

Hepatitis C Emerging Therapy Update: Reports From the Liver Meeting 2012



Project ID: 5021

Target Audience This activity has been designed to meet the educational needs of gastroenterologists, hepatologists, physician assistants, and nurse practitioners involved in the care of patients with Hepatitis C.

Statement of Need/Program Overview The purpose of this activity is to enhance the care of patients with Hepatitis C.

Objectives Upon completion of this activity, the participant will be better prepared to:

- To assess the efficacy and safety of new antiviral agents currently under development for the treatment of chronic hepatitis C
- To recognize the advantages offered by the new antiviral agents currently under development for the treatment of chronic hepatitis C when compared to current therapy with boceprevir or telaprevir + PegIFN + RBV

Format This activity is an enduring material and consists of an eNewsletter.

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Triple therapy regimens for the treatment of genotype 1 hepatitis C have been standard therapy since 2011.¹ The current treatment regimens include pegylated interferon (PegIFN), ribavirin (RBV), and a direct-acting antiviral (DAA) agent. Physicians can choose between two DAA agents, either boceprevir (Victrelis®) or telaprevir (Incivek™). Sustained viral response (SVR) rates with triple-therapy regimens have improved considerably when compared to earlier treatment regimens with interferon (IFN) or PegIFN monotherapy or IFN or PegIFN used in combination with RBV. A registration trial for boceprevir combined with PegIFN and RBV reported an overall SVR rate of 63% in previously untreated genotype 1 patients compared to an SVR rate of 38% for patients treated with PegIFN and RBV in a control arm of the study; the treatment duration in both arms of the study was 48 weeks.^{1,2} A similar overall SVR rate of 75% was reported for a registration trial utilizing telaprevir combined with PegIFN and RBV in previously untreated genotype 1 patients compared to an SVR rate of 44% for patients treated with PegIFN and RBV in a control arm of the study; the treatment duration in both arms of the study was 48 weeks.^{1,3} The current standard of care for previously untreated genotype 2 or 3 patients is dual therapy with PegIFN and RBV for a duration of 24 weeks; response rates reported for genotype 2 or 3 patients range from 70% up to 90%.⁴

Current treatment regimens are demanding, both for the patient and for health professionals caring for the patient. Efficacy is compromised in certain patient types, such as patients who have failed previous therapy, cirrhotic patients and black patients, the limitation of injection administration, long recommended treatment durations ranging from 24 to 48 weeks or longer, and side effects are common and can be severe.^{1,4} Thus, the search continues for improved therapeutic alternatives. This newsletter is based on an overview by Robert S. Brown, Jr., MD, MPH,* of data from selected new therapies for chronic hepatitis C presented at the The Liver Meeting® 2012, the 63rd Annual Meeting of the American Association for the Study of Liver Diseases, which took place November 9 - 13, 2012 in Boston, MA. Table 1 lists the new agents reviewed in this newsletter along with the sponsoring corporation and the mechanisms of action. The goals for improved therapeutic regimens for the treatment of chronic hepatitis C, compared to current PegIFN/RBV treatment regimens, are listed in Table 2.

Agent	Sponsor	Activity
Oral Direct-Acting Antivirals		
ABT-267	Abbott	NS5A inhibitor
ABT-333	Abbott	Non-nucleoside NS5B polymerase inhibitor
ABT-450	Abbott	NS3/4 protease inhibitor
BI201335 (Feldaprevir)	Boehringer Ingelheim	NS3/4A protease inhibitor
BI207127	Boehringer Ingelheim	Non-nucleoside NS5B polymerase inhibitor
BMS-650032 (Asunaprevir)	Bristol-Myers Squib	NS3 protease inhibitor
BMS-790052 (Daclatasvir)	Bristol-Myers Squib	NS5A replication complex inhibitor
BMS-791325	Bristol-Myers Squib	Non-nucleoside NS5B polymerase inhibitor
GS-7977 (Sofosbuvir)	Gilead	Uridine nucleotide analog NS5B polymerase inhibitor
GS-5885	Gilead	NS5A protein inhibitor
TMC435	Janssen	NS3/4A protease inhibitor
Interferon		
Peginterferon Lambda-1a	Bristol-Myers Squib	Type III interferon immune modular

Table 1: Selected antivirals under development for the treatment of chronic hepatitis C utilized in studies reported at The Liver Meeting® 2012.

