Correspondence

Elimination Half-Life May Explain the Relative Efficacy of Boceprevir and Telaprevir in the Treatment of Hepatitis C Virus Genotype 1

TO THE EDITOR—In their very comprehensive meta-analysis, Kieran and colleagues compared the efficacy of telaprevir and boceprevir as third agents in the treatment of chronic hepatitis C virus (HCV); they found a significantly greater efficacy rate for telaprevir in the specific setting of prior relapers as compared to standard pegylated interferon/ribavirin therapy [1]. Such a meta-analysis is so far the only attempt to compare the 2 new antivirals, which have been released into the market without any preference for either agent in treatment recommendations [2]. A number of parameters have been proven to influence the outcome of anti-HCV treatment, such as genetic variation in IL-28B, the type of pegylated interferon administered, baseline HCV RNA, ribavirin pharmacokinetic exposure, and degree of liver fibrosis. As stated by the authors, dependency of the treatment outcome on the third drug may thus be rather variable, and even of borderline significance when multiple favorable factors coincide in the same patient. We believe that in addition to what was suggested by the authors in terms of possible reasons accounting for the higher efficacy of telaprevir in prior relapers, its longer elimination half-life (9–11 hours) as compared to boceprevir (3.4 hours) should also be taken into consideration [3, 4]. In anti–human immunodeficiency virus therapy, a longer half-life is the major determinant of what we call “forgiveness,” such as the property of maintaining effective concentrations in spite of a missed dose of the drug/ regimen [5]. In the field of antiretroviral therapy, where numerous head-to-head comparisons have been made, a tendency to a better virologic outcome is almost always recognizable in favor of the regimen containing the drug(s) with a longer half-life [6–8], with the notable exception of integrase inhibitors (for which being associated with a faster viral clearance may compensate for the drug shorter half-life) [9]. Although patients’ adherence has been far less characterized in the HCV setting than in antiretroviral therapy, we might reasonably envisage how patients under triple anti-HCV therapy taking oral drugs 3 times daily are at risk of suboptimal adherence. Supposing an equal degree of nonadherence, effective pharmacokinetic exposure of telaprevir persists longer than in the case of boceprevir intake when a dose is missed, thus allowing a greater chance of maintaining adequate antiviral concentration despite irregular drug intake. This pharmacokinetic property of telaprevir has been recently further testified by the successful validation of twice-daily intake of the drug at equal total daily dose [10]. Because controlled head-to-head comparative trials between telaprevir and boceprevir are unlikely to be performed (and might soon lose interest with the new anti-HCV drugs being developed) the meta-analytic comparison carried out by the authors might remain the sole study to rely upon. Based on these considerations, we believe that whenever a patient’s adherence is perceived to be particularly at risk, the choice of telaprevir might provide an advantage in terms of pharmacokinetic coverage.

Notes

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Andrea Calcagno, Lucio Boglione, Francesco Giuseppe Di Rosa, Giovanni Di Perri, and Stefano Bonora
Infectious Diseases Unit, Department of Medical Sciences, University of Torino, Italy

References


Correspondence: Andrea Calcagno, MD, DTM&H, Ospedale Amedeo di Savoia, Clinica Universitaria I piano, Corso Svizzera 164, Torino 10159, Italy (andrea.calcagno@unito.it).

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