CME NEWSLETTER

Reporting from

The 47th Annual Meeting of the European Association for the Study of the Liver (EASL)

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

EASL*
April 18-22, 2012
Barcelona, Spain

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*This coverage is not sanctioned by the conference organizers and is not an official part of the conference proceedings.

Introduction

This newsletter is based on the continuing medical education program The 47th Annual EASL: Online Expert Poster Review and Discussion. *This program provided updates on important presentations made during the 47th Annual Meeting of the European Association for the Study of the Liver (EASL) and is available online at* http://www.viraled.com/modules/info/easl_2012_poster_program.html

The faculty for this program consisted of Douglas T. Dieterich, MD from Mount Sinai School of Medicine, New York, New York; Paul Y. Kwo, MD from Indiana University School of Medicine, Indianapolis, Indiana; Jürgen Rockstroh, MD from the University of Bonn, Bonn, Germany; and Paul J. Pockros, MD from The Scripps Clinic, La Jolla, California.

EASL Posters

Efficacy and safety of protease inhibitors for severe hepatitis C recurrence after liver transplantation: a first multicentric experience. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 47. Coilly A, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_47_and_8.html

This poster described a study that was designed to assess the efficacy and safety of triple therapy for HCV in liver transplant (LT) patients (n=28) at 5 French transplant centers. The patients had active HCV genotype (GT) 1 chronic hepatitis and were all men who were treated with an HCV protease inhibitor (PI) (boceprevir [BOC], n=17, telaprevir [TVR], n=11). The recipient IL28B genotype was CC in 7 patients: 6 (35%) taking BOC and 1 (9%) taking TVR. Sixteen patients used cyclosporine and 12 used tacrolimus. Pegylated interferon (PegIFN) and ribavirin (RBV) dosages ranged between 1 and 1.5 mg/kg/week and 600 to 1,200 mg BID, respectively. TVR 750 mg TID and BOC 800 mg TID were initiated at week 0 and week 4, respectively.

At week 8, 70% of TVR patients and 75% of BOC patients had a virological response (VR, defined as a reduction <2 $\log_{10}$ of HCV RNA), and 70% of TVR vs. 56% of BOC patients had a complete virological response (CVR, defined as undetectable HCV RNA). Anemia was the main adverse event, occurring in 71% of BOC and 55% of TVR patients. There were 26 (93%) of patients who were treated with erythropoietin (EPO) and 4 (14%) required red blood cell transfusion (BOC=3, TVR=1). Dosage reduction in calcineurin inhibitors (CNIs) was constantly required: 1.3 fold with cyclosporine and 5 fold with tacrolimus in the BOC group and 4 fold with cyclosporine and 35 fold with tacrolimus in the TVR group.

Discussion: Dr. Pockros pointed out that because of concerns about drug-drug interactions, the investigators hospitalized the patients during the first week they received triple combination HCV therapy, and measured CNI titers each day.

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Safety of telaprevir or boceprevir in combination with peginterferon alfa/ribavirin, in cirrhotic non responders. First results of the French Early Access program (ANRS CO20-CUPIC). 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 8. Hezode C, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_47_and_8.html

Investigators studied the use of BOC and TVR in combination with PegIFN + RBV in cirrhotic non-responders in the French Early Access program (CUPIC). Prior to this analysis, the number of patients with cirrhosis studied with BOC and TVR was limited: only 247 (with TVR) and 115 (with BOC). The study consisted of HCV GT1 patients with compensated cirrhosis (Child Pugh A) and included relapsers, partial responders, and null responders.

The primary objective of this study was to determine the rate of SVR, with an interim analysis to evaluate safety and tolerability among patients included in the CUPIC cohort who received at least 16 weeks of antiviral treatment. There were 455 patients included in the final analysis. Patients received BOC in one study arm and TVR in the other.

