LUTATHERA®
(lutetium Lu 177 dotatate)
injection, for intravenous use

Understanding Radiation Safety With LUTATHERA

Key information about radiation exposure and guidelines for radiation safety when caring for patients being treated with LUTATHERA

INDICATION

LUTATHERA® (lutetium Lu 177 dotatate) is indicated for the treatment of adult and pediatric patients aged 12 years and older with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Radiation Exposure:** Treatment with LUTATHERA contributes to a patient's overall long-term cumulative radiation exposure and is associated with an increased risk for cancer. Radiation can be detected in the urine for up to 30 days following LUTATHERA administration. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with LUTATHERA consistent with institutional good radiation safety practices, patient management procedures, Nuclear Regulatory Commission patient release guidance, and instructions to the patient for follow-up radiation protection at home.

Please see additional Important Safety Information throughout and full Prescribing Information.

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With LUTATHERA, beta radiation can be effectively used for GEP-NETs within safe limits[1-3]

LUTATHERA delivers beta minus (β^-) radiation to SSTR+ GEP-NETs[1]

- Beta radiation damages the DNA of SSTR+ cells, ultimately killing the cells[1,4]
- Radiation may also damage neighboring cells[1]

Limited penetration of β^- radiation[1]

- Maximum penetration in tissue is **2.2 millimeters** (mean, 0.67 mm)

Half-life of 6.65 days[1]

- Within **48 hours**, 65% is excreted through urine
- Within **14 days**, >99% is eliminated

GEP-NETs, gastroenteropancreatic neuroendocrine tumors; SSTR+, somatostatin receptor-positive.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression:** In the NETTER-1 clinical trial, myelosuppression occurred more frequently in patients receiving LUTATHERA with long-acting octreotide compared with patients receiving high-dose long-acting octreotide (all grades/grade 3/4): anemia (81%/0 vs 54%/1%), thrombocytopenia (53%/1% vs 17%/0), and neutropenia (26%/3% vs 11%/0). In NETTER-1, platelet nadir occurred at a median of 5.1 months following the first dose. Of the 59 patients who developed thrombocytopenia, 68% had platelet recovery to baseline or normal levels. The median time to platelet recovery was 2 months. Fifteen of the 19 patients in whom platelet recovery was not documented had post-nadir platelet counts.

Please see additional Important Safety Information throughout and full Prescribing Information.

Radiation exposures to the care team were within ICRP limits of 20 mSv per year[2,3,*]

Radiation exposure following treatment with Lutetium 177 on the LUTATHERA dosing regimen was tested in an outpatient study with 4 sequentially treated patients in a 4-bed room[2]

Exposure to nurses was similar to that of a flight crew on regular round-trip flights from Los Angeles to Honolulu[2,5]

Exposure is 14.5 µSv on a 5.2-hour flight from Los Angeles to Honolulu[5]

Mean whole-body radiation exposures per treatment day: 6.8 µSv (nuclear medicine technologist); 33.2 µSv (nurse)[2]

*Averaged over a defined period of 5 years, with no single year exceeding 50 mSv.[3]

Seventy-six patients with progressive, metastatic NETs received 4 cycles of 7.8 GBq of Lutetium 177 at 8-week intervals in an outpatient setting at 1 treatment center. Four patients were treated sequentially on each therapy day in a 4-bed room in the hospital's day procedure unit, with each patient remaining until radiation exposure was below the release limit. Radiation exposures to HCPs and caregivers were monitored by personal dosimeter. Twenty-five carers were provided with electronic dosimeters. In the nearby staff office with a 50% staff occupancy factor, the mean (range) exposure rate measured on 10 different therapy administration days was 1.6 µSv/h (1.3–2.0 µSv/h), and at the nursing station with 100% staff occupancy it was 3.5 µSv/h (2.9–4.0 µSv/h).[2]

µSv, microsievert; GBq, gigabecquerel; HCPs, health care professionals; ICRP, International Commission on Radiological Protection; mSv, millisievert; NETs, neuroendocrine tumors.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression (continued):** Among these 15 patients, 5 improved to grade 1, 9 to grade 2, and 1 to grade 3. Monitor blood cell counts. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of myelosuppression.

Please see additional Important Safety Information throughout and full Prescribing Information.

