Foreword

New Hepatitis C Therapies

Jean-Michel Pawlotsky, MD, PhD[1]

[1] National Reference Center for Viral Hepatitis B, C, and D, Department of Virology, Hôpital Henri Mondor, Université Paris-Est & INSERM U955, Créteil, France

Semin Liver Dis 2014;34:7–8.

Hepatitis C virus (HCV) will appear in the history of human medicine as a unique case of speedy "discovery to cure." Indeed, blood-borne non-A, non-B hepatitis was not recognized as an important medical entity until the late 1970s. The causative agent, HCV, was identified in 1989. Only 25 years later, new highly active antiviral drug combinations are reaching the Western world's markets, bringing the hope for possible therapeutic eradication….

This unforeseeable outcome should not be seen as a "miracle," but as the result of a conjunction of efforts and favorable circumstances. These include (1) the outstanding work of pioneer researchers in transfusion medicine and viral hepatitis who identified non-A, non-B hepatitis as an infectious disease transmitted by blood, likely caused by a viral agent, and characterized its epidemiology; (2) the discovery of HCV, one of the most important of the 20th century, that used an original approach based on molecular biology methods, subsequently used to discover a large number of other viruses; (3) the work of academic research laboratories that developed the in vitro models required to unravel the HCV life cycle and screen large chemical compound libraries in the search for specific antiviral inhibitors; (4) the enormous amounts of money made available by the financial world for HCV drug development, based on the assumption of a quick return-on-investment due to the size and accessibility of the HCV treatment market; (5) the invaluable experience acquired by biotech and larger pharmaceutical companies in the successful preclinical and clinical development of antiviral drugs against HIV; and (6) the worldwide investment of academic clinical teams in phase I to III clinical trials that offered their patients early access to the new therapies and will finally move many of the drugs they tested to approval. Thus, the current HCV therapeutic revolution is the result of an exemplary collaboration between academic and private entities that may serve as an example for future therapeutic developments in other disease areas.

In this exciting context, the enormous volume of bench research and clinical data generated and presented over the past few years has also created a lot of confusion. Thus, this issue of *Seminars in Liver Disease* is particularly timely in summarizing the state of the art in new HCV drug development. In the first article, Daniel Rupp and Ralf Bartenschlager describe the HCV life cycle, its different steps and actors, and the potential targets it offers for antiviral interventions. I then present the classes of new HCV drugs approved or still in clinical development, their mechanisms of action, and the basic concepts on which highly efficient curative strategies are founded. Current and future interferon-containing strategies are described by Andrew Aronsohn and Donald Jensen. The results of interferon-free regimens are split into two articles: strategies including a nucleoside/nucleotide analogue are discussed by Jordan Feld, while Tania Welzel and Stefan Zeuzem present the new nucleoside/nucleotide-free drug regimens. Specific aspects of HCV treatment in the liver transplant setting are discussed by Sabela Lens, Martina Gambato, Maria-Carlota Londoño, and Xavier Forns in their contribution, while Mark Sulkowski presents the new treatment approaches available for the HIV–HCV coinfected population. Because a therapeutic approach based solely on antiviral drugs may not be sufficient to eradicate HCV infection, which involves 184 million people worldwide with a still high incidence in many areas, Jonathan Honegger, Yan Zhou, and Christopher Walker discuss the reality of the need for a prophylactic or protective vaccine and present the results of preclinical studies with different HCV vaccine approaches. Finally, because HCV infection is not limited to countries that will be able to afford the cost of new curative therapies, the global HCV issue is discussed by Maud Lemoine and Mark Thursz, with special focus on access to care in resource-constrained areas. All of these authors should be lauded for their enthusiastic participation, the quality of their work, and their commitment to produce their piece quickly after the November 2013 Liver Meeting, to provide the readers with complete, up-to-date information.

Are we foreseeing the end of the HCV story? Probably just the beginning of the end. With such high infection cure rates, access to therapy, including broad-scale screening, diagnosis, access to care facilities, medication cost coverage, etc., is going to become a

Address for correspondence Jean-Michel Pawlotsky, MD, PhD, Department of Virology, Hôpital Henri Mondor, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Créteil, France (e-mail: jean-michel.pawlotsky@hmn.aphp.fr).

Issue Theme New Hepatitis C Therapies; Guest Editor, Jean-Michel Pawlotsky, MD, PhD

DOI http://dx.doi.org/10.1055/s-0034-1371178.
ISSN 0272-8087.

major issue, both in the developed and developing world. Eradicating infection from the nearly 200 million infected individuals worldwide with antiviral drugs may take decades. Cured infections will not all mean cured patients. Indeed, patients with cirrhosis remain at high risk for life-threatening complications, such as liver decompensation or hepatocellular carcinoma, after they definitively eliminate infection.

Nevertheless, we should not deny ourselves the pleasure of realizing that the HCV infection cure rates will be over 95% with the new all-oral, interferon-free strategies, a situation that nobody would have foreseen only 3 years ago. I hope this issue of *Seminars in Liver Disease* will help its readers to understand how the field got where it currently is and in what direction it is now moving. We, scientists and physicians involved in HCV research and care, should be proud of our collective achievements and full of hope for our HCV-infected patients. The beginning of the end just means that this end will have an end, and we will probably see it.