Reviewer’s report

Title: Keratin 8 variants and prognosis of patients with alcoholic cirrhosis

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Reviewer: TREPO Eric

Reviewer’s report:

In this manuscript the authors study the association between various K8 variants and the presence of HCC as well as mortality. They report that none of these variants have significant impact regarding these outcomes. The topic is interesting and relevant, considering the role of keratins in various liver diseases. The manuscript is also well written. My comments are as follows:

I) Major comment:

Although this work is interesting and the analyses clearly performed, the authors do not distinctly state its limits which should be stated in the Discussion section. Thus, in genetic association studies a replication cohort is strongly recommended to exclude false negative/positive results. Moreover, since the results reported are negative and the frequency of the mutated variants low, the authors should calculate the power of the analyses with respect to the mains outcomes (HCC and mortality).

Furthermore, a SUGESTION to overcome this limitation could be to genotype the cohort for a “positive control” that already showed a reproducible association with HCC in various cohorts (e.g. PNPLA3 rs738409 C>G).

II) Minor comments:

a) Please correct the sentence which claims that “14 patients harbored amino-acid-altering K8 variants” when the sum of variants (in brackets) is 13.

b) The objectives of the study at the end of the introduction section are confusing. I suggest that the authors clearly outline the primary (presence of HCC) and secondary (mortality) aims.

c) In Table 2, please replace the word mRNA by DNA or cDNA.

d) I suggest the authors suppress from the Abstract, the sentence claiming that K8 R341H variant may predispose to non-HCC-related liver mortality. Indeed, this does not take into account multiple testing corrections and is invalidated by log-rank analysis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests