

Long Term Results Utilizing High Dose Intra-Arterial Melphalan Delivered via Percutaneous Hepatic Perfusion (PHP) for Patients with Unresectable Hepatic Metastases from Primary Neuroendocrine Tumors

Abstract:

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 predominant hepatic metastases from MNET.

Methods: Between December 2001 and October 2009, 30 MNET patients (mean age: 46 y, range: 13-72y; M: 16, F: 14; gastrointestinal neuroendocrine: 23, carcinoid: 7) 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 hemofiltration. Treatment course consisted of four PHPs every 28-35 days. Survival curves were estimated by the Kaplan-Meier method.

Results: Thirty patients received 83 treatments (median: 3/pt); 1 patient was not treated due to hepatic arterial anatomic limitations. Mean MEL dose was 185 mg (median: 182, range: 90-220). Reversible grade III/IV toxicities observed were hematologic (77%) and hepatic (23%). Mean hospital stay was 3.4 days/PHP (median: 3, range: 1-21). An overall radiographic response was seen in 17 of 24 evaluable patients (71%; complete n=2, partial n=15). There was one treatment-related mortality (3.3%) secondary to complications of cholangitis in a patient with previous biliary reconstruction. Two patients had disease progression while on active therapy (6.7%). Median overall survival was 39 months.

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.