Hepatitis C “Revolution” May Transform Liver Cancer Outcomes
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Novel agents that target the replication of the hepatitis C virus (HCV) are poised to have a far-reaching impact on the prevention and recurrence of hepatocellular carcinoma (HCC) and have shown the ability to reverse liver fibrosis, including cirrhosis in patients with end-stage HCC, according to a leading liver disease expert.

Improved outcomes for patients who have been diagnosed with HCC or are at risk of developing the disease are among the benefits that potentially could flow from a “revolution” in the treatment of chronic HCV that has unfolded in recent years, said Michael P. Manns, MD, in delivering a keynote address at the 2015 World Congress on GI Cancer.

“HCV is the number 1 indication for liver transplantation in the US and Europe, and a major cause of liver cancer,” said Mann, who is director of the Department of Gastroenterology, Hepatology and Endocrinology at the Medical School of Hannover, Germany. “There are approximately 185 million carriers worldwide. Although there is no vaccine, it is the first curable chronic infection, and elimination of the virus prolongs survival in hepatocellular carcinoma.”

Moreover, HCV therapies can dramatically change the treatment paradigm for HCC, Mann indicated. “The goal in 10 to 20 years is to have no more liver transplantation due to HCV-positive hepatocellular carcinoma and for all transplant patients to be free of HCV,” he said. “The vision for the future is to have no more hepatitis C-associated liver cancer, which can only be realized with global access to therapies.”

The correlation between eradicating HCV and improving liver-related health outcomes is supported by a body of clinical trial evidence, Mann indicated during his presentation.

“Achieving sustained virological response for 12 weeks [SVR12] constitutes cure in 95.5% of cases,” he said. Cure of infection has been shown to reduce the incidence of HCC, liver-related mortality, and even all-cause mortality (both P <.001), for example, from cardiovascular disease.1

Breakthroughs Lauded

“The revolution in chronic HCV treatment was the result of a masterpiece of translational research,” Mann commented. From 2001 to 2011, the standard treatments for patients with chronic HCV were variations of pegylated- (PEG) interferon alfa-2a or alfa-2b plus ribavirin. These treatments yielded SVR in 40% to 50% of patients infected with genotypes 1 or 4 and an SVR of 60% to 90% in genotypes 2 or 3.2

In the past four years, treatment options have mushroomed. In 2011, the FDA approved telaprevir (Incivek) and boceprevir (Victrelis), both for patients with HCV genotype 1 in combination with PEG-interferon and ribavirin.

Since November 2013, the FDA has approved four new treatments for chronic HCV, some of which do not require PEG-interferon. These therapies are simeprevir (Olysio), sofosbuvir (Sovaldi), ledipasvir and sofosbuvir (Harvoni), and the Viekira Pak. Harvoni is a fixed-dose tablet combination of ledipasvir and sofosbuvir that replaced a regimen of one weekly PEG-interferon injection plus 11 or 12 pills daily.
Viekira Pak is a four-drug regimen (ombitasvir, paritaprevir and ritonavir tablets co-packaged with dasabuvir tablets).

These new treatments each inhibit viral replication at one of three stages that result in SVR in 92% to 100% of chronically infected individuals, said Manns.

He pinpointed four stages at which viral eradication could impact patients with HCC: (1) treatment early in the course of infection to prevent the development of HCC; (2) prior to resection to prevent recurrence; (3) before and after liver transplantation; and (4) in patients with simultaneous HCC undergoing transcatheter arterial chemoembolization (TACE)/sorafenib and palliative treatment.

Manns said successful HCV treatment does prevent liver cancer and achieving HCV SVR has been associated with a decrease in the development of HCC over a 10-year follow-up period (P <.001).3

“Suppression of HCV replication reduces risk for HCC in patients with HCV cirrhosis,” he said. “Successful HCV therapy prevents fibrosis progression, and has even been shown to reverse fibrosis, including cirrhosis.”

“HCV treatment in the management of HCC lowers the risk of HCC recurrence after curative treatment with radiofrequency ablation or surgery,” added Manns. Results from interferon-based treatments given prior to curative HCC treatment showed an effect on curative HCC treatment wherein patients achieving SVR had prolonged recurrence-free survival compared with patients who did not achieve eradication of the virus (P <.01).

The public health implications of eradicating the virus are enormous, Manns indicated. “HCV infection accounts for approximately 25% of liver disease leading to transplantation in Europe,” he said.

Additionally, de novo HCC, which often develops in patients on the transplant waiting list, is due to HCV in 66% of cases, said Mann. Pretransplant sofosbuvir plus ribavirin has been shown to decrease HCV recurrence posttransplant by 70% to 75%; remaining continuously free of virus for a greater number of days prior to transplant decreases the risk of viral recurrence (P <.001).4 “Prevention of HCV recurrence is possible in Child A cirrhosis and treatment of HCV posttransplant is highly efficacious in compensated and decompensated liver disease,” said Mann.

Whether patients with late-state HCC receiving palliative care would benefit from HCV treatment remains controversial. The SOLAR-1 trial showed high efficacy and improved liver function in patients with advanced cirrhosis following treatment of HCV genotypes 1 and 4 with sofosbuvir plus ribavirin5 but Manns cautioned that this treatment was not recommended for patients with impaired kidney function with a glomerular filtration rate <30. “The urgent unmet need in decompensated liver disease is defining the point of no return,” he said.

References


