var drug_url = "telaprevir-drug";

Telaprevir *(Incivek)*

Discontinued

Discontinued. This treatment has been discontinued.

Table of Contents

Drug Summary

Although telaprevir was a promising direct-acting antiviral agent that had impact in the hepatitis C treatment field during 2011 to 2013, it was subsequently replaced by newer direct-acting antiviral agents that were more effective, better tolerated, and more convenient. Based on the dwindling role of telaprevir after newer direct-acting antiviral agents were approved, Vertex pharmaceuticals discontinued the sales and distribution of telaprevir in the United States in October 2014. Telaprevir does have some current importance since persons who previously failed a telaprevir-based regimen may have developed resistant associated variants, which could potentially impact subsequent therapy.

Class and Mechanism

Telaprevir (*Incivek*) is a NS3/4A hepatitis C protease inhibitor. Specifically, telaprevir inhibits the proteolytic cleavage of the HCV encoded polyprotein, an essential step in the viral life cycle for the production of mature forms of the viral proteins NS4A, NS4B, NS5A, and NS5B.

Manufacturer for United States

Telaprevir (*Incivek*) is no longer manufactured in the United States. Telaprevir (Figure 1) was previously manufactured by Vertex Pharmaceuticals. Vertex pharmaceuticals discontinued the sales and distribution of telaprevir in the United States in October 2014, primarily due to available alternative treatments and diminishing market demands. The drug telaprevir was formerly known as VX-950 and was co-developed by Vertex Pharmaceuticals and Johnson & Johnson.

Cost and Medication Access

In 2014, Vertex Pharmaceuticals discontinued its sales of telaprevir in the United States.

Adverse Effects

The most significant adverse effects reported in the main registration trials and in post-marketing experience were rash, anorectal complaints, and anemia. When comparing triple therapy of telaprevir, peginterferon, and ribavirin with dual therapy of peginterferon and ribavirin alone significant differences were noted with rash (56% versus 34%), anemia (36% versus 17%), and anorectal complaints that include anorectal discomfort, anal pruritus, and hemorrhoids (29% versus 7%). In most cases, the rash that develops is eczematous or maculopapular in character and mild to moderate in severity; the rash is typically manageable with good skin care and topical emollients or corticosteroids. In some instances, however, telaprevir has caused serious skin rashes, including Steven's Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Toxic Epidermal Necrolysis (TEN). Teleprevir has a black box warning for fatal and non-fatal serious skin reactions.

Key Drug Interactions

For complete information on telaprevir-related drug interactions, see the Drug Interactions section in the Telaprevir (*Incivek*) Prescribing Information.

Clinical Trials

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ADVANCE (Study 108)

This phase 3, double-blind, placebo-controlled trial examined the effiacacy of telaprevir in combination with peginterferon and ribavirin in treatment-naïve patients with genotype 1 infection. Investigators randomized 1,088 patients to one of three treatment arms: (1) telaprevir for the first 8 weeks plus peginterferon and ribavirin (T8/PR group) followed by an additional 12 or 36 weeks of peginterferon and ribavirin; (2) telaprevir for the first 12 weeks in combination with peginterferon plus ribavirin (T12/PR group), followed by an additional 12 or 36 weeks of peginterferon and ribavirin, or (3) a placebo-controlled arm of peginterferon plus ribavirin for 48 weeks (PR group). In the two telaprevir groups, patients who had undetectable HCV RNA at week 4 and 12 (defined as an extended rapid virologic response [eRVR]) completed a 24-week course of therapy while those who did not meet this response-guided treatment criterion completed 48 weeks. Sustained virologic response at week 24 post treatment (SVR24) was observed in 72% in the T8/PR group, 79% in the T12/PR group, and 46% in the control arm (PR group). Among all patients treated with telaprevir, 58% had an eRVR and received a total of 24 weeks of therapy. Thus, in treatment-naive patients with genotype 1 chronic HCV infection, the addition of telaprevir to peginterferon and ribavirin significantly improved the treatment responses when compared with peginterferon and ribavirin alone. Further, use of telaprevir shortened the duration of therapy in most patients from 48 to 24 weeks.

