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Telaprevir

Updated: March 10, 2016.

OVERVIEW

Introduction

Telaprevir is an oral, direct acting hepatitis C virus (HCV) protease inhibitor that is used in combination with other antiviral agents in the treatment of chronic hepatitis C, genotype 1. Telaprevir has not been linked to instances of acute liver injury during therapy, but has been linked to cases of severe cutaneous reactions such as DRESS and Stevens Johnson syndrome which can be associated with mild hepatic injury. In addition, when combined with peginterferon and ribavirin, telaprevir has been associated with cases of hepatic decompensation in patients with preexisting cirrhosis.

Background

The hepatitis C virus is a small RNA virus that is a major cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma in the United States as well as worldwide. Various approaches to antiviral therapy of chronic hepatitis C have been developed, starting in the 1980s with interferon alfa which was replaced in the 1990s by long acting forms of interferon (peginterferon), to which was added the oral nucleoside analogue, ribavirin. Between 2010 and 2015, several potent oral, direct acting anti-HCV agents were developed and combinations of these found to have marked activity against the virus, allowing for highly effective therapy without use of interferon with treatment courses of 12 to 24 weeks only. These direct acting agents included HCV protease (NS3/4) inhibitors, structural replication complex (NS5A) inhibitors and the HCV RNA polymerase (NS5B) inhibitors. The HCV protease inhibitors block the activity of the viral encoded protease that is essential in the posttranslational modification of the viral polypeptide, cleaving it into a series of structural and nonstructural (NS: enzyme) regions. The HCV proteases that have been developed are polypeptide-like molecules, modified amino acids that that resemble the specific amino acid sequence that the protease cleaves and act as competitive inhibitors of the protease enzyme. At least four HCV protease inhibitors (all having the suffix: -previrs) have been approved for use in the United States: boceprevir [2012], telaprevir [2012], simeprevir [2013] and paritaprevir [2014].

Telaprevir (tel a' pre vir) was one of the first HCV specific protease inhibitors developed as therapy of chronic hepatitis C. Like other HCV protease inhibitors, telaprevir blocks the activity of the viral encoded protease (HCV nonstructural [NS] region 3/4) that is essential in the posttranslational modification of the viral polypeptide that is cleaved into a series of structural and nonstructural (enzyme) regions. When used by itself, telaprevir results in rapid inhibition of HCV RNA levels, but resistance develops rapidly in a high proportion of patients. When combined with peginterferon and ribavirin, it was shown to provide a sustained inhibition of HCV RNA with a low rate of antiviral resistance. Triple therapy with telaprevir, peginterferon and ribavirin, when given for 44 to 48 weeks, increased the sustained virological response (SVR) rate from 40% to 50% (peginterferon and ribavirin alone) to 70% to 85% in patients with genotype 1. Telaprevir was approved for use

in the United States in 2011 for patients with chronic hepatitis C, genotype 1, to be used in combination with peginterferon and ribavirin. Since that time, telaprevir has been replaced by more potent and better tolerated oral antiviral agents that can be given in combination without peginterferon. For these reasons, telaprevir was withdrawn by the sponsor in 2015. Telaprevir was previously available under the brand name Incivek (formerly VX950) as tablets of 375 mg. The recommended dose was 750 mg three times daily for the first 12 of the 24 or 48 weeks of combination therapy. The side effects of telaprevir were difficult to separate from those of peginterferon and ribavirin, but the triple therapy was associated with a higher rate of many side effects, including anemia, fatigue, itching, rash, anal pruritus and burning and gastrointestinal upset. Rash was particularly common with telaprevir therapy occurring in at least half of patients and occasionally being associated with DRESS or Stevens Johnson syndrome.

Hepatotoxicity

In large randomized controlled trials, triple therapy with telaprevir, peginterferon and ribavirin was associated with a high rate of adverse events that often required dose adjustments and led to early discontinuation in 5% to 20% of patients. However, serum ALT elevations and clinically apparent liver injury were not generally mentioned as adverse events of therapy. Telaprevir, however, was associated with a high rate of rash, which was sometimes associated with features of hypersensitivity, including rare instances of DRESS and Stevens Johnson syndrome. These severe cutaneous reactions are often accompanied by laboratory evidence of hepatic injury (ALT and alkaline phosphatase elevations). In reported cases, however, the rash and other features of hypersensitivity have overshadowed the hepatic injury and none were reported to be associated with jaundice.

