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Characterizing Long-Term Hematologic Toxicity After ^{177}Lu-DOTATATE: A Real-World Analysis of Patients with Gastrointestinal Neuroendocrine Tumors

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BACKGROUND

Lutetium-177 (^177Lu)-DOTATATE peptide receptor radionuclide therapy (PRRT) is an important treatment for well-differentiated, advanced, somatostatin receptor–positive gastrointestinal neuroendocrine tumors (GI-NETs). Although generally well tolerated, hematologic toxicity remains clinically relevant, and long-term data beyond one year are limited. We performed a comprehensive assessment of incidence, severity, longitudinal trends, and correlates of hematologic toxicity following ^177Lu-DOTATATE.

METHODS

We performed an observational retrospective analysis of adults (≥18 years) with histologically confirmed GI-NETs who received ≥1 cycle of ^177Lu-DOTATATE between 2017 and 2024 and had baseline laboratory data within 30 days before treatment. Patients were excluded for known hematologic malignancy, concurrent cytotoxic chemotherapy during PRRT, or inadequate follow-up for toxicity grading, defined as no laboratory follow-up through one year. Hemoglobin, white blood cell and platelet counts were monitored at baseline and approximately 3, 6, 12, and 24 months. Toxicity was graded by CTCAE v6.0. Treatment delays, interruption/discontinuation, supportive interventions, and development of MDS were recorded. Descriptive statistics were used; exploratory associations were evaluated using Fisher's exact test.

RESULTS

Sixty-three treatment-course records were analyzed. Hematologic toxicity was common but mostly low grade. Grade ≥2 anemia occurred in 19/63 (30.2%), including Grade ≥3 anemia in 7/63 (11.1%). Anemia peaked at approximately 12 months, when Grade ≥2 anemia was observed in 13/62 (21.0%), improving to 6/47 (12.8%) at 24 months. Thrombocytopenia was the most clinically relevant toxicity. Grade ≥2 thrombocytopenia occurred in 9/63 (14.3%), including Grade ≥3 thrombocytopenia in 5/63 (7.9%). Clinically significant thrombocytopenia peaked at 6 months (6/63, 9.5%), decreasing to 4/62 (6.5%) at 12 months and 2/47 (4.3%) at 24 months. The strongest association was treatment

exposure: patients receiving >4 treatments had higher composite Grade ≥2 anemia/thrombocytopenia than those receiving four treatments (8/14, 57.1% vs 9/46, 19.6%; p≈0.015), and higher Grade ≥3 toxicity (5/14, 35.7% vs 2/46, 4.3%; p≈0.006). Tumor grade and metastatic burden showed no clear association. Five patients (7.9%) required treatment delay, interruption, or discontinuation; four (6.3%) required transfusion support and/or hospitalization. Three patients (4.8%) developed therapy-related MDS; two occurred after 8 treatments at approximately 9 and 15 months, and one after 3 treatments at approximately 12 months. Two additional patients had persistent multilineage cytopenias with macrocytosis concerning for MDS without confirmatory marrow evaluation.

CONCLUSIONS

Hematologic toxicity after ^{177}Lu-DOTATATE was frequent and predominantly low-grade, though Grade ≥3 cytopenias and MDS occurred in a clinically meaningful minority. Higher treatment exposure and repeat PRRT were associated with more severe cytopenias, supporting careful patient selection and closer monitoring during extended or repeat therapy. Delayed, persistent cytopenias warrant long-term follow-up and marrow evaluation when clinically indicated.

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