Hepatitis C: Emerging Therapies

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:

- Assess the potential advantages of direct-acting antiviral agents currently under investigation for the treatment of chronic hepatitis C compared to current treatment options with telaprevir/PegIFN/ribavirin, boceprevir/PegIFN/ribavirin, or PegIFN/RBV.
- Recognize that PegIFN-free treatment regimens utilizing direct-acting antiviral agents for the treatment of chronic hepatitis C are possible with compounds currently under investigation.
- Identify patient populations with chronic hepatitis C for whom data from drugs currently under investigation are lacking.

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Chief of the Division of Gastroenterology and Hepatology and Vincent Astor Professor of Medicine at Weill Cornell Medical College New York, NY. Grants/Research Support: Schering, Tibotec, Roche, Genentech, Pharmasset, Anadys, Boehringer Ingelheim, Novartis, Gilead, Vertex, GlobeImmune, Human Genome Sciences, Pfizer, Bristol Myers Squibb and Zymogenetics Consultant: Bristol Myers Squibb, Novartis, Gilead, Schering, Merck, Pfizer, Vertex, GlobeImmune, Human Genome Sciences, Boehringer Ingelheim, Pharmasset, Zymogenetics, TIbotec, Abbott, Roche, Genentech, Anadys, Sanofi-Aventis, Achillion, Glaxo Smith Kline and Biolex. Advisory Board Membership: Schering, Merck, Gilead, Bristol Myers Squibb, Novartis, Roche, Genentech Speaker Bureau for:Schering, Merck, Gilead, Bristol Meyers Squibb and Roche/Genentech.

Dr. Jacobson has disclosed that there will be discussion about the use of products for non-FDA approved indications.

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All staff at the Annenberg Center for Health Sciences at Eisenhower have nothing to disclose.

All staff with The Chronic Liver Disease Foundation have nothing to disclose.

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Interferon (IFN) alfa was approved for the treatment of chronic hepatitis C in 1991, the first effective treatment for a disease that was formerly known as non-A, non-B hepatitis. Initially, IFN was used as monotherapy and the recommended treatment duration was 6 months. Unfortunately, only 6% of those receiving this treatment regimen achieved clearance (sustained viral response [SVR]), of the hepatitis C virus (HCV). Adjustments in treatment duration and the introduction of new therapies over the past 20 years have resulted in significant, incremental improvements in SVR rates (Figure 1).[1]

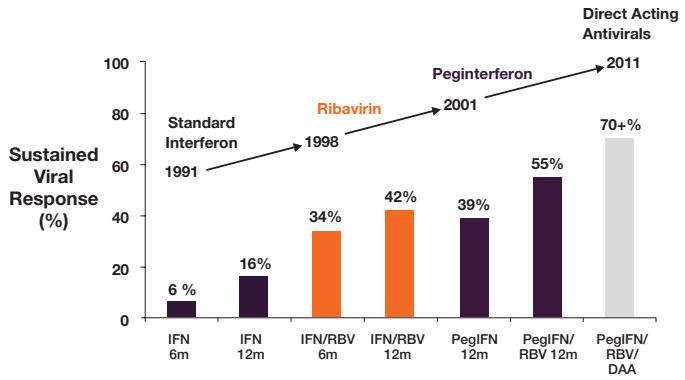

Figure 1: Milestones in therapy of hepatitis C. IFN, interferon; RBV, ribavirin; PegIFN, pegylated interferon; DAA, direct-acting antivirals. Adapted from FDA Advisory Committee Meeting Materials.[1]