Another exception to the absence of hepatic complications of telaprevir therapy occurred in patients with advanced fibrosis or cirrhosis, among whom de novo, seemingly spontaneous hepatic decompensation occurred in a proportion of subjects. Decompensation was particularly common among patients with advanced fibrosis or cirrhosis and those with a previous history of decompensation. The cause of the decompensation was not clear and the separate role of telaprevir in contrast to peginterferon and ribavirin could not be defined. Nevertheless, in postmarketing studies of triple therapy of chronic hepatitis C with cirrhosis, decompensation was reported in 2% to 8% of patients, and deaths from hepatic failure in 1% to 3%.

Likelihood score: E* (unproven but suspected cause of liver injury).

Mechanism of Injury

The mechanism by which telaprevir might cause liver injury is not known. It is metabolized in the liver largely via the cytochrome P450 system, predominantly CYP 3A4, and liver injury may be due to production of a toxic or immunogenic metabolite. It is also a substrate of P-glycoprotein (P-gp). Telaprevir is also susceptible to multiple drug-drug interactions and can cause increases in serum concentrations of drugs that depend upon CYP 3A4 metabolism or P-gp. The other adverse effects of telaprevir, particularly when combined with peginterferon and ribavirin, may predispose to events that might lead to hepatic decompensation in a susceptible patient. Triple therapy using telaprevir (as well as with boceprevir and simeprevir) can cause anemia, neutropenia, thrombocytopenia, severe infections, gastrointestinal upset, dehydration and rash, all of which might help precipitate hepatic decompensation in a patient with underlying cirrhosis or advanced fibrosis.

Outcome and Management

Rash is common with telaprevir therapy and several cutaneous reactions can be accompanied by evidence of hepatic injury. There is no reason to suspect cross sensitivity to the cutaneous hypersensitivity between telaprevir and other oral antivirals active against hepatitis C. Triple therapy using telaprevir or other protease inhibitors combined with peginterferon and ribavirin should be considered inadvisable in patients with preexisting cirrhosis, particularly those with a prior history of hepatic decompensation. On the other hand, hepatic

decompensation has been reported even with all-oral antiviral therapy of hepatitis C, although the rates reported with non-interferon and non-ribavirin containing regimens were quite low (<1%).

