Preliminary Experience with Intra-arterial I-131 MIBG Hepatic Infusion for Progressive Metastatic Neuroendocrine Tumors: A Work in Progress

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Systemic I-131 MIBG (MIBG) therapy is an established treatment modality for neuroendocrine tumors (NETs); however, because of the relatively low radiation dose that can be delivered, it is mostly palliative; significant anatomical tumor responses are rare. In hopes of increasing delivered hepatic tumor dose, direct intra-arterial (IA) infusion seems promising. This work in progress documents our early intra-hepatic MIBG experience in 6 patients with a variety of late stage NETs, predominantly metastatic to the liver. Clinical, biochemical, hematological and radiographic responses, as well as the side effect profile of IA infusion of I-131 MIBG in an ongoing group of NET patients (pts.) that have demonstrated progressive disease (PD) despite standard therapy are being studied.

Materials and Methods (Cont.)
A femoral artery catheter was positioned into the common hepatic artery and an infusion of 7.4 GBq high specific activity MIBG (> 1.2 MBq/mg) was done via a lead shielded infusion pump over 30 minutes without moving the pt in the radiology special procedures suite with appropriate radiation safety precautions in place. Pre-treatment tumor markers, CT/MRI scans, CMPs, hematologic profiles, OctreoScans and MIBG scans were obtained, with follow-up lab, quality of life questionnaires, and radiographic studies.

Results
Our 1st pt (MG carcinoid) showed a minor response (decrease in tumor size by 25–50%), and good clinical and tumor marker responses. The 2nd and 3rd pts. (unknown primary and MG carcinoid) have expired at 7 & 9 weeks post Rx of PD before a second cycle could be given. The 4th pt, (MG carcinoid) initially had an excellent clinical and biomarker response with drop in pancreastatin from 9,587 to 1,095 post 1st cycle. Post 2nd cycle, her NKA declined from 144 preRx to 61 ng/ml. She continues to have a Karnofski Performance Score (KPS) of 90-100 post 3rd cycle; however, her pancreastatin has again increased to 3,024 ng/ml, and her NKA to 82 ng/ml. The 5th pt. (BP carcinoid—see below) expired 7 months after her 1st Rx. Her 3rd cycle was cancelled when she developed a pancreatic metastasis. The 6th pt (rectal carcinoid) has had her 2nd cycle withheld while investigation for possible PD takes place. Catheterization caused no problems in any pt. No carcinoid crisis was observed. Mild nausea without vomiting developed in 1 pt. Mild-moderate reversible thrombocytopenia (Grade 2-3) developed in 3 pts. Overall side effects were no different than in our larger group of advanced NET pts. treated with IV MIBG therapy.

Conclusions
Intra-arterial therapy with MIBG appears to be a safe alternative to standard IV treatment. Despite the higher mean tumor uptake from IA administration demonstrated by other workers, clinical efficacy and side effects appear to be no different, and mortality is greater (likely due to selection bias) thus far in this small group of advanced NET patients. A larger group will have IA MIBG therapy in an attempt to assess its potential benefit.

Background

Materials and Methods

From August, 2010 to February, 2012, selected NET pts. from our Neuroendocrine Tumor Clinic have been offered up to 3 cycles of IA infusions of MIBG, each infusion delivering 7.4 GBq (200 mCi) MIBG for isolated or predominant hepatic metastases, unresponsive to multiple therapies. Thus far, 6 pts. (5 females, 1 male, mean age, 67.3 yrs.) have received a total of 11 hepatic IA infusions of MIBG. Verification of pretreatment intense MIBG hepatic tumor uptake via I-123 MIBG scanning was done.

Results (Cont.)

(A) Pt. #1: Pre first IA MIBG treatment coronal CT with large 6.9 cm segment 1 metastasis (B) Selective angiogram demonstrating metastatic tumor hypervascularity (C) Post MIBG Rx SPECT CT fusion with intense uptake in caudate lobe metastasis (D) Coronal CT 3mo post 3rd cycle of 7.4 GBq I-131MIBG showing significant necrosis with central fluid (E) Pt # 5: Angiogram shows large left lobe vascular metastasis. (F) Post 1st Rx MIBG with intense uptake in large metastasis (G) Progressive disease with a pancreatic metastasis developing 9 wks. after 2nd Rx. Her 3rd cycle I-131 MIBG was cancelled. She expired 6 wks. later.