The approval of ribavirin (RBV) in 1998 for use in combination with IFN increased SVR rates to 34%, and the approval of pegylated interferon (PegIFN) in 2001 resulted in SVR rates of 39% when used as monotherapy and 55% when used in combination with RBV. SVR rates from earlier registration trials utilizing IFN, PegIFN, and RBV included patients with genotypes 2 and 3 in addition to genotype 1. The approval of the direct-acting antivirals (DAAs) boceprevir and telaprevir in 2011 resulted in SVR rates of 63% to 79% in treatment-naive patients when used in combination with PegIFN and RBV.[2] The registration trials for boceprevir/PegIFN/RBV or telaprevir/PegIFN/RBV included only genotype 1 patients. Despite these advances, treatment of chronic hepatitis C continues to be problematic. Thirty percent of genotype 1 chronic hepatitis C patients fail to achieve SVR, efficacy in certain patient types (e.g., previously treated patients, cirrhotic patients, and black patients) is limited, and PegIFN must be administered subcutaneously. In addition, recommended treatment durations for boceprevir/PegIFN/RBV or telaprevir/PegIFN/RBV are lengthy, ranging between 24 and 48 weeks, and adverse events are common and may be severe. Thus, the search continues for therapies with better efficacy, efficacy in all patient types, orally effective IFN-free treatments, shorter-duration treatments, and treatments with improved side-effect profiles. Numerous compounds are currently under investigation for the treatment of chronic hepatitis C, and the results of some of these studies were reported at the International Liver Congress™ 2012, the annual meeting of the European Association for the Study of the Liver (EASL) that took place in Barcelona, Spain in April, 2012. Ira M. Jacobson, MD, Chief, Division of Gastroenterology and Hepatology at Weill Cornell Medical College in New York, NY, has reviewed the efficacy and safety reports of new DAAs for the treatment of chronic hepatitis C from selected studies presented at the 2012 EASL meeting.[3] Dr. Jacobson's review will be the focus of this newsletter.

The compounds included in this review, along with their sponsors and mechanisms of action, are listed in Table 1. It is important to note that all the agents reviewed are in preliminary states of development and that none of the studies were head to head, thus precluding direct comparison. Endpoints varied between studies, ranging from sustained viral response rates at 4 weeks following cessation of therapy (SVR4) to sustained viral response rates at 24 weeks (SVR24), the endpoint for therapy currently utilized in registration trials. Nevertheless, compared to current therapy, it appears that some of the agents under development will offer better efficacy, that some future regimens will have

shorter durations, and that orally effective, interon-free regimens will become available. While safety profiles looked favorable for the future agents, study populations were generally too small and study durations too short to make definitive statements on safety for many agents.

Compound	Manufacturer	Activity
ABT-072	Abbott	Non-nucleoside NS5B polymerase inhibitor
ABT-333	Abbott	Non-nucleoside NS5B polymerase inhibitor
ABT-450	Abbott/Enanta	NS3 protease inhibitor
Asunaprevir (BMS-650032)	Bristol-Myers Squibb	NS3 protease inhibitor
BI201335	Boehringer-Ingelheim	NS3 protease inhibitor
BI207127	Boehringer-Ingelheim	Non-nucleoside NS5B polymerase inhibitor
Daclatasvir (BMS-790052)	Bristol-Myers Squibb	NS5A replication complex inhibitor
GS-7977 (PSI-71977)	Gilead (Pharmasset)	Uridine nucleotide analog NS5A polymerase inhibitor
TMC435	Tibotec/Medvir	NS3/4A protease inhibitor

Table 1: Selected direct-acting antiviral agents for the treatment of chronic hepatitis C presented at the International Liver Congress™ 2012, the sponsoring manufacturer, and the agent's activity as reported by the sponsor.

Studies in treatment-naive HCV patients

Table 2 summarizes the results of selected studies with DAA compounds in treatment-naive chronic hepatitis C patients. Four studies involved only genotype 1 patients; three studies had genotype 2/3 study arms in addition to a genotype 1 study arm. Three studies involved combinations of an NS3 protease inhibitor, an NS5B non-nucleoside polymerase inhibitor, and RBV in genotype 1 patients with treatment durations ranging from 12 weeks to 40 weeks. Lawitz et al utilized ABT-450/r + ABT-072 + RBV with a treatment duration of 12 weeks and an SVR24 endpoint; Poordad et al studied ABT-450r + ABT-333 + RBV with a treatment duration of 12 weeks and an SVR12 endpoint; and Zeuzem et al administered BI201335 + BI207127 + RBV for treatment durations of 16, 28, and 40 weeks, respectively, and an SVR12 endpoint.[4,5,6] While SVR12 values were used in two of the studies, there is reportedly a high degree of concordance between the SVR12 and SVR24 values such that regulatory authorities in both Europe and the United States have proposed changing the primary endpoint for future registration trials to SVR12. SVR4 study results also show a high degree of concordance with SVR24 endpoints.[3] SVR rates for studies utilizing an NS3 protease inhibitor in combination with an NS5B non-nucleoside polymerase inhibitor and RBV ranged from 56% to 95%. Patients treated with ABT-450/r + ABT-072 + RBV (all IL28B CC) achieved an SVR24 of 91%, patients treated with ABT-450/r + ABT-333 + RBV achieved an SVR12 of 93% to 95% (ABT-450/r was administered at two dosage levels), and patients who received BI201335 + BI207127 + RBV achieved an SVR12 of 56% to 68% (three treatment durations were studied).[4,5,6]

		Treatment-Naive Patients				
Study	Drug Combination	n	Genotype	Treatment Duration (Wks)	Endpoint	% Response
Lawitz et al[4]	ABT-450/r+ ABT-072 + RBV	11	1 (all IL28B Genotype cc)	12	SVR24(<10 IU/mL)	91
Poordad et al[5]	ABT-450r + ABT-333 + RBV	33	1	12	SVR12(<25 IU/mL)	93-95
Gane et al[10]	GS-7977 + RBV	25	1	12	SVR4(<10 IU/mL)	88
	GS-7977 + PegIFN + RBV	10	2/3	8	SVR4(<10 IU/mL)	100
Zeusem et al[6]	BI201335 + BI207127 t+ RBV	316	1	16, 28, & 40	SVR12(<10 IU/mL)	56-68
	BI201335 + BI207127	46	1	28	SVR12(<10 IU/mL)	39
Sulkowski et al[7]	Daclatasvir + GS-7977	29	1	24	SVR4 (<10 IU/mL)	100
		30	2/3	24	SVR4(<10 IU/mL)	88-100
	Daclatasvir + GS-7977 + RBV	15	1	24	SVR4(<10 IU/mL)	100
		14	2/3	24	SVR4 (<10 IU/mL)	79
Suzuki et al[8]	Daclatasvir + Asunaprevir	22	1b	24	SVR12(<25 IU/mL)	64

Table 2: Summary of selected studies of direct-acting antiviral compounds in chronic hepatitis C treatment-naive patients. None of the studies were head to head.

Only one study (Zeuzem et al) involved study arms comparing an NS3 protease inhibitor/NS5B non-nucleoside polymerase inhibitor ± RBV in treatment-naive genotype 1 patients. Treatment durations for the BI201335 + BI207127 + RBV study arms were 16 weeks, 28 weeks, and 40 weeks; the treatment duration for the BI201335 + BI207127 arm was 28 weeks. SVR12 rates were higher in each of the RBV-containing arms (56% to 68%) than in the arm that included the NS3 protease inhibitor/NS5B

non-nucleoside polymerase inhibitor without RBV. The results suggest that RBV enhances the response of a NS3 protease inhibitor/NS5B non-nucleoside polymerase inhibitor combination.[6] In contrast, a study by Sulkowski et al of the NS5A inhibitor, daclatasvir, combined with the NS5B polymerase inhibitor, GS-7977 ± RBV found that SVR4 rates were 100% in genotype 1 study arms with and without RBV when administered for 24 weeks; RBV appeared to be unnecessary for the treatment of genotype 1 patients when used with daclatasvir/GS-7997. The same study also included arms in which daclatasvir/GS-7977 ± RBV were administered to genotype 2/3 patients. When used in genotype 2/3 patients, daclatasvir/GS-7977 without RBV resulted in SVR4 rates of 88% to 100%, while daclatasvir/GS-7977 with RBV resulted in an SVR4 rate of 79%. Treatment duration was 24 weeks in all treatment arms.[7] Daclatasvir was also studied in combination with the NS3 protease inhibitor asunaprevir by Suzuki et al. in genotype 1b Japanese patients who were ineligible for or intolerant to PegIFN/RBV therapy. Genotype 1b is the most common subtype of genotype 1 outside North America. Treatment duration was 24 weeks, and the SVR12 rate was 64%.[8,9]

