New therapies increase survival rates in post-transplant liver cancer patients

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A recent study found that sirolimus-based immunosuppression following liver transplantation in patients with non-resectable hepatocellular carcinoma (liver cancer) significantly increases survival rates for this patient population. Results of this study appear in the April issue of *Hepatology*, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases (AASLD).

According to the NIH, hepatocellular carcinoma (HCC) is a common type of liver cancer, and one of the few cancers in the U.S. in which the number of new cases is expected to rise over the next two decades. Liver transplantation is an important treatment option for selected patients with non-resectable HCC, but the ideal immunosuppression protocol is still a matter of debate. To date, no single protocol has gained widespread acceptance.

Researchers at the University of Alberta led by Dr. Christian Toso set out to define the immunosuppressant regimen associated with the best survival after liver transplantation for HCC. This study was not designed to look at the effect of specific drugs, but at protocols containing specific drugs. Based on data from the Scientific Registry of Transplant Recipients, the researchers evaluated 2491 adult recipients of isolated liver transplantation for HCC and 12167 for non-HCC diagnoses between March 2002 and March 2009. All patients remained on stable maintenance immunosuppression protocols for at least six months post-transplant. The unique outcome variable of the study was patient survival; all deaths were taken into account in the analysis whether they

were associated with HCC or not.

In a multivariate analysis, only anti-CD25 antibody induction and sirolimus-based maintenance therapy were associated with improved survivals after transplantation for HCC. The other studied drugs, including calcineurin-inhibitors, did not demonstrate a significant impact. To determine whether the observed effects were due to a direct impact of the drug on tumor or more on liver transplant in general, the research team conducted a similar analysis on non-HCC patients. While anti-CD25 induction was again associated with a trend toward improved survival, sirolimus showed a trend toward lower rates of survival in non-HCC recipients, confirming the specificity of its beneficial impact to cancer patients.

"Of all protocols, sirolimus-based immunosuppression was the only one associated with an improved post-transplantation survival specific to HCC patients, further reinforcing the clinical evidence of its anti-cancer properties," Dr. Toso concluded. "The use of anti-CD25 antibodies demonstrated similar trends to improved survival in both HCC and non-HCC patients. These observations, together with previous reports combining anti-CD25 antibody induction and delayed introduction of CNIs, speak in favor of the use of this drug after liver transplantation in general."

He adds, "Like any potent immunosuppressive drug, sirolimus is linked to a potential for development of numerous side effects. In general however, we believe that these side effects are relatively minor and easy to manage, and that the data revealed by the present study justify a broader use of protocols including sirolimus after liver transplantation for patients with HCC."

In another recent study on hepatocellular carcinoma, researchers from Seoul Veterans Hospital compared hepatic resection (HR) to

radiofrequency ablation (RFA) to treat patients with very early-stage HCC, defined as asymptomatic solitary HCC less than 2cm. Very early stage HCC can be an ideal indication for HR because of the low potential risk of microscopic seeding. According to AASLD guidelines, HR is the treatment of choice for patients with very early stage HCC.

Researchers compared HR and percutaneous RFA for the treatment of compensated cirrhotic patients with very early stage HCC using a Markov model to simulate a randomized trial to compare the overall survival of patients treated with HR, RFA or the combined approach of primary RFA followed by HR for cases of initial local failure.

Team leader Dr. Yun Ku Cho explains the rational behind the study. "Usually, RFA is inferior to HR in terms of local recurrence, which is known to be a significant adverse prognostic factor for survival. However, if initial local treatment failure following RFA can be further treated by HR, survival outcomes of patients treated with primary RFA may be improved." He concluded, "The results of this study matched such an expectation, with both study groups achieving nearly identical overall survival rates. Considering that RFA is much less invasive as compared to HR, this study highly suggests that RFA may deserve to be considered as a primary treatment for very early stage HCC."

More information:

Article: "Sirolimus-based Immunosuppression Is Associated with Increased Survival after Liver Transplantation for Hepatocellular Carcinoma." Christian Toso, Shaheed Merani, David L. Bigam, James Shapiro, Norman Kneteman. Hepatology; Published Online: November 13, 2009 (DOI: 10.1002/hep.23437); Print Issue Date: April 2010. www3.interscience.wiley.com/jo … l/122684403/abstract

Article: "Hepatic Resection versus Radiofrequency Ablation for Very

Early Stage Hepatocellular Carcinoma: A Markov Model Analysis." Yun Ku Cho, Jae Kyun Kim, Wan Tae Kim, Jin Wook Chung; Published Online: November 30, 2009 (DOI: 10.1002/hep.23466); Print Issue Date: April 2010. www3.interscience.wiley.com/jo … l/123194754/abstract

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