Exposure to caregivers was similar to that of a chest x-ray[2,6]

X-ray exposure is 100 µSv[6]

Mean total exposure during the day of therapy and at home for up to 5 days: 90 µSv (median, 40 µSv [range, 10 µSv-470 µSv])[2]

Patients are only discharged from the treatment center when radiation exposure to others does not exceed regulatory thresholds[7]

Seventy-six patients with progressive, metastatic NETs received 4 cycles of 7.8 GBq of Lutetium 177 at 8-week intervals in an outpatient setting at 1 treatment center. Four patients were treated sequentially on each therapy day in a 4-bed room in the hospital's day procedure unit, with each patient remaining until radiation exposure was below the release limit. Radiation exposures to HCPs and caregivers were monitored by personal dosimeter. Twenty-five carers were provided with electronic dosimeters. In the nearby staff office with a 50% staff occupancy factor, the mean (range) exposure rate measured on 10 different therapy administration days was 1.6 µSv/h (1.3–2.0 µSv/h), and at the nursing station with 100% staff occupancy it was 3.5 µSv/h (2.9–4.0 µSv/h).[2]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Secondary Myelodysplastic Syndrome and Leukemia:** In NETTER-1, with a median follow-up time of 76 months in the main study, myelodysplastic syndrome (MDS) was reported in 2.3% of patients receiving LUTATHERA with long-acting octreotide compared with no patients receiving high-dose long-acting octreotide. In ERASMUS, a phase 2 clinical study, 16 patients (2.0%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to onset was 29 months (range, 9-45 months) for MDS and 55 months (range, 32-125 months) for acute leukemia.

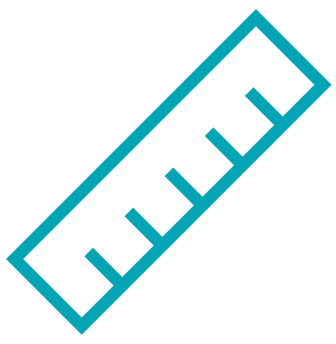
Please see additional Important Safety Information throughout and full Prescribing Information.

Radiation safety guidelines for HCPs

Treatment safety guidelines for HCPs: ALARA (As Low As Reasonably Achievable)[8]

Following the principles of ALARA can help minimize radiation exposure. These principles include avoiding unnecessary exposure to radiation by using 3 protective measures[8]:

Minimize the time spent near radioligand therapy



Maximize the distance from radioligand therapy

Use appropriate shielding from radioligand therapy

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity:** In ERASMUS, 8 patients (<1%) developed renal failure 3 to 36 months following LUTATHERA. Two of these patients had underlying renal impairment or risk factors for renal failure (eg, diabetes or hypertension) and required dialysis. Administer the recommended amino acid solution before, during, and after LUTATHERA to decrease the reabsorption of lutetium Lu 177 dotatate through the proximal tubules and decrease the radiation dose to the kidneys. Advise patients to hydrate and to urinate frequently before, on the day of, and on the day after administration of LUTATHERA. Monitor serum creatinine and calculated creatinine clearance.

Please see additional Important Safety Information throughout and full Prescribing Information.

Radiation safety guidelines for patients

Posttreatment safety guidelines for patients (NANETS/SNMMI consensus and Mayo Clinic recommendations)

Your treatment center may provide more specific guidance, but here are some frequently discussed topics regarding posttreatment LUTATHERA radiation precautions.

Staying hydrated

Patients should drink liquids and urinate frequently before, on the day of, and on the day after administration of LUTATHERA.[1]

Using the toilet

For at least 3 days, patients should use the toilet in a seated position (even for men) and flush the toilet twice after use.[9]

Showering and personal hygiene

For at least 7 days, patients should shower daily. For at least 3 days, patients should use separate towels and washcloths and wash laundry separately from the rest of their household.[9,10]

NANETS, North American Neuroendocrine Tumor Society;
SNMMI, Society of Nuclear Medicine and Molecular Imaging.

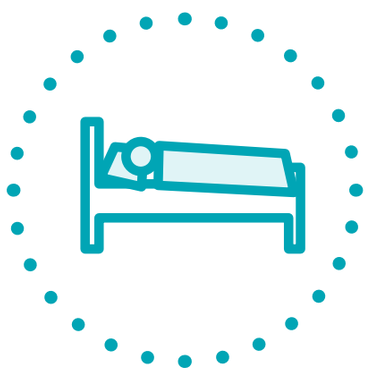
IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity (continued):** Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of renal toxicity. Patients with baseline renal impairment may be at increased risk of toxicity due to increased radiation exposure; perform more frequent assessments of renal function in patients with baseline mild or moderate impairment. LUTATHERA has not been studied in patients with baseline severe renal impairment (creatinine clearance <30 mL/min) or those with end-stage renal disease.

Please see additional Important Safety Information throughout and full Prescribing Information.

