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Interim Results of an Open-label, Single-Arm Trial of Ultratrace I-131-Iobenguane in Patients with Metastatic Pheochromocytoma/Paraganglioma (Pheo)

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Background: The primary aim of this study was to evaluate the therapeutic efficacy of no carrier added (nca) I-131-MIBG in pheo as measured by >50% reduction of all antihypertensives for ≥6 months. Secondarily, to evaluate safety and assess for objective and biomarker responses.

Methods: Patients with metastatic pheo causing hypertension were treated with up to two 500 mCi doses of ^{131}I-nca-MIBG 3-6 months apart. Administered dose was limited by pretreatment organ dosimetry (Emami 1991). Response and toxicity were evaluated for at least 1 year or until death.

Results: 41 patients (16-72 years) received at least one treatment (full analysis; FA); 34 patients received 2 treatments (per protocol; PP). All patients were followed at least 1 year or until death. The primary endpoint of sustained reduction in antihypertensives was achieved in 35% (PP) and 32% (FA). 25/41 subjects who received at least 1 treatment had ≥50% reduction in antihypertensives, mean duration 8.3±6.9 months (range 0.1–22.1 months). Objective PR was seen in 41% (PP) and 34% (FA). 56% of PP had at least objective MR. All PP subjects and 90% in FA had at least stable disease. At 8 months there was a 53±31% reduction in ChromograninA from baseline in PP. Median survival to date is 31 months.

Primary toxicity was myelosupression: Grade 3 (27%), Grade 4 (30%). Grade 3 GI disorders were 36%. Biomarker response correlated to objective and antihypertensive responses. Thrombocytopenia was the most common treatment-emergent SAE (n=4) related to study drug. No other treatment-emergent SAE was related to study drug in >2 subjects.

Conclusions: 12 of 34 in PP in this study met the primary endpoint, which correlated with objective and biomarker responses in this disease with no approved, efficacious therapies. Toxicity for all patients was tolerable and predominantly limited to myelosupression.