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HIGH DOSE INTRA-ARTERIAL MELPHALAN DELIVERED VIA PERCUTANEOUS HEPATIC PERFUSION (PHP) FOR PATIENTS WITH UNRESECTABLE HEPATIC METASTASES FROM PRIMARY NEUROENDOCRINE TUMORS

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Introduction. Patients hepatic MNET are faced with multiple treatment strategies including resection, ablation, and a variety of regional therapies which have been successfully utilized in this heterogeneous group of patients. Treatment options for patients with diffuse hepatic disease are more limited. This study examines a minimally invasive PHP with melphalan (MEL) for patients with isolated or redominant hepatic metastases from MNET.

Methods. Between December 2001 and July 2007, 21 MNET patients (mean age: 47 y; M: 13, F: 8; pancreatic neuroendocrine: 17, carcinoid: 4) were enrolled on one of two IRB approved PHP protocols. Analysis included PHP parameters, complications, toxicities, response, progression-free (PFS) and overall survival (OS). PHP consisted of a 30 minute hepatic artery infusion of MEL via a percutaneously placed catheter with hepatic venous hemofiltration using a double balloon catheter (Delcath Systems, Inc.) positioned in the retrohepatic inferior vena cava with in-line charcoal filtration. Treatment course consisted of four PHPs every 28-35 days. Survival curves were estimated by the Kaplan-Meier method.

Results. Twenty patients received 60 treatments (median: 3/pt); 1 patient was not treated due to hepatic arterial anatomic limitations. Mean MEL dose was 183 mg (median: 186, range: 90-220). Reversible grade III/IV toxicities observed were hematologic (53%) and hepatic (27%). Mean hospital stay was 2.5 days/PHP. An overall radiographic response was seen in 12 of 16 evaluable patients (75%; complete n=2, partial n=10) with an additional minor response (21% tumor reduction persisting for 43 months). At a median potential follow-up of 21 months, progression of intrahepatic disease has been observed in 3 patients (43, 24, 18 months, respectively) and two additional patients have died secondary to progression of extrahepatic disease. There was one treatment related mortality (5%) and 1 patient had disease progression on therapy (5%). Median duration of ongoing hepatic response is 12 months (mean: 16, range: 5-31) in 8 patients. Median PFS and OS have not been achieved.

Conclusions. This study shows that PHP with MEL has efficacy in patients with diffuse MNET of the liver too extensive for resection, ablation, or embolization strategies. Responses to therapy tend to be durable, with repeat therapy effective upon progression