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

MENU

**For your patients with SSTR+ GEP-NETs,[1-3]**

# START STRONG WITH LUTATHERA

**1st and only radioligand therapy**
to change the trajectory of GEP-NETs

*Not an actual patient.*
*Hypothetical patient case.*

## »1L *Meet Alison, a 1L patient with aggressive GEP-NETs[1,5,6]*

FDA approval was based on the efficacy and safety of **NETTER-1**, a phase 3, randomized, open-label, multicenter study in 229 patients with well-differentiated, grade 1/2 advanced GEP-NETs after SSA progression.[2-4]

**NETTER-2** was a phase 3, randomized, open-label, multicenter study in 226 patients with metastatic or advanced GEP-NETs.[1,5]

1L, first line; FDA, US Food and Drug Administration; GEP-NETs, gastroenteropancreatic neuroendocrine tumors; SSA, somatostatin analogue; SSTR+, somatostatin receptor-positive.

## 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.

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

NOVARTIS

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# 1L ALISON

## A patient with high grade 2/3 GEP-NETs[1,5,6]

### Alison's disease characteristics are similar to those of participants in the NETTER-2 study[1,2,5,6]

- **Newly diagnosed** (within the last 6 months), well-differentiated SSTR+ GEP-NET
- **Primary tumor site:** 54% pancreas, 30% small intestine, 5% rectum, 4% stomach, 7% other
- **Ki-67 index:** ≥10% to ≤55% (tumor grade 2/3)
- **Disease burden:** moderate to severe
- **Karnofsky PS:** 90-100
- **Nonfunctional and functional tumors** can be treated with LUTATHERA

Select study characteristics. Not an exhaustive list.

*Not an actual patient.*
*Hypothetical patient case.*

## Because of her aggressive disease, Alison and her doctor chose to start strong with 1L LUTATHERA

**NETTER-2** is a phase 3, randomized, open-label, active comparator, multicenter study of the efficacy of LUTATHERA with 30 mg octreotide LAR (n=151) vs 60 mg octreotide LAR (n=75) in patients with newly diagnosed, well-differentiated, grade 2/3 advanced SSTR+ GEP-NETs. SSA-naive patients were eligible, as well as patients previously treated with SSAs in the absence of progression. The primary end point of the study was centrally assessed PFS.[1,5,*]

* In NETTER-2, 44 patients (19.5%) received prior treatment in the absence of progression, including CAPTEM (1 patient), everolimus (1 patient), and SSAs (42 patients, with the majority receiving 1 or 2 doses).[5,6]

CAPTEM, capecitabine and temozolomide; LAR, long-acting release; PFS, progression-free survival; PS, performance status.

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

- **Radiation Exposure (continued):** Radiation can be detected in the urine for up to 30 days following LUTATHERA administration.

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# NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) select recommendations[7]

National Comprehensive Cancer Network® (NCCN®)

**NCCN RECOMMENDED**

**PRRT with lutetium Lu 177 dotatate (LUTATHERA®) is NCCN Guidelines® recommended** as a systemic therapy option for SSTR+, well-differentiated GEP-NET patients*

## ≫1L

### Grade 1/2

- **NCCN Category 2A Preferred** as an alternative first-line option for certain patients with locoregional advanced disease and/or distant metastases of gastrointestinal or pancreatic NETs (Ki-67 ≥10% and clinically significant tumor burden)†

### Grade 3

- **Category 2A** for locally advanced and/or metastatic NETs with unresectable, clinically significant tumor burden or evidence of progression and favorable biology
- **Category 2B** for locally advanced and/or metastatic NETs with unresectable, asymptomatic, low tumor burden and favorable biology

**NCCN Guidelines recommendations for 1L are based on data from the NETTER-2 study**

*NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

†Consider for pancreatic NETs.

NCCN, National Comprehensive Cancer Network; NETs, neuroendocrine tumors; PRRT, peptide receptor radionuclide therapy.

