Identifying Hepatitis C Virus Genotype 2/3 Patients Who Can Receive a 16-Week Abbreviated Course of Peginterferon Alfa-2a (40KD) Plus Ribavirin

Moises Diago,[1] Mitchell L. Shiffman,[2] Jean-Pierre Bronowicki,[3] Stefan Zeuzem,[4] Maribel Rodriguez-Torres,[5] Stephen C. Pappas,[6] Andreas Tietz,[7] and David R. Nelson[8]

The objective of this analysis was to compare sustained virological response (SVR) and relapse rates in patients with a rapid virological response (RVR, HCV RNA <50 IU/mL at week 4) randomized to 24 or 16 weeks of treatment with peginterferon alfa-2a (40KD) 180 μg/week plus ribavirin 800 mg/day in the multinational ACCELERATE study. The analysis was restricted to patients who received treatment for 80% or more of the planned duration. Of 1309 eligible patients, 863 individuals (65.9%) achieved an RVR and were included in this analysis (458 assigned to 16 weeks and 405 assigned to 24 weeks). The overall SVR rate was significantly higher in patients randomized to 24 weeks of treatment (91% versus 82%; $P = 0.0006$) and among patients infected with genotype 2 (92% versus 81%; $P = 0.0010$) but not genotype 3 (90% versus 84%; $P = 0.1308$). Relapse rates were significantly lower among all patients randomized to 24 weeks of treatment: overall (6% versus 15%, $P < 0.0001$); in those infected with genotype 2 (5% versus 17%, $P = 0.0001$), and genotype 3 (7% versus 14%, $P = 0.0489$). SVR rates in patients with a viral load of 400,000 IU/mL or less randomized to 24 and 16 weeks of treatment were similar, 95% and 91% ($P = 0.2012$). Significant pretreatment predictors of SVR included assignment to 24 weeks of treatment ($P = 0.0006$), absence of advanced fibrosis on liver biopsy ($P = 0.0032$), lower HCV RNA level ($P = 0.0017$), and lower body weight ($P < 0.0001$). *Conclusion*: The standard 24-week regimen of peginterferon alfa-2a (40KD) plus ribavirin is significantly more effective than an abbreviated 16-week regimen in genotype 2/3 patients who achieve an RVR. Abbreviated regimens may be considered in patients with a low baseline viral load who achieve an RVR. (HEPATOLOGY 2010; 51:1897-1903)

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; MLR, multiple logistic regression; OR, odds ratio; RVR, rapid virological response; SVR, sustained virological response.

From the [1]Hepatology Section, Hospital General de Valencia, Valencia, Spain; [2]Hepatology Section, Virginia Commonwealth University Medical Center, Richmond, VA; [3]Department of Hepatology and Gastroenterology, INSERM U724, CHU de Nancy, Vandoeuvre-les-Nancy, France; [4]J.W. Goethe University Hospital, Frankfurt, Germany; [5]Fundacion de Investigacion de Diego, Santurce, Puerto Rico; [6]St Luke's Center for Liver Disease, Houston, TX; [7]Roche, Basel, Switzerland; and; and [8]University of Florida, Gainsville, FL.

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Address reprint requests to: Moises Diago, Hospital General De Valencia, Av. Tres Cruces 2, 46014 Valencia, Spain. E-mail: mdiagom@meditex.es; fax: +34 963 987 906.

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The standard of care for patients with chronic hepatitis C is the combination of pegylated interferon plus ribavirin.[1-4] When treatment-naive patients infected with hepatitis C virus (HCV) genotype 2 or 3 are treated with the standard of care for 24 weeks, sustained virological response (SVR) rates generally exceed 65% and may reach 80% or higher.[5-7] Treatment for longer durations does not increase efficacy in these individuals.[5,6] Given that a consistently high cure rate can be achieved with a 24-week combination regimen in these individuals, several studies have evaluated shorter treatment durations in patients with HCV genotype 2 or 3 infection.[7-10]

The large randomized multinational ACCELERATE trial was designed to test the hypothesis that treatment for 16 weeks in patients with HCV genotype 2 or 3 infection was noninferior to treatment for 24 weeks, as defined by a 6% noninferiority margin. The study demonstrated that 24 weeks of treatment is significantly more effective than 16 weeks of treatment with peginterferon alfa-2a (40KD) 180 μg/week plus ribavirin (800 mg/day). Overall SVR rates in the trial were 70% and 62%, respectively ($P < 0.001$).[7]

