



Center for
Cancer Research

Surgery Branch

Surgical Metabolism Section

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U.S. Department of Health
And Human Services
National Institutes of Health

June 01, 2006

Re: Treatment of Patients with Metastatic Neuroendocrine Tumors

Dear Colleague:

This letter is to inform you about a clinical trial currently enrolling patients with neuroendocrine tumors metastatic to the liver. The purpose of this trial is to examine the utility of high-dose, intra-arterial melphalan delivered through the hepatic artery via a percutaneous (PHP) approach utilizing the Delcath® catheter system. The primary endpoints of this trial are overall response rate and duration of response. Secondary endpoints include determination of disease-free and overall survival in treated patients along with examining patterns of recurrence in those patients who have responded to therapy.

This is a single arm study utilizing high-dose, infusional melphalan delivered via a catheter placed in the hepatic artery. The protocol calls for four treatments delivered at 28-day intervals. Prior to the third treatment, patients will undergo radiologic assessment of response, and patients with evidence of response to therapy stable disease (RECIST criteria) will be offered two additional treatments at 28-day intervals. After completion of therapy patients will be followed at 1 to 3 month intervals. Expected hospital length of stay is 2 to 4 days at each treatment.

The rationale for examining this therapy for patients with metastatic neuroendocrine tumors includes a previously reported overall response rate of 6 of 12 patients treated with high-dose melphalan via a surgical approach (Surgery 2005;138:1003-8). A small cohort (n=4) of patients treated as part of our Phase I dose-escalation PHP trial with the Delcath system had metastatic neuroendocrine tumors, with 2 observed complete responses of 24 months duration (J Clin Oncol 2005;23:3465-3474.). Early results in the present phase II study, support previous observations.

Eligibility criteria for study entry include:

- Histologically proven neuroendocrine tumor metastatic to the liver. In patients with extrahepatic disease (including primary tumors), the life-limiting component of disease must be in the liver.
- Adequate liver function as manifest by a total serum bilirubin ≤ 2.0 mg/dL and a PT within 2 seconds of the upper normal limit. AST/ALT must be ≤ 10 times upper limit of normal.



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Additional information about this trial or other clinical trial may be found at <http://Clinicaltrials.gov>. The clinicaltrials.gov identifier for this study is NCT00091455.

For additional information about this trial please feel free to contact me at the address below. Additional contacts include study nurse coordinators Susan Ohl (ohlsu@mail.nih.gov) and Cynthia Helsabeck (helsabec@mail.nih.gov).

All care for these patients will be provided at no cost to the patient at the Clinical Center, National Institutes of Health.

Every effort will be made to keep you fully informed of the results of the treatment and to promptly return the patient to your care for joint follow-up and collaboration with the National Cancer Institute.

Thank you for considering this treatment option for your patients.

Sincerely,

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