Peginterferon and Ribavirin Treatment in African American and Caucasian American Patients With Hepatitis C Genotype 1

HARI S. CONJEEVARAM,* MICHAEL W. FRIED,† LENNOX J. JEFFERS,§ NORAH A. TERRAULT,¶ THELMA E. WILEY–LUCAS,‖ NEZAM AFDHAL,# ROBERT S. BROWN,** STEVEN H. BELLE,†† JAY H. HOOFNAGLE,§§ DAVID E. KLEINER,‖‖ and CHARLES D. HOWELL,¶¶ for the Virahep-C Study Group

*University of Michigan, Ann Arbor, Michigan; †University of North Carolina, Chapel Hill, North Carolina; §University of Miami, Miami, Florida; ¶University of California, San Francisco, San Francisco, California; ‖Rush University, Chicago, Illinois; #Beth Israel Deaconess Medical Center, Boston, Massachusetts; **New York-Presbyterian Medical Center, New York, New York; ††Graduate School of Public Health at the University of Pittsburgh, Pittsburgh, Pennsylvania; §§National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland; ‖‖National Cancer Institute, Baltimore, Maryland; ¶¶University of Maryland, Baltimore, Maryland

Background & Aims: **Compared with Caucasian Americans (CA), African Americans (AA) with chronic hepatitis C are less likely to respond to interferon-based antiviral therapy.** ***Methods:*** **In a multicenter treatment trial, 196 AA and 205 CA treatment-naive patients with hepatitis C virus (HCV) genotype 1 infection were treated with peginterferon alfa-2a (180 μg/wk) and ribavirin (1000–1200 mg/day) for up to 48 weeks. The primary end point was sustained virologic response (SVR).** ***Results:*** **Baseline features were similar among AA and CA, including HCV-RNA levels and histologic severity, but AA had higher body weights, a higher prevalence of diabetes and hypertension, and lower alanine transaminase levels ($P < .001$ for all). The SVR rate was 28% in AA and 52% in CA ($P < .0001$). Racial differences in viral responses were evident as early as treatment week 4. Breakthrough viremia was more frequent among AA than CA (13% vs 6%, $P = .05$); relapse rates were comparable (32% vs 25%, $P = .30$). Proportions of patients with serious adverse events and dose modifications and discontinuations were similar among AA and CA. In multiple regression analyses, CA had a higher SVR rate than AA (relative risk, 1.96; 95% confidence interval, 1.48–2.60; $P < .0001$). Other factors independently associated with higher SVR included female sex, lower baseline HCV-RNA level, less hepatic fibrosis, and more peginterferon taken.** ***Conclusions:*** **AA with chronic hepatitis C genotype 1 have lower rates of virologic response to peginterferon and ribavirin than CA. These differences are not explained by disease characteristics, baseline viral levels, or amount of medication taken.**

Population-based surveys indicate that 1.3% of the US population, approximately 3.2 million Americans, have chronic hepatitis C virus (HCV) infection, as shown by detection of anti-HCV and HCV RNA in serum.[1] Chronic hepatitis C is now the leading cause of chronic liver disease and the most common indication for liver transplantation in the United States.[2,3] HCV-related cirrhosis accounts for up to 50% of newly diagnosed cases of hepatocellular carcinoma and for approximately 10,000 deaths per year.[4]

Pegylated alfa interferon (peginterferon) in combination with ribavirin given for 24 or 48 weeks is standard therapy for chronic hepatitis C.[5] In controlled clinical trials, combination therapy yielded sustained virologic response (SVR) rates of 54%–63%.[6–8] Several factors were associated with a higher likelihood of SVR, the most important being HCV genotype.[5–8] SVR rates were 75%–80% in patients with HCV genotypes 2 or 3. In patients with genotype 1, the most common HCV genotype in the United States, SVR rates were only 40%–50%.

Response rates also vary among ethnic and racial groups. Most striking is the lower SVR rate among African Americans (AA) compared with Caucasian Americans (CA) and Asians.[9–12] AA also have a higher prevalence of HCV infection (anti-HCV rates of 3.0% overall) and are more likely to have genotype 1 than other racial groups.[1] Despite these racial differences, AA have been underrepresented in most trials of therapy in hepatitis C, making it difficult to estimate response rates in this population accurately.[10] Two recent studies that enrolled larger numbers of AA than previous studies documented lower response rates in AA compared with non-Hispanic whites with HCV genotype 1 infec-

Abbreviations used in this paper: AA, African Americans; CA, Caucasian Americans; EVR, early virologic response; MEMS, Medication Event Management System; SVR, sustained virologic response.