Only one study investigated the effect of an NS5B polymerase inhibitor (GS-7997) in combination with RBV in genotype 1 patients; treatment duration was 12 weeks. The SVR4 rate was 88% (22/25) with this two-drug combination. In the same study, the SVR4 rate was 100% following administration of a combination of GS-7997, PegIFN, and RBV for only 8 weeks in genotype 2/3 patients.[10]

As with PegIFN/RBV therapy, both host and viral factors may affect response when polymerase inhibitor/protease inhibitor therapy that does not include PegIFN is used for treating patients with genotype 1 HCV. A single nucleotide polymorphism near the IL28B gene predicts a patient's response to HCV treatment with PegIFN/RBV. Patients with the CC genotype achieve a twofold greater rate of SVR than those with the TT or CT genotypes when treated with PegIFN/RBV.[11] It appears that SVR rates following treatment with certain polymerase inhibitors/protease inhibitors ± RBV will show similar differences in response rates according to the IL28B genotype as illustrated in the analysis of response rates for BI201335 + BI207127 ± RBV depicted in Figure 2.

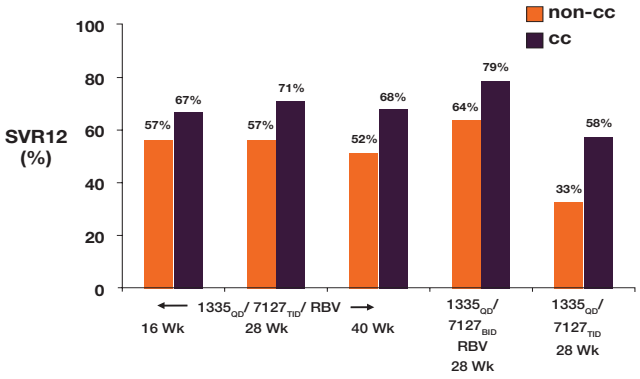

Figure 2: SVR12 according to IL28B gene following treatment with various dosing regimens of BI201335 and BI207127 ± RBV in treatment-naive patients with genotype 1 HCV infection. SVR12 rates are higher for patients with the CC genotype than with the non-CC genotype for every dosing regimen tested.[6]

Response rates in each study arm are higher in patients with the CC genotype than in those with the non-CC genotype.[6] Similarly, the SVR rate following treatment with PegIFN/RBV is higher in those infected with genotype 1b than in those infected with genotype 1a and it appears that a similar SVR differential will occur following treatment with certain polymerase inhibitors/protease inhibitors ± RBV.[12] An analysis of response rates for BI201335 + BI207127 ± RBV according to genotype 1 subtype is illustrated in Figure 3.

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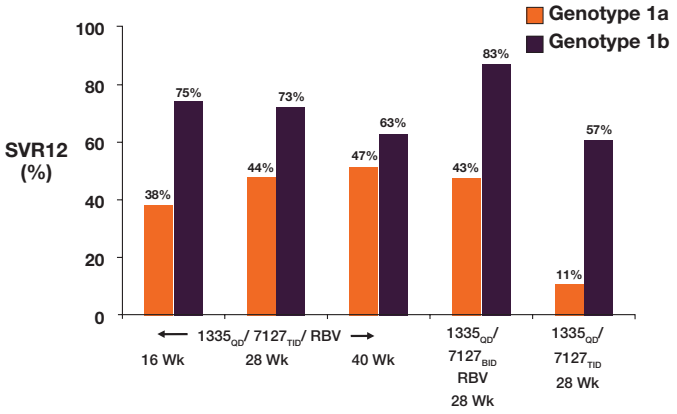

