

Direct-acting antivirals: Revolutionizing SVR rates in HCV.

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Received: 04-Aug-2025, Manuscript No. AAVRJ-25-171359; Editor assigned: 05-Aug-2025, PreQC No. AAVRJ-25-171359(PQ); Reviewed: 19-Aug-2025, QC No. AAVRJ-25-171359; Revised: 23-Aug-2025, Manuscript No. AAVRJ-23-171359(R); Published: 30-Aug-2025, DOI:10.35841/aavrj-9.3.209

Introduction

Hepatitis C virus (HCV) infection has long posed a global health challenge, affecting over 58 million people worldwide and contributing to significant morbidity and mortality due to liver cirrhosis and hepatocellular carcinoma. For decades, treatment relied on interferon-based regimens, which were plagued by low sustained virological response (SVR) rates, severe side effects, and poor patient adherence. The advent of direct-acting antivirals (DAAs) has transformed the therapeutic landscape, offering cure rates exceeding 95%, shorter treatment durations, and improved tolerability. This article explores how DAAs have revolutionized SVR outcomes in HCV, the mechanisms behind their efficacy, and the implications for global elimination efforts [1].

Sustained virological response (SVR) is defined as the absence of detectable HCV RNA in the blood 12 or 24 weeks after completing therapy. SVR is considered a virological cure and is associated with reduced liver-related complications, improved quality of life, and decreased mortality. Achieving SVR is the primary goal of HCV treatment, and DAAs have dramatically increased the likelihood of reaching this milestone [2].

DAAs target specific nonstructural proteins essential for HCV replication. These include: By directly interfering with the viral life cycle, DAAs suppress viral replication with high potency and specificity, leading to rapid viral clearance. The first wave of DAAs, approved in 2011, included protease inhibitors like telaprevir and boceprevir, which were used in combination with pegylated interferon and ribavirin. While these improved SVR rates, they retained many of the adverse effects of interferon-based therapy. The second wave, beginning in 2013, introduced interferon-free regimens. Sofosbuvir, a nucleotide analog NS5B inhibitor, became a cornerstone of DAA therapy.

Combination regimens such as sofosbuvir-ledipasvir (Harvoni), sofosbuvir-velpatasvir (Epclusa), and glecaprevir-pibrentasvir (Mavyret) offered pan-genotypic coverage, simplified dosing, and shortened treatment durations to 8–12 weeks [3].

DAAs have demonstrated remarkable efficacy across all HCV genotypes. Clinical trials and real-world studies consistently report SVR rates above 95% in treatment-naïve and treatment-experienced patients. Even traditionally difficult-to-treat populations—such as those with cirrhosis, HIV coinfection, or renal impairment—have benefited from DAA therapy. For example, the ASTRAL-1 trial showed that sofosbuvir-velpatasvir achieved SVR12 in 99% of patients across genotypes 1–6. Similarly, the POLARIS-2 study reported SVR rates of 95% with glecaprevir-pibrentasvir in diverse patient populations [4].

Real-world data from national registries and cohort studies confirm the high effectiveness of DAAs outside clinical trials. Countries like Egypt, which once had the highest HCV prevalence globally, have implemented mass treatment programs using DAAs, dramatically reducing disease burden. However, challenges remain in ensuring equitable access. High drug costs initially limited availability, but the introduction of generics and global health initiatives has expanded access in low- and middle-income countries. The World Health Organization aims to eliminate HCV as a public health threat by 2030. DAAs are central to this goal, enabling scalable treatment with minimal monitoring [5].

Conclusion

Direct-acting antivirals have revolutionized the treatment of hepatitis C, transforming a once-chronic, stigmatized disease into a curable condition. With SVR rates exceeding 95%,

improved safety profiles, and pan-genotypic coverage, DAAs represent one of the greatest achievements in antiviral therapy. As we move toward HCV elimination, continued investment in access, innovation, and public health infrastructure will ensure that the benefits of DAAs reach all who need them.

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