Treatment of HCV in Persons with Cirrhosis

This is a PDF version of the following document:
Module 5:   Treatment of Hepatitis C Infection
Lesson 4:   Treatment of HCV in Persons with Cirrhosis

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https://www.hepatitisC.uw.edu/go/treatment-infection/treatment-cirrhosis/core-concept/all.

Background

Introduction

Individuals with chronic hepatitis C virus (HCV) infection and cirrhosis have an increased risk of developing severe liver-related complications, including hepatic decompensation, hepatocellular cancer, and death. Accordingly, any person with chronic HCV infection who is diagnosed with cirrhosis should be considered a high priority for HCV treatment. When considering the general approach to the treatment of hepatitis C in persons with cirrhosis, it is essential to determine (1) whether the individual received prior HCV treatment and experienced virologic failure and (2) whether their cirrhosis is compensated or decompensated (Figure 1). For persons with chronic HCV infection and decompensated cirrhosis, HCV treatment plans and goals are more complicated and require management by a liver specialist.

Distinguishing Compensated and Decompensated Cirrhosis

One important step in treating HCV in persons with cirrhosis is to determine whether the cirrhosis is compensated or decompensated.[1,2] The Child-Turcotte-Pugh score is an important component of determining the severity of cirrhosis and predicts morbidity and mortality (Figure 2).[3,4] The treatment approach and goals are divergent based on the classification of compensated versus decompensated cirrhosis. In particular, HCV protease inhibitor-based regimens are not recommended for use in persons with decompensated cirrhosis due to the risk of hepatotoxicity with some direct-acting antiviral (DAA) medications and lack of data with other DAAs.[5]

- **Compensated Cirrhosis**: In general, individuals with compensated cirrhosis have mild hepatic impairment (Child-Turcotte-Pugh class A) and generally do not have clinical manifestations of decompensated disease, specifically jaundice, ascites, variceal hemorrhage, or hepatic encephalopathy.
- **Decompensated Cirrhosis**: Individuals should be considered to have decompensated cirrhosis if they have moderate or severe liver disease (Child-Turcotte-Pugh class B or C, or a score of 7 or higher). Individuals with decompensated cirrhosis often have experienced one or more of the following: ascites, jaundice, variceal hemorrhage, or hepatic encephalopathy.[1,3] Individuals who have significant clinical improvement after experiencing one feature of hepatic decompensation should be evaluated on a case-by-case basis to determine whether they could be considered for treatment similar to patients with compensated cirrhosis. Even if they recover from the acute event, they are still considered to have decompensated cirrhosis.

Impact of Treating HCV in Persons with Cirrhosis

Reduction in Cirrhosis-related Complications After HCV Treatment

Multiple studies, most from the interferon era, have shown that successful treatment of HCV in persons with compensated cirrhosis will decrease the incidence of subsequent cirrhosis-related complications, including hepatic failure, hepatocellular carcinoma, and liver-related deaths.[6,7,8,9] In one international, multicenter study, investigators followed 530 adults with chronic hepatitis C and advanced fibrosis or cirrhosis after treatment with interferon-based therapy and found that patients who achieved a sustained virologic response (SVR) had substantially lower hepatic-related complications and lower mortality (Figure 3).[7]

Regression and Reversal of Hepatic Fibrosis after HCV Treatment

Multiple studies have shown that persons with chronic HCV and cirrhosis have significant improvement in inflammatory grade and fibrosis severity following HCV therapy and achievement of a sustained virologic response (SVR) (Figure 4).[7,10] Several studies have shown regression in hepatic fibrosis following the achievement of an SVR with DAA-based treatments, in addition to improvements in laboratory parameters for hepatic function.[11,12,13,14,15,16,17]

Treating HCV in Persons with Compensated Cirrhosis

HCV Treatment Goals in Persons with Compensated Cirrhosis

The most important immediate goal of treatment is to achieve a sustained virologic response, which is required before observing the subsequent benefit in liver-related and other outcomes. The next intermediate-term priority with treatment is to decrease the patient's risk of developing hepatic decompensation. The long-term goals are to diminish the risk of developing HCV-related hepatocellular carcinoma and death.

HCV Treatment Data in Persons with Compensated Cirrhosis

The following is a summary of clinical trials involving persons with compensated cirrhosis. This summary illustrates the high effectiveness of DAA regimens even among patients with cirrhosis.

