Endoscopic ultrasonography-guided portal injection chemotherapy for hepatic metastases

D. Faigel[1], D. Lake[2], T. Landreth[1], C. Kelman[1], R. Marler[1]

[1]Mayo Clinic, Scottsdale, AZ, United States, [2]Arizona State University, Tempe, AZ, United States

Introduction: We hypothesized that endoscopic ultrasonography-guided portal injection chemotherapy (EPIC) using irinotecan-loaded microbeads may achieve increased intrahepatic concentrations, while decreasing systemic exposure. This may achieve enhanced efficacy for the treatment of diffuse liver metastases, while decreasing systemic toxicities.

Materials and Methods: In eight anesthetized 35 kg pigs, EPIC was performed transgastrically using the linear-array echoendoscope and a 22 g fine-needle aspiration. In four animals, irinotecan (100 mg) loaded onto 75-150 micron liquid chromatography (LC) beads was injected. In four animals, saline was injected into the portal vein and unloaded irinotecan (100 mg) was injected into the jugular vein. Plasma (every 15 min), and at 1 h bone marrow, liver and skeletal muscle samples were obtained. Irinotecan and SN-38 (active metabolite) concentrations were assayed by LC/mass spectrometry.

Results: The procedure was performed safely in all eight animals. Compared with systemic administration, EPIC resulted in almost twice the hepatic concentration of irinotecan (6242 *vs.* 3692 ng/g) and half the systemic concentrations in plasma (1092 *vs.* 2762 ng/mL), bone marrow (815 *vs.* 1703 ng/mL) and skeletal muscle (521 *vs.* 1058 ng/g). SN-38 levels were lower with EPIC (liver: 166 *vs.* 681 ng/g; plasma: 1.8 *vs.* 2.4 ng/mL; bone marrow: 0.9 *vs.* 1.4 ng/mL; muscle 4.6 *vs.* 9.2 ng/g). Liver histology showed the beads within small portal venules.

Conclusions: EPIC using irinotecan-loaded microbeads can enhance hepatic exposure to irinotecan, while decreasing systemic concentrations. SN-38 levels were lower with EPIC indicating that a substantial portion of the irinotecan was still loaded onto beads. The microbeads may act as a reservoir resulting in prolonged hepatic drug exposure.

Status of the presenting author: Chief resident.

The authors declare: No significant relationship.