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tion.[11,12] The reasons for these differences in response rates are not known.

The Study of Viral Resistance to Antiviral Therapy of Chronic Hepatitis C (Virahep-C) was designed to assess the rates of response to peginterferon combination therapy for hepatitis C among AA and CA and to evaluate clinical, immunologic, virologic, and host genetic reasons for the lack of response to treatment. The primary goal of this study was to elucidate the mechanisms of antiviral resistance among patients who fail to respond to the optimal current regimen of therapy.

Materials and Methods

Patient Sample

Adult patients between the ages of 18 and 70 years with chronic HCV genotype 1 infection who had not been treated previously were eligible for enrollment. Patients were required to have HCV RNA in serum, compensated liver disease, and histologic evidence of chronic hepatitis C on liver biopsy examination performed within the previous 18 months. An increased serum alanine transaminase level was not required. Only patients who designated themselves as "African American/black" or "Caucasian/white" and not as "Both" or "Other" were eligible for enrollment. Persons not born in the United States were excluded. Other exclusion criteria included hemoglobin level less than 11 g/dL in women or less than 12 g/dL in men, neutrophil count less than 1000 cells/mm^3, and platelet count less than 75,000 cells/mm^3. The protocol and consent form were approved by the institutional review boards of the participating institutions. All patients gave informed written consent. In addition, the study was monitored by an independent Data Safety and Monitoring Board.

Study Design

Study participants, recruited at 8 US clinical centers between July 2002 and December 2003, were treated for up to 48 weeks with peginterferon alfa-2a (Pegasys; Roche Pharmaceuticals, Nutley, NJ) 180 μg/wk and ribavirin (Copegus; Roche Pharmaceuticals) 1000 or 1200 mg/day based on body weight of 75 kg or less. The study was designed to enroll equal numbers of AA and CA at all centers. Patients were monitored at 1- to 2-week intervals for the first 8 weeks and every 4 weeks thereafter. Virologic response was assessed at week 24. Those who had positive qualitative serum HCV RNA were considered nonresponders, and therapy was stopped. Responding patients were continued on therapy for another 24 weeks and assessed for SVR at 24 weeks after stopping treatment.

Specific dose-adjustment guidelines for peginterferon and ribavirin were followed for treatment-related neutropenia, thrombocytopenia, and anemia. Because constitutional neutropenia is common among AA, dose reductions were not undertaken until the neutrophil count was less than 500 cells/mm^3.[13] For peginterferon, a level 1 decrease was from 180 to 135 μg, a level 2 decrease was from 135 to 90 μg, and a level 3 decrease was from 90 to 45 μg. Treatment was stopped for neutrophil counts less than 250 cells/mm^3 and for platelet counts less than 25,000 cells/mm^3. For hematologic adverse events (anemia), the ribavirin dose reduction was from 1200 to 800 mg/day or 1000 to 600 mg/day for hemoglobin levels of 8.5–10 g/dL. When the hemoglobin level decreased to less than 8.5 g/dL, ribavirin was stopped permanently. For nonhematologic adverse events, ribavirin dose reduction was performed stepwise in decrements of 200 mg/day to the lowest dose of 400 mg/day. For other adverse effects considered to be possibly related to either drug, stepwise dose reductions were performed at the discretion of the investigator.

Clinical Assessment and End Points

The primary end point of therapy was an SVR that was defined as the absence of detectable HCV RNA in serum 24 weeks after therapy was stopped. Treatment nonresponse was defined as detectable serum HCV RNA at treatment week 24; virologic breakthrough was defined as the lack of detectable HCV RNA at treatment week 24, but reappearance of detectable HCV RNA between weeks 24 and 48 of treatment; and virologic relapse was defined as a lack of detectable HCV RNA in serum at the end of therapy, but reappearance of HCV RNA 24 weeks later. At week 24 and time points thereafter, missing HCV RNA data were considered a nonresponse.

