Advances in the Management of Hepatitis C
• This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the sponsorship of Annenberg Center for Health Sciences at Eisenhower and the Chronic Liver Disease Foundation. Annenberg Center for Health Sciences at Eisenhower is accredited by the ACCME to provide continuing medical education for physicians.

• This program is supported by an educational grant from Kadmon Pharmaceuticals and Merck.
Educational Objectives

• Incorporate new treatment options like boceprevir or telaprevir in combination with pegylated interferon and ribavirin in the treatment of genotype 1 hepatitis C

• Describe response guided therapy with approved protease inhibitors in combination with pegylated interferon and ribavirin

• Recognize primary adverse reactions seen in registration trials of protease inhibitors

• Provide optimal aggressive treatment or referral for patients with HCV
Treatment
Milestones in Therapy of CHC
Average SVR Rates from Clinical Trials

- **IFN 6m**
- **IFN 12m**
- **IFN/RBV 12m**
- **Peg-IFN 12m**
- **Peg-IFN/RBV/ DAA**

Standard Interferon 1991
Ribavirin 1998
Peginterferon 2001
Direct Acting Antivirals 2011

SVR (%)

6% 16% 34% 42% 39% 55% 70+%

Adapted from US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring MD.
New Products with an Indication for the Treatment of Chronic Hepatitis C

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Acting Antiviral (Protease Inhibitors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boceprevir</td>
<td>Victrelis™</td>
<td>Merck Pharmaceuticals Inc</td>
</tr>
<tr>
<td>Telaprevir</td>
<td>Incivek™</td>
<td>Vertex Pharmaceuticals Inc</td>
</tr>
</tbody>
</table>

- Both compounds act by inhibiting HCV nonstructural NS3/4A protease and are referred to as direct acting antivirals (DAAs)

Direct Acting Antivirals Utilize Response Guided Therapy (RGT) for Most Patients

- Treatment algorithms individualize treatment based on virologic response of patient
- Goals of RGT
  - Shorten therapy in those who exhibit favorable viral kinetics
  - Identify subjects who are unlikely to have a response
    - Limit side effects
    - Cost

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring MD.
Telaprevir
Telaprevir Phase 3 Clinical Trials

- **ADVANCE**: Previously untreated genotype 1 HCV
- **ILLUMINATE**: Previously untreated genotype 1 HCV
- **REALIZE**: HCV genotype 1 patients who failed previous treatment (relapsers, partial responders and null responders)
ADVANCE: Treatment Arms

T/PR, 8 wks (n=364)
T/PR, 12 wks (n=364)
PR (control arm) 48 weeks (n=361)

T, Telaprevir 750 mg TID
P, Peg-IFN alfa-2a 180 μg/wk
R, RBV 1000-1200 mg/day

eRVR*; extended rapid viral response, undetectable HCV RNA at wks 4 and 12
ADVANCE: Treatment Arms (Untreated Patients)

T/PR, 12 wks (n=364)

- eRVR*
  - PR 12 wks (n=246) Follow-up 24 wks SVR 89%
  - no eRVR* PR 36 wks Follow-up 24 wks SVR 54%

PR (control arm) 48 weeks (n=361) Follow-up 24 wks SVR 44%

*EVR; extended rapid viral response: undetectable HCV RNA at wks 4 and 12

T, Telaprevir 750 mg TID
P, Peg-IFN alfa-2a 180 μg/wk
R, RBV 1000-1200 mg/day

ADVANCE: Treatment-Naïve Patients Conclusions

- Telaprevir-containing regimens, compared to Peg-IFN/RBV alone, were associated with a significant increase in the rates of SVR overall and in all subgroups of patients analyzed.
- The majority of patients treated with telaprevir had undetectable HCV RNA at weeks 4 and 12 and received only 24 weeks of total therapy.
- The significant improvement in SVR rates and the capacity for response-guided therapy to shorten the duration of treatment among patients who have a rapid response represent important advances.

