Dropout Rate From the Liver Transplant Waiting List Because of Hepatocellular Carcinoma Progression in Hepatitis C Virus–Infected Patients Treated With Direct-Acting Antivirals

TO THE EDITOR:

We have read with interest the article recently published by Zanetto et al. in *Liver Transplantation* regarding the effect on radiologic progression of hepatocellular carcinoma (HCC) after the treatment with direct-acting antivirals (DAAs) for hepatitis C virus (HCV) in patients listed for liver transplantation.[1] Although a previous call for attention to a higher, early, and aggressive HCC recurrence following the treatment with DAAs has been observed,[2] Zanetto et al. reported similar outcomes while on the waiting list between patients treated with DAAs and controls in terms of dropout (8.7% versus 4.3%) and HCC radiological progression (35% versus 17%, respectively). Although both studies proposed a novel discussion whether DAAs promote an immunological disruption and tumor growth, its causal inference is still far away to reach robustness.

The radiological HCC progression during the waiting list in previous studies ranges 4%-6% and close to 20% at 6 and 12 months of listing, respectively.[3,4] The study by Zanetto et al. is limited by the fact that the nonrandom intervention already biases the results, even after adjusting for confounding variables such as serum alpha-fetoprotein values.[5] Likewise, neither the intervention assignment nor the radiological evaluation were blinded from baseline variables. Finally, a sample size estimation is lacking. Observing "nonsignificant" differences in this study might be far away from the real effect as a consequence of this lack of power. In fact, the study published by Roayaie et al. might have gone through the reported confidence interval limits (95% CI of 17% to 40%).[6] Ultimately, although the clinical question is novel, this research does not "illuminate" but rather "deepens the confusion" on this topic and further demands a randomized intervention study.

Federico Piñero, M.D., M.S.C.E.
Marcelo Silva, M.D.
Hepatology and Liver Transplant Unit
School of Medicine
Hospital Universitario Austral
Austral University
Buenos Aires, Argentina

Address reprint requests to Federico Piñero, M.D., M.S.C.E., Hepatology and Liver Transplant Unit, School of Medicine, Hospital Universitario Austral, Avenida Presidente Perón 1500, (B1629HJ) Pilar, Buenos Aires, Argentina. Telephone: + 54 0230 448 2000; FAX: + 54 0230 448 2236; E-mail: fpinerof@cas.austral.edu.ar

Received September 14, 2017; accepted October 1, 2017.

Federico Piñero and Marcelo Silva received a Clinical Research Grant from the National Institute of Cancer, Argentina.

Copyright © 2017 by the American Association for the Study of Liver Diseases.

View this article online at wileyonlinelibrary.com.

DOI 10.1002/lt.24962

Potential conflict of interest: Nothing to report.

REFERENCES

1) Zanetto A, Shalaby S, Vitale A, Mescoli C, Ferrarese A, Gambato M, et al. Dropout rate from the liver transplant waiting list because of hepatocellular carcinoma progression in hepatitis C virus–infected patients treated with direct-acting antivirals. Liver Transpl 2017;23:1103-1112.
2) Reig M, Mariño Z, Perelló C, Iñarrairaegui M, Ribeiro A, Lens S, et al. Unexpected high rate of early tumor recurrence in patients

with HCV-related HCC undergoing interferon-free therapy. J Hepatol 2016;65:719-726.
3) Cucchetti A, Cescon M, Bigonzi E, Piscaglia F, Golfieri R, Ercolani G, et al. Priority of candidates with hepatocellular carcinoma awaiting liver transplantation can be reduced after successful bridge therapy. Liver Transpl 2011;17:1344-1354.
4) Mehta N, Dodge JL, Goel A, Roberts JP, Hirose R, Yao FY. Identification of liver transplant candidates with hepatocellular carcinoma and a very low dropout risk: implications for the current organ allocation policy. Liver Transpl 2013;19:1343-1353.
5) Piñero F, Tisi Baña M, de Ataide EC, Hoyos Duque S, Marciano S, Varón A, et al.; for Latin American Liver Research, Education and Awareness Network (LALREAN). Liver transplantation for hepatocellular carcinoma: evaluation of the alpha-fetoprotein model in a multicenter cohort from Latin America. Liver Int 2016;36:1657-1667.
6) Roayaie S, Obeidat K, Sposito C, Mariani L, Bhoori S, Pellegrinelli A, et al. Resection of hepatocellular cancer ≤2 cm: Results from two Western centers. Hepatology 2013;57:1426-1435.