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

- **Radiation Exposure (continued):** 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.**

# NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) select recommendations[7]

National Comprehensive Cancer Network® (NCCN®)
NCCN
RECOMMENDED

**PRRT with lutetium Lu 177 dotatate (LUTATHERA®) is NCCN Guidelines® recommended** as a systemic therapy option for SSTR+, well-differentiated GEP-NET patients*

## »2L

### Grade 1/2

- **Category 1 Preferred** for locoregional advanced disease and/or distant metastases—mid-gut NETs with progression on octreotide LAR/lanreotide
- **Category 2A Preferred** for locoregional advanced disease and/or distant metastases of gastrointestinal or pancreatic NETs after progression on octreotide LAR/lanreotide

**NCCN Guidelines recommendations for 2L are based on data from the NETTER-1 study**

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2L, second line.

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

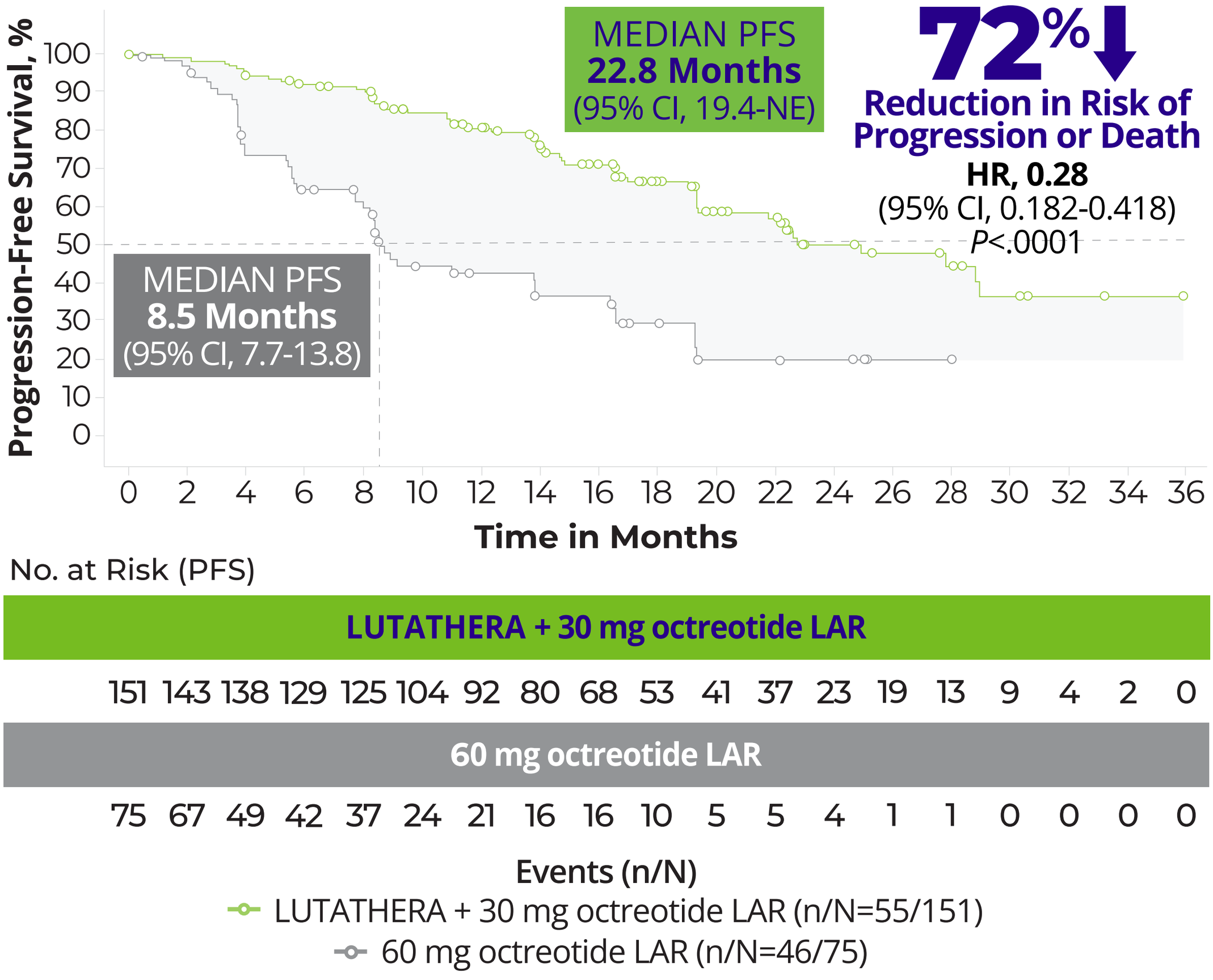
- **Myelosuppression:** In the NETTER-1 clinical trial, myelosuppression occurred more frequently in patients receiving LUTATHERA with long-acting octreotide compared with patients receiving high-dose long-acting octreotide (all grades/grade 3/4): anemia (81%/0 vs 54%/1%), thrombocytopenia (53%/1% vs 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.

