Adversе Events in Targeted Radionuclide Therapy

Harrison Agordzo MSc,[1] Jagruti Shah, MD, Erin Grady, MD PhD, John Kwofie, Donald Samaan, Kip E Guja, MD PhD[1],
Stanford University, Stanford Health Care

2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

ABSTRACT

Targeted radionuclide therapy (TRT) plays an important role in management of oncology patients, particularly those with thyroid cancer, prostate cancer, or neuroendocrine tumor. Use of TRTs has expanded rapidly in recent years, with approval of new agents and indications. The number of ongoing TRT clinical trials suggests that this trend is likely to continue in the future.

Adequate knowledge of potential adverse events and their management is essential for treating physicians to optimize outcomes in patients undergoing TRT. The authors review adverse events that may occur in TRT; their clinical manifestations, incidence, risk factors, and management; and strategies to prevent or decrease their risk of occurrence.

CONTACT

Harrison Agordzo, MSc.
Stanford University
480 Oak Rd, Stanford CA
hagordzo@stanford.edu
415-553-0884

INTRODUCTION

Radiopharmaceutical therapy (RPT) involves the use of radionuclides that are either linked to specific tumor-targeting agents (e.g. peptides or small molecules) or concentrate in tumors through natural physiological mechanisms that are increased in tumor cells (e.g. bone turnover in osseous metastases). Radioiodine therapy for thyroid cancer has been in use for more than 8 decades and is the most widely implemented RPT. Therapies not approved by the U.S. Food and Drug Administration (FDA) (eg, lead 212–based and actinium 225–based TRT agents) are beyond the scope of this article. Other bone-targeting agents such as samarium 153 and strontium 89 are also not addressed in this article because of their limited use in current clinical practice, since the advent of these newer therapeutic agents. 90Y microspheres are β-emitting embolic agents delivered percutaneously via a hepatic arterial microcatheter for local therapy of primary or metastatic liver malignancy. These devices exploit the dominance of hepatic arterial flow to tumor tissue, wherein normal liver tissue is supplied primarily by the portal vein, and tumor tissue is supplied predominantly by the hepatic artery.

METHODS AND MATERIALS

The RPT agents discussed herein include Lu-177 PSMA-617 (Pluvicto®), Lu-177 DOTATATE (Lutathera®), Ra-223 dichloride (Xofigo®), and high-specific activity (HSA) I-131 MIBG (Azedra®) and I-131 MIBG. The prototypical RPT agent, I-131 NaI has already been covered extensively in the literature and therefore is only briefly discussed here, with a focus primarily on the newer Lu-177-based agents. Lu-177 PSMA-617 is a beta emitting agent conjugated to vipivotide tetraxetan, a ligand that targets prostate-specific membrane antigen (PSMA), which is overexpressed on prostate cancer tumor cells.

Lu-177 PSMA-617 was FDA approved in 2022 for patients with PSMApositive metastatic castration-resistant prostate cancer previously treated with androgen receptor pathway inhibition and taxane-based chemotherapy.

RESULTS

Patients with bulky or extensive liver metastases can experience increased epigastric pain and nausea after TRT. This is shown in figure1.
These liver pain flare reactions are thought to be mediated by increased inflammation and edema secondary to tumor cell injury, resulting in stretching of the hepatic capsule and stimulation of pain fibers (56). Data on the incidence of liver pain flare related to TRT are limited, but one small study of 12 patients with metastatic neuroendocrine tumor treated with 177Lu-DOTATATE showed an incidence of 8% (one of 12) for grade 2–3 pain thought to be related to liver metastases (53). Patients with suspected liver pain flare can be treated with corticosteroids and analgesics, with additional antiemetics for any associated nausea or vomiting.

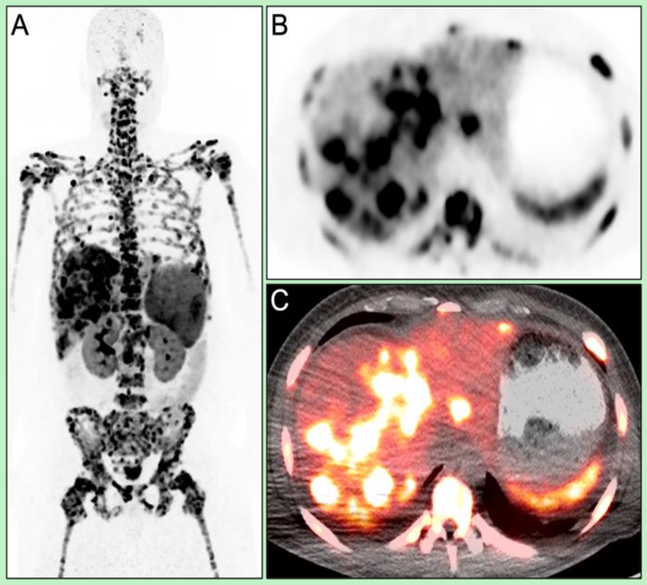

Figure 1. A 38-year-old man at risk for liver (epigastric) pain flare, bone pain flare, and hematologic (marrow) toxicity

