

Prediction of PRRT outcome using multimodality imaging in patients with GEP-NETs: results from a prospective phase II clinical trial - The Lumen trial -

Magdalena Mileva, Gwennaëlle Marin, Hugo Levillain, Carlos Artigas, Camille Van Bogaert, Clémentine Marin, Rachele Danieli, Bruno Vanderlinden, Zéna Wimana, Patrick Flamen, Ioannis Karfis

Jules Bordet Institute,
Hôpital Universitaire de Bruxelles (H.U.B)



Disclosures

- Nothing to declare



Introduction

Peptide receptor radionuclide therapy (PRRT)

- ✓ Validated and effective systemic treatment option in the clinical management of patients with advanced neuroendocrine tumours (NETs) expressing somatostatin receptors (SSTRs).
 - ✗ Lack of strong biomarkers for predicting PRRT efficacy, particularly imaging biomarkers ("imaging – based" treatment).
 - ?
- Can molecular imaging play a crucial role not only for the selection of patients, but also for predicting response to PRRT?



Study objective

Aim: To predict ^{177}Lu -DOTATATE treatment outcome using ^{68}Ga -DOTATATE PET/CT imaging and tumour dosimetry



Prospective, monocentric,
phase II clinical-imaging study:

The **LuME**n study

^{177}Lu -octreotate treatment prediction using
Multimodality imaging in refractory
neuro**End**ocrine tumours

Primary endpoint:

- Lesion-based Time to Progression (TTP)

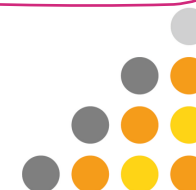
Secondary endpoints:

- Progression-free survival (PFS)
- Best morphological response (RECIST 1.1)

Population:

- ≥ 18 years old
- Metastatic or locally advanced, unresectable histologically proven GEP-NETs
- Grades 1-3
- Progressive as per RECIST 1.1/clinically/SSTR-PET/CT within 12mo before inclusion
- SSTR+ disease

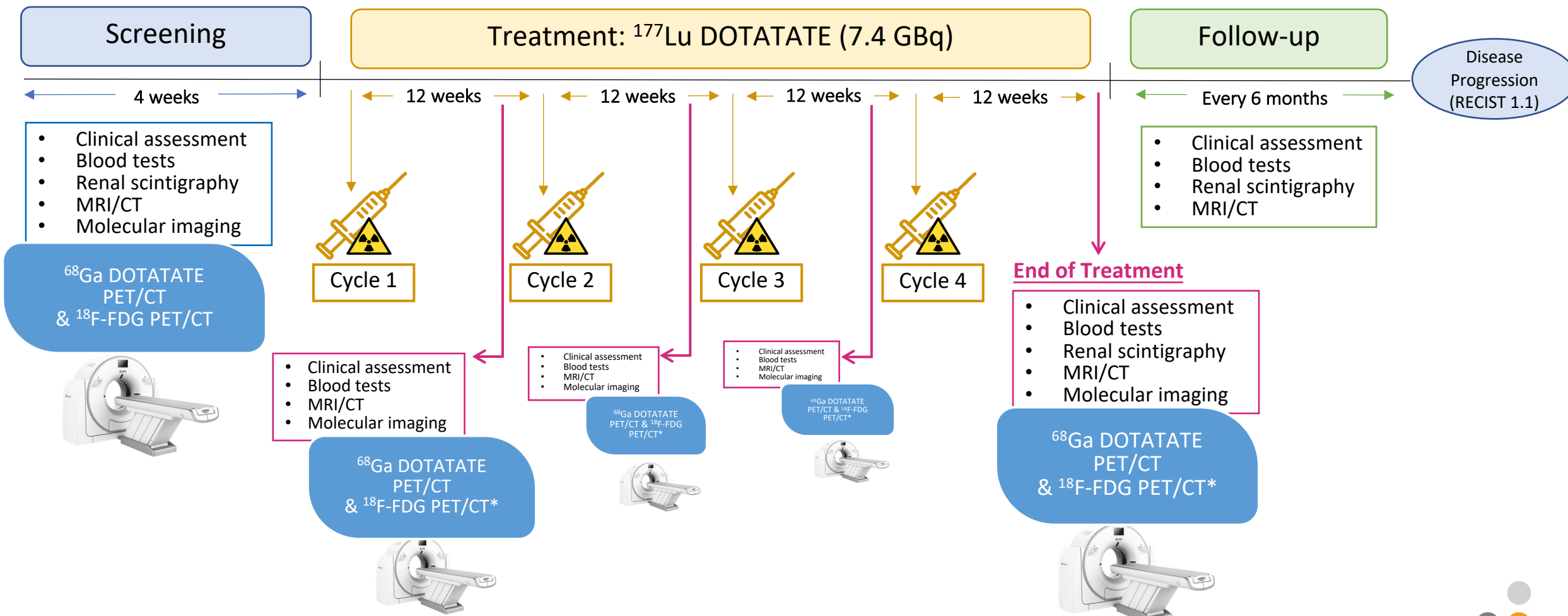
Clinicaltrial.gov identifier: NCT01842165



