Persons With Hepatocellular Carcinoma

Hepatitis C virus (HCV) infection is a leading cause of hepatocellular carcinoma (HCC) (Fiehn, 2024). Attention to the subpopulations of individuals with chronic hepatitis C and a prior history of HCC or current HCC is needed. This section discusses specific considerations around HCV treatment in these populations. Although there may be special considerations for timing of HCV treatment as it relates to HCC diagnosis and treatment, generally treatment regimen recommendations are unchanged from those for people without HCC detailed throughout this guidance. There is insufficient evidence to recommend modification in the duration of antiviral therapy or the addition of ribavirin based upon a prior history or current HCC.

Recommendation for Hepatitis C Treatment in Persons With Current or Prior Hepatocellular Carcinoma

RECOMMENDED	RATING
There is insufficient evidence to recommend modification of antiviral treatment duration or the addition of ribavirin based on a prior history or current hepatocellular carcinoma.	IIb, C

Hepatitis C Treatment in Persons With a Prior History of Hepatocellular Carcinoma: Impact of Direct-Acting Antiviral Therapy on Hepatocellular Carcinoma Occurrence/Recurrence

Recommendation for Treating Hepatitis C in Persons With a Prior History of Hepatocellular Carcinoma

RECOMMENDED	RATING
A prior history of hepatocellular carcinoma is not a contraindication to hepatitis C treatment.	I, A

Multiple observational cohort studies have demonstrated a decreased risk for incident HCC in persons with HCV-associated cirrhosis following direct-acting antiviral (DAA) therapy with sustained virologic response (SVR) (Kanwal, 2017); (Singer, 2018). However, several small cohort reports early in the DAA era raised concern regarding the potential effect of DAA-associated virologic suppression in people with a history of HCC. This was initially documented in a single-center study from Spain involving 58 persons with HCV infection and a history of HCC who were treated with interferon-free DAA therapy and appeared to have unexpectedly high rates of HCC recurrence post treatment (Reig, 2016). An early meta-analysis of 24 studies (n=1820 participants) revealed a pooled point estimate for HCC recurrence after DAA therapy of 25.1% (95% confidence interval [CI] 19.4%–31.2%). But among 9 studies (n=947) with a comparator arm of untreated and/or interferon-treated persons, DAA-treated persons experienced similar or lower rates of HCC recurrence. In 5 studies that reported relative risk of recurrence with 95% confidence intervals, DAA-treated persons had a

lower pooled HCC recurrence risk compared with untreated persons (pooled odds ratio [OR] 0.55; 95% CI 0.25–0.85) (Saraiya, 2018). Many uncontrolled studies and cohort analyses have been limited by misclassification of HCC complete response prior to DAA therapy, ascertainment bias of HCC recurrence, and inclusion of persons with advanced HCC, a history of prior HCC recurrence, and/or undergoing noncurative intent treatment modalities.

Multiple observational cohort studies have further clarified the relationship between DAA therapy and HCC recurrence. A North American retrospective cohort study involving 793 adults with HCV-associated HCC with a complete response to oncologic treatment were evaluated for HCC recurrence risk based on exposure or nonexposure to DAA therapy. The investigators concluded that DAA therapy was not associated with HCC recurrence (hazard ratio [HR] 0.90; 95% CI 0.70–1.16). Further, among persons with DAA-induced SVR, the risk of death was reduced (HR 0.29; 95% CI 0.18–0.47) (Singal, 2019). A similar Korean retrospective cohort study involving 1021 adults with HCV-related HCC who received curative treatment were evaluated for risk of HCC recurrence and all-cause mortality based on exposure or nonexposure to DAA therapy. DAA therapy was associated with a significantly lower risk of HCC recurrence (HR 0.05; 95% CI 0.007–0.354) and lower all-cause mortality (HR 0.063; 95% CI 0.009–0.451) (Ahn, 2022). A prospective cohort of 163 consecutive Italian adults with HCV-related cirrhosis and first diagnosis of early Barcelona-Clinic Liver Cancer (BCLC) stage 0/A HCC with complete radiologic response after curative resection or ablation compared HCC recurrence risk in those who underwent DAA therapy versus 328 participants with a comparable HCV and HCC history who did not receive DAA therapy. Compared with the DAA-untreated group, the DAA-treated group experienced no difference in HCC recurrence (HR 0.70; 95% CI 0.44–1.13). However, the investigators noted a decrease in hepatic decompensation (HR 0.32; 95% CI 0.13–0.84) and decreased all-cause mortality (HR 0.39; 95% CI 0.17–0.91) for the DAA-treated group (Cabibbo, 2019). A multicenter, retrospective cohort study evaluated the outcomes of 566 adults with HCV-related cirrhosis and treatment-naive HCC based on those with DAA-induced SVR before HCC diagnosis (n=135) compared with those with active HCV viremia (n=431) at the time of HCC diagnosis. Initial HCC treatment was nonsurgical for all participants, who were followed until liver transplantation, last follow-up, or death. Compared with persons with active viremia, DAA-induced SVR was associated with a significantly reduced risk of hepatic decompensation (OR 0.18; 95% CI 0.06–0.59); there was no significant difference in overall survival between the study groups (Parikh, 2022). A systematic review with meta-analysis and meta-regression involving 41 studies (n=13,875 participants) evaluating HCC occurrence or recurrence further confirmed that DAA therapy was not associated with an increased risk of either HCC occurrence (relative risk [RR] 0.68; 95% CI 0.18–2.55) or recurrence (RR 0.62; 95% CI 0.11–3.45) (Waziry, 2017). The collective evidence signals an overall neutral or protective effect of DAA therapy on HCC recurrence, and a decreased risk for hepatic decompensation and all-cause mortality. Therefore, available data do not support a history of HCC as a contraindication to DAA therapy.

