

Format for ANSWERING REVIEWERS

August 25, 2012



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: TUMORES OH WJHEPATOLOGY VERSIÓN DEFINITIVA.doc).

Title: "Incidence, risk factors and outcome of *de novo* tumors in liver transplant recipients focusing on alcoholic cirrhosis"

Author: Carlos Jiménez-Romero; Iago Justo-Alonso; Félix Cambra-Molero; Alejandro Manrique-Municio; Jorge Calvo-Pulido; Alvaro García-Sesma; Manuel Abradelo-Usera; Oscar Caso-Maestro; Enrique Moreno-González:

ESPS Manuscript NO: 12684

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

REVISOR 504591

- 1) First, I have corrected the grammatical errors
- 2) Of course, the majority of data of the series are related to overall incidence of *de novo* tumors, because there are few series comparing AC and non-AC OLT patients. I have reconsidered the title and I have changed it according your advice (... "focusing in alcoholic cirrhosis").
- 3) I have also performed 3 Tables: 1. Considering the overall incidence and other variables of most important *de novo* tumor series. Table 2. Considering comparative series (AC patients vs. non-AC patients who underwent OLT). Table 3. Risk factors for development *de novo* tumors in patients who underwent OLT for AC.

REVISOR 5191

- 1) I have corrected the grammatical errors
- 2) I have also inserted a "Method" section
- 3) I have reviewed the immunosuppression section as you advised me

REVISOR 2530754

- Regarding the incidence of *de novo* tumors, almost all series refer as the term "incidence". In addition, the papers usually report the incidence among the transplant population. Of course, is also important to compare with non-transplant population and to calculate the SIR. I have followed your recommendation and I have included in Table 1 the SIR that show some series.

- I have also performed a Table 2, with series that compare the incidence of *de novo* tumors in AC-patients vs non-AC patients who underwent OLT.

In relation with immunosuppression, I have emphasize, as summary, that "there are no randomized control studies....".

-We think that AC patients, usually smokers, should be subjected to specific pre-OLT protocol, as we have added in premalignant condition section.

-The grammatical errors have been corrected.

There are no published controlled trials demonstrating the effect of m-TORi in preventing the novo tumors, but according to our experience is possible to perform a combination of m-TORi with low doses of CNI and even their substitution especially after one year elapsed the OLT. In this situation, in our experience the acute rejection is rare.

REVISOR 54275

The data about the risks of de novo tumors in smokers non-AC patients are very interesting, but to our knowledge there are not studies reflecting this question. Perhaps this can be a future line of investigation.

I have carried out a Table 3, showing the risk factors related to most frequent tumors in patients who underwent OLT for AC.

With respect to title I have changed it for a more general adding "focusing on alcoholic cirrhosis", as was suggested by revisor 504591.

3 References and typesetting were corrected

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

Sincerely yours,

Carlos Jiménez Romero, MD, PhD