Design

The LuMEEn study

¹⁷⁷Lu-octreotate treatment prediction using
Multimodality imaging in refractory
neuroEndocrine tumours



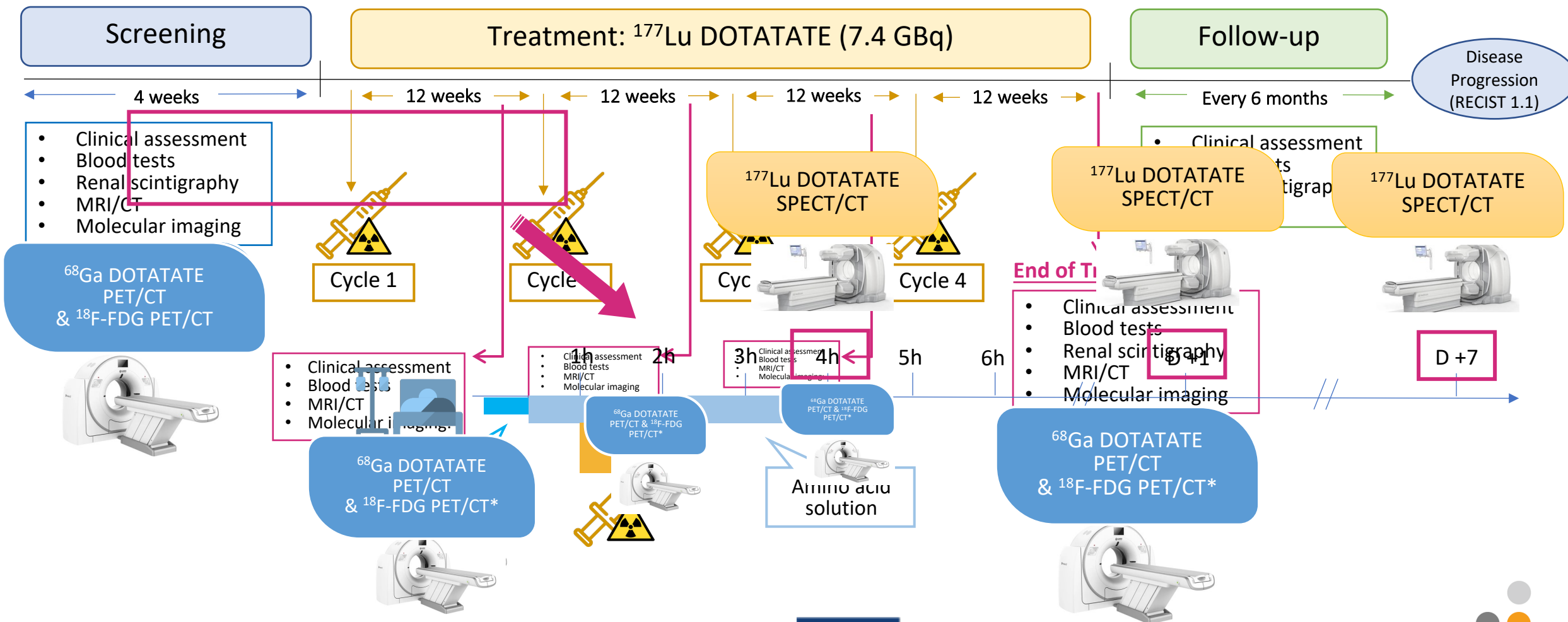
*Repeated if positive at screening



Design

The LuMEEn study

¹⁷⁷Lu-octreotate treatment prediction using
Multimodality imaging in refractory
neuroEndocrine tumours



Methodology and image analysis

Step 1:

⁶⁸Ga DOTATATE
PET/CT



Max 5 target lesions
PETEdge Tool (MIM6.9)



Cycle 1

Step 2:

¹⁷⁷Lu DOTATATE
SPECT/CT



Same target lesions
Region-growing tool
(MIM6.9)

10-12
weeks p.i.

Step 3:

⁶⁸Ga DOTATATE
PET/CT



Same target lesions
PETEdge Tool (MIM6.9)

Baseline

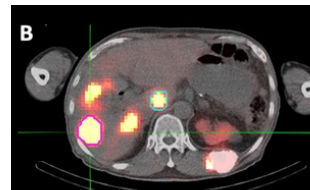
Uptake parameters

SUVmax
SUVmean
tumour-to-spleen ratio
tumour-to-blood ratio

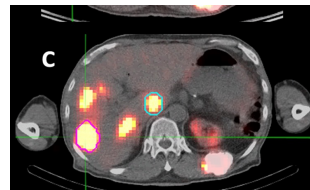
Volumetric parameters

SSTR-TV
TL-SSTR expression

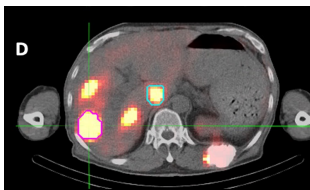
4h p.i.



1 day p.i.



7 days p.i.



Absorbed dose
(Gy) at Cycle 1

Change after C1

Uptake parameters

SUVmax
SUVmean
tumour-to-spleen ratio
tumour-to-blood ratio.

Volumetric parameters

SSTR-TV
TL-SSTR expression

Methodology and image analysis