PANGENOTYPIC REGIMENS

Glecaprevir-Pibrentasvir

- Glecaprevir-Pibrentasvir in Cirrhosis: Pooled Analysis: The efficacy of glecaprevir-pibrentasvir for 12 or 16 weeks was evaluated in a pooled analysis of 308 adults with HCV genotypes 1, 2, 3, 4, 5, and 6 and compensated cirrhosis.[18] Cirrhosis status was determined by FibroScan in 70% of the study subjects, and 41% were treatment-experienced with prior peginterferon-based therapy. The Child-Turcotte-Pugh score was 5 in 86% of those enrolled. Using an intent-to-treat analysis, SVR12 was achieved in 96% (297/308) of the study participants.[18] The SVR12 rates by HCV genotype showed 94% with HCV genotype 1, 97% with genotype 3, and 100% with genotypes 2, 4, 5, or 6.[18] There were no DAA-associated serious adverse events and no grade 3-4 elevations in hepatic aminotransferase levels. Grade 3 hyperbilirubinemia developed in 3 study participants; this occurred without associated abnormalities in other liver parameters, and it resolved without treatment discontinuation.[18]
- EXPEDITION-8: In this single-arm trial, glecaprevir-pibrentasvir was administered for 8 weeks to 343 treatment-naïve adults with compensated cirrhosis and HCV genotypes 1, 2, 3, 4, 5, or 6.[19] By intention-to-treat analysis, the SVR12 response rates were 98% overall.[19]

Sofosbuvir-Velpatasvir

- ASTRAL-1: The ASTRAL-1 trial enrolled treatment-naïve and treatment-experienced adults with genotype 1, 2, 4, 5, or 6.[20] Individuals with compensated cirrhosis were not excluded.[20] The SVR12 rate with 12 weeks of sofosbuvir-velpatasvir treatment in participants with cirrhosis was 99% (120 of the 121), and the SVR12 rate was identical to participants without cirrhosis.[20]
- ASTRAL-2: In this randomized, placebo-controlled trial, participants with HCV genotype 2 received a 12-week treatment course with sofosbuvir-velpatasvir or sofosbuvir plus ribavirin.[21] Individuals with cirrhosis were not excluded.[21] All 19 participants with cirrhosis and HCV genotype 2 achieved an SVR12 with sofosbuvir-velpatasvir treatment.[21]
- ASTRAL-3: The ASTRAL-3 study enrolled persons with HCV genotype 3, and among the 80 participants with cirrhosis who received sofosbuvir-velpatasvir, the SVR12 rates were 93% for treatment-naïve and 89% for treatment-experienced participants.[21]
- Sofosbuvir-Velpatasvir in Patients with Compensated Cirrhosis and HCV Genotype 3 (Spain): Additional data from Spain suggest that persons with HCV genotype 3 and cirrhosis should undergo baseline NS5A resistance testing and those with pretreatment NS5A resistance-associated substitutions may benefit from the addition of ribavirin to reduce the risk of viral relapse.[22]

Sofosbuvir-Velpatasvir-Voxilaprevir

- POLARIS-2: In this phase 3, active-comparator, open-labeled trial, 314 patients with chronic hepatitis C genotypes 1, 2, or 3 with prior direct-acting antiviral (DAA) therapy without an NS5A inhibitor were randomized to receive either sofosbuvir-velpatasvir-voxilaprevir or sofosbuvir-velpatasvir for 12 weeks.[23] Compensated cirrhosis was present in 46% and prior sofosbuvir exposure in 80% of patients.[23] The overall sustained virologic response rates were 98% and 90% for the sofosbuvir-velpatasvir-voxilaprevir and sofosbuvir-velpatasvir arms, respectively; among those participants with cirrhosis, 98% (82 of 84) achieved an SVR12 in the sofosbuvir-velpatasvir-voxilaprevir arm compared with 86% (59 of 69) in the sofosbuvir-velpatasvir arm.[23] Virologic relapse was confirmed at week 4 for one sofosbuvir-velpatasvir-voxilaprevir patient and 14 sofosbuvir-velpatasvir participants, of whom 8 had genotype 3a.[23]

NON-PANGENOTYPIC REGIMENS

Elbasvir-Grazoprevir

- Integrated Analysis of Treatment in Persons with Compensated Cirrhosis: In this study, investigators performed an integrated analysis of 6 elbasvir-grazoprevir phase 2/3 clinical trials to determine SVR12 treatment responses in 402 study participants with HCV genotypes 1, 4, or 6 and compensated cirrhosis.[24] Participants received treatment with elbasvir-grazoprevir, with or without weight-based ribavirin; the treatment duration was 12 weeks for treatment-naïve participants (n = 169) and 12, 16, or 18 weeks for treatment-experienced subjects (n = 233).[24] Notably, platelet counts of less than 100,000 cells/mm^3 and serum albumin of less than 3.5 g/dL were present in only 25% and 6% of participants, respectively. Overall, using an intention-to-treatment analysis, SVR12 occurred in 96% of treatment-naïve participants and ranged from 89 to 100% among treatment-experienced subjects.[24] Genotype 1a patients were most likely to experience viral relapse, with the strongest predictor for treatment failure being the presence of baseline NS5A resistance-associated substitutions. Asymptomatic grade 3-4 increases in hepatic aminotransferase levels were observed in 2.3%.[24]