Compared to PegIFN/RBV, new therapeutic regimens for the treatment of chronic hepatitis C should offer:
<ul style="list-style-type: none"> • Improved efficacy • Efficacy in all patient types including previously treated patients, cirrhotic, and black patients • Oral effectiveness, IFN-free • Shorter treatment duration • Improved side-effect profile

Table 2: Goals for new therapeutic regimens for the treatment of chronic hepatitis C.

Oral IFN-free DAA HCV therapeutic regimens

Feldaprevir (BI201335) + BI207127 ± RBV in treatment naive genotype 1 HCV patients. Zeuzem et al presented the final results of the SOUND-C2 Phase IIB clinical trial, which utilized feldaprevir (an NS3/4A protease inhibitor) and BI207127 (a non-nucleoside NS5B polymerase inhibitor) ± RBV administered to treatment-naive genotype 1 HCV patients.⁵ Of the five study arms reported, the most effective dosing regimen consisted of feldaprevir 120 mg QD + BI 207127 600 mg twice daily + RBV 1000 - 1200 mg QD administered for 28 weeks. This regimen resulted in an SVR at 12 weeks following completion of therapy (SVR12) of 69% (54/75 patients treated; intent to treat [ITT] analysis). Genotype 1b patients were more responsive to this regimen than genotype 1a patients, with an 85% (41/48) SVR12 rate for 1b patients compared to a 43% (13/30) SVR12 rate for genotype 1a patients. IL28B patient genotype also influenced SVR12 rates; CC genotype patients had an 84% (16/19) SVR12 rate, while non-CC genotype patients had a 64% (38/59) SVR12 rate. SVR12 rates were lowest in the treatment arm that did not utilize RBV

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and therefore, RBV was considered a necessary component of feldaprevir/BI207127 treatment. The tolerability of the feldaprevir 120 mg QD + BI 207127 600 mg twice daily + RBV 1000 - 1200 mg QD treatment regimen was the most favorable of the 5 treatment arms, with an 8% discontinuation rate due to adverse experiences.

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Sofosbuvir (GS-7977) + RBV ± GS-5885 in genotype 1 treatment naïve and prior null responders. The ELECTRON trial investigated the effectiveness of sofosbuvir (a uridine nucleotide analog NS5B polymerase inhibitor) ± RBV in genotype 1, 2, and 3 patients.⁶ The ELECTRON study consisted of 11 arms and included both treatment-naïve and treatment-experienced patients. High rates for SVR24 were observed with sofosbuvir + RBV administered for 12 weeks in treatment naïve (100%) genotype 2/3 HCV patients; treatment-experienced genotype 2/3 patients treated with sofosbuvir + RBV for 8 weeks achieved an SVR12 rate of 64%. While 12 weeks of sofosbuvir + RBV produced an SVR12 rate of 84% in treatment-naïve genotype 1 patients, the SVR12 rate was only 10% for prior null-responder genotype 1 patients. The trial was extended to determine if the addition of a second DAA agent, an NS5A protein inhibitor, GS-5885, would enhance responses in genotype 1 patients. The combination of sofosbuvir + GS-5885 + RBV administered for 12 weeks resulted in an SVR4 of 100% in both treatment-naïve and prior null-responder genotype 1 HCV patients. It should be noted, however, that while SVR4 rates were available for all patients (n=25) in the treatment-naïve arm, only 3 patients were included in the analysis of prior null-responder patients (n=9). The authors concluded that the addition of GS-5885 increased the efficacy of sofosbuvir + RBV; no additional safety or tolerability issues were detected.

Efficacy of Sofosbuvir (GS-7977) + RBV in difficult to treat genotype 1 patients. The SPARE trial investigated the effects of sofosbuvir (a uridine nucleotide analog NS5B polymerase inhibitor) + RBV in difficult-to-treat genotype 1 HCV patients.⁷ Subjects included those with IL28B CT/TT genotype, high HCV viral load, high body mass index, black race, and advanced liver fibrosis. Patient baseline demographics are listed in Table 3. In 2 arms of the trial, sofosbuvir (400 mg daily) was studied with either full-dose RBV (1000 – 2000 mg daily; n = 25) or reduced-dose RBV (600 mg daily; n = 25) administered for 24 weeks. The intent-to-treat SVR4 rate was 72% when sofosbuvir was used with full-dose RBV and 56% when used with low-dose RBV. A third arm of the study limited

enrollment to patients with early-stage liver fibrosis but had patient demographics that were otherwise similar to the other 2 study arms. Ten patients in the third arm received sofosbuvir + full-dose RBV for 24 weeks and achieved an intent-to-treat SVR12 rate of 90%; the modified intent-to-treat SVR12 rate was 100%. There were no safety issues or drug-related discontinuations in this study.

