J Med.* 2002;347:975-982.

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