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Short Communication

Hepatic Arterial Infusion Chemotherapy (HAIC) Combined with Regorafenib and PD-1 Inhibitors in the Treatment of Liver Metastases of Colorectal Cancer after Failure of Second-Line Chemotherapy: A Single-Arm Prospective, Open-Label Phase II Clinical Trial

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ABSTRACT

Hepatic metastases are common in colorectal cancer. However, few therapeutic options are available after failure of second-line treatment. This study aims to explore the efficacy and safety of Hepatic Arterial Infusion Chemotherapy (HAIC) combined with Regorafenib and PD-1 inhibitors in the treatment of liver metastases of colorectal cancer after failure of second-line chemotherapy.

Keywords: Hepatic Arterial Infusion Chemotherapy (HAIC); Regorafenib; PD-1 inhibitors; Liver metastases; Colorectal cancer

ABOUT THE STUDY

Colorectal Cancer (CRC) ranks the third in morbidity rate and fourth in mortality of all human cancers globally [1]. Approximately 60% of patients with colorectal cancer will develop liver metastasis during the course of their disease [2]. Traditional radical resection and surgical resection are the only radical treatments for mCRC patients. However, just 10-20% of the patients can receive radical resection upon diagnosis. For the remaining majority, chemotherapy is the standard treatment option for liver metastases of colorectal cancer. Following failure of second line treatment, Regorafenib and Fruquintinib are recommended as third-line treatment. However, high moderate and or severe AEs influence the choice of therapy. Despite the plurality of therapeutic options, the curative effects remain unsatisfactory. Therefore, more effective therapeutic options are required.

Hepatic Arterial Infusion Chemotherapy (HAIC) is a local treatment used in the treatment of unresectable colorectal cancer liver metastases. The efficacy of HAIC has been well established in multiple studies, including prospective randomized studies [3,4]. In theoretical terms, HAIC is more effective than intravenous chemotherapy because of its first-pass metabolism and topical accumulation of chemotherapeutic agents in the liver. In the clinical experiments, HAIC can achieve a higher local response rate than systemic chemotherapy and remain effective when patients have failed to respond to previous chemotherapy.

In recent years, the use of immune checkpoint inhibitors offered new hopes for metastatic colorectal cancer. Anti-Programmed cell Death-1 (PD-1) blockade in tumors with Deficient Mismatch Repair (dMMR) metastatic colorectal cancer showed tremendous efficacy. However, the population of dMMR/Microsatellite Instability (MSI-H) is very low, representing only 5% of patients in the metastatic setting. Unfortunately, PD-1 inhibitors have been ineffective in Micro-Satellite Stable (MSS) metastatic colorectal cancer [5,6]. Regorafenib is a multi-targeted tyrosine kinase inhibitor approved for use in refractory colorectal cancer. In the phase III correct trial, Regorafenib significantly improved survival in treatment-refractory metastatic colorectal cancer [7]. Theoretically, HAIC combined with Regorafenib and PD-1 inhibitors in the treatment of liver metastases of colorectal cancer will be better than that of immune and targeting therapy.

Therefore, we designed a study to try and address clinically relevant questions about liver metastases of colorectal cancer after failure of second-line chemotherapy. This study aims to explore the efficacy and safety of HAIC combined with Regorafenib and PD-1 inhibitors in the treatment of liver metastases of colorectal cancer after failure of second-line

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chemotherapy. It can provide meaningful guidance for further clinical studies while offering an opportunity to improve treatment options for patients with liver metastases of colorectal cancer after failure of second-line chemotherapy in the future.

CONCLUSION

This was an open-label, single-arm, phase II study. Major inclusion criteria are listed as follows. Pathologically or cytologically confirmed colorectal cancer, with liver metastases, who were unable to undergo surgical resection (among the patients whose age was over 18 years old), when signing the informed consent form against second-line or second-line targeted therapy, failure was observed with standard chemotherapy (FOLFOX, FOLFIRI, XELOX) macromolecule targeted therapy.

Key inclusion criteria includes active gastrointestinal bleeding which occurs within half a year, followed by uncontrolled hypertension after drug therapy (which can be defined as: Systolic blood pressure >160 mmHg and or diastolic blood pressure >100 mmHg). Detailed selection criteria are provided at Objective Response Rate (ORR) was the primary endpoint in this study. Secondary endpoints include Progression Free Survival (PFS), Hepatic Progression Free Survival (HPFS), Disease Control Rate (DCR) Overall Survival (OS) and Adverse Event (AE). The efficacy was evaluated based on the Modified Response Evaluation Criteria in Solid Tumors (MRECIST). The participants were assessed by the same assessor at baseline and during the treatment period. A total of 41 participants are anticipated to be enrolled in these studies. The implementation period for this study was September 2022 through September 2025. During the study, the transportation cost of patients was sponsored by Bayer, and the insurance fee of the clinical trial was sponsored by Shanghai Henlius Biopharmaceutical Company.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
2. Ghiringhelli F. Hype and hope of hepatic arterial infusion for colorectal cancer. Hepatobiliary Surg Nutr. 2021;10(2):235-237.
3. Chang AE, Schneider PD, Sugarbaker PH, Simpson CO, Culnane MA, Steinberg SM. A prospective randomized trial of regional versus systemic continuous 5-fluorodeoxyuridine chemotherapy in the treatment of colorectal liver metastases. Ann Surg. 1987;206(6): 685-693.
4. Nishiofuku H, Tanaka T, Aramaki T, Boku N, Inaba Y, Sato Y, et al. Hepatic arterial infusion of 5-fluorouracil for patients with liver metastases from colorectal cancer refractory to standard systemic chemotherapy: A multicenter, retrospective analysis. Clin Colorectal Cancer. 2010;9(5):305-310.
5. Le DT, Kim TW, van Cutsem EV, Geva R, Jäger D, Hara H, et al. Phase II open-label study of pembrolizumab in treatment-refractory, microsatellite instability–high/mismatch repair–deficient metastatic colorectal cancer: KEYNOTE-164. J Clin Oncol. 2020;38(1):11-19.
6. Ghiringhelli F, Fumet JD. Is there a place for immunotherapy for metastatic microsatellite stable colorectal cancer?. Front Immunol. 2019;10:1816.
7. Grothey A, van Cutsem EV, Sobrero A, Siena S, Falcone A, Ychou M, et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (correct): An international, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet. 2013;381(9863):303-312.