COMPETE Trial – Peptide Receptor Radionuclide Therapy (PRRT) with ^{177}Lu-Edotreotide vs. Everolimus in progressive GEP-NET.

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PASSION FOR PRECISION

Background

There are only limited treatment options for metastasized gastroentero-pancreatic neuroendocrine tumors (GEP-NETs). Current standard therapies include somatostatin analogs and targeted drugs such as Everolimus and Sunitinib. While these treatments rarely induce objective tumor remission, disease stabilization may be achieved for limited periods of time. Median PFS with Everolimus in prospective phase III trials is 11 months. A subset of patients may benefit from systemic chemotherapy.

PRRT has recently emerged as a promising option providing more durable response and potentially higher objective response rates. This therapy uses IV-infused radiolabeled somatostatin analogues to deliver radioactivity directly to metastases, destroying the tumor cells but sparing most of the surrounding tissue.

PRRT with radiolabeled SSTR-ligands, such as ^{177}Lu-DOTATATE has shown great results in the treatment of progressive midgut NET, with median progression-free survival (mPFS) of 33.0 months, and disease control rates 65%, respectively. ^{177}Lu-Edotreotide is an innovative PRRT agent, with favorable safety profile, and promising efficacy. A first retrospective study on ^{177}Lu-Edotreotide PRRT in metastasized GEP-NET reported a median PFS of 34.5 months in patients who received ≥2 treatment cycles. A direct comparison of PRRT vs. medical therapy has not yet been performed. This is where the COMPETE trial takes effect.

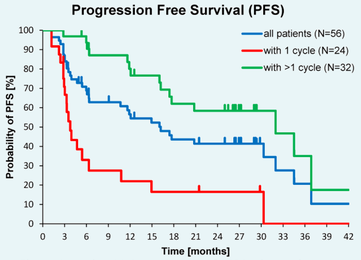


Figure 1. Kaplan-Meier estimates of PFS in the study population depending on number of ^{177}Lu-Edotreotide PRRT cycles.

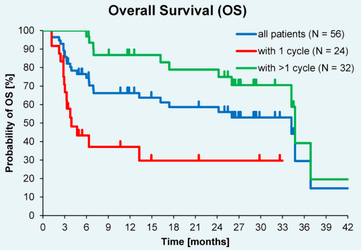


Figure 2. Kaplan-Meier estimates of OS in the study population depending on number of ^{177}Lu-Edotreotide PRRT cycles

Method

Trial design

COMPETE is a prospective, randomized, controlled, open-label, multi-centers phase III study to evaluate the efficacy and safety of ^{177}Lu-Edotreotide PRRT in comparison with Everolimus in patients with inoperable, progressive, somatostatin receptor-positive (SSTR$^+$) GEP-NETs. The study is ongoing in 12 countries and 43 sites and currently recruiting patients.

300 patients will be randomized with progressive GEP-NET: 200 will receive max. 4 cycles of ^{177}Lu-Edotreotide PRRT (7.5 GBq/cycle) every 3 months or until diagnosis of progression; 100 will receive 10 mg Everolimus daily for 24 months, or until diagnosis of progression. Study treatment duration per patient is 24 months.

Study Objectives

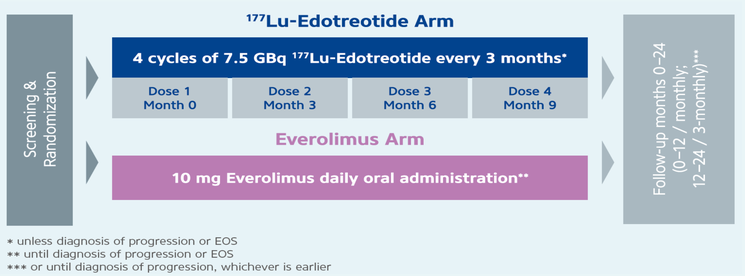
Primary Objective

is to demonstrate the efficacy of PRRT with ^{177}Lu-Edotreotide to prolong median progression-free survival (mPFS) in patients with inoperable, progressive, SSTR$^+$ GEP-NET, compared to Everolimus.

Secondary Objectives

assess objective response rates (ORR), defined as the proportion of patients achieving partial response (PR) or complete response (CR) as best outcome, after treatment with ^{177}Lu-Edotreotide, compared to Everolimus. To assess overall survival (OS), defined as the time from the date of randomization until death.

Treatment & Assessments – 24 months



* unless diagnosis of progression or EOS
** until diagnosis of progression or EOS
*** or until diagnosis of progression, whichever is earlier

Figure 4. Medication administration plan: ^{177}Lu-Edotreotide vs. Everolimus.

Mode of Action

Lock and Key Principle

Targeted radiopharmaceuticals contain a targeting molecule and a radioisotope. The targeting molecule binds to the tumor specific receptor according to the lock and key principle. In most cases the targeting molecule can be used for both diagnostics as well as therapy – only the radioisotope has to be changed. This opens up the way for Theranostics in Precision Oncology.

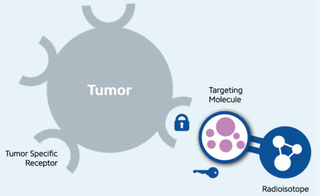


Figure 3. Lock and key principle of PRRT with targeting molecule and medical radioisotope.

Main Inclusion Criteria

- Written informed consent
- Male or female ≥18 years of age
- Histologically and clinically confirmed diagnosis of well-differentiated NET of non-functional gastroenteric origin (GE-NET) or both functional or non-functional pancreatic origin (P-NET), tumor grade G1 or G2 (Ki-67 <20%), unresectable or metastatic
- Measurable disease per RECIST 1.1, on CT/MRI scans, defined as at least 1 lesion with ≥1 cm in longest diameter, and ≥2 radiological tumor lesions in total
- Somatostatin receptor positive (SSTR$^+$) disease, as evidenced by SSTR imaging (SRI) within 4 months prior to randomization
- Radiological disease progression, defined as: Progressive disease per RECIST 1.1. criteria, evidenced by CT/MRI with ≥90 days interval during 12 months prior to randomization
- Karnofsky performance status (KPS) scale ≥70
- Life expectancy of at least 6 months
- Glomerular filtration rate (GFR, MDRD) ≥60 mL / min / 1.73 m^2

Conclusion

COMPETE was designed to extend scientific knowledge of PRRT in the treatment of NETs. Accordingly, a broad indication was chosen with non-functional GE-NETs / functional or nonfunctional P-NETs. Everolimus, the current standard of care therapy, was chosen as comparator. This study is also the first to test PRRT as a first-line therapy in subset of NETs. The trial results could therefore influence the future treatment algorithm of NETs.

References

Clinical Phase II Trial

Baum et al., 2016, Theranostics, doi: 10.7150/thno.13702

Please use this QR code by scanning it with your phone camera or find the publication at: www.thno.org/v06p0501.htm

Clinical Phase III Trial COMPETE

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