Impact of chronic hepatitis virus infection on the feasibility and efficacy for Asian patients with hepatocellular carcinoma in phase I clinical trials


1Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan, 2National Cancer Center Hospital, Tokyo, Japan, 3Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan, 4Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: In Asia, chronic hepatitis B and C virus infections (CHVI) are major risk factors for liver fibrosis and hepatocellular carcinoma (HCC). Patients with advanced HCC have limited effective therapeutic options and are potential candidates for early phase clinical trials for new anti-cancer agents. The impact of CHVI on the feasibility and efficacy for patients with HCC in Phase I trials (P-IIs) has not been reported or elucidated in Western countries.

Methods: We retrospectively analyzed the characteristics and outcomes of HCC patients participating in P-IIs, with emphasis on CHVI. Patients testing positive for anti-hepatitis C virus (HCV) antibody or hepatitis B virus surface antigen (HBsAg) were diagnosed with CHVI.

Results: Eighty-five patients were enrolled in P-IIs at our center. There were no significant differences in the clinical and laboratory variables, including the liver function test results, between the 46 (54%) CHVI-positive and 39 (46%) CHVI-negative patients in this study. The median time to treatment failure (TTF) and overall survivals (OS) from enrollment of the P-I were 60 days (95% confidence interval [CI]: 51–85) and 112 days (95% CI: 67–178), respectively. There is no significant difference between positive and negative for hepatitis virus in the best response based on the RECIST. The frequency of abnormal liver function test (LFT) adverse events (grade ≥ 3) was significantly different among CHVI-positive and -negative patients. No patient discontinued P-I treatment secondary to abnormal LFT results or developed reactivation of hepatitis virus, and no treatment-related mortality was observed. Multivariate analysis revealed that the number of prior systemic treatments significantly contributed to poor TTF (HR: 2.1, 95% CI: 1.3–3.6, P = 0.004) and that poor Eastern Cooperative Oncology Group Performance Status significantly contributed to poor OS (HR: 1.9, 95% CI: 1.3–3.6, P = 0.04).

Conclusions: CHVI did not independently predict TTF and OS. Abnormal LFT adverse events could be related to CHVI but did not lead to discontinuation of P-I treatment. Thus, patients advanced HCC with CHVI can be enrolled in the P-IIs.

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