The investigators reported undetectable HCV RNA in 86% of TVR users and 71% of BOC users (per protocol). However, the safety profile among cirrhotic patients treated in CUPIC was poor. Serious adverse events (SAEs) were found in 48% of TVR patients and 38% of BOC patients. Anemia was reported in both groups: Grade 2, 20% with TVR and 23% with BOC, and Grade 3/4, 10% with TVR and 10% with BOC. EPO use was reported in 57% of TVR patients and 66% of BOC patients. There was also a high rate of discontinuation due to SAEs (14% for TVR and 7% for BOC). The researchers concluded that patients with cirrhosis should be treated cautiously and should be monitored carefully, especially because of a high incidence of anemia with poor response to EPO.

Discussion: Dr. Pockros noted that anemia in patients who are treated with BOC seemed to appear more slowly than in those receiving TVR, which allows more time to respond to this issue. Dr. Kwo said that the lead-in allows for some RBV dose adjustments prior to adding the direct-acting antiviral agent (DAA).

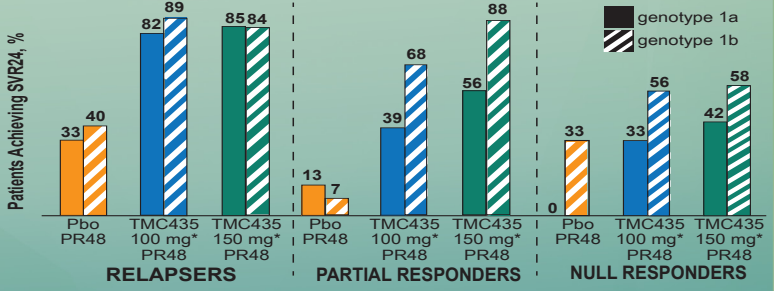
TMC435 in HCV genotype 1 patients who have failed previous pegylated interferon/ribavirin treatment: final SVR 24 results of the ASPIRE TRIAL. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 2. Zeuzem S, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_2.html

This poster described the ASPIRE study, a randomized, double-blind phase IIb trial that used TMC435 – an investigational once-daily oral HCV NS3/4A protease inhibitor – with PegIFN + RBV in HCV GT1 patients who had failed previous PegIFN + RBV treatment. Patients with null-response, partial-response, or relapse to prior PegIFN + RBV therapy were randomized to one of seven treatment arms: TMC435 (100 or 150 mg QD) for 12, 24 or 48 weeks in combination with PegIFN + RBV and placebo for 48 weeks, or placebo + PegIFN + RBV for 48 weeks. The primary endpoint was SVR24 (HCV RNA <25 IU/mL at week 72). Secondary endpoints included virologic response at other time points, viral breakthrough and relapse rates, safety, and tolerability.

The investigators reported that overall SVR24 rates were significantly higher with TMC435 + PegIFN + RBV compared with PegIFN + RBV alone. With TMC435 150 mg combined with PegIFN + RBV, SVR24 was achieved by 85% of prior relapsers, 75% of prior partial responders, and 51% of prior null responders. The SVR24 rates with the 150 mg dose of TMC435 were equal or superior to those of the 100 mg dose. The results in patients with HCV GT 1a and 1b are shown in Figure 1. Viral breakthrough and relapse were found to be associated with mutations similar to those reported previously. Once-daily TMC435 was well tolerated in this population; phase III clinical trials for TMC435 150 mg are ongoing.

Figure 1. ASPIRE Trial: SVR24 by Prior Response and HCV Genotype Subtype



* Duration Pooled; Pbo = placebo; PR = PegIFN + RBV.

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Interferon-free treatment with a combination of mericitabine and danoprevir/r with or without ribavirin in treatment-naive HCV genotype 1-infected patients. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 1412. Gane EJ, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_1412.html

Mericitabine (MCB) and danoprevir (DNV, RG7227) are DAAs that are being studied in INFORM-SVR, a randomized, double blind, parallel group phase IIb study. Researchers are investigating the safety and efficacy of response-guided treatment (RGT) with MCB in combination with ritonavir-boosted DNV (DNV/r) with and without RBV for 12 or 24 weeks in treatment-naive patients with GT1 chronic HCV infection.

