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Evaluation of the Features of Long Term Hematologic Toxicity in Neuroendocrine Patients Treated with Peptide Receptor Radionuclide Therapy(PRRT)

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Background: Peptide receptor radionuclide therapy (PRRT) for neuroendocrine tumors (NET) may offer partial or complete objective response in up to 30% of patients (1). In order to deliver treatment in a safe and effective manner, long-term adverse events involving the bone marrow should be considered. Our objective was to evaluate the clinical characteristics of patients treated with PRRT who developed secondary hematologic malignancies as a long-term toxicity.

Methods: Patients eligible for evaluation received radionuclide therapy for histologically proven unresectable, advanced neuroendocrine tumor between April 1997 and December 2010. Parameters including age, gender, time interval from diagnosis to secondary hematologic malignancy, total cumulative radiolabel dose (GBq), and treatments were analyzed by descriptive statistics. Comparative analysis was performed using t- and z-tests.

Results: A total of 172 patients were eligible for evaluation. All patients received at least one cycle of MIBG, Indium-111 or Lutecium-177. Of those, 3.5% (n=6) patients had identified secondary hematologic malignancies (4 patients with acute myeloid leukemia and 2 patients with myelodysplastic syndrome). Mean interval from NET diagnosis to secondary hematologic malignancy was 7.5 years. Mean age of NET diagnosis was 36.0 (SD 14.2) and 53.2 (SD 11.1) years for patients with and without documented secondary hematologic malignancy respectively ($p=0.02$). The male:female ratio was lower for patients with secondary hematologic malignancy (1:5) compared to those without (85:87) ($p=0.057$). Patients with a secondary hematologic malignancy received a mean cumulative dose of 59.4 GBq (32.1-96.6 GBq). Two patients received concurrent chemotherapy containing epirubicin.

Conclusions: The rate of secondary hematologic malignancy was higher than in phase I study (2) but similar to rates reported in case series (3). This finding is compounded by the concurrent use of chemotherapy. Possible risk factors are female gender and young age at diagnosis. Efforts are ongoing to better delineate risk factors for secondary hematologic malignancies.