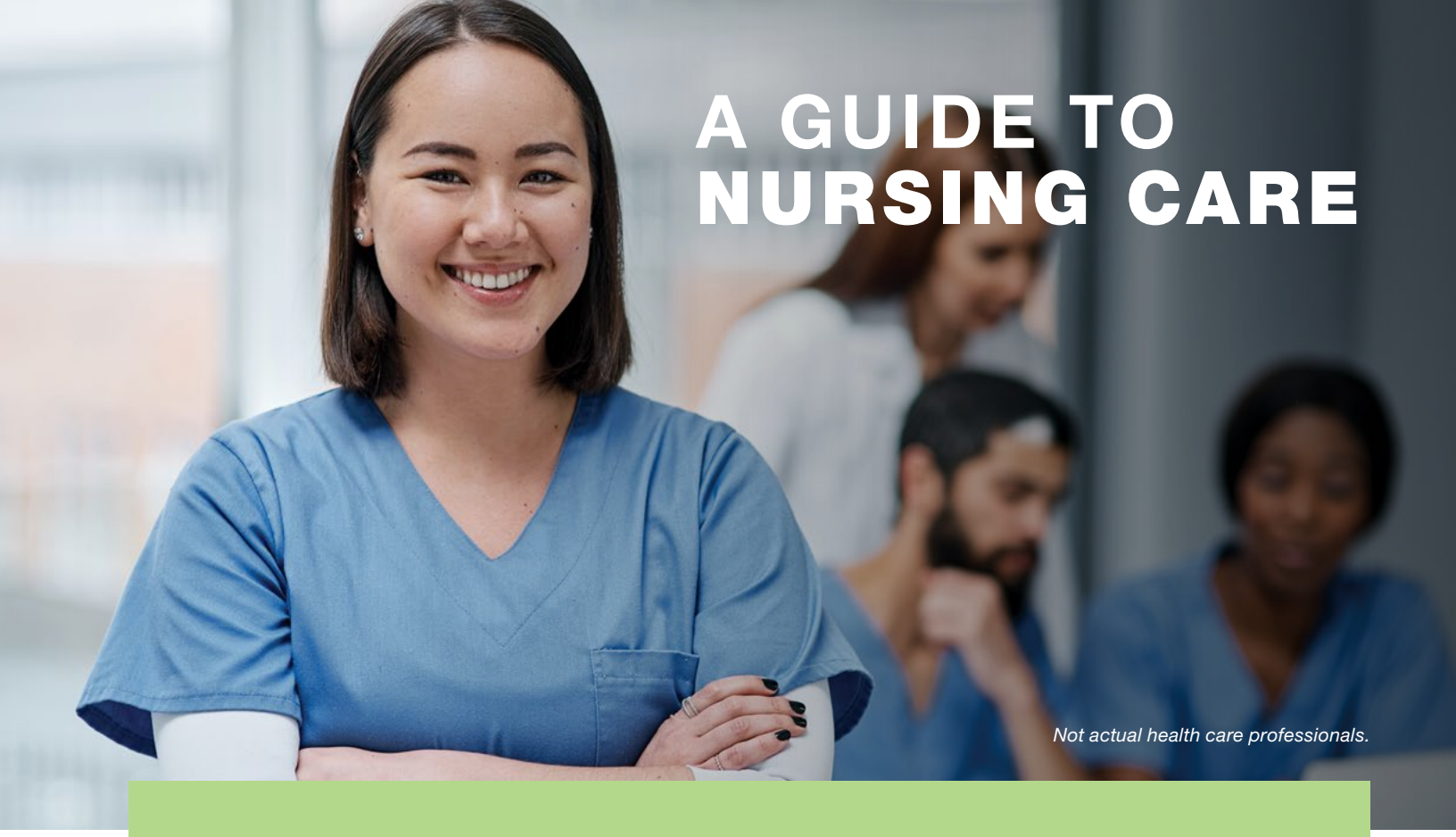

Learn more about **LUTATHERA** and see how it may help patients with GEP-NETs[1]

GEP-NETs, gastroenteropancreatic neuroendocrine tumors.

INDICATION

LUTATHERA® (lutetium Lu 177 dotatate) is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

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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When Treating Patients With GEP-NETs,

A MULTIDISCIPLINARY TEAM APPROACH IS RECOMMENDED

The roles and responsibilities outlined here provide general guidance for those involved in the treatment process with LUTATHERA. It is important to keep in mind that guidelines may vary by institution.

