February 15, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Manuscript 5924 revised)

Title: Impact of immunosuppression minimization and withdrawal in long-term HCV liver transplant recipients

Author: Tommaso Maria Manzia, Roberta Angelico, Paolo Ciano, Jon Mugweru, Kofi Owusu, Daniele Sforza, Luca Toti and Giuseppe Tisone

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5924

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
(1)
(2)

3 References and typesetting were corrected

The English editing has been made by mother tongue authors: Jon Mugweru, Kofi Owusu, Wake forest Institute, Winston Salent, NC, USA

Authors referees response:

Referee 1

	The manuscript must be re-submitted with tables clearly reported and readable.

Author response: The table have been re-submitted readable in the format required.

Referee 2

Comments To Authors	The course of hepatitis C infection after liver transplantation (OLT) is influenced by the immunosupression (IS). IS withdrawal could benefit these patients by delaying the pregression of liver damage. The impact of IS withdrawal has only been evaluated by the Tor Vergata group in Rome. This interesting paper introduces three groups of patients after OLT: (CNI group; MMF group and TOL group). The numbers are small and it is a retrospective study. Authors do not describe the total number of patients transplanted in the center from 1993 to 2013 (total number, and HCV patients) to better understand how many were included in this study. All where cadaveric OLT? Living related? There could

be significant bias in the groups. The authors do not give detailed information on the history of the groups in the immediate post OLT period (how many had rejection after OLT, how many received boluses of steroids, or antibodies after OLT, CMV infection, etc). Table 1 is almost illegible but apparently it says that hey had no rejection episodes?…. What was the reason for beeing only with MMF (renal insufficiency only ?? How bad was it …..) Table 1 is almost illegible: Please redo…. the table…. is important to put donor age, amount of steatosis of donor livers, ischemia times, CMV infection post OLT?, etc as they are variables important for the evolution of hepatitis C after OLT. Other consideration: There is one patients in the MMF group with hep B and C cirrosis…..this patients should be removed from the grupo (confound)

Referee 2: The course of hepatitis C infection after liver transplantation (OLT) is influenced by the immunosupression (IS). IS withdrawal could benefit these patients by delaying the pregression of liver damage. The impact of IS withdrawal has only been evaluated by the Tor Vergata group in Rome. This interesting paper introduces three grups of patients after OLT: (CNI group; MMF group and TOL group). The numbers are small and it is a retrospective study. Authors do not describe the total number of patients transplanted in the center from 1993 to 2013 (total number, and HCV patients) to better understand how many were included in this study. All where cadaveric OLT? Living related? There could be significant bias in the groups.
Author response: that's interesting point. The data were added in the study population session.

Referee 2: The authors do not give detailed information on the history of the groups in the immediate post OLT period (how many had rejection after OLT, how many received boluses of steroids, or antibodies after OLT, CMV infection, etc). Table 1 is almost illegible but apparently it says that hey had no rejection episodes?….
Author response: All LT recipients included in the study received in the immediate post-operative period IS regimen based on CNI (Cyclosporine or Tacrolimus) ± Azathioprine ± steroids. Azathioprine and steroids were withdrawal within the first 3 months from LT. None received boluses of steroids and antibodies therapy during the entire follow-up period. No rejection were recorded. CMV infection was reported in 1 case in TOL group, 2 cases of CNI group and 1 case of MMF group. These data have been added both in Table 1 and in the text.

Referee 2: What was the reason for beeing only with MMF (renal insufficiency only ?? How bad was it …..)
Author response: we clarified in the text.

Referee 2: Table 1 is almost illegible: Please redo…. the table…. is important to put donor age, amount of steatosis of donor livers, ischemia times, CMV infection post OLT?, etc as they are variables important for the evolution of hepatitis C after OLT.
Author response: Table 1 was rewritten with all suggested data (i.e. donor age, amount of steatosis of donor livers, ischemia times, CMV infection post OLT).

Referee 2: Other consideration: There is one patients in the MMF group with hep B and C cirrosis…..this patients should be removed from the group (confound)
Author response: The HCV-HBV recipient undergone LT for cirrhosis HCV-related; in the past medical history an HBV infection was reported but at the time transplant and during the entire follow-up period he was HBV-DNA PCR negative, HBsAg negative, anti-HBs antibodies positive. No HBV therapy either before and after LT was given. In the study this patients was considered as only an HCV.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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