Hepatitis C Treatment in Persons With Early-Stage Hepatocellular Carcinoma

Recommendation for Treating Hepatitis C in Persons With Early-Stage Hepatocellular Cancer	
RECOMMENDED	RATING
Direct-acting antiviral therapy may be deferred until 4 months to 6 months after initial therapy for early-stage hepatocellular carcinoma in order to maximize virologic response.	IIb, B

Among persons with HCV infection and early-stage HCC, expeditious management of HCC should be prioritized. Furthermore, achievement of adequate HCC treatment prior to HCV treatment can increase the likelihood of HCV infection cure. A single-center retrospective study of 421 adults with chronic hepatitis C and cirrhosis—of whom 33% (n=139) had active HCC or a prior history of HCC—evaluated the SVR rates in participants with HCC compared with those without HCC. The rate of DAA failure to attain SVR in participants with HCC was 21% compared with 12% in those without HCC (Prenner, 2017). In a multivariable analysis, the strongest predictor of DAA treatment failure was the presence of active HCC at the time of HCV treatment initiation (adjusted odds ratio [AOR] 8.5; 95% CI 3.90–18.49). Similarly, a large retrospective cohort study from the US Veterans Affairs health care system identified 17,847 HCV treatment recipients, among whom 624 persons had a diagnosis of HCC prior DAA treatment initiation, including 142 persons with HCC who received a liver transplant prior to DAA therapy. The presence of HCC was associated with a lower likelihood of SVR overall (AOR 0.38; 95% CI 0.29–0.48) (Beste, 2017). A large systematic review with meta-analysis of 56 studies evaluated the effectiveness of DAA treatment for hepatitis C among 5,522 adults with HCV infection and HCC. In the 42 studies (n=4178) in which all persons with HCC received curative management, the pooled SVR rate was 90.4% (95% CI 88.3%–92.4%). The pooled SVR rate was lower in the 9 studies (n=361) in which all persons received noncurative HCC management; pooled SVR rate was 82.5% (95% CI 73.9%–91.2%).Notably, stratified analysis demonstrated that this difference was not due to cirrhosis status (He, 2020). Additionally, in evaluating HCC recurrence risk in the context of hepatitis C treatment, the interval between HCC cure and HCV treatment has been associated with recurrence risk. In the original report of unexpectedly high HCC recurrence in the context of DAA therapy, it was noted that HCC recurrence was significantly higher in persons who received DAA therapy less than 4 months after HCC treatment completion compared with those whose DAA therapy occurred more than 4 months after HCC treatment completion (55% and 21%, respectively) (Reig, 2016); (Tsai, 2016). Although the number of persons with recurrence in this study was small, it would be reasonable to defer HCV antiviral therapy for 4 months to 6 months after completion of HCC treatment with high likelihood of cure.

