Reviewer 1

The authors retrospectively assessed the effectiveness and safety of DAA in HCV-infected patients with or without concurrent mental illness. They found that the SVR12 rates by PP analysis were comparable in patients with or without mental illness, while the proportion of patients who were lost-to follow-up was higher in patients with mental illness, compared to those without. Furthermore, the safety profile was comparable between groups.

1.Please indicate clearly all the statistical number throughout the manuscript for those with p values > 0.05. Just state > 0.05 was not acceptable and non-professional.

Thank you for this comment. According to the request, we have reported the exact p-values also for p > 0.05. Exact p-values are reported throughout the manuscript, except when p was lower than 0.0001 as, according to various guidelines, it is accepted to report as p<0.0001 (in fact, guidelines of journals such as NEJM or The Lancet accept reporting already as <0.001).2.

2.Figure 1B was not clearly demonstrated. What was the comparators in Figure 1B subgroups, e.g. anxiety vs. non-anxiety (in mental illness group) or anxiety vs, non-anxiety (whole group). Please show all the numbers of patients with SVR/index group in the columns in Figures 1A and 1B.

Thank you for this comment. Indeed, Figure 1B was not clearly described. In Figure 1B, there is a comparison of SVR in a given mental disease to SVR in the entire control group (group B). This has now been clarified in the figure legend.

3. The authors should show in the details of the univariate analysis, with an assumption of cut-off p value (such as < 0.10) set by the authors to enter multivariate analysis. To sum up, re-do the Table 4 to show the details of uni- and multi-variate analyses. Just show the multivariate analysis subjectively was not acceptable. Furthermore, re-organize the statistical wordings in the text accordingly.

The variables which are known to be the potential independent factors predicting the failure to achieve SVR were the subject of numerous previous studies, including our

previous analysis conducted on the data collected in the Epi-Ter database. According to statistical guidelines, one of the approaches to selecting variables for multiple analyses is using variables already well proven in the literature to be related to the outcome. Therefore, we have selected these variables, which were previously reported to affect response to antiviral treatment in HCV, as explained in the methodology description supported by the references, plus this mental illness which was found to have lower SVR (i.e., bipolar disorder) as compared to the control group (group B).

4. The authors should show the potential drug-drug interaction profiles before the initiation of DAA therapy, e.g. how many patients adjusted or switched mental illness co-medications before DAAs. How many patients were treated with DAAs who also were on co-medications which were considered contraindicated for use? Please add a supplementary summary Table to show the detailed information of patients who had switch or termination of co-medication (particularly mental ill-related drugs) before being treated with DAAs, in group A and B patients.

An analysis of potential drug-drug interactions was carried out before the start of DAA therapy using as an online tool on the University of Liverpool website. The data in the database take into account information from baseline to 12 weeks after the end of therapy, and there are no data on the number of patients who had their psychiatric treatment modified, as well as the nature of these modifications. We have added this information to the Limitations.

The only psychiatric drug whose use was associated with potential interactions with DAA therapy used in the studied population was carbamazepine, administered in 3 patients from group A and 12 from group B due to epilepsy. This drug was not changed because it was the only one giving clinical stability from a psychiatric (in case of group A) or neurological (in case of group B) point of view. Among psychiatric patients, all responded to DAA therapy; no safety issues were reported during treatment. This information was in the discussion:

"Although this drug is not recommended in combination with DAAs because it can reduce their levels below therapeutic levels, all patients completed the treatment as planned without adverse events and achieved SVR."

Among 12 patients treated with carbamazepine in group B 11 responded to therapy and one was lost to follow-up without SVR assessment; no safety issues were also noticed in this group.

Now we have added the following sentence to the Results "Safety"

"All patients with mental diseases using carbamazepine completed the treatment as planned without adverse events and achieved SVR."

5. Figure 5: The information was not clear. What did it mean Tx discontinuation? Also what did it mean Tx modification? Did the authors mean discontinuation or dose modification of DAA or co-medications or both? What was the proportion of patients who resumed Tx after discontinuation? Conventionally, the dose of DAA should not be modified. If Tx modification indicated DAA dose modification, it seemed violation to label recommendation.

Modification of therapy involved only a change in the dose of ribavirin according to the label, while discontinuation of therapy was permanent, and no patient subsequently returned to treatment. The applicable information was added in Results.

6. The abstract should clearly defined ITT and PP analyses in Methods, and should show the SVR12 rates with ITT and PP forms. Please show the switch or termination of co-medications in each group in the abstract.

Thank you for this comment. Now we have added the suggested sentence in the Abstract and Materials and Methods. According to the information provided earlier, we do not have data regarding the substitution or termination of psychiatric medications.

Reviewer 2

This is nice retrospective study of the efficacy and tolerability of DAA anti-HCV treatment in patients with mental disorders at country level. Due to scarce data on the efficacy and tolerability of DAA treatment of HCV in patients with mental health disorders and just few full text publications with large cohorts of patients enrolled, this

study should be welcomed. Despite of the fact that the appropriate methods used and a quality of the manuscript is good, some points need to be clarified.

1. Authors found that the 16.7% of patients from group A had previously been treated with interferon, however, it is not clear what proportion of this patients did not respond due to premature discontinuation of the treatment due to AE, did all these patients achieve response with DAAs, and what was the rate of AE in them in compare to control?

Thank you for drawing attention to this important aspect. We have added these sentences to the Results „ characteristics of the studied group"

"34 patients discontinued interferon-based therapy due to adverse events. During current therapy, 12/34 (35%) had mild adverse events, the most common of which was headache (n=3), and one patient in this group experienced an increase of insomnia. All patients in this group completed therapy as planned, 31 achieved SVR, and 1 patient was lost to follow-up."

2. Authors noted higher lost of follow-up rate in group A in comparison to the control, but they did not provide possible explanation or additional analysis, then discussing this fact as a part of the adherence problem, they mentioned 2 publications (Ref.39 and Ref.44), which both are not relevant for this discussion as the first one was performed in psychiatric nursing homes and the second one included patients participated in clinical trials with GLE/PIB, other words the adherence in these patients was very well controlled. This study represented data, obtained in a real-world settings, in which adherence was not carefully controlled and difference in the lost of follow-up numbers may be clinically important and indicate to the lower adherence to the treatment.

The sentence "In patients with available SVR, we did not observe significant differences in the effectiveness of DAA therapy depending on the diagnosis of mental illness, which is consistent with reports from other RWE cohorts." with references 39 and 44 cited concerns the fact that after excluding patients lost to follow-up from the analysis, efficacy in the psychiatric patient population is comparable to that obtained in patients without psychiatric conditions. We have now added a citation regarding the issue of non-adherence [Wedemeyer et al.].

3.At the page 13 of the manuscript authors said that "To the best of our knowledge, this is the first study to address the problem of treating chronic hepatitis C in patients with mental disorders, highlighting the differences in specific psychiatric illnesses." Unfortunately, it is not true as in 2022 excellent analysis of the efficacy of HCV treatment in mental health disorders patients from 7 countries was published in which such differences were described. (Wedemeyer, H.; et al. Global Real-World Evidence of Sofosbuvir/Velpatasvir as a Highly Effective Treatment and Elimination Tool in People with Hepatitis C Infection Experiencing Mental Health Disorders. Viruses 2022, 14, 2493. https://doi.org/10.3390/v14112493). Authors should correct discussion section of the manuscript accordingly and discuss their data against the results from this study.

Thank you very much for this valid comment. The suggested paper was discussed in the manuscript and the above-mentioned sentence was modified accordingly. References in the manuscript have been renumbered after this item was added.