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

# 1L Start strong with ~3x longer PFS in 1L[1,5]

## LUTATHERA + SSA demonstrated statistically significant mPFS compared with SSA alone[1,5]

### Median PFS (Primary End Point)




- PFS was defined as the time from randomization to first documented disease progression or death due to any cause. Centrally assessed according to RECIST v1.1 criteria[1]
- The primary PFS analysis data cutoff was July 20, 2023. Median duration of follow-up was 23.2 months (from randomization to cutoff date)[5]

HR, hazard ratio; mPFS, median progression-free survival; NE, not evaluable; RECIST, Response Evaluation Criteria in Solid Tumors.

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression (continued):** 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.**

# NETTER-2 adds to the breadth of data for LUTATHERA in patients with GEP-NETs, which were established by the pivotal NETTER-1 study[2,5]

**~3X**
**longer PFS**
**in patients after progression on an SSA[2,5,8]**

- Primary analysis: mPFS was **not reached** with LUTATHERA + SSA **vs 8.5 months** with SSA alone (HR, 0.21 [95% CI, 0.13-0.32]; *P*<.0001)[2,3]
- Updated analysis: mPFS was **28.4 months** with LUTATHERA + SSA vs **8.5 months** with SSA alone (HR, 0.21 [95% CI, 0.14-0.33])[8,*]

**NETTER-1** was a pivotal, phase 3, randomized, multicenter, open-label study of LUTATHERA with 30 mg octreotide LAR (n=116) vs 60 mg octreotide LAR (n=113) in patients with locally advanced, inoperable, or metastatic SSTR+ GEP-NETs. The primary end point of the study was centrally assessed PFS.[2-4]

*The updated PFS analyses are based on post hoc assessments conducted after the prespecified primary analysis and are observational only. They were not powered for statistical significance and the results should be interpreted with caution.

## 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.
- **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.

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

# Start with the established safety and proven tolerability of LUTATHERA[1-3,5]

## Consistent safety profile with no new safety signals in NETTER-2[5,9]

- Most common AEs (≥20%) included nausea, abdominal pain, and diarrhea[5]
- In NETTER-2, 2% of patients reduced dose, and 2% discontinued treatment[5]

## Demonstrated long-term safety at 5 years with no new safety signals reported[9,*]

| 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[9] |
| **Grade ≥3 Treatment-Related SAEs During the Entire Study** |
| 7 (6%) of 111 patients treated in the LUTATHERA arm[9] |

*Cutoff date for final analysis was January 18, 2021.[9]

AEs, adverse events.

