Poster W1007

Rapid Virologic Response to Peginterferon alfa and Ribavirin Treatment of Chronic Hepatitis C Predicts Sustained Virologic Response and Relapse

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Background

- Assessing viral response to pegylated interferon (PEG-IFN) alfa plus ribavirin (RBV) helps predict treatment outcomes among patients with chronic hepatitis C
- Hepatitis C virus (HCV) RNA levels decrease rapidly after initiation of treatment with IFN-based antiviral therapy[1,2]
- Two important milestones during the early stages of treatment that can help predict treatment outcomes are
  - Rapid virologic response (RVR): undetectable HCV RNA at week 4 of treatment
  - Early virologic response (EVR): undetectable HCV RNA at week 12 of therapy or a ≥2 $\log_{10}$ decline in HCV RNA from baseline at week 12 of therapy
- Virologic response milestones can help individualize therapy so that the likelihood of attaining sustained virologic response (SVR) is maximized and the likelihood experiencing relapse is minimized for each patient
- Virologic response-guided therapy is becoming an increasingly important component of hepatitis C treatment

Aim

- To determine the value of assessing viral kinetics (RVR) during therapy with PEG-IFN alfa plus RBV in predicting relapse and SVR by evaluating relapse rates among patients with and without RVR and by compiling positive predictive values (PPVs) and negative predictive values (NPVs) of RVR for SVR

Methods

Selection of Studies

- Data from published PEG-IFN alfa plus RBV clinical studies in which RVR was assessed and predictive values and relapse rates were provided or able to be calculated
  - RVR was defined as undetectable HCV RNA at week 4 of treatment; the lower limit of detection was <50 IU/mL in most studies
- Predictive values
  - PPV was defined as attaining RVR and SVR
  - NPV was defined as not attaining RVR or SVR
  - If predictive values were not reported but RVR and SVR rates were available, PPVs and NPVs were calculated as follows:

$$\text{PPV} = \frac{\text{Patients who attain RVR and SVR}}{\text{Patients who attain RVR}} \times 100$$

$$\text{NPV} = \frac{\text{Patients who do not attain RVR or SVR}}{\text{Patients who do not attain RVR}} \times 100$$

- Relapse was defined as having undetectable HCV RNA at the end of treatment (EOT) but detectable HCV RNA levels during follow-up
  - If relapse rates were not provided but EOT and SVR rates were available, relapse was calculated as follows:

$$\frac{\text{Patients with undetectable HCV RNA at EOT – patients with detectable HCV RNA during follow-up}}{\text{All patients with EOT}} \times 100$$

  - Actual relapse rates may differ because of patients lost during follow-up

Results

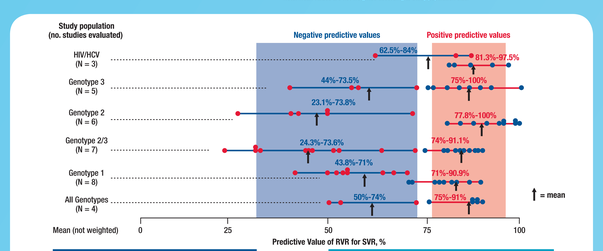
Predictive Value of RVR

- NPV and PPV values for RVR are presented in **Tables 1** and **2** and **Figure 1**
- Overall, the NPV ranged between 23% and 84%
- Overall, the PPV ranged between 71% and 100%

Table 1. Negative and Positive Predictive Values of Rapid Virologic Response for Sustained Virologic Response

	NPV	PPV
	Mean (range [n])	
All genotypes	61.1 (50-74 [3])	86.1 (75-91 [6])
G1	58.1 (44-71 [9])	79.4 (71-91 [7])
G2/3	46.0 (24-74 [11])	83.7 (74-91 [10])
G2	47.8 (23-74 [6])	91.9 (78-100 [10])
G3	58.8 (44-74 [4])	85.3 (75-100 [8])
HIV/HCV	75.9 (63-84 [3])	88.0 (81-98 [5])

n = number of observations for each range; NPV = negative predictive value; PPV = positive predictive value; G = genotype; HCV = hepatitis C virus.
Note: Mean values are not weighted according to study population size.



Note: Ranges may include multiple data points (● or ●) from a single study.

Figure. 1. Overall data summary. NPV = negative predictive value; PPV = positive predictive value; RVR = rapid virologic response; SVR = sustained virologic response.