Ledipasvir-Sofosbuvir

- ION-1: The ION-1 trial enrolled HCV treatment-naïve adults, with and without compensated cirrhosis, to receive 12 or 24 weeks of ledipasvir-sofosbuvir.[25] Among the subjects enrolled with compensated cirrhosis, 97% (63 of 65) achieved an SRV12; the results were similar with 12 or 24 weeks of therapy.[25] In this study, the addition of ribavirin did not significantly improve SVR12 rates.
- ION-2: In this trial, treatment-experienced adults with HCV genotype 1 were treated with 12 or 24 weeks of ledipasvir-sofosbuvir, with or without ribavirin.[26] Among those individuals with cirrhosis, SVR12 rates were lower if they received ledipasvir-sofosbuvir for 12 weeks (86%) versus 24 weeks (100%).[26] In this study, the addition of ribavirin did not significantly improve SVR12 rates.[26]
- SIRIUS: In the SIRIUS trial, 155 treatment-experienced adults with HCV genotype 1 and compensated cirrhosis received 12 weeks of ledipasvir-sofosbuvir plus ribavirin or 24 weeks of ledipasvir-sofosbuvir; the SVR12 rates were 96% for participants in the 12-week group and 97% in the 24-week group.[27] In a post-hoc analysis of 7 clinical trials, investigators analyzed data from 513 adults with HCV genotype 1 and compensated cirrhosis who received ledipasvir-sofosbuvir, with or without ribavirin.[28] The treatment-naïve subjects did equally well with either a 12- or 24-week treatment course, but treatment-experienced individuals had lower response rates with 12 compared with 24 weeks; ribavirin did not significantly improve SVR rates.[28]

Recommended HCV Treatment with Compensated Cirrhosis

For individuals with compensated cirrhosis (Child-Turcotte-Pugh Class A) the AASLD-IDSA HCV Guidance provides recommendations for initial treatment and retreatment (when prior therapy has failed).[29,30] Treatment of persons with decompensated cirrhosis should be managed by a liver specialist.

- Treatment-naïve persons with compensated cirrhosis should undergo screening to see if they are eligible for the simplified treatment approach for persons with compensated cirrhosis as outlined in the AASLD-IDSA HCV Guidance.[31] The recommended pangenotypic DAA regimens for simplified therapy—glecaprevir-pibrentasvir or sofosbuvir-velpatasvir—are effective in patients with or without cirrhosis.[31,32,33] When treating with glecaprevir-pibrentasvir, the dosing and duration of treatment are the same when treating persons without cirrhosis and those with compensated cirrhosis.[31] If, however, treatment with sofosbuvir-velpatasvir is being considered for a person with compensated cirrhosis, a baseline HCV genotype should be obtained, since this treatment regimen may need to be adjusted if the person has HCV genotype 3.[31] Further, in this situation, if this baseline genotype screening identifies HCV genotype 3, then resistance-associated substitution (RAS) testing is recommended, and the regimen may require adjustment based on this result.[31]
- Treatment-experienced persons with compensated cirrhosis should be managed based on the prior treatment received as outlined in the AASLD-IDSA HCV Guidance.[30] In this context, treatment-experienced refers to individuals who did not achieve an SVR12 with prior treatment or had virologic relapse shortly after completing therapy (i.e., prior therapy failed). Persons who achieve an SVR12 with prior treatment but later reacquires HCV should be managed the same as treatment-naïve individuals.

Although the treatment recommendations for persons with and without cirrhosis have significant overlap, there are, in some instances, key differences in the recommended regimens, duration of therapy, or inclusion of ribavirin.[29,30] Thus, when treating HCV in persons with compensated cirrhosis (particularly if they are treatment experienced), the AASLD-IDSA HCV Guidance should be reviewed to ensure that the regimen is appropriate for that particular patient with cirrhosis.[29,30,31,33]

Treating HCV in Persons with Decompensated Cirrhosis

Definition of Decompensated Cirrhosis

Individuals with cirrhosis should have a Child-Turcotte-Pugh score calculated; they are considered to have decompensated cirrhosis if the score is 7 or higher (Child-Turcotte-Pugh class B or C).[1,2,3]

HCV Treatment Goals in Persons with Decompensated Cirrhosis

The treatment of persons with decompensated cirrhosis (Child-Turcotte-Pugh class B or C) can be potentially challenging given the high rate of clinical events and complications that may occur in persons with decompensated cirrhosis.

