

a series of fact sheets written  
by experts in the field of liver  
disease

## Drugs in Development: *Telaprevir* (Incivek™)

Alan Franciscus, Editor-in-Chief

Telaprevir is an HCV protease inhibitor that has completed three phase 3 clinical trials. The information in this fact sheet represents top-line results only and therefore only limited data was available to report on. It is important to know that the data that was released doesn't give us the information we need to really understand the efficacy, safety and tolerability of telaprevir. But the information provided is a good starting point and I will update this fact sheet as more information is released. Telaprevir was given in combination with pegylated interferon

**Note:** HCSP has developed separate fact sheets for telaprevir and boceprevir because the studies were not head-to-head studies—that is they did not directly compare the drugs. Additionally, it is difficult to compare the results of the studies because the clinical trials were designed using different criteria such as differences in on-treatment response guidance rules, lead-in phase vs. no lead-in phase, different brands of pegylated interferon and different periods of treatment duration.

### **<sup>1</sup>ADVANCE**

The ADVANCE study included 1,095 HCV genotype 1 treatment-naïve patients (never been treated). Twenty percent of the patient population in the study were African American, Black, Hispanic or Latino, and 20% had advanced fibrosis or cirrhosis. The treatment was guided by type of on-treatment response to the medicines. There was no lead-in phase—the triple combination of telaprevir, pegylated interferon and ribavirin was started at day one.

The study contained three arms. The different arms and the SVR or sustained virological response rates\* are listed below:

- **12-week telaprevir arm:** 12 weeks of telaprevir, pegylated interferon and ribavirin followed by an additional 12 or 36 weeks of pegylated interferon and ribavirin (without telaprevir) depending on the type of on-treatment response; **SVR = 79%**
- **8-week telaprevir arm:** 8 weeks of telaprevir, pegylated interferon and ribavirin followed by 16 or 40 weeks of pegylated interferon and ribavirin (without telaprevir) depending on the type of on-treatment response; **SVR = 69%**
- **Standard of care arm (SOC):** 48 weeks of pegylated interferon plus ribavirin; **SVR = 44%**

In a subanalysis it was found that:

- Blacks achieved a 62% SVR compared to 25% SVR in the control arm
- Hispanics achieved a 74% SVR compared to 39% in the control arm
- People with bridging fibrosis/cirrhosis achieved a 62% SVR compared to 33% SVR in the control arm.

**Note:** The on-treatment response was guided by the following rules:

- People who were HCV RNA (viral load) undetectable (<25 IU/mL) at week 4 and week 12 were treated for a total of 24 weeks
- Patients who were not HCV RNA undetectable at week 4 or week 12, but who were undetectable by week 24 were treated for a total of 48 weeks

### **<sup>1</sup>ILLUMINATE**

This study included 540 HCV genotype 1 treatment-naïve patients (never been treated). The aim of this study was to find out if there was a benefit in extending the total treatment duration from 24 weeks to 48 weeks.

The use of erythropoiesis-stimulating agents (Epogen/Procrit) was not allowed in the study.

## Overall SVR

- **SVR = 72%** —patients who received the triple combination of telaprevir, pegylated interferon, ribavirin

The study was response guided—patients who were HCV RNA negative at weeks 4 and 12 of treatment were randomized at treatment week 20 to receive either 24 or 48 weeks total treatment duration.

In a subanalysis it was found that:

- Black patients achieved an 88% SVR
- Hispanic patients achieved an 94% SVR

Based on the data in this study, there was no benefit seen in extending the treatment duration from 24 to 48 weeks for treatment-naïve HCV genotype 1 patients.

## ***REALIZE***

The REALIZE study included HCV genotype 1 prior non-SVR patients — 354 relapsers, 124 partial responders, and 184 null response patients.\* The only data provided on the patient population was that 89% of patients had a high HCV RNA viral load (greater than or equal to 800,000 IU/mL) and 26% of the patients had cirrhosis—both are considered poor predictors of treatment response. All the patients were HCV genotype 1 evenly divided between subtypes 1a and 1b.