Table 2. Positive and Negative Predictive Values of Rapid Virologic Response for Sustained Virologic Response

Study	Treatment Regimen	Treatment Duration, wk	RVR, % (n/N) No RVR, % (n/N)	PPV, % (n/N)	NPV, % (n/N)
All genotypes					
Davis et al[1,a]	PEG-IFN alfa-2b (1.5) + RBV (800)	48	29.4 (150/511) 70.6 (361/511)	88.7 (133/150)	— 59.4 (221/361)
Wong et al[1,a]	PEG-IFN alfa-2b (1.5) + RBV (>10.6 mg/kg)	48	30	91	52
Ferenci et al[1,a,b]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	48	66.7 (302/453) 33.3 (151/453)	— —	75 74
			26.6 (119/448)	87 (103/119)	—
Shiffman et al[b]	PEG-IFN alfa-2b (1.5) + RBV (1000-1200)	24/48	36 (117/324)	88 (91/103)	—
	PEG-IFN alfa-2b (1.5) + RBV (1200)	24/48	24 (155/646)	87 (125/144)	—
G1					
Segadas-Soares et al[7]	PEG-IFN alfa-2b (1.5) + RBV (1000-1250)	48	34 (35/103) 66 (68/103)	71 (25/35) —	— 71 (48/68)
Reddy et al[8]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	48	15.8 (90/569)	83.3 (75/90)	—
Jensen et al[9,a,c]	PEG-IFN alfa-2a (180) + RBV (800)	48	16.0 (40/250) 83.2 (208/250)	72.5 (29/40) —	— 64.9 (135/208)
	PEG-IFN alfa-2a (180) + RBV (1000-1200)	48	20.3 (55/271) 77.5 (210/271)	90.9 (50/55) —	— 56.2 (118/210)
Berg et al[10]	PEG-IFN alfa-2a (180) + RBV (800)	48	22.2 (51/230)	84.3 (43/51)	—
		—	77.8 (179/230)	—	56.4 (101/179)
		72	15.6 (35/225)	77.1 (27/35)	—
		—	84.4 (190/225)	—	50.5 (96/190)
Sanchez-Tapias et al[11]	PEG-IFN alfa-2a (180) + RBV (800) Note: All patients had detectable HCV RNA at week 4	48	0 (0/165)	—	67.9 (112/165)
		72	0 (0/161)	—	54.7 (88/161)
Ferenci et al[12]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	24	27.9 (104/373)	77 (80/104)	—
		48[d]	0 (0/105)	—	43.8 (46/105)
		72[e]	0 (0/108)	—	57.4 (62/108)
G2/3					
Dalgard et al[13,d]	PEG-IFN alfa-2b (1.5) + RBV (800-1400)	G2/3: 14	77.9 (95/122)	89.5 (85/95)	—
		G2: 14	91.3 (21/23)	90.5 (19/21)	—
		G3: 14	74.8 (74/99)	89.2 (66/74)	—
		G2/3: 24	22.1 (27/122)	—	44.4 (12/27)
		G2: 24	8.7 (2/23)	—	50 (1/2)
		G3: 24	25.3 (25/99)	—	44.0 (11/25)
Mangia et al[14]	PEG-IFN alfa-2b (1.0) + RBV (1000-1200)	G2/3: 24	64.3 (45/70)	—	—
			35.7 (25/70)	—	52.0 (13/25)
		G2: 24	66.0 (35/53)	88.6 (31/35)	—
			33.9 (18/53)	—	50.0 (9/18)
		G3: 24	58.8 (10/17)	100 (10/10)	—
			41.2 (7/17)	—	57.1 (4/7)
Dalgard et al[15] North-C	PEG-IFN alfa-2b (1.5) + RBV (800-1400)	G2/3: 14	100 (140/140)	81.1 (120/148)	
		G2: 14[b]	100 (29/29)	93 (27/29)	
		G3: 14[b]	100 (110/110)	84 (93/110)	NR
		G2/3: 24	100 (150/150)	90.7 (136/150)	
		G2: 24[b]	100 (31/31)	97 (30/31)	
		G3: 24[b]	100 (115/115)	92 (106/115)	
		G2/3: 24	0 (0/126)	—	45.2 (57/126)
Shiffman et al[16,e] ACCELERATE	PEG-IFN alfa-2a (180) + RBV (800)	G2/3: 16	66.8 (469/732)	79.1 (387/489)	—
			30.0 (220/732)	—	73.6 (162/220)
		G2: 16	69.1 (257/372)	77.8 (200/257)	—
			27.7 (103/372)	—	73.8 (76/103)
		G3: 16	64.2 (230/358)	80.4 (185/230)	—
			32.7 (117/358)	—	73.5 (86/117)
		G2/3: 24	64.3 (470/731)	85.1 (400/470)	—
			33.8 (247/731)	—	55.5 (137/247)
		G2: 24	69.4 (247/356)	85.0 (210/247)	—
			28.1 (100/356)	—	47.0 (47/100)
		G3: 24	59.3 (219/369)	85.4 (187/219)	—
			39.3 (145/369)	—	60.7 (88/145)
Von Wagner et al[17,e]	PEG-IFN alfa-2a (180) + RBV (800-1200) 152 patients were randomly assigned to 16 or 24 weeks' treatment based on RVR status	G2/3 with RVR: 16	100 (71/71)	81.6 (58/71)	—
		G2/3 with RVR: 24	100 (71/71)	80.3 (57/71)	—
		G2/3 without RVR: 24	0 (0/11)	—	63.6 (7/11)
		G2 with RVR: 16	100 (19/19)	94.7 (18/19)	—
		G2 with RVR: 24	100 (19/19)	94.7 (18/19)	—
		G3 with RVR: 16	100 (51/51)	76.5 (39/51)	—
		G3 with RVR: 24	100 (52/52)	75.0 (39/52)	—
Mecenate et al[18]	PEG-IFN alfa-2a (180) + RBV (800-1200) Patients were randomly assigned to 12 or 24 weeks' treatment based on RVR status	G2/3 with RVR: 12	100 (60/60)	74	—
		G2/3 with RVR: 24	100 (60/60)	84	—
		G2/3 without RVR: 24	0 (0/60)	—	46
Yu et al[19]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	G2: 16	86.0 (43/50)	100 (43/43)	—
			14.0 (7/50)	—	42.8 (3/7)
		G2: 24	87.0 (87/100)	97.7 (85/87)	—
			13.0 (13/100)	—	23.1 (3/13)
Willems et al[20]	PEG-IFN alfa-2a (180) + RBV (800)	G2/3: 24	0 (0/21)	—	33.3 (7/21)
		G2/3: 48	0 (0/30)	—	33.3 (10/30)
	PEG-IFN alfa-2a (180) + RBV (1000-1200)	G2/3: 24	0 (0/34)	—	35.3 (12/34)
		G2/3: 48	0 (0/37)	—	24.3 (9/37)
HIV/HCV Coinfection					
Crespo et al[21,f]	PEG-IFN alfa-2b (1.5) + RBV (800)	G1/4: 48	24.2 (16/66)	81.3 (13/16)	84.0 (42/50)
		G1/4: 48	75.8 (50/66)		
		G2/3: 24	55.6 (20/36)	85.0 (17/20)	
		G2/3: 24	44.4 (16/36)	—	62.5 (10/16)
Payan et al[22]	PEG-IFN alfa-2b (1.5) or IFN alfa-2b (3 MU 3× wk) + RBV (800)	48	—	97.5	81.3
Rodrigues-Torres et al[23]	PEG-IFN alfa-2a (180) + RBV (800)	G1: 48	—	82	—
		G2/3: 48	—	94	—

