



Clinical Summary Series

HAI Therapy for Unresectable CRLM

Combined hepatic arterial infusion pump and systemic chemotherapy in the modern era for chemotherapy-naïve patients with unresectable colorectal liver metastases

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BACKGROUND

In colorectal cancer patients with metastatic disease confined to the liver, resection of the primary tumor and liver metastases is associated with long-term survival and cure. However, the majority of patients with colorectal liver metastases (CRLM) present with unresectable disease. Previous studies have demonstrated that hepatic artery infusion (HAI) therapy in combination with systemic chemotherapy (SYS) may improve rates of conversion to resection (CTR) compared with SYS alone. Chemotherapy-naïve patients have been shown to have higher response rates and rates of CTR following HAI plus SYS compared with patients who were pre-treated. The aim of the present study was to evaluate CTR rate and survival outcomes of HAI plus SYS as initial treatment in the modern era.

RESULTS

The overall response rate was 79%, and disease control was achieved in 95% of patients. Four patients (7%) had a complete response (CR). CTR was achieved in 55% of patients. Overall, 36 of 58 (62%) patients achieved CTR or CR. Median OS for the entire cohort was 53.0 months. In comparison, median OS in patients who achieved CTR or CR was 141.7 months, while median OS in patients who did not achieve either CTR or CR was 28.0 months. Three- and five-year OS for the entire cohort were 65% and 45%, respectively. Among patients who achieved CTR or CR, three- and five-year OS were 88% and 72%. Three- and five-year OS among patients who achieved neither CTR nor CR were 27% and 0%. Twelve patients (21%) had no evidence of disease at last follow-up (median 122 months, range 15–210 months): 5 patients after initial treatment and 7 patients after salvage therapy for recurrence.

METHODS

This single-center retrospective cohort study conducted at Memorial Sloan Kettering Cancer Center included 58 chemotherapy-naïve patients with unresectable CRLM who underwent HAI pump placement without liver resection between January 2003 and May 2019. Assessment for resectability was performed by a multidisciplinary team. Irresectability was defined as technical unresectable (a margin-negative resection requiring resection of three hepatic veins, both portal veins or the retrohepatic inferior vena cava, or a resection leaving fewer than two adequately perfused and drained segments). Patients had a median of 12 liver metastases. Ninety-one percent of patients had five or more metastases, and 57% had 10 or more. RAS and BRAF mutations were present in 33% and 17% of patients, respectively.

All patients received HAI therapy consisting of floxuridine and dexamethasone and concomitant SYS consisting of escalating doses of oxaliplatin and irinotecan or a combination of fluorouracil and leucovorin concurrent with either oxaliplatin or irinotecan. Primary endpoints were radiologic response rate, rate of CTR, and overall survival (OS) from the time of pump placement.

“Nearly two-thirds of patients achieved a complete response or proceeded to conversion surgery, which was associated with prolonged survival.”



FIGURE 1
Median OS for Chemotherapy-Naïve Unresectable CRLM Patients Treated with HAI Therapy + SYS

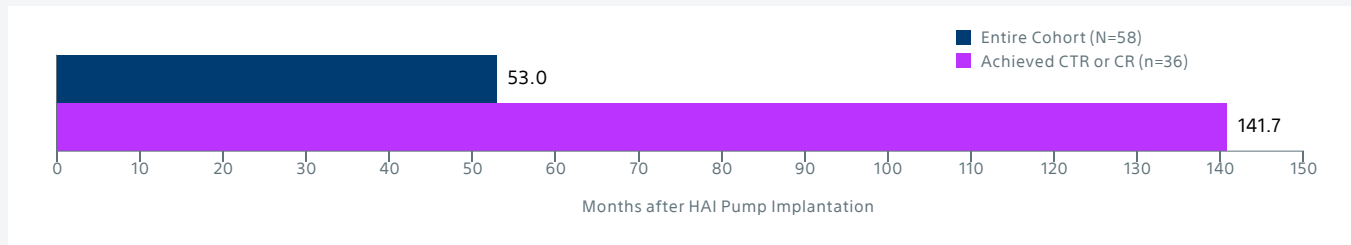


FIGURE 2
OS for Chemotherapy-Naïve Unresectable CRLM Patients Treated with HAI + SYS

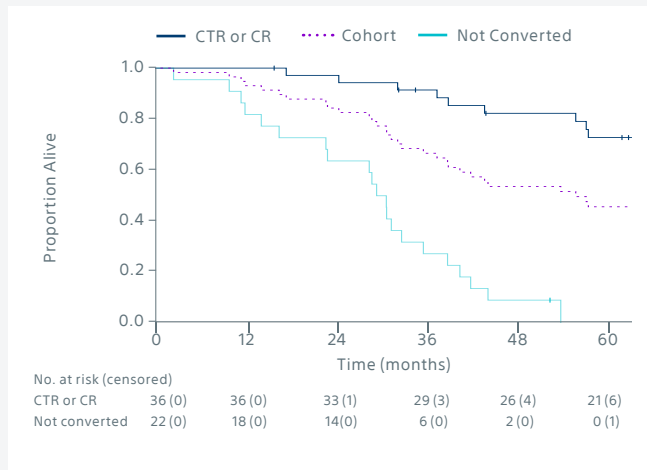
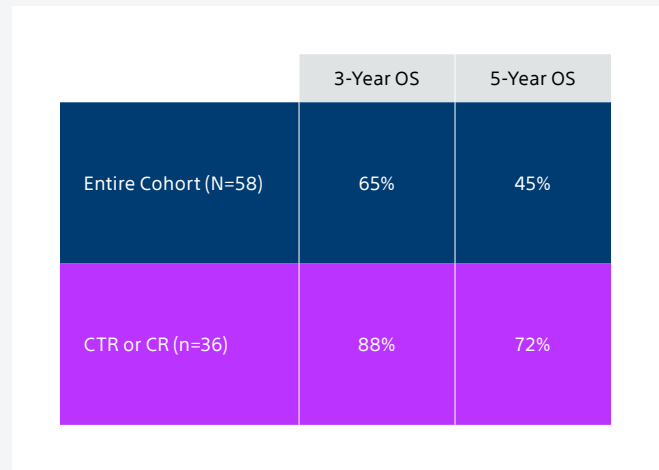


FIGURE 3
3- and 5-Year OS for Chemotherapy-Naïve Unresectable CRLM Patients Treated with HAI + SYS



LIMITATIONS

Limitations of this study include possible selection bias due to its retrospective nature, lack of a control group comparison, and the subjective determination of resectability. Favorable patient and tumor characteristics (median age 56, 66% left-sided tumors, and 61% baseline CEA ≤ 200 ng/mL) may also have contributed to study outcomes.

CONCLUSION

This study showed that chemotherapy-naïve patients with unresectable CRLM who received HAI + SYS had a high rate of CTR or CR, which was associated with prolonged survival.



[Pump HCP Indications, safety, and warnings](#)

TAKEAWAYS

- 62% of chemotherapy-naïve patients with unresectable CRLM who received HAI + SYS underwent CTR or achieved CR without resection.
- Median OS was five times greater (141.7 vs. 6.1 months) and three-year OS was more than three times greater (88% vs. 27%) among patients who achieved CTR or CR compared with patients who achieved neither CTR nor CR.
- 72% of patients who achieved CTR or CR were alive at 5 years vs. 0% of patients who did not achieve either.
- 21% of patients had no evidence of disease at last follow-up (median 122 months).