Figure 3: SVR12 according to HCV genotype 1a or 1b subtype following treatment with various dosing regimens of BI201335 and BI207127 ± RBV in treatment-naive patients with genotype 1 HCV infection. SVR12 rates are higher for patients with genotype 1b than with genotype 1a for every dosing regimen tested.[6]

Response rates in each study arm are higher in genotype 1b patients than in genotype 1a patients.[6] The differential response rates depending on IL28B CC vs. non-CC or 1a vs. 1b subtype may be a nonissue; however, when genotype 1 patients are treated with two potent drugs with at least one agent also possessing a high barrier to resistance (Figure 4).

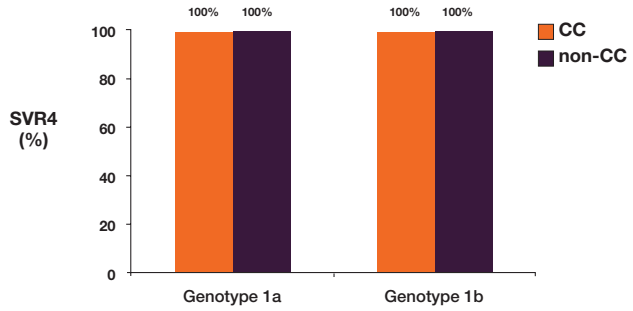

Figure 4: SVR4 according to HCV genotype 1 subtype and IL28B genotype following administration of daclatasvir and GS-7977 ± RBV in treatment-naive patients with genotype 1 HCV infection. SVR4 rates were 100% regardless of genotype 1 subtype or IL28B genotype.[7]

One hundred percent of treatment-naive genotype 1 patients receiving daclatasvir and GS-7977 ± RBV achieved SVR4 regardless of IL28B genotype or HCV genotype 1 subtype; of 44 patients treated, 32 had HCV genotype 1a, 12 had HCV genotype 1b, 16 patients were IL28B CC, and 11 were IL28B CT or TT (IL28B genotype data were missing for one patient).[7]

Efficacy results for new agents in treatment-naive patients with cirrhosis were reported in one study. Soriano and colleagues analyzed the effects of BI201335 + BI207127 ± RBV administered to patients with biopsy or Fibroscan-confirmed cirrhosis enrolled in the SOUND-C2 clinical trial. Treatment durations ranged between 16 weeks and 42 weeks. The pooled SVR12 rate for the RBV-containing arms was 56%; the SVR12 rate for the study arm containing only BI201335 + BI207127 was 33%, indicating a positive effect of RBV on SVR with this combination of DAA agents (Table 3).[13]

	Patients With Cirrhosis					
Study	Drug Combination	n	Genotype	Treatment Duration (Wks)	Endpoint	% Response
Soriano et al[13]	BI201335 + BI207127 + RBV	31	1	16, 28, & 40	SVR12(<10 IU/mL)	56
	BI2011335 + BI207127	3	1	28	SVR12(<10 IU/mL)	33

Table 3: Summary of a selected study of direct-acting antiviral compounds in chronic hepatitis C treatment-naive patients with biopsy or Fibroscan-confirmed cirrhosis.

None of the studies with investigational agents reported subgroup analyses for treatment-naive black patients.