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ILLUMINATE (Study 111)

This open-label phase 3 trial involved treatment-naïve patients with genotype 1 chronic HCV who received therapy with telaprevir plus peginterferon and ribavirin. All patients received telaprevir for 12 weeks, but treatment duration with peginterferon and ribavirin varied depending on whether patients had undetectable HCV RNA levels at weeks 4 and 12 (extended rapid virologic response [eRVR]). Patients with an eRVR were randomized at week 20 to receive peginterferon plus ribavirin for an additional 4 (T12/PR24 group) or 28 more weeks (T12/PR48 group). All of the patients who do not achieve eRVR received a total of 48 weeks of peginterferon and ribavirin (T12PR48). Among the 540 subjects enrolled, 352 (65%) achieved an eRVR. Among the 352 patients who achieved an eRVR, the SVR24 rates were comparable in the T12/PR24 group (92%) and the T12/PR48 group (88%). The patients who did not achieve eRVR had SVR24 rate of 64%. This study demonstrated that response guided therapy is an appropriate strategy in treatment-naive patients with genotype 1 HCV who are receiving treatment with telaprevir plus peginterferon and ribavirin. This strategy, however, may not be valid for patients with cirrhosis. For the subset of cirrhotic patients in this study, the response-guided therapy approach appeared to have suboptimal efficacy– among the 30 patients who achieved eRVR, the SVR rates were 61% for T12/PR24 versus 92% for T12/PR48.

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OPTIMIZE (C211)

In this phase 3, dosing trial, 740 treatment-naive patients with genotype 1 chronic hepatitis C were randomized to receive a 12-week course of telaprevir at a dose of 1125 mg bid or 750 mg every 8 hours, in combination with peginterferon and ribavirin. All patients received 12 weeks of telaprevir with peginterferon and ribavirin, followed by peginterferon and ribavirin for a duration that depended on the response to therapy. Specifically, patients with an undetectable HCV RNA level after 4 weeks of therapy received a total of 24 weeks whereas all others received 48 weeks. The SVR12 rates were nearly identical in the two treatment dosing arms of telaprevir: 74% in the twice daily group and 73% in the every 8 hour group. Among those subjects who achieved an undetectable HCV RNA level at week 4, the SVR response rates were particularly good (86% in the twice daily group and 85% in the every 8 hour group).

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REALIZE (Study C216)

This phase 3 randomized, double-blind, trial enrolled 663 patients with chronic HCV genotype 1 infection who were previously treated with peginterferon plus ribavirin and did not achieve SVR, including prior relapsers and non-responders. The nonresponders included two subgroups: prior partial responders and prior null responders. Subjects were randomized in a 2:2:1 ratio to one of three regimens: (a) telaprevir combined with peginterferon plus ribavirin for 12 weeks, followed by 36 weeks of peginterferon plus ribavirin (T12/PR48), (b) peginterferon plus ribavirin given for a lead-in phase of 4 weeks, followed by 12 week of telaprevir plus peginterferon and ribavirin, followed by 32 weeks of peginterferon plus ribavirin (Lead In-T12/PR48), or (c) placebo-controlled arm of peginterferon plus ribavirin for 48 weeks (PR48). The SVR rates were markedly higher in the telaprevir-treated patients (64% without lead in and 66% with lead in) when compared with the peginterferon plus ribavirin alone (17%). There were notable differences in SVR according to prior treatment history: the best SVR rates were achieved in prior relapsers, intermediate SVR rates with prior partial responders, and poor SVR rates were seen with prior null responders. Overall, this study

demonstrated that with hepatitis C treatment experienced patients, the addition of telaprevir to peginterferon and ribavirin markedly improves SVR rates, irrespective of whether a lead-in phase is used.

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Figures

Figure 1 Telaprevir (*Incivek*) Box

Photo: Andrew Karpenko, University of Washington

Figure 2 Telaprevir (*Incivek*) Tablet

Photo: Andrew Karpenko, University of Washington