Pivotal phase III COMPOSE trial will compare ^{177}Lu-edotreotide with best standard of care for well-differentiated aggressive grade 2 and grade 3 gastroenteropancreatic neuroendocrine tumors

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Background

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs), which represent approximately 70% of NETs, frequently develop metastatic disease with limited treatment options.[1]

Current standard therapies for the subset of well-differentiated high grade 2 and grade 3 GEP-NETs include cytoreductive procedures, somatostatin analogues, molecular targeted therapies (everolimus or sunitinib), chemotherapy and peptide receptor radionuclide therapy (PRRT), with no specified sequence of use.[2–4]

PRRT may stabilize disease and induce objective tumor responses. This treatment uses radiolabeled somatostatin analogues to selectively target somatostatin receptor expressing (SSTR+) tumor cells.[5]

No-carrier-added (n.c.a.) ^{177}Lu-edotreotide is an innovative radiolabeled somatostatin analogue with a favorable safety profile and promising efficacy.[5,6] Retrospective data in metastatic GEP-NETs treated with two or more ^{177}Lu-edotreotide cycles demonstrated a progression-free survival (PFS) of at least 30 months (Figure 1A). Overall survival estimates are presented in Figure 1B.

The currently recruiting Phase III COMPETE trial compares the efficacy and safety of 177Lu-edotreotide, versus everolimus, in grade 1 and grade 2 GEP-NETs.

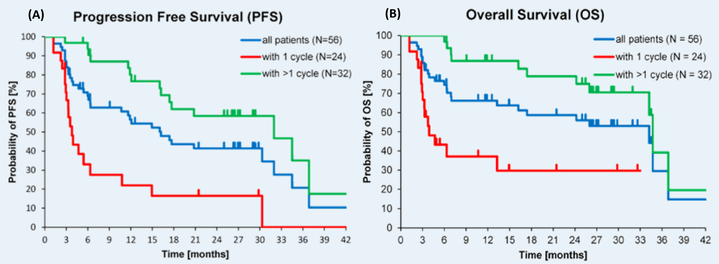

Figure 1. Kaplan-Meier estimates of (A) PFS and (B) OS in the study population depending on number of n.c.a. ^{177}Lu-edotreotide PRRT cycles.[6]

Mode of Action

PRRT contains a targeting molecule, which binds to the tumor specific receptor according to the **lock and key principle** (Figure 2), and a radioisotope. The targeting molecule can be used for both therapeutics and diagnostics; only the radioisotope has to be changed. This leads the way for theranostics in precision oncology.

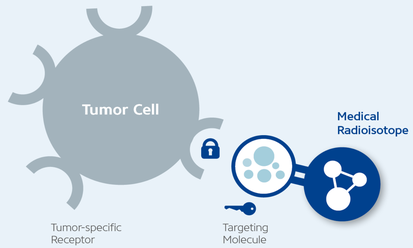

Figure 2. Lock and key principle of PRRT

Conclusions

Study recruitment for **COMPOSE** commenced in September 2021.

COMPOSE will **evaluate targeted radionuclide therapy** with **^{177}Lu-edotreotide** for patients with **well-differentiated high grade 2 and grade 3 SSTR+ GEP-NETs**, including for first-line therapy, compared to best standard of care.

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Clinical Phase III Trial COMPOSE NCT04919226:
Find more trial information on
www.itm-gep-net-trials.com; ClinicalTrials.gov

Main Inclusion/Exclusion Criteria

Inclusion Criteria:

- Patients aged ≥18 years
- Histologically confirmed diagnosis of unresectable, well-differentiated (high grade 2 or grade 3) GEP-NETs
- SSTR+ disease

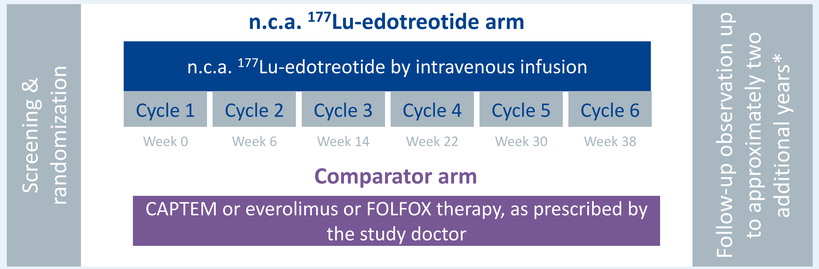
Exclusion Criteria:

- Prior PRRT
- Any major surgery within 4 weeks prior to randomization
- Other known malignancies
- Serious non-malignant disease
- Renal, hepatic, cardiovascular, or hematological organ dysfunction, potentially interfering with the safety of the trial treatments

CAPTEM: capecitabine-temozolomide; FOLFOX: folinic acid, fluorouracil and oxaliplatin; GEP-NET: gastroenteropancreatic neuroendocrine tumor; n.c.a.: no-carrier-added; OS: overall survival; PFS: progression-free survival; PRRT: peptide receptor radionuclide therapy; RECIST: response evaluation criteria in solid tumors; SSTR+: somatostatin receptor expressing.

Methods

COMPOSE is a prospective, randomized, controlled, open-label, multi-center, Phase III trial, in patients with well-differentiated, high grade 2 and grade 3 (Ki-67 index 15–55%), SSTR+ GEP-NETs. This trial is to evaluate the efficacy, safety and patient-reported outcomes of first- or second-line treatment with n.c.a. ^{177}Lu-edotreotide PRRT compared to best standard of care. COMPOSE was recently opened and is planned to recruit patients in 10 countries.



*Treatment response, tumor progression, survival data, information on further antineoplastic treatments and secondary malignancies

Figure 3. Summary schedule of treatments and follow-up consultation

COMPOSE aims to randomize 202 patients 1:1 to a defined number of cycles of ^{177}Lu-edotreotide or an active comparator. As shown in Figure 3, patients will receive either:

- PRRT with n.c.a. ^{177}Lu-edotreotide consisting of six cycles (7.5 GBq n.c.a. ^{177}Lu-edotreotide per cycle), administered as intravenous infusion (101 patients)

or:

- Either CAPTEM, everolimus, or FOLFOX, as chosen by the study doctor and administered according to local prescribing information, until diagnosis of progression or end of study (101 patients)

Study Endpoints

- **Primary:** Progression-free survival assessed every 12 weeks until disease progression (RECIST v1.1) or death, whichever occurs earlier.
- **Key Secondary:** Overall survival assessed up to 2 years after disease progression

References

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