# EVOLVING ROLE OF RADIOLIGAND THERAPY IN NETs

**Neuroendocrine tumours (NETs)** arise from hormone-secreting cells. **Treatment options vary** and include surgery, somatostatin analogues, radiotherapy, chemotherapy, targeted agents, and peptide receptor radionuclide therapy (PRRT).

## PRRT IS HERE TO STAY

Building on the results of NETTER-1, the recent COMPETE study consolidated the role of **PRRT as a very effective 2nd line treatment**, with $^{177}$Lu-edotreotide ($^{177}$Lu-DOTATOC) showing superior efficacy to everolimus.

Expert experience shows that NETs are **not as rare as once thought.**

As patients may live with the disease for many years,*[1]* **optimising care needs collaboration** over the whole of the patient's journey.

## Build a good team

**Partnerships with patients, caregivers & HCPs**

Best outcomes achieved with **multi-disciplinary collaborations and shared and informed decision-making with the patient** to support improved, knowledgeable, and better-coordinated/-aligned NET medical teams. *[2]*

## PAIRING THE RIGHT PATIENT WITH THE RIGHT TREATMENT

**Optimising treatment strategies** needs an **understanding of the clinical trial data and how studies differ.**

| | COMPETE *[3]* | COMPOSE *[4,5]* | NETTER-1 *[5,6]* | NETTER-2 *[7]* |
|---|---|---|---|---|
| **Tumour type** | G1/G2 well-differentiated GEP-NETs | G2/G3 well-differentiated GE-NETs or P-NETs Ki67 ≥15% and ≤55% | G1/G2 well-differentiated, metastatic midgut | G2/G3 well-differentiated GEP-NETs Ki67 ≥10% and ≤55% |
| **Study treatment** | $^{177}$Lu-edotreotide | $^{177}$Lu-edotreotide | $^{177}$Lu-DOTATATE | $^{177}$Lu-DOTATATE + octreotide LAR |
| **Comparator** | Everolimus | SoC | Octreotide LAR | Octreotide LAR |
| **Treatment line** | 1st and 2nd line | 1st and 2nd line | 2nd line | 1st line |
| **Efficacy results** | Median PFS 23.9 months with $^{177}$Lu-edotreotide vs 14.1 months with everolimus (*p=0.022*) | Expected 2027 | Median PFS not reached with $^{177}$Lu-DOTATATE vs 8.4 months with octreotide LAR (*p<0.001*) Estimated risk of death 60% lower with $^{177}$Lu-DOTATATE vs octreotide LAR (*p=0.004*) | Median PFS 22.8 months with $^{177}$Lu-DOTATATE vs 8.5 months with octreotide LAR (*p<0.0001*) |
| **Key efficacy outcome** | Clinically relevant and statistically significant benefit in PFS vs everolimus | Expected 2027 | Markedly longer PFS with $^{177}$Lu-DOTATATE vs high-dose octreotide LAR alone | Significantly extended PFS with combination vs octreotide LAR alone |
| **Key safety outcome** | Well-tolerated with favourable safety results | Expected 2027 | Limited acute toxic effects | Consistent with the established profile |

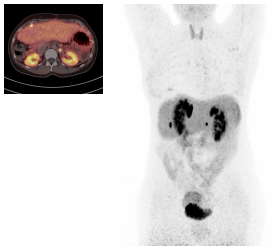
## Imaging

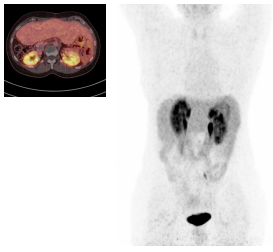
**To support diagnosis :**

- **MRI** of the abdomen and pelvis with a contrast agent or CT of abdomen and pelvis with arterial phase of liver
- **Somatostatin receptor** functional imaging at diagnosis
- **Gallium-68** and, in the US, copper-64 radioisotopes at diagnosis
- **DOTATATE/DOTATOC PET/CT** if surgery indicated, to identify "occult disease"

**Patient with P-NET** despite multiple treatments, including several surgeries, chemotherapy, SSAs, and everolimus.

**Same patient** showing complete response after PRRT.





*Source: Images kindly provided by Dr Ieva Ciuciulkaite, Dept. of Nuclear Medicine, University Hospital Essen, Germany*

## Managing adverse events*

- Most important for patients is **nausea during infusion of PRRT**. This is not associated directly with PRRT itself, but adjunct renal-protection agents *[8]*
- For regulators, renal dose-effects and potential renal toxicity are fundamental; **there are long-term data to show that PRRTs are renally well-tolerated** *[9]*
- For HCPs using maintenance therapy, long term bone marrow function effects are most relevant, although **they are infrequent** *[10]*

**Expert opinion*

*G, grade, GE, gastroenteral; HCP, healthcare practitioner; Ki67, Kiel 67; LAR, long-acting release; CT, computerised tomography; Lu, lutetium; MRI, magnetic resonance imaging; P, pancreatic; PET, positron emission tomography; PFS, progression-free survival; SoC, standard of care; SSA, somatostatin analogue: US, United States.*

### References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