	Sofosbuvir + Full-Dose RBV (N=25)	Sofosbuvir + Low-Dose RBV (N=25)	Sofosbuvir + Full-Dose RBV (N=10)
Median age (range)	54 (30 – 65)	55 (26 – 78)	54 (30 – 65)
Male sex (%)	20 (80%)	14 (56%)	4 (40%)
Genotype 1a (%)	20 (80%)	16 (64%)	6 (60%)
African American (%)	18 (72%)	23 (92%)	9 (90%)
Median BMI (range)	28 (22 – 44)	30 (19 – 47)	26 (22 – 43)
IL28B CT/TT (%)	21 (84%)	21 (84%)	6 (67%)
Median HCV RNA log (IQR)	6.16 (5.37 – 6.41)	6.05 (5.49 – 6.36)	6.85 (5.80 – 7.21)
Advanced fibrosis (%)	6 (24%)	7 (28%)	0

Table 3: Baseline patient demographics for the SPARE trial, a study of sofosbuvir + RBV in difficult-to-treat HCV-infected genotype 1 patients.⁷

Daclatasvir (BMS-790052)+ sofosbuvir (GS-7977) ± RBV in treatment naïve patients chronically infected with HCV genotype 1, 2, or 3. Sulkowski and colleagues reported on the efficacy and safety of daclatasvir (an NS5A replication complex inhibitor) + sofosbuvir (a uridine nucleotide analog NS5B polymerase inhibitor) ± RBV in treatment-naïve patients chronically infected with HCV genotype 1, 2, or 3.⁸ The study consisted of 7 arms, 3 for genotype 2/3 with a total of 44 patients, and 5 for genotype 1 with a total of 126 patients (Table 4). SVR4 rates for the various study arms are illustrated in Figure 1. Depending on treatment regimen, HCV patients with genotype 1, 2 or 3 treated with daclatasvir + sofosbuvir ± RBV achieved SVR4 rates between 86% and 100%. The virologic response did not vary according to IL28B genotype, viral subtype, or the administration of RBV. Daclatasvir + sofosbuvir with or without RBV was generally well tolerated.

<ul style="list-style-type: none"> • Randomized 44 genotype 1 and 44 genotype 2/3, non-cirrhotic HCV patients 1:1:1 to: <ul style="list-style-type: none"> – Sofosbuvir for 7 days, then daclatasvir + sofosbuvir for 23 weeks – Daclatasvir + sofosbuvir for 24 weeks – Daclatasvir + sofosbuvir + RBV for 24 weeks • An additional 82 genotype 1 patients were randomized 1:1 to daclatasvir + sofosbuvir or daclatasvir + sofosbuvir ± RBV for 12 weeks • Dosing: <ul style="list-style-type: none"> – Daclatasvir 60 mg daily – Sofosbuvir 400 mg daily – RBV 1000 - 1200 mg per day in genotype 1 and 800 mg per day in genotype 2/3 patients

Table 4: Study design and dosing for daclatasvir + sofosbuvir ± RBV in treatment-naïve patients chronically infected with HCV genotype 1, 2, or 3.⁸

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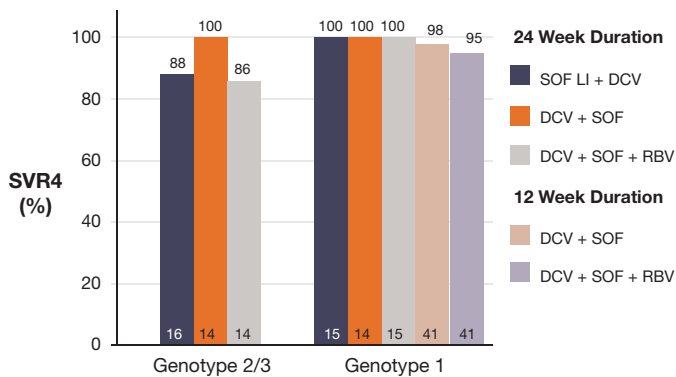


Figure 1: SVR4 rates for treatment-naïve patients infected with HCV genotype 2/3 or genotype 1 treated with differing regimens of daclatasvir (DCV) + sofosbuvir (SOF) ± ribavirin (RBV). SOF lead-in (LI) patients received 1 week of sofosbuvir monotherapy followed by sofosbuvir + daclatasvir for 23 weeks.⁸

