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Response to fibrolamellar hepatocellular carcinoma versus conventional hepatocellular carcinoma: better 5-year survival or artefactual result of research methodology?

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We are grateful for the opportunity to reply to Dr Njei's letter, which raised the question of whether a better 5-year survival for patients with fibrolamellar hepatocellular carcinoma (fHCC) versus patients with hepatocellular carcinoma (HCC) (that we recently reported), was real or an artefact of research methodology.[1] In the letter, results of a meta-analysis were presented which were interpreted to show that the survival of fHCC and HCC do not differ in non-cirrhotic patients. We disagree with this interpretation of the results.

In the meta-analysis, 11 studies were included in the overall analysis, while three of the 11 were included in a subset analysis of non-cirrhotic patients. The overall analysis resulted in an OR=2.09, 95% CI1.38 to 3.16, while the subset analysis resulted in an OR=1.69, 95% CI 0.69 to 4.17. Based on these results, it was concluded that the survival of fHCC was significantly better in the main analysis, but not in the subset analysis of non-cirrhotic patients. It should be noted, however, that the two 95% CIs overlap to the extent that one CI entirely encompasses the other CI, thus the two ORs are not statistically significantly different. It should also be noted that the subset analysis was based on very small numbers (n=32 fHCC; n=64 HCC). It cannot be concluded from these results that there is any difference in results of the two analyses. It also cannot be concluded that 'survival in fHCC is similar to conventional HCC in non-cirrhotic liver patients, but better than conventional HCC in cirrhotic liver patients' as this comparison was not done. There was no analysis presented which included only persons with cirrhosis.

In our retrospective Surveillance, Epidemiology and End Results analysis, which lacks information on underlying liver diseases, including cirrhosis, we reported that patients with fHCC experienced significantly better 5-year relative survival (34%) than patients with HCC-not otherwise specified (16%).[2] In a recently published followup study, we show that fHCC patients experienced better survival despite larger tumour size distribution. The better survival, however, was found but only among cases younger than 40 years of age.[3]

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In summary, the fact that different registries may provide different data clearly underscores the need for better prospective and comprehensive tumour registries to study this rare disease.

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