Cancer Chemother Pharmacol (2011) 68:1641–1642
DOI 10.1007/s00280-011-1778-6

REPLY

Sorafenib for hepatocellular carcinoma according to Child-Pugh class of liver function

Jeong Eun Kim · Baek-Yeol Ryoo · Yoon-Koo Kang

Published online: 9 November 2011

The authors would like to thank Dr. Farinati and colleagues for their interest in our paper. We totally agree with Dr. Farinati on the importance of identifying proper patients for sorafenib.

As most patients with HCC have underlying cirrhosis of various etiologies, patients die not only from progression of HCC but also aggravation of the underlying cirrhosis. The most commonly used parameters to assess cirrhosis is the Child-Pugh score (CPS). Considering that death from cirrhosis could potentially mask antitumor efficacy of sorafenib, the 2 phase III trials, SHARP [4] and Asia–Pacific trials [5], selected HCC patients with underlying Child-Pugh class A (CPA) cirrhosis. But, in practice, many patients have poorer liver function when sorafenib is considered, which hinders physicians from prescription of the agent. While it is generally agreed that sorafenib could not be used for the patients with Child-Pugh class C (CPC) cirrhosis because of the poor prognosis and significant liver function deterioration, controversy lies with patients with Child-Pugh class B (CPB) cirrhosis [6]. The confusion and controversy have really focused on the use of sorafenib in patients with CPB cirrhosis. One phase I study showed no substantial differences in the incidence of adverse events between CPA and CPB patients [3]. And another phase II study showed that pharmacokinetics (PK) of sorafenib was comparable with similar drug-related toxicity profiles between the CPA and CPB patients [2]. On the other hand, a study showed that CPB patients suffered more frequent worsening of their liver function [1]. These studies, however, included CPB patients at various clinical statuses.

Our report is based on the assumption that some patients in CPB could be safely treated with systemic treatment including sorafenib, and could also be included in clinical trials for new agents. To identify these patients, we compared the efficacy and toxicity of sorafenib according to CPS in CPB patients (CPB 7 vs. CPB 8–9). According to our results, sorafenib efficacy and survival outcomes were worse in CPB patients than in CPA patients. But the incidence of adverse events was comparable in CPB 7 with in CPA. But the low incidence of adverse events in CPB 7 might be related with the short duration of sorafenib treatment because of the lower efficacy. To minimize this effect, the number of patients who discontinued sorafenib because of cirrhosis-related complications was analyzed; a significant number of patients with CPB 8–9 required sorafenib discontinuation because of the cirrhosis-related complications in comparison to CPB 7.

In conclusion, sorafenib should not be used in patients with CPC. In patients with CPB, sorafenib could not be recommended as a standard treatment because of the lower efficacy; but, selected patients with CPB cirrhosis (i.e., CPB 7) may be included with CPA in the future clinical trials with sorafenib or other novel agents. In the era of enormous clinical trials for HCC, a better and applicable index is required to assess liver function and guide therapy.

J. E. Kim · B.-Y. Ryoo · Y.-K. Kang (✉)
Department of Oncology, Asan Medical Center,
University of Ulsan College of Medicine,
86 Asanbyeongwon-gil, Songpa-gu, Seoul 138-736, Korea
e-mail: ykkang@amc.seoul.kr

References

1. Abou-Alfa GK (2009) Commentary: sorafenib—the end of a long journey in search of systemic therapy for hepatocellular carcinoma, or the beginning? Oncologist 14:92–94

2. Abou-Alfa GK, Schwartz L, Ricci S, Amadori D, Santoro A, Figer A, De Greve J, Douillard J-Y, Lathia C, Schwartz B, Taylor I, Moscovici M, Saltz LB (2006) Phase II study of sorafenib in patients with advanced hepatocellular carcinoma. J Clin Oncol 24: 4293–4300
3. Furuse J, Ishii H, Nakachi K, Suzuki E, Shimizu S, Nakajima K (2008) Phase I study of sorafenib in Japanese patients with hepatocellular carcinoma. Cancer Sci 99:159–165
4. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc J-F, de Oliveira AC, Santoro A, Raoul J-L, Forner A, Schwartz M, Porta C, Zeuzem S, Bolondi L, Greten TF, Galle PR, Seitz J-F, Borbath I, Haussinger D, Giannaris T, Shan M, Moscovici M, Voliotis D, Bruix J, the SHARP Investigators Study Group (2008) Sorafenib in advanced hepatocellular carcinoma. N Engl J Med 359:378–390
5. Poon D, Anderson BO, Chen LT, Tanaka K, Lau WY, Van Cutsem E, Singh H, Chow WC, Ooi LL, Chow P, Khin MW, Koo WH (2009) Management of hepatocellular carcinoma in Asia: consensus statement from the Asian oncology summit 2009. Lancet Oncol 10:1111–1118
6. Worns MAMD, Weinmann AMD, Pfingst K, Schulte-Sasse CMD, Messow C-M, Schulze-Bergkamen HMDP, Teufel AMDP, Schuchmann MMDP, Kanzler SMDP, Duber CMDP, Otto GMDP, Galle PRMDP (2009) Safety and efficacy of sorafenib in patients with advanced hepatocellular carcinoma in consideration of concomitant stage of liver cirrhosis. J Clin Gastroenterol 43: 489–495