- **Immediate Treatment Goal**: The immediate treatment goal for individuals with decompensated cirrhosis differs based on candidacy for liver transplantation. For those who are not a candidate for liver transplantation, the short-term goal of therapy is to achieve an SVR, with the hope that some degree of liver decompensation will reverse as a result of therapy, which could then stabilize or improve their clinical condition.
- **Intermediate Treatment Goal**: For persons with chronic HCV infection and decompensated cirrhosis who are candidates for liver transplantation, there are a variety of factors to consider in the decision on timing of DAA therapy.[34] The primary rationale for pretransplantation treatment of HCV is to reduce the risk of liver disease progression and the risk of HCV reinfection of the new liver—thus improving posttransplantation outcomes. Pretransplantation HCV treatment has been shown to be a cost-effective strategy in the United States.[35] In addition, for some individuals with decompensated cirrhosis, HCV treatment may prevent the need for a liver transplant.[36] In a European study that evaluated 103 persons with chronic HCV who were on an active liver transplant list due to decompensated cirrhosis, treatment with DAA therapy resulted in delisting 19% at 60 weeks after treatment.[37] However, HCV treatment is not recommended in all patients prior to transplantation, particularly if their liver disease is severe and transplantation is urgent. The goal in this scenario would be to shorten organ wait times, opening up the possibility of receipt from a donor who has HCV infection, as DAA therapy has been shown to have comparable efficacy posttransplantation.[38]

HCV Treatment Regimens for Persons with Decompensated Cirrhosis

The efficacy of DAAs in patients with decompensated cirrhosis is lower than in those with compensated disease, ranging from 70 to 90% depending on the study size and the severity of liver disease. In a multicenter study from Canada, among 868 patients with cirrhosis who underwent DAA therapy, 81% of those with Child-Turcotte-Pugh class B or C disease achieved an SVR12 compared with 90% of individuals with Child-Turcotte-Pugh class A disease.[39] Clinical progression was defined as liver failure, hepatocellular carcinoma, liver transplantation, or death.[39] Achieving an SVR was associated with event-free survival in those with Child-Turcotte-Pugh class A disease but not in those with Child-Pugh class B or C.[39] Real-world data suggest that although DAA therapy can reduce the risk of clinical progression in patients with cirrhosis, it may not provide sufficient, timely benefit for patients with severe liver disease who may need to consider liver transplantation in addition to antiviral therapy.

The following summarizes the existing clinical trial data that have evaluated the efficacy of NS5A-NS5B inhibitor combinations in patients with decompensated liver disease.

Ledipasvir-Sofosbuvir plus Ribavirin

- SOLAR-1: (Cohorts A and B): In Cohort A of the phase 2 SOLAR-1 study, investigators prospectively enrolled 108 adults with hepatitis C genotype 1 or 4 infection and decompensated liver disease (Child-Turcotte-Pugh class B or C).[40] A total of 108 participants were randomized to receive either a

12-week or 24-week course of ledipasvir-sofosbuvir plus ribavirin; the ribavirin dose started at 600 mg per day and then was titrated up as tolerated.[40] Overall, 65% of patients were HCV treatment experienced. Patients receiving the 12-week regimen had an SVR12 rate of 87%, which was similar to the SVR12 rate of 89% in the 24-week regimen; these data excluded 6 patients who underwent liver transplantation.[40] The results were similar in the Child-Turcotte-Pugh class B and C groups. Overall, the regimen of ledipasvir-sofosbuvir plus ribavirin was safe and well tolerated.

- SOLAR-2: In a similar phase 2 trial (SOLAR 2), investigators evaluated 12 or 24 weeks of ledipasvir-sofosbuvir plus ribavirin in adults with HCV genotype 1 or 4 and advanced liver disease.[41] The study cohort A included adults with Child-Turcotte-Pugh class A, B, or C who had not undergone liver transplantation.[41] In participants with Child-Turcotte-Pugh class B, the SVR12 rates were 87% with 12 weeks of treatment and 96% with 24 weeks. For those with Child-Turcotte-Pugh class C, the SVR12 rates were 85% with 12 weeks of treatment and 78% with 24 weeks.[41]

Sofosbuvir-Based Regimens

- **Sofosbuvir Plus Ribavirin in Decompensated Cirrhosis**: In an open-label, nonrandomized, phase 2 trial, 50 adults with Child-Turcotte-Pugh class A or B cirrhosis and portal hypertension were randomized to receive immediate or deferred HCV treatment with sofosbuvir 400 mg once daily plus weight-based ribavirin 1,000 to 1,200 mg divided twice daily.[42] The immediate group received treatment for 48 weeks; the deferred group was observed during the first 24 weeks and then received 48 weeks of therapy.[42] Overall, 72% (33 of 46) of the participants achieved an SVR12. The results were better in those with Child-Turcotte-Pugh class A (78%) than in those with Child-Turcotte-Pugh class B (68%). For the 37 participants who had paired baseline and end-of-treatment hepatic venous gradient measurements, those who achieved an SVR12 had clinically meaningful reductions in portal pressure.[42]