Radiation safety guidelines for patients (continued)



Sleeping

For at least 3 days, patients should sleep in a separate bed and avoid intimate contact.[9]

Interacting with others

For at least 3 days, patients should use a general distance guideline of no closer than 3 feet for no more than 1 hour per day. They should try to maintain a distance of 6 feet from others and minimize use of public transportation and public facilities.[9]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hepatotoxicity:** In ERASMUS, 2 patients (<1%) were reported to have hepatic tumor hemorrhage, edema, or necrosis, with 1 patient experiencing intrahepatic congestion and cholestasis. Patients with hepatic metastasis may be at increased risk of hepatotoxicity due to radiation exposure. Monitor transaminases, bilirubin, serum albumin, and the international normalized ratio during treatment. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of hepatotoxicity.

Please see additional Important Safety Information throughout and full Prescribing Information.

LUTATHERA has a well-established safety profile[1,11,12]

NETTER-2 safety data are consistent with the established profile of LUTATHERA seen in NETTER-1[1,11,12]

- **In NETTER-2:** The most common grade 3/4 adverse events (>3% in either arm) were lymphocyte count decreased (5% vs 0%), GGT increased (5% vs 3%), small intestinal obstruction (3% vs 0%), and abdominal pain (3% vs 4%) for LUTATHERA + 30 mg octreotide LAR vs 60 mg octreotide LAR, respectively[12]
- **In NETTER-1:** The most common grade 3/4 adverse reactions with a higher incidence in the LUTATHERA arm were lymphopenia (44%), increased GGT (20%), vomiting (7%), nausea (5%), increased AST (5%), increased ALT (4%), hyperglycemia (4%), and hypokalemia (4%)[1]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; LAR, long-acting release.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema, occurred in patients treated with LUTATHERA. Monitor patients closely for signs and symptoms of hypersensitivity reactions, including anaphylaxis, during and following LUTATHERA administration for a minimum of 2 hours in a setting in which cardiopulmonary resuscitation medication and equipment are available. Discontinue the infusion upon the first observation of any signs or symptoms consistent with a severe hypersensitivity reaction and initiate appropriate therapy. Premedicate patients with a history of grade 1/2 hypersensitivity reactions to LUTATHERA before subsequent doses. Permanently discontinue LUTATHERA in patients who experience grade 3/4 hypersensitivity reactions.

Please see additional Important Safety Information throughout and full Prescribing Information.

No new safety signals were reported in the 5-year, long-term follow-up for NETTER-1[13,*]

Adverse Events	During the long-term follow-up, only serious adverse events (SAEs) deemed related to treatment with LUTATHERA and AEs of special interest (hematotoxicity, cardiovascular events, and nephrotoxicity, regardless of causality) in the LUTATHERA arm were reported[13]
Grade ≥3 Treatment-Related SAEs During the Entire Study	7 (6%) of 111 patients treated in the LUTATHERA arm[13]
Incidence of Treatment-Related SAEs During the Long-Term Follow-Up Period	**3 (3%) of 111 patients treated with LUTATHERA[13]** — 2 (1.8%) patients experienced at least 1 grade ≥3 SAE (1 grade 5 MDS event)[13] — 1 (0.9%) patient experienced an SAE leading to study discontinuation[13]

*Cutoff date for final analysis was January 18, 2021.[13]

AEs, adverse events; MDS, myelodysplastic syndrome.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Neuroendocrine Hormonal Crisis:** Neuroendocrine hormonal crises, manifesting with flushing, diarrhea, bronchospasm, and hypotension, occurred in <1% of patients in ERASMUS and typically occurred during or within 24 hours following the initial LUTATHERA dose. Two (<1%) patients were reported to have hypercalcemia. Monitor patients for flushing, diarrhea, hypotension, bronchoconstriction, or other signs and symptoms of tumor-related hormonal release. Administer intravenous somatostatin analogues, fluids, corticosteroids, and electrolytes as indicated.

Please see additional Important Safety Information throughout and full Prescribing Information.