Several smaller trials have selected patients for abbreviated treatment on the basis of the virological response at week 4.[8-10] The results of one of these trials with peginterferon alfa-2b (12KD) 1.0 μg/kg/week plus ribavirin (1000/1200 mg/day) suggested that individuals with a rapid virological response (RVR), defined as HCV RNA less than 50 IU/mL at week 4, achieved an SVR rate after 12 weeks of treatment that was similar to that achieved in patients receiving the standard 24-week regimen (85% versus 91%, respectively).[9] However, a larger trial that randomized patients to peginterferon alfa-2b (12KD) 1.5 μg/kg/week plus ribavirin (800-1400 mg/day) with an RVR to 14 or 24 weeks of treatment concluded that the shorter treatment duration was inferior to the longer duration, with SVR rates of 86% and 93%, respectively.[11] The difference in SVR rates between the two treatment durations in these two studies was attributable to higher relapse rates in patients assigned to the abbreviated treatment regimen.[9,11] The ACCELERATE trial also showed that SVR rates were lower in patients with an RVR who were treated for 16 or 24 weeks (79% versus 85%).[7]

The ACCELERATE trial randomized more than 1400 genotype 2 or 3 patients, 65% of whom achieved an RVR.[7] Based on an intention-to-treat analysis, SVR rates among patients randomized to longer treatment durations may be lower because of higher dropout rates compared with patients randomized to shorter treatment durations. Therefore, a conservative approach to comparing the efficacy of two identical regimens differing only in treatment duration is to restrict analyses to patients who complete the scheduled treatment duration. The large database from this trial provides an opportunity to determine whether a specific subgroup of genotype 2 or 3 patients who achieve an RVR and complete scheduled treatment, for example, those with low baseline HCV RNA levels, can be treated with an abbreviated regimen without compromising SVR rates.

Patients and Methods

Study Design and Patients. The inclusion and exclusion criteria, study design, and primary results of ACCELERATE are reported elsewhere.[7] Briefly, treatment-naive patients with chronic HCV genotype 2 or 3 infection were randomized to receive treatment with peginterferon alfa-2a (40KD) (PEGASYS®, Roche, Basel, Switzerland) 180 μg/week plus ribavirin (COPEGUS®, Roche) 800 mg/day for either 16 or 24 weeks. Eligible patients had quantifiable HCV RNA (COBAS® AMPLICOR HCV MONITOR Test, v2.0: limit of quantitation 600 IU/mL) and elevated serum alanine aminotransferase levels. All patients were required to have undergone a liver biopsy before enrollment.

Assessment of Virological Response. Serum HCV RNA levels were measured by qualitative polymerase chain reaction assay (COBAS® AMPLICOR HCV Test, v2.0, limit of detection 50 IU/mL) at weeks 4, 12, at the end of the scheduled treatment period (week 16 or 24), and at weeks 12 and 24 after completion of the scheduled treatment period. The primary efficacy end-point in ACCELERATE was SVR defined as undetectable serum HCV RNA at the end of follow-up (week 40 in patients randomized to 16 weeks of treatment and week 48 in those randomized to 24 weeks of treatment). Virological relapse was defined as detection of HCV RNA in serum during follow-up in a patient that was confirmed to have been HCV RNA-negative at the end of treatment. Patients without an end-of-treatment HCV RNA result or without post-treatment HCV RNA data were not included in relapse rate calculations. The impact of ribavirin exposure on SVR rates was evaluated by calculating the amount of drug received by a patient (percentage of the planned total dose). Physician-initiated dose reductions for adverse events and laboratory abnormalities and patient compliance as recorded in diaries were included in these calculations.

Analysis Populations and Statistics. The efficacy analysis was conducted in all randomized patients with an RVR that were included in the per-protocol population who completed the scheduled treatment duration of 16 or 24 weeks. Patients were excluded from the per-protocol population when they had (1) major protocol deviations, or (2) treatment interruptions or early discontinuations resulting in less than 13 doses of peginterferon alfa-2a (40KD) or less than 13 weeks of treatment with ribavirin in patients randomized to 16 weeks, and less than 19 doses of peginterferon alfa-2a (40KD) or less than 19 weeks of treatment with ribavirin in patients randomized to 24 weeks of treatment. Use of the standard population rather than the intention-to-treat population ensures that differences in SVR rates or relapse rates are not influenced by a higher dropout rate in patients randomized to the longer treatment duration.