Sofosbuvir-Velpatasvir

- ASTRAL-4: The ASTRAL-4 trial was a randomized, open-label, phase 3 trial designed to examine the safety and efficacy of the fixed-dose combination of sofosbuvir-velpatasvir with or without ribavirin in adults with HCV genotypes 1, 2, 3, 4, or 6 and decompensated cirrhosis.[43] Treatment-naïve and treatment-experienced individuals with Child-Pugh-Turcotte class B disease were randomized to one of three arms: (1) sofosbuvir-velpatasvir for 12 weeks (n = 90), (2) sofosbuvir-velpatasvir plus ribavirin for 12 weeks (n=87), or (3) sofosbuvir-velpatasvir for 24 weeks (n = 90). All three regimens were highly efficacious among participants with HCV genotypes 1, 2, 4, and 6.[43] Among participants with HCV genotype 3, the treatment groups without ribavirin had lower SVR12 rates (50%, 85%, and 50%, respectively).[43] The MELD scores improved over baseline in those with a baseline MELD score of less than 15 and in those with a baseline MELD score of 15 or greater (Figure 5).[43]
- Sofosbuvir-Velpatasvir in Patients with Decompensated Cirrhosis Study (Japan): Another open-label trial that enrolled patients with decompensated cirrhosis randomized 102 participants 1:1 to sofosbuvir-velpatasvir with or without ribavirin.[44] Most (77%) had CTP class B disease and 78% had HCV genotype 1 infection.[44] The SVR12 rates were the same, 92% (47 of 51) in both groups.[44] Of 91 patients who achieved SVR, 26% demonstrated improvement in their CTP score from baseline to post-treatment week 12. Most adverse events were attributed to progression of liver disease or ribavirin toxicity.[44]

Guidance for HCV Treatment with Decompensated Cirrhosis

The AASLD-IDSA HCV Guidance addresses this group of patients in the section Unique Patient Populations: Patients with Decompensated Cirrhosis.[5] The key recommendation from the guidance is that general management and treatment of all patients with decompensated cirrhosis should be performed by a medical practitioner highly experienced in managing persons with chronic HCV infection and decompensated cirrhosis. Accordingly, referral of these patients to an expert, ideally at a transplant center, is strongly recommended. Patients with decompensated cirrhosis include patients who may or may not be a candidate for liver

transcription and may include patients with hepatocellular carcinoma.

Summary Points

- For all patients with chronic hepatitis C and cirrhosis, it is important to determine whether they have compensated cirrhosis or decompensated cirrhosis.
- Treatment of HCV in persons with compensated cirrhosis (Child-Turcotte-Pugh class A) is a high priority because of the risk of developing severe liver-related complications.
- For persons with HCV-related cirrhosis, treatment of HCV with an SVR is associated with significant reversal in hepatic fibrosis and reduced risk of developing hepatocellular carcinoma.
- For persons with HCV and compensated cirrhosis, the regimen choice and duration is generally similar to those without cirrhosis, except for a longer duration, and in select circumstances, the addition of ribavirin.
- With the use of HCV DAA treatment, individuals with HCV and compensated cirrhosis can have comparable SVR12 rates as those without cirrhosis, especially with adjustments in therapy duration when indicated.
- Treatment of HCV is recommended in persons with decompensated cirrhosis who are eligible for liver transplantation, since the transplanted liver will become infected with HCV in all patients who have detectable HCV RNA levels at the time of liver transplantation. In addition, posttransplantation HCV infection is associated with an accelerated course of liver disease.
- Treatment of HCV in persons with decompensated cirrhosis should be performed only by a medical provider who has experience in treating HCV in persons with decompensated cirrhosis.