Daclatasvir (BMS-790052) + asunaprevir (BMS-650032)+BMS-791325 regimen for treatment-naïve genotype 1 HCV patients. Everson and colleagues reported on an IFN-free and RBV-free study of daclatasvir (an NS5A replication complex inhibitor) + asunaprevir (an NS3 protease inhibitor) + BMS-791325 (a non-nucleoside NS5B polymerase inhibitor) treatment regimen in treatment-naïve genotype 1 HCV patients.⁹ Patients (N=32) were randomized 1:1 to receive daclatasvir (60 mg daily) + asunaprevir (200 mg BID) + BMS-791325 (75 mg BID) for either 24 or 12 weeks. The SVR4 rates are illustrated in Figure 2. The IFN-free and RBV-free triple DAA combination resulted in 94% SVR4 rates after both 12 and 24 weeks of treatment. The combination of daclatasvir + asunaprevir + BMS-791325 was well tolerated, and no patients discontinued due to adverse events.

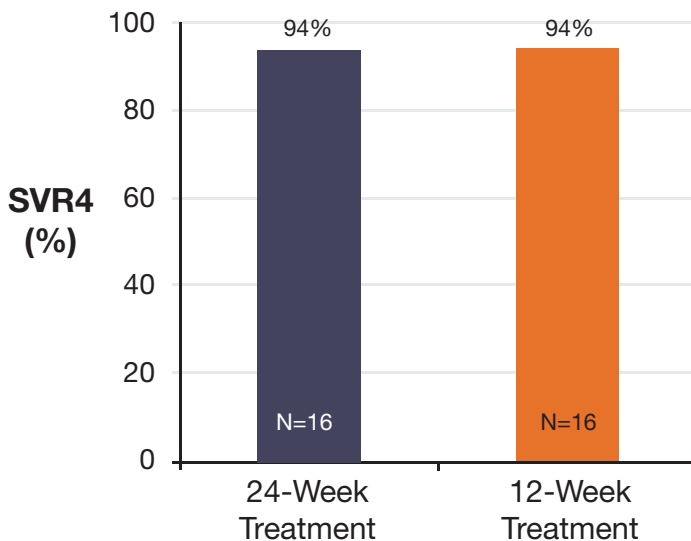


Figure 2: SVR4 rates for treatment-naïve patients infected with HCV genotype 1 treated with daclatasvir + asunaprevir + BMS-791325 for 24 weeks or 12 weeks.⁹

ABT-450r, ABT-267, ABT-333 and RBV in treatment naïve and prior null responders with genotype 1 HCV infection. The results of a study utilizing various combinations of ABT-450r (an NS3/4 protease inhibitor dosed with ritonavir), ABT-267 (an NS5A inhibitor), ABT-333 (a non-nucleoside NS5B polymerase inhibitor) and RBV were reported by Kowdley and associates.¹⁰ Trial data reported at The Liver Meeting® 2012 consisted of 5 arms for treatment naïve genotype 1 HCV patients and 2 arms for prior null-responder genotype 1 HCV patients. ABT-450/r was dosed at either 100 mg/100 mg or 200 mg/100 mg daily, ABT-267 was dosed at 25 mg daily, ABT-333 was dosed at 400 mg BID, and RBV was weight-dosed. Intent-to-treat SVR12 rates for 5 study arms in treatment-naïve patients and 2 study arms in prior null responders are illustrated in Figure 3. The 12-week 3 DAA + RBV regimens showed the greatest efficacy in both treatment-naïve (SVR12 = 97.5%) and prior null-responder (SVR12 = 93.3%) populations. High SVR12 rates were observed in both IL28B CC and IL28B non-CC genotypes and in both 1a and 1b HCV genotypes. No study-drug-related serious adverse events were observed, and only 2 of 448 patients discontinued treatment due to adverse events attributed to a study drug by the investigator. Fatigue, headache, insomnia, and nausea were the most common adverse events reported.