Team Members, Roles, and Responsibilities When Treating With LUTATHERA

MEDICAL ONCOLOGY PRACTICE

Identify

- Patient with GEP-NET in the foregut, midgut, or hindgut[1]

Refer

- Referring oncologist confirms SSTR presence and may order SSTR imaging[1,2]

NUCLEAR MEDICINE OR RADIATION ONCOLOGY PRACTICE

Test

- Conduct molecular imaging test for tumor localization[1,2]

MEDICAL ONCOLOGY PRACTICE

Determine

- Whether treatment with LUTATHERA is appropriate[1]

Refer

- Referring oncologist prescribes LUTATHERA, if appropriate, and refers patient to treatment site[1]

NURSE OR OTHER HEALTH CARE PROFESSIONAL

Confirm

- Discontinue long-acting SSA ≥4 weeks prior to the administration of LUTATHERA[1]
- Administer short-acting octreotide as needed; discontinue at least 24 hours prior to initiating LUTATHERA[1]
- Patient undergoes periodic laboratory testing as needed[1]
- Pregnancy status must be verified for women of childbearing potential[1]

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. 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.

When Treating Patients With GEP-NETs,

A MULTIDISCIPLINARY TEAM APPROACH IS RECOMMENDED (continued)

NUCLEAR MEDICINE OR RADIATION ONCOLOGY PRACTICE

Administer

- Patient treated with LUTATHERA
- Recommended treatment cycle is administered 4 times at 8-week intervals[1]

NURSE OR OTHER HEALTH CARE PROFESSIONAL

On day of infusion

- Patient checks in for treatment
- Assessment, expectations of the day, orientation of the room
- Administer antiemetics before the recommended amino acid solution to prevent nausea and vomiting[1,2]
- Initiate an IV sterile amino acid solution containing L-lysine and L-arginine 30 minutes before administering LUTATHERA. Continue the infusion during and for at least 3 hours after the completion of the infusion of LUTATHERA. Do not decrease the dose of the amino acid solution if a reduced dose of LUTATHERA is administered. Premedicate patients who have had prior grade 1/2 hypersensitivity reactions to LUTATHERA. Do not rechallenge patients who experience grade 3/4 hypersensitivity reactions to LUTATHERA[1]
- Patient is treated with LUTATHERA
- After treatment, discharge instructions are given[1,2]
- Dispose of any unused medicinal product or waste material in accordance with local and federal laws[1]

MEDICAL ONCOLOGY PRACTICE

or

NUCLEAR MEDICINE OR RADIATION ONCOLOGY PRACTICE

After treatment with LUTATHERA

- Long-acting octreotide 30 mg IM is administered between 4 and 24 hours after each dose of LUTATHERA. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose of LUTATHERA. Short-acting octreotide may be given for symptomatic management during treatment with LUTATHERA, but must be withheld for at least 24 hours before each LUTATHERA dose[1]
- Patient is monitored for adverse reactions, and laboratory abnormalities[1]

After the treatment course is completed

- Long-acting octreotide 30 mg IM should continue every 4 weeks until disease progression or for 18 months following treatment initiation at the discretion of the physician[1]
- Continue to follow up with laboratory tests and adverse events as deemed necessary[1]

IM, intramuscular; IV, intravenous; SSA, somatostatin analog; SSTR, somatostatin receptor.

"You play a key role in the multidisciplinary team approach and are an essential touchpoint for patients in your care"

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.

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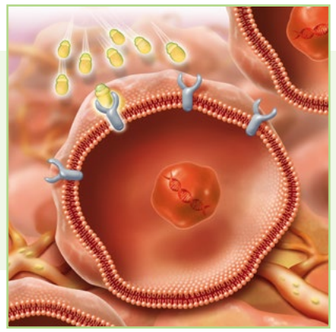
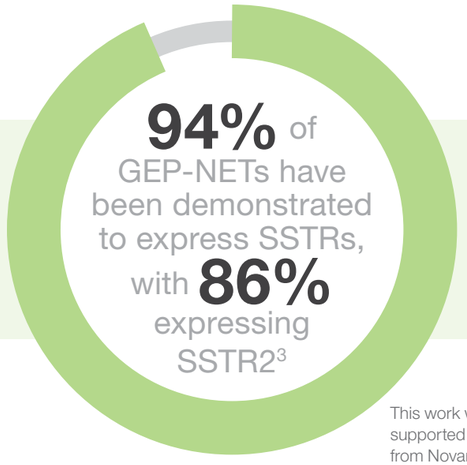
THE SCIENCE BEHIND LUTATHERA

LUTATHERA is a peptide receptor radionuclide that binds to SSTRs on the surface of cells that express this receptor.[1]





This work was supported by grants from Novartis.

Due to the high density of SSTR expression on GEP-NETs, they may be considered for targeted treatment with LUTATHERA.[1,3]

***Your knowledge of GEP-NETs and SSTR expression can help patients have a better understanding of the role of a targeted approach with* LUTATHERA[1]**

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. 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.