Hepatitis C Treatment in Persons with Advanced Hepatocellular Carcinoma

Recommendation for Treating Hepatitis C in Persons With Advanced Hepatocellular Carcinoma

RECOMMENDED	RATING
Persons diagnosed with advanced hepatocellular carcinoma who have hepatitis C infection should undergo treatment for hepatitis C unless they have palliative goals of care.	IIa, B

There has been a rapid advancement in the development of effective therapies for the treatment of advanced HCC (Peng, 2024); (Fong, 2023); (Singal, 2023); (Chen, 2022); (Guven, 2022); (Park, 2019). Previously, hepatitis C treatment was not recommended for those with advanced HCC due to poor HCC-related outcomes. However, in addition to improved survival of people with advanced HCC, emerging data suggest that HCV antiviral therapy may improve overall survival (OS). Thus, the timing and benefit of HCV antiviral therapy in the setting of advanced HCC should be considered.

Multiple retrospective studies have shown improved OS among persons with HCC who attain SVR compared with those who remain viremic (Kuwano, 2022); (Li, 2022); (Mori, 2022); (Seko, 2022); (Shao, 2021); (Yeh, 2021); (Luo, 2020); (Sou, 2019); (Bruno, 2017); (Kawaoka, 2017). The safety and tolerability of DAAs provide

even people with advanced cirrhosis and HCC the highly probable opportunity to attain SVR. A retrospective study from Japan among 359 persons with HCV-associated advanced HCC who received first-line systemic chemotherapy reported that those with SVR had a median OS of 38.4 months (95% CI 16.5–60.3) compared with 14.3 months (95% CI 10.9–17.7) in HCV viremic persons. Multivariate analysis demonstrated that SVR was the prognostic factor most strongly associated with OS. Furthermore, SVR was associated with improved liver function, better response to first-line HCC therapy, and a higher likelihood of receiving additional HCC treatment (Minami, 2022). Other small studies have shown similar findings (Mori, 2022); (Lin, 2020). A retrospective cohort study (n=1684; 122 HCV DAA treated, 1,562 HCV untreated) utilizing Taiwanese administrative health data showed that after propensity score matching, persons with advanced HCC (identified as those receiving sorafenib) had improved OS with DAA treatment compared with those whose HCV infection was untreated. The median survival was 20.2 months in the DAA treatment group compared with 11.1 months in the HCV infection untreated group (Tsai, 2021). Another retrospective study pooled data from 2 US and 6 Asian centers and compared outcomes in persons with HCV-associated HCC between 1,239 untreated persons and 437 treated persons with DAA-induced SVR. Using propensity score matching to reduce differences between the groups, the investigators found that OS was better in persons with DAA-induced SVR in all subgroups compared with those in the HCV untreated group. Multivariable analysis indicated that SVR was independently associated with a 66% reduction in the risk of 5-year liver-related mortality and a 63% reduction in the risk of 5-year all-cause mortality. Among persons with advanced HCC receiving noncurative intent therapy, after propensity score matching (92 SVR, 97 untreated), the median survival for the SVR group was 27.4 months (95% CI 16.0–53.6) compared with 19.7 months (95% CI 11.5–36.1) in the untreated group (Dang, 2020). Although the numbers were limited in those with advanced HCC, the investigators speculated that HCV treatment may improve liver function and thus an individual's ability to tolerate HCC therapy.

Collectively, the data from multiple retrospective studies show improved overall and liver-related survival in people with advanced HCC and HCV infection who received DAA treatment compared with those who remained HCV viremic. Prospective data would be helpful to confirm these results and clarify if there are people with advanced HCC who are not well served by DAA treatment. As systemic therapy for HCC continues to improve, it is likely that the benefits of HCV treatment and SVR in those with HCV-associated advanced HCC will become more robust.

There are minimal drug-drug interactions described if concurrently treating an individual with DAAs and HCC systemic therapies. Among the currently recommended treatment agents, there is a potential drug-drug interaction between regorafenib and both sofosbuvir/velpatasvir and glecaprevir/pibrentasvir that can cause a mild increase in regorafenib concentration. In the setting of sofosbuvir/velpatasvir therapy, concentrations of both sofosbuvir/velpatasvir and regorafenib can be increased due to inhibition of breast cancer resistance protein. In the setting of glecaprevir/pibrentasvir therapy, concentrations of regorafenib may increase due to weak inhibition of cytochrome P450 3A4. There are no drug-drug interactions expected with the use of DAAs in combination with atezolizumab plus bevacizumab, lenvatinib, nivolumab, pembrolizumab, or ramucirumab. Dosing and treatment regimens are not impacted by these drug-drug interactions.

There are insufficient data on the cost-effectiveness of treating HCV in individuals with advanced HCC.

