Porto, 4th August, 2020

Dear Editor,

We kindly thank you for the opportunity to submit a new revised version of the manuscript Manuscript NO 57096: " The HIPPOCRATES Project: a proof of concept of a collaborative program for HCV microelimination in a prison setting".
We found the comments very thoughtful and instructive and we have addressed all of the points raised.
We hope that you consider the current manuscript acceptable for publication.

On behalf of all the co-authors, we are looking forward to hearing from you.

Yours sincerely,

Rui Gaspar

Reviewer #1:

The authors have responded to all my comments and incorporated the responses into the manuscript. Two final detailed remarks: -page 9 line 5 the sentence "There were two patients that refused treatment and eight patients started treatment in another institution after being moved". should be integrated into the results and not the methods -page 11 line 4 "and testing negative for HIV" should be deleted because in contradiction with the next sentence

We thank the Reviewer for the comments.
The changes have been made accordingly and added to the text.

Reviewer #2:

We thank the Reviewer for the comments.
We have already made the changes suggested (as forward).

Specific Comments to Authors: Strong points -The authors report an interesting experience of microelimination of HCV in prison with systematic screening as part of a national strategy and an investment by all professionals in prison, prison staff and health care providers but also including hospital hepatologists, and a risk reduction strategy with maintenance of care after release of prisoners. The paper is well written and easy to read To be discussed: However, this experience is not applicable in many prisons on European territory. Moreover, it is expensive and time-consuming. Thus, the authors should justify their spectacular results with more precise data concerning the training of prison staff which is essential, the role of nurses ... and the applicability of their model to other structures.

1) Systematic screening of all prisoners for hepatitis viruses and HIV at the time of their incarceration is not usual and appears to be a key strategy even if little practiced. The results of other studies that never reached this level of care could be cited for comparison. Ex the retrospective study of Quebec with on-demand screening leading to screening carried out in 7% of cases with 2 patients in total treated (for an initial population of 4,930 inmates)The hepatitis C virus cascade of care in a Quebec provincial prison: a retrospective cohort study. Kronfli N, Dussault C, Klein MB, Lebouché B, Sebastiani G, Cox J. CMAJ Open. 2019 Dec 3;7(4):E674-E679. doi: 10.9778/cmajo.20190068. Print 2019 Oct-Dec. PMID: 31796509 The results of other organized strategies could be cited as in the United Kingdom where the results are good but not excellent Detection, stratification, and treatment of hepatitis C positive prisoners in the United Kingdom prison estate: Development of a pathway of care to facilitate the elimination of hepatitis C in a London prison. Connoley D, Francis-Graham S, Storer M, Ekeke N, Smith C, Macdonald D, Rosenberg W. J Viral Hepat. 2020 May 25. doi: 10.1111/jvh.13336. Online ahead of print. PMID: 32449969 Also to mention the Georgian experience An evaluation of the hepatitis C testing, care and treatment program in the country of Georgia's corrections system, December 2013 - April 2015.

Harris AM, Chokoshvili O, Biddle J, Turashvili K, Japaridze M, Burjanadze I, Tsertsvadze T, Sharvadze L, Karchava M, Talakvadze A, Chakhnashvili K, Demurishvili T, Sabelashvili P, Foster M, Hagan L, Butsashvili M, Morgan J, Averhoff F. BMC Public Health. 2019 May 10;19(Suppl 3):466. doi: 10.1186/s12889-019-6783-4. PMID: 32326938 - There is no discussion of the rate of refusal of screening, as screening seems legislated ? If not, how many patients refused to enter the program?

We thank the Reviewer for the comments.
In the prison included in our study, all the prisoners are screened at admission.
Therefore, there is no chance of refusal to be tested to HCV infection.
The changes have been made accordingly and added to the text.
The references were also added to the text.

