A Comprehensive Review of Direct Acting Antivirals in Chronic Viral Hepatitis Therapy

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Abstract

Chronic viral hepatitis is a global public health concern a fecting millions of people worldwide. Terw r á a ' wor ò / clearance. Additionally, we discuss the challenges and future prospects of DAA therapy, emphasizing the potential for achieving sustained virologic responses and eventually eradicating chronic viral hepatitis.

Keywords: Chronic viral hepatitis; Antiviral; hepatitis C virus

Introduction

Chronic viral hepatitis is caused by the hepatitis B virus (HBV) and hepatitis C virus (HCV) and is a leading cause of liver-related morbidity and mortality globally. Traditional treatment options, such as interferon-based therapies, had limited success in achieving sustained virologic responses and were o en associated with signi cant adverse e ects. e emergence of direct acting antivirals (DAAs) has transformed the landscape of chronic viral hepatitis therapy [1].

DDAs on the other hand constitute a more recent development based on increasing knowledge of the molecular biology of the hepatitis viruses. In the case of HCV, the resolution of the 3-dimensional structure of important viral enzymes such as the NS3 serine protease and the RNA dependent RNA polymerase, and the in vitro models of viral replication that have allowed the study of virus entry, replication, morphogenesis, and identi ed host factors that are required for this process, have been invaluable in the design and testing of drugs under development. Such drugs act directly as viral lifecycle inhibitors [2]. e current choices of treatment will be reviewed in turn for each virus, as well as results from current clinical or preclinical trials with other agents in development, and which most likely will truly revolutionize future treatment approaches.

Classes of direct acting antivirals

DAAs can be classi ed into di erent groups based on their targets and mechanisms of action. We discuss the major classes of DAAs, including nucleoside/nucleotide analogs, non-nucleoside polymerase inhibitors, protease inhibitors, and NS5A inhibitors, highlighting how they inhibit viral replication through direct interactions with viral enzymes [3].

Hepatitis B virus

e mature virion or Dane particle measuring 45 nm in diameter is spherical in nature and consists of an outer envelope comprised of the hepatitis B surface proteins in a lipid bilayer derived from the host. e envelope encloses the nucleocapsid of the virus which is composed of the self-assembling core protein. is in turn encloses the viral genome

the HBeAg status of the patient as explained below. DNA remains in episomal form and in its transcriptionally active state associates with histones and other proteins, and through recruitment of a number of liver speci c transcription factors serves as the template for viral transcript synthesis by host RNA polymerase II. Most antiviral agents so far have been unable to prevent the replenishment of the DNA pool from genonic HBV-DNA recycled from immature core particles in the cytoplasm to the nucleus, or to radically eliminate DNA-containing hepatocytes [7].

DAA therapy for chronic hepatitis C

In this section, we provide an in-depth analysis of DAAs used in the treatment of chronic hepatitis C. We explore the di erent combinations and regimens available, including pan-genotypic therapies, and discuss their high cure rates and shorter treatment durations compared to traditional interferon-based therapies.

Mutations

Natural stable variants of the virus give rise to well-recognized serological subtypes and genotypes. However, HBV has a higher mutation rate than other DNA viruses base substitutions per site per year, through error prone steps in the replication cycle of the virus. ese may occur during pgRNA synthesis by the cellular RNA polymerase II, as RNA polymerases show inherently low copying delity, but also during reverse transcription due to the lack of proof reading capacity by the viral polymerase [8]. Fluctuations in the composition of the intracellular nucleotide pools are another possible contributing factor. A lot of these mutations are lethal to the virus, but those which o er it a replication advantage facilitate immune escape, or cause resistance to antiviral drugs, as explained later, can be preferentially selected.

Safety and tolerability of DAAs

While DAAs have shown remarkable e cacy, we also critically examine their safety pro les and potential drug interactions. Addressing the challenges related to drug resistance and adverse events is crucial to optimizing treatment outcomes [9].

Challenges and future prospects

Despite the tremendous success of DAAs, several challenges remain, including the cost of treatment, access to therapy in resource-limited settings, and the persistence of chronic hepatitis B covalently closed circular DNA. We discuss ongoing research e orts and potential strategies to overcome these obstacles.

e road to eradication

We conclude the review by highlighting the potential for achieving sustained virologic responses with DAAs and the eventual eradication of chronic viral hepatitis [10]. We emphasize the importance of early diagnosis, increased awareness, and access to a ordable treatment to accelerate progress towards global hepatitis elimination goals.

Conclusion

Direct acting antivirals have revolutionized the landscape of