The amount of drug taken was monitored using the electronic Medication Event Management System (MEMS) (Aardex, Zug, Switzerland) caps placed on both the peginterferon and ribavirin containers.[14] MEMS caps record the date and time the containers are opened, an indication of medication use. Patients were advised to open the bottles as per the dosage regimen daily and not place pills in weekly pill containers. Patients were asked about their medication use at weeks 4, 12, 24, 36, and 48 during the treatment period but were not queried about possible lapses in medication use at the end of the study. By multiplying the number of cap openings by the dose prescribed per opening, the estimated total dose of each drug taken was calculated. The proportion of maximum dose taken for 24 weeks of treatment (maximum value = 1.0) was calculated as the total estimated dose taken divided by the maximum dose possible had there been no dose reductions or discontinuations. Although patients were instructed on the use of the MEMS caps at the baseline visit, neither patients nor clinical center personnel received data from the caps during the course of the study.

Laboratory and Viral Testing

Routine blood counts and biochemical liver tests including alanine and aspartate transaminase levels were performed at local laboratories. Liver biopsies were scored under code by the study pathologist (D.E.K.) using the Ishak et al[15] modification of the histologic activity index that scores necroinflammatory changes from 0 to 18 and fibrosis from 0 to 6. Steatosis was graded on a scale of 0 to 4 based on the percentage of cells with fat.

Serum HCV-RNA levels were tested at a central laboratory (SeraCare BioServices, Gaithersburg, MD) using the COBAS Amplicor Hepatitis C Virus Monitor Test, version 2.0 assay (sensitivity, 600 IU/mL; Roche Molecular Diagnostics, Alameda, CA). Samples that tested negative using this quantitative assay were tested in duplicate using the Amplicor assay (sensitivity 50 IU/mL; Roche Molecular). HCV genotyping was performed using a line-probe hybridization assay (VERSANT HCV Genotype Assay; Bayer, Tarrytown, NY).

Statistical Analysis

The study was designed to enroll 400 patients with equal numbers of AA and CA, which would provide 80% power to detect a difference in SVR between racial groups assuming SVR rates of 26% vs 40% using a 2-sided test with an α value of .05. Primary analyses were performed using all patients who were eligible at the time they took their first dose of drug.

Baseline demographic, clinical, and virologic characteristics of the racial groups were compared using the χ^2 test for association with continuity correction or exact tests for differences in proportions. The nonparametric Wilcoxon rank-sum test was used to compare racial differences in distributions of continuous data. Proportions of AA and CA with SVR were compared using the χ^2 test of association with continuity correction. Because this was a prospective study, the association between race and SVR after adjusting for potential confounders was assessed through step-wise fitted multiple Poisson regression models with sandwich estimator of the variance to calculate the relative risk using variables identified in univariable analysis.[16] Factors with a P value of less than .25 in univariable analyses were eligible for entry and those with a P value of less than .05 were retained in the multiple regression model for predicting SVR. Results are reported as relative risks with 95% confidence intervals. Statistical analyses were performed using SAS 8.02 (SAS Institute, Cary, NC) and the R language and environment.[17]

Results

Baseline Features

Of 535 patients screened, 401 met the entry criteria and were enrolled. The 2 groups that consisted of 196 AA and 205 CA did not differ significantly in regards to sex, age, estimated duration of infection, suspected source of infection, or alcohol use (Table 1). Education greater than high school level was less common among AA. AA patients were heavier and were more likely to have a history of diabetes and hypertension compared with CA. AA had lower serum ALT values than CA but similar liver histologic scores for necrosis, inflammation, fibrosis, and steatosis. AA were also more likely than CA to have genotype 1b and less likely to have genotype 1a. HCV-RNA levels at baseline were similar in the 2 racial groups.

Virologic Response Rates

The primary end point, SVR, was achieved in 28% of AA compared with 52% of CA patients ($P < .0001$). Differences in virologic response to therapy between the 2 groups were seen as early as week 4 and persisted (Figure 1). At 24 weeks, 46% of AA patients compared with 74% of CA patients were HCV RNA negative and were eligible to continue on therapy to 48 weeks. Breakthroughs in virologic response on treatment were more common among AA than CA patients (13% vs 6%; $P = .05$), whereas relapse rates after treatment were comparable (32% vs 25%; $P = .30$).