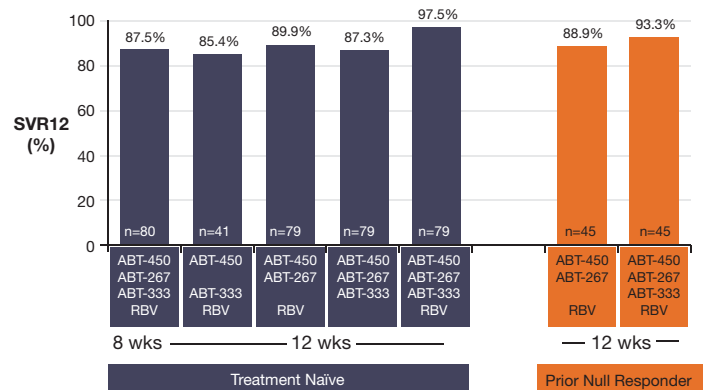


Figure 3: SVR12 rates in treatment-naïve and prior null-responder genotype 1 HCV patients treated with varying combinations of ABT-450/r, ABT-267, ABT-333 and ribavirin for 8 or 12 weeks.¹⁰

A new pegylated interferon

PegIFN lambda-1a compared to PegIFN alfa-2a in treatment naïve genotype 1 and 4 HCV patients. The efficacy and safety of 120-µg, 180-µg and 240-µg doses of PegIFN lambda-1a compared to a 180-µg dose of PegIFN alfa-2a was evaluated in treatment-naïve genotype 1 and 4 HCV patients enrolled in the phase 2b EMERGE trial.¹¹ PegIFN lambda-1a is a type III IFN that exerts antiviral effects through a unique receptor with limited distribution outside the liver, which may result in

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an improved tolerability profile compared to PegIFN alfa-2a. EMERGE efficacy and safety results are summarized in Table 5. Compared to PegIFN alfa, treatment with PegIFN lambda was associated with comparable efficacy, but with an improved safety profile. The authors indicated that the 180- μ g dose was selected for Phase III PegIFN lambda-1a trials.

Efficacy and safety results, %	Lambda 120 μ N=98	Lambda 180 μ N=102	Lambda 240 μ N=104	Alfa 180 μ N=103
HCV RNA undetectable				
RVR (Week 4)	6.1	14.7	16.3	5.8
SVR 24 (Week 72)	45.9	37.3	39.4	36.9
Adverse events/dose reductions				
Serious adverse events	6.1	2.9	8.7	6.8
IFN dose reductions	6.1	7.8	73.1*	28.2
RBV dose held/reduced	11.2	10.8	11.5	33.0
Flu-like symptoms	17.3	12.7	7.7	45.6
Musculoskeletal symptoms	21.4	15.7	21.2	46.6
Laboratory abnormalities				
Hemoglobin <10 g/dL or >3.4 g/dL below baseline	27.8	22.8	18.6	62.1
Neutrophils <1000/mm ³	1.0	2.0	1.0	42.7
Platelets <100,000/mm ³	0	2.0	0	19.4
ALT >5 x ULN	1.0	1.0	9.8	3.9
Direct bilirubin >1.2 mg/dL	0	5.0	12.7	1.9

*Study protocol modified May 2011 and lambda 240- μ g dose was reduced to 180 μ g due to increased hepatic laboratory abnormalities.

Table 5: Efficacy and safety results for three dosages of peginterferon lambda-1a + weight-based RBV compared to peginterferon alfa-1a + weight-based RBV.¹¹

IFN plus DAA HCV therapeutic regimens

Sofosbuvir (GS-7977) + PegIFN + RBV in treatment naïve patients with HCV genotype 1, 4, and 6. The results of the ATOMIC trial, a Phase IIb study of sofosbuvir (a uridine nucleotide analog NS5B polymerase inhibitor) + PegIFN + RBV in treatment-naïve genotype 1, 4, and 6 HCV patients, were reported by Hassanein et al.¹² The trial consisted of 3 arms: 1) Sofosbuvir (400 mg) + PegIFN + RBV for 12 weeks in genotype 1 patients, 2) Sofosbuvir (400 mg) + PegIFN + RBV for 24 weeks in genotype 1, 4, and 6 patients, and 3) Sofosbuvir (400 mg) + PegIFN + RBV for 12 weeks followed by either sofosbuvir monotherapy or sofosbuvir + RBV for an additional 12 weeks in genotype 1 patients. Overall, SVR12 was achieved by 90% or more of patients in each arm of the study (Figure 4). The SVR12 rate for patients infected with genotype 4 (n=11) in the 24 week sofosbuvir + PegIFN + RBV study arm was 82%; the SVR12 rate for patients infected with genotype 6 (n=5) was 100%. All regimens were well tolerated with a safety profile similar to that of PegIFN + RBV.