In this study, patients were randomized (1:1) to receive a combination of MCB (1,000 mg bid) and DNV/r (100 mg/100 mg BID) + either RBV (Arm A) or placebo (Arm B) for 12 or 24 weeks. In both arms, patients achieving an early extended rapid virological response (eRVR2, defined as unquantifiable HCV RNA [<43 IU/mL]) between week 2 to week 8, and with undetectable HCV RNA (<15 IU/mL) at week 10, were re-randomized (1:1) at week 12 to either discontinue treatment (total therapy duration: 12 weeks) or continue the assigned regimen until week 24 (total therapy duration: 24 weeks). The primary outcome of the trial is SVR24.

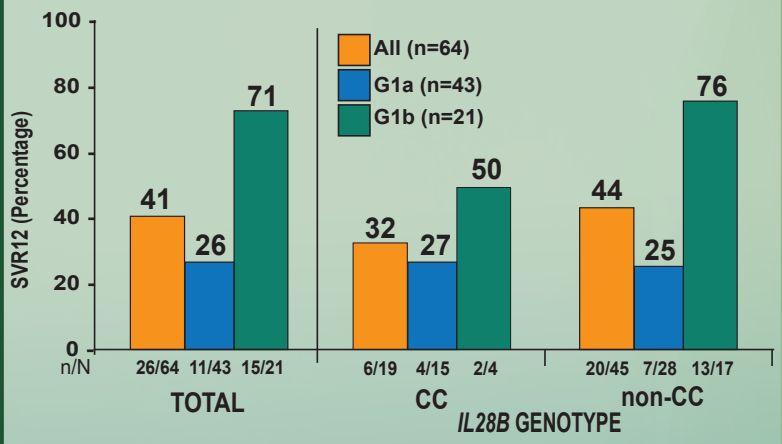
A total of 169 patients were randomized to treatment (Arm A, n=83; Arm B, n=86) and received at least one dose of study medication. Randomization to 12 weeks of treatment in Arm A and to the whole of Arm B was stopped prematurely due to high relapse rates, and patients in Arm B were offered follow-on with PegIFN + RBV therapy. As a result, only 20/169 patients were randomized to 12 weeks of treatment (Arm A, n=17; Arm B, n=3) and, for the efficacy analyses, Arm A (24 weeks of treatment), was the key group analyzed.

The efficacy population consisted of 64 patients who received MCB combined with DNV/r and RBV for 24 weeks; 43 patients with HCV GT1a and 21 with GT1b. SVR12 rates for GT1a and 1b patients receiving 24 weeks of MCB plus DNV/r and RBV treatment are shown in Figure 2. Overall, 41% of patients achieved SVR12 (26/64). SVR12 rates were higher among patients with HCV GT1b (71%) compared with patients with GT1a infection (26%). When SVR12 rates were stratified according to IL28B genotype (CC and non-CC), 32% of patients with IL28B CC genotype, and 44% with non-CC genotype achieved SVR12. Among patients in Arm A treated with MCB combined with DNV/r and RBV for 24 weeks, 60% (26/43) of HCV GT1a-infected patients achieved an eRVR2, compared with 48% (10/21) of patients with HCV GT1b infection.

Among patients who received at least one dose of the study medication, 26 patients experienced breakthrough: 8 in Arm A (8/83; 10%) and 18 in Arm B (18/86; 21%). Breakthrough rates were higher among HCV GT1a patients (Arm A: 6/56; 11%; Arm B: 15/57; 26%) compared with GT1b patients (Arm A: 2/27; 7%; Arm B: 3/29; 10%).