The absence of an early virologic response (EVR), as defined by a lack of detectable HCV RNA or a 2-log decrease from baseline level at week 12 of treatment, has been shown to predict lack of SVR accurately.[5,6,18] In this study, EVR was less common among AA than CA (61% vs 78%, $P = .0003$). Although the negative predictive value of EVR was similar between AA and CA (97% vs 100%), the positive predictive value was less for AA patients (43% vs 67%, $P < .0001$). Substituting earlier time points (weeks 4 and 8) and more rigorous criteria (lack of detectable HCV RNA) to define an EVR did not improve the negative predictive values for achieving a sustained response in either racial group (data not shown).

Side Effects, Dose Modifications, and Medication Taken

The respective proportions of participants with serious adverse events, at least 1 dose reduction, or drug discontinuation were similar between AA and CA patients (Table 2). Serious adverse events included 3 deaths among AA. Two deaths occurred after stopping therapy and were considered unrelated: 1 resulted from postoperative complications of cholecystectomy and 1 resulted from cardiac ischemia related to cocaine use. One death occurred on therapy, was attributed to pyelonephritis, and was judged as possibly related to peginterferon treatment. None of the deaths could be linked to neutropenia. Including these 3 patients, treatment was discontinued in a similar proportion of AA and CA patients.

Importantly, assessments using the MEMS caps methodology indicated that the proportion of the total maximum dose taken of both peginterferon and ribavirin during the first 24 weeks was significantly less among AA than CA (Table 2). Thus, 54% of AA compared with 73% of CA took at least 80% of the maximum doses of both drugs ($P < .0001$), the criteria typically used in assessing compliance in combination therapy of hepatitis C.[19]

Table 1. Baseline Characteristics of Virahep-C Participants

Characteristic	African Americans (n = 196)	Caucasian Americans (n = 205)	*P* value[a]
Male, n (%)	127 (64.8)	134 (65.4)	.99
Age, *y*	49.0 (45.0, 52.5)	48.0 (43.0, 52.0)	.08
Estimated duration of infection, *y*	(n = 144) 25.0 (17.5, 32.0)	(n = 158) 27.0 (19.0, 33.0)	.15
Suspected source of infection, n (%)[b]			
Injection drug use	94 (48.0)	106 (51.7)	.52
Blood or blood products	39 (19.9)	48 (23.4)	.46
Other	35 (17.9)	23 (11.2)	.08
Unknown	28 (14.3)	28 (13.7)	.97
Education, n (%)	(n = 191)	(n = 202)	.04
>High School	104 (54.5)	132 (65.4)	
≤High School	87 (45.6)	70 (34.7)	
Weight (*kg*)	(n = 194) 87.5 (78.6, 100.9)	82.3 (72.7, 95.5)	.001
Body mass index, kg/m^2	(n = 193) 29.3 (26.4, 34.0)	(n = 203) 27.6 (24.4, 31.5)	.0003
History of diabetes, n (%)	30 (15.3)	9 (4.4)	.0004
History of hypertension, n (%)	84 (42.9)	43 (21.0)	<.0001
Current alcohol use (drinks/day), n (%)[c]	(n = 188)	(n = 201)	
<1	164 (87.2)	178 (88.6)	.81
1 to <2	11 (5.9)	14 (7.0)	.81
≥2	13 (6.9)	9 (4.5)	.41
Currently smoking, n (%)	78 (41.3)	70 (34.5)	.20
Alanine transaminase level, *IU/L*	59.0 (40.0, 88.0)	74.0 (51.0, 138.0)	<.0001
Aspartate transaminase level, *IU/L*	51.0 (33.5, 69.0)	52.0 (37.0, 87.0)	.06
Albumin level, *g/dL*	4.1 (3.8, 4.3)	4.2 (4.0, 4.4)	<.0001
Total bilirubin level, *mg/dL*	.6 (.4, .8)	.7 (.5, .9)	.0007
Prothrombin time, international normalized ratio	1.0 (.9, 1.1)	1.0 (.9, 1.1)	.83
Hemoglobin level, *g/dL*	14.3 (13.5, 15.1)	15.0 (13.9, 15.9)	<.0001
White blood cell count, 10^3 cells/mm^3	5.8 (4.7, 7.5)	6.2 (4.9, 7.4)	.08
Neutrophil count, 10^3 cells/mm^3	2.7 (2.0, 8.8)	3.3 (2.6, 4.2)	<.0001
Platelet count, 10^3 cells/mm^3	214.5 (168, 268)	207 (162, 244)	.11
Ishak necroinflammatory score, 0–18	8 (6, 9)	8 (6, 10)	.56
Ishak fibrosis score, 0–6	2 (1, 3)	2 (1, 3)	.45
Bridging, n (%)	57 (29.4)	60 (29.3)	.99
Cirrhosis, n (%)	10 (5.2)	19 (9.3)	.16
Steatosis (≥5% present), n (%)	56 (28.9)	77 (37.6)	.08
HCV subtype, n (%)[d]			
1a	92 (46.9)	118 (57.6)	.04
1b	90 (45.9)	58 (28.3)	.0004
Other (1, 1a/b)	14 (7.1)	29 (14.2)	.04
HCV RNA level, $\times 10^6$ IU/mL	6.4 (5.6, 6.7)	6.5 (5.7, 6.8)	.08

