Clinical Summary Series

HAI Therapy for Unresectable Intrahepatic Cholangiocarcinoma

Hepatic Arterial Infusion Pump Chemotherapy in Patients With Unresectable Intrahepatic Cholangiocarcinoma—PUMP-2 Trial

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BACKGROUND

Three-year overall survival (OS) for patients with unresectable advanced intrahepatic cholangiocarcinoma (iCCA) confined to the liver treated with systemic gemcitabine-cisplatin in the ABC trials was 3%. Over 70% of these patients die of hepatic disease progression[1], and therefore, locoregional treatments such as hepatic arterial infusion (HAI) therapy may improve survival. A recent meta-analysis documented a pooled three-year OS of 39.5% for comparable patients treated with HAI therapy. The purpose of this study was to validate the impact of HAI on overall survival in a prospective multicenter trial.

METHODS

PUMP-2 is a prospective, multicenter, single-arm phase II trial of 50 patients with unresectable advanced iCCA treated with HAI in 2020-2022 at three centers in the Netherlands.

Patients received up to 6 cycles of HAI floxuridine (starting dose 0.12 mg/kg/day). Systemic gemcitabine and cisplatin were administered concurrently or sequentially, depending on prior treatment exposure, following standard dosing protocols.

The primary endpoint was 1-year OS compared to historical control of similar patients. Secondary endpoints included other overall survival outcomes, progression-free survival (PFS), and objective response rate (ORR).

The PUMP-2 Trial achieved its primary endpoint, demonstrating a 1-year OS of 80% compared with 47% in the historical cohort ($p < 0.001$) and showed a 3-year OS of 32%.

[1] Yamashita S, Koay EJ, Passot G, et al: Local therapy reduces the risk of liver failure and improves survival in patients with intrahepatic cholangiocarcinoma: A comprehensive analysis of 362 consecutive patients. Cancer 123:1354-1362, 2017

RESULTS

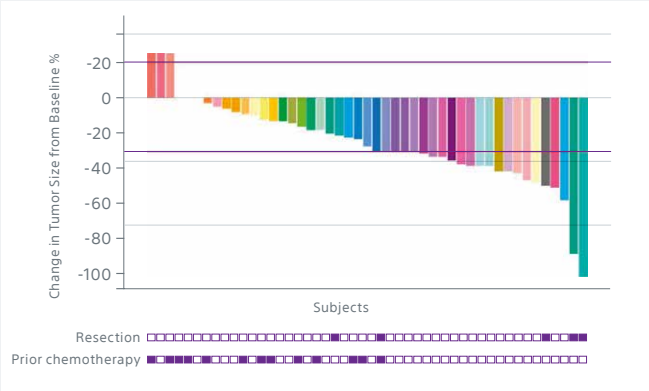
Combined HAI and systemic gemcitabine-cisplatin was administered as first-line treatment in 35 patients (70%) and second-line treatment in 2 patients; 11 patients (22.0%) who had received systemic treatment prior to enrollment received HAI therapy alone. The remaining 2 patients were unable to initiate HAI therapy but are included in the analysis. All 6 planned cycles of floxuridine were completed in 33 patients (66%).

Median follow-up was 43.1 months. Response is shown in Figure 1, with partial response was observed in 44% of patients, with 84% disease control at six months. The trial met its primary endpoint, demonstrating a significantly improved 1-year OS rate of 80.0% compared to 47% in the historical cohort treated with gem-cis alone ($p < 0.001$); 2-Year and 3-Year OS were 50% and 32% respectively. Additional survival outcomes, including those from diagnosis are shown in Table 1.

Notably, five patients (10%) were converted to surgical resection, including one with a complete pathologic response.

FIGURE 1

Waterfall Plot Showing Response



Response Rate	44%
Response in 1st Line Setting	59%
Disease Control at 6 Months	84%

TABLE 1

Survival Outcomes

	Measure	Outcome	95% CI
From Pump Placement	1-Year OS	80.0%	69.6%-91.9%
	Median OS	22.3 m	19.7-35.9 m
	3-Year OS	31.5%	20.4-48.6%
	PFS	11.4 m	9.0-12.4m
	hPFS	12.1 m	11.1-17.1 m
From Diagnosis	Median OS	28.6 m	23.2-40.0 m
	3-Year OS	37.6%	26.2-53.9%

CONCLUSIONS & TAKEAWAYS

- Addition of HAI to systemic chemotherapy significantly improves survival in patients with unresectable liver-confined iCCA.
- Results of this study are consistent with a previously published meta-analysis documenting 3-year OS > 30% in patients with unresectable iCAA treated with HAI therapy and superior to the 3-year OS reported in the ABC trials (2.8%) and historical control (3%).
- HAI should be considered for patients with advanced iCCA confined to the liver.