Studies in HCV patients previously treated with PegIFN/RBV

Considerable research activity has been targeted to the large pool of patients who have failed previous treatment with PegIFN/RBV. Prior non-responders are usually defined based on the type of non-response they experienced with previous therapy: A null response (<2-$\log_{10}$ reduction in HCV-RNA at week 12 of prior treatment with Peg-IFN/RBV), a partial response (≥2-$\log_{10}$ reduction in HCV-RNA at week 12, but not achieving HCV RNA undetectable at end of treatment with Peg-IFN/RBV), or relapse (HCV-RNA undetectable at end of treatment with Peg-IFN/RBV, but HCV RNA detectable within 24 weeks of treatment follow-up).[14]

Table 4 summarizes the results of selected studies with investigational agents in treatment-experienced patients. Four studies involved only genotype 1 patients, while one study had both a genotype 1

arm and a genotype 2/3 arm. One study involved a combination of an NS5A inhibitor and an NS3 protease inhibitor, one study utilized a combination of an NS3 protease inhibitor, a non-nucleoside NS5B polymerase inhibitor, and RBV, and one study involved a uridine nucleotide analog NS5B polymerase inhibitor in combination with RBV. Two studies included Peg-IFN in the drug regimen, one with an NS5A replication complex inhibitor, an NS3 protease inhibitor, RBV, and Peg-IFN, and one with an NS3/4A protease inhibitor, RBV, and Peg-IFN.

Suzuki et al studied the combination of daclatasvir and asunaprevir administered for 24 weeks. All patients in this trial were Japanese with HCV genotype 1b. The SVR12 in prior null responders was 91%. While not shown in Table 4, the SVR12 in an arm of the study that included patients who were ineligible or intolerant to Peg-IFN–containing treatment regimens and who received daclatasvir/ asunaprevir therapy identical to that administered to the prior null responders was 64%.[8]

Treatment-Experienced Patients							
Study	Drug Combination	n	Prior Response	Genotype	Treatment Duration (Wks)	Endpoint	% Response
Poordad et al[5]	ABT-450/r*+ ABT-333 + RBV	6	Null	1	12	SVR12(<25 IU/mL)	50
		11	Partial	1	12	SVR12(<25 IU/mL)	46
Gane et al[10]	GS-7997 + RBV	8	Null	1	12	SVR4(<10 IU/mL)	11
		15	Non-responsder	2/3	12	SVR4(<10 IU/mL)	80
Suzuki et al[8]	Daclatasvir + Asunaprevir	21	Null	1b	24	SVR12(<25 IU/mL)	91
Lok et al[15]	Daclatasvir + Asunaprevir + Peg-IFN + RBV	41	Null	1	24	SVR4(<10 IU/mL)	95-95
Zeuem et al[16]	TMC435 + PegIFN + RBV	101	Null	1	TMC 12-48; PegIFN/RBV 48	SVR24(<25 IU/mL)	38-59
		137	Partial	1	TMC 12-48; PegIFN/RBV 48	SVR24(<25 IU/mL)	48-86
		158	Relapser	1	TMC 12-48; PegIFN/RBV 48	SVR24(<25 IU/mL)	77-89

Table 4: Summary of selected studies of direct-acting antiviral compounds in chronic hepatitis C treatment-experienced patients (patients who failed previous therapy with PegIFN/RBV). None of the studies were head to head.

Poordad et al utilized a combination of ABT-450r + ABT-333 + RBV administered for 12 weeks in HCV genotype 1 patients with either a prior null response or a prior partial response. The SVR12 was 50% (3/6) in the prior null-responder study arm and 46% (5/11) in the prior partial-responder study arm. For comparison, the combination of ABT-450r + ABT-333 + RBV administered for 12 weeks to treatment-naive genotype 1 patients produced an SVR 12 rate of 93% to 95% (Table 2).[5]

Gane et al reported the results of a study utilizing a combination of the polymerase inhibitor GS-7997 + RBV, but without a protease inhibitor, administered for 12 weeks. The combination resulted in an SVR4 of 11% when administered to genotype 1 prior null-responder patients and an SVR4 of 80% when administered to genotype 2/3 prior non-responder patients. For comparison, in the same study GS-7997 + RBV administered for 12 weeks to treatment-naive genotype 1 patients resulted in an SVR4 rate of 88%, while 100% of treatment-naive genotype 2/3 patients had an SVR 4 when GS-7997 + RBV + PegIFN administered for 8 weeks (Table 2).[10]