Patients who failed to achieve a 2 log10 drop at 12 wks or had detectable HCV RNA by 24 wks were discontinued as virologic failures.

eRVR; extended rapid viral response, undetectable HCV RNA at wks 4 and 12


T, Telaprevir 750 mg TID
P, Peg-IFN alfa-2a 180 μg/wk
R, RBV 1000-1200 mg/day

*Patients who failed to achieve a 2 log10 drop at 12 wks or had detectable HCV RNA by 24 wks were discontinued as virologic failures
†eRVR; extended rapid viral response, undetectable HCV RNA at wks 4 and 12

SVR
92%

SVR
90%
Telaprevir-containing regimens were associated with a significant increase in the rates of SVR.

58% treated with telaprevir had undetectable HCV RNA at weeks 4 and 12 and received only 24 weeks of therapy.

The duration of treatment among patients was shortened in patients who have an eRVR.

A 24-week telaprevir-based regimen was non-inferior to a 48-week telaprevir based regimen among patients who achieved eRVR (92% SVR compared to 90%).
REALIZE: Treatment Arms

Week 4  Week 12  Week 16

T12/PR48
TVR/Peg/RBV  Pbo/Peg/RBV  Peg/RBV  Follow-Up

T12(DS)/PR48
Pbo/Peg/RBV  TVR/Peg/RBV  Peg/RBV  Follow-Up

Pbo/PR48
PBO/Peg/RBV  Peg/RBV  Follow-Up

T, Telaprevir 750 mg TID
P, Peg-IFN alfa-2a 180 μg/wk
R, RBV 1000-1200 mg/day

REALIZE: Treatment Arms (previous non-response patients)

T12/PR48
- TVR/Peg/RBV
- Peg/RBV
- Follow-Up

Pbo/PR48
- PBO/Peg/RBV
- Peg/RBV
- Follow-Up

T, Telaprevir 750 mg TID
P, Peg-IFN alfa-2a 180 μg/wk
R, RBV 1000-1200 mg/day

REALIZE: SVR by Response to Previous Peg-IFN/RBV Therapy

**All Patients**
- **Relapsers**: 86%
- **Partial Responders**: 59%
- **Null Responders**: 32%

**Cirrhosis Patients**
- **Relapsers**: 87%
- **Partial Responders**: 34%
- **Null Responders**: 14%

### SVR by Response to Previous Peg-IFN/RBV Therapy

- **All T12/PR48**
- **Pbo/PR48**
The addition of telaprevir to Peg-IFN/RBV significantly increased rates of SVR for HCV genotype 1 patients who failed previous treatment with Peg-IFN/RBV.

A lead-in Peg-IFN/RBV phase did not improve SVR rates.

SVR rates were highest in prior relapsers (86%), intermediate those with prior partial responses (59%), and lowest in prior null responders (32%).

Telaprevir Indications and Usage
# Telaprevir/Peg-IFN/RBV Treatment Guidelines:
## Recommended Treatment Duration

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>HCV-RNA</th>
<th>Triple Therapy Tel/Peg-IFN/RBV</th>
<th>Dual Therapy Peg-IFN/RBV</th>
<th>Total Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment-Naïve and Prior Relapse Patients</strong></td>
<td>Undetectable at Weeks 4 and 12</td>
<td>First 12 weeks</td>
<td>Additional 12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td></td>
<td>Detectable (1000 units/mL or less) at Weeks 4 and/or 12</td>
<td>First 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
<tr>
<td><strong>Prior Partial and Null Responder Patients</strong></td>
<td>All patients</td>
<td>First 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>

Telaprevir/Peg-IFN/RBV Treatment Guidelines: Discontinuation of Dosing

• Treatment Futility Rules: All Patients

<table>
<thead>
<tr>
<th>HCV-RNA</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4 or Week 12: &gt;1000 units/mL</td>
<td>Discontinue telaprevir and Peg-IFN and RBV (telaprevir treatment complete at 12 weeks)</td>
</tr>
<tr>
<td>Week 24: Detectable</td>
<td>Discontinue Peg-IFN and RBV</td>
</tr>
</tbody>
</table>

• If Peg-IFN or RBV is discontinued for any reason, telaprevir must also be discontinued

Boceprevir
Boceprevir Phase 3 Clinical Trials

- **SPRINT-2**: Previously untreated genotype 1 HCV
- **RESPOND-2**: HCV genotype 1 patients who failed previous treatment (relapsers and partial responders)
SPRINT-2: Treatment Arms