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity (continued):** 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.**

# Demonstrated long-term safety at 5 years with no new safety signals reported[9,*] (continued)

## Incidence of Treatment-Related SAEs During the Long-Term Follow-Up Period

**3 (3%) of 111 patients treated with LUTATHERA[9]**

— 2 (1.8%) patients experienced at least 1 grade ≥3 SAE (1 grade 5 MDS event)[9]

— 1 (0.9%) patient experienced an SAE leading to study discontinuation[9]

## MDS or Acute Leukemia

**No new cases were reported during long-term follow-up[9]**

— 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[2,9]

— 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[2,a]

*Cutoff date for final analysis was January 18, 2021.[9]

[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.[2]

MDS, myelodysplastic syndrome; SSTR, somatostatin receptor.

## 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.

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

# Demonstrated long-term safety at 5 years with no new safety signals reported[9,*] (continued)

| 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[9] |
| **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[9] |

*Cutoff date for final analysis was January 18, 2021.[9]

## IMPORTANT SAFETY INFORMATION (continued)
## WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity (continued):** 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.
- **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.

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

# IMPORTANT SAFETY INFORMATION (continued)
# WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity Reactions (continued):** 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.
- **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.
- **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.**

# 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.

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

## 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.**

**References: 1.** Data on file. Novartis Pharmaceuticals Corp; 2021. **2.** Lutathera. Prescribing information. Novartis Pharmaceuticals Corp. **3.** 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. **4.** US Food and Drug Administration. FDA approves lutetium Lu 177 dotatate for treatment of GEP-NETS. Updated January 26, 2018. Accessed June 1, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lutetium-lu-177-dotatate-treatment-gep-nets **5.** 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. **6.** Data on file. CAAA601A22301 Clinical Study Report. Novartis Pharmaceuticals Corp; 2024. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed July 22, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **8.** Kunz P, Benson A, Bodei L, et al. The phase 3 NETTER-1 study of $^{177}$Lu-DOTATATE in patients with midgut neuroendocrine tumours: updated progression-free survival analyses. Poster presented at: North American Neuroendocrine Tumor Society (NANETS) Annual Multidisciplinary Medical Symposium; November 4-6, 2021; Chicago, IL. **9.** 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. **10.** Data on file. LUTATHERA ROME extract. Novartis Pharmaceuticals Corp; May 2025.

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# START STRONG WITH LUTATHERA

## The first and only radioligand therapy to change the trajectory of GEP-NETs

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## SUPERIOR EFFICACY IN 2 PHASE 3 TRIALS

### LUTATHERA + SSA demonstrated 3x longer PFS vs SSA alone[2,5,8]

**1L** Primary analysis: mPFS of 22.8 months with LUTATHERA + SSA vs 8.5 months with SSA alone (HR, 0.28 [95% CI, 0.18-0.42]; *P*<.0001)[5]

**2L** Primary analysis: mPFS NR with LUTATHERA + SSA vs 8.5 months with SSA alone (HR, 0.21 [95% CI, 0.13-0.32]; *P*<.0001)[2,3]

Updated analysis: mPFS of 28.4 months with LUTATHERA + SSA vs 8.5 months with SSA alone (HR, 0.21 [95% CI, 0.14-0.33])[8]

## ESTABLISHED SAFETY & PROVEN TOLERABILITY

### Consistent safety profile with no new safety signals in NETTER-1* and NETTER-2 with 5-year follow-up in NETTER-1[5,9]

- Most common AEs (≥20%) across trials: nausea, abdominal pain, diarrhea (NETTER-1 and NETTER-2), vomiting, fatigue, thrombocytopenia, musculoskeletal pain, and decreased appetite (NETTER-1)[2,3,5]
- In NETTER-1 and NETTER-2, respectively: 7% and 2% of patients reduced dose, 5% and 2% of patients discontinued treatment[3,5]

## Real-world experience with LUTATHERA: Trusted by HCPs to treat >18,000 patients over 7 years[4,10,†]

***START HERE:* www.LUTATHERA-HCP.com**

*Cutoff date for final analysis was January 18, 2021.
†Internal data tracking as of May 2025.

HCPs, health care professionals; NR, not reached.

## 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.

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