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# A Prospective Phase II Single-Arm Trial on Neoadjuvant Peptide Receptor Radionuclide Therapy (PRRT) with <sup>177</sup>Lu-DOTATATE Followed by Surgery for Pancreatic Neuroendocrine Tumors (NeoLuPaNET)

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## BACKGROUND

Surgical resection of Nonfunctioning Pancreatic Neuroendocrine Tumor (NF-PanNET) is curative in most of the cases. Neoadjuvant treatments in patients with resectable NF-PanNET at high-risk of recurrence have never been investigated. Aim of this study was to test the safety and efficacy of neoadjuvant PRRT with <sup>177</sup>Lu-DOTATATE followed by surgery in patients with resectable high-risk NF-PanNET.

## METHODS

This was a multi-center single-arm phase 2 trial. Treatment was PRRT with <sup>177</sup>Lu-DOTATATE (Lutathera®) followed by surgery in patients with high-risk of recurrence resectable NF-PanNET. "High-risk NF-PanNET" was defined by the presence of at least one of the following characteristics: tumor size > 4 cm, nearby organ/s invasion, Ki67 >10%, vascular invasion, single liver metastasis, nodal involvement. The primary endpoints were postoperative morbidity and mortality. The secondary endpoint was the rate of objective radiological response.

## RESULTS

Among 34 patients screened, 31 were enrolled in the study. Twenty-six (84%) patients tolerated 4 cycles of <sup>177</sup>Lu-DOTATATE whereas 4 patients did not complete 4 cycles for adverse events or unsafe absorbed dose. One patient voluntarily interrupted treatment after 2 cycles and 2 patients refused to undergo surgery after <sup>177</sup>Lu-DOTATATE. No patient had progressive disease after neoadjuvant <sup>177</sup>Lu-DOTATATE. A partial radiological response was observed in 18 patients (58%) whereas 13 patients (42%) had stable radiological disease. Overall, 29 patients underwent surgery after a median period of 119 days (113–142.5 days) from the last cycle of <sup>177</sup>Lu-DOTATATE. Surgical resection of NF-PanNET was achieved in 28 patients (96.5%) whereas one patient underwent only exploratory laparotomy for unresectable vascular invasion.

Pancreaticoduodenectomy ( $n=11$ ) and distal pancreatectomy ( $n=11$ ) were the most frequent types of operation. At final histology, the majority of patients who underwent resection had a NF-PanNET G2 ( $n=16$ ) and a nodal involvement (N1) was present in the 52% of cases. There was no postoperative mortality. Severe postoperative complications occurred in the 24% of patients and postoperative pancreatic fistula was the most frequent complication after surgery (34%).

## **CONCLUSIONS**

Neoadjuvant PRRT with  $^{177}\text{Lu}$ -DOTATATE followed by surgery for NF-PanNET is safe and effective demonstrating evidence of a high rate-of radiological response. (ClinicalTrials.gov registration: NCT04385992).

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