**Peginterferon α-2b/Ribavirin 48 wks (PR Control)**
- **PR**
- Placebo + PR

**Boceprevir Response-Guided Therapy (RGT)**
- **PR**
- Boceprevir + PR
- Placebo + PR

**Boceprevir/PR 48 wks (BOC/PR48)**
- **PR**
- Boceprevir + PR

**Boceprevir 800 mg TID**
- P, Peg-IFN alfa-2b 1.5 mcg/kg/wk
- R, RBV 600-1400 mg/day

**Early Responder** (HCV-RNA TW 8-24 undetectable)

**Late Responder** (HCV-RNA TW 8 detectable-TW 24 undetectable)

**Futility**

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27, 2011, Silver Spring MD.
SPRINT-2 Treatment-Naïve Patients Conclusions

- Addition of boceprevir to PR standard-of-care resulted in a statistically significant increase in efficacy in treatment-naïve patients
- Using RGT, 44% of patients received only 28 weeks of treatment and achieved a SVR rate of 96%
- Boceprevir/PR significantly improved efficacy in the difficult to treat black patients
  - RGT is the recommended regimen
- Boceprevir/PR improved efficacy in the difficult to treat cirrhotic patients
  - Patients with cirrhosis may need 44 weeks of boceprevir treatment

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27, 2011, Silver Spring MD.
RESPOND-2: Treatment Arms

Boceprevir 800 mg TID
P, Peg-IFN alfa-2b 1.5 μg/kg/wk
R, RBV 600-1400 mg/day

Peginterferon α-2b/Ribavirin 48 wks (PR Control)
PR | Placebo + PR

Boceprevir Response-Guided Therapy (RGT)
PR | Boceprevir + PR

Boceprevir/PR 48 wks (BOC/PR48)
PR | Boceprevir + PR

Early Responder (HCV-RNA TW 8-12 undetectable)
Late Responder (HCV-RNA TW 8 detectable-TW 12 undetectable)

TW 0  TW 4  TW 8  TW 12  TW 36  TW 48  FW 24
Futility

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27, 2011, Silver Spring MD.
RESPOND-2: Treatment Arms

Peginterferon α-2b/Ribavirin 48 wks (PR Control)

- Placebo + PR

Boceprevir Response-Guided Therapy (RGT)

- Boceprevir + PR
- Early Responder (HCV-RNA TW 8-12 undetectable)
- Late Responder (HCV-RNA TW 8 detectable-TW 12 undetectable)

Boceprevir/PR 48 wks (BOC/PR48)

- Boceprevir + PR

Boceprevir 800 mg TID
P, Peg-IFN alfa-2b 1.5 mcg/kg/wk
R, RBV 600-1400 mg/day

SVR
23%
88%
72%
60%

RESPOND-2: Treatment Arms

**Peginterferon α-2b/Ribavirin 48 wks (PR Control)**
- **PR**
  - Placebo + PR
  - SVR: 23%

**Boceprevir Response-Guided Therapy (RGT)**
- **PR**
  - Boceprevir + PR
  - Early Responder (HCV-RNA TW 8-12 undetectable)
    - SVR: 88%
  - Late Responder (HCV-RNA TW 8 detectable-TW 12 undetectable)
    - SVR: 72%

**Futility**
- Futility rule: HCV RNA TW 12 ≥ 100 U/ml; TW24 detectable: **STOP TREATMENT**

RESPOND-2 Previous Treatment Failure Conclusions

- Adding boceprevir to PR for the Treatment Failure population resulted in a statistically significant ~3-fold increase in SVR

- RGT allowed a shorter duration of treatment in 44% of patients (early responders) who achieved 89% SVR

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27, 2011, Silver Spring MD.
Regardless of a patient’s historic response classification the addition of boceprevir substantially increased SVR:

- Highest responses in relapsers
- Robust response in non-responders
- RGT is the optimal regimen

Boceprevir/PR also improves efficacy in the difficult to treat cirrhotic patients

- Patients with cirrhosis may need 44 weeks of boceprevir treatment

US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27, 2011, Silver Spring MD.
Boceprevir Indications and Usage
**Boceprevir/Peg-IFN/RBV**  
**RGT Guidelines**