Drug Class: Antiviral Agents, Hepatitis C Agents, HCV Protease Inhibitors

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Telaprevir – Incivek®

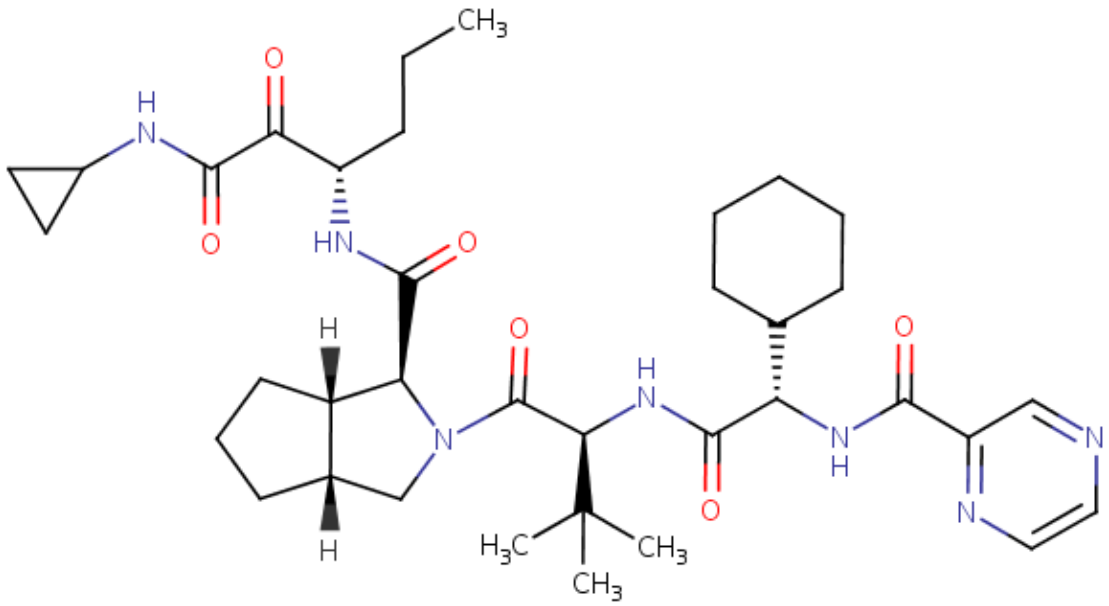
DRUG CLASS

Hepatitis C Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Telaprevir	402957-28-2	C36-H53-N7-O6	

ANNOTATED BIBLIOGRAPHY

References updated: 10 March 2016

[Abbreviation used: SVR, sustained virological response.]

Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013.

(Multi-authored textbook of hepatotoxicity published in 2013 does not discuss oral, direct acting antiviral agents used to treat hepatitis C).

Kim JL, Morgenstern KA, Lin C, Fox T, Dwyer MD, Landro JA, Chambers SP, et al. Crystal structure of the hepatitis C virus NS3 protease domain complexed with a synthetic NS4A cofactor peptide. Cell 1996; 87: 343-55. PubMed PMID: 8861917.

(Report of the crystal structure of the NS3/4 region of HCV with detailed description of the active serine protease catalytic site, the target for subsequent development of specific inhibitors of the HCV protease).

Lawitz E, Rodriguez-Torres M, Muir AJ, Kieffer TL, McNair L, Khunvichai A, McHutchison JG. Antiviral effects and safety of telaprevir, peginterferon alfa-2a, and ribavirin for 28 days in hepatitis C patients. J Hepatol 2008; 49: 163-9. PubMed PMID: 18486984.

(Among 12 patients treated with telaprevir, peginterferon and ribavirin for 4 weeks, all became HCV RNA negative by 28 days, and all 8 patients who continued peginterferon and ribavirin thereafter for up to 48 weeks had an SVR; during telaprevir therapy, 4 patients developed rash; no mention of de novo ALT elevations).

Hézode C, Forestier N, Dusheiko G, Ferenci P, Pol S, Goeser T, Bronowicki JP, et al.; PROVE2 Study Team. Telaprevir and peginterferon with or without ribavirin for chronic HCV infection. N Engl J Med 2009; 360: 1839-50. PubMed PMID: 19403903.

(Among 334 patients with previously untreated chronic hepatitis C, genotype 1, who received various regimens of peginterferon, ribavirin and telaprevir, SVR rates were higher with telaprevir, but were also increased by ribavirin; common adverse events included rash and pruritus; no mention of hepatic complications or de novo ALT elevations).

McHutchison JG, Everson GT, Gordon SC, Jacobson IM, Sulkowski M, Kauffman R, McNair L, et al; PROVE1 Study Team. Telaprevir with peginterferon and ribavirin for chronic HCV genotype 1 infection. N Engl J Med 2009; 360: 1827-38. PubMed PMID: 19403902.

(Among 240 patients with chronic hepatitis C, genotype 1, who received various regimens of peginterferon, ribavirin and telaprevir, SVR rates were higher with telaprevir and adverse events of rash, pruritus, nausea and diarrhea were more common in groups receiving telaprevir, severe rash occurring in 5-9% of patients; no mention of ALT elevations or hepatic adverse events).

McHutchison JG, Manns MP, Muir AJ, Terrault NA, Jacobson IM, Afdhal NH, Heathcote EJ, et al.; PROVE3 Study Team. Telaprevir for previously treated chronic HCV infection. N Engl J Med 2010; 362: 1292-303. PubMed PMID: 20375406.

(Among 453 patients with previously treated chronic hepatitis C, genotype 1, treated with one of 4 regimens of peginterferon, ribavirin and telaprevir, SVR rates were higher with telaprevir [24-51% vs 14%] as were serious adverse events [17-24% vs 11%], rash occurring in at least half of patients on telaprevir, usually within 1-4 weeks of starting requiring discontinuation in 5%; no mention of ALT elevations or liver related adverse events).