PEG-IFN = pegylated interferon; RBV = ribavirin; NR = not reported; G = genotype; HCV = hepatitis C virus; PPV = positive predictive value; NPV = negative predictive value; RVR = undetectable HCV RNA or >2 $\log_{10}$ decrease from baseline in HCV RNA; PEG-IFN alfa-2b is expressed in μg/kg/wk; PEG-IFN alfa-2a is expressed in μg/wk; RBV is expressed in mg/day except where otherwise stated.
[a] The studies by Davis et al and Wong et al are retrospective analyses of the PEG-IFN alfa-2b + RBV registration study reported by Manns et al (*Lancet* 2001;358:958-965). The study by Ferenci and colleagues is a retrospective analysis of the PEG-IFN alfa-2a + RBV registration study reported by Fried et al (*N Engl J Med*; 2002;347:975-982). The study by Jensen and colleagues is a retrospective analysis of the clinical trial originally reported by Hadziyannis (*Ann Intern Med*. 2004;140:346-355). [b] RVR = undetectable HCV RNA (<50 IU/mL) or >2 $\log_{10}$ drop at week 4. [c] Week 4 virologic data were not available for all patients; hence, RVR = no RVR = 100%. [d] RVR = undetectable (<50 IU/mL) HCV RNA at weeks 4 and 8. [e] RVR = HCV RNA <600 IU/mL at week 4. [f] RVR = undetectable (<100 IU/mL) HCV RNA at week 4. [1] All patients had detectable HCV RNA at week 4 and an unquantifiable or a 2 $\log_{10}$ drop in HCV RNA at week 12. [2] Per-protocol analysis: n = 139 treated for 14 weeks and n = 146 treated for 24 weeks. [3] Patient numbers not available. [4] All patients had detectable HCV RNA at week 4.
[a] Based on patients with undetectable HCV RNA at weeks 4, 12, and 24.

