Long-Term Care Updates

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A Review of Hepatitis C Screening and Treatment in Long-Term Care Facilities

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Introduction

In the general population, but especially in long-term care facilities, there is a significant yet underrecognized group affected by the hepatitis C virus (HCV). Studies such as those conducted by Gallo et al. and Chien et al. have revealed high rates of anti-HCV positivity among institutionalized elderly individuals, indicating the need for structured screening strategies within this setting.[1,2] HCV infection, if left undiagnosed and untreated, can lead to chronic liver disease, ranging from mild to severe, including cirrhosis and liver cancer.[3]

HCV has six genotypes, each categorized based on similar genes.[4] HCV genotypes 1a and 1b are the predominant genotypes found in North America, followed by genotypes 2 and 3. Fortunately, all HCV genotypes can now be cured by direct-acting antivirals (DAAs), with some treatment options being pangenotypic, meaning they can cure all genotypes equally effectively. These pangenotypic therapies include glecaprevir/pibrentasvir (Mavyret®) and sofosbuvir/velpatasvir (Epclusa®), which have emerged as prominent choices recommended by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) for treating HCV in treatment-naïve adults with or without compensated cirrhosis.[5]

Additionally, advancements in HCV treatment have simplified care and expanded access, aligning with global efforts to eliminate HCV. Lewis et al. estimated that 2.2 million noninstitutionalized civilian U.S. adults had HCV between January 2017 and March 2020, with one-third of these cases being unaware of their infection.[6] Screening strategies recommended by the Centers for Disease Control and Prevention (CDC) include targeting at-risk populations, including individuals with a history of injection drug use, HIV infection, blood transfusion or organ donor recipients, anyone who has received maintenance hemodialysis, and those with persistently abnormal alanine aminotransferase (ALT) levels.[3]

It is now recommended that all adults 18 years and older be screened for HCV at least once in their lifetime, emphasizing the importance of proactive screening initiatives, particularly in long-term care settings.[3] Recognizing the unique challenges and opportunities presented by HCV in long-term care facilities and implementing comprehensive screening and treatment protocols are essential steps toward improving the health outcomes of this population.

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Glecaprevir/pibrentasvir (Mavyret®)

Glecaprevir/pibrentasvir (G/P) (Mavyret®) is a pangenotypic HCV treatment option approved in 2017 for patients at least 3 years of age and older.[7] G/P may be used in patients with or without compensated cirrhosis (Child-Pugh class A). G/P does not require renal dose adjustments but is contraindicated in moderate or severe hepatic impairment (Child-Pugh class B or C) and a history of hepatic decompensation.[8]

G/P works synergistically to inhibit critical enzymes necessary for the replication of HCV.[7] Glecaprevir acts as a protease inhibitor (PI), while pibrentasvir inhibits the NS5A protein, both of which are essential for viral replication and assembly. The recommended dosage of G/P is three tablets (glecaprevir 100 mg/pibrentasvir 40 mg per tablet) taken by mouth once daily with food for a duration of 8 to 16 weeks.[8] This convenient once-daily dosing regimen enhances patient adherence and simplifies treatment protocols. See Tables 1 & 2 for more dosing information.

Table 1. HCV Treatment-Naïve Glecaprevir/Pibrentasvir Dosing[5]

HCV Genotype	Comorbidities	Adult Dose/Duration
1-6	± Compensated cirrhosis ± HIV/HCV coinfection	Take 3 tablets by mouth once daily for **8 weeks**

Table 2. HCV Treatment-Experienced Glecaprevir/Pibrentasvir Dosing[5]

HCV Genotype	Comorbidities	Treatment- Experienced With:	Adult Dose/Duration
1-6	± Compensated cirrhosis ± HIV/HCV coinfection	Glecaprevir/pibrentasvir	Take 3 tablets by mouth once daily + sofosbuvir (400 mg) and weight-based ribavirin for **16 weeks**
1-6	± Compensated cirrhosis ± HIV/HCV coinfection	Multiple DAA failures (sofosbuvir/velpatasvir/ voxilaprevir or sofosbuvir + glecaprevir/pibrentasvir)	Take 3 tablets by mouth once daily + sofosbuvir (400 mg) and weight-based ribavirin for **16 weeks** *Treatment may be extended to **24 weeks** in difficult-to-treat scenarios or failure following sofosbuvir + glecaprevir/pibrentasvir)
1-6	± Compensated cirrhosis ± HIV/HCV coinfection	Sofosbuvir-based treatments (without prior NS5A inhibitor + NS3/4 PI exposure or genotype 3 with sofosbuvir/NS5A inhibitor exposure)	Take 3 tablets by mouth once daily for **16 weeks**

