Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: McHutchison JG, Lawitz EJ, Shiffman ML, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. N Engl J Med 2009;361:580-93. DOI: 10.1056/NEJMoa0808010.

Appendix Table 1

A: Final Logistic Regression Model* for SVR Status Using Stepwise Variable Selection&

Population: Randomized Patients Who Received at Least One Dose of Study Medication

Effect	Odds Ratio	95% CI	P - Value
METAVIR Fibrosis (F0/1/2 vs F3/4)	2.163	1.627-2.874	<.001
Baseline viral load (IU/mL, ≤ 600,000 vs >600,000)	3.319	2.688-4.099	<.001
Race (Caucasian vs African American)	3.039	2.396-3.855	<.001
Hepatic steatosis (No: 0% vs Yes: >0%)	1.608	1.358-1.903	<.001
Baseline fasting glucose (mmol/L, <5.6 vs ≥ 5.6)	1.428	1.185-1.721	<.001
ALT (Elevated vs Normal)	1.332	1.080-1.644	0.007

B: Final Logistic Regression Model* for Relapse Status Using Stepwise Variable Selection&

Population: Patients Who Were HCV-RNA Negative at End of Treatment and Whose End of Follow-Up Evaluation Was Not Missing

Effect	Odds Ratio	95% CI	P - Value
Treatment (Peg2b 1.0/RBV vs Peg2a/RBV)	0.592	0.436 - 0.803	<0.001
Treatment (Peg2b 1.5/RBV vs Peg2a/RBV)	0.713	0.534 - 0.951	0.02
METAVIR Fibrosis (F3/4 vs F0/1/2)	1.956	1.307 - 2.928	0.001
Baseline viral load (IU/mL, >600,000 vs ≤ 600,000)	2.633	1.872 - 3.705	<0.001
Age(Years, >40 vs ≤ 40)	2.053	1.368 - 3.080	<0.001
Hepatic steatosis (Yes: >0% vs No: 0%)	1.477	1.136 - 1.920	0.004
Baseline fasting glucose (mmol/L, ≥ 5.6 vs <5.6)	1.554	1.185 - 2.039	0.002
ALT (Normal vs Elevated)	1.469	1.073 - 2.012	0.02

*Potential predictors included the following pre-specified factors: treatment regimen (Peg2b 1.0/RBV, Peg2b 1.5/RBV, Peg2a/RBV), METAVIR fibrosis (F0/1/2, F3/4), baseline viral load (IU/mL, ≤ 600,000, >600,000), age(years, ≤ 40, >40), gender (Male, Female), race (Caucasian, African American), hepatic steatosis (No: 0%, Yes: >0%), BMI (≤ 20, >20-25, >25-30, >30), ALT(Elevated , Normal), smoking status (Current, Former, Never), baseline genotype(1A, 1B), assigned ribavirin dose(mg/kg/day, continuous) $, baseline weight (kg, continuous) $, as well as the following three post-hoc factors: baseline fasting glucose (mmol/L, <5.6, ≥ 5.6), baseline hemoglobin (g/dL, continuous) $, and baseline platelet count (continuous) $.

& Model selection: stepwise selection procedure used a significance level of 0.05 for variables to both enter and stay in the final model.

$All continuous variables (baseline hemoglobin, baseline platelet count, assigned ribavirin dose, and baseline weight) were standardized as: (variable value – mean)/Standard Deviation.

Appendix Table 2: P-Values[1] for Treatment by Subgroup Interactions and Other Model Effects for Subgroups Based on Patient Characteristics at Baseline

	Treatment Effect Specification (Pairwise) [2]		
Subgroup/Effect	(Peg2b 1.0, Peg2b 1.5)	(Peg 2b1.5, Peg 2a)	(Peg2b 1.0, Peg 2a)
METAVIR Fibrosis (0/1/2, 3/4)			
Treatment	0.29	0.50	0.71
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.06	0.75	0.11
Baseline viral load (IU/mL, >600,000, ≤ 600.000)			
Treatment	0.47	0.35	0.10
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.99	0.41	0.40
Race (African American, Caucasian)			
Treatment	0.12	0.44	0.02
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.18	0.62	0.06
Age (Years, ≤ 40, >40)			
Treatment	0.23	0.60	0.08
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.46	0.67	0.23
Gender (Male, Female)			
Treatment	0.19	0.83	0.12
Subgroup	0.38	0.04	0.70
Treatment*Subgroup	0.01	0.20	0.23
Hepatic steatosis (No, Yes)			
Treatment	0.50	0.41	0.14
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.88	0.94	0.94
BMI (≤ 20, >20-25, >25-30, >30)			
Treatment	0.80	0.42	0.27
Subgroup	0.87	0.76	0.26
Treatment*Subgroup	0.18	0.16	0.97
ALT (Normal, Elevated)			
Treatment	0.88	0.36	0.44
Subgroup	0.04	0.01	0.24
Treatment*Subgroup	0.20	0.37	0.68

Smoking status (Current, Former, Never)			
Treatment	0.47	0.60	0.21
Subgroup	0.45	0.17	0.94
Treatment*Subgroup	0.13	0.29	0.70
Baseline fasting glucose (mmol/L, <5.6, ≥ 5.6)			
Treatment	0.51	0.43	0.15
Subgroup	<0.001	<0.001	<0.001
Treatment*Subgroup	0.98	0.53	0.55
Baseline genotype (1a, 1b)			
Treatment	0.97	0.97	0.97
Subgroup	0.86	0.46	0.41
Treatment*Subgroup	0.92	0.66	0.84
Baseline weight (kg, continuous)			
Treatment	0.81	0.36	0.25
Subgroup	0.51	0.11	0.14
Treatment* Subgroup	0.94	0.39	0.36
Hemoglobin (g/dL, continuous)			
Treatment	0.52	0.47	0.18
Subgroup	0.61	0.07	0.23
Treatment * Subgroup	0.57	0.50	0.21
Platelet count (continuous)			
Treatment	0.28	0.87	0.36
Subgroup	0.006	<0.001	0.006
Treatment*Subgroup	0.17	0.99	0.17
Assigned ribavirin dose (mg/kg/day, continuous)			
Treatment	0.52	0.88	0.34
Subgroup	0.01	0.03	0.003
Treatment* Subgroup	0.57	0.84	0.36

[1] Table entries are the nominal p-values for the corresponding model effect, obtained from a logistic regression model with SVR status as the dependent variable and treatment, subgroup, and the treatment by subgroup interaction as independent variables.

[2] Treatment effect is a variable with two levels which correspond to the two treatment regimens specified in the column heading.