COMPOSE: Phase III Trial of ^{177}Lu-edotreotide versus Standard of Care in Well-differentiated (WD) Aggressive Grade 2 and Grade 3 Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

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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]

Therapeutic algorithm for well-differentiated (WD) high-grade 2 and grade 3 gastroenteropancreatic neuroendocrine tumors (G2 + G3 GEP-NETs) is not well established. Current options include cytoreductive procedures, somatostatin analogues, everolimus, sunitinib, chemotherapy and peptide receptor radionuclide therapy (PRRT), with no specified sequence of use.[2–4]

Peptide Receptor Radionuclide Therapy (PRRT) could be useful in high grade NETs, however there is a lack of prospective evidence. ^{177}Lu-edotreotide is an innovative radiolabeled somatostatin analogue with a favorable safety profile and efficacy [5].

The ongoing Phase III trial COMPETE in G1 and G2 GEP-NETs is exploring the efficacy and safety of ^{177}Lu-edotreotide, in comparison to everolimus. COMPOSE is a complementary study with the aim of extending the therapeutic options for ^{177}Lu-edotreotide to high grade NETs.

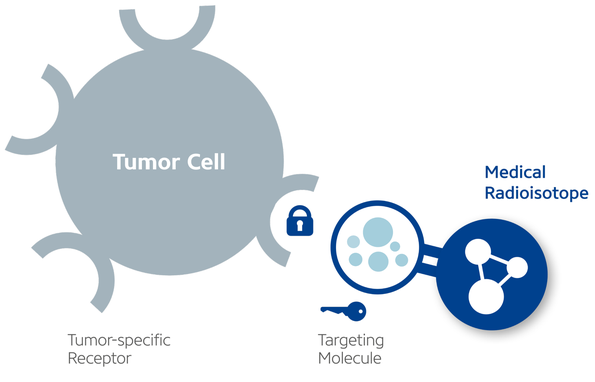

Figure 1. PRRT mode of action

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
- Renal, hepatic, cardiovascular, or hematological organ dysfunction, potentially interfering with the safety of the trial treatments

Conclusions

COMPOSE will contribute with the first prospective controlled data for ^{177}Lu-edotreotide, CAPTEM, FOLFOX and everolimus in the treatment of patients with high G2 and G3 GEP-NETs, clarifying the positioning of ^{177}Lu-edotreotide in the therapeutic algorithm.

References

1. Severi S, et al. Onco Targets Ther 2017;10:551–557; 2. Uri I & Grozinsky-Glasberg S. Clin Diabetes Endocrinol 2018;4:16; 3. Pavel M, et al. Ann Oncol 2020;31:844–860; 4. Sonbol MB & Halfdanarson TR. Curr Treat Options Oncol 2019;20:74; 5. Baum RP, et al. Theranostics 2016;6:501-510; 6. Strosberg J, et al. N Engl J Med 2017;376:125–135.

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compose

STUDY DESIGN

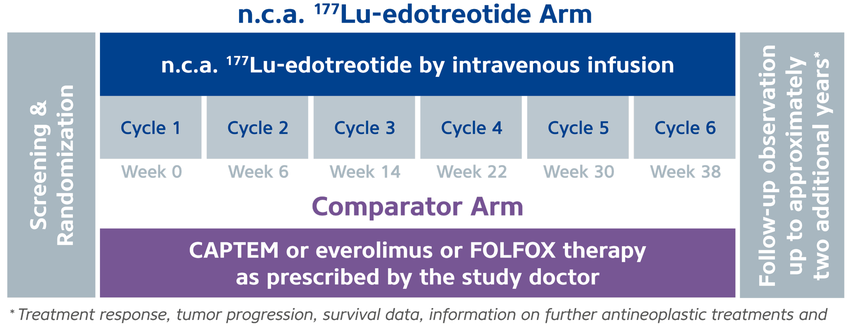
COMPOSE (NCT04919226) is a prospective, randomized, controlled, open-label, multi-center, Phase III trial, in patients with well-differentiated, high grade 2 and grade 3, SSTR+ GEP-NETs. This trial is to evaluate the efficacy, safety and patient-reported outcomes of first- or second-line treatment with n.c.a. ^{177}Lu-edotreotide PRRT compared to best standard of care.

Primary endpoint is progression free survival, assessed every 12 weeks until disease progression (RECIST v1.1) or death. Secondary outcomes include overall survival, assessed up to 2 years after disease progression.

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 2, 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).
- Either CAPTEM, everolimus, or FOLFOX, as chosen by the study doctor and administered according to local prescribing information (101 patients).

Recruitment commenced in September 2021 with first patient screened in France.



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

Figure 2. Summary schedule of treatments and follow-up consultation