The baseline demographic and disease characteristics in the two treatment groups of the analysis population were compared using the chi-squared test for categorical data and *t* test for continuous data to verify whether the restriction to the specified analysis population had any relevant impact on the comparability of two treatment groups. SVR and relapse rates in the two treatment groups were compared with the use of the Cochran-Mantel-Haenszel test, stratified according to country of residence and HCV genotype. The common odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. The noninferiority margin specified in the study protocol for the primary analysis[7] was 6%, which was equivalent to an OR of 0.70 when assuming an SVR rate of 80% in the 24-week group. On this basis, the 16-week and 24-week regimens were considered equivalent if the lower limit of the 95% CI for the OR was at least 0.70. Because the current analysis was post hoc, no inferiority margin was assumed, the study results were known, and the subgroups lacked adequate power.

Multiple logistic regression (MLR) models were used to identify baseline factors associated with SVR and relapse in patients who achieved an RVR and who were treated for 16 or 24 weeks. Pretreatment factors considered in the analysis included assigned treatment duration at randomization plus the following baseline factors: age, sex, race (white versus nonwhite), body weight, HCV genotype (3 versus 2), serum alanine aminotransferase quotient, serum HCV RNA level, and the pretreatment liver biopsy result (no bridging fibrosis/cirrhosis versus bridging fibrosis/cirrhosis).

In the current analysis, all statistical tests are exploratory, and thus a significant result ($P < 0.05$) cannot be considered as formal proof of efficacy. Furthermore, the presence of nonsignificant test results cannot be considered as a formal proof of noninferiority. No adjustment of the significance level of 0.05 was considered necessary because of the exploratory nature of the analysis.

Table 1. Baseline Characteristics of Patients With an RVR and Who Completed Designated Treatment

Characteristic	Assigned to 16 Weeks' Treatment (N = 458)	Assigned to 24 Weeks' Treatment (N = 405)	*P*-Value*
Mean age, years ± SD	45.7 ± 9.8	44.9 ± 10.5	0.2955
Male sex, n (%)	274 (59.8)	251 (62.0)	0.5184
Mean weight, kg ± SD	79.4 ± 17.2	79.8 ± 17.3	0.7033
Mean BMI, kg/m^2 ± SD	27.2 ± 5.2	27.3 ± 5.2	0.7669
Race, n (%)			
White	400 (87.3)	353 (87.2)	0.7439
Black	11 (2.4)	13 (3.2)	
Other	47 (10.3)	39 (9.6)	
Histological diagnosis, n (%)			
No cirrhosis or bridging fibrosis	359 (78.4)	329 (81.2)	0.2987
Cirrhosis or bridging fibrosis	99 (21.6)	76 (18.8)	
HCV genotype, n (%)			
2	243 (53.1)	212 (52.3)	0.8346
3	215 (46.9)	193 (47.7)	
Mean HCV RNA level, log^{10} IU/mL ± SD	6.17 ± 0.93	6.16 ± 0.91	0.8528
HCV RNA level ≤400,000 IU/mL, n (%)	122 (26.6)	100 (24.7)	0.5139

*Chi-squared test for categorical variables and *t* test for continuous variables assuming equal variances.

Results

The per protocol population comprised 1309 individuals, of whom 863 patients (65.9%) achieved an RVR at week 4, completed designated treatment, and were included this analysis. Of the 863 patients included in the analysis, all were considered for the determination of SVR, with patients missing post-treatment HCV RNA values considered as nonresponders. Forty patients were excluded from the analysis of relapse because of missing HCV RNA values at end of treatment (n = 24), breakthrough (n = 5), or missing post-treatment HCV RNA values in patients with response at end of treatment (n = 11).

