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

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Introduction

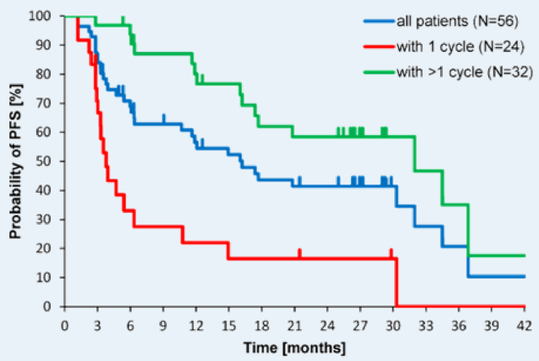
Gastroenteropancreatic neuroendocrine tumors (GEP-NETs), which frequently develop metastatic disease, represent an estimated 70% of NETs.[1]

There are limited treatment options with current standard therapies for well-differentiated aggressive grade 2 and grade 3 (Ki-67 index 15–55%) GEP-NETs; however, these may include somatostatin analogues; targeted radionuclide therapies (TRT); molecular targeted therapies (everolimus or sunitinib); chemotherapy; and cytoreductive procedures.[2–4]

TRT, which uses radiolabeled somatostatin analogues to selectively target somatostatin receptor expressing tumor cells, may stabilize disease and induce objective tumor responses.[5]

The radiolabeled somatostatin analogue ^{177}Lu-edotreotide has demonstrated promising efficacy and a favorable safety profile. Retrospective data in metastatic GEP-NETs treated with two or more ^{177}Lu-edotreotide cycles demonstrated nearly 30 months progression free survival (Figure 1).[6]

Figure 1. *Kaplan-Meier estimates of progression free survival in the study population depending on number of n.c.a. ^{177}Lu-edotreotide TRT cycles[6]*



CAPTEM: capecitabine-temozolomide; FOLFOX: folinic acid, fluorouracil and oxaliplatin; GEP-NETs: gastroenteropancreatic neuroendocrine tumors; n.c.a: non-carrier added; TRT: targeted radionuclide therapy; RECIST: response evaluation criteria in solid tumors; SSTR+: somatostatin receptor-positive

Method

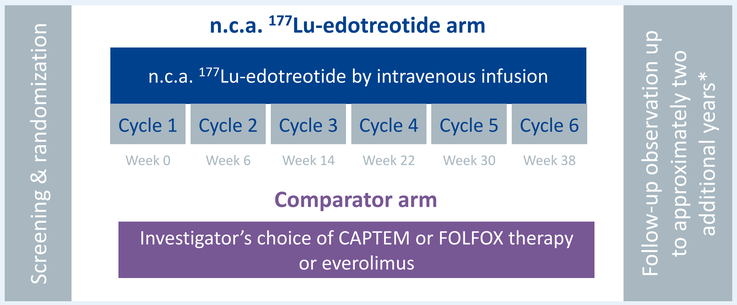
Trial Design

COMPOSE (NCT04919226), a prospective, randomised, controlled, open-label, multi-center Phase III study, aims to extend therapeutic options for patients with well-differentiated aggressive grade 2 and grade 3, somatostatin receptor-positive (SSTR+), GEP-NETs.

COMPOSE evaluates efficacy, safety, and patient-reported outcomes of first- or second-line treatment with ^{177}Lu-edotreotide TRT.

Patients will be randomised 1:1 (Figure 2) to:

- Up to six cycles ^{177}Lu-edotreotide (7.5 GBq per cycle), administered as an intravenous infusion (at least 101 patients) at 6- to 8-week intervals or
- Investigator's choice of CAPTEM, FOLFOX or everolimus, administered according to local prescribing information, until diagnosis of progression or end of study (at least 101 patients)



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

Figure 2: *Summary schedule of treatments and follow-up consultation*

Study Outcomes

Primary

- Progression-free survival assessed every 12 weeks until disease progression (RECIST v1.1) or death, whichever occurs earlier

Secondary

- Overall survival assessed up to 2 years after disease progression

Results

COMPOSE recruitment commenced in September 2021 and currently includes 29 open sites in Australia, France, India, Italy, the Netherlands, Spain, Sweden, the United Kingdom, and the United States. More sites and countries will follow.

Conclusion

COMPOSE results are expected to inform about optimal treatment options for patients with well differentiated aggressive grade 2 and grade 3 SSTR+ GEP-NETs, including for first-line therapy.

References

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Clinical Phase III Trial COMPOSE NCT04919226: ClinicalTrials.gov

Find more trial information on www.itm-gep-net-trials.com

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