HOW LUTATHERA WORKS

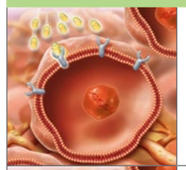
LUTATHERA is a targeted treatment that uses radiation to damage SSTR-positive cells and neighboring cells.[1]

LUTATHERA has a **2-part approach** that targets and enters SSTR-positive cells, releasing energy in the form of radiation that damages them and nearby cells.[1]

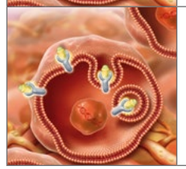
In other words, LUTATHERA serves as a "key" that specifically seeks and connects with the "lock," or SSTRs, on target cells.[1]

1

PRECISION TARGETING FOR SSTR CELLS



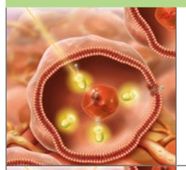
LUTATHERA is designed to contain a tumor-targeting component that helps find cells with SSTRs, including GEP-NET cancer cells.[1]



Once it finds these target cells, LUTATHERA is designed to bind to the SSTRs located on the outside of the cells.[1]

2

ENTERS THE CELL



After LUTATHERA binds to the SSTRs, it is designed to enter into the cell.[1]

LUTATHERA delivers radiation that causes damage to the SSTR-positive cells and nearby cells.[1]

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.
- **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.

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ADMINISTRATION SETUP OF GRAVITY METHOD FOR LUTATHERA

Administration Guidelines

These are not inclusive of every step; please refer to the full Prescribing Information (section 2.5) for detailed instructions.

ANTIEMETICS	• Premedication with antiemetics must be given before amino acid solution infusion[1]
AMINO ACID SOLUTION	• Intravenous sterile amino acid solution containing L-lysine and L-arginine must begin 30 minutes before the start of LUTATHERA[1] —Continue the amino acid solution infusion during and for at least 3 hours after the completion of the infusion of LUTATHERA[1] —Do not decrease the dose of the amino acid solution if a reduced dose of LUTATHERA is administered[1] —Use a 3-way valve to administer the amino acid solution using the same venous access as LUTATHERA or administer in the patient's other arm (separate venous access)[1]
HYPERSENSITIVITY PROPHYLAXIS AND MONITORING	• Premedicate patients who have had prior grade 1/2 hypersensitivity reactions to LUTATHERA. Do not rechallenge patients who experience grade 3/4 hypersensitivity reactions to 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 where 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[1]
MONITORING FOR NEUROENDOCRINE HORMONAL CRISIS	• Monitor patients for flushing, diarrhea, hypotension, bronchoconstriction, or other signs and symptoms of tumor-related hormonal release. Please see Important Safety Information and full Prescribing Information for additional information[1]
ADMINISTRATION METHOD FOR LUTATHERA[a]	• The gravity method, peristaltic pump method, or the syringe pump method may be used for the administration of the recommended dosage[1] • Use the peristaltic pump or syringe pump method when administering a reduced dose of LUTATHERA following a dosage modification for an adverse reaction. When using the gravity method for a reduced dose, adjust the LUTATHERA dose before the administration to avoid the delivery of an incorrect volume of LUTATHERA[1]

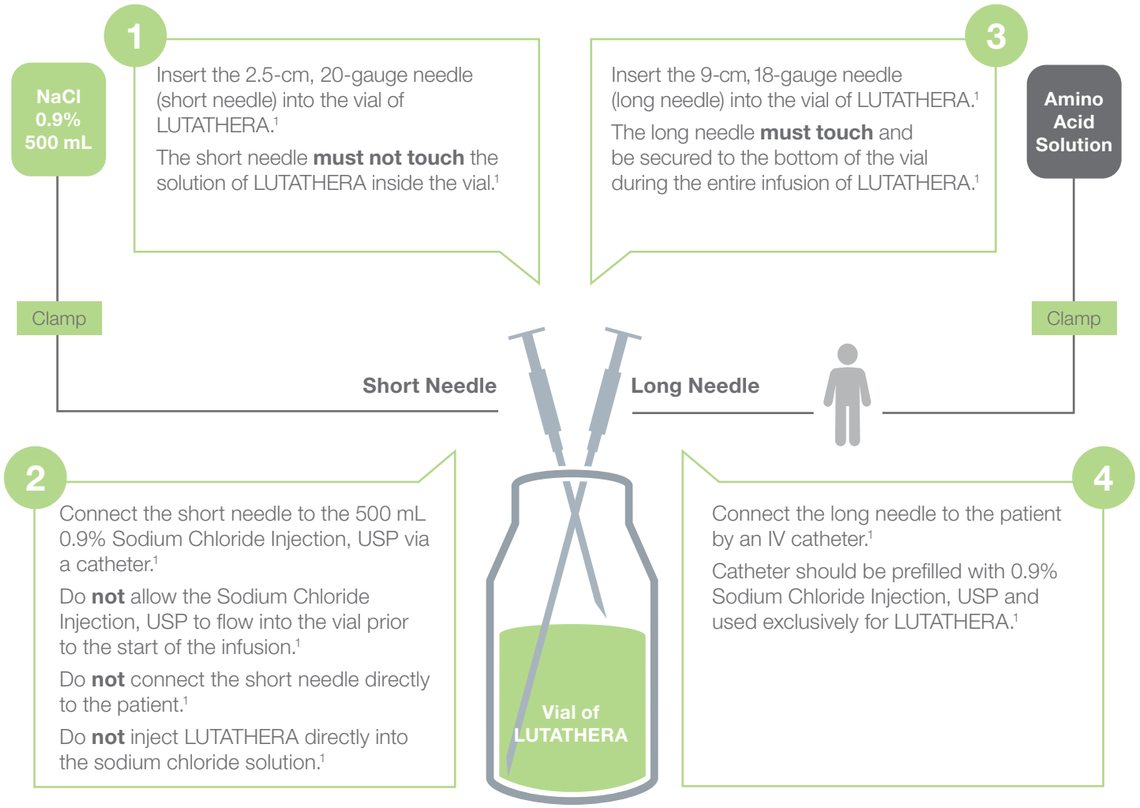
[a]Refer to the full Prescribing Information for instructions on the gravity method, peristaltic pump method, and the syringe pump method.