NOTE. Continuous variables are represented by median (25th percentile, 75th percentile).
[a]The Wilcoxon rank-sum test was used to compare distributions for continuous variables, Pearson's χ^2 test was used to compare percentages.
[b]$P = .27$.
[c]$P = .54$.
[d]$P = .0005$.

Factors Associated With Response

Factors associated with SVR were analyzed by univariable, followed by multivariable, regression models (Table 3). In univariable analysis, factors associated with higher SVR included CA race, female sex, more than high school education, lower weight, lower baseline HCV-RNA level, less degree of fibrosis, and higher proportion of maximum dose taken of both interferon and ribavirin. A history of diabetes and, to a lesser extent, a history of hypertension was associated with lower response rates. Finally, several laboratory features possibly related to fibrosis and cirrhosis were associated with a decreased likelihood of SVR, including lower white blood cell and platelet counts.

In multivariable analysis, CA race was associated significantly with higher SVR after adjusting for all other significant factors (relative risk, 1.96; 95% confidence interval, 1.48–2.60; $P < .0001$) Factors other than race that were associated independently with higher SVR included female sex, lower baseline HCV-RNA level,

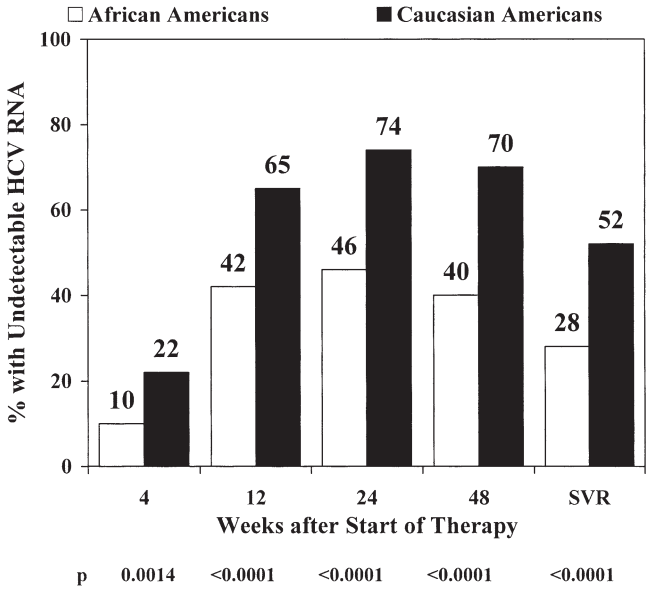

Figure 1. Percentages of participants with undetectable serum HCV-RNA levels (<50 IU/mL) by racial group at selected time points. □, AA; ■, CA.

lower Ishak fibrosis scores, and greater amounts of maximum peginterferon dose taken (Table 3). However, none of these factors accounted for the differences in response rate by race.

Multivariable analysis of factors associated with an SVR uncovered an interaction between race and baseline HCV-RNA levels (Figure 2). Response rates were markedly different between AA and CA patients with high initial levels of HCV RNA. In contrast, after controlling for other factors, response rates were similar in the 2 racial groups among patients with low initial levels of HCV RNA. The lack of interactions between race and the other factors in the model or factors that did not enter the model indicated that the model was similar for AA and CA participants.

