

February 27, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format

Title: Alpha-1 Antitrypsin Deficiency and the Risk of Hepatocellular Carcinoma in End-Stage Liver Disease

Authors: Clara Antoury, MD; Rocio Lopez, MPH, MS; NizarZein, MD; James K. Stoller, MD, MS; NaimAlkhouri, MD

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 16069

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 reviewers:

Reviewer 1:

- a. The diagnosis of HCC was based on imaging (US followed by CT scan for confirmation), biopsy, or examination of the explanted liver.
- b. Concomitant etiologies in patients with A1ATD/HCC were not excluded
- c. The average age at time of diagnosis of A1ATD cirrhosis was similar between patients with HCC and patients without HCC (53 +/- 11.46 and 55 +/- 10.22 respectively)
- d. The average age at time of diagnosis of HCC in patients with A1ATD was 53 +/- 11.46 compared to 58 +/- 7.93 in patients without A1ATD.
- e. The average AFP value at time of diagnosis of HCC in patients with A1ATD was 27.6.
- f. Of the four patients with A1ATD/HCC, two had a single HCC focal lesion with BCLC stage A3, one subject had bifocal disease and one subject had multi-nodular HCC (BCLC stage B).
- g. Given the small size of patients with A1ATD/HCC, no meaningful comparison of AFP/BCLC stadium can be done between these patients and the rest of the HCC/non A1ATD group.

Reviewer 3:

- a. We included in the revised manuscript the number of deaths in each of the subgroup (30.15 % of patients with HCC and 24.6% in the overall cohort)
  - b. 3 out of 4 patients with A1ATD/HCC have mild to moderate airflow obstruction according to their PFTs. The 4<sup>th</sup> patient did not have PFTs done. Not enough patients with A1ATD had PFTs in our system in order to make any meaningful statistical estimate of their overall lung function.
3. References and typesetting were corrected

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

Sincerely Yours,

A handwritten signature in cursive script that reads "Clara Antoury". The signature is written in black ink and has a long, sweeping underline that extends to the right.

Clara Antoury, MD

Department of Medicine,

Cleveland Clinic Foundation,

Email: [antourc@ccf.org](mailto:antourc@ccf.org)

Ph: 440-364 3714