C37

Systemic Toxicity after Delayed Peptide Receptor Radionuclide Therapy in Patients with Metastatic Neuroendocrine Tumors

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Background: Somatostatin analogues tagged with radioactive ^{90}Yttrium and ^{177}Lutetium have been used to treat disseminated and inoperable NETs –peptide receptor radionuclide therapy (PRRT). Given the lack of availability of PRRT in the United States (US), treatment with PRRT is often offered later in the disease course. We hypothesized that delayed PRRT with more advanced disease and a greater number of prior liver-directed and systemic therapies would be at risk of developing more severe drug toxicities.

Methods: We performed a retrospective study of all patients seen at the Hospital of the University of Pennsylvania with disseminated, somatostatin-receptor positive NETs referred to University Basel Hospital (UBH) for PRRT (N=16) from 2005 to 2013. All patients had disseminated NETs with liver involvement. Cross-sectional imaging was performed within 12 weeks of PRRT. Tumor burden was graded using RECIST criteria 3-6 months after therapy and standardized laboratory studies were drawn at 1, 6, and 12 months post treatment to assess for systemic toxicity.

Outcomes: In our cohort, 7 patients (41%) had progression of disease (median 11 mos, range 4-28 mos) and 5 patients (31%) had stable disease at date of last cross-sectional imaging (10 mos, 5-16 mos) post-PRRT. Four patients have had treatment within the last three months with no follow up imaging available yet.

Within 1 year of PRRT, 11 patients (69%) developed new onset bone marrow dysfunction, 4 patients (25%) kidney dysfunction and 5 patient (31%) liver dysfunction. Of the latter five patients, four developed decompensated liver failure characterized by ascites and two died from liver disease. The patients who developed decompensated liver failure had received the greatest number of liver-directed therapies (3.75 therapies of 3 different types) prior to PRRT. Three patients had declines in CrCl to <60 mL/min and 1 patient to <30 mL/min. Eleven patients developed hematologic toxicity (anemia, n= 6, thrombocytopenia, n= 6, leucopenia, n =2)

Conclusion: Treatment toxicity was more frequent and more severe than reported in the current literature, though all patients showed clinical evidence of anti-tumor efficacy of PRRT therapy. Given its systemic efficacy and tolerability in less pre-treated patients, earlier consideration of PRRT therapy may improve outcomes.