Among patients with an eRVR2, 80% with GT1b and 31% with GT1a achieved SVR12. IL28B genotype (CC and non-CC) appeared to have less impact on SVR12 rates relative to differences observed between GT1a and 1b patients. Breakthrough rates were higher among patients who did not receive RBV, indicating that RBV plays an important role in preventing viral breakthrough.

Figure 2. SVR12 Rates in Patients Receiving 24 Weeks of MCB + DNV/r + RBV (Arm A) by HCV Genotype and IL28B Genotype



Discussion: Dr. Pockros said that the overall SVR rate in the study – 41% – was somewhat disappointing, especially in the GT1a patients (26%), a genotype that is more common in the United States. He said he doesn't think the data indicate that this regimen is robust enough to move forward with in either GT1a or GT1b patients. However, some researchers are investigating whether we can use this type of regimen if we add a nonnucleoside polymerase inhibitor to the MCB, which might protect against resistant variants.

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Early versus delayed treatment of acute hepatitis C: Final results of the randomized controlled German HEP-NET acute HCV-III study. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 48. Deterding K, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_48.html

The HEP-Net-Acute-HCV-III study is a prospective, randomized trial in patients with symptomatic acute hepatitis C comparing the efficacy and safety of immediate PegIFN treatment for 6 months (Arm A) vs. delayed treatment with PegIFN + RBV for 6 months, starting 12 weeks after randomization in patients who were still HCV RNA positive (Arm B). All asymptomatic patients were assigned to early treatment with PegIFN (Arm C). 132 patients (66% GT1, 63% icteric) were recruited by 72 centers. The intent-to-treat (ITT) analysis included all patients and the completer analysis was based on all patients who completed 24 weeks of follow-up after treatment or 60 weeks of observation (arm B).

ITT virological response rates were 76% in Arm A (n=49), 54% in the delayed treatment Arm B (n=52; *P*=0.02 vs. arm A) and 75% in arm C. The completer analysis showed SVRs of 90% in Arm A (37/41), 90% in Arm B (28/31), and 95% in Arm C (18/19). In arm B, sustained spontaneous HCV clearance was documented for 11 out of 52 patients (21%). Female gender and HCV GT1 infection but not IL28B-genotype were associated with HCV RNA negativity at week 12 in the observation arm B. The lower ITT SVR in Arm B was mainly due to drop-outs during the first 12 weeks observation period. However, delayed PegIFN and RBV treatment remained highly effective as all Arm B patients who completed treatment and follow-up achieved SVR (n=14).

This large prospective, randomized European trial on acute hepatitis C treatment showed that early, immediate treatment with PegIFN was highly effective in both symptomatic and asymptomatic patients. Delayed PegIFN + RBV treatment resulted in lower overall response rates in this real-life treatment setting. However, the investigators concluded that if adherence can be assured, delayed combination therapy seems to be of similar efficacy to immediate treatment in symptomatic patients and may be recommended in particular for women infected with HCV GT1.

Discussion: In addition to potential improvements in efficacy, Dr. Rockstroh noted that treating patients immediately may have cost advantages and that treating people acutely infected with HCV might decrease the number of people who could transmit HCV to others.

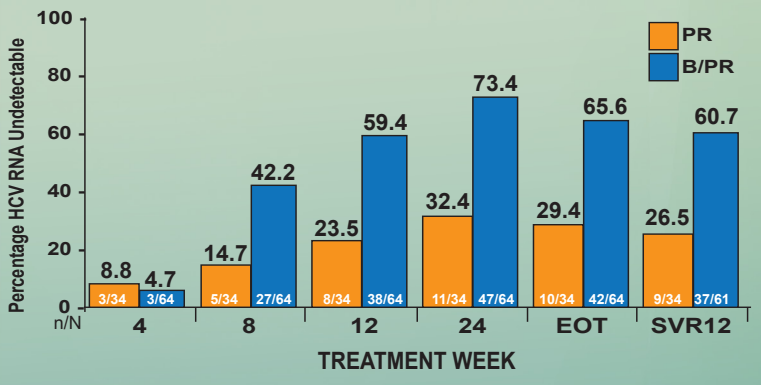
Boceprevir plus peginterferon/ribavirin for the treatment of HCV/HIV co-infected patients: end of treatment (week 48) interim results. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 50. Mallolas J, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_50.html

In this study with HCV/HIV co-infected patients (HCV GT1, HIV RNA <50 copies/mL), participants were randomized 2:1 to receive PegIFN (1.5 µg/kg/wk) + RBV (600-1,400 mg/day, by weight) + BOC 800 mg TID or PegIFN + RBV + placebo for 44 weeks, after a 4-week lead-in of PegIFN + RBV. The primary efficacy endpoint was SVR, undetectable plasma HCV RNA 24 weeks after end of treatment (EOT). Secondary endpoints and planned interim analyses included proportion of subjects with undetectable HCV RNA at treatment week 4, 8, 12, 24 and 48/EOT. During the study, 34 control and 64 experimental patients were treated. The majority were non-cirrhotic (95%), white (82%), and male (69%). Most participants had high baseline HCV RNA (88%) and HCV GT1a (65%).

At treatment week 48/EOT, the rate of undetectable HCV RNA was 66% in the BOC arm and 29% in the control arm. The SVR12 for the BOC arm was 61% and for the control arm was 26% (Figure 3). The researchers concluded that the addition of BOC to PegIFN + RBV for the treatment of HIV/HCV co-infected patients was associated with higher rates of undetectable HCV RNA at all time points, including SVR12. The safety and tolerability profile was consistent with that observed in HCV-monoinfected patients.

Figure 3. Virological Response Over Time



Discussion: Dr. Rockstroh said these findings indicate that HIV/HCV co-infected patients can also benefit from the use of DAAs. He noted that while 7 patients in the study had HIV breakthrough, there were no differences between arms, so there was not a higher rate of breakthrough in patients receiving BOC than in those receiving placebo.

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Alisporivir plus ribavirin is highly effective as interferon-free or interferon-add-on regimen in previously untreated HCV-GT2 or GT3 patients: SVR12 results from VITAL-1 Phase 2b study. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 1405. Pawlotsky JJ-M, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_1405.html

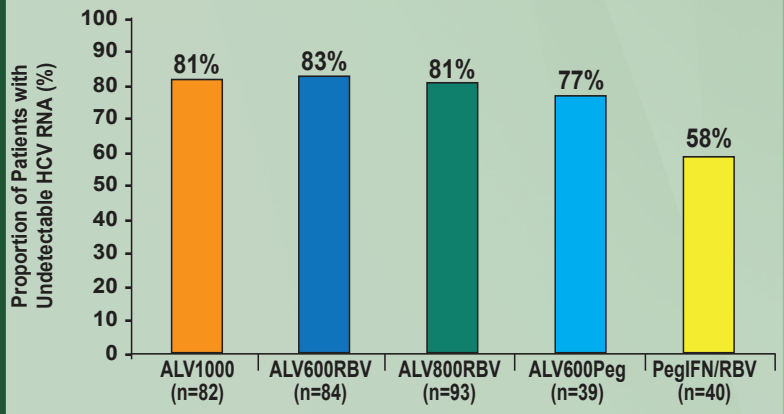
Alisporivir (ALV) is a host targeting antiviral (HTA) with pangenotypic anti-HCV activity that was studied in VITAL-1, an international, multicenter trial in HCV GT2/3 patients. The study was designed to determine rates of HCV clearance with interferon-free treatment – ALV alone or ALV + RBV and with delayed add-on PegIFN to ALV + RBV.