The baseline characteristics of patients with an RVR who completed treatment were similar, with no significant differences (all *P*-values > 0.2) by treatment group (Table 1). The mean overall age of patients with an RVR was 45 to 46 years, 60% to 62% were male, 87% were white, and 2% to 3% were black. Approximately 25% to 27% had a low baseline serum HCV

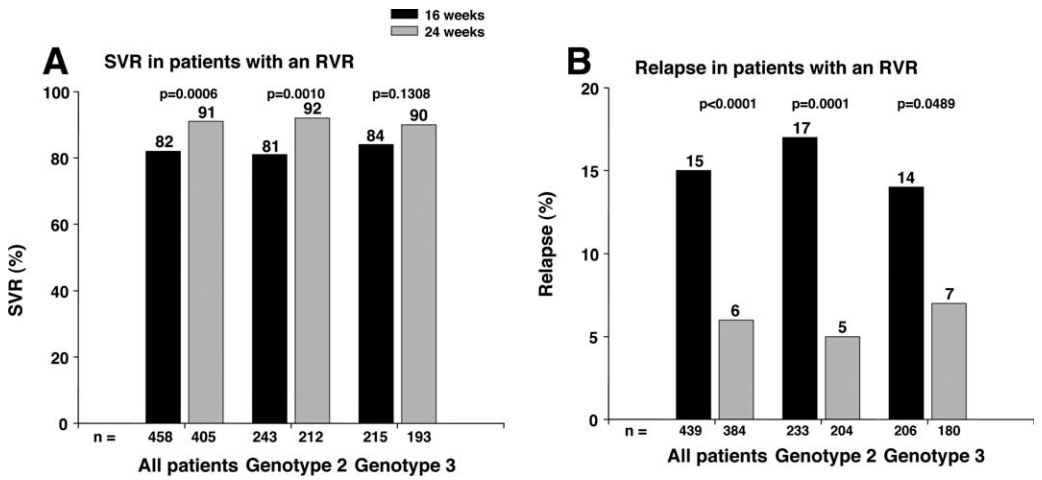

Fig. 1. (A) SVR and (B) relapse rates according to treatment duration. Only patients confirmed to be HCV RNA–negative at the end-of-treatment were included in the calculation of relapse rates.

RNA levels (≤400,000 IU/mL), 19% to 22% had advanced fibrosis (bridging fibrosis or cirrhosis), and 52% to 53% were infected with HCV genotype 2.

SVR rates exceeded 80% in patients with an RVR regardless of HCV genotype or the assigned treatment duration (Fig. 1A). The SVR rate was significantly lower in patients randomized to 16 than 24 weeks of treatment, overall (82% [377/458] versus 91% [367/405]; OR 0.49, 95% CI 0.32-0.74; $P = 0.0006$) and in those infected with genotype 2 (81% [196/243] versus 92% [194/212]; OR 0.38, 95% CI 0.21-0.69; $P = 0.0010$) but not genotype 3 (84% [181/215] versus 90% [173/193]; OR 0.63, 95% CI 0.35-1.15; $P = 0.1308$).

Virological relapse rates during follow-up were consistently and significantly higher in patients randomized to the shorter treatment duration (Fig. 1B). The relapse rates in patients randomized to 16 and 24 weeks of treatment, respectively, were 15% (67/439) and 6% (23/384) overall (OR 2.77, 95% CI 1.69-4.55; $P < 0.0001$); 17% (39/233) and 5% (10/204) among patients infected with HCV genotype 2 (OR 3.82, 95% CI 1.85-7.89; $P = 0.0001$); and 14% (28/206) and 7% (13/180) among those infected with HCV genotype 3 (OR 1.99, 95% CI 1.00-3.99; $P = 0.0489$).

Among genotype 2/3 patients with a low baseline viral load (HCV RNA level ≤400,000 IU/mL) who achieved an RVR and completed scheduled treatment, there was no statistically significant difference in SVR rates among patients randomized to 16 and 24 weeks of treatment, being 91% (111/122) and 95% (95/100), respectively ($P = 0.2012$). Furthermore, among genotype 2/3 patients with a low baseline viral load (HCV RNA level ≤400,000 IU/mL) who achieved an RVR and completed scheduled treatment, there was no statistically significant difference in relapse rates among patients randomized to 16 and 24 weeks of treatment, being 5% (6/114) and 1% (1/96), respectively ($P = 0.1373$).

Predictors of SVR and Relapse by MLR Analysis. Baseline factors that were identified as significant and independent predictors of SVR among genotype 2/3 patients with an RVR who completed the designated treatment duration included assignment to 24 weeks of treatment (OR 2.12, 95% CI 1.38-3.24; $P = 0.0006$), absence of advanced fibrosis on liver biopsy (OR 2.06, 95% CI 1.27-3.33; $P = 0.0032$), lower HCV RNA level (OR 1.52, 95% CI 1.17-1.97; $P = 0.0017$), and lower body weight (OR 1.03, 95% CI 1.02-1.04; $P < 0.0001$).