Montaudié H, Passeron T, Cardot-Leccia N, Sebbag N, Lacour JP. Drug rash with eosinophilia and systemic symptoms due to telaprevir. Dermatology 2010; 221: 303-5. PubMed PMID: 20798484.

(57 year old woman with chronic hepatitis C developed rash, fever, fatigue and lymphadenopathy 6 weeks after starting telaprevir with peginterferon and ribavirin [ALT 61 U/L, eosinophils 2,700/μL, HCV RNA negative, bilirubin and Alk P not given], resolving with prednisone therapy, but with subsequent HCV relapse; had previously received peginterferon and ribavirin without rash).

Sherman KE, Flamm SL, Afdhal NH, Nelson DR, Sulkowski MS, Everson GT, Fried MW, et al.; ILLUMINATE Study Team. Response-guided telaprevir combination treatment for hepatitis C virus infection. N Engl J Med 2011; 365: 1014-24. PubMed PMID: 21916639.

(Among 540 previously untreated patients with chronic hepatitis C, genotype 1, treated with telaprevir [12 weeks] and ribavirin and peginterferon [for 12, 24 or 48 weeks], the overall rate of SVR was 72%, rash 37% and any serious adverse event 9%; no mention of ALT elevations or liver related adverse events).

Zeuzem S, Andreone P, Pol S, Lawitz E, Diago M, Roberts S, Focaccia R, et al; REALIZE Study Team. Telaprevir for retreatment of HCV infection. N Engl J Med 2011; 364: 2417-28. PubMed PMID: 21696308.

(Among 663 patients with previously treated chronic hepatitis C, genotype 1, who were treated with various regimens of telaprevir [12 weeks] with or without 48 weeks of peginterferon and ribavirin, SVR rates were higher with telaprevir [64-66% vs 17%] as were side effects of fatigue, gastrointestinal upset, pruritus, rash, anemia and neutropenia; no mention of liver related adverse events).

Jacobson IM, McHutchison JG, Dusheiko G, Di Bisceglie AM, Reddy KR, Bzowej NH, Marcellin P, et al.; ADVANCE Study Team. Telaprevir for previously untreated chronic hepatitis C virus infection. N Engl J Med 2011; 364: 2405-16. PubMed PMID: 21696307.

(Among 1088 patients with previously untreated chronic hepatitis C, genotype 1, who were treated with peginterferon and ribavirin with vs without 12 weeks of telaprevir, SVR rates were higher with telaprevir [69-75% vs 44%], but serious adverse events rates were similar [9% vs 7%]; one case of Stevens Johnson syndrome and one liver disease death occurred in telaprevir groups, but few details were provided).

Telaprevir (Incivek) and boceprevir (Victrelis) for chronic hepatitis C. Med Lett Drugs Ther 2011; 53: 57-9. PubMed PMID: 21778964.

(Concise review of the efficacy, safety and costs of boceprevir and telaprevir, shortly after their approval for use as a part of triple therapy of chronic hepatitis C, genotype 1, in the US, mentions side effects of rash, anemia, fatigue, pruritus, nausea and anorectal pruritus and burning, but not ALT elevations or clinically apparent liver injury).

Hayashi N, Okanoue T, Tsubouchi H, Toyota J, Chayama K, Kumada H. Efficacy and safety of telaprevir, a new protease inhibitor, for difficult-to-treat patients with genotype 1 chronic hepatitis C. J Viral Hepat 2012; 19: e134-42. PubMed PMID: 22239511.

(Among 141 previously treated Japanese patients with chronic hepatitis C, genotype 1, treated with telaprevir [12 weeks] with ribavirin and peginterferon [24 weeks], the overall SVR rate was 76% and serious adverse event rate 11%, most troublesome being anemia and rash; no mention of ALT elevations or hepatotoxicity).

Sulkowski MS, Sherman KE, Dieterich DT, Bsharat M, Mahnke L, Rockstroh JK, Gharakhanian S, et al. Combination therapy with telaprevir for chronic hepatitis C virus genotype 1 infection in patients with HIV: a randomized trial. Ann Intern Med 2013; 159: 86-96. PubMed PMID: 23685940.