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Figures

Figure 1 General Approach to Hepatitis C Treatment in Adults with Cirrhosis

Abbreviation: American Association for the Study of the Liver (AASLD) and Infectious Disease Society of America (IDSA)
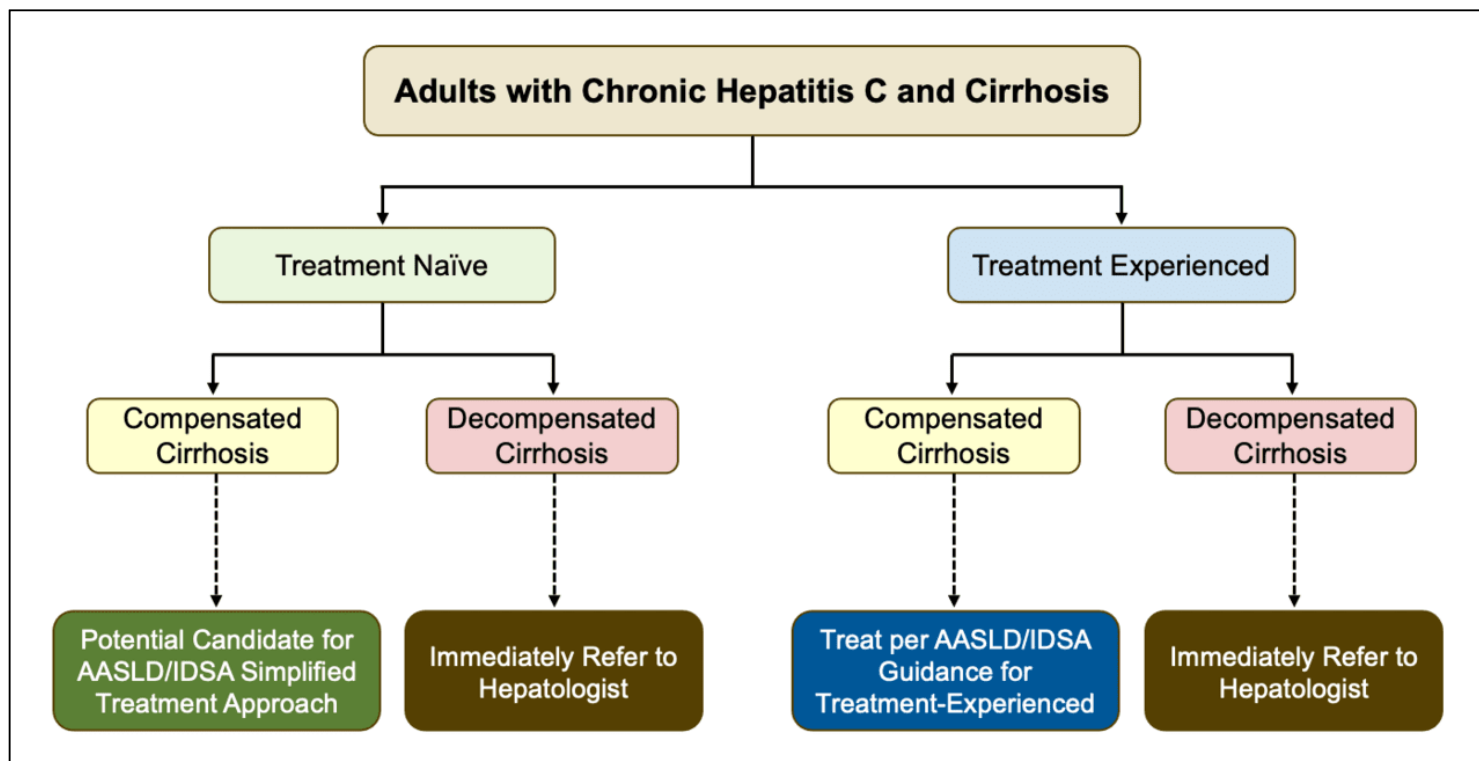
Figure 2 Child-Turcotte-Pugh Classification for Severity of Cirrhosis

The Child-Turcotte-Pugh (CTP) classification system utilizes two clinical parameters (encephalopathy and ascites) and three laboratory values (bilirubin, albumin, and prothrombin time). Patients are classified as class A, B, or C based on their total points.

Source: Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973;60:646-9.

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	**Points***		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
***Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)**			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			
Class C = 10 to 15 points (most severe liver disease)			

