



PRESS RELEASE

Advanced Accelerator Applications Announces Start of Phase III Study Investigating Radioligand Therapy Lutathera® as First-Line Treatment in Patients with Advanced GEP-NETs

Saint-Genis-Pouilly, France, March 25, 2020 - Advanced Accelerator Applications S.A. (AAA), a Novartis company, today announced that the first patient has been treated in the NETTER-2 Phase III clinical study investigating Lutathera® (USAN: lutetium Lu 177 dotatate / INN: lutetium (¹⁷⁷Lu) oxodotreotide) given as first-line treatment, for Grade 2 and Grade 3 advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in combination with long-acting octreotide.

NETTER-2 is a multi-center, randomized, open-label study to evaluate the efficacy and safety of Lutathera in combination with long-acting octreotide (30mg), given as first line treatment in comparison to patients treated with high dose, long-acting octreotide (60mg) alone. Lutathera treatments will be administered every eight weeks for a total of four doses, followed by three years of post-treatment monitoring.

The primary objective of NETTER-2 is prolonged Progression Free Survival (PFS) in patients with high proliferation rate tumors (G2 and G3). Approximately 222 patients are expected to be enrolled in the NETTER-2 study at approximately 50 sites across the US, Canada, Europe, Brazil, China and South Korea.

“We are encouraged by the impact Lutathera has had in treatment of neuroendocrine tumors since its launch, and are eager to explore its potential in first line therapy of more aggressive tumors,” said Geromo Gericke, M.D., Global Head of Research and Development at Advanced Accelerator Applications.

The NETTER-2 study follows the pivotal Phase III NETTER-1 study comparing treatment with lutetium ¹⁷⁷Lu-dotatate (Lutathera) plus long-acting octreotide (30mg) to high dose, long-acting octreotide (60 mg) in patients with inoperable, progressive, somatostatin receptor positive midgut carcinoid tumors.¹

Lutathera is approved for treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors in the United States,² and for the treatment of unresectable or metastatic, progressive, well differentiated (G1 and G2), somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) in adults in Europe.³ Lutathera is also approved in Switzerland, Canada and Israel.

LUTATHERA®

Patient Important Safety Information

What is LUTATHERA?

LUTATHERA® (lutetium Lu 177 dotatate) is a prescription medicine used to treat adults with a type of cancer known as gastroenteropancreatic neuroendocrine tumors (GEP-NETs) that are positive for the hormone receptor somatostatin, including GEP-NETs in the foregut, midgut, and hindgut.

IMPORTANT SAFETY INFORMATION²:

What are the possible serious side effects of LUTATHERA?

LUTATHERA® can cause **serious side effects** and if you experience these side effects, your healthcare provider may need to adjust or stop your treatment. You should always follow your healthcare provider's instructions. Serious side effects may include:

- **Radiation exposure:** Treatment with LUTATHERA will expose you to radiation which can contribute to your long-term radiation exposure. Overall radiation exposure is associated with an increased risk for cancer. The radiation will be detectable in your urine for up to 30 days following administration of the drug. It is important to minimize radiation exposure to household contacts consistent with good radiation safety practices.
- **Bone marrow problems:** Treatment with LUTATHERA increases the risk of myelosuppression, a condition in which bone marrow activity is decreased, resulting in drop in blood cell counts. You may experience blood-related side effects such as low red blood cells (anemia), low numbers of cells that are responsible for blood clotting (thrombocytopenia), and low numbers of a type of white blood cells (neutropenia). People with low blood cell counts are at higher risk of developing serious side effects associated with LUTATHERA. Speak with your healthcare provider if you experience any signs or symptoms of infection, fever, chills, dizziness, shortness of breath or increased bleeding or bruising. Your healthcare provider may need to adjust or stop your treatment accordingly.
- **Secondary bone marrow and blood cancers:** Other serious conditions that you may develop as a direct result of treatment with LUTATHERA include blood and bone marrow disorders known as secondary myelodysplastic syndrome and cancer known as acute leukemia. Your healthcare provider will routinely check your blood counts and tell you if they are too low.
- **Kidney problems:** Treatment with LUTATHERA will expose your kidneys to radiation and may impair their ability to work as normal. You may be at an increased risk for lower kidney function after LUTATHERA treatment if you already have kidney impairment before treatment. In some cases, patients have experienced kidney failure after treatment with LUTATHERA. Your healthcare provider will monitor changes and provide you with an amino acid solution before, during, and after LUTATHERA to help protect your kidneys. You should stay well hydrated before, during, and after your treatment. You should urinate frequently during and after administration of LUTATHERA. Your doctor will monitor your kidney function and may withhold, reduce, or stop your LUTATHERA treatment accordingly.
- **Liver problems:** In clinical studies of LUTATHERA, less than 1% of patients were reported to have tumor bleeding (hemorrhage), swelling (edema) or tissue injury (necrosis) to the liver. If you have tumors in your liver, you may be more likely to experience these side-effects. Signs that you may be experiencing liver damage include increases in blood markers called ALT, AST and GGT. Your healthcare provider will monitor your liver using blood tests and may need to withhold, reduce, or stop your LUTATHERA treatment accordingly.
- **Hormonal gland problems (carcinoid crisis):** During your treatment you may experience certain symptoms that are related to hormones released from your cancer. These symptoms may include flushing; diarrhea, difficulty breathing (bronchospasm), and low blood pressure (hypotension), and may occur during or within the 24 hours after your first LUTATHERA treatment. Your healthcare provider will monitor you closely. Speak with your healthcare provider if you experience any of these signs or symptoms.
- **Pregnancy warning:** Tell your healthcare provider if you are pregnant or you or your partner plan to become pregnant before taking LUTATHERA. LUTATHERA can harm your unborn baby.

Females should use an effective method of birth control during treatment and for 7 months after the final dose of LUTATHERA. Males with female partners should use an effective method of birth control during treatment and for 4 months after the final dose of LUTATHERA.

- **Breastfeeding warning:** You should not breastfeed during treatment with LUTATHERA and for 2.5 months after your final dose of LUTATHERA.
- **Fertility problems:** Treatment with LUTATHERA may cause infertility. This is because radiation absorbed by your testis and ovaries over the treatment period falls in the range of exposure where temporary or permanent infertility may occur.

What other medicines may interact with LUTATHERA?

Tell your healthcare provider if you are taking any other medications, including somatostatin analogs. Somatostatin analogs may affect how your LUTATHERA treatment works. Your healthcare provider may ask you to stop taking your long-acting somatostatin analogs 4 weeks before LUTATHERA treatment. You may continue taking short-acting somatostatin analogs up to 24 hours before your LUTATHERA treatment.

What are the most common side effects of LUTATHERA?

The most common and most serious side effects of LUTATHERA include: vomiting, nausea, decreased blood cell counts, increased liver enzymes, decreased blood potassium levels, and increased glucose in the bloodstream.

Talk to your doctor if you have a side effect that bothers you or does not go away. There are other possible side effects of LUTATHERA. For more information, and to learn more about LUTATHERA, talk to your doctor or healthcare provider.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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preferences of physicians and patients; general political and economic conditions; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Advanced Accelerator Applications S.A.

Advanced Accelerator Applications, S.A. (AAA), a Novartis company, is developing targeted radioligand therapies and precision imaging radioligands for oncology indications. We are committed to transforming patients' lives by leading innovation in nuclear medicine. AAA has a legacy as a leader in radiopharmaceutical drugs for Positron Emission Tomography (PET) and Single-Photon Emission Computed Tomography (SPECT) diagnostic imaging. For more information, please visit: <https://www.adacap.com>.

References

1. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 Trial of 177Lu-Dotatate for Midgut Neuroendocrine Tumors. N Engl J Med 2017; 376:125-35.
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