No new safety signals were reported in the 5-year, long-term follow-up for NETTER-1[13,*] (continued)

MDS or Acute Leukemia	**No new cases were reported during long-term follow-up[13]** — MDS incidence from the Prescribing Information for LUTATHERA: In NETTER-1, with a median follow-up time of 76 months in the main study, MDS was reported in 2.3% of patients receiving LUTATHERA with long-acting octreotide compared with no patients receiving high-dose, long-acting octreotide[1,13] — In ERASMUS, 16 patients (2.0%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to onset was 29 months (range, 9-45 months) for MDS and 55 months (range, 32-125 months) for acute leukemia[1,a]
Diffuse Large B-Cell Lymphoma	One patient developed diffuse large B-cell lymphoma during long-term follow-up that was deemed unrelated to treatment with LUTATHERA[13]
Nephrotoxicity of Grade ≥3, Regardless of Causality	Reported in 6 (5%) of 111 patients in the LUTATHERA arm and 4 (4%) of 112 patients in the control arm during the study[13]

*Cutoff date for final analysis was January 18, 2021.[13]

[a] ERASMUS study design: Retrospective safety data are available from 1214 patients in ERASMUS, an international, single-institution, single-arm, open-label trial of patients with SSTR-positive tumors (neuroendocrine and other primaries). The median duration of follow-up was >4 years.[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

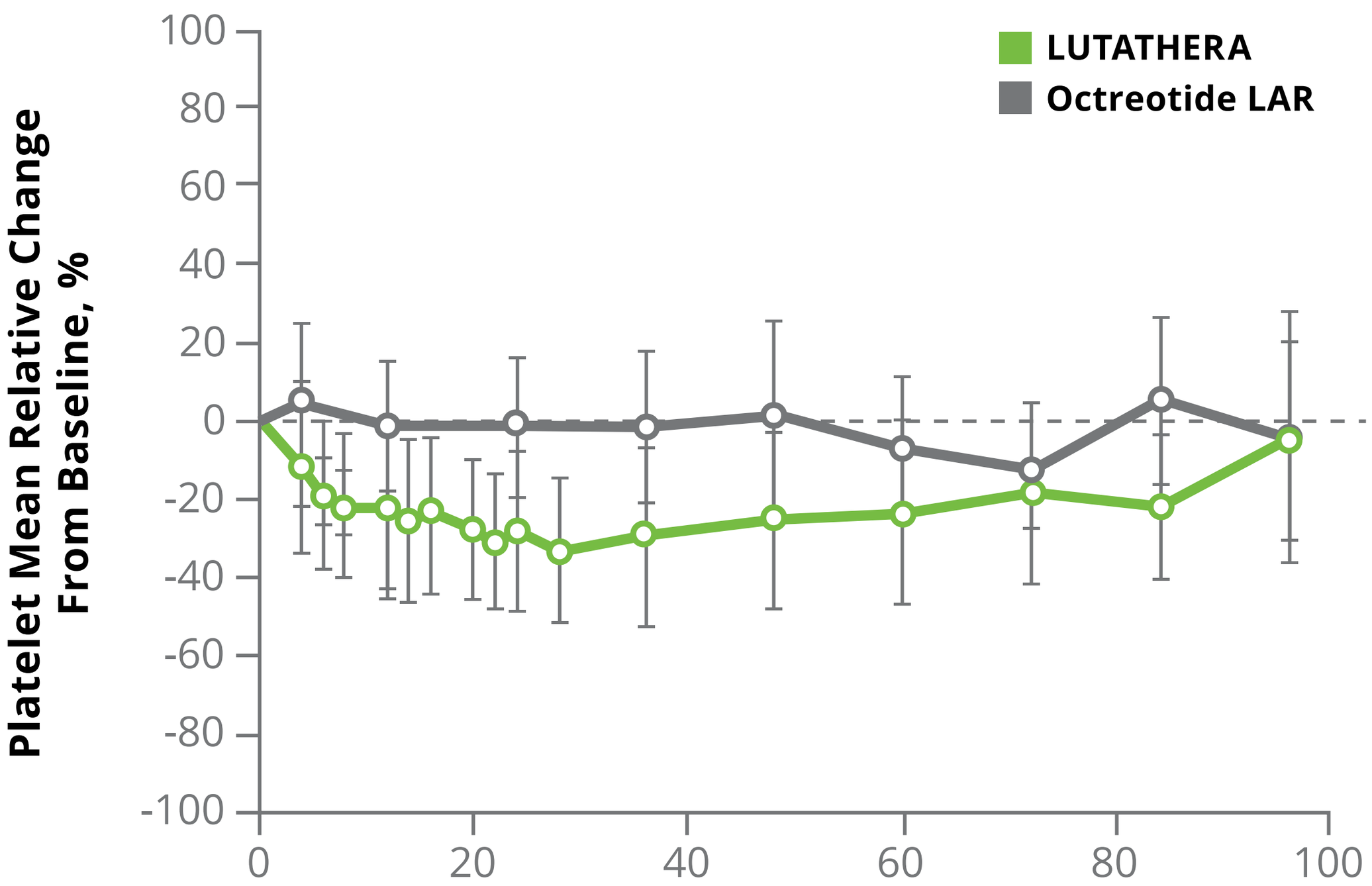
- **Embryo-Fetal Toxicity:** LUTATHERA can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to initiating LUTATHERA. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LUTATHERA and for 7 months after the last dose.

