Reviewer's report

Title: Safety and efficacy of direct-acting antivirals for chronic hepatitis C in patients with chronic kidney disease

Version: 1 Date: 18 Jun 2019

Reviewer: M Jadoul

Reviewer's report:

Iliescu et al have studied, in a prospective observational study, the safety and efficacy of one direct-acting antiviral agent (DAA) regimen (PROD) for chronic hepatitis C in patients with chronic kidney disease.

Their results are largely confirmatory of those published in several smaller-sized studies but still may deserve publication, after appropriate major revision along the suggestions below.

General comments

1. The most important concern is related to the selection of the study participants. We are told that this is a prospective observational study but the reader should know whether these were all consecutive patients with CKD and chronic hepatitis C seen at the outpatient liver clinic at this hospital in Bucharest, etc… Were some patients that were referred not treated? This information is key to understand whether there is a referral or treatment bias and to what extent the study results may be generalized to CKD patients in general. For instance, can the authors clarify whether all HD patients with chronic hepatitis C HD some units were referred or is there some selection bias too (frequent in such observational studies)?

2. The manuscript is much too long and should be markedly shortened. In addition, the added value of the detailed description of the results in the various subpopulations is unclear. Can some grouping spare some space?

3. The authors mention the use of Fibromax as the test to assess the extent of liver fibrosis. Has Fibromax been validated in CKD and especially in end-stage kidney disease patients? Please provide a reference and clarify.

4. The abstract should stress that whereas some of the previous studies were RCT data, this is a real-world study with the advantages of that approach.

5. The paper should absolutely include key references that are missing, such as the main results with other DAA regimens in late CKD/dialysis: the C-surfer by Roth et al Lancet 2015 and Bruchfeld et al 2017 Lancet Gastro-enterology Hepatology, and the Expedition results by Gane et al New England Journal of Medicine 2017 + KDIGO executive

6. The authors mention in the introduction that approximately 180 million people are currently affected by HCV globally. This reference is outdated and should be adapted according to the most recent figures: Polaris Observatory HCV Collaborators: Global prevalence and genotype distribution of hepatitis C virus infection in 201: a modelling study. Lancet Gastroenterol Hepatol 2017.

7. The authors should stress in the conclusion of the abstract that the SVR rate is 100%. The reader might thus wonder why they conclude that interferon-free regimens in such patients need further investigation!

8. The authors analyze the results in the HCV-infected population presenting cryoglobulinemia but it isn't clear from the lengthy paper how cryoglobulinemia was defined. Based on the presence of cryoglobulin in blood or was it based on clinical diagnosis? Please clarify.

9. The authors mention on the second page of the results that the use of DAAs was associated with a reduction of proteinuria. It should be clarified whether other drugs were given concomitantly or started such as ACE-inhibitors or angiotensin receptor blockers.

Specific comments

1. Results: regarding HCV infection population undergoing hemodialysis. The authors mention that 27 were males. Useless to mention that 21 were women if total = 48.

2. In the section of HCV infection with CKD due to diabetic or hypertensive nephropathy "a jeun" should be "fasting" in English.

3. Similarly, in the last section of the methods, "anamnesis" should be "history".

4. In the section about kidney transplant recipients, tacrolimus "doses" should be "dosages", and 2 "mg/week" instead of 2 "ng/week".

5. ref 41 should be updated.

6. Table 1: all figures should be rounded, limiting the number of decimals.

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