In the study, 340 treatment-naïve HCV GT2 or GT3 patients were randomized to 5 arms: 1) ALV 1,000 mg QD monotherapy (ALV1000, n=83); 2) ALV 600 mg QD + RBV (ALV600/RBV, n=84); 3) ALV 800 mg QD + RBV (ALV800/RBV, n=94); 4) ALV 600 mg QD + PegIFN (ALV/PegIFN, n=39); or 5) PegIFN + RBV (n=40). Patients in ALV-containing arms that achieved RVR (week 4 undetectable HCV RNA <25 IU/mL) continued on the initial treatment for 24 weeks, while those with detectable HCV RNA continued with ALV + PegIFN + RBV triple therapy from week 6 to week 24. End-of-Treatment Response (ETR) and SVR12 rates were analyzed separately for patients who received ALV-based, interferon-free treatment, and overall for patients in each arm receiving interferon-free and interferon add-on regimen.

The SVR12 – the proportion of patients with undetectable HCV RNA (%) (ITT population) – is shown in Figure 4. The SVR12 for the per protocol population (PPP) was 91% for ALV1000, 91% for ALV600/RBV, 94% for ALV800/RBV, 86% for ALV600/PegIFN, and 74% for PegIFN + RBV.

ALV treatments were well tolerated with lower discontinuation rates and markedly lower flu-like symptoms compared with PegIFN + RBV. The investigators concluded that alisporivir + RBV represents an effective interferon-free option in HCV GT2/3 patients, achieving high SVR rates. Alone or with RBV, ALV was found to maintain on-treatment HCV control, confirming ALV's high barrier to resistance.

Figure 4. Overall SVR 12 for All Treatment Groups (ITT Population)



Discussion: Dr. Rockstroh stated that the addition of RBV appeared to provide an added antiviral effect in this setting. Other trials with alisporivir have raised concerns about pancreatitis, but those studies combined alisporivir with PegIFN + RBV. Dr. Kwo suggested that the future drug development of alisporivir will be without the use of interferon.

GS-7977 PROTON and ELECTRON: 100% concordance of SVR4 with SVR24 in HCV GT1, GT2, & GT3. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 7. Lawitz E, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_7.html

GS-7999 (formerly PSI-7977), is a specific nucleotide analog inhibitor of HCV NS5B that demonstrated >90% EOT response and SVR12 in interferon-containing and interferon-free regimens, and across HCV genotypes 1, 2, and 3. Positive predictive value (PPV) and negative predictive value (NPV) of SVR4 and SVR12 for viral cure (SVR24) were assessed.

In PROTON, GS-7977 400 mg (n=47) in a 12+12 regimen with PegIFN + RBV in HCV GT1, and GS-7977 400 mg + PegIFN + RBV (n=24) for 12 weeks in HCV GT2/3 were studied. ELECTRON evaluated GS-7977 + PegIFN + RBV (n=30), GS-7977 + RBV (n=10), and GS-7977 monotherapy (n=10) in HCV GT2 or GT3. HCV RNA was assessed with Roche COBAS TaqMan (LOD 15 IU/mL) at post-therapy weeks 4, 12, and 24.

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117 subjects with HCV GT1, 2, or 3 received GS-7977 400 mg QD in ELECTRON or PROTON and achieved HCV RNA <LOD at EOT. There were 4 of 10 subjects on GS-7977 monotherapy who experienced relapse, versus 1 in 107 receiving GS-7977 + RBV ± PegIFN. All relapses occurred within 4 weeks after therapy discontinuation. To date, no relapse has been reported across the GS-7977 program after SVR4, regardless of treatment duration. 100% concordance was demonstrated for SVR4 and SVR12 with SVR24 in subjects with HCV GT1-3. This was true for regimens containing PegIFN (n=91) and for regimens not containing PegIFN (n=16).

Discussion: Dr. Rockstroh said that we may need to change our use of predictors of response with some patients. Dr. Kwo suggested that host factors will have to be considered in treatment decisions as we move toward an era of interferon-free therapy.