Discussion

In this study, response rates to the current, optimal regimen of antiviral therapy of hepatitis C were significantly lower among AA compared with CA patients (28% vs 52%). This difference was not explained by factors known to be associated with poor response such as baseline HCV-RNA levels, sex, age, weight, degree of fibrosis, or amount of drug taken, even though AA and CA patients differed in the frequency of several of these predictive factors (body weight, amount of drug taken). Factors that predicted an SVR in AA patients were the same as those that predicted response among CA patients, although racial differences in SVR varied somewhat by baseline viral levels.

Failure to take the full doses of drugs often is cited as a reason for poor response to therapy of hepatitis C.[19] Side effects of interferon and ribavirin can be troublesome and lead to dose reductions or early termination of treatment. Indeed, in this study, 36% of patients had at least one dose reduction, and another 17% discontinued therapy early. However, rates of dose reduction and discontinuation were similar among AA and CA patients, so that changes in the prescribed doses of the medications were unlikely to be the reason for the racial differences in SVR. This study also included a careful analysis of the actual amounts of drugs taken. Assessment of amounts of peginterferon and ribavirin taken using the MEMS caps methodology suggested that the proportion of maximum dose of both drugs was lower among AA than CA. Furthermore, the proportion of maximum dose taken was a significant factor associated

Table 2. Participants With Serious Adverse Events, Dose Reductions, or Dose Discontinuations

	AA (N = 196)	CA (N = 205)	*P* value
Serious adverse events, n (%)			
Patients with at least 1 serious adverse event	30 (15.3)	33 (16.1)	.64
Related to drug, severe in nature	12 (6.1)	16 (7.8)	.94
Dose reductions, n (%)			
Peginterferon only	10 (5.1)	8 (3.9)	.73
Ribavirin only	43 (21.9)	48 (23.4)	.82
Both	15 (7.7)	21 (10.2)	.46
Dose discontinuations, n (%)[a]	38 (19.4)	29 (14.1)	.20
Proportion of total maximum dose taken (first 24 weeks)			
Peginterferon (median, 25th–75th)	.96 (.88–1.00)	1.00 (.93–1.00)	.02
≥80%	152 (80.4)	178 (87.3)	.065
Ribavirin (median, 25th–75th)	.86 (.63–.97)	.94 (.81–.99)	.0002
≥80%	106 (56.4)	152 (75.6)	<.0001
Both drugs, n (%)			
100	4 (2.1)	9 (4.4)	.26
80–80	99 (53.8)	146 (73.0)	<.0001

[a]Includes 3 deaths.

Table 3. Relationship Between SVR and Each Variable of Interest in Univariable and Multivariable Analysis

Variable	Univariable analysis		Multivariable analysis	
	Relative risk (95% Confidence interval)	*P* value	Relative risk (95% Confidence interval)	*P* value
CA race	1.89 (1.46–2.46)	<.0001	1.96 (1.48–2.60)	<.0001
Male sex	.73 (.58–.93)	.01	.74 (.60–.91)	.004
Age, per 5 years	.97 (.89–1.03)	.24		
Estimated years infected, per year	1.01 (.99–1.02)	.37		
Education (≤high school)	.72 (.55–.94)	.02		
Weight (*kg*) per 5 kg	.94 (.91–.97)	.0004		
Body mass index, kg/m^2	.98 (.96–1.00)	.07		
History of diabetes	.49 (.26–.91)	.02		
History of hypertension	.76 (.57–1.01)	.06		
Use of antidepressant drugs	1.06 (.75–1.50)	.73		
Current alcohol consumption	1.02 (.76–1.36)	.90		
Currently smoking	1.13 (.89–1.45)	.31		
Alanine transaminase level (*IU*) per 100 IU	1.05 (.90–1.22)	.53		
Asparate transaminase level (*IU*) per 100 IU	.75 (.55–1.02)	.06		
Prothrombin time, international normalized ratio	.89 (.31–2.59)	.83		
Hemoglobin, *g/dL*	.95 (.87–1.04)	.26		
White blood cells, per 10^3 cells/mm^3	1.05 (.996–1.11)	.07		
Platelet count, per 10^5 cells/mm^3	1.27 (1.09–1.47)	.003		
Genotype, 1a vs not 1a	.92 (.73–1.17)	.50		
Baseline viral level, log_{10} *IU/mL*	.76 (.66–.88)	.0002	.58 (.45–.75)	<.0001
Ishak necroinflammatory score	.99 (.96–1.04)	.87		
Ishak fibrosis score	.89 (.81–.97)	.006	.89 (.83–.96)	.004
Cirrhosis	.58 (.30–1.12)	.10		
Steatosis score	.88 (.72–1.08)	.21		
Proportion maximum peginterferon dose taken for first 24 weeks, per .1-increase	1.43 (1.20–1.70)	<.0001	1.41 (1.20–1.65)	<.0001
Proportion maximum ribavirin dose taken for first 24 weeks, per .1-increase	1.20 (1.12–1.28)	<.0001		
Interaction of baseline viral level and CA race, log_{10} *IU/mL*			1.43 (1.08–1.89)	.01