<table>
<thead>
<tr>
<th>ASSESSMENT (HCV-RNA Results)†</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At TW8</strong></td>
<td><strong>At TW 24</strong></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>Previously Untreated Patients</strong></td>
<td></td>
</tr>
<tr>
<td>Undetectable</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>
| Detectable                    | Undetectable   | 1. Continue all three medicines and finish through TW36; *and then*  
                                |                | 2. Administer Peg-IFN and RBV and finish through TW48  |
| **Previous Partial Responders or Relapsers** |                |                |
| Undetectable                  | Undetectable   | Complete three medicine at TW36  |
| Detectable                    | Undetectable   | 1. Continue all three medicines and finish through TW36; *and then*  
                                |                | 2. Administer Peg-IFN and RBV and finish through TW48  |

†In clinical trials, HCV-RNA in plasma was measured using a Roche COBAS® TaqMan® assay with a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL. Boceprevir (VICTRELIS™) Prescribing Information. Schering Corporation, a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ. May, 2011.
• Treatment Futility

- If the patient has HCV-RNA results $\geq 100$ IU/mL at TW12, then discontinue three-medicine regimen

- If the patient has confirmed, detectable HCV-RNA at TW24, then discontinue three-medicine regimen

Contraindications to DAA/Peg-IFN/RBV Combination Therapy
Both Boceprevir/Peg-IFN/RBV and Telaprevir/Peg-IFN/RBV Combination Therapy have Similar Contraindications

- Contraindications to Peg-IFN and RBV also apply to boceprevir and telaprevir combination therapy
- Both boceprevir and telaprevir combination therapies are contraindicated in:
  - Women who are or may become pregnant
  - Men whose female partners are pregnant

Both Boceprevir/Peg-IFN/RBV and Telaprevir/Peg-IFN/RBV Combination Therapy have Similar Contraindications (cont)

- Both boceprevir and telaprevir are contraindicated when combined with drugs that:
  - Are highly dependent on CYP3A for clearance if elevated plasma concentrations are associated with serious and/or life-threatening events
  - Strongly induce CYP3A and may lead to lower exposure and loss of efficacy of telaprevir

- Refer to the respective prescribing information for recommendations based on established or potentially clinically significant drug interactions before initiating therapy with boceprevir or telaprevir

Adverse Reactions
Telaprevir/Peg-IFN/RBV Combination Therapy: Clinical Trial Adverse Reactions

- Safety assessment based on data from pooled clinical trials including:
  - 1797 subjects who received telaprevir combination therapy
  - 493 who received Peg-IFN/RBV
- Serious AEs occurred in 3% of subjects who received telaprevir combination therapy vs. none of the subjects treated with Peg-IFN/RBV
  - The most frequent serious AEs in subjects treated with telaprevir combination therapy were skin disorders (rash and/or pruritus) and anemia

14% of subjects discontinued telaprevir due to AEs

Rash, anemia, fatigue, pruritus, nausea, and vomiting were the most frequent AEs leading to discontinuation of telaprevir
The most commonly reported adverse reactions (>35% of subjects regardless of causality assessment) were fatigue, anemia, nausea, headache, and dysgeusia when boceprevir was used in combination with Peg-IFN/RBV (n=2095).
Conclusions
A New Era In the Treatment of Hepatitis C: Direct Acting Antivirals: Conclusions

• DAAs, in combination with PegIFN and RBV, achieve SVRs in 65% to 75% of treatment naïve genotype 1 CHC patients and in 60% to 65% of genotype 1 CHC patients previously treated with Peg-IFN/RBV
  - In previously treated patients SVR rates are highest in prior relapsers, intermediate in prior partial responders, and lowest in prior null responders

• Response guided therapy utilizes on-treatment viral response to determine appropriate treatment duration
  - Treatment durations of only 24 or 28 weeks can be utilized in many treatment naïve patients
As with Peg-IFN/RBV therapy, DAA/Peg-IFN/RBV therapy is associated with significant side effects
  - Most adverse events are similar to those seen with Peg-IFN/RBV therapy
  - Most adverse events can be managed

Both boceprevir and telaprevir are contraindicated when combined with drugs that are highly dependent on CYP3A for clearance or that strongly induce CYP3A
  - Drug interactions may affect blood levels of either the DAA or of the co-administered drug

Resistance may develop to either boceprevir or telaprevir and is frequently associated with treatment failure
Select EASL 2012 Abstracts
Boceprevir & Telaprevir
100% SVR in IL28B CC Patients Treated with 12 Weeks of Telaprevir, Peginterferon and Ribavirin in the PROVE 2 Trial


