Background: There are few treatment options for unresectable hepatic MNET. Fewer than 10% of pancreatic NET patients demonstrate objective response to everolimus, sunitinib or octreotide. Regional therapies are used, but treatment options for patients with diffuse hepatic disease are limited.

Materials and Methods: We used minimally-invasive PHP to give a 30 minute hepatic artery infusion of melphalan 3 mg/kg with extracorporeal hemofiltration using specially-designed catheters positioned in the retrohepatic IVC and jugular venous return of filtered blood. Treatment was every 4–5 wks up to 4 cycles in consecutive IRB-approved phase 1 and 2 studies at NCI Surgery Branch, Bethesda. Delcath Systems, Inc., NY, USA sponsored the studies. Patients had MNET, limited treatable extrahaepatic disease, adequate hepatic reserve (Bili <3.0, PT within 2 seconds of normal, LFTs <10× ULN), no portal hypertension and adequate hepatic vascular access. The primary objective of this analysis was objective response rate by RECIST. We also studied acute peri-procedural events, later-onset AEs post-day 5 of each cycle, progression-free (PFS) and overall survival (OS).

Results: From Dec 2001 to Feb 2010, we treated 23 MNET patients (9 with extrahepatic disease), median 15 lesions, 12 with <25%, 5 with 25–50% and 6 >50% liver replacement; the majority had pancreatic NET (n = 17). Median cycles were 3/pt, total 68; median dose 180 mg (126–220); 2 cycles not given due to sclerotic hepatic artery and hypercalcemia. 1 patient received 4 cycles in 2004 and a further 3 cycles upon progression in 2008. Acute procedure-related grade 3–4 changes were transaminitis (22% cycles), thrombocytopenia (21% cycles), anemia (16% cycles) and hyperbilirubinemia (9% cycles) plus 1 tumour lysis, 1 carcinoid crisis and 1 CNS hemorrhage. Later-onset grade 3–4 AEs were mainly hematological: neutropenia (47% cycles), thrombocytopenia (29% cycles) and anemia (15% cycles). The 1 treatment-related death was due to gastric ulcer at day 74 post-cycle 1. There were 79% objective responses in 15 of 19 evaluable patients (2 CR, 13 PR, 3 SD, 1 PD). Median hepatic PFS was 39 months (n = 20) and OS was not yet reached (n = 23).

Conclusions: Percutaneous hepatic perfusion with melphalan has substantial efficacy in patients with diffuse MNET of the liver too extensive for resection, ablation or embolization strategies. Responses to therapy are durable, with a 39-month PFS and the option of retreatment upon progression.