Dual oral therapy with the NS5A inhibitor daclatasvir (BMS-790052) and NS3 protease inhibitor asunaprevir (BMS-650032) in HCV genotype 1B-infected null responders or ineligible/intolerant to peginterf. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 14. Suzuki F, et al.

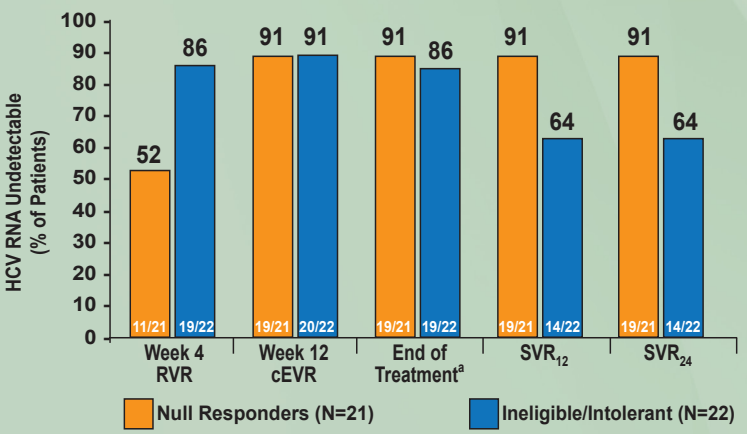
Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_14.html

This poster described an open-label, phase 2a study (AI447-017) that evaluated daclatasvir, an NS5A replication complex inhibitor + asunaprevir, a selective inhibitor of HCV NS3 protease, in non-cirrhotic Japanese adults with HCV GT1b infection with PegIFN + RBV intolerance or prior null response to PegIFN + RBV.

The study enrolled 21 null responders (<2 $\log_{10}$ HCV RNA reduction after 12 weeks of PegIFN + RBV, group A) and 22 patients ineligible for interferon-containing regimens for medical reasons or who discontinued PegIFN + RBV after <12 weeks due to intolerance (group B). Patients received daclatasvir 60 mg QD and asunaprevir 200 mg BID (initially 600 mg BID in 10/21 subjects in group A) for 24 weeks. Addition of PegIFN + RBV was permitted for group A patients with virologic failure.

The investigators reported that HCV RNA was undetectable at week 12 (cEVR) in 91% of patients in both groups. SVR12 was achieved by 91% and 64% of patients in groups A and B, respectively. Three patients discontinued prematurely for adverse events, 1 for lack of efficacy, 2 due to patient request, and 1 (group A) for lack of efficacy requiring addition of PegIFN + RBV. The SVR24 findings were reported at EASL: 91% for the null responder group and 64% for the ineligible/intolerant group (Figure 5)

Figure 5. Undetectable HCV RNA by Patient Group



[a] End of Treatment = Week 24 or last on-treatment visit for patients who discontinued early Intention to treat (missing = failure) analysis

Discussion: Dr. Dieterich said that a difference between the Japanese HCV epidemic and the situation in the United States is that the Japanese patients are about 10 years older – the median age of the intolerant group was 68 years, and they often had other diseases that would not allow them to take interferon. He speculated that the low SVR24 in the ineligible/intolerant group (64%) may be attributable to low adherence.

A 12-week interferon-free regimen of ABT-450/r, ABT-072, and ribavirin was well tolerated and achieved sustained virologic response in 91% treatment-naïve HCV IL28B-CC genotype-1-infected subject. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 13. Lawitz E, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_13.html