Figure 3 Clinical Events Related to HCV Treatment Response

Abbreviations: HCC = hepatocellular cancer

Source: van der Meer AJ, Veldt BJ, Feld JJ, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA. 2012;308:2584-93.
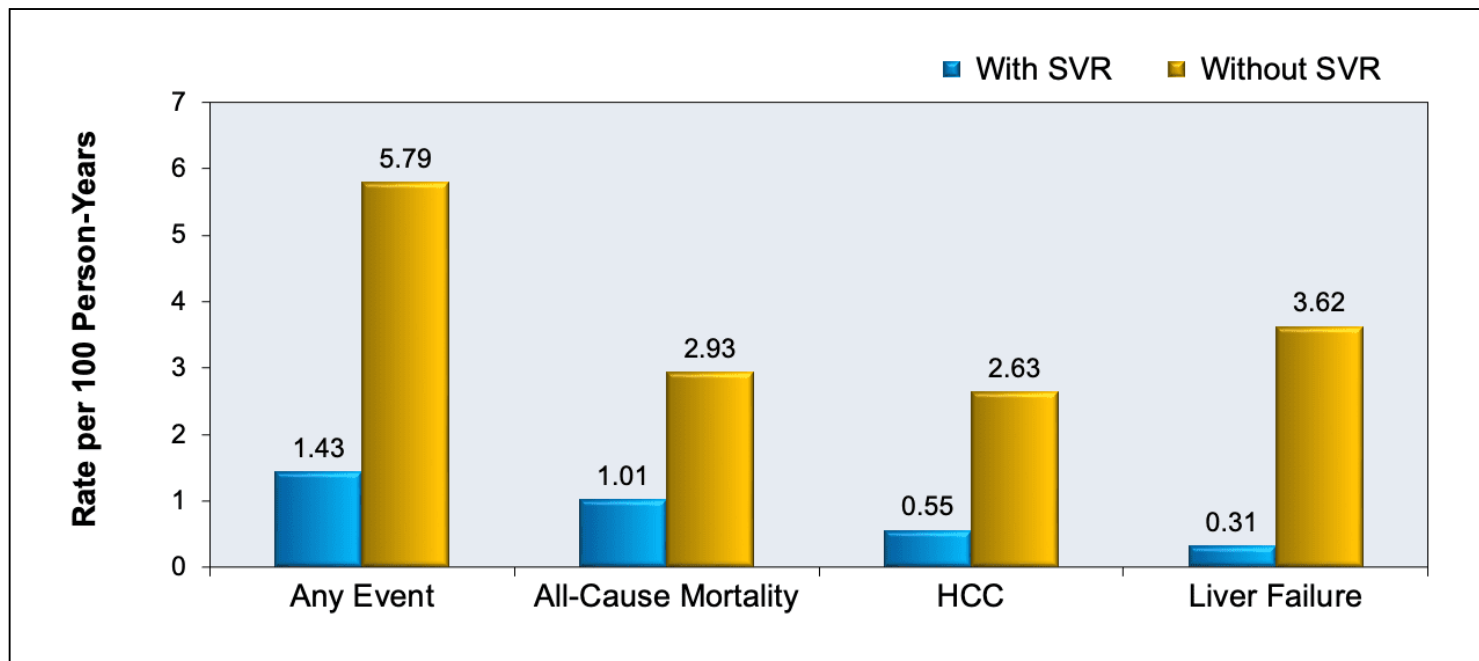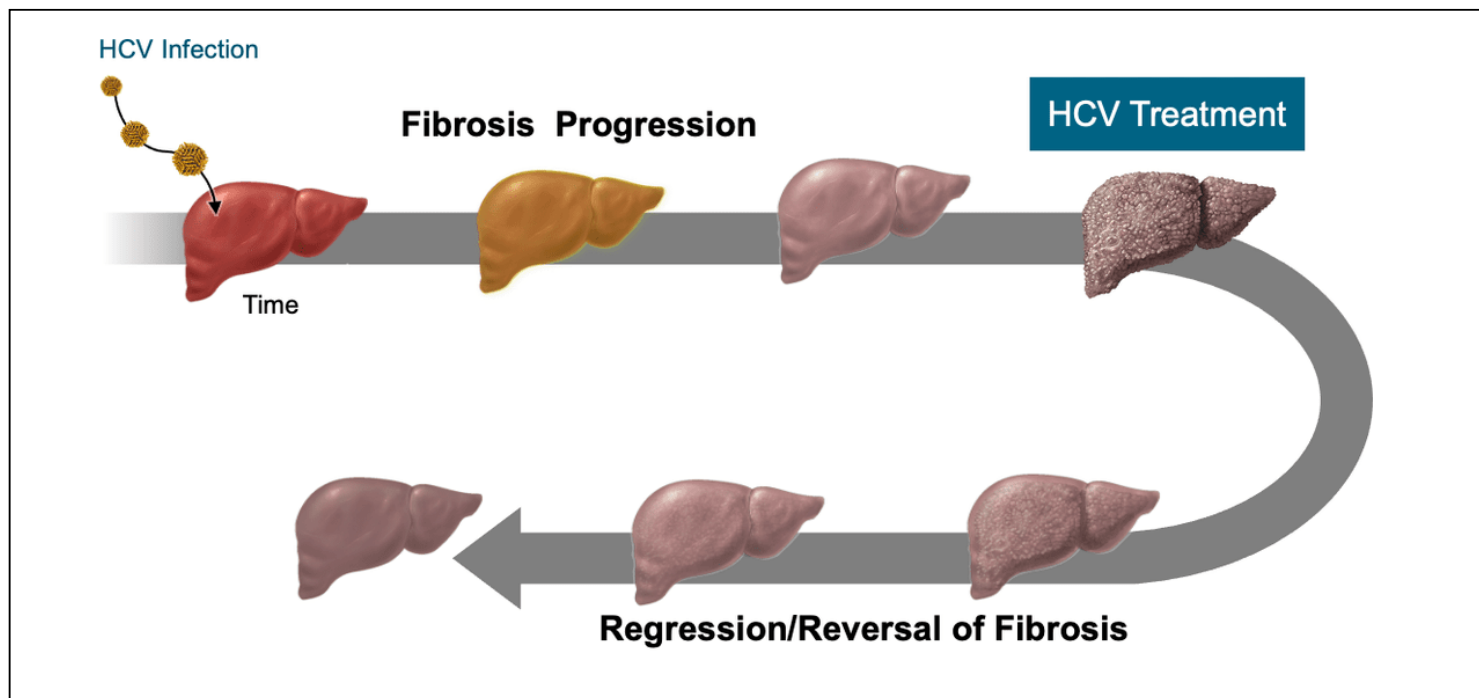
Figure 4 Regression of Liver Cirrhosis Following Hepatitis C Treatment