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

ADMINISTRATION SETUP OF GRAVITY METHOD FOR LUTATHERA (continued)

Short- and Long-Needle Instructions

These are not inclusive of every step; please refer to the full Prescribing Information (section 2.5) for detailed instruction on the gravity method, peristaltic pump method, and the syringe pump method.



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 analogs, fluids, corticosteroids, and electrolytes as indicated.
- **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. Advise males with female partners of reproductive potential to use effective contraception during treatment with LUTATHERA and for 4 months after the last dose.

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TREATMENT REGIMEN FOR LUTATHERA

LUTATHERA is approved as a 4-dose treatment regimen, given once every 8 weeks.[1]

RECOMMENDED DOSAGE	• The recommended dosage of LUTATHERA is 7.4 GBq (200 mCi) IV, every 8 weeks (±1 week), for a total of 4 doses[1]
DOSE MODIFICATION	• The dosage of LUTATHERA should be modified based on hematologic, renal, hepatic, hypersensitivity, or other nonhematologic adverse reactions (see full Prescribing Information)[1]
ADVERSE REACTIONS	• Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on severity of adverse reactions (see full Prescribing Information)[1]
USE OF SSAs	• Discontinue long-acting SSAs for at least 4 weeks prior to initiating LUTATHERA[1] • Administer short-acting octreotide as needed for symptom management; discontinue at least 24 hours prior to initiating LUTATHERA[1] • Administer long-acting octreotide 30 mg IM between 4 and 24 hours after each dose of LUTATHERA. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose of LUTATHERA[1] • Continue long-acting octreotide 30 mg IM every 4 weeks after completing LUTATHERA until disease progression or for 18 months following treatment initiation at the discretion of the physician[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

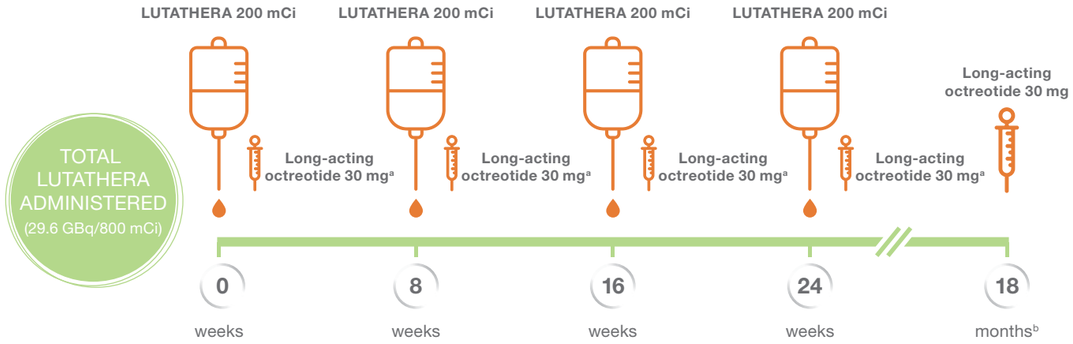
- **Risk of Infertility:** LUTATHERA may cause infertility in males and females. Radiation absorbed by testes and ovaries from the recommended cumulative LUTATHERA dose falls within the range in which temporary or permanent infertility can be expected following external beam radiotherapy.

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

TREATMENT REGIMEN FOR LUTATHERA (continued)

Treatment Regimen for LUTATHERA[1]

Administer premedications and concomitant medications as recommended in the full Prescribing Information. Monitor patients with laboratory testing as needed.[1]



Long-acting SSAs should be discontinued for at least 4 weeks prior to initiating LUTATHERA.[1]

Short-acting octreotide may be given for symptomatic management during treatment with LUTATHERA, but must be withheld for at least 24 hours before each dose of LUTATHERA.[1]

[a]Administer long-acting octreotide 30 mg IM between 4 and 24 hours after each dose of LUTATHERA. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose of LUTATHERA.[1]
-The interval between infusions may be extended up to 16 weeks in the case of a dose modification due to an adverse reaction. Permanently discontinue LUTATHERA in patients who experience grade 3/4 hypersensitivity reactions.[1] Please see the Prescribing Information for additional information on dose modifications.