Please see additional Important Safety Information throughout and full Prescribing Information.

Hematologic cell counts trended back to baseline over 2 years[14]

Hematologic events from NETTER-1: Mean relative change from baseline over time[14]

Platelet count relative changes



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

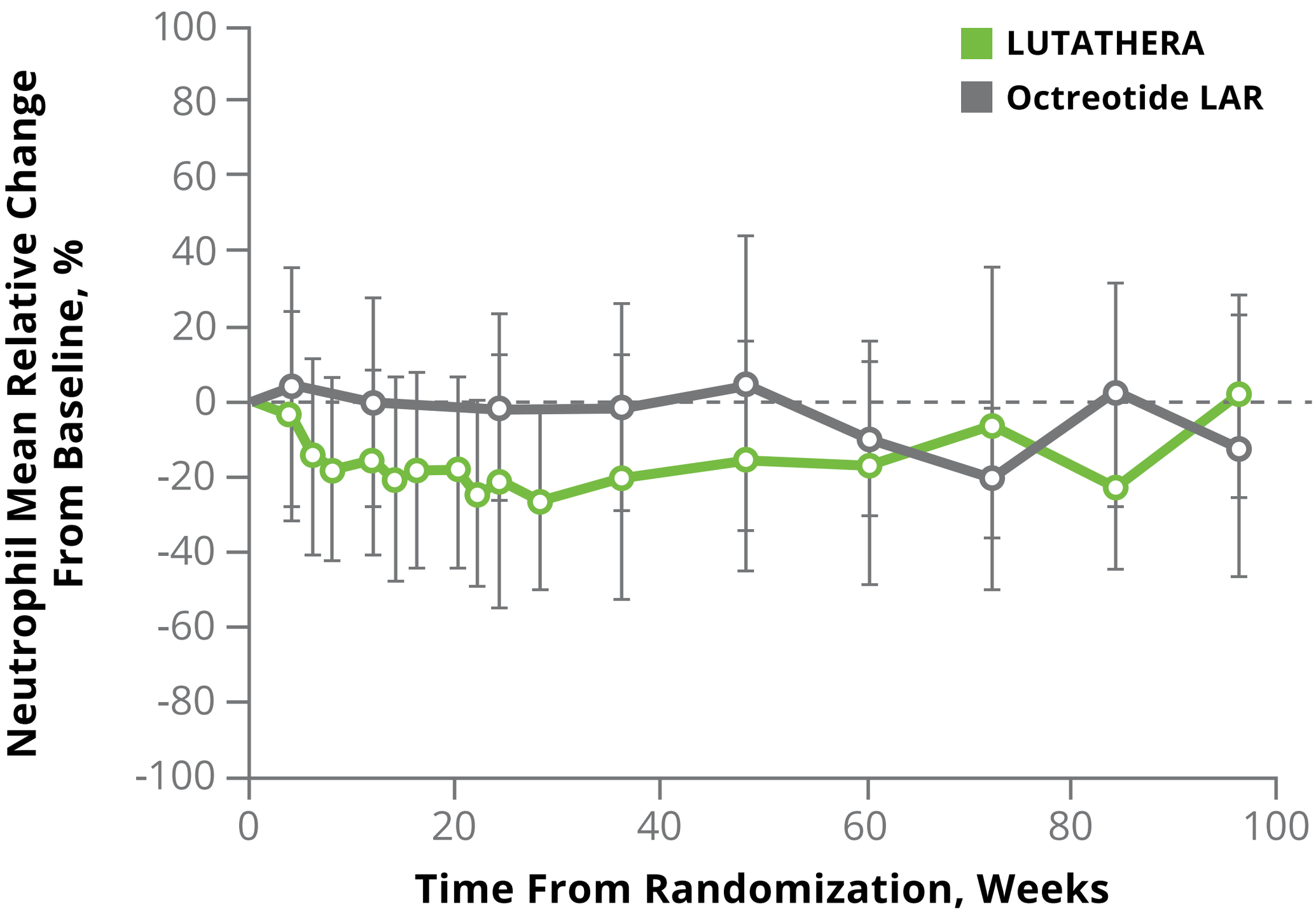
- **Embryo-Fetal Toxicity (continued):** Advise males with female partners of reproductive potential to use effective contraception during treatment with LUTATHERA and for 4 months after the last dose.
- **Risk of Infertility:** LUTATHERA may cause infertility in males and females. Radiation absorbed by testes and ovaries from the recommended cumulative LUTATHERA dose falls within the range in which temporary or permanent infertility can be expected following external beam radiotherapy.