This study investigated the use of ABT-450, a NS3 HCV protease inhibitor (dosed with low-dose ritonavir, ABT-450/r), and ABT-072, a non-nucleoside NS5B polymerase inhibitor. This pilot study was the first interferon-free evaluation of ABT-450/r + ABT-072 + RBV in GT1-infected subjects. Eleven treatment-naïve, non-cirrhotic HCV GT1-infected subjects with IL28B rs12979860 genotype CC were enrolled in an open-label study that assessed the safety, tolerability, pharmacokinetics, and antiviral activity of ABT-450/r 150/100 mg QD + ABT-072 400 mg QD + weight-based RBV 1,000-1,200 mg/day dosed twice-daily for 12 weeks. Of the 11 subjects, 8 (73%) subjects were male, 9 (82%) were white, and 3 (27%) reported Latino ethnicity. At baseline, the

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median age was 56 years (range 41-66) and mean HCV RNA was 6.9 $\log_{10}$ IU/mL – 100% with BL HCV RNA >800,000 IU/mL. Eight (73%) subjects were infected with GT1a.

All 11 subjects completed 12 weeks of treatment and were followed for 24 weeks post-treatment. A rapid decrease in HCV RNA level was observed with treatment and all subjects had HCV RNA levels <25 IU/mL by week 3. All subjects maintained HCV RNA <25 IU/mL from weeks 4 through 12 of treatment, and all had undetectable HCV RNA from week 5 to the end of treatment. One subject relapsed at post-treatment week 8, while 10 subjects (91%) achieved SVR24 and 82% achieved SVR36. Most reported AEs were mild in severity; the most common were headache, fatigue, nausea, and dry skin. No additional relapses seen among 10 subjects with 48-week post-treatment data available.

Discussion: Dr. Kwo noted that there was a late relapse at SVR36. He said this should be viewed as a cautionary finding, although Dr. Dieterich noted that this was only one patient.

A randomized trial comparing ribavirin dose reduction versus erythropoietin for anemia management in previously untreated patients with chronic hepatitis C receiving boceprevir plus peginterferon/riba. 47th EASL, Barcelona, Spain, April 18-22, 2012. Abst. 1419. Poordad FF, et al.

Available at: http://www.viraled.com/modules/info/easl_2012_poster_program_abstract_1419.html

The study in this poster compared two approaches – RBV dose reduction (DR) and EPO – for the management of anemia during treatment with BOC + PegIFN + RBV. Treatment-naive HCV G1 patients (n=687) with baseline hemoglobin (Hb) 12-15 g/dL (female) or 13-15 g/dL (male) were enrolled in the multinational, open-label trial. Patients received PegIFN + RBV for 4 weeks, then BOC + PegIFN + RBV for 24 or 44 weeks (depending on HCV RNA level at treatment week 8). Investigators could use a secondary management strategy such as EPO, RBV DR, or transfusion in patients with Hb ≤8.5 g/dL to prevent study discontinuation. The primary endpoint was the comparison of sustained virologic response (SVR) between arms (24 or 44 weeks).

During the study, a total of 500 patients developed anemia (Hb ≤10 g/dL or were expected to reach that nadir before next visit) and were randomized to receive RBV DR (by 200-400 mg/d) or EPO (40,000 units/week subcutaneously). SVR and relapse rates were comparable between arms. Multivariate logistic regression analyses for SVR revealed treatment differences (EPO vs. RBV DR) were not statistically significant for subgroups, including gender, age, fibrosis score, baseline Hb, and time to anemia onset. SVR rates in patients receiving only primary anemia management were similar in the RBV DR (69%) and EPO (68%) groups. Patients who received additional secondary intervention had a numerically higher SVR rate than those who only received primary intervention: 82% and 76% for the RBV DR and EPO groups, respectively. Safety profiles were similar regardless of anemia management strategy. The investigators reported that SVR rates of 71% were achieved in anemic patients receiving BOC + PegIFN + RBV using either RBV DR or EPO and that these data support RBV DR for primary anemia management.

Discussion: Dr. Dieterich noted that research suggests we can dose-reduce RBV without affecting SVR rates with either of the two HCV protease inhibitors. Dr. Kwo said the study showed that either strategy for managing anemia is appropriate.