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## One year Follow-up for the Phase I MTD study of Ultratrace Iobenguane I 131 in Patients with Malignant Pheochromocytoma/Paraganglioma (Pheo)

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**Background:** I-131-iobenguane, a substrate for the norepinephrine transporter, has been shown to be effective in the treatment of neuroendocrine cancers such as Pheo. Non-radioactive iobenguane has been shown to inhibit uptake of radioiodinated iobenguane by tumors and has potential to cause cardiovascular AEs. Ultratrace iobenguane I 131 (Ultratrace) is devoid of cold iobenguane thereby enhancing tumor accumulation of radiolabeled iobenguane and limiting iobenguane dose dependent AEs.

**Methods:** Adult patients with metastatic/recurrent Pheo with a least 1 Ultratrace-avid CT-measurable lesion were enrolled. A 3+3 dose escalation design was used, initiated at 6.0 mCi/kg and escalated in 1.0 mCi/kg increments. Safety and efficacy data were obtained, including tumor markers and assessment of CT and bone scans by two blinded reviewers per RECIST.

**Results:** Twenty-one patients were treated: 3 at 6 mCi/kg (0/3 DLTs), 6 at 7 mCi/kg (1/6 DLTs), 6 at 8 mCi/kg (1/6 DLTs), and 6 at 9 mCi/kg (2/6 DLTs). The DLTs were neutropenia (2), febrile neutropenia (1), and thrombocytopenia (1). Two patients died within the 12 month efficacy follow-up (disease progression, thalamic infarction). The best overall response was 3 (14%) PRs, 14 (67%) SDs, 2 (10%) PDs, and 2 (10%) NEs. All 3 PRs were documented at the 3 month visit, and have continued; 2 at 12 months, and 1 at 18 months. Mean serum chromogranin A and vanillylmandelic acid levels decreased through 9 months. Furthermore, 5 of 15 (33%) patients on anti-hypertensives at the time of treatment reduced or discontinued following treatment.

**Conclusions:** The MTD in this dose escalation study was 8 mCi/kg. A single dose of Ultratrace iobenguane I 131 demonstrated clinical benefit and stabilized or reduced tumor dimensions and tumor marker levels. Objective tumor response was durable.