(Among 62 patients with chronic hepatitis C, genotype 1, and HIV coinfection treated with telaprevir or placebo [12 weeks] and peginterferon and ribavirin [48 weeks], SVR rates were higher with telaprevir [74% vs 45%] as were serious adverse events [5% vs 0 in first 12 weeks]; no mention of ALT elevations or hepatic adverse events).

Hézode C, Fontaine H, Dorival C, Larrey D, Zoulim F, Canva V, de Ledinghen V, et al.; CUPIC Study Group. Triple therapy in treatment-experienced patients with HCV-cirrhosis in a multicentre cohort of the French Early Access Programme (ANRS CO20-CUPIC) - NCT01514890. J Hepatol 2013; 59: 434-41. PubMed PMID: 23669289.

(Among 497 patients with chronic hepatitis C, genotype 1, and cirrhosis treated in a French early access program with 48 weeks of peginterferon and ribavirin with either boceprevir or telaprevir, serious adverse events occurred in 197 patients [40%], hepatic decompensation in 12 [2.4%], severe infection in 24 [4.8%], and 6 patients died [1.5%], the serious complications typically arising in the first 12 weeks of therapy).

Coilly A, Roche B, Dumortier J, Leroy V, Botta-Fridlund D, Radenne S, Pageaux GP, et al. Safety and efficacy of protease inhibitors to treat hepatitis C after liver transplantation: a multicenter experience. J Hepatol 2014; 60: 78-86. PubMed PMID: 23994384.

(Among 37 patients with severe recurrent chronic hepatitis C, genotype 1, after liver transplantation who were treated with peginterferon, ribavirin and either boceprevir or telaprevir for up to 48 weeks, 6 [16%] had an SVR, 10 [27%] a severe infection and 3 [8%] died).

Park C, Jiang S, Lawson KA. Efficacy and safety of telaprevir and boceprevir in patients with hepatitis C genotype 1: a meta-analysis. J Clin Pharm Ther 2014; 39: 14-24. PubMed PMID: 24237070.

(Analysis of efficacy and safety of telaprevir and boceprevir in triple therapy in 10 controlled trials of 4421 patients with chronic hepatitis C, genotype 1; serious adverse events were higher with triple therapy than with peginterferon and ribavirin alone).

Colombo M, Fernández I, Abdurakhmanov D, Ferreira PA, Strasser SI, Urbanek P, Moreno C, et al. Safety and on-treatment efficacy of telaprevir: the early access programme for patients with advanced hepatitis C. Gut 2014; 63: 1150-8. PubMed PMID: 24201995.

(Among 1587 patients with chronic hepatitis C, genotype 1, and cirrhosis treated with telaprevir [12 weeks] combined with peginterferon and ribavirin [for 24 or 48 weeks], serious adverse events were common during the first 16 weeks leading to drug discontinuation in 12% of patients and death in 7 patients; rash developed in 13% of patients, led to drug discontinuation in 5% and was compatible with Stevens Johnson syndrome in one).

Hézode C, Fontaine H, Dorival C, Zoulim F, Larrey D, Canva V, De Ledinghen V, et al.; CUPIC Study Group. Effectiveness of telaprevir or boceprevir in treatment-experienced patients with HCV genotype 1 infection and cirrhosis. Gastroenterology 2014; 147: 132-142. PubMed PMID: 24704719.

(Among 511 patients with cirrhosis and chronic hepatitis C, genotype 1, and cirrhosis treated with triple therapy using telaprevir or boceprevir for 48 weeks, 91 [18%] patients had an SVR, severe adverse events occurred in 50%, including liver decompensation in 43 [8%], severe infections in 28 [5.5%] and death in 11 [2.2%]).

Burton JR Jr, O'Leary JG, Verna EC, Saxena V, Dodge JL, Stravitz RT, Levitsky J, et al. A US multicenter study of hepatitis C treatment of liver transplant recipients with protease-inhibitor triple therapy. J Hepatol 2014; 61: 508-14. PubMed PMID: 24801415.