[b]Continue long-acting octreotide 30 mg IM every 4 weeks after completing LUTATHERA until disease progression or for 18 months following treatment initiation at the discretion of the physician.[1]

GBq, gigabecquerel; mCi, millicurie.

***You are a key source of information to help your patients prepare and plan ahead for the administration of* LUTATHERA**

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%).

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.

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RADIATION EXPOSURE

Radiation Associated With LUTATHERA

TYPES OF RADIATION EMITTED	• LUTATHERA decays to stable hafnium (Hf-177), with a half-life of 6.647 days, by emitting beta minus (β-) radiation with a maximum energy of 0.498 MeV (79%) and photonic radiation (γ) of 0.208 MeV (11%) and 0.113 MeV (6.2%)[1]
PENETRATING RADIATION	• The maximum radiation penetration of LUTATHERA in tissue is 2.2 mm, and the mean penetration is 0.67 mm[1]
PATIENT EXPOSURE	• Patients are discharged from the treatment center only when radiation exposure to third parties does not exceed regulatory thresholds[2]

Radiation Exposure in HCPs and Caregivers Following Outpatient Treatment With Lutetium 177[4]

Methods

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.[4]

Radiation study results

HEALTH CARE PROFESSIONALS	Mean whole-body exposures per therapy treatment day with 4 patients when administering Lutetium 177 ranged from 6.8 µSv (nuclear medicine technologist) to 33.2 µSv (nurse). 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), whereas that at the nursing station with 100% staff occupancy was 3.5 µSv/h (2.9–4.0 µSv/h).[4,a]
CAREGIVERS	Mean total exposure during the day of therapy and at home for a period of up to 5 days was 90 µSv, with a median exposure of 40 µSv and range of 10 µSv to 470 µSv.[4,a,b]
Exposures to HCPs and caregivers were within the limits recommended by the International Commission on Radiological Protection.[4]	

[a]For reference, radiation exposure is 14.5 µSv on a 5.2-hour flight from Los Angeles to Honolulu.[5]
[b]Twenty-five caregivers were provided with electronic dosimeters.[4]

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS

Somatostatin and its analogs competitively bind to somatostatin receptors and may interfere with the efficacy of LUTATHERA. Discontinue long-acting somatostatin analogs at least 4 weeks and short-acting octreotide at least 24 hours prior to each LUTATHERA dose. Administer short- and long-acting octreotide during LUTATHERA treatment as recommended.

Glucocorticoids can induce downregulation of subtype 2 somatostatin receptors. Avoid repeated administration of high doses of glucocorticoids during treatment with LUTATHERA.

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

RADIATION SPILL PROCEDURES

If a radiation spill occurs, you should always follow the guidance of your institution's radiation safety department. The information below is guidance from the National Radiation Commission for additional consideration.[6]

FOR MINOR SPILLS[6]	
NOTIFY	Notify persons in the area that a spill has occurred.
PREVENT THE SPREAD	Cover the spill with absorbent paper.
CLEANUP	Use disposable gloves and absorbent paper. Carefully fold the absorbent paper with the clean side out and place in a labeled plastic bag for transfer to a radioactive waste container. Also put contaminated gloves and any other contaminated disposable material in the bag.
SURVEY	With a low-range radiation detection survey meter, check the area around the spill. Also check your hands, clothing, and shoes for contamination.
REPORT	Report the incident to the Radiation Safety Officer (RSO).
DOCUMENT	Complete any necessary forms for documentation.

FOR MAJOR SPILLS[6]	
CLEAR THE AREA	Notify all persons not involved in the spill to vacate the room.
PREVENT THE SPREAD	Cover the spill with absorbent paper, but do not attempt to clean it up. To prevent the spread of contamination, limit the movement of all personnel who may be contaminated.
SHIELD THE SOURCE	If possible, shield the spill. This should be done only if it can be done without further contamination or a significant increase in radiation exposure.
CLOSE THE ROOM	Lock or otherwise secure the area to prevent entry.
CALL FOR HELP	Notify the RSO immediately.
PERSONNEL DECONTAMINATION	Remove contaminated clothing and flush contaminated skin with lukewarm water and then wash with mild soap. If contamination remains, induce perspiration by covering the area with plastic. Then wash the affected area again to remove any contamination that was released by the perspiration.
CLEANUP	The RSO will supervise the cleanup of the spill and complete any necessary forms for documentation.

HCPs, health care professionals; NETs, neuroendocrine tumors.

IMPORTANT SAFETY INFORMATION (continued)

SPECIFIC POPULATIONS

Lactation: Because of the potential risk for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with LUTATHERA and for 2.5 months after the last dose.

