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Therapy-Related Myeloid Neoplasms After Radioligand Therapy in Neuroendocrine Tumors: A Multicenter Real-World Analysis

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BACKGROUND

Therapy-related myeloid neoplasms (t-MNs), including myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML), represent an uncommon but serious long-term hematological toxicity associated with radioligand therapy (RLT). Real-world data on the incidence of t-MNs and associated risk factors following RLT in are limited. We sought to investigate the incidence and risk factors of t-MN in patients with NETs treated with 177Lu-Dotatate.

METHODS

We conducted a multicenter retrospective cohort study using the TriNetX research network. Adult patients with NETs who received 177Lu-dotatate were identified, with first administration defined as the index date. The primary outcome was development of t-MNs (incident MDS or AML) with a 12-month latency period after target treatment. Incidence was calculated and Cox proportional hazards models were used to evaluate associations between baseline covariates and t-MN risk. Covariates included age, sex, race, primary tumor site (small bowel, colon, pancreas, lung), liver and bone metastases, prior alkylating chemotherapy (temozolomide exposure), chronic kidney disease (CKD), and nicotine or alcohol dependence. Treatment pathways were assessed for 177Lu-Dotatate re-treatment and temozolomide duration.

RESULTS

A total of 1,811 patients met the inclusion criteria. Mean age at index was 65.4 ± 10.9 years; 977 (54.0%) were male, and 1,503 (83.0%) were White. Median follow-up duration was 20.5 months. Following 177Lu-Dotatate, 37 of 1,807 patients (2.05%) developed MDS, and 15 of 1,804 patients (0.83%) developed AML, with an overall incidence of t-MNs 2.88% (52/1,804). At baseline, mean age (67.1 ± 9.3 vs 65.4 ± 11.0 years, p=0.27) and sex (males 42.0% vs 54.2%, p=0.14) were comparable between

patients who did and did not develop t-MNs. On multivariable Cox proportional analysis, higher age at index (HR 1.03; 95% CI 1.01–1.07; p=0.048) and baseline CKD (HR 2.69; 95% CI 1.32–5.49; p=0.006) were independently associated with increased risk of t-MNs. Sex, race, primary tumor site, presence of liver or bone metastases, alkylating chemotherapy exposure, and nicotine or alcohol dependence were not significantly associated with t-MN risk. Evaluation of treatment pathways demonstrated similar 177Lu-Dotatate re-treatment rates (2.33% vs 2.77%, p=1.0), and comparable receipt of temozolomide for ≥12 months (18.6% vs 16.4%, p=0.66) between groups that did and did not develop t-MNs, respectively.

CONCLUSIONS

In this large real-world cohort of NET patients treated with 177Lu-dotatate, t-MNs were uncommon but clinically significant. Older age and CKD were associated with increased risk, whereas repeat 177Lu-Dotatate and alkylating chemotherapy exposure were not associated with increased t-MN incidence. These findings may inform risk stratification, patient counseling, and long-term hematologic surveillance following 177Lu-Dotatate.

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