Please see additional Important Safety Information throughout and full Prescribing Information.

Hematologic cell counts trended back to baseline over 2 years[14] (continued)

Hematologic events from NETTER-1: Mean relative change from baseline over time[14] (continued)

Neutrophil count relative changes



IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

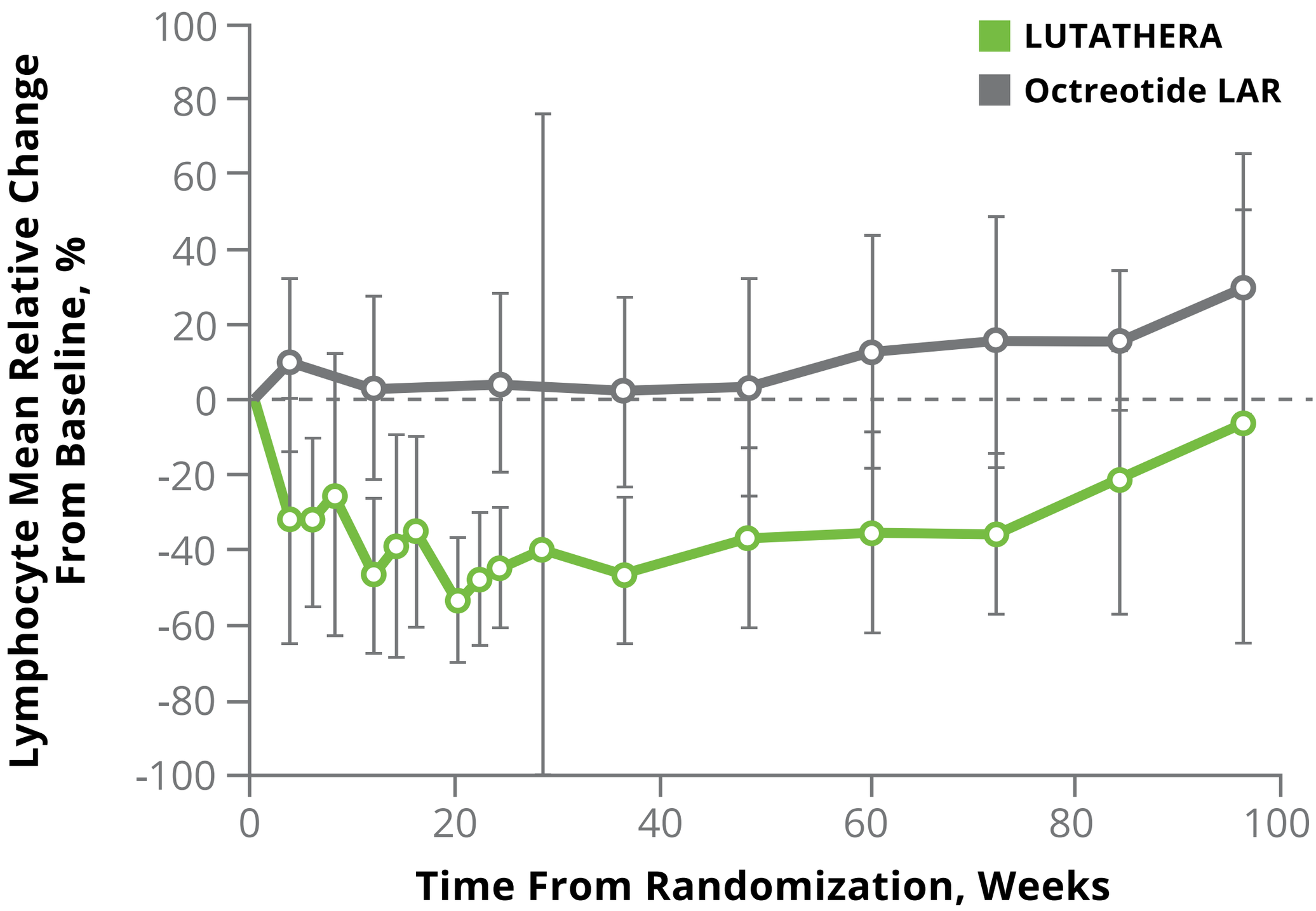
The most common grade 3/4 adverse reactions (≥4% with a higher incidence in the LUTATHERA arm) observed in NETTER-1 were lymphopenia (44%), increased gamma-glutamyl transferase (20%), vomiting (7%), nausea (5%), increased aspartate aminotransferase (5%), increased alanine aminotransferase (4%), hyperglycemia (4%), and hypokalemia (4%).

