Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer

Kemeny N, Huang Y, Cohen AM, Shi W, Conti JA, Brennan MF, Bertino JR, Turnbull ADM, Sullivan D, Stockman J, Blumgart LH, Fong Y
New England Journal of Medicine. 1999;341(27):2039-48.

BACKGROUND

At the time of this study, 2-year survival after resection of colorectal liver metastases (CRLM) was approximately 65% . Three out of four resected patients would experience disease recurrence within 2 years with half of these patients recurring in the liver. Unlike the blood supply for healthy liver cells which is mostly derived from the portal vein, hepatic metastases derive their blood supply largely from the hepatic artery. Because floxuridine is rapidly metabolized by the liver, Infusion of floxuridine directly into the hepatic artery exposes the metastases to high drug concentrations while minimizing or eliminating systemic toxicity. In an effort to reduce the recurrence rate and improve survival, Memorial Sloan Kettering Cancer Center researchers conducted a randomized clinical trial (RCT) to test the efficacy of adjuvant hepatic artery infusion (HAI) of Floxuridine following resection of CRLM.

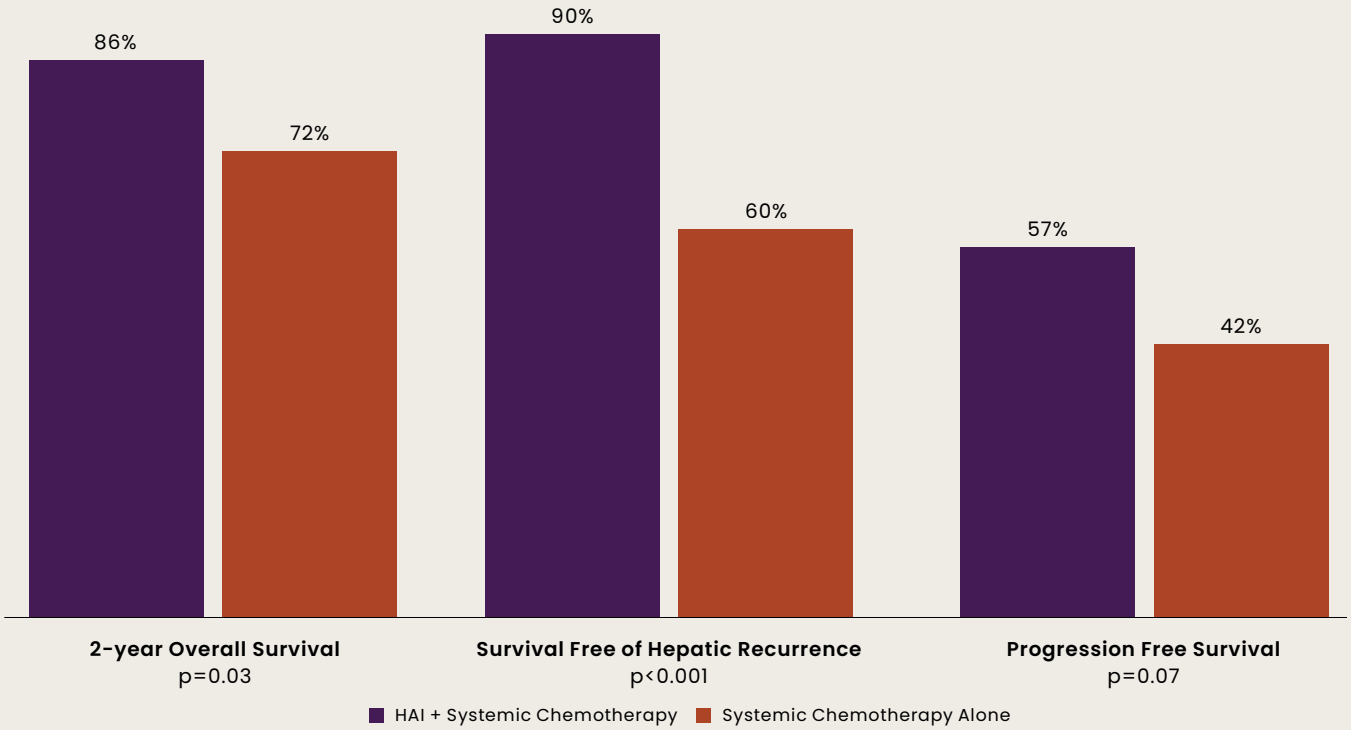
METHODS

Patients (N=156) undergoing complete CRLM resection were randomly assigned to receive HAI plus systemic chemotherapy (N=74) or systemic chemotherapy alone (N=82). Outcomes included overall 2-year survival, survival free of hepatic progression, and overall progression-free survival (PFS) at 2 years. Follow-up ranged from 16 to 95 months with a median of 62.7 months.

RESULTS

The randomized groups had no significant differences at baseline. At 2 years after resection, the survival rate was 86% for patients receiving HAI plus systemic chemotherapy and 72% for those with systemic chemotherapy alone (p=0.03). Median survival was 72.2 months in the HAI cohort, more than a year longer than the monotherapy group (59.3 months), thus meeting the primary end point of superior 2-year OS. At 2 years, patients treated with systemic chemotherapy alone had 2.34 (95%CI: 1.10-4.98, p=0.027) times the risk of death than those with HAI plus systemic chemotherapy, controlling for covariates. The overall progression free survival rates were 57% in the HAI therapy group and 42% in the chemotherapy only group (P=0.07). Survival rate free of hepatic recurrence was 90% in the combined group and 60% in the monotherapy group (p<0.001), demonstrating the power of HAI in controlling cancer in the liver.

2-Year Actuarial Survival Rates between HAI + Systemic Chemotherapy and Systemic Chemotherapy Alone



LIMITATIONS

The RCT was not powered to detect differences beyond 2 years. The study was conducted before the availability of modern chemotherapeutics such as oxaliplatin and irinotecan.

CONCLUSION

This RCT demonstrated that HAI as an adjuvant therapy after liver resection for CRLM resulted in significantly improved survival and hepatic progression free survival at 2 years. A similar trend was observed for overall PFS, but did not reach statistical significance (p=0.07).

TAKEAWAYS

- No RCTs conducted to date were able to demonstrate a statistically significant survival improvement for patients treated with systemic adjuvant chemotherapy alone after CRLM resection.
- However, in this RCT III study Kemeny et al, 1999 demonstrated that the addition of HAI to systemic chemotherapy after CRLM resection in the adjuvant setting significantly improved survival at 2 years compared to adjuvant chemotherapy alone.