Hepatitis C Treatment in Persons With Hepatocellular Carcinoma in the Liver Transplant Setting

Recommendation for Treating Hepatitis C in Liver Transplant Candidates With Hepatocellular Carcinoma

RECOMMENDED	RATING
Persons diagnosed with hepatitis C and hepatocellular carcinoma who are candidates for liver transplantation should be treated for hepatitis C before or after transplant in conjunction with their liver transplant practitioners, taking into consideration planned hepatocellular carcinoma therapies, the likelihood of hepatitis C antiviral treatment response, and transplant access.	I, C

HCC remains a common indication for liver transplantation in the United States and around the world. However, the important impact of HCV antiviral treatment on the risk for HCV-related HCC is highlighted by the overall decline in liver transplant rates for HCC in this population since the widespread availability of DAAs.

While all liver transplant recipients with HCV must be treated to attain SVR and optimize graft and patient survival, the timing of treatment (before or after transplantation) and ideal regimen may depend on the individual's liver function, likelihood of treatment response, and urgency for transplantation on the waiting list, as detailed in the section on Persons Who Develop Recurrent HCV Infection Post Liver Transplantation. The lower SVR rates observed among people who are undergoing concomitant treatment for early-stage HCC on the liver transplant wait list may be an important consideration (along with Child-Turcotte-Pugh class) in determining optimal timing of DAA treatment, with posttransplant response rates potentially being higher in some persons (Tse, 2020).

The impact of DAA therapy on the risk of HCC recurrence post liver transplant has also been studied. While there has been at least 1 report from a single center, retrospective cohort study of increased HCC recurrence in DAA-treated liver transplant recipients (HR 5.2; 95% CI 0.9–29.81) (Lim, 2020), other reports have not supported this association (Tse, 2020); (Vidal, 2020); (Zanetto, 2017); (Younossi, 2016). Nonetheless, HCV treatment remains an important priority in the liver transplant population due to improved OS in persons with SVR as well as decreased rates of significant HCV recurrence and graft failure (Tabrizian, 2021). Whether there are additional considerations for graft selection in transplant recipients with HCV-related HCC, including the use of HCV-viremic donors, remains uncertain.

Related References

Ahn YH, Lee H, Han JE, et al. Effect of direct-acting antivirals for hepatitis C virus-related hepatocellular carcinoma recurrence and death after curative treatment. *J Liver Cancer*. 2022; 22:125-135.

Beste LA, Green PK, Berry K, et al. Effectiveness of hepatitis C antiviral treatment in a USA cohort of veteran patients with hepatocellular carcinoma. *J Hepatol*. 2017; 67(1):32-39.

Bruno S, Di Marco V, Iavarone M, et al. Improved survival of patients with hepatocellular carcinoma and compensated hepatitis C virus-related cirrhosis who attained sustained virological response. *Liver Int*. 2017 Oct;37(10):1526-1534. doi: 10.1111/liv.13452.

Cabibbo G, Celsa C, Calvaruso V, et al; HCV (RESIST-HCV) and Italian Liver Cancer (ITA.LI.CA.) Group. Direct-acting antivirals after successful treatment of early hepatocellular carcinoma improve survival in HCV-cirrhotic patients. *J Hepatol*. 2019 Aug;71(2):265-273. doi: 10.1016/j.jhep.2019.03.027.

Chen YH, Wang CC, Chen YY, Wang JH, Hung CH, Kuo YH. Low-dose nivolumab in advanced hepatocellular carcinoma. *BMC Cancer*. 2022;22(1):1153. doi:10.1186/s12885-022-10271-6.

Dang H, Yeo YH, Yasuda S, et al. Cure with interferon-free direct-acting antiviral is associated with increased survival in patients with hepatitis C virus-related hepatocellular carcinoma from both East and West. *Hepatology*. 2020;71(6):1910-1922. doi: 10.1002/hep.30988.

Fiehn F, Beisel C, Binder M. Hepatitis C virus and hepatocellular carcinoma: carcinogenesis in the era of direct-acting antivirals. *Curr Opin Virol*. 2024;67:101423. doi: 10.1016/j.coviro.2024.101423.

Fong KY, Zhao JJ, Sultana R, et al. First-line systemic therapies for advanced hepatocellular carcinoma: a systematic review and patient-level network meta-analysis. *Liver Cancer*. 2022;12(1):7-18. doi: 10.1159/000526639.