Special considerations must be taken for patients in long-term care settings, as they may have comorbid conditions or be on concurrent medications that could interact with G/P. It is crucial to assess each patient's overall health status and potential drug interactions to ensure the safe and effective use of G/P in managing HCV. Avoid concomitant use with carbamazepine, efavirenz, and St. John's wort as they may significantly decrease plasma concentrations of G/P, leading to reduced therapeutic effect and potential HCV treatment failure.[8] Additionally, G/P is contraindicated with atazanavir or rifampin. G/P may increase the serum concentration of statins, and atorva-, simva-, and lovastatin should be avoided during G/P treatment. Rosuvastatin should be limited to 10 mg daily and pravastatin doses should be reduced by 50% during treatment.[8]

The safety profile of G/P is generally favorable, with most side effects being mild to moderate. Common adverse effects include nausea, fatigue, and headache. Patients should be instructed to take each dose with their evening meal to help with nausea, increase absorption, and decrease daytime fatigue. Hepatic decompensation and failure have been reported, typically within the first 4 weeks of treatment. Monitor ALT and symptoms of liver disease such as weakness, nausea, vomiting, jaundice, or significantly elevated bilirubin, alkaline phosphatase, or INR during treatment.[8]

Clinical studies have demonstrated G/P's high efficacy across various genotypes of HCV, including challenging cases with prior treatment failures or the presence of liver cirrhosis. The treatment regimen has shown 12-week post-treatment sustained virologic response (SVR12) rates of over 95%, indicating a strong likelihood of achieving a cure when the virus remains undetectable 12 weeks after completing therapy. This high success rate makes G/P a preferred option for a broad spectrum of patients.

The ENDURANCE-1 and ENDURANCE-3 trials evaluated the effectiveness of G/P in 1,208 non-cirrhotic HCV patients, showing high SVR12 rates: 99.1% for 8 weeks and 99.7% for 12 weeks in genotype 1, and 95% for 8 and 12 weeks in genotype 3. Adverse events were minimal, indicating G/P is highly effective and well-tolerated for HCV genotype 1 or 3 without cirrhosis.[9] The ENDURANCE-5,6 trial evaluated 84 adults with HCV genotype 5 or 6 infection receiving G/P orally once daily for 8 or 12 weeks based on cirrhosis status. The study showed a 97.6% SVR12 rate, with 95.7% for genotype 5 and 98.4% for genotype 6. Serious adverse events occurred in 6% of patients, none related to G/P, and did not lead to treatment discontinuation, concluding that G/P is highly effective and well-tolerated in patients with HCV genotype 5 or 6 and compensated liver disease.[10]

The EXPEDITION-2 study assessed G/P's efficacy and safety in 153 treatment-naïve and experienced patients coinfected with HCV genotypes 1-6 and HIV-1. Participants achieved SVR12 rates of 98% (8 weeks) and 100% (12 weeks). The regimen was well-tolerated, with mostly mild to moderate adverse events, and showed no significant interactions with HIV-1 antiretroviral drugs, supporting its use as an effective treatment option for coinfected patients.[11]The EXPEDITION-8 trial assessed an 8-week G/P regimen in 343 treatment-naïve patients with compensated cirrhosis and chronic HCV genotypes 1-6, achieving SVR12 rates of 99.7% (per-protocol) and 97.7% (intention-to-treat). The regimen was well-tolerated, with mostly mild adverse events and rare serious adverse events, showing efficacy comparable to a 12-week regimen.[12]

Sofosbuvir/velpatasvir (Epclusa®)