RVR as a Predictor of Relapse

- SVR rates were higher and relapse rates were lower among patients who attained RVR than among those with detectable HCV RNA at week 4 (**Tables 3** and **4**)
  - Relapse rates were as high as 16% among patients who attained RVR and as high as 75% among those who did not attain RVR
  - SVR rates were 64% to 100% and 16% to 77%, respectively

Table 3. End-of-Treatment Response → Sustained Virologic Response → Relapse Among Patients With and Without Rapid Virologic Response

Genotype	RVR	EOTR, % (n)	SVR, % (n)	Relapse, % (n)
1	Yes	73-97 (6)	64-91 (9)	0-16 (8)
	No	56-70 (6)	16-49 (9)	26-75 (6)
2/3	Yes	82-100 (7)	79-91 (9)	2-11 (7)
	No	52-82 (4)	26-76 (11)	4-59 (8)*
2	Yes	91-100 (5)	78-100 (11)	0-10 (7)
	No	50-100 (5)	26-77 (7)	0-43 (5)
3	Yes	90-100 (3)	77-100 (9)	0-16 (5)
	No	41-84 (3)	26-56 (5)	0-33 (3)

RVR = rapid virologic response; EOTR = end-of-treatment response; SVR = sustained virologic response; n = number of observations for each range.
*Data updated since time of abstract submission.

Summary

- Patients who attain RVR have a high likelihood of attaining SVR
- Approximately 50% to 60% of patients who do not attain RVR will also not attain SVR
  - Mean NPVs were 58.1% in G1, 47.8% in G2, and 58.8% in G3 patients
  - However, according to this analysis, NPV (no RVR or SVR) is not sufficiently predictive of treatment failure to warrant withdrawal of treatment at week 4
- Regardless of genotype, the risk for relapse is low among patients who attain RVR
  - Generally, less than 10% of patients with EOT responses who attain RVR will have relapses
  - In contrast, relapse rates are higher among patients with EOT responses who have detectable HCV RNA at week 4

Table 4. End-of-Treatment Responses, Sustained Virologic Responses, and Relapse Rates Among Patients With and Without Rapid Virologic Response