Guven DC, Erul E, Sahin TK, Dizdar O, Yalcin S, Sahin IH. The benefit of immunotherapy in patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Future Oncol*. 2022;doi:10.2217/fon-2022-0642.

He S, Lockart I, Alavi M, Danta M, Hajarizadeh B, Dore GJ. Systematic review with meta-analysis: effectiveness of direct-acting antiviral treatment for hepatitis C in patients with hepatocellular carcinoma. *Aliment Pharmacol Ther*. 2020;51(1):34-52. doi: 10.1111/apt.15598.

Kanwal F, Kramer J, Asch SM, et al. Risk of hepatocellular cancer in HCV patients treated with direct-acting antiviral agents. *Gastroenterology*. 2017; 153(4):996-1005.

Kawaoka T, Aikata H, Teraoka Y, et al. Impact of hepatitis C virus eradication on the clinical outcome of patients with hepatitis C virus-related advanced hepatocellular carcinoma treated with sorafenib. *Oncology*. 2017;92(6):335-346. doi: 10.1159/000458532.

Kuwano A, Yada M, Nagasawa S, et al. Hepatitis C virus eradication ameliorates the prognosis of advanced hepatocellular carcinoma treated with sorafenib. *J Viral Hepat*. Jul 2022;29(7):543-550. doi: 10.1111/jvh.13681.

Li X, Wang J, Ding X, et al. Clinical study of lenvatinib in the treatment of hepatitis virus-related hepatocellular carcinoma and antiviral therapy. *Front Pharmacol*. 2022;13:1032881.

Lim N, Singh D, Jackson S, Lake JR. Recurrence of hepatocellular carcinoma in hepatitis C virus (HCV) liver transplant recipients treated with pretransplant direct-acting antiviral (DAA) therapy. *Gastrointest Tumors*. 2020;7(4):134-143. doi: 10.1159/000510341.

Lin WC, Lin YS, Chang CW, et al. Impact of direct-acting antiviral therapy for hepatitis C-related hepatocellular carcinoma. *PLoS One*. 2020;15(5):e0233212. doi: 10.1371/journal.pone.0233212.

Luo Y, Zhang Y, Wang D, Shen D, Che YQ. Eradication of hepatitis C virus (HCV) improves survival of hepatocellular carcinoma patients with active HCV infection - a real-world cohort study. *Cancer Manag Res*. 2020;12:5323-5330. doi: 10.2147/CMAR.S254580.

Minami Y, Aoki T, Chishina H, et al. Prognostic factors for overall survival in patients with HCV-related HCC undergoing molecular targeted therapies: beyond a sustained virological response. *Cancers (Basel)*. 2022;14(19):4850. doi: 10.3390/cancers14194850.

Mori Y, Matsuda S, Sato M, et al. The impact of antiviral therapy for hepatitis C virus on the survival of patients after hepatocellular carcinoma treatment. *Intern Med*. 2022;61(18):2721-2729. doi: 10.2169/internalmedicine.8456-21.

Parikh ND, Mehta N, Hoteit MA, et al. Association between sustained virological response and clinical outcomes in patients with hepatitis C infection and hepatocellular carcinoma. *Cancer*. 2022;128(19):3470-3478. doi: 10.1002/cncr.34378.

Park J, Cho J, Lim JH, Lee MH, Kim J. Relative efficacy of systemic treatments for patients with advanced hepatocellular carcinoma according to viral status: a systematic review and network meta-analysis. *Target Oncol*. 2019;14(4):395-403. doi: 10.1007/s11523-019-00651-7.

Peng W, Pan Y, Xie L, et al. The emerging therapies are reshaping the first-line treatment for advanced hepatocellular carcinoma: a systematic review and network meta-analysis. *Therap Adv Gastroenterol*. 2024;17:17562848241237631. doi: 10.1177/17562848241237631.

Prenner SB, VanWagner LB, Flamm SL, et al. Hepatocellular carcinoma decreases the chance of successful hepatitis C virus therapy with direct-acting antivirals. *J Hepatol*. 2017; 66(6):1173-1181.

Reig M, Marino Z, Perello C, et al. Unexpected high rate of early tumor recurrence in patients with HCV-related HCC undergoing interferon-free therapy. *J Hepatol*. 2016;65(4):719-726. doi: 10.1111/apt.14823.

Saraiya N, Yopp AC, Rich NE, Odewole M, Parikh ND, Singal AG. Systematic review with meta-analysis: recurrence of hepatocellular carcinoma following direct-acting antiviral therapy. *Aliment Pharmacol Ther*. 2018;48(2):127-137. doi: 10.1111/apt.14823.