The use of erythropoiesis-stimulating agents (Epoen/Procrit) was not allowed in this study.

Overall, 65% in the telaprevir containing groups achieved an SVR compared to 17% in the groups that received the current standard of care— pegylated interferon and ribavirin — without telaprevir. The SVR rates of the **telaprevir containing groups** vs. **standard of care groups** by type of prior Non-SVR are listed below.

The side effects of all three clinical trials were similar across all treatment arms. The treatment discontinuation rates were also similar between all the arms in all three studies including the arms that did not contain telaprevir.

On November 23, 2010 Vertex announced that it had submitted an application to the Food and Drug Administration for marketing approval. Vertex has also requested and been granted a priority review. FDA approval of telaprevir, pegylated interferon plus ribavirin is expected mid-2011. Health Canada has also granted telaprevir a Priority Review.

On December 20, 2010, Janssen-Cilag (Johnson & Johnson in Europe) will seek approval from the European Medicines Agency (EMA) for a new investigational treatment for the chronic genotype 1 hepatitis C virus (HCV). JNJ owns the commercial rights to Telaprevir in Europe.

## ***\*Definitions:***

**Sustained virological response (SVR):** is defined as undetectable HCV RNA (viral load) 24 weeks after the last dose of medicine was taken.

**Relapser:** a person who was undetectable at the completion of at least 42 weeks of therapy but who became detectable during the 24 week follow-up period.

**Partial responder:** a person who achieved at least a 2 log<sub>10</sub> reduction in HCV RNA (viral load) at week 12, but who was never HCV RNA undetectable by week 24 of treatment.

**Null responder:** a person who achieved LESS than a 2 log<sub>10</sub> reduction in HCV RNA by week 12.

*Example: 2 log drop = 15,000,000 IU/ml to 150,000 IU/ml; a viral load that starts at 15,000,000 IU/ml and does not decrease to 150,000 IU/ml or lower.*

## **REALIZE RESULTS**

<b>Type of Prior Non-SVR</b>	<b>Telaprevir Containing Groups</b>	<b>Standard of Care Groups</b>
Relapsers	86% SVR	24%
Partial responders	57% SVR	15%
Null responders	31% SVR	5%

<sup>1</sup>Triple combination (telaprevir, pegylated interferon, ribavirin). Telaprevir was not given for more than 12 weeks.

### *Quick Reference Guide:*

#### **Summary—Top Line Results:**

- All three studies included on-treatment response guided therapy.
- The side effects were similar across all treatment arms including the arms that did and did not receive telaprevir.
- Telaprevir (in combination with pegylated interferon and ribavirin) was only given for 8 to 12 weeks—then followed by a treatment with pegylated interferon and ribavirin.
- Treatment-naïve patients were treated for a total treatment duration ranging from 24 weeks up to 48 weeks.
- Patients retreated with telaprevir, pegylated interferon plus ribavirin were treated for a total treatment duration of 48 weeks.

#### **Treatment Naïve (never been treated):**

- All groups that received telaprevir plus pegylated interferon and ribavirin
  - ◆ SVR or cure rates from 69% to 75%

#### **Treatment Experienced (prior pegylated/ribavirin non-SVR):**

- All groups that received telaprevir plus pegylated interferon and ribavirin
  - ◆ SVR or cure rates from 31 to 86% (depending on type of prior response)

FDA approval of the combination of telaprevir, pegylated interferon and ribavirin is expected mid-2011

*Source: Company press release*

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- *Telaprevir*

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- *Patient Assistance Programs*
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- *Pregnancy Categories*
- *Reporting Drug Side Effects*
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## **• hcsPFACTsheet •**

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#### **Executive Director**

**Editor-in-Chief, HCSP Publications**  
Alan Franciscus

#### **Design**

Paula Fener

#### **Production**

C.D. Mazoff, PhD

#### **Contact information:**

Hepatitis C Support Project  
PO Box 427037  
San Francisco, CA 94142-7037

[alanfranciscus@hcvadvocate.org](mailto:alanfranciscus@hcvadvocate.org)

The information in this fact sheet is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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