Reviewer's report

Title: Hepatitis B virus variants in an HIV-HBV co-infected patient at different periods of antiretroviral treatment with and without lamivudine.

Version: 4 Date: 16 July 2004

Reviewer: Flor Helene H Pujol

Reviewer's report:

General

This paper describes the follow up of a haemodialysis patient, coinfected with HBV and HIV and the genetic characterization of the HBV isolates circulating during antiretroviral treatment, with or without lamivudine and during withdrawal of treatment. A triple mutation in the HBV polymerase appeared after reintroduction of lamivudine, which confers resistance to lamivudine and may restore replication ability. The substitution observed in the surface gene might be reducing the antigenicity of this antigen.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. A high viral load was observed in the 3 samples tested, measured by an in-house PCR titration procedure. This is quite unusual in haemodialysis patients. Was this in-house method validated against international standards? Were these determinations performed in duplicated or triplicate? These answers would help to clarify the significance of an increase in one log of viral load in 2001.
2. HBV serological markers in the time points when the molecular analyses were performed would be useful for the interpretation of the results. In particular, the HBe/anti-HBe status and the correlation of HBsAg positivity with the mutation pattern would be useful to explain the high viral load observed and an eventual reduction in antigenicity.
3. The appearance of quasispecies observed during the absence of lamivudine treatment and the reemergence of the wild type strain, which leads to the presence of stop codons in the S gene and then to non replication competent strains, is not discussed, particularly correlated with the high viral load observed.
4. How were detected the two variants L/V and D/E by direct sequencing?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors should reduce the number of references
2. YSDD mutation has also been described for the HBV polymerase during lamivudine treatment.
3. The legend of Figure 2 should mention the bootstrap value.
4. Abstract: line 5 of conclusions: “..., which was independent” instead of “..., which was high independent”
5. Materials and Methods: DNA extraction…: “August 2000”.

Discretionary Revisions (which the author can choose to ignore)

1. The designation of subgenomic groups inside HBV genotype A is confusing. The authors might
adopt the new nomenclature (Aa and Ae) which has recently been proposed.

**What next?:** Accept after discretionary revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

None