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PATIENT MANAGEMENT BEFORE AND DURING TREATMENT WITH LUTATHERA

Helpful Information to Discuss With Your Patients on the Recommended Actions They Can Take After Receiving Treatment With LUTATHERA

REQUIRED ACTIONS	
	**Staying hydrated** • Drink liquids and urinate frequently before, on the day of, and on the day after administration of LUTATHERA[1]
	**Breastfeeding** • Do not breastfeed during treatment with LUTATHERA and for 2.5 months after your last infusion of LUTATHERA[1]
	**Using birth control** Use effective birth control during treatment with LUTATHERA and for: • 7 months after your last dose if you are a woman of reproductive potential[1] • 4 months after your last dose if you are a man with a female partner who is able to become pregnant[1]

***You play an important part in making sure your patients and their loved ones are aware of the radiation safety guidelines while being treated with* LUTATHERA[1]**

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.

IMPORTANT RADIATION GUIDELINES WHEN COUNSELING PATIENTS

CONSIDERATIONS AS RECOMMENDED BY THE NANETS/SNMMI CONSENSUS GUIDELINES AND MAYO CLINIC GUIDELINES[2,7]	
	**Using the toilet** • For at least 3 days, use the toilet in a seated position and flush the toilet twice after use, and use separate towels and washcloths[2]
	**Showering** • For at least 7 days, shower daily[7]
	**Sleeping** • For at least 3 days, sleep in a separate bed and avoid intimate contact[2]
	**Interacting with others** • For at least 3 days, use a general distance guideline of no closer than 3 feet for not more than 1 hour per day. Try to maintain a distance of 6 feet from others. Minimize public transportation and use of public facilities[2] • For at least 3 days, avoid going to work[2]

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

Refer to these general guidelines and to specific guidelines provided by NANETS, SNMMI, the Mayo Clinic, and your institution when counseling your patients

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. 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.

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COMMON AND/OR SERIOUS SIDE EFFECTS FROM THE NETTER-1 TRIAL

The safety of LUTATHERA was evaluated in NETTER-1, a pivotal phase 3, randomized, multicenter, open-label, active-control trial.[1,8]

The Most Common (>15%) All-Grade Side Effects of LUTATHERA[a]
Nausea (65%)[1]
Vomiting (53%)[1]
Fatigue (38%)[1]
Abdominal pain (26%)[1]
Diarrhea (26%)[1]
Decreased appetite (21%)[1]
Headache (17%)[1]
Dizziness (17%)[1]
Peripheral edema (16%)[1]

- The most common (≥4%) 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]
- 6% of patients required a dose reduction, and 13% of patients discontinued LUTATHERA[1]
  —5 patients discontinued due to renal-related events[1]
  —4 patients discontinued due to hematologic toxicities[1]

[a]Adverse reactions occurring at a higher incidence in patients receiving LUTATHERA and long-acting octreotide compared with long-acting octreotide.[1]

IMPORTANT SAFETY INFORMATION (continued)

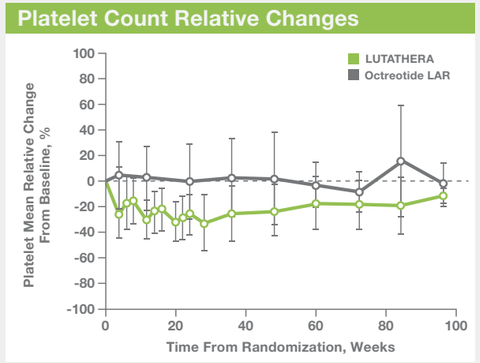
WARNINGS AND PRECAUTIONS (continued)

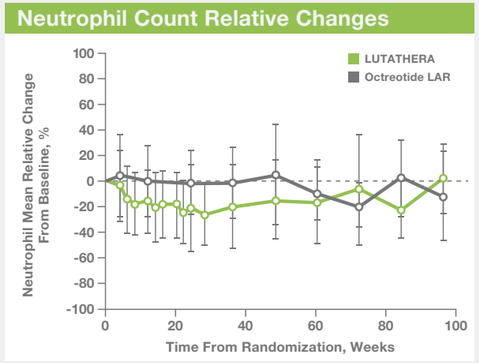
- **Secondary Myelodysplastic Syndrome and Leukemia:** In NETTER-1, with a median follow-up time of 76 months in the main study, myelodysplastic syndrome (MDS) was reported in 2.3% of patients receiving LUTATHERA with long-acting octreotide compared with no patients receiving high-dose long-acting octreotide. 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.