with SVR. We do not have an explanation for the differences in dose taken based on MEMS caps among AA and CA, although this is being analyzed carefully in more detail. Nevertheless, in multivariable analysis, the differences in response rates between AA and CA could not be attributed to the differences in the amount of peginterferon or ribavirin actually taken.

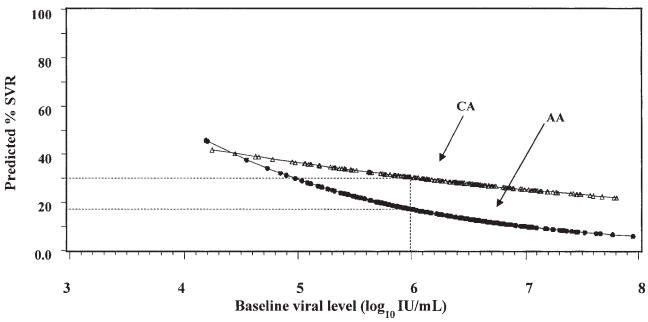

Figure 2. Relationship between baseline viral level (log_{10} IU/mL) and adjusted predicted percentage with SVR by race. The predicted probability of an SVR by baseline viral level is shown separately for AA and CA using the example of a man with an Ishak fibrosis score of 2 on pretreatment liver biopsy examination who took 80% of the maximum peginterferon dose during the first 24 weeks of treatment.

Other factors found to be associated with lower response rates in both AA and CA patients were male sex, greater degrees of fibrosis on liver biopsy examination, and higher initial levels of HCV RNA, findings consistent with previous studies of combination therapy for hepatitis C.[5–8,11] Interestingly, modeling response rates by race showed an interaction between baseline HCV-RNA levels and race (Figure 2). After controlling for sex, fibrosis scores, and amount of peginterferon taken, SVR rates were strikingly lower in AA than CA with high viral levels but were more similar at lower viral levels. These post hoc analyses using statistical modeling techniques deserve validation by prospective evaluation but suggest that AA and CA patients with low levels of HCV RNA ($\leq 10^5$ IU/mL) may have similar SVR rates.

Testing for HCV-RNA levels before and after 12 weeks of treatment with peginterferon and ribavirin has been proposed as a means to identify patients who are unlikely to have an SVR and thus allow early discontin-

uation of therapy.[5,18] In this study, an EVR at week 12 had a high negative predictive value for an SVR in both racial groups. However, the positive predictive value was significantly less among AA than among CA patients (43% vs 67%, $P = .0003$).

The findings from this study suggest that the reduced response rate to combination therapy of hepatitis C among AA compared with CA is not caused by clinical patient characteristics, disease severity, or amount of medication taken. Even after controlling for important factors associated with a response to combination therapy (HCV-RNA levels, sex, hepatic fibrosis, amount of drug taken), race remained significantly and independently associated with sustained response. Separate analyses of virologic, immunologic, genetic, and host interferon signaling responses were built into the design of the Virahep-C and are currently addressing the biologic causes of nonresponse in therapy of hepatitis C.

Appendix

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at doi:10.1053/j.gastro.2006.06.008.

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Address requests for reprints to: Hari Conjeevaram, MD, MS, Division of Gastroenterology, The University of Michigan, 3912 Taubman Center, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109-0362. e-mail: omsairam@umich.edu; fax: (734) 936-7392.

