Expensiveness of hepatitis C virus polymerase inhibitor sofosbuvir: a warrant for therapeutic drug monitoring of compliance

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We read with interest the recent article by Ippolito *et al.* [1] on the need for a close virological monitoring of hepatitis C therapy with new directly acting agents (DAAs). Sofosbuvir, the first commercially available hepatitis C virus (HCV) RNA polymerase inhibitor, expands the therapeutic revolution initiated in 2011 with first-generation HCV protease inhibitors [2]. This drug still increases the rate of sustained virological response, regardless of the viral genotype, and with a reduced duration of therapy (3–6 months). In addition, it can be associated with other DAAs including daclatasvir and simeprevir, which avoids using the poorly tolerated pegylated interferon and ribavirin in some treatment combinations. Notwithstanding, sofosbuvir use has raised some non-medical concern due to its very high cost, which is ~66,000 Euros or 84,000 USD for a 12-week course of therapy [3]. In addition, in several indications based on current guidelines, the duration of sofosbuvir-based therapies is 24 weeks and not 12 weeks [4]. We do agree with Ippolito *et al.* that tight virological monitoring of these highly efficient but expensive HCV therapies is needed [1]. Nonetheless, there are other issues that deserve to be addressed, which are DAA compliance and exposure. Both can be assessed by therapeutic drug monitoring (TDM), which is currently not recommended [4].

Our attention was recently attracted by nonresponse to an 8-week course of therapy with sofosbuvir and ribavirin in a 73-year-old HIV-negative woman with HCV genotype 1b infection. Indeed, HCV RNA level was 5.6 $\log_{10}$ IU/mL at baseline, and 5.4 and 5.6 $\log_{10}$ IU/mL after 4 and 8 weeks of therapy, respectively. In this case, sofosbuvir TDM was not available in our institution, but ribavirin concentration trough was undetectable at week 8 of therapy, suggesting possible concurrent noncompliance to sofosbuvir, although sofosbuvir-plus-rivabirin therapy does not have 100% success.

TDM can allow detecting suboptimal drug exposure related to noncompliance, and its cost is negligible compared to the great expense of a full course of therapy with sofosbuvir [3]. HCV cure is now an achievable goal for a large majority of patients, but at a high financial cost, and this considerable therapeutic advance could be locked by cheap laboratory testing, at least in the case of non-response. TDM should also apply to other newly available DAAs whose price is in the same order of magnitude as that of sofosbuvir [3].

Transparency declaration

All authors declare no conflicts of interest.

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