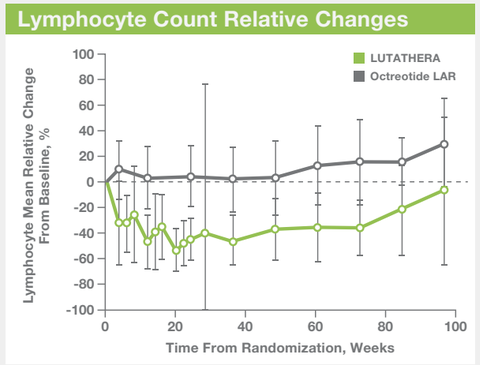
Please see additional Important Safety Information throughout and full Prescribing Information.

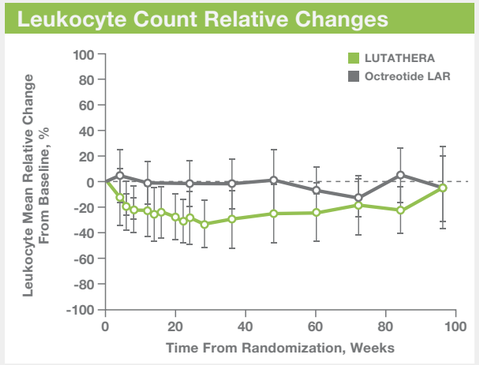
HEMATOLOGIC EVENTS

Hematologic Events From NETTER-1: Mean Relative Change From Baseline Over Time[8]









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

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. 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.

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LONG-TERM SAFETY RESULTS

ERASMUS, A RETROSPECTIVE, LONG-TERM (MEDIAN FOLLOW-UP, >4 YEARS), OPEN-LABEL TRIAL[1]	
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).[1]
ADMINISTRATION	LUTATHERA 7.4 GBq (200 mCi) was administered every 6 to 13 weeks for up to 4 doses with or without octreotide. Retrospective medical record review was conducted on a subset of 811 patients to document serious adverse reactions.[1] • 81% of patients in the subset received a cumulative dose ≥22.2 GBq (≥600 mCi)[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

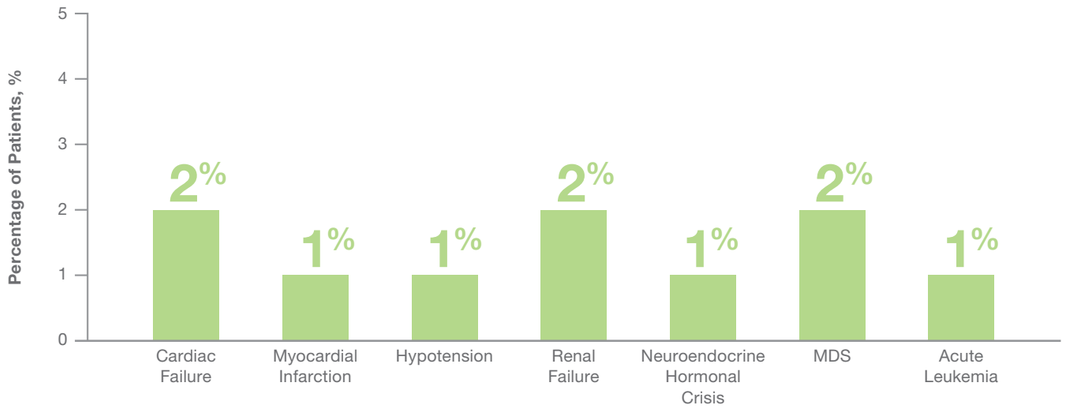
- **Hepatotoxicity:** In ERASMUS, 2 patients (<1%) were reported to have hepatic tumor hemorrhage, edema, or necrosis, with 1 patient experiencing intrahepatic congestion and cholestasis. Patients with hepatic metastasis may be at increased risk of hepatotoxicity due to radiation exposure. Monitor transaminases,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

LONG-TERM SAFETY RESULTS (continued)

In ERASMUS, a retrospective study analyzing long-term (median, >4 years) follow-up after treatment with LUTATHERA, the serious adverse reactions included[1]:

Serious Adverse Reactions



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

Please see Warnings and Precautions for myelosuppression, MDS, and leukemia. Monitor blood cell counts. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of adverse reactions.[1]

The safety of* LUTATHERA *was evaluated in 2 studies[1]

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 analogs, fluids, corticosteroids, and electrolytes as indicated.

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WARNINGS AND PRECAUTIONS FOR LUTATHERA

Events Reported in the NETTER-1 and ERASMUS Clinical Trials

RISK FROM 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[1] • Minimize radiation exposure to patients, medical personnel, and household contacts during and following 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[1]
MYELOSUPPRESSION	• In NETTER-1, 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[1] • Of the 59 patients who developed thrombocytopenia, 68% had platelet recovery to baseline or normal levels[1] —The median time to platelet recovery was 2 months[1] —Fifteen of the 19 patients in whom platelet recovery was not documented had post-nadir platelet counts. Among these 15 patients, 5 improved to grade 1, 9 to grade 2, and 1 to grade 3[1] • Monitor blood cell counts. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of myelosuppression[1]
SECONDARY MDS AND LEUKEMIA	• 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] • 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]
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[1] • 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[1] • Monitor serum creatinine and calculated creatinine clearance. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of renal toxicity[1] • 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[1]

