Reviewer’s report

Title: Warfarin and boceprevir interaction causing subtherapeutic INR: a case report

Version: 1  Date: 30 August 2014

Reviewer: Sam Schulman

Which of the following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

1. The authors report a case with suspected interaction between the protease inhibitor boceprevir and the oral anticoagulant warfarin, resulting in increased metabolism of warfarin and hypoprothrombinemia. The putative mechanism is induction of CYP1A2 and CYP2C9, although in vitro studies did not provide evidence for that. The authors should in the discussion use the Naranjo probability scale to support the probability of the interaction (Clin Pharmacol Ther 1981;30:239-45).

2. It is stated in the discussion that interferon and warfarin have no known significant interactions with warfarin, referring to the warfarin package insert, which surely is incomplete. A literature search should have been performed. It
would show that ribavirin has been reported to have a similar inhibiting effect on warfarin (Ann Pharmacother 2002;36:72-4). The mechanism here seems to be via induction of factor VII mRNA (J Thromb Haemost 2006;4:469-70). This needs to be discussed and is it not possible that the mechanism for the boceprevir interaction could be of a similar nature in view of the conflicting information regarding cytochrome P450?

3. The discussion regarding HIV protease inhibitors is superfluous and I suggest deleting “In a pharmacokinetic open-label randomized study …for darunavir/r.”

4. The data on INRs and warfarin doses in relation the events would have been more reader friendly in a graph rather than the table.

Minor comments
1. Case report, line 5: pulmonary embolism, for which …
2. Discussion, line 6 from the end: … his 9/25/12 visit, at which …
3. Discussion, line 3 from the end: … visits, at which times he stated that he did not …

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Declaration of competing interests:**

No competing interests