4CPS-132

UNDERSTANDING THE TYPES AND CAUSES OF ^{177}LU-OXODOTREOTIDE REGIMEN MODIFICATIONS TO IDENTIFY A TYPICAL PATIENT PROFILE

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WHAT WAS DONE

- **Lutathera® (^{177}Lu-oxodotreotide)** is indicated for the treatment of patients with inoperable or metastatic, progressive, well-differentiated (G1, G2) gastroenteropancreatic neuroendocrine tumors (GEP-NETs). **The standard therapeutic regimen (STR) consists of 4 injections of 7.4 GBq, spaced 8 ± 1 week**.
- In routine clinical practice, **treatment regimen modifications (TRM)** are frequently required due to biological toxicities: **Half-dose administration (HD), Extension of the inter-cycle interval (ICI) or Treatment discontinuation (TD)** *[1]*. These modifications remain poorly documented in the literature 1 *[2-4].*
- This lack of data provides the rationale for evaluating real-world treatment regimen modifications in patients treated with Lutathera®.

WHY IT WAS DONE

- To describe treatment regimen modifications and to develop a statistical model for predicting the risk of regimen changes.

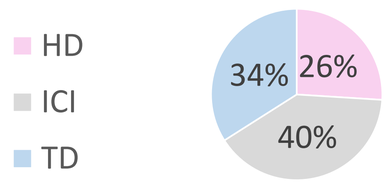
HOW IT WAS DONE

- **Single-center retrospective descriptive study conducted between June 24, 2016 and October 31, 2024,** including all patients who completed Lutathera® treatment, regardless of the number of cycles received (from 1 and 4) and excluding patients enrolled in clinical trials and retreatment protocols (> 4 cycles).
- Collected data included demographic and biological characteristics, GEP-NET-related information and biological parameters (including complete blood count and renal function tests) assessed before each administration. Biological toxicities were graded according to **the NCI-CTCAE v5.0 criteria**.
- Baseline predictors of treatment regimen modification were assessed using **multivariate logistic regression**. Survival was compared using the log-rank test.

WHAT WAS ACHIEVED

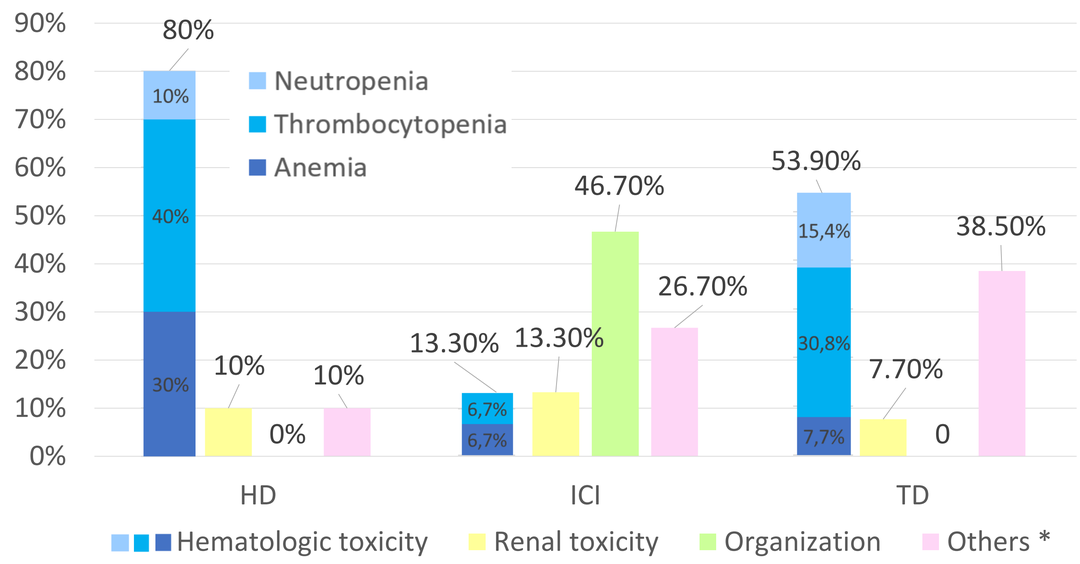
From 24 June 2016 to 31 October 2024, 77 patients met inclusion criteria
M/F = 1.57
Mean age = 67.9 ± 10.3 years

Types of TRM



A total of 38 modifications were identified, involving 24 patients.