Baseline factors that predicted relapse among genotype 2/3 patients during follow-up were for the most part the opposite of those that predicted SVR: assignment to 16 weeks of treatment (OR 2.96, 95% CI 1.76-4.95; $P < 0.0001$), presence of advanced fibrosis on liver biopsy (OR 2.42, 95% CI 1.43-4.12; $P = 0.0011$), higher HCV RNA level (OR 1.96, 95% CI 1.40-2.74; $P < 0.0001$), and higher body weight (OR 1.03, 95% CI 1.01-1.04; $P = 0.0002$). Male sex was also a significant predictor of relapse in this analysis (OR 1.79, 95% CI 1.02-3.16; $P = 0.0426$).

Based on the outcome of the current MLR analysis, rates of SVR and relapse in the two treatment groups were estimated for each baseline covariate shown to be an independent predictor of response (Table 2). Rates for genotype, sex, age, and alanine aminotransferase

Table 2. Rates of SVR and Relapse Among Subgroups of Patients

Characteristic	SVR			Relapse		
	Assigned to 16 Weeks' Treatment (N = 458)	Assigned to 24 Weeks' Treatment (N = 405)	Difference: 16 Minus 24 Weeks (%)	Assigned to 16 Weeks' Treatment (N = 439)	Assigned to 24 Weeks' Treatment (N = 384)	Difference: 16 Minus 24 Weeks (%)
Genotype, n/N (%)						
2	196/243 (81)	194/212 (92)	−10.9	39/233 (17)	10/204 (5)	11.8
3	181/215 (84)	173/193 (90)	−5.5	28/206 (14)	13/180 (7)	6.4
2/3	377/458 (82)	367/405 (91)	−8.3	67/439 (15)	23/384 (6)	9.3
HCV RNA, n/N (%)						
≤400,000 IU/mL	111/122 (91)	95/100 (95)	−4.0	6/114 (5)	1/96 (1)	4.2
>400,000 IU/mL	266/336 (79)	272/305 (89)	−10.0	61/325 (19)	22/288 (8)	11.1
Cirrhosis, n/N (%)						
No	306/359 (85)	301/329 (91)	−6.3	41/342 (12)	16/312 (5)	6.9
Yes	71/99 (72)	66/76 (87)	−15.1	26/97 (27)	7/72 (10)	17.1
Age, n/N (%)						
≤40 years	116/127 (91)	119/130 (92)	−0.2	9/123 (7)	5/120 (4)	3.2
>40 years	261/331 (79)	248/275 (90)	−11.3	58/316 (18)	18/264 (7)	11.5
Sex						
Male	212/274 (91)	227/251 (92)	−0.2	54/261 (21)	16/237 (7)	13.9
Female	165/184 (79)	140/154 (91)	−11.3	13/178 (7)	7/147 (5)	2.5
Body weight, n/N (%)						
<65 kg	82/92 (89)	70/75 (93)	−4.2	6/87 (7)	2/70 (3)	4.0
≥65 kg	295/366 (81)	297/330 (90)	−9.4	61/352 (17)	21/314 (7)	10.6
ALT ratio, n/N (%)						
≤3	248/296 (84)	230/258 (89)	−5.4	39/284 (14)	16/243 (7)	7.2
>3	129/162 (81)	137/147 (90)	−13.6	28/155 (18)	7/141 (5)	13.1
No. of positive predictors						
≥2	197/220 (90)	184/193 (93)	−3.3	13/208 (6)	7/188 (4)	2.5
≤1	180/238 (76)	183/207 (88)	−12.8	54/231 (23)	16/196 (8)	15.21

Positive predictors: Noncirrhosis, HCV RNA ≤400,000 IU/mL, body weight <65 kg, age ≤40 years.
ALT, alanine aminotransferase.

ratio are also presented for completeness, because they were significant predictors in the intention-to-treat analysis.[7] The results show that for RVR patients with low viral load, low age, or low body weight, rates of SVR in both groups range from 89% to 95%, with differences between the two groups less than 5%. When a patient had at least two of the four positive predictors, low viral load, low age, low body weight, and noncirrhosis, then the SVR rate was 90% in the 16-week group and 93% in the 24-week group,