Poster 1094
47th Annual Meeting of the European Association for the Study of the Liver
Barcelona, Spain
April 21, 2012
100% SVR in IL28B CC Patients Treated with 12 Weeks of Telaprevir/PegIFN/RBV in the PROVE 2 Trial: Results

SVR According to IL28B Genotype and Treatment

<table>
<thead>
<tr>
<th></th>
<th>T12PR12 n=44</th>
<th>T12PR24 n=37</th>
<th>T12P12 n=29</th>
<th>PR48 n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC n/n (%)</td>
<td>12/12 (100)</td>
<td>15/16 (94)</td>
<td>3/4 (75)</td>
<td>7/11 (64)</td>
</tr>
<tr>
<td>CT n/n (%)</td>
<td>12/27 (44)</td>
<td>12/18 (67)</td>
<td>4/22 (18)</td>
<td>5/16 (31)</td>
</tr>
<tr>
<td>TT n/n (%)</td>
<td>1/5 (20)</td>
<td>1/3 (33)</td>
<td>0/3 (0)</td>
<td>1/4 (25)</td>
</tr>
</tbody>
</table>

100% SVR in IL28B CC Patients Treated with 12 Weeks of Telaprevir/PegIFN/RBV in the PROVE 2 Trial: Conclusion

- 12 weeks of the triple combination of telaprevir, peginterferon and ribavirin are sufficient to cure IL28B CC treatment-naïve patients infected with HCV genotype 1 without cirrhosis

Futility Rules in Telaprevir Combination Treatment


Oral Presentation 55
47th Annual Meeting of the European Association for the Study of the Liver
Barcelona, Spain
April 20, 2012
Futility Rules in Telaprevir Combination Treatment: Results

- Patients with HCV RNA >1000 IU/mL at week 4:
  - Treatment-naïve patients: 1.6% (14/903)
  - Prior relapsers: 0.7% (1/145)
  - Prior partial responders: 0% (0/49)
  - Prior null responders: 14% (10/72)
  - None of these patients achieved an SVR with continued PR treatment (telaprevir was discontinued per protocol)
  - 24/25 patients reached HCV RNA nadir at or prior to week 4, typically at week 2, with a subsequent increase in HCV RNA levels by week 4

Futility Rules in Telaprevir Combination Treatment: Results (cont)

- Patients with HCV RNA levels between 100 - 1000 IU/mL at week 4:
  - Prior treatment-naïve: 1.8% (16/903)
  - Prior treatment experienced: 2.6% (7/266)
  - 22% (5/23) achieved SVR with continued treatment

- Modeling data confirmed patients with 100 - 1000 IU/mL at week 4 would benefit from continued telaprevir and PegIFN/RBV treatment, but patients with >1000 IU/mL would not

A futility rule of >1000 IU/mL at week 4 identified and predicted treatment-naïve or -experienced patients unlikely to achieve an SVR.

This futility rule prevented unnecessary exposure to telaprevir and PegIFN/RBV in patients unlikely to benefit from further treatment.

24/25 of these patients had reached HCV RNA nadir by week 4 and were experiencing viral breakthrough.

Safety of Telaprevir or Boceprevir in Combination with Peginterferon alfa/Ribavirin in Cirrhotic Non Responders. First Results of the French Early Access Program (ANRS C020-CUPIC)


Oral Presentation 8
47th Annual Meeting of the European Association for the Study of the Liver
Barcelona, Spain
April 19, 2012
Safety of Telaprevir or Boceprevir in Combination with PegIFN/RBV in Cirrhotic Non Responders: Results

<table>
<thead>
<tr>
<th></th>
<th>Telaprevir/ PegIFN/RBV (n=169)</th>
<th>Boceprevir/ PegIFN/RBV (n=138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median treatment / PI duration (days)</td>
<td>112.0 / 85.0</td>
<td>113.0 / 84.0</td>
</tr>
<tr>
<td>Serious adverse events / Discontinuation</td>
<td>87 (51%) / 20 (12%)</td>
<td>41 (30%) / 10 (7%)</td>
</tr>
<tr>
<td>Death</td>
<td>3 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Anemia Grade 2 (8.0 - &lt;10.0 g/dL) / Grade 3-4 (&lt;8.0 g/dL)</td>
<td>54 (32%) / 23 (14%)</td>
<td>39 (28%) / 8 (6%)</td>
</tr>
<tr>
<td>EPO use / Blood transfusion</td>
<td>94 (56%) / 32 (19%)</td>
<td>71 (51%) / 8 (6%)</td>
</tr>
</tbody>
</table>

