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REPLY

Reply to "Hepatocellular carcinoma in thalassemia and other hemoglobinopathies"

We thank Dr Mancuso and colleagues for their knowledgeable comments about our study.[1] In particular, one point raised is that the study does not address the question of the rates of patients with hepatocellular carcinoma (HCC) with and without concomitant cirrhosis.

This information is important because several studies have revealed a significant rate of HCC in patients with thalassemia and a noncirrhotic liver (mainly non–transfusion-dependent thalassemia).[2–4] However, as clearly stated in Table S1 of our article, among 80 patients who developed HCC, 63 of the 75 patients for whom the data were available (i.e., 84%) had a concomitant diagnosis of cirrhosis. We were not able to develop this issue in depth in our article for reasons of space, but we would like to take the opportunity offered by Mancuso and colleagues to clarify some further specifics.

Only for 30 of the patients with cirrhosis do we have the date of the diagnosis: 25 of 30 (83%) had a previous diagnosis, and 5 of 30 (17%) had a simultaneous diagnosis.

In patients with a previous diagnosis of cirrhosis, the median time between the diagnosis of cirrhosis and the diagnosis of HCC was 7.5 years (interquartile range, 5.2–13.1 years).

In addition, although we could not assess the role of cirrhosis as a risk factor for the development of HCC because we did not have these data for the control population that did not develop cancer, in our population, cirrhosis was present in the majority of the patients who developed HCC without differences according to the type of hemoglobinopathy.

Furthermore, cirrhosis was present in 83% of patients with transfusion-dependent thalassemia (45 of 54), in 92% of patients with non–transfusion-dependent thalassemia (12 of 13), and in 75% of patients with sickle cell disease (6 of 8; $p = .5$). Notably, nine of the patients who developed HCC in the absence of cirrhosis were still positive for anti-HCV.

Finally, Mancuso and colleagues claim that our study does not help in solving the debate about the treatment of HCC in the setting of thalassemia and other hemoglobinopathies because it does not contain specific data.[5]

Seven patients with hemoglobinopathy and HCC underwent liver transplantation in our population (the data are already present in Table S1 of our article). Apart from two who had a history of heart disease, the patients had no major comorbidities. They were diagnosed with HCC after 2001 (between 2001 and 2020), and the transplant was performed a median of 2.1 years after the HCC diagnosis. The number is too small to say whether, as is desirable, there has been an increase in the number of transplant-eligible patients over time. However, five of them were still alive at the last follow-up (median after liver transplantation, 6.4 years; range, 0.1–17.2 years). The remaining two patients died because of liver failure and sepsis 1.9 and 8 months after transplantation, respectively.

Although larger studies are needed to clarify the role of liver transplantation in patients with hemoglobinopathies, our work also contributes to reinforcing the concept, expressed by Mancuso and colleagues, that liver transplantation can be a therapeutic option to be considered in select cases, and it increases the published cases in this regard.[6,7]

We conclude by pointing out that even the proper management of liver cancer in a person with hemoglobinopathy and the eventual choice of transplantation cannot disregard a multidisciplinary evaluation in which an expert in hemoglobinopathies plays an important role in giving proper weight to the patient's clinical situation, life expectancy (as related to the underlying pathology), iron status, and past comorbidities.

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CONFLICTS OF INTEREST STATEMENT

Filomena Longo reports acting as an independent contractor for Bristol-Myers Squibb and Vertex Pharmaceuticals. The other authors declare no conflicts of interest.

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