Reference	Treatment/CHC Study Population	Treatment Duration, wk	Patients With RVR, n/N (%)				Patients Without RVR, n/N (%)			
			All	EOTR	SVR	REL	All	EOTR	SVR	REL
Mixed genotype										
Davis et al[1]	PEG-IFN alfa-2b (1.5) + RBV (800)	48	150/511 (29.4)	—	133/150 (88.7)	—	361/511 (70.6)	—	140/361 (38.8)	—
Ferenci et al[b]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	48	302/453 (67)	—	226/302 (75)	—	151/453 (33.3)	—	39/151 (26)	—
G2/3										
Mangia et al[14]	PEG-IFN alfa-2b (1.0) + RBV (1000-1200)	G2/3: 12/24	n = 133	126/133 (95)	113/133 (85)	13/126 (10.3)	n = 80	54/80 (68)	51/80 (64)	3/54 (5.6)
		G2: 12/24	n = 102	98/102 (96)	89/102 (87)	9/98 (9.2)	n = 58	45/58 (78)	42/58 (72)	3/45 (6.7)
		G3: 12/24	n = 31	28/31 (90)	24/31 (77)	4/28 (14.3)	n = 22	9/22 (41)	9/22 (41)	0/9 (0)
		G2/3: 24	n = 45	42/45 (93)	41/45 (91)	1/42 (2.4)	n = 25	13/25 (52)	12/25 (48)	1/13 (7.7)
		G2: 24	n = 35	32/35 (91)	31/35 (89)	1/32 (3.1)	n = 18	10/18 (56)	9/18 (50)	1/10 (10.0)
		G3: 24	n = 10	10/10 (100)	10/10 (100)	0/10 (0)	n = 7	3/7 (43)	3/7 (43)	0/3 (0)
Von Wagner et al[17]	PEG-IFN alfa 2a (180) + RBV (800-1200) 152 patients were randomly assigned to 16 or 24 weeks' treatment based on RVR status	G2/3: 16	n = 71	67/71 (94.4)	58/71 (81.7)	9/67 (13)	—	—	—	—
		G2: 16	n = 19	—	18/19 (94.7)	—	—	—	—	—
		G3: 16	n = 51	—	39/51 (76.5)	—	—	—	—	—
		G2/3: 24	n = 71	60/71 (84.5)	57/71 (80.3)	3/60 (5)	n = 11	8/11 (72)	4/11 (36)	4/8 (50)
		G2: 24	n = 19	—	18/19 (94.7)	—	—	—	—	—
		G3: 24	n = 52	—	39/52 (75.0)	—	—	—	—	—
Dalgard et al[13]	PEG-IFN alfa-2b (1.5) + RBV (800-1400)	G2/3: 14	n = 95	95/95 (100)	85/95 (90)	10/95 (10)	—	—	—	—
		G2: 14	n = 21	21/21 (100)	19/21 (91)	2/21 (9.5)	—	—	—	—
		G3: 14	n = 74	74/74 (100)	66/74 (89)	8/74 (10.8)	—	—	—	—
		G2/3: 24	—	—	—	—	n = 27	22/27 (81.5)	15/27 (56)	7/22 (31.8)
		G2: 24	—	—	—	—	n = 2	1/2 (50)	1/2 (50)	0/1 (0)
		G3: 24	—	—	—	—	n = 25	21/25 (84)	14/25 (56)	7/21 (33.3)
Dalgard et al (North C)[15]	PEG-IFN alfa-2b (1.5) + RBV (800-1400) 298 patients with RVR were randomly assigned to 14 or 24 weeks' treatment	G2/3: 14	n = 148	136/148 (91.9)	120/148 (81.1)	16/148 (10.8)	—	—	—	—
		G2: 14	n = 29	—	27/29 (93)[c]	2/29 (7)[c]	—	—	—	—
		G3: 14	n = 119	—	93/110 (84)[c]	17/110 (16)[c]	—	—	—	—
		G2/3: 24	n = 150	144/150 (96.0)	136/150 (90.7)	8/150 (5.3)	—	—	—	—
		G2: 24	n = 31	—	30/31 (97)[c]	1/31 (3)[c]	—	—	—	—
		G3: 24	n = 119	—	106/115 (92)[c]	9/115 (8)[c]	—	—	—	—
Shiffman et al (ACCELERATE)[16]	PEG-IFN alfa-2a (180) + RBV (800)	G2/3: 16	487/730 (67)	—	(79)	—	243/730 (33)	—	(26)	—
		G2: 16	257/372 (69)	—	(78)	—	115/372 (31)	—	(26)	—
		G3: 16	230/358 (64)	—	(80)	—	128/358 (36)	—	(26)	—
		G2/3: 24	466/725 (64)	—	(85)	—	259/725 (36)	—	(45)	—
		G2: 24	247/356 (69)	—	(85)	—	109/356 (31)	—	(53)	—
		G3: 24	219/369 (59)	—	(85)	—	150/369 (41)	—	(39)	—
Willems et al[20] Post hoc analysis of patients without RVR from Hadziyannis[24] and Fried[25] studies	PEG-IFN alfa-2a (180) + RBV (800)	24[a]	—	—	—	—	n = 21	—	14/21 (67)	5/19 (26)
		48[a]	—	—	—	—	n = 30	—	20/30 (67)	3/23 (13)
	PEG-IFN alfa-2a (180) + RBV (1000-1200)	24[a]	—	—	—	—	n = 34	—	22/34 (65)	7/29 (24)
		48[a]	—	—	—	—	n = 37	—	28/37 (76)	1/27 (4)
		48[b]	—	—	—	—	—	—	61	—
Yu et al[19]	PEG-IFN alfa-2a (180) + RBV (1000-1200)	G2: 16-week treatment arm	43/50 (86)	43/43 (100)	43/43 (100)	0/43 (0)	7/50 (14)	7/7 (100)	4/7 (57)	3/7 (42.9)
		G2: 24-week treatment arm	87/100 (87)	87/87 (100)	85/87 (98)	2/87 (2.3)	13/100 (13)	11/13 (84.6)	10/13 (77)	1/11 (9.1)
G1										
Segadas-Soares et al[7]	PEG-IFN alfa-2b (1.5) + RBV (1000-1250)	48[a]	51/167 (31)	—	38/51 (75)	—	116/167 (69)	—	27/116 (23)	—
Jensen et al[9] Post hoc analysis of Hadziyannis et al[24]	PEG-IFN alfa-2a (180) + RBV	RBV 800: 24 (n = 101)	18/101 (18)	17/18 (94)	16/18 (89)	1/17 (6)	81/101 (80)	51/81 (63)	13/81 (16)	38/51 (75)
		RBV 1000-1200: 24 (n = 118)	33/118 (28)	32/33 (97)	29/33 (88)	3/32 (9)	84/118 (71)	59/84 (70)	19/84 (23)	40/59 (68)
		RBV 800: 48 (n = 250)	40/250 (16)	29/40 (73)	29/40 (73)	0/29 (0)	208/250 (83)	116/208 (56)	73/208 (35)	43/116 (37)
		RBV 1000–1200: 48 (n = 271)	55/271 (20)	52/55 (93)	49/52 (91)	3/52 (6)	210/271 (77)	132/210 (63)	92/210 (44)	40/132 (30)
Berg et al[10]	PEG-IFN alfa 2a (180) + RBV (800) G1 patients with HCV RNA >1000 IU/mL at baseline	48	51/230 (22)	46/51 (90.2)	43/51 (84)	3/46 (7)	179/230 (77.8)	—	78/179 (44)	—
		72	35/225 (16)	32/35 (91.4)	27/35 (77)	5/32 (16)	190/225 (84.4)	—	94/190 (49)	—
Sanchez-Tapias et al[11]	PEG-IFN alfa-2a (180) + RBV (800)	No RVR: 48	—	—	—	—	n = 165	101/165 (61)	53/165 (32)	48/101 (48)*
		No RVR: 72	—	—	—	—	n = 161	99/161 (61)	73/161 (45)	26/99 (26)
		RVR: 24 (G2/3, G1 LVL)	n = 148	—	117/148 (79)	—	—	—	—	—
		RVR: 48 (G1 HVL)	n = 46	—	29/46 (64)	—	—	—	—	—
HIV/HCV										
Crespo et al[21]	PEG-IFN alfa-2b (1.5) + RBV (800)	G1/4: 48	16/66 (24)	13/16 (81)	13/16 (81)	0/13 (0)	50/66 (76)	13/50 (26)	8/50 (16)	5/13 (38)
		G2/3: 24	20/36 (56)	18/20 (90)	17/20 (85)	1/18 (5.5)	16/36 (44)	11/16 (69)	6/16 (38)	5/11 (45.5)

