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Unboosted fosamprenavir is associated with low drug exposure in HIV-infected patients with mild–moderate liver impairment resulting from HCV-related cirrhosis—authors' response

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Sir,

We have read with attention the interesting comment on our paper[1] written by Lanzafame *et al*.[2]

In their comment, Lanzafame *et al*.[2] report data on amprenavir therapeutic drug monitoring (TDM) in 18 patients taking fosamprenavir; 3 out of the 18 had cirrhosis (two decompensated and one in Child–Pugh class A). They did not find an association between low fosamprenavir C_{trough} and usage of unboosted fosamprenavir in cirrhotic patients. On the contrary, they found a strict relationship between low amprenavir C_{trough} and lack of adherence. Hence, they have suggested that patients with cirrhosis included in our study were 'selective drug takers' with undetectable HIV-RNA, hypothesizing that the low levels, selectively found in cirrhotic patients in our study, were related to poor adherence. We thank Lanzafame *et al*.[2] for their useful observation; we are aware of the fact that the lack of a systematic assessment of the adherence to antiviral treatment is a limitation of our study. Even if we cannot exclude that a low adherence selectively present in cirrhotic patients could be the cause of our finding, there are two pieces of evidence that do not support this hypothesis: (i) only in 1 out of 3 cirrhotic patients with a C_{trough} <400 ng/mL could a lack of adherence be supposed on the basis of the accounts of drug discharge from our pharmacy—the other cirrhotic patients self-reported a good adherence confirmed by accounts of drug discharge from our pharmacy; and (ii) it has been demonstrated that the maintenance of virological response in patients with poor adherence treated with a non-boosted protease inhibitor is very uncommon.[3,4]

However, we think that the experience of Lanzafame *et al*.,[2] as well as ours, has added additional data to our knowledge on this issue; nevertheless larger studies on TDM are needed in order to draw a definitive conclusion about the optimal schedule of fosamprenavir in cirrhotic patients.

Moreover, given that: (i) an association between higher levels of fosamprenavir and hepatotoxicity has never been demonstrated; (ii) our data and data from another study[5] do not support this association; (iii) the direct hepatotoxicity of the drug has not been demonstrated while other concentration-independent mechanisms, such as idiosyncratic reactions, liver steatosis or immune reconstitution,[6] may be involved in liver damage in co-infected subjects treated with highly active antiretroviral therapy; and (iv) suboptimal drug exposure could cause virological failure, especially in heavily pre-treated patients, we think that it could be reasonable to follow the recommendation to boost fosamprenavir in cirrhotic patients reported in the recently modified summary of product characteristics for fosamprenavir. This recommendation probably ensures an adequate drug exposure and does not seem to be associated with additional liver toxicity.

However, our experience and that of Lanzafame *et al*.[2] strongly supports strict clinical and laboratory monitoring of antiretroviral therapy efficacy and toxicity in patients with cirrhosis.

Transparency declarations

None to declare.

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