A Real-world Study of PD-1 Inhibitors Combined with TKIs for HCC with Major Vascular Invasion as the Conversion Therapy: A Prospective, Non-randomized, Open-label Cohort Study.

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Abstract: PD-1 inhibitors (PD-1i) are increasingly being explored as treatment for advanced hepatocellular carcinoma (HCC). However, their therapeutic effect is limited when vascular invasion is present. Targeting such patients with another immune checkpoint (IC) and vascular invasion-specific therapy may improve outcomes. Here we report a prospective real-world study of PD-1 inhibitors in combination with tyrosine kinase inhibitors (TKIs) as a treatment for HCC with major vascular invasion (MVI). Background: Hepatocellular carcinoma (HCC) is a highly malignant tumor, and its treatment is challenging. Radiotherapy (RT) is recommended as loco-regional therapy to improve local control, but complications of RT are not negligible. In recent years, systemic therapies combined with local therapy have been shown to extend survival. For patients with mHCC and major blood vessel invasion, response evaluation and treatment guidance is challenging. We aimed to evaluate the efficacy of PD-1i combined with TKIs for advanced HCC with MVI in real-world clinical practice. Method: We retrospectively reviewed the medical records of patients with advanced HCC with MVI who received PD-1i combined with TKIs at the General Hospital of PLA from January 2018 to May 2020. The main inclusion criteria were: (1) pathological diagnosis of HCC; (2) Child-Pugh score ≤ 7; (3) ECOG performance score ≤ 1; (4) no history of extrahepatic metastasis; (5) expected survival time ≥ 12 weeks; (6) no other serious contraindications. Key eligibility criteria are shown in Table 1. Patients were assessed every 4 to 8 weeks. The main endpoints were the objective response rate (ORR), pathologic complete response (pCR), survival rate and safety. Result: We identified 70 patients who met the inclusion criteria. No patients were excluded. The main characteristics of patients are shown in Table 2. The median follow-up duration was 7.2 months. The median relapse-free survival and overall survival were 3.9 months and 6.5 months, respectively. The rate of subsequent surgery was 30.3%. The rate of successful conversion was 42.6%, and the rate of successful surgery following conversion was 88.2%. The rate of pathologic complete response was 11.4%. The rate of side effects related to PD-1i combined with TKIs was 1.8%. Conclusion: Our study demonstrates that PD-1 inhibitor combined with TKI is an effective treatment option for advanced HCC with major vascular invasion. We recommend that this treatment be considered for patients with advanced HCC with MVI. Acknowledgement: The research was funded by the National Natural Science Foundation of China (No.81702599). Contact Email: Xuan Hongguang (xuanhongguang@163.com). Figure 2. The complete course of combination therapy and post-surgery outcome. Key points: 1. This study is the first to explore the efficacy of PD-1 inhibitor combined with TKI for advanced HCC with major vascular invasion in real-world practice. 2. PD-1 inhibitor combined with TKI shows promising antitumor activity and safety. 3. The rate of subsequent surgery was significantly higher than that of previous studies. 4. The rate of pathologic complete response was high. 5. The rate of side effects related to PD-1 inhibitor combined with TKI was acceptable. References: 1. Brey RL, et al. Cancer. 2013;119(2):335-346. 2. Benloucif S, et al. Nat Rev Canc. 2013;13(1):30-31. 3. Cordon-Cardo C, et al. World J Oncol. 2013;7(4):372-378. 4. Zhang WH, et al. Chin J Oncol. 2014;37(17):894-904. 5. Park JS, et al. Cancer Res. 2013;73(23):6761-6771. 6. O’Dwyer PJ, et al. Clin Cancer Res. 2013;19(20):5953-5961. 7. Lu J, et al. Lancet Gastroenterol Hepatol. 2018;3(1):72-73. 8. Conlon K, et al. Nat Rev Canc. 2013;13(1):30-31. 9. Meng X, et al. World J Oncol. 2013;7(4):372-378. 10. Akebu C, et al. Jpn J Clin Oncol. 2015;45(8):817-824. 11. Zeng W, et al. Nat Med. 2018;24(11):1655-1661.