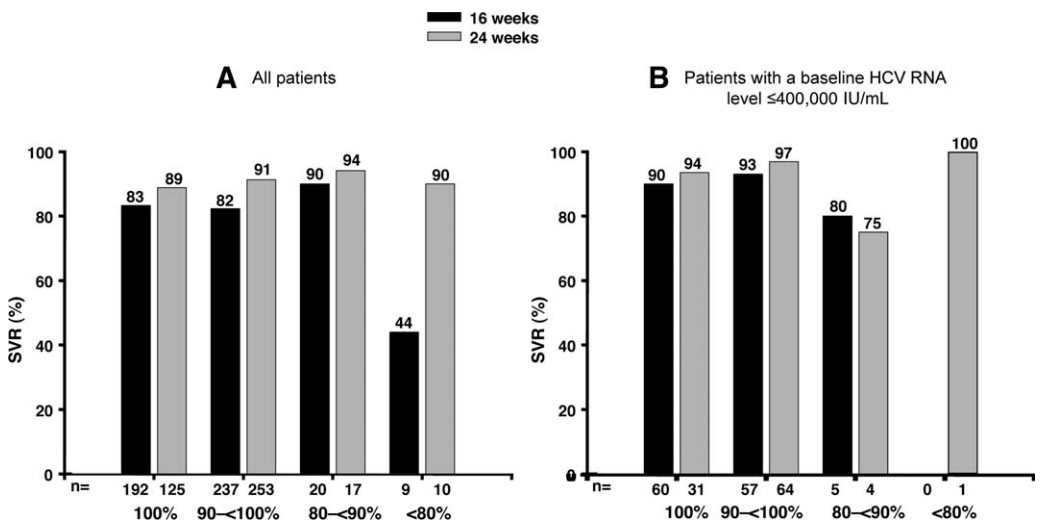

Fig. 2. SVR rates according to exposure to ribavirin in patients with an RVR who completed the designated treatment duration. (A) All patients. (B) Patients with a baseline HCV RNA level ≤400,000 IU/mL.

whereas the relapse rates were 6% and 4%, respectively. The difference in SVR rate between the 16-week and 24-week groups remains low (87% versus 88%) in all treated patients (intention-to-treat patients) with RVR and at least two positive predictors.

Impact of Dose Reductions on SVR. Among patients with an RVR and who completed treatment, SVR rates were consistently higher in those who completed 24 weeks of treatment compared with 16 weeks of treatment regardless of the extent of ribavirin exposure (Fig. 2A). Only a small number of patients had ribavirin exposure that was less than 80% of the planned dose (19/863, 2%); thus, it is not possible to comment on the effect of large or prolonged dose reductions on SVR rates in individuals with an RVR. The results were generally similar when the analysis was restricted to those patients with a baseline HCV RNA level less than 400,000 IU/mL, although most patients had exposure to ribavirin that was 90% or more of the planned dose (Fig. 2B).

Discussion

The results of this analysis confirm the findings of the intention-to-treat analysis of ACCELERATE in showing that SVR rates are higher in genotype 2/3 patients with an RVR who are treated for 24 weeks than 16 weeks. However, it should be noted that for genotype 3 patients the difference in SVR between 24 and 16 weeks was not statistically significant (Δ = 6%) in contrast to the difference in genotype 2 patients (Δ = 11%). In the original analysis, SVR rates in patients with an RVR treated for 24 and 16 weeks were 85% and 79%, respectively ($P = 0.02$).[7] The current analysis included only patients who had an RVR and who completed the planned treatment duration without relevant treatment interruptions (at least 19 doses of peginterferon alfa-2a in the 24-week treatment group and at least 13 doses in the 16-week treatment group). This approach has the advantage of compensating for the difference in withdrawal rates between the two treatment arms. More than twice as many patients withdrew from the 24-week treatment group than from the 16-week treatment group (13% versus 6%), which has the effect of reducing the difference between the two treatment durations in an intention-to-treat analysis. After application of this criterion, the SVR rates were 91% in those randomized to 24 weeks and 82% in those randomized to 16 weeks of treatment ($P = 0.0006$). Most patients achieved an end-of-treatment response (data not shown); thus, the key factor behind this 9% difference in SVR rates was a higher relapse rate in patients randomized to 16 weeks of treatment (15% versus 6%, $P < 0.0001$).