Seko Y, Moriguchi M, Takahashi A, et al. Hepatitis C virus eradication prolongs overall survival in hepatocellular carcinoma patients receiving molecular-targeted agents. *J Gastroenterol*. 2022;57(2):90-98. doi: 10.1007/s00535-021-01837-5.

Shao C, Shao PP, Chen WT, Lin CC, Lin WR, Yeh CT. Direct-acting antiviral therapy improves the outcome of chronic hepatitis C/intermediate-stage B hepatocellular carcinoma patients. *Anticancer Res*. 2021;41(4):2007-2016. doi: 10.21873/anticanres.

Singal AG, Llovet JM, Yarchoan M, et al. AASLD practice guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology*. 2023;78(6):1922-1965. doi: 10.1097/HEP.0000000000000466.

Singal AG, Rich NE, Mehta N, et al. Direct-acting antiviral therapy for hepatitis c virus infection is associated with increased survival in patients with a history of hepatocellular carcinoma. *Gastroenterology*. 2019;157(5):1253-1263.e2.

Singer AW, Reddy KR, Telep LE, et al. Direct-acting antiviral treatment for hepatitis C virus infection and risk of incident liver cancer: a retrospective cohort study. *Aliment Pharmacol Ther*. 2018; 47(9):1278-1287.

Sou FM, Wu CK, Chang KC, et al. Clinical characteristics and prognosis of HCC occurrence after antiviral therapy for HCV patients between sustained and non-sustained responders. *J Formos Med Assoc*. 2019;118(1 Pt 3):504-513. doi: 10.1016/j.jfma.2018.10.017.

Tabrizian P, Saberi B, Holzner ML, et al. Outcomes of transplantation for HBV- vs. HCV-related HCC: impact of DAA HCV therapy in a national analysis of >20,000 patients. *HPB (Oxford)*. 2022;24(7):1082-1090. doi: 10.1016/j.hpb.2021.11.018.

Tsai HY, Chang HP, Chen CJ, Hsu WL, Huang LY, Lee PC. Effects of direct-acting antiviral therapy for patients with advanced hepatocellular carcinoma and concomitant hepatitis C-A population-based cohort study. *Eur Rev Med Pharmacol Sci*. 2021;25(23):7543-7552. doi: 10.26355/eurrev_202112_27454.

Tsai PC, Huang CF, Yu ML. Unexpected early tumor recurrence in patients with hepatitis C virus-related hepatocellular carcinoma undergoing interferon-free therapy: issue of the interval between HCC treatment and antiviral therapy. *J Hepatol*. 2017;66(2):464. doi: 10.1016/j.jhep.2016.10.035.

Tse CS, Yang JD, Mousa OY, et al. Direct-acting antiviral therapy in liver transplant patients with hepatocellular carcinoma and hepatitis C. *Transplant Direct*. 2020;7(1):e635. doi: 10.1097/TXD.0000000000001049.

Vidal RIO, Vidal EIO, Pereira BB, et al. Risk factors for hepatocellular carcinoma recurrence and survival after liver transplantation in patients with HCV-related cirrhosis. *Biomed Res Int*. 2020;2020:1487593. doi: 10.1155/2020/1487593.

Waziry R, Hajarizadeh B, Grebely J, et al. Hepatocellular carcinoma risk following direct-acting antiviral HCV therapy: a systematic review, meta-analyses, and meta-regression. *J Hepatol*. 2017; 67:1204-1212.

Yeh ML, Kuo HT, Huang CI, et al. Eradication of hepatitis C virus preserves liver function and prolong survival in advanced hepatocellular carcinoma patients with limited life expectancy. *Kaohsiung J Med Sci*. 2021;37(2):145-153. doi: 10.1002/kjm2.12303.

Younossi ZM, Stepanova M, Saab S, et al. The impact of viral hepatitis-related hepatocellular carcinoma to post-transplant outcomes. *J Viral Hepat*. 2016;23(1):53-61. doi: 10.1111/jvh.12449.

Zanetto A, Shalaby S, Vitale A, et al. Dropout rate from the liver transplant waiting list because of hepatocellular carcinoma progression in hepatitis C virus-infected patients treated with direct-acting antivirals. *Liver Transpl*. 2017;23(9):1103-1112. doi: 10.1002/lt.24790.

Last Update: January 15, 2025