Hepatic Arterial Infusion Chemotherapy for Post-transplant Recurrent Hepatocellular Carcinoma after Failure of Tyrosine Kinase Inhibitors

Jinfa Lai , MD [1,2] **Ming Zhao, MD** [1,2]

1 Department of Minimally Invasive Interventional Radiology, Sun Yat-sen University Cancer Center, Guangzhou, People's Republic of China.

2 State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, People's Republic of China.

HAIC for post-LT r-HCC

INTRODUCTION

Liver transplantation (LT) is a first-line treatment for hepatocellular carcinoma (HCC) patients within the Milan criteria, but HCC recurrence after LT still remains the leading cause of death[1] .

For LT patients, the management of recurrent HCC after LT have not a specific recommendation in the international clinical guidelines [2-3]. Therapeutic strategies of recurrent HCC depend on disease characteristic and location of lesions [4-5].. Palliative treatments such as tyrosine kinase inhibitor (TKI), adjuvant chemotherapy or regional therapy are considered in this scenario [2-3].

Recently, many studies have observed that oxaliplatin-based Hepatic arterial infusion chemo-therapy (HAIC) can significantly improve survival benefit, even better than sorafenib, in advanced primary HCC[6-7].

AIM

We aim to evaluate the safety and efficacy of hepatic arterial infusion chemotherapy for HCC patients with TKIs-refractory after LT.

METHOD

Eighteen cohort patients who presented with HCC recurrence after LT were eligible for systematic therapy between January 2016 and January 2019 were enrolled in this study. We investigated whether HAIC using oxaliplatin and fluorouracil can improve survival benefit for HCC patients after LT who experienced TKIs resistance. The radiologic response was evaluated by follow-up radiologic imaging for all patients each 3-4 weeks. Survival outcome was evaluated from HCC recurrence to death by the Kaplan-Meier survival curve.

RESULTS

A total of 18 patients, nine patients relapsed within 6 months after LT (Early recurrence group), and the remaining beyond 6 months (Late recurrence group). Objective response was obtained in 44% and stable disease in 50%. Median survival time (MST) was 24 months (95% CI: 8.8-39.2) in the whole cohort. In subgroup analysis, survival outcome was significantly improved in the late recurrence group than early recurrence group (MST 32.7 vs. 17.4 months, p=0.027). There were no severe adverse events related with HAIC.

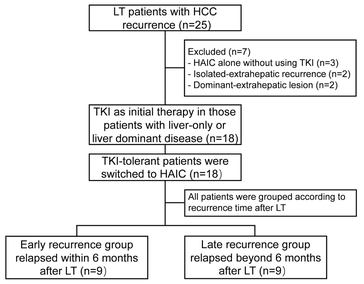

Fig.1. *The diagram shows the selection criteria for patients enrolled in the study.*

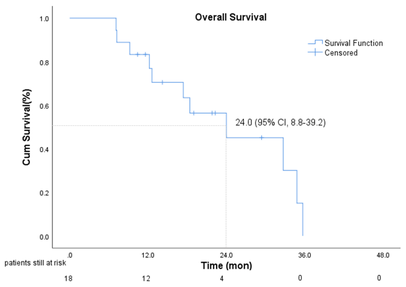

Fig.2. *Kaplan-Meier analysis of overall survival from HCC recurrence in the whole cohort.*

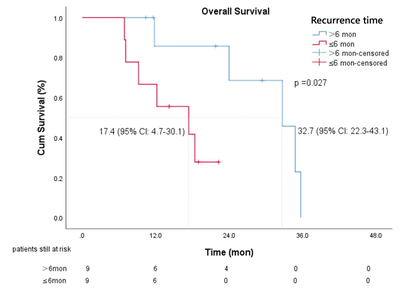

Fig.3. *Comparison of overall survival between patients in the early recurrence group and the late recurrence group.*

Table 1. *Incidence of HAIC-related adverse events in patients with hepatocellular carcinoma recurrence after liver transplantation.*

Adverse effects	Toxicity grade (n=18)	
	Any grade	Grade ≥3
Fatigue	1 (5.6%)	0
Nausea/Vomiting	3 (16.7%)	0
Diarrhea	0	0
Neutropenia	2 (11.1%)	0
Thrombocytopenia	0	0
Anemia	0	0
Alopecia	0	0
Stomatitis	0	0
Neurotoxicity	4 (22.2%)	0
Liver dysfunction	2 (11.1%)	0

CONCLUSIONS

HAIC may be a feasible treatment for LT patients with HCC recurrence suffering TKIs refractory. It seems to improve overall survival and has acceptable safety profile in those patients.

REFERENCES

[1] Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. The New England journal of medicine 1996; 334:693-9.

[2] EASL Clinical Practice Guidelines: Liver transplantation. Journal of hepatology 2016; 64:433-85.

[3] Benson AB, D'Angelica MI, Abbott DE, et al. Guidelines Insights: Hepatobiliary Cancers, Version 2.2019. Journal of the National Comprehensive Cancer Network : JNCCN 2019; 17:302-10.

[4] de'Angelis N, Landi F, Carra MC, Azoulay D. Managements of recurrent hepatocellular carcinoma after liver transplantation: A systematic review. World journal of gastroenterology 2015; 21:11185-98.

[5] Verna EC, Patel YA, Aggarwal A, et al. Liver Transplantation for Hepatocellular Carcinoma: Management After the Transplant. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2019.

[6] Lyu N, Lin Y, Kong Y, et al. FOXAI: a phase II trial evaluating the efficacy and safety of hepatic arterial infusion of oxaliplatin plus fluorouracil/leucovorin for advanced hepatocellular carcinoma. Gut 2018; 67:395-6.

[7] Lyu N, Kong Y, Mu L, et al. Hepatic arterial infusion of oxaliplatin plus fluorouracil/leucovorin vs. sorafenib for advanced hepatocellular carcinoma. Journal of hepatology 2018; 69:60-9.

ACKNOWLEDGEMENTS

We thank all the patients and their family's members for their permission in this study.

CONTACT INFORMATION

The authors have no conflicts of interest to disclose.