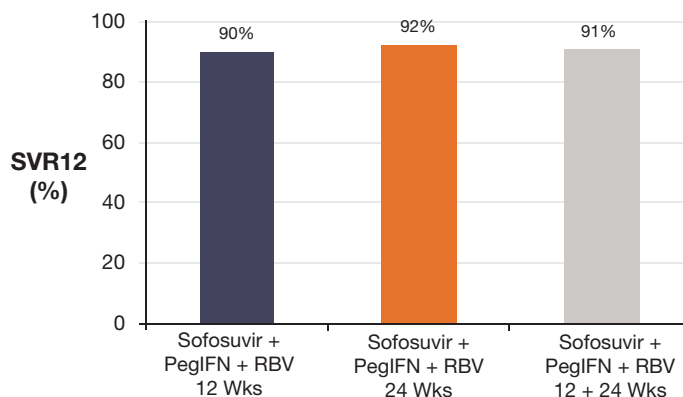


Figure 4: SVR12 rates for the three arms of the ATOMIC trial in genotype 1, 4, and 6 HCV patients. Sofosbuvir + PegIFN + RBV was administered for either 12 or 24 weeks, or for 12 weeks followed by 12 weeks of sofosbuvir or 12 weeks of sofosbuvir + RBV.¹²

Efficacy and tolerability of simeprevir (TMC435) + PegIFN + RBV for treatment of HCV genotype 1 infection in patients with Metavir score F3 and F4. A post hoc analysis of subsets of genotype 1 HCV patients with Metavir score F3 and F4 enrolled in the PILLAR and ASPIRE trials was presented by Poordad and colleagues.¹³ Patients in the PILLAR trial were treatment naïve and received PegIFN + RBV alone or in combination with simeprevir (an NS3/4A protease inhibitor) at doses of 75 or 150 mg once daily for 12, 24 or 48 weeks. The PILLAR analysis included only patients with Metavir F3. Patients in ASPIRE were treatment-experienced and received PegIFN + RBV alone or in combination with simeprevir at doses of 100 or 150 mg once daily for 12, 24 or 48 weeks. Patients in the ASPIRE analysis included both Metavir F3 and F4 patients. Response guided total PegIFN/RBV duration was 24 or 48 weeks in PILLAR and 48 weeks in ASPIRE. The post hoc analysis evaluated efficacy and safety for those patients receiving simeprevir 150 mg in either trial and treatment duration groups were pooled. SVR24 rates for patients receiving either PegIFN/RBV or simeprevir + PegIFN/RBV are illustrated in Figure 5. SVR24 rates in treatment-experienced F3/F4 patients varied according to prior response to PegIFN/RBV; SVR rates were 65% (17/26) in prior relapsers, 67% (14/21) in prior partial responders, and 33% (7/21) in prior null responders. Simeprevir was generally well tolerated, with comparable rates between simeprevir + PegIFN + RBV and PegIFN + RBV in F3/F4 patients for adverse events, hematologic laboratory toxicities, and incidences of rash and anemia. Transient mild-to-moderate bilirubin elevations, not associated with ALT/AST changes, rarely led to discontinuation.

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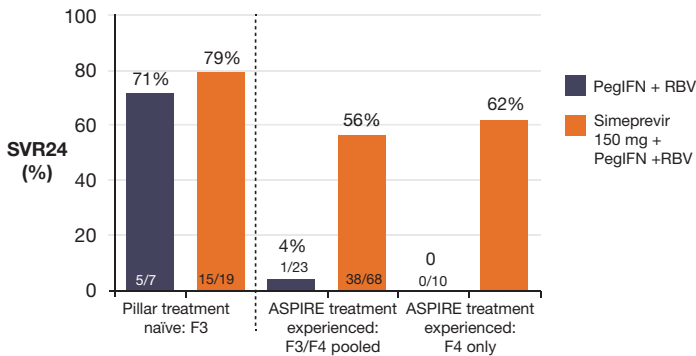


Figure 5: SVR24 rates in Metavir F3 and F4 patients who received simeprevir + PegIFN + RBV compared to PegIFN + RBV. Post hoc analysis performed on F3 patients from the PILLAR (treatment-naïve) trial and F3/F4 patients from the ASPIRE (treatment-experienced) trial.¹³

Pooled safety analysis of PILLAR and ASPIRE trials:
Simeprevir (TMC435) + PegIFN + RBV compared to PegIFN + RBV. Fried and associates reported on the safety analysis of pooled data from the PILLAR (treatment-naïve genotype 1 HCV patients) and ASPIRE (treatment-experienced genotype 1 HCV patients) trials.¹⁴ The analysis included only the 150-mg daily dose of simeprevir + PegIFN + RBV (PILLAR and ASPIRE combined N = 355) compared to PegIFN + RBV (PILLAR and ASPIRE combined N = 143) from each trial. Simeprevir 150 mg daily was the dose chosen for Phase III trials. Data for selected adverse events are presented in Table 6. Simeprevir + PegIFN + RBV was well tolerated by both treatment-naïve and treatment-experienced HCV patients. The incidence of overall and serious adverse events for simeprevir + PegIFN + RBV was similar to the incidence in the PegIFN + RBV control arms of the studies. No difference in mean change over time in hemoglobin, platelets, or neutrophils was observed between simeprevir and control patients. Transient bilirubin elevations were mild and reversible and were not associated with AST/ALT elevations.