(Among 81 patients with recurrent hepatitis C, genotype 1, after liver transplant who were treated with triple therapy using peginterferon, ribavirin and either boceprevir or telaprevir, the overall SVR rate was 63%, the serious adverse event rate was not reported, but 27% required hospitalization, 15% early drug discontinuation and 7 patients [9%] died of liver failure).

Gordon SC, Muir AJ, Lim JK, Pearlman B, Argo CK, Ramani A, Maliakkal B, et al; HCV-TARGET study group. Safety profile of boceprevir and telaprevir in chronic hepatitis C: real world experience from HCV-TARGET. J Hepatol 2015; 62: 286-93. PubMed PMID: 25218788.

(Among 2084 patients with chronic hepatitis C, genotype 1, treated in clinical practice with peginterferon, ribavirin and either boceprevir or telaprevir for up to 48 weeks, the overall SVR rate was 52%, serious adverse event rate 12% while hepatic decompensation occurred in 3% and 5 patients [0.25%] died, all from hepatic failure; rash was a common side effect [63% with telaprevir and 34% with boceprevir] and was graded as serious in 8 patients [0.5%], 2 [0.1%] with DRESS).

Verna EC, Saxena V, Burton JR Jr, O'Leary JG, Dodge JL, Stravitz RT, Levitsky J, et al.; CRUSH-C Consortium. Telaprevir- and boceprevir-based triple therapy for hepatitis C in liver transplant recipients with advanced recurrent disease: a multicenter study. Transplantation 2015; 99: 1644-51. PubMed PMID: 25715116.

(Among 54 patients with advanced, recurrent chronic hepatitis C, genotype 1, after liver transplantation, who were treated with peginterferon, ribavirin and either boceprevir or telaprevir for up to 48 weeks, the SVR rate was 50%, but hepatic decompensation arose in 24% and 6 patients [11%] died).

Neukam K, Munteanu DI, Rivero-Juárez A, Lutz T, Fehr J, Mandorfer M, Bhagani S, et al. Boceprevir or telaprevir based triple therapy against chronic hepatitis C in HIV coinfection: real-life safety and efficacy. PLoS One 2015; 10: e0125080. PubMed PMID: 25923540.

(Among 159 patients with chronic hepatitis C, genotype 1, treated in health care clinics in 5 European countries with peginterferon, ribavirin and either boceprevir or telaprevir for up to 48 weeks, the overall SVR rate was 63%, while 4 patients [2.5%] developed hepatic decompensation, one of whom died to hepatic failure).

Bailly F, Pradat P, Virlogeux V, Zoulim F. Antiviral Therapy in Patients with Hepatitis C Virus-Induced Cirrhosis. Dig Dis 2015; 33: 613-23. PubMed PMID: 26159282.

(Review of the status of antiviral therapy of chronic hepatitis C with cirrhosis summarizing the high rate of adverse events including hepatic decompensation and death with peginterferon based regimens combined with boceprevir or telaprevir, and the more effective and better tolerated all-oral regimens).

Ferenci P, Kozbial K, Mandorfer M, Hofer H. HCV targeting of patients with cirrhosis. J Hepatol 2015; 63: 1015-22. PubMed PMID: 26100497.

(Review of the status of antiviral therapy of chronic hepatitis C with cirrhosis, suggests that genotype 1 infected patients should receive an all-oral regimen such as sofosbuvir with ledipasvir or daclatasvir or the triple combination of dasabuvir with ombitasvir and paritaprevir, the major issues being duration of therapy and the role of ribavirin).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-1352. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 12 were attributed to antiviral agents, but all were antiretroviral agents and no case was attributed to the oral direct acting agents used to treat hepatitis C).

European Association for Study of Liver. EASL Recommendations on Treatment of Hepatitis C 2015. J Hepatol 2015; 63: 199-236. PubMed PMID: 25911336.

(Guidelines for the antiviral therapy of chronic hepatitis C from the European liver disease research and academic society).

AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. Hepatology 2015; 62: 932-54. PubMed PMID: 26111063.

(Guidelines for the antiviral therapy of chronic hepatitis C from the US liver and infectious diseases research and academic societies).