Assignment to 24 weeks of treatment was the most important predictor of SVR in the MLR analysis; conversely, assignment to the 16-week regimen was the most important predictor of relapse in the MLR analysis. Other predictors of SVR included the absence of advanced fibrosis on the pretreatment liver biopsy, a lower HCV RNA level, and lower body weight, all of which are well established as predictors of treatment success in patients with chronic hepatitis C.

In the original intention-to-treat analysis, the overall SVR rates did not differ significantly between treatment groups when only patients with a baseline HCV RNA level 400,000 IU/mL or less were included (82% in those treated for 24 weeks and 81% in those treated for 16 weeks).[7] The results of the current analysis supports this finding that patients achieving an RVR with a baseline serum HCV RNA level of 400,000 IU/mL or less can be treated for 16 weeks without compromising SVR rates because there was no statistically significant difference between those treated for 24 weeks and those treated for 16 weeks (95% versus 91%, $P = 0.2012$).

The authors of other studies of abbreviated regimens for genotype 2 or 3 patients have reported higher relapse rates in patients assigned to the shorter treatment duration.[9,11,12] The increase in the probability of relapse was twofold to threefold greater in patients assigned to abbreviated 12- to 14- week regimens, which is in close agreement with the 2.5-fold higher relapse rate in patients assigned to the 16-week regimen in the current analysis.

In addition to higher voluntary withdrawal rates in patients treated for longer duration, it is possible that differences in treatment exposure may have an effect on SVR rates in patients randomized to different treatment durations. For this reason we included an exposure analysis in the current analysis. Few patients had exposure levels below 80% of the planned dose of ribavirin or peginterferon alfa-2a (40KD); thus, we cannot comment on the impact of large or long-term dose reductions on the probability of achieving an SVR. Most patients had a ribavirin exposure level that was 90% to 100% of the planned amount. Among patients with 80% or greater exposure to ribavirin, the SVR rates were consistently higher in patients assigned to the longer treatment duration. Moreover, there was no trend toward a reduction in SVR rates with decreasing exposure in these individuals.

It is now clear from the results of ACCELERATE and another recently completed large randomized noninferiority study[11] that 24 weeks of treatment produces significantly higher SVR rates than abbreviated regimens and that abbreviated regimens expose patients to a significantly higher probability of virological relapse during follow-up, even in patients with an RVR. In spite of the greater efficacy of the standard treatment duration in their study, Dalgard et al.[11] argued that it would be cost-effective to assign all genotype 2 or 3 patients to abbreviated treatment and to immediately retreat those who relapse. Such a policy assumes that all patients have the same probability of relapse and that all patients will be willing to immediately reenroll for a longer treatment duration. The results of the current analysis and that reported by Mangia et al.[13] suggest that the first assumption is incorrect; the probability of relapse varies according to several well-established predictors of treatment success. Adopting this approach would require physicians to counsel all patients to prepare themselves for the possibility of undergoing two consecutive courses of treatment, with a total treatment duration of 40 weeks. However, Mangia et al. reported that patients infected with genotype 2 or 3 who achieved an RVR but who relapsed after an abbreviated 12-week course of treatment with peginterferon alfa-2b plus ribavirin could achieve an SVR rate of 70% with a second 24-week course of the same treatment.[13]

The current analysis has shown that several subgroups of patients with an RVR have an acceptable risk:benefit ratio for contemplation of abbreviated therapy in addition to those that have a low baseline serum HCV RNA level. Given that advanced fibrosis was a stronger predictor of relapse in patients with RVR after 16 weeks of treatment (relapse rate of 27%), it is reasonable to exclude all such patients from abbreviated treatment.

Rather than reducing the treatment duration in patients who experience adverse events that must be managed by dose reductions, physicians should encourage continued treatment for the full 24-week duration to maximize the probability of SVR.

Overall, this analysis shows that for patients infected with HCV genotype 2 or 3 and who achieve an RVR at week 4, the standard 24-week treatment duration produces significantly higher SVR rates than an abbreviated 16-week regimen. Shortening the treatment duration should be considered only in patients with a low baseline HCV RNA level and without bridging fibrosis/cirrhosis who achieve an RVR. The difference in SVR rates is attributable to a significantly higher rate of virological relapse in patients treated with the abbreviated regimen.

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