Safety of Telaprevir or Boceprevir in Combination with PegIFN/RBV in Cirrhotic Non Responders: Results (cont)

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Telaprevir/ PegIFN/RBV (n=169)</th>
<th>Boceprevir/ PegIFN/RBV (n=138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia Grade 3-4 (&lt;1000/mm$^3$) / G-CSF use</td>
<td>21 (12%) / 5 (3%)</td>
<td>14 (10%) / 7 (5%)</td>
</tr>
<tr>
<td>Thrombopenia Grade 3-4 (&lt;50000/mm$^3$ / Thrombopoietin use</td>
<td>37 (22%) / 1 (1%)</td>
<td>10 (7%) / 1 (1%)</td>
</tr>
<tr>
<td>Rash Grade 3 / SCAR</td>
<td>11 (7%) / 0 (0%)</td>
<td>1 (1%) / 0 (0%)</td>
</tr>
<tr>
<td>Grade 3-4 infection / Other AEs</td>
<td>4 (2%) / 90 (53%)</td>
<td>1 (1%) / 44 (32%)</td>
</tr>
</tbody>
</table>

The safety profile of telaprevir/PegIFN/RBV or boceprevir/PegIFN/RBV in cirrhotic patients was poor and associated with significant adverse event rates of 30% to 51% compared to those reported in phase III trials of 9% to 14%.

Data suggest that triple therapy must be administered cautiously with intensive safety monitoring in these patients.
Ribavirin Dose Modification in Treatment-Naïve and Previously Treated Patients who Received Telaprevir Combination Treatment: No Impact on Sustained Virologic Response in Phase 3 Studies


Poster 1162
47th Annual Meeting of the European Association for the Study of the Liver
Barcelona, Spain
April 21, 2012
### RBV Dose Modification Has No Impact on SVR in Patients Receiving Telaprevir Combination Treatment: Results

#### SVR rates in treatment naïve patients by RBV dose/day

<table>
<thead>
<tr>
<th>RBV Dose Reductions</th>
<th>Patients Affected, n/N (%)</th>
<th>SVR, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T12PR</td>
<td>PR</td>
</tr>
<tr>
<td>Any dose reduction</td>
<td>446/885 (50%)</td>
<td>62/354 (18%)</td>
</tr>
<tr>
<td>Received ≤600 mg</td>
<td>395/885 (45%)</td>
<td>38/354 (11%)</td>
</tr>
<tr>
<td>Received 800-1000 mg/day</td>
<td>51/885 (6%)</td>
<td>24/354 (7%)</td>
</tr>
<tr>
<td>Never reduced</td>
<td>439/885 (50%)</td>
<td>292/354 (82%)</td>
</tr>
</tbody>
</table>

RBV Dose Modification Has No Impact on SVR in Patients Receiving Telaprevir Combination Treatment: Results

SVR rates in previously treated patients by RBV dose/day

<table>
<thead>
<tr>
<th>RBV Dose Reductions</th>
<th>Prior Relapse, n/N (%)</th>
<th>Prior Partial, n/N (%)</th>
<th>Prior Null, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T12PR48</td>
<td>PR</td>
<td>T12PR48</td>
</tr>
<tr>
<td>Received ≤600 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received 800-1000 mg/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never reduced</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Ribavirin dose-reductions among previously treated patients:
  - Prior relapse: 56/145 (39%) T12PR48 and 13/68 (19%) PR
  - Prior partial: 15/49 (31%) T12PR48 and 7/27 (26%) PR
  - Prior null: 13/72 (18%) T12PR48 and 7/37 (19%) PR

In treatment-naïve and previously treated patients who received telaprevir combination treatment, RBV dose reduction was more frequent than in the control group.

RBV dose reduction, including dose reduction to 600 mg/day, had no substantial effect on SVR rates in patients treated with telaprevir combination therapy.