Kawaguchi Y, Iwane S, Kumagai T, Yanagita K, Yasutake T, Ide Y, Otsuka T, et al. Efficacy and safety of telaprevir, pegylated interferon α-2b and ribavirin triple therapy in Japanese patients infected with hepatitis C virus genotype 1b. Intern Med 2015; 54: 2551-60. PubMed PMID: 26466688.

(Among 106 Japanese patients with chronic hepatitis C, genotype 1b, treated with peginterferon, ribavirin and telaprevir for 24 weeks, 93 [88%] had a SVR, but adverse events were frequent including rash [28%], anemia [76%] and 31% discontinued telaprevir early; no mention of ALT elevations or hepatotoxicity).

Janczewska E, Flisiak R, Zarebska-Michaluk D, Kozielewicz D, Berak H, Dobracka B, Librant-Suska M, et al. Effect of peginterferon or ribavirin dosing on efficacy of therapy with telaprevir in treatment-experienced patients with chronic hepatitis C and advanced liver fibrosis: a multicenter cohort study. Medicine (Baltimore) 2015; 94: e1411. PubMed PMID: 26402801.

(Among 211 treatment experienced patients with chronic hepatitis C, genotype 1, and advanced liver disease [68% with cirrhosis] treated with peginterferon, ribavirin and telaprevir, 118 [56%] had an SVR, 31 [15%] had a serious adverse reaction, and 4 died; but no death was attributed to treatment and there was no mention of ALT elevations or hepatotoxicity).

Lepida A, Colombo M, Fernandez I, Abdurakhmanov D, Ferreira PA, Strasser SI, Urbanek P, et al. Final results of the telaprevir access program: FibroScan values predict safety and efficacy in hepatitis C patients with advanced fibrosis or cirrhosis. PLoS One 2015; 10: e0138503. PubMed PMID: 26398503.

(Among 1722 patients with chronic hepatitis C, genotype 1, and advanced fibrosis who wwere treated with peginterferon, ribavirin and telaprevir, 1139 [64%] had an SVR and common adverse events were anemia [56%], rash [30%] and pruritus [16%]; no mention of ALT elevations or hepatotoxicity).

Coilly A, Dumortier J, Botta-Fridlund D, Latournerie M, Leroy V, Pageaux GP, Agostini H, et al. Multicenter experience with boceprevir or telaprevir to treat hepatitis C recurrence after liver transplantation: when present becomes past, what lessons for future? PLoS One 2015; 10: e0138091. PubMed PMID: 26394142.

(Among 81 patients with recurrent hepatitis C after liver transplantation who were teated with peginterferon, ribavirin and either telaprevir or boceprevir, 38 [47%] had an SVR, 22 [27%] a serious adverse event, 10 [12%] acute rejection, and 4 [5%] died, largely of infectious complications; no mention of ALT elevations or hepatotoxicity).

Salmerón J, Vinaixa C, Berenguer R, Pascasio JM, Sánchez Ruano JJ, Serra MÁ, Gila A, et al; Alhambra Spanish Study Group. Effectiveness and safety of first-generation protease inhibitors in clinical practice: Hepatitis C virus patients with advanced fibrosis. World J Gastroenterol 2015; 21: 9163-74. PubMed PMID: 26290644.

(Among 1057 patients with chronic hepatitis C who were treated with peginterferon, ribavirin and either telaprevir or boceprevir at 38 Spanish hospitals, 635 [60%] had an SVR, and adverse events were largely hematologic; no mention of ALT elevations or hepatotoxicity).

Ueda Y, Ikegami T, Soyama A, Akamatsu N, Shinoda M, Ishiyama K, Honda M, et al. Simeprevir or telaprevir with peginterferon and ribavirin for recurrent hepatitis C after living donor liver transplantation: A Japanese multicenter experience. Hepatol Res 2016 Feb 22. [Epub ahead of print] PubMed PMID: 26899352.

(Among 79 patients with chronic hepatitis C, genotype 1, after liver transplantation who were treated wtih peginterferon, ribavirin and either simeprevir [n=79] or telaprevir [n=36], the SVR rates were 56% vs 69%, serious adverse event rates 11% vs 25%, and immune mediated graft dysfunction occurred in 8% vs 11%).