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

WARNINGS AND PRECAUTIONS FOR LUTATHERA (continued)

Events Reported in the NETTER-1 and ERASMUS Clinical Trials (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[1] • 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[1]
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 where 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[1] • 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[1]
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[1] • Monitor patients for flushing, diarrhea, hypotension, bronchoconstriction, or other signs and symptoms of tumor-related hormonal release. Administer intravenous SSAs, fluids, corticosteroids, and electrolytes as indicated[1]
EMBRYO-FETAL TOXICITY	• Based on its mechanism of action, LUTATHERA can cause fetal harm when administered to a pregnant woman. There are no available data on LUTATHERA use in pregnant women. No animal studies using lutetium Lu 177 dotatate have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, radioactive emissions, including those from LUTATHERA, can cause fetal harm[1] • Verify the pregnancy status of females of reproductive potential prior to initiating LUTATHERA[1] • 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. Advise males with female partners of reproductive potential to use effective contraception during treatment with LUTATHERA and for 4 months after the last dose[1]
RISK OF INFERTILITY	• LUTATHERA may cause infertility in males and females. The recommended cumulative dose of 29.6 GBq of LUTATHERA results in a radiation-absorbed dose to the testes and ovaries within the range in which temporary or permanent infertility can be expected following external beam radiotherapy[1]

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NOVARTIS PATIENT SUPPORT

What Is Novartis Patient Support?

Novartis Patient Support is a comprehensive support program designed to help your patients start and stay on LUTATHERA. We support you throughout your patient's journey, including:

- **Insurance Support**
- **Financial Support**
- **Product Acquisition**
- **Coding & Billing Support**

Novartis Patient Support Co-pay Savings

We help make treatment more affordable for your patients through co-pay savings.

$25 CO-PAY*

Eligible patients may pay as little as $25 per dose.*
Enrollment in Novartis Patient Support is required to determine eligibility and participation.

*Limitations apply. Valid only for those patients with commercial insurance. Not valid under Medicare or any other federal or state program. Offer subject to a maximum benefit per course of treatment. See complete Terms and Conditions in the Enrollment Forms for details.

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. 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.

NOVARTIS PATIENT SUPPORT (continued)

Co-pay Savings Start With Enrollment

Eligible patients are considered for co-pay savings when they enroll in Novartis Patient Support. Ensure patients have completed and signed the Enrollment Form for Novartis Patient Support to activate assessment eligibility.

To complete and submit an Enrollment Form, visit www.novartis-patientsupport.com/RLT or call us at 1-844-638-7222.

Additional Financial Support May Be Available for Patients Without Private Insurance

To find out if patients are eligible for other financial support, call Novartis Patient Support at 1-844-638-7222, Monday through Friday, from 8:00 AM to 8:00 PM ET.

Patients must be enrolled in Novartis Patient Support to be considered for financial support.

Visit www.novartis-patientsupport.com/RLT for more information

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%).

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.

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NOTES:

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

REFERENCES:

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8. 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.

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HAVING A GREATER UNDERSTANDING OF LUTATHERA CAN HELP STRENGTHEN THE ONGOING CARE FOR PATIENTS WITH GEP-NETS[1]

Not an actual health care professional.

With LUTATHERA, a **multidisciplinary team** approach that includes a medical oncologist, nuclear medicine or radiation oncologist, RSO, and advanced clinical practice and other nurses is recommended[2]

LUTATHERA is a peptide receptor radionuclide that **binds to SSTRs** on the surface of cells that express this receptor[1]

LUTATHERA is a **targeted treatment** that uses radiation to damage SSTR-positive cells and neighboring cells[1]

Safety was assessed in the pivotal NETTER-1 trial and long-term ERASMUS trial (median, >4 years)[1]

- In the NETTER-1 study, 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]

Treatment with LUTATHERA consists of a **4-dose treatment regimen**, **given every 8 weeks (±1 week),** as an IV infusion[1]

×4

Patients are discharged from the treatment center only when radiation exposure to third parties does not exceed regulatory thresholds[2]

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS

Somatostatin and its analogs competitively bind to somatostatin receptors and may interfere with the efficacy of LUTATHERA. Discontinue long-acting somatostatin analogs at least 4 weeks and short-acting octreotide at least 24 hours prior to each LUTATHERA dose. Administer short- and long-acting octreotide during LUTATHERA treatment as recommended.

Glucocorticoids can induce downregulation of subtype 2 somatostatin receptors. Avoid repeated administration of high doses of glucocorticoids during treatment with LUTATHERA.

SPECIFIC POPULATIONS

Lactation: Because of the potential risk for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with LUTATHERA and for 2.5 months after the last dose.

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

Scan the QR code or go to LUTATHERA-HCP.com to find a list of LUTATHERA treatment centers in the United States.

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