The addition of PegIFN appears to enhance response rates when added to a combination of an NS5A replication inhibitor (daclatasvir), a protease inhibitor (asunaprevir), and RBV in prior nonresponders. Lok et al achieved an 85% to 95% SVR 24 rate when null responders were administered daclatasvir + asunaprevir + PegIFN + RBV for 24 weeks--the highest SVR rate for prior null responders among the studies reported at EASL 2012.[15]

Very respectable SVR 24 rates were also obtained with the protease inhibitor TMC435 when combined with PegIFN + RBV. This combination, reported by Zeuzem et al, produced SVR rates of 38% to 59% in prior null responders, 48% to 86% in prior partial responders, and 77% to 89% in prior relapsers. TMC435 was administered at two different doses, and each dose of TMC435 was administered for three different durations (12 weeks, 24 weeks and 48 weeks); PegIFN/RBV was administered for 48 weeks in all six arms of the study. Administration of

TMC435 at the higher dose for 48 weeks along with PegIFN/RBV for 48 weeks appeared to be the most efficacious regimen in this study.[16]

Conclusions

Poster and oral presentations of results reported at EASL 2012 utilizing combinations of novel DAA agents provide proof of concept that future therapies for chronic hepatitis C will be improved relative to current treatment with boceprevir/PegIFN/RBV or telaprevir/PegIFN/RBV for genotype 1 patients or with PegIFN/RBV for genotype 2/3 patients. Results presented at EASL 2012 suggest that DAA agents currently under investigation, compared to treatment with current therapies may offer:

1. Enhanced efficacy in genotypes 1, 2, and 3.
2. Enhanced efficacy in both treatment-naive and treatment-experienced patients.
3. Orally administered IFN-free treatment combinations.
4. Regimens that allow treatment durations as short as 12 weeks for many patient populations.

Safety profiles and resistance profiles for the newer agents look promising; however, large confirmatory Phase 3 studies will be needed to confirm the profiles. Additional data are needed in difficult-to-treat patients, including nulls responders, black patients, and patients with cirrhosis.

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This material supported by an educational grant from Janssen and Vertex Pharmaceuticals.

Posttest

Project ID: 5021

If you wish to receive acknowledgement of participation for this activity, please complete this posttest, evaluation form, and request for credit (pages 9-12) and fax to 973-939-8533. Required with 70% passing

1. **All of the following statements are true regarding our current understanding of agents currently under investigation for the treatment of genotype 1 chronic hepatitis C when compared to currently approved therapies, except:**
   A. Better efficacy appears possible
   B. The same treatment regimen for all patients regardless of prior response or genotype appears possible
   C. Shorter treatment durations appear possible
   D. IFN-free treatment regimens appear possible

2. **As reported by Sulkowski et al, which HCV patient type achieved an SVR4 of 100% following treatment with daclatasvir + GS-7977 ± RBV for 24 weeks?**
   A. Genotype 1 prior null responders to PegIFN/RBV
   B. Genotype 1 prior partial responders to PegIFN/RBV
   C. Genotype 1 prior relapsers following PegIFN/RBV
   D. Treatment naive genotype 1 patients

3. **In the study of BI201335 + BI207127 ± RBV by Zeuzem et al, what was the effect of the IL28B gene on SVR rates in treatment-naive patients with genotype 1 HCV?**
   A. Patients with the CC genotype achieved higher SVR rates than those with TT or CT genotypes
   B. Patients with the TT or CT genotypes achieved higher SVR rates than those with the CC genotype
   C. Patients with the CC or CT genotypes achieved higher SVR rates than those with the TT genotype
   D. Patients with the CC, TT, or CT genotype achieved similar SVR rates

