AB044. P-12. Phase 1 study of hepatic arterial infusion (HAI) therapy with floxuridine (FUDR) combined with systemic gemcitabine and oxaliplatin in patients with locally advanced intrahepatic cholangiocarcinoma (ICC)

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Background: The standard of care for unresectable intrahepatic cholangiocarcinoma (ICC) is palliative systemic chemotherapy with cisplatin and gemcitabine. The use of hepatic arterial infusion (HAI) floxuridine (FUDR) with systemic chemotherapy may improve outcomes. We conducted a phase 1 study of HAI FUDR with systemic gemcitabine and oxaliplatin.

Methods: We enrolled patients in three cohorts: FUDR 0.16 mg/kg/day ×14 days (Cohort 1), FUDR 0.12 mg/kg/day ×14 days with gemcitabine 1,000 mg/m^2 on days 1, 8, 15 (Cohort 2), and FUDR 0.10 mg/kg/day ×14 days with gemcitabine 800 mg/m^2 days 1, 15 and oxaliplatin 85 mg/m^2 days 1, 15 (Cohort 3). The primary endpoint was the recommended phase 2 dose (RP2D). Dose limiting toxicities (DLTs) were assessed during cycle 1. Secondary objectives were response rate and survival.

Results: We enrolled 24 patients, 6 male, age range 42–81 years (median 64). No DLTs were observed in Cohort 1. In Cohort 2, the addition of gemcitabine 1,000 mg/m^2 days 1, 8, 15 resulted in grade 3 LFT elevation in 2 patients; for subsequent patients, the gemcitabine dose was reduced to 800 mg/m^2. No DLT were observed in Cohort 3. Most patients experienced stable disease (SD) or partial response (PR). Conversion to resectable disease occurred in all cohorts.

Conclusions: Administration of FUDR via HAI pump in combination with systemic gemcitabine and oxaliplatin is well-tolerated in patients with unresectable cholangiocarcinoma. Preliminary analysis suggests a high rate of response and disease control, with some patients proceeding to resection. Based on Cohort 3, the RP2D is FUDR 0.10 mg/kg/day ×14 days, with gemcitabine 800 mg/m^2 days 1, 15 and oxaliplatin 85 mg/m^2 days 1, 15 for future studies. Future studies of this promising regimen will utilize this dosing schedule.

Keywords: Cholangiocarcinoma; hepatic arterial infusion pump; liver-direct therapy; FUDR; bile duct cancer

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