Prospective Phase II trial of combination hepatic artery infusion and systemic chemotherapy for unresectable colorectal liver metastases: long term results and curative potential

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BACKGROUND

Many patients with colorectal cancer will develop liver metastases (CRLM), with the liver often being the only site of distant disease. Complete resection is required for best survival outcomes, but up to 85% of patients present with unresectable disease. Conversion to resection with current systemic chemotherapy regimens is low (13 – 27%). Hepatic artery infusion (HAI) therapy allows for precise delivery of chemotherapy to the liver and, in combination with systemic chemotherapy, has demonstrated promising superior response rates of 55-88% with a nearly 50% conversion rate. The purpose of this study was to assess conversion to resection and evaluate long-term OS in patients with unresectable CRLM treated with HAI and systemic chemotherapy.

METHODS

This phase II single-center prospective trial included 64 patients with unresectable CRLM treated concurrently with HAI and systemic chemotherapy. Patients had high disease burden (e.g., 14 liver tumors [median]) and the majority (67%) had received previous chemotherapy. The primary endpoint was conversion to complete gross resection greater than twice the historical rate of 15% with systemic chemotherapy alone. Secondary endpoints included overall survival (OS), progression-free survival (PFS), hepatic progression-free survival (HPFS), tumor response rate and treatment-related toxicities and complications.

> "Combination HAI and SYS chemotherapy is an effective treatment regimen in patients with unresectable CRLM with a high rate of conversion to resection and long-term survival."

RESULTS

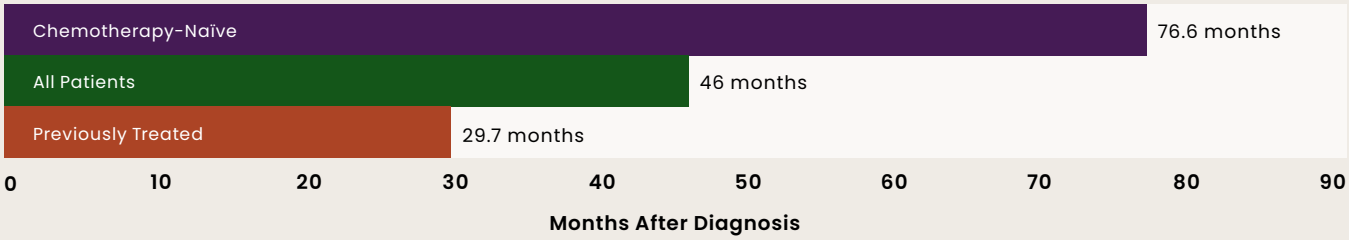
The study met the primary endpoint of >30% conversion to resection with more than half (52%) converted to resection at a median of 5 months (range: 2-22) post treatment initiation.

The overall response rate was 73% (67% and 86% in previously treated and chemotherapy-naïve patients, respectively).

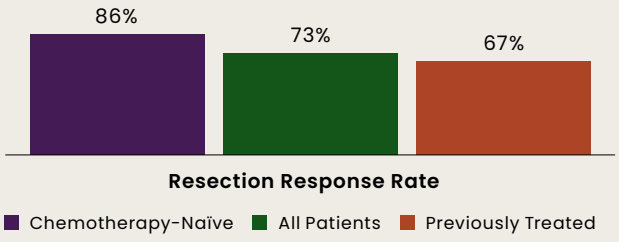
Median OS was 46 months (95%CI: 32.3-59.7) overall; 76.6 months (95%CI: 38.3-not reached (NR)) for chemotherapy-naïve patients and 29.7 months (95%CI: 21.5-40.2) for those previously treated (p=0.022). Five-year OS was 35.8% overall: 51.9% (95%CI: 29.1-70.6) and 27.9% (95%CI:15.6-41.6) for chemotherapy-naïve and previously treated patients, respectively. Multivariable analysis found conversion to resection (p<0.001) as the only variable significantly associated with prolonged OS.

Median HPFS was 16 months overall. Median PFS was 13 months (95%CI: 9-16), longer for chemotherapy-naïve vs. previously treated patients (19.7 vs. 10 months, p=0.021). Age (p=0.048) and conversion to resection (p=0.016) were significantly associated with PFS in multivariable analysis.

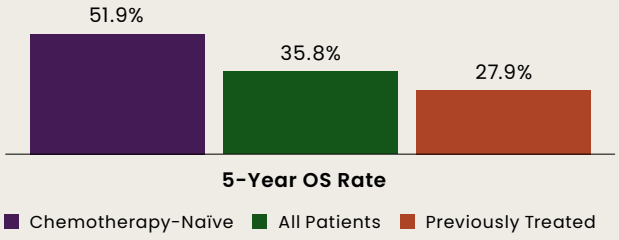
Median Overall Survival for Unresectable Patients Receiving HAI + Systemic Chemotherapy



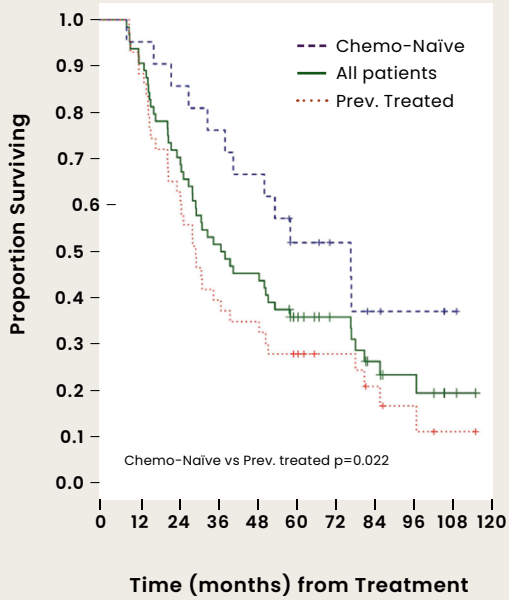
Response Rate to HAI Therapy



5-Year Overall Survival Rate



Overall Survival for Patients Receiving HAI + Systemic Chemotherapy



LIMITATIONS

The study's patient selection process may have resulted in a sample with different characteristics than those of the overall CRLM patient population. The definition of irresectability was not standardized and may reflect institutional bias.

CONCLUSION

This study demonstrated that the combination of HAI and systemic chemotherapy is an effective treatment for patients with unresectable CRLM resulting in high rate of conversion to resection and prolonged survival.

TAKEAWAYS

- For unresectable CRLM patients, Hepatic Artery Infusion resulted in **high response rates in chemo-naive and previously treated patients (86% and 67% respectively)**. Overall response rate was **73%**.
- Patients in this study had high disease burden and the majority underwent previous chemotherapy treatment, yet **more than half (52%) converted to resection** using combination HAI and systemic chemotherapy.
- Patients who converted to resection after treatment with combination of HAI and systemic therapy had **5-year OS of 62%**, which is comparable to that of patients who are initially resectable, and higher than that of patients treated with systemic chemotherapy alone.