2) This approach assumes the availability of several specialist doctors in situ in the strategy of going towards, which is rarely obtained in practice

We thank the Reviewer for the comments.
Our team included only 3 hepatologists who were responsible for all the moves to the prison setting to perform all the fibroscans and the outpatient clinics. All the procedures were performed by the same 3 Hepatologists and any problems concerning these patients were seen by the prison's doctor and reported to the hospital team.
The changes have been made accordingly and added to the text.

3) The strategy presupposes a daily distribution of drugs by prison staff who thus have a crucial role: how are they trained? Do they also distribute TSOs? Do prison guards have a key role in education for prevention of reinfection risks both in prison and after discharge?

We thank the Reviewer for the comments.
The prison staff was responsible to distribute the DAAs to our patients and were instructed by the medical team before the beginning of the program. They were already previously in charge of distributing the opioid substitution therapy. Although being instructed about the prevention measures, medical education was mainly performed by our team in every opportunity.
The changes have been made accordingly and added to the text.

4) -It presupposes the availability of a FibroScan in each prison and a national investment in the process

We thank the Reviewer for the comments.
The degree of fibrosis was evaluated using the portable Fibroscan 430 mini model from Echosens® (owned by our department),
The changes have been made accordingly and added to the text.

5) There is no clear description of a strategy for renewing screening during the stays of patients with longer sentences, even if a low rate of reinfection is suggested. What is the

long-term screening strategy? It would thus be useful to specify the average length of stay in the prison environment considered.

We thank the Reviewer for the comments.
Our strategy is to re-screen every year. The average length of stay in prison was 2 years.
The changes have been made accordingly and added to the text.

6) In the same vein, there is little prescription of 8 weeks Maviret treatment which could favor the reduction in the length of the treatment and therefore microelimination. Why ? Determining the genotype in all patients is expensive. Was it useful? What justification for the genotype in the management of a simplified route? In a correctional system what about temporality? Other usable techniques TRODs GeneXpert in the perspectives could be evoked ?

We thank the Reviewer for the comments.
In the beginning of our program Maviret and also Epclusa were not available - that was the reason for less prescription of these drugs - therefore, determining genotype was important in order to select the treatment. Nowadays, it could be a step forward treatment simplification.
Regarding TRODs GeneXpert would extremely useful but unfortunately we do not have acess.
The changes have been made accordingly and added to te text.

7) The role of medical specialists is highlighted and little is said about nurses, who nevertheless have a key role in therapeutic compliance. It seems that the prison staff is the almost exclusive interlocutor of prisoners apart from medical specialists

We thank the Reviewer for the comments.
In Portugal, unfortunately, most of the tasks are attributable to medical team. Although, one of the authors (Jorge Tavares) is a nurse and developed a major role as he was a very important link with the patients, not only for therapeutic compliance but also highlighting the measures to prevent reinfection.
The changes have been made accordingly and added to the text.

8) After this prospective study, do the authors intend to carry out prevalence and comparative incidence studies over the before / after period? Although it seemed that the rate of de novo infection and reinfection was low even during detention in this study, this is not the experience of other prison systems where infection can be acquired up to 70% cases in prison even if drug injection is not permitted (The role of prison-based interventions for hepatitis C virus (HCV) micro-elimination among people who inject drugs in Montréal, Canada. Godin A, Kronfli N, Cox J, Alary M, Maheu-Giroux M. Int J Drug Policy. 2020 Apr 8:102738. doi: 10.1016/j.drugpo.2020.102738. Online ahead of print. PMID: 32278651

We thank the Reviewer for the comments.

We intend to continue the study and determine the rate of de novo infection and reinfection - we think that our strategy of education even before the beginning of the treatment could be an important tool to achieve a low rate of new infections. This study was also cited in our references.

Minor comments Laboratory data page 8: add HIV testing

We thank the Reviewer for the comments.
The changes have been made accordingly.

Reviewer #3:
For global eradication of HCV, DAA therapy for prisoner is very important. This manuscript deserves publication.