4. **In the study of BI201335 + BI207127 ± RBV by Zeuzem et al, what was the effect of the genotype 1 subtype on SVR rates in treatment-naive HCV patients?**
   A. SVR 12 rates were the same in subtypes 1a and 1b
   B. SVR 12 rates were higher in subtype 1a than in subtype 1b
   C. SVR 12 rates were higher in subtype 1b than in subtype 1a
   D. Only patients with subtype 1b were included in the study

5. **What was the effect of the type of prior non-response on SVR 24 when HCV patients were re-treated with a combination of TMC435 + PegIFN + RBV as reported by Zeuzem et al?**
   A. SVR24 rates were approximately the same for prior null responders, partial responders, and relapsers
   B. SVR24 rates were highest for prior null responders
   C. SVR24 rates were highest for prior partial responders
   D. SVR24 rates were highest for prior relapsers

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Evaluation

Project ID: 5021

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?	*This learning objective did (or will) increase/ improve my:*	*High Impact*	*Moderate Impact*	*No Impact*	*Not Applicable*
• Assess the potential advantages of direct-acting antiviral agents currently under investigation for the treatment of chronic hepatitis C compared to current treatment options with telaprevir/ PegIFN/ribavirin, boceprevir/PegIFN/ribavirin, or PegIFN/RBV	***Knowledge***	❑	❑	❑	❑
	Competence	❑	❑	❑	❑
	Performance	❑	❑	❑	❑
	Patient Outcomes	❑	❑	❑	❑
• Recognize that PegIFN-free treatment regimens utilizing direct-acting antiviral agents for the treatment of chronic hepatitis C are possible with compounds currently under investigation	***Knowledge***	❑	❑	❑	❑
	Competence	❑	❑	❑	❑
	Performance	❑	❑	❑	❑
	Patient Outcomes	❑	❑	❑	❑
• Identify patient populations with chronic hepatitis C for whom data from drugs currently under investigation are lacking	***Knowledge***	❑	❑	❑	❑
	Competence	❑	❑	❑	❑
	Performance	❑	❑	❑	❑
	Patient Outcomes	❑	❑	❑	❑

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)*:

❑ Patient care or patient-centered care
❑ Practice-based learning and improvement
❑ Interpersonal and communication skills
❑ Employ evidence-based practice
❑ Interdisciplinary teams
❑ Professionalism
❑ Quality improvement
❑ Medical knowledge
❑ System-based practice
❑ Utilize informatics
❑ None of the above

- 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.*

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Impact of the Activity

	Strongly Agree	Agree	Disagree	Strongly Disagree	Not Applicable
• The educational activity has enhanced my professional effectiveness in treating patients	❑	❑	❑	❑	❑
• The educational activity will result in a change in my practice behavior	❑	❑	❑	❑	❑

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

❑ Create/revise protocols, policies, and/or procedures
❑ Change the management and/or treatment of my patients
❑ This activity validated my current practice
❑ I will not make any changes to my practice
❑ Other, please specify: _____

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

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

❑ Lack of experience
❑ Lack of resources (equipment)
❑ Lack of time to assess/counsel patients
❑ Lack of consensus of professional guidelines
❑ Lack of opportunity (patients)
❑ Lack of administrative support
❑ Reimbursement/insurance issues
❑ Patient compliance issues
❑ No barriers
❑ Cost
❑ Other _____

• 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:
Annenberg Center For Health Sciences at Eisenhower

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Evaluation

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*Please do not use abbreviations. We need current and **complete** information to assure delivery of participation acknowledgement.*

Degree *(please mark appropriate box and circle appropriate degree)*

❑ MD/DO ❑ PharmD/RPh ❑ NP/PA ❑ RN ❑ Other _____

Full Name *(please print clearly)*

Last Name: First Name: Middle Initial:

Street Address:

City: State or Province: Postal Code:

Phone: Ext: Fax:

Specialty:

E-mail Address:

Date Completed: _____

Attestation to time spent on activity is required

❑ I participated in the entire activity and claim *1.0 AMA PRA Category 1 Credit(s)™*.

❑ I participated in only part of the activity and claim _____credits

❑ I do not wish to claim credits