

**Study Settings**

**Primary objective**

Compare Progression Free Survival (PFS) after treatment with 177Lu-DOTATATE 60 mg and Octreotide LAR 30 mg in patients with progressive midgut NETs.

**Secondary objectives**

- Compare the Objective Response Rate (ORR) between the two arms.
- Compare Pharmacokinetic and pharmacodynamic data.
- Evaluate the safety and tolerability of 177Lu-DOTATATE.
- Compare the health related quality-of-life (QoL) as measured by the EORTC QLQ-G.I.21 questionnaire.

**Study Endpoints**

Tumor Response Rate (currently evaluable patients)

- **Prior Cancer Treatments at Enrollment (ITT population, N=229)**
  - DMT (Dose Modifying Toxicity).
  - No DMT

**Participants in 51 Centers - 8 Countries**

- **Tumor Response Rate (currently evaluable patients)**
  - Octreotide LAR 60 mg: 16 (6%)
  - 177Lu-DOTATATE: 34 (29%)

**Safety and Tolerability (ITT population, N=229)**

- **Any adverse event**
  - 108 (47%)
  - 95 (42%)

- **Grade 3/4 adverse events**
  - 29 (13%)
  - 25 (11%)

- **N = 229 (ITT)**
  - Number of events: 30
  - **177Lu-DOTATE: 23**
  - **Octreotide LAR 60 mg: 7**

- **Withdrawals due to adverse events**
  - 7 (3%)
  - 3 (2%)

**Summary and Conclusions**

- In this first prospective randomized study in patients with progressive midgut NETs, 177Lu-DOTATATE was superior to Octreotide LAR 60 mg in terms of PFS (HR 0.39, 95% CI 0.209 – 0.701, p = 0.0012). All progression were centrally confirmed and independently reviewed for eligibility (SAP).

- One patient withdrew due to adverse events (n=30).

- While few treatment options are now up to now available, 177Lu-DOTATATE appears as a major advance in this patient population.

**Acknowledgements**

We thank the patients and investigators participating in this trial.

**NETTER-1 Study Objectives and Design**

- Evaluate the efficacy and safety of 177Lu-DOTATATE vs LAR Octreotide in patients with progressive midgut NETs.
- Inclusion criteria: Patients ≥18 years of age.
- Exclusion criteria: Karnofsky performance score < 60.

**Results**

**Participants**

- 229 patients had liver as a primary site of metastasis (84% vs. 83% in the 177Lu-DOTATATE vs comparator arm, respectively).

**PRIMARY endpoints (ITT population, N=229)**

- **Progression free survival (PFS) [months]**
  - 177Lu-DOTATATE: 8.4 months
  - Octreotide LAR 60 mg: 4.2 months

- **ORR (CR + PR)**
  - 177Lu-DOTATATE: 19% (11-26%)
  - Octreotide LAR 60 mg: 3% (0-6%)

- **PFS**
  - Median PFS: Not reached
  - P = 0.0186 (CI 95%)

**Overall survival (interim analysis)**

- **Median OS**
  - 177Lu-DOTATATE: 22.7 months
  - Octreotide LAR 60 mg: 17.2 months

- **Number of deaths**
  - 177Lu-DOTATATE: 13
  - Octreotide LAR 60 mg: 22

**Adverse events**

- **Treatment-related serious adverse events (n=229)**
  - 10 SAEs
  - ≥ 10 patient withdrawals

- Currently available safety data confirms the results of the previous phase II study.

**Methodology and Design**

- Protocol consists of a cumulative dose of 20.8 GBq of 177Lu-DOTATATE at 4.74 GBq every 4 weeks, until the control treatment with 30 mg Octreotide LAR is compared to 60 mg Octreotide LAR every 4 weeks.
- Design objective was to compare patients randomized to the 2 arms (1:1).
- Randomization was centrally assessed in both arms, every 12 weeks (91 patients) from the randomization data, according to the RECIST criteria. Efficacy is blindly and independently assessed through image review by qualified readers.
- Patients who had previously received first line disease progression or unacceptably toxic therapy, or inability to/willingness to comply with study requirements or consent withdrawal.

**NETTER-1 Study population**

- 229 patients treated with 177Lu-DOTATATE arm, only 5% patients experienced DMT (Dose Modifying Toxicity).

**Population Characteristics at Enrolment (ITT population, N=229)**

- Only available in 98 patients

- **Chromogranin A (µg/L)**
  - Grade 2: 76/40 (66/34%)
  - Grade 3/4: 81/32 (72/28%)

- **Patients who completed trt phase, N=102**

- **Primary tumor site**
  - Other: 47 (27%)
  - Chemo-embolization: 90 (78%)
  - Prior ablation: 93 (82%)

- **Previous treatment**
  - Progression free survival (PFS) [months]
  - 177Lu-DOTATATE: 8.4 months
  - Octreotide LAR 60 mg: 4.2 months

- **ORR (CR + PR)**
  - 177Lu-DOTATATE: 19% (11-26%)
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- **PFS**
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- **Overall survival (interim analysis)**
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- **Number of deaths**
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  - Octreotide LAR 60 mg: 22

- **Progression-free Survival**
  - N = 229 (ITT)

- **Safety analysis**
  - Treatment-related serious adverse events (n=229) (1): 10 SAEs
  - ≥ 10 patient withdrawals

- Currently available safety data confirms the results of the previous phase II study.

**Study Design**

- Treatment: Patients in 51 centers - 8 countries.