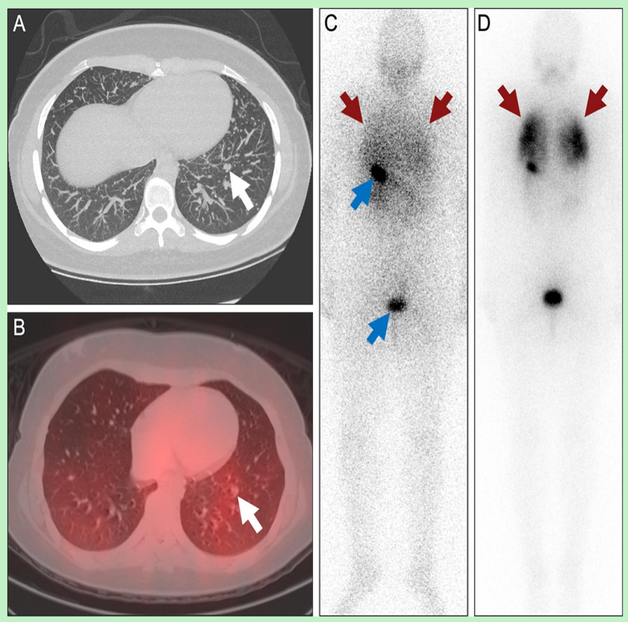

Figure 2. Extensive radioiodine-avid pulmonary metastases from differentiated thyroid cancer, at increased risk for pulmonary toxicity, in a 21-year-old woman with metastatic papillary thyroid cancer who had undergone thyroidectomy. She was treated with a dosimetry-based dose of 131I–sodium iodide

DISCUSSION

In 131I–sodium iodide therapy for thyroid cancer, the incidence of acute sialadenitis varies from 2% to 67% and the incidence of chronic sialadenitis ranges from 11% to 43% (61,62). Salivary gland toxicity related to 177Lu–PSMA-617 TRT including dry mouth and loss of taste is usually mild and transient, with variable incidence ranging from 20% to 60%. The incidence of xerostomia in the multicenter VISION and TheraP trials of 177Lu–PSMA-617 was 38.8% and 60%, respectively. An example patient with xerostomia after 177Lu–PSMA-617 TRT is shown below in figure 3. In general, the risk of salivary gland toxicity from TRT increases with the number of radiopharmaceutical cycles and the total radiation dose to the salivary glands

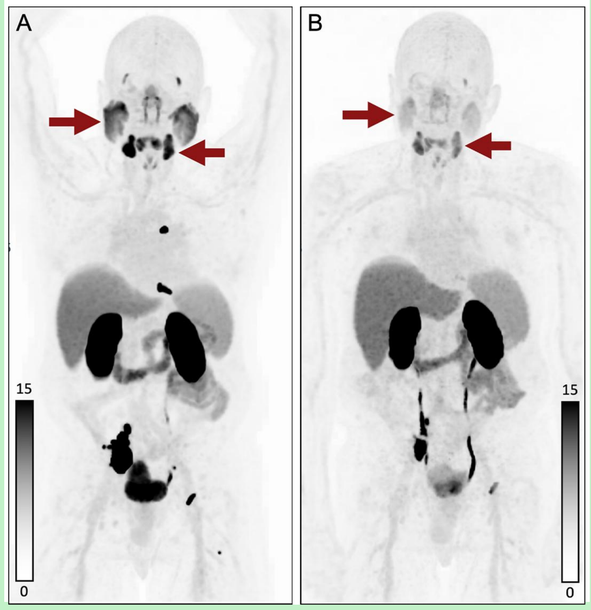

Figure 3. Salivary gland toxicity after ^{177}Lu–PSMA-617 therapy in an 84-year-old man. The patient had metastatic castration-resistant prostate cancer and was treated with six cycles of ^{177}Lu–PSMA-617 therapy; he developed symptomatic dry mouth (xerostomia)

CONCLUSIONS

In summary, while RPT is generally well-tolerated and has proven to be very effective, adverse events do occur and should be recognized and managed appropriately. Identifying patients at risk and implementation of preventative strategies or closer monitoring can improve patient safety and outcomes.

REFERENCES

1. NRC. Preliminary Evaluation of Radiopharmaceutical Extravasation and Medical Event Reporting. https://www.nrc.gov/docs/ML2122/ML21223A085.pdf. Published 2021. Updated
2. Duan H, Ferri V, Fisher GA, Shaheen S, Davidzon GA, Iagaru A, et al. Evaluation of Liver and Renal Toxicity in Peptide Receptor Radionuclide Therapy for Somatostatin Receptor Expressing Tumors: A 2-Year Follow-Up. Oncologist 2022;27(6):447-452.