Proportion of Patients, %	PILLAR and ASPIRE combined: Overall treatment duration	
	Peg/IFN + RBV n=143	Simeprevir 150 mg + PegIFN +RBV n=355
Grade 3 or 4 AEs	31	35
Serious AEs	6	9
AEs leading to simeprevir/placebo discontinuation	2	5
AEs leading to discontinuation of any study drug	9	9
AEs most frequently reported (>25% of patients in pooled overall simeprevir 150 mg group)		
Fatigue	46	74
Influenza-like illness	29	5
Pruritus (all types)	34	37
Headache	45	41
Nausea	25	26
AEs of clinical interest (regardless of causality; documented with other agents in the protease inhibitor class)		
Rash or pruritus combined (all types)	24	29
Rash (all types), Grade 3	0	1
Rash (all types), Grade 4	0	0
Anemia, at least Grade 2	11	11
Neutropenia	19	26

Table 6: Pooled safety analysis from the PILLAR and ASPIRE trials of simeprevir 150 mg + PegIFN + RBV compared to PegIFN + RBV.¹⁴

Summary

Significant improvements in the treatment of hepatitis C appear imminent based on reports of studies presented at The Liver Meeting® 2012. Although most data are preliminary, depending on the treatment regimen, efficacy in 100% of genotype 1 patients appears possible. Several IFN-free, orally effective combinations of DAA agents avoid the problems associated with injecting IFN and, more importantly, the significant side effects associated with IFN. Preliminary results suggest that IFN-free combinations of DAA agents can be as effective as IFN-containing treatment regimens. Treatment regimens with a duration of 12 weeks have shown excellent efficacy, which is a welcome improvement compared to the 24- to 48-week treatment duration recommended for current therapy for genotype 1 chronic HCV (boceprevir or telaprevir in combination with PegIFN/RBV). Additional data are needed for difficult-to-treat patients including those with cirrhosis and black patients.

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Posttest

If you wish to receive acknowledgement of participation for this activity, please complete this posttest, evaluation form, and request for credit (pages 8-11) and fax to 973-939-8533.
Required with 70% passing

- 1. Which of the following statements is true concerning the SOUND-C2 clinical trial that utilized feldaprevir + BI207127 ± ribavirin?**
 - a. Patients with genotype 1a HCV had a higher SVR12 rate than those with genotype 1b
 - b. IL28B non-CC patients had a higher SVR12 rate than CC patients
 - c. Ribavirin was not considered a necessary component of the treatment regimen
 - d. The most effective dosing regimen consisted of feldaprevir 120 mg QD + BI207127 600 mg twice daily + ribavirin 1000 - 1200 mg QD administered for 28 weeks

- 2. In an extension of the ELECTRON trial, the addition of GS-5885 to sofosbuvir + ribavirin:**
 - a. Achieved 100% SVR4 rates in both treatment-naïve and prior null-responder genotype 1 HCV patients
 - b. Had little effect on SVR4 response rates for either treatment-naïve or prior null-responder patients compared to sofosbuvir + ribavirin
 - c. Enhanced SVR4 rates in treatment-naïve, but not in prior null-responder patients
 - d. Was terminated early because of safety/tolerability issues with GS-5885

- 3. The study of daclataxvir + sofosbuvir ± ribavirin in treatment-naïve patients infected with HCV genotype 1, 2, or 3 found that:**
 - a. Patients with genotype 1a HCV were more responsive than those with genotype 1b
 - b. IL28B non-CC patients were more responsive than CC patients
 - c. Ribavirin was not considered a necessary component of the treatment regimen
 - d. Treatment durations of 48 weeks provided the best SVR4 rates

