First Real Life Evidence of New Direct-acting Antivirals (DAA) in Co-infected HIV HCV Patients: Better than Ever

To the Editor—Direct-acting antiviral (DAA)-based anti-hepatitis C virus (HCV) therapies currently provide amazing opportunities to cure almost all HCV-positive patients. However, these results were obtained in clinical trials. We read the points raised by Shafran with interest [1], proposing that all future phase 3 anti-HCV clinical trial programmes should include human immunodeficiency virus (HIV)-coinfected participants with HCV-monoinfected patients, because HIV coinfection does not affect sustained
virological response (SVR) rates or toxicity with treatments containing DAA. At that time, few data were available on HIV and HCV coinfection, and none of them, to our knowledge, were obtained in real life. Here, we retrospectively analyze the efficacy and safety of DAA-based anti-HCV therapies administered over a 1-year period in real life to HIV-coinfected patients from a cohort of 1700 HIV-positive patients, including 600 HCV-coinfected patients monitored in our infectious diseases unit in the public hospitals of Marseille in southeastern France. The primary and secondary endpoints were virological response at the end of treatment and at 12 weeks of treatment. We treated 55 HIV-HCV coinfected patients. The mean age was 51 years, 75% were male, and all were white. At the baseline of DAA-based HCV treatment, all the patients received combined antiretroviral therapy (cART) and the median length of HIV treatment was 18.5 years. Plasma HIV-1 RNA level was suppressed under stable antiretroviral therapy including integrase inhibitors (69%), nonnucleoside reverse transcriptase inhibitors (29%), protease inhibitors (33%), and CCR5 inhibitors (11%). The mean CD4 count was 600 cells/mm³ (range, 70–1682). In terms of hepatitis C, HCV RNA level was >800 000 copies/mL in 32% of the patients, and the median duration of HCV infection was 21 years (range, 11–34). Thirty-one percent of the patients were HCV-treatment-naïve, and 48% had previously been treated twice or more and were relapers (50%) or nonresponders (50%). Most of them had advanced liver disease (75%). HCV genotype was 1a, 1b, 3, and 4 in 41%, 13%, 30%, and 16% of patients, respectively. Guidance on recommended DAA-based protocols changed during the study period (April 2014–April 2015). All patients received sofosbuvir (SOF), a nucleotide polymerase inhibitor, as a single fixed dose. SOF was combined with a NS5A inhibitor, daclastavir (DCV) (35/55), for 24 weeks (30/35) or ledipasvir (LDV) (14/55), in a majority of cases (12/14) for 12 weeks. Four patients received SOF plus ribavirine (RBV) for 24 weeks and 2 SOF plus peglated-interferon (PegIFN) + RBV for 12 weeks. Virological response at the end of treatment (EOT) was observed in all patients treated for 12 or 24 weeks, and 94.5% achieved SVR at week 12 (Figure 1). Only 3 patients experienced a relapse between weeks 4 and 8 after the end of treatment; all with HCV-compensated cirrhosis, 1 with genotype 1a and 2 with genotype 4. We searched for an explanation for these failures, using therapeutic drug monitoring and drug resistance genotyping, as routinely performed in our institution. Pharmacokinetic data were only available for 1 patient and revealed a suboptimal sofosbuvir Cmax at week 4 (22 ng/mL; expected range: 603 ± 47 ng/mL). Amino acids associated with reduced susceptibility to HCV NS5A
inhibitors were observed at positions 28 (28L) and 30 (30R) in sequences obtained for the 2 patients infected with HCV genotype 4 after treatment completion, and at position 58 (58L) for 1 of them. Good tolerance was observed with only Grade 1 adverse effects during the first month. The most common adverse events were insomnia (23%), asthenia (19%), and headache (16%). No HIV breakthrough was observed.

These results represent the first evidence, to our knowledge, of the high potency and tolerability of DAA-based therapy in the real life treatment of HIV-positive patients, including a large proportion at an advanced stage of liver fibrosis. The availability of new DAA gives hope that the majority of coinfected individuals can clear HCV. Currently, one major limitation of DAA-based treatment uptake is the cost of these medications. However, this may be bypassed as the result of the emergence of generic drugs [2]. Moreover, studies examining the benefit of all-oral therapy vs interferon-based therapy have reached the same conclusion, that all-oral therapy can be cost effective when compared to interferon-based treatment for HCV [3].

Note
Potential conflicts of interest. Funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Amélie Menard,1 Philippe Colson,2,3 Dhiver Catherine,1 Ravaux Isabelle,1 Tomei Christelle,1 Line Meddeb,1 Souad Ben Ali,2 Caroline Solas,5 and Andreas Stein1,2
1Pôle des Maladies Infectieuses et Trophiques Clinique et Biologique, Service de Maladies Infectieuses, Fondation Institut Hospitalo-Universitaire (IHU) Méditerranée Infection, 2Aix Marseille Université, URMITE, UMR126, CNRS 7279, IRD 198, INSERM 1025, 3Aix Marseille Université, UMR126, CNRS 7279, IRD 198, INSERM 1025, 4Pôle des Maladies Infectieuses et Trophiques Clinique et Biologique, Fédération de Bactériologie-Hygiène-Virologie, Fondation IHU Méditerranée Infection, 5Service d’hepato-gastro-entérologie, and Laboratoire de Pharmacocinétique et Toxicologie, Faculté de Pharmacie, Aix-Marseille University, INSERM UMR 911-CER, Centre Hospitalo-Universitaire Timone, AP-HM, 264, rue Saint-Pierre, 13385 Marseille cedex 05, France

References

Correspondence: A. Ménard, Infectious disease, Pôle des Maladies Infectieuses et Trophiques Clinique et Biologique, Service de Maladies Infectieuses, Fondation IHU Méditerranée Infection, Centre Hospitalo-Universitaire Conception, France (amelie.menard@ap-hm.fr).

Clinical Infectious Diseases® 2016;62(7):947–9
© The Author 2016. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail journals.permissions@oup.com. DOI: 10.1093/cid/civ1215