Please see additional Important Safety Information throughout and full Prescribing Information.

Hematologic cell counts trended back to baseline over 2 years[14] (continued)

Hematologic events from NETTER-1: Mean relative change from baseline over time[14] (continued)

Lymphocyte count relative changes



IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

In ERASMUS, the following serious adverse reactions have been observed with a median follow-up time of >4 years after treatment with LUTATHERA: myelodysplastic syndrome (2%), acute leukemia (1%), renal failure (2%), hypotension (1%), cardiac failure (2%), myocardial infarction (1%), and neuroendocrine hormonal crisis (1%). Patients should be counseled and monitored in accordance with the LUTATHERA Prescribing Information.

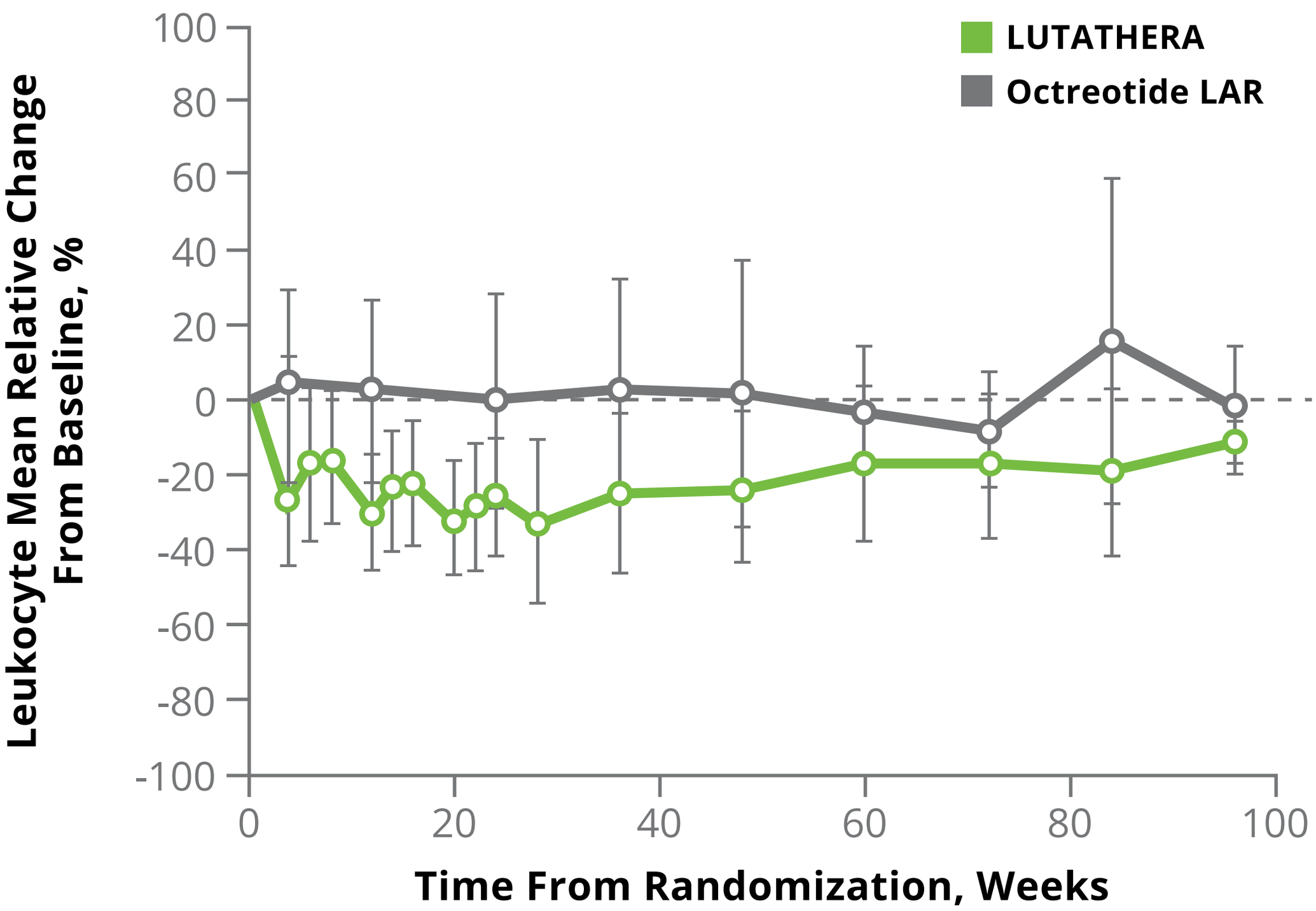
Adverse reactions observed in pediatric patients were similar to those observed in adults treated with LUTATHERA.

