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]

PRRT uses radiolabeled somatostatin analogues to selectively target somatostatin receptor expressing (SSTR$^+$) tumor cells.[2] It may be able to stabilize disease and induce objectively evaluable tumor response; however, there is a lack of prospective evidence.

No-carrier-added (n.c.a.) ^{177}Lu-edotreotide is an innovative radiolabeled somatostatin analogue with a favorable safety profile and promising efficacy.[2,3] Figure 1A, utilizing retrospective data in metastatic GEP-NETs, shows progression-free survival of at least 30 months following treatment with two or more cycles of ^{177}Lu-edotreotide. Figure 1B shows overall survival estimates.[3]

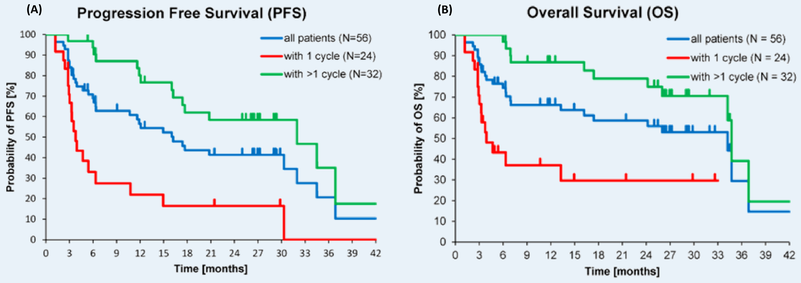


Figure 1. Kaplan-Meier estimates of (A) PFS and (B) OS in the study population depending on number of n.c.a. ^{177}Lu-edotreotide PRRT cycles[3]

COMPETE, a Phase III trial in grade 1 and grade 2 GEP-NETs comparing the efficacy and safety of ^{177}Lu edotreotide versus everolimus, has recently completed patient recruitment.[4]

Aims

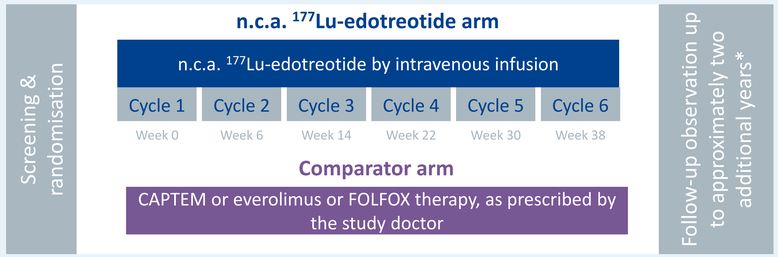
COMPOSE aims to extend the therapeutic options for ^{177}Lu-edotreotide to aggressive grade GEP-NETs.

Materials and Methods

- **COMPOSE** (NCT04919226) is a prospective, randomized, controlled, open-label, multi-center Phase III study, in patients with well-differentiated aggressive 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 ^{177}Lu edotreotide PRRT compared to best standard of care.

COMPOSE aims to randomize 202 patients 1:1 to a defined number of cycles ^{177}Lu-edotreotide or an active comparator (Figure 3)

- 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
- CAPTEM, everolimus, or FOLFOX, according to investigator´s choice and administered according to local prescribing information, until diagnosis of progression or end of study (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

Materials and Methods (cont)

Primary endpoint

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

Key secondary endpoint

- Overall survival, assessed up to 2 years after disease progression

Results

Recruitment for **COMPOSE** commenced in September 2021.

Conclusion

It is expected that **COMPOSE** will inform optimal treatment options for patients with well differentiated aggressive grade 2 and grade 3 SSTR$^+$ GEP-NETs, including for first-line therapy.

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

References

1. Severi S, et al. Onco Targets Ther 2017;10:551–557; 2. Strosberg J, et al. N Engl J Med 2017;376:125–135; 3. Baum RP, et al. Theranostics 2016;6:501-510.
4. ClinicalTrials.gov Identifier: NCT03049189

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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