- 4. Comparing PegIFN lambda-1a to PegIFN alfa-2a:**
 - a. PegIFN lambda-1a is orally effective; PegIFN alfa-2a must be given parenterally
 - b. PegIFN lambda-1a exerts antiviral effects through a unique receptor with limited distribution outside the liver resulting in improved tolerability compared to PegIFN alfa-2a
 - c. The dose of PegIFN lambda-1a is one-half that of PegIFN alfa-2a, thus resulting in improved tolerability
 - d. The incidence of adverse events and laboratory abnormalities for PegIFN lambda-1a 180 µg was similar to the incidence for PegIFN alfa-2a 180 µg

- 5. Potential advances in the treatment of chronic hepatitis C as reported at The Liver Meeting® 2012 suggest all of the following appear possible with agents currently being studied except:**
 - a. Efficacy in 100% of genotype 1 HCV patients
 - b. IFN-free, orally effective combinations of DAA agents
 - c. Improved side-effect profiles compared to PegIFN/RBV
 - d. Treatment durations as short as 2 weeks

Evaluation

Annenberg Center for Health Sciences at Eisenhower respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form.

How well did this activity meet the following learning objectives?

	<i>This learning objective did (or will) increase/ improve my:</i>	<i>High Impact</i>	<i>Moderate Impact</i>	<i>No Impact</i>	<i>Not Applicable</i>
<ul style="list-style-type: none"> To assess the efficacy and safety of new antiviral agents currently under development for the treatment of chronic hepatitis C 	Knowledge	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Competence	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Performance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Patient Outcomes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<ul style="list-style-type: none"> To recognize the advantages offered by the new antiviral agents currently under development for the treatment of chronic hepatitis C when compared to current therapy with boceprevir or telaprevir + PegIFN + RBV 	Knowledge	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Competence	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Performance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Patient Outcomes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Impact of the Activity

• Please indicate which of the following American Board of Medical Specialties/Institute of Medicine core competencies were addressed by this educational activity (*select all that apply*):

- | | | |
|--|--|--|
| <input type="checkbox"/> Patient care or patient-centered care | <input type="checkbox"/> Interdisciplinary teams | <input type="checkbox"/> System-based practice |
| <input type="checkbox"/> Practice-based learning and improvement | <input type="checkbox"/> Professionalism | <input type="checkbox"/> Utilize informatics |
| <input type="checkbox"/> Interpersonal and communication skills | <input type="checkbox"/> Quality improvement | <input type="checkbox"/> None of the above |
| <input type="checkbox"/> Employ evidence-based practice | <input type="checkbox"/> Medical knowledge | |

• The content of this activity matched my current (or potential) scope of practice.

- No _____
- Yes, please explain _____

• Was this activity scientifically sound and free of commercial bias* or influence?

- Yes _____
- No, please explain _____

* Commercial bias is defined as a personal judgment in favor of a specific product or service of a commercial interest.

Evaluation

Impact of the Activity

	<i>Strongly Agree</i>	<i>Agree</i>	<i>Disagree</i>	<i>Strongly Disagree</i>	<i>Not Applicable</i>
• The educational activity has enhanced my professional effectiveness in treating patients	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
• The educational activity will result in a change in my practice behavior	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

• How will you change your practice as a result of participating in this activity (*select all that apply*)?

- | | |
|--|---|
| <input type="checkbox"/> Create/revise protocols, policies, and/or procedures | <input type="checkbox"/> I will not make any changes to my practice |
| <input type="checkbox"/> Change the management and/or treatment of my patients | <input type="checkbox"/> Other, please specify: _____ |
| <input type="checkbox"/> This activity validated my current practice | _____ |

• What new information did you learn during this activity? _____

• Please indicate any barriers you perceive in implementing these changes.

- | | |
|---|---|
| <input type="checkbox"/> Lack of experience | <input type="checkbox"/> Reimbursement/insurance issues |
| <input type="checkbox"/> Lack of resources (equipment) | <input type="checkbox"/> Patient compliance issues |
| <input type="checkbox"/> Lack of time to assess/counsel patients | <input type="checkbox"/> No barriers |
| <input type="checkbox"/> Lack of consensus of professional guidelines | <input type="checkbox"/> Cost |
| <input type="checkbox"/> Lack of opportunity (patients) | <input type="checkbox"/> Other _____ |
| <input type="checkbox"/> Lack of administrative support | _____ |

• If you indicated any barriers, how will you address these barriers in order to implement changes in your knowledge, competency, performance, and/or patients' outcomes? _____

• Comments to help improve this activity? _____

• Recommendations for future CME/CPE topics. _____

To assist with future planning, please attest to time spent on activity:

I spent ____ hours on this program

Accredited by:



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