Please see additional Important Safety Information throughout and full Prescribing Information.

Hematologic cell counts trended back to baseline over 2 years[14] (continued)

Hematologic events from NETTER-1: Mean relative change from baseline over time[14] (continued)

Leukocyte count relative changes



IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS

Discontinue long-acting somatostatin analogues at least 4 weeks and short-acting octreotide at least 24 hours prior to each LUTATHERA dose.

SPECIFIC POPULATIONS

Lactation: Advise patients not to breastfeed during LUTATHERA treatment.

Please see additional Important Safety Information throughout and full Prescribing Information.

MENU

Stay confident in the targeted power of LUTATHERA for SSTR+ GEP-NETs[1]

View the full efficacy and safety profile at LUTATHERA-hcp.com

Not an actual patient.

References: 1. Lutathera. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Calais PJ, Turner JH. Radiation safety of outpatient ^{177}Lu-octreotate radiopeptide therapy of neuroendocrine tumors. *Ann Nucl Med.* 2014;28(6):531-539. **3.** US Department of Health and Human Services: Radiation Emergency Medical Management. International Commission on Radiological Protection (ICRP) guidance for occupational exposure. Updated May 3, 2024. Accessed January 28, 2025. https://remm.hhs.gov/ICRP_guidelines.htm **4.** O'Neill E, Kersemans V, Allen PD, et al. Imaging DNA damage repair in vivo after ^{177}Lu-DOTATATE therapy. *J Nucl Med.* 2020;61(5):743-750. **5.** Friedberg W, Copeland K, Duke FE, O'Brien K III, Darden EB Jr. Radiation exposure during air travel: guidance provided by the Federal Aviation Administration for air carrier crews. *Health Phys*. 2000;79(5):591-595. **6.** United States Environmental Protection Agency. Radiation sources and doses. Updated February 22, 2024. Accessed June 30, 2024. https://www.epa.gov/radiation/radiation-sources-and-doses **7.** Siegel JA. Guide for diagnostic nuclear medicine. Society of Nuclear Medicine; 2001. Accessed August 30, 2024. https://www.nrc.gov/docs/ML0222/ML022250828.pdf **8.** U.S. Centers for Disease Control and Prevention. Guidelines for ALARA—as low as reasonably achievable. Updated February 26, 2024. Accessed August 9, 2024. https://www.cdc.gov/radiation-health/safety/alara.html **9.** Hope TA, Abbott A, Colucci K, et al. NANETS/SNMMI procedure standard for somatostatin receptor-based peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE. *J Nucl Med*. 2019;60(7):937-943. **10.** Kendi AT, Halfdanarson TR, Packard A, Dundar A, Subramaniam RM. Therapy with ^{177}Lu-DOTATATE: clinical implementation and impact on care of patients with neuroendocrine tumors. *AJR Am J Roentgenol*. 2019;213(2):309-317. **11.** Strosberg J, El-Haddad G, Wolin E, et al; for the NETTER-1 trial investigators. Phase 3 trial of ^{177}Lu-dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017;376(2):125-135. **12.** Singh S, Halperin D, Myrehaug S, et al. [^{177}Lu]Lu-DOTA-TATE plus long-acting octreotide versus high-dose long-acting octreotide for the treatment of newly diagnosed, advanced grade 2-3, well-differentiated, gastroenteropancreatic neuroendocrine tumours (NETTER-2): an open label, randomised, phase 3 study. *Lancet*. 2024;403(10446):2807-2817. **13.** Strosberg JR, Caplin ME, Kunz PL, et al; NETTER-1 investigators. ^{177}Lu-dotatate plus long-acting octreotide versus high-dose long-acting octreotide in patients with midgut neuroendocrine tumours (NETTER-1): final overall survival and long-term safety results from an open-label, randomised, controlled, phase 3 trial. *Lancet Oncol*. 2021;22(12):1752-1763. **14.** Strosberg J, El-Haddad G, Wolin E, et al; for the NETTER-1 trial investigators. Phase 3 trial of ^{177}Lu-dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017;376(2)(suppl):125-135.

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LUTATHERA®
(lutetium Lu 177 dotatate)
injection, for intravenous use

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