CHC = chronic hepatitis C; RVR = rapid virologic response; EOTR = end-of-treatment response; SVR = sustained virologic response; REL = relapse rate; PEG-IFN = pegylated interferon; RBV = ribavirin; G = genotype; HCV = hepatitis C virus; LVL = low viral load; HVL = high viral load. PEG-IFN alfa-2b is expressed in μg/kg/wk; PEG-IFN alfa-2a is expressed in μg/wk; RBV is expressed in mg/day.
[a] P = .003 vs 72-week arm.
[b] Cohort included treatment-naive patients (62%), nonresponders (25%), and relapsers (13%). [c] Patients with available HCV RNA test results 24 weeks after the end of treatment.

Conclusions

- RVR is an excellent positive but a poor negative predictor for SVR; relapse rates are lower in patients who attain RVR than in those who do not
- RVR is a powerful tool and can be a patient motivator in future studies and a component of response-guided therapy in clinical practice
- The relative value of RVR for predicting SVR, relapse, or both with PEG-IFN alfa-2a– or alfa-2b–based therapy cannot be determined from these studies because of variations in study designs
  - However, preliminary results from the IDEAL trial, the largest study comparing the 2 regimens, demonstrated lower relapse rates with PEG-IFN alfa-2b (1.5 mg/kg/wk)–based therapy than with PEG-IFN alfa-2a–based therapy (24% vs 32% [95% CI –13.2%, –2.8%])[26]

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