A second pangenotypic treatment option for Hepatitis C is the once-daily combination of sofosbuvir and velpatasvir (S/V), marketed under the brand name Epclusa®. The mechanism of action of S/V is two-fold: sofosbuvir induces chain termination during viral replication by inhibiting HCV NS5B RNA polymerase and velpatasvir inhibits the viral protein NS5A. S/V is administered as a single tablet containing 400 mg sofosbuvir and 100 mg velpatasvir once daily with or without food for 12 weeks, regardless of previous treatment history. S/V alone is sufficient for patients with compensated cirrhosis (Child-Pugh class A), while the addition of ribavirin is recommended for patients with decompensated cirrhosis (Child-Pugh class B or C).[13]

Several clinical trials have demonstrated that S/V is highly effective at curing HCV, with 99% SVR12 across genotypes 1,2,4,5, and 6,[14,15] and 95% SVR12 in genotype 3.[15] ASTRAL-1 was a phase 3 double-blind placebo-controlled trial that involved 706 patients with HCV genotypes 1, 2, 4, 5, and 6, who were either treatment-naïve or previously treated, including those with compensated cirrhosis. Researchers found that the rate of sustained virologic response among patients who received 12 weeks of S/V was 99% (95% CI, 98 to >99), which significantly exceeded the prespecified performance goal of 85% (P<0.001). Overall, S/V was well-tolerated, with only 2% of patients experiencing a serious adverse event and only one patient discontinuing treatment due to an adverse event.[14] ASTRAL-2 and -3 were two randomized controlled trials for patients with HCV genotypes 2 and 3, regardless of whether they were treatment-naïve or previously treated, and with or without compensated cirrhosis. Among patients with HCV genotype 2, the SVR12 in the S/V group was 99% (95% CI, 96 to 100) and for patients with HCV genotype 3, the SVR12 in the S/V group was 95% (95% CI, 92 to 98) demonstrating superiority over sofosbuvir-ribavirin for both HCV genotypes 2 and 3.[15] Finally, the ASTRAL-4 trial was a phase 3 open-label study involving 267 treatment-naïve or previously treated patients with HCV of any genotype (1-6) presenting with Child-Pugh class B decompensated cirrhosis. A high SVR12 was observed in patients with decompensated cirrhosis treated with S/V with or without ribavirin for 12 weeks and with S/V for 24 weeks.[16]

While generally well-tolerated for most patients, there are several considerations for patients in the long-term care setting. Clinical trials for S/V involved 156 subjects aged 65 and over, which accounted for 12% of the total number of subjects in the phase 3 clinical trials. No significant differences in safety or effectiveness were observed between these older subjects and younger subjects. However, some older individuals may have greater sensitivity, although no specific dosage adjustment is recommended for geriatric patients. No dosage adjustment is necessary for patients with mild, moderate, or severe renal impairment, including end-stage renal disease (ESRD) requiring dialysis. However, there is no safety data available for subjects with both decompensated cirrhosis and severe renal impairment, including ESRD requiring dialysis.[13]

There is a risk of HBV reactivation in patients coinfected with HBV and HCV. Due to serious DDIs, coadministration of S/V with amiodarone, rifampin, St. John's wort, and carbamazepine is not recommended. Coadministration with statins may increase the risk of myopathy and rhabdomyolysis, so caution is warranted when statin therapy is necessary in patients taking S/V. Acid-reducing agents (such as antacids, proton pump inhibitors (PPIs), and H2 antagonists) decrease the solubility of velpatasvir, which could lead to reduced efficacy of S/V and virologic failure. Patients should separate antacids from S/V by 4 hours and not exceed doses comparable to 40 mg famotidine daily for H2 antagonists. Coadministration with PPIs should generally be avoided, however, if necessary, S/V may be taken with food and 4 hours before omeprazole, though this has not been studied with other PPIs.[13]

Conclusion

The development of highly effective pangenotypic therapies such as glecaprevir/pibrentasvir (Mavyret®) and sofosbuvir/velpatasvir (Epclusa®) has simplified and increased access to treatment, supporting global efforts to eradicate HCV in as little as eight weeks of therapy. It is essential to establish thorough screening and treatment protocols for HCV in long-term care facilities to prevent complications and improve health outcomes. The high rates of anti-HCV positivity among elderly individuals in institutionalized care highlight the necessity of early detection and intervention. Understanding the unique challenges and opportunities presented by HCV in long-term care settings is crucial for addressing its impact on this vulnerable population.

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