- **Causes of TRM**



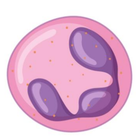
* Medical precaution measures, clinical worsening, diagnosis of an intercurrent malignancy

Approximately 2/3 of TRM (n = 25/38) were performed outside the SmPC recommandations.

Among these modifications, **dose reductions to 75–90%** of the planned activity, rather than the standard 50% reduction were observed, as well as modifications due for **low-grade toxicities** and inter-cycle delays related to **organizational constraints.**

- **Baseline predictors of TRM**

Thrombocytopenia
Platelets < 150 G/L

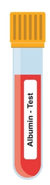


Neutropenia
Neutrophils < 2 G/L

Presence of bone metastases

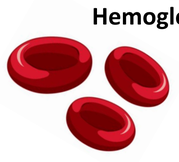
Lymphopenia
Lymphocytes < 2 G/L

Factors associated with the probability of modification of the Lutathera® treatment regimen using an optimal multivariate model



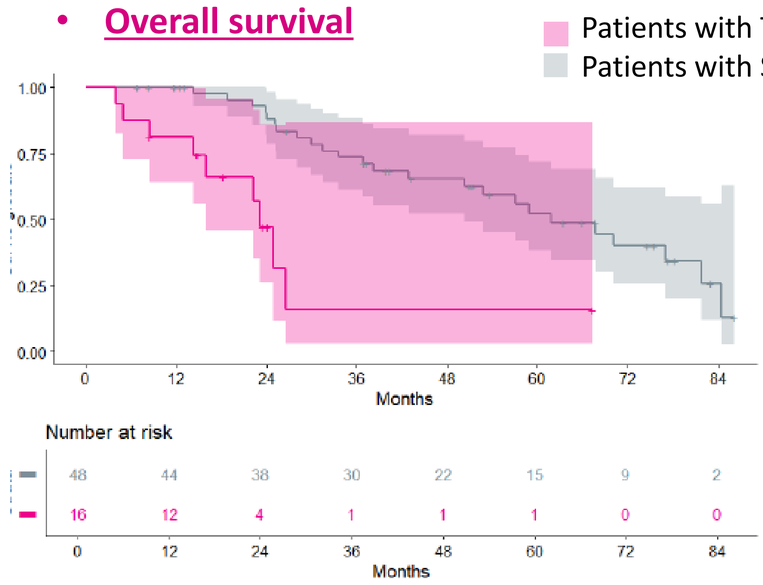
Hypoalbuminemia
Albumin < 35 g/L

Anemia
Hemoglobin < 12 g/dL



Prothrombin time
PT < 70%

- **Overall survival**



Overall survival was significantly reduced in the TRM group: 24.2 vs. 67.7 months; log-rank p = 0.0001

WHAT IS NEXT

- The model will be validated in external multicenter cohorts to assess its robustness and reproducibility.
- In parallel, the integration of data from other centers will help refine the predictive framework and contribute to the harmonization of clinical practices in the management of patients with NETs.

[1] J. Strosberg, *et al*. Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors. *N Engl J Med* **2017**, *376*, 125–135. **[2]** N. S. Minczeles, *et al*. Long-Term Outcomes of Submaximal Activities of Peptide Receptor Radionuclide Therapy with ^{177}Lu-DOTATATE in Neuroendocrine Tumor Patients. *J Nucl Med* **2023**, *64*, 40–46. **[3]** D. M. V. de Vries–Huizing, *et al*. Haematotoxicity during Peptide Receptor Radionuclide Therapy: Baseline Parameters Differences and Effect on Patient's Therapy Course. *PLoS ONE* **2021**, *16*, e0260073. **[4]** A. Khatami, *et al*. Toxicity and Tolerability of ^{177}Lu-DOTA-TATE PRRT with a Modified Administered Activity Protocol in NETs of Variable Origin – A Phase 2 Registry Study. *Curr Radiopharm* **2022**, *15*, 123–133.