Q









Home ▶ All Journals ▶ Medicine ▶ Expert Review of Gastroenterology & Hepatology ▶ List of Issues ▶ Volume 7, Issue 5 ▶ The hepatitis C virus NS5A inhibitor dac ....

## Expert Review of Gastroenterology & Hepatology >

Volume 7, 2013 - <u>Issue 5</u>

 $\begin{array}{c|c} 92 & 11 & 0 \\ \text{Views} & \text{CrossRef citations to date} & \text{Altmetric} \end{array}$ 

Editoria

# The hepatitis C virus NS5A inhibitor daclatasvir has a dual mode of action and leads to a new virus half-life estimate

Jeremie Guedj, Harel Dahari, Susan L Uprichard & Alan S Perelson

Pages 397-399 | Published online: 10 Jan 2014



- Full Article
- Figures & data
- References
- **66** Citations
- **Metrics**

**➡** Reprints & Permissions

Read this article

Share

# The hepatitis C virus NS5A inhibitor daclatasvir has a dual mode of action and leads to a new virus half-life estimate

Expert Rev. Gastroenterol. Hepatol. 7(5), 397-399 (2013)



Jeremie Guedi

INSERM, UMR 738, Université Paris Diderot, Sorbonne Paris Cité, Paris 75018, France



### Harel Dahari

oyola University Medica nter, Maywood, IL 60153.

Theoretical Biology and Biophysics, Los Alamos I Laboratory, Los Alamos, NM 87545, USA



Susan L Uprichard

oyola University Medical Center, Maywood, IL 60153,



Alan S Perelson

Author for corresponde Biophysics, Las Alamas Nationa Laboratory, Los Alamos, NM 87545, USA Tel.: +1 505 667 6829 asp@lanl.gov



www.expert-reviews.com

**KEYWORDS:** daclatasvir • hepatitis C virus • multiscale model • NSSA inhibitor • viral kinetics

10.1586/17474124.2013.811050

© 2013 Informa UK Ltd

ISSN 1747-4124

"We employed mathematical modeling to decipher the origin of the very rapid viral decline observed in the first hours following initiation of daclatasvir, a first-in-class NS5A inhibitor, where one dose of daclatasvir led to a 1000-fold decrease in viral levels within approximately 12 h."

(HCV) affects approximately 160 mil- protein 5A. In a recent paper published lion people worldwide [1] and is the leading cause of cirrhosis, liver cancer and of Sciences [5], we employed mathematistandard of care in the western world was the very rapid viral decline observed in weekly injections of pegylated-interferon (peg-IFN)-α and daily oral ribavirin (RBV), but viral eradication was achieved in less than 50% in treatment-naive HCV genotype 1 patients, the most prevalent approximately 12 h [6]. genotype in western world [3].

Since the approval in 2011 of two pro- Hepatitis C viral dynamics, tease inhibitors (PIs), telaprevir (TVR) and boceprevir, in combination with effectiveness peg-IFN/RBV, the landscape of anti-HCV of direct antiviral agents targeting different clinical development, holding the promise that a universal cure can be achieved. Although results from clinical trials, often obtained in small populations of highly selected patients, should be taken with caution, short, tolerable, pan-genotype and IFN-free regimens appear to be attainable within the next couple of years.

has been an increasing appeal from the industry and academics to use viral kinetic mathematical modeling to anticipate, ral effectiveness of interferon, as well as to evaluate and rationalize the effectiveness of these new antiviral strategies [4]. This is half-life of 2.7 h [7]. Importantly, if HCV particularly true in the case of agents that target proteins with complex or ill-defined

Chronic infection with hepatitis C virus functions, such as the HCV nonstructural in Proceedings of the National Academy liver transplantation [2]. Until 2011, the cal modeling to decipher the origin of the first hours following initiation of daclatasvir (DCV), a first-in-class NS5A inhibitor, where one dose of DCV led to a 1000-fold decrease in viral levels within

# virion half-life & drug antiviral

One of the most important results of viral therapy has been rapidly changing. Dozens kinetic modeling was to introduce the idea that viral load level observed in a patient stages of the viral lifecycle are currently in reflects the balance between the antagonist processes of production and clearance of the virus. By blocking viral production from infected cells, the initiation of antiviral treatment disrupts this equilibrium and the clearance of the virus is no longer efficiently compensated. Thus, the rate of viral decline observed early after treatment initiation can be used to calculate the virus half-life. This In this highly dynamical context, there basic idea was used by Neumann et al. to fit the viral decline observed during interferon therapy and to estimate the antiviobtain the original estimate of the HCV is rapidly eliminated from the circulation, it implies that large quantities of the virus

# Financial & competing interests disclosure

Portions of this work were performed under the auspices of the US Department of Energy (under contract DE-AC52-06NA25396) and supported by NIH grants (R56/R01-AI078881, P20-GM103452, OD011095, AI028433 and HL109334). AS Perelson has been a consultant for Bristol-Myers Squibb. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

# Related research 1

People also read

Recommended articles

Cited by 11

Information for

R&D professionals

Editors

**Authors** 

Librarians

Societies

Opportunities

Reprints and e-prints

Advertising solutions

Accelerated publication

Corporate access solutions

Open access

Overview

Open journals

**Open Select** 

**Dove Medical Press** 

F1000Research

Help and information

Help and contact

Newsroom

All journals

Books

### Keep up to date

Register to receive personalised research and resources by email



Sign me up













Copyright © 2025 Informa UK Limited Privacy policy Cookies Terms & conditions

Taylor and Francis Group

Accessibility