This graphic shows progression of hepatic fibrosis in persons with untreated chronic hepatitis C, which can regress and reverse following treatment with direct-acting antiviral agents.
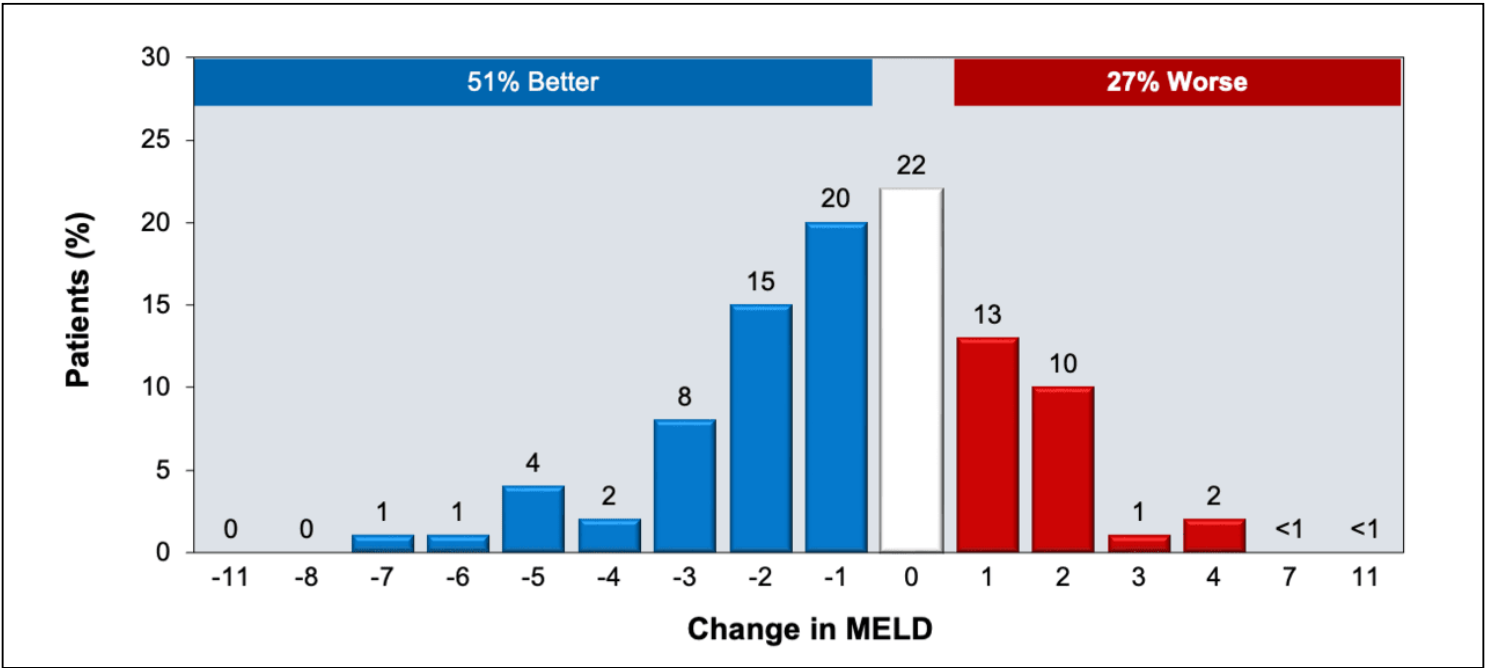
Illustration: David H. Spach, MD

Figure 5 (Image Series) - Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis: ASTRAL4 (Image Series) - Figure 5 (Image Series) - Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis: ASTRAL4
Image 5A: ASTRAL4: Change in MELD Score in Adults with Baseline MELD Score Less than 15

Abbreviations: MELD = Model for End-Stage Liver Disease (MELD)

Source: Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. N Engl J Med. 2015;373:2618-28.

Figure 5 (Image Series) - Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis: ASTRAL4
Image 5B: ASTRAL4: Change in MELD Score in Adults with Baseline MELD Score of 15 or Greater

Abbreviations: MELD = Model for End-Stage Liver Disease (MELD)

Source: Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. N Engl J Med. 2015;373:2618-28.