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Members of Virahep-C contributing to the study include: *from the Beth Israel Deaconess Medical Center, Boston, MA:* Nezam Afdhal, MD (Principal Investigator), Tiffany Geahigan, PA-C, MS (Research Coordinator); *from the New York-Presbyterian Medical Center, New York, NY:* Robert S. Brown, Jr., MD, MPH (Principal Investigator), Lorna Dove, MD, MPH (Co-Investigator), Shana Stovel, MPH (Study Coordinator), Maria Martin (Study Coordinator); *from the University of California, San Francisco, San Francisco, CA:* Norah Terrault, MD, MPH (Principal Investigator), Stephanie Straley, PA-C, Eliana Agudelo, PA-C, Melissa Hinds, BA (Clinical Research Coordinator), Jake Heberlein (Clinical Research Coordinator); *from Rush University, Chicago, IL:* Thelma E. Wiley, MD (Principal Investigator), Monique Williams, RN (Study Coordinator); *from the University of Maryland, Baltimore, MD:* Charles D. Howell, MD (Principal Investigator), Kelly Gibson (Project Coordinator), Karen Callison, RN (Study Coordinator), Jane Lewis, RN (Study Coordinator); *from the University of Miami, Miami, FL:* Lennox J. Jeffers, MD

(Principal Investigator), Shvawn McPherson Baker, PharmD (Co-Investigator), Maria DeMedina, MSPH (Project Manager), Carol Hermitt, MD (Project Coordinator); *from the University of Michigan, Ann Arbor, MI:* Hari S. Conjeevaram, MD, MS (Principal Investigator), Robert J. Fontana, MD (Co-Investigator), Donna Harsh, MS (Study Coordinator); *from the University of North Carolina, Chapel Hill, NC:* Michael W. Fried, MD (Principal Investigator [K24 DK066144]), Scott R. Smith, PhD (Co-Investigator), Dickens Theodore, MD, MPH (Co-Investigator), Steven Zacks, MD, MPH, FRCPC (Co-Investigator [K23 DK064762]), Roshan Shrestha, MD (Co-Investigator), Karen Dougherty, NP (Co-Investigator), Paris Davis (Study Coordinator), Shirley Brown (Study Coordinator); *from St. Louis University, St. Louis, MO:* John E. Tavis, PhD (Principal Investigator), Adrian Di Bisceglie, MD (Co-Investigator), Ermei Yao, PhD (Co-Investigator), Maureen Donlin, PhD (Co-Investigator), Nathan Cannon, BS (Graduate Student), Ping Wang, BS (Lab Technician); *from Cedars-Sinai Medical Center, Los Angeles, CA:* Huiying Yang, MD, PhD (Principal Investigator), George Tang, PhD (Project Scientist), Dai Wang, PhD (Project Scientist); *from the University of Colorado Health Sciences Center, Denver, CO:* Hugo R. Rosen, MD (Principal Investigator), James R. Burton, MD (Co-Investigator), Jared Klarquist (Lab Technician); *from Veteran's Administration, Portland, OR:* Scott Weston (Lab Technician); *from Indiana University, Bloomington, IN:* Milton W. Taylor, PhD (Principal Investigator), Corneliu Sanda, MD (post-doctoral associate), Takuma Tsukahara, MS (statistician), Mary Ferris (lab assistant); *from the Data Coordinating Center, Graduate School of Public Health at the University of Pittsburgh, Pittsburgh, PA:* Steven H. Belle, PhD (Principal Investigator), Richard A. Bilonick, PhD (Statistician), Geoffrey Block, MD (Co-Investigator), Jennifer Cline, BS (Data Manager), Marika Haritos, MS (Statistician), KyungAh Im, MS (Statistician), Stephanie Kelley, MS (Data Manager), Sherry Kelsey, PhD (Co-Investigator), Laurie Koozer, BA (Project Coordinator), Sharon Lawlor, MBA (Data Coordinator), Stephen B. Thomas, PhD (Co-Investigator), Abdus Wahed, PhD (Statistician), Yuling Wei, MS (Project Coordinator), Leland J. Yee, PhD (Consultant), Song Zhang, MS, MD (Statistician); *from the National Institute of Diabetes and Digestive and Kidney Diseases:* Patricia Robuck, PhD, MPH (Project Scientist), James Everhart, MD, MPH (Scientific Advisor), Jay H. Hoofnagle, MD (Scientific Advisor), Edward Doo, MD (Scientific Advisor), T. Jake Liang, MD (Scientific Advisor), Leonard B. Seeff, MD (Scientific Advisor); *from the National Cancer Institute:* David E. Kleiner, MD, PhD (Central Pathologist).