Symposium III

# Chemotherapy for Recurrent Hepatocellular Carcinoma after Liver Transplantation

Catholic University

Myung-Ah Lee

Surgical treatment seemed to show better survival in selected patient for recurrent hepatocellular carcinoma (HCC) after liver transplantion (LT). However, some patients recurred with unresectable state, such as distant organ metastasis. In these patients, systemic chemotherapy is indicated. Unfortunately, there was no effective cytotoxic chemotherapeutic agent for the HCC. In one trial conducted in Korea, several agent such as 5-FU, cisplatin, oxaliplatin, gemcitabine and capecitabine, S-1 were tried as 1st line chemotherapy for the 24 patients with recurrent HCC after LT. No objective response was observed and the median overall survival was 11 months (4.6-17.4 months). This result was disappointing although the patients were treated with heterogenous chemotherapy regimen, and small sample size. In this patients population, most of patients were treated with chemotherapy and the immunosuppressive agents at the same time. Therefore, grade 3/4 hematologic toxicity were 20-30%, causing the dose intensity was only 81% (median: 85%, 37-100%). For another reason, the immunosuppressive agent maybe a major factor. The response to chemotherapy in recurrenct HCC after LT was poorer than in non-transplanted group, because it can makes the growth rate of the tumor greater. The unique immune status by immunosuppressive agent except sirolimus-based maybe another factor that it might influence the response of chemotherapy.

Sorafenib is the only accepted systemic therapy for the HCC by FDA. But there is few data of the sorafenib for the recurrent HCC after LT (Table 1). Although we could not make any conclusion from these data because all these studies included very small number of patients, and analyzed retrospectively, we could find some idea for the treatment of LT patients. Patients who underwent transplantation usually take multiple immunosuppressive medication, and it may interact with sorafenib, causing unwanted toxicity, such as hand foot toxicity, diarrhea, dry skin, and neutropenia. Therefore, the dose of sorafenib shoud be titrated from low dose, or required dose reduction. As seen Table l, mTOR inhibitor was used as immunosuppressive agent with sorafenib. There are preclinical data for the synergistic effect of sorafenib and everolimus, especially to inhibit tumor, without drug interaction.

To identify the optimal dose and schedule of sorafenib with the adequate immunosuppression, further

**Table 1.** Sorafenib for the recurrent HCC after LT

| Trial | No | Regimen | Response | OS | TTP |
|---|---|---|---|---|---|
| Worns MA (2009) | 4 | Sorafenib | | | 8.9 mon |
| Kim R. (2010) | 9 | Sorafenib | 1 CR | | |
| | | Everolimus | 4 SD | | |
| Validivieso A (2010) | 5 | Sorafenib | | 18.8 mon | |
| | | Everolimus | | | |
| Yoon DH (2010) | 13 | Sorafenib | 6 SD | 5.4 mon | 2.9 mon |

OS: Overall survival, TTP: Time to progression.

large clinical trial wll be warranted.

## References


1. Lee JO, Kim DY, Lim JH. Palliative chemotherapy for patients with recurrent hepatocellular carcinoma after liver transplantation. J Gastroenterol Hepatol 2009;24: 800-805.
2. Kim R, El-Gazzaz G, Tan A, et al. Safety and feasibility of using sorafenib in recurrent hapatocellular carcinoma after orthotopic liver transplantation. Oncology 2010;79:62-66.
3. Valdivieso A, Bustamante J, Gastaca M, et al. Management of hepatocellular carcinoma recurrence after liver transplantation. Transplant Proc 2010:42:660-662.
4. Yoon DH, Ryoo BY, Ryu MH et al. Sorafenib fior recurrent hepatocellular carcinoma after liver transplantation. Jpn J Clin Oncol 2010;40(8):768-773.
5. Safety and efficacy of sorafenib in patients with advanced hepatocellular carcinoma in consideration of concomitant stage of liver cirrhosis. Worns MA, Weinmann A, Pfingst K, et al. J Clin Gastroenterol 2009;43:489-495.