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PET/CT

Same target lesions
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Baseline:

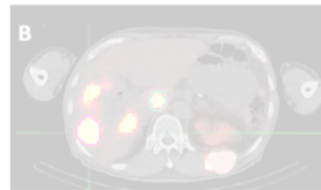
Uptake parameters

SUVmax
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tumour-to-spleen ratio
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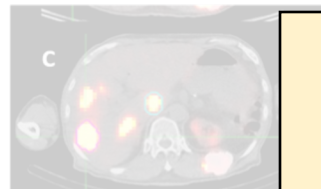
Volumetric parameters

SSTR-TV
TL-SSTR expression

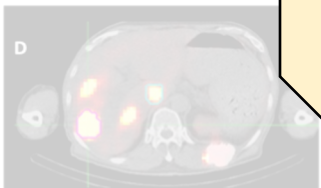
4h p.i.



1 day p.i.



7 days p.i.



Change after Cycle 1:

Uptake parameters

Parameters were assessed in individual lesions & on a patient level using the average lesion values (+minimal and maximal for tumor absorbed dose)

Population characteristics (N = 37)

Gender, n (%)	
male	19 (51)
female	18 (49)
Mean age (SD) at inclusion, y	66 ± 8.1
Median (IQR) time since diagnosis, y	3.4 (1.7-7.7)
Primary tumour site, n (%)	
small intestinal	23 (62)
pancreatic	10 (27)
colorectal	4 (11)
Tumour grade, n (%)	
grade 1	12 (32)
grade 2	22 (59)
grade 3	3 (8)
Site of metastasis, n (%)	
liver	32 (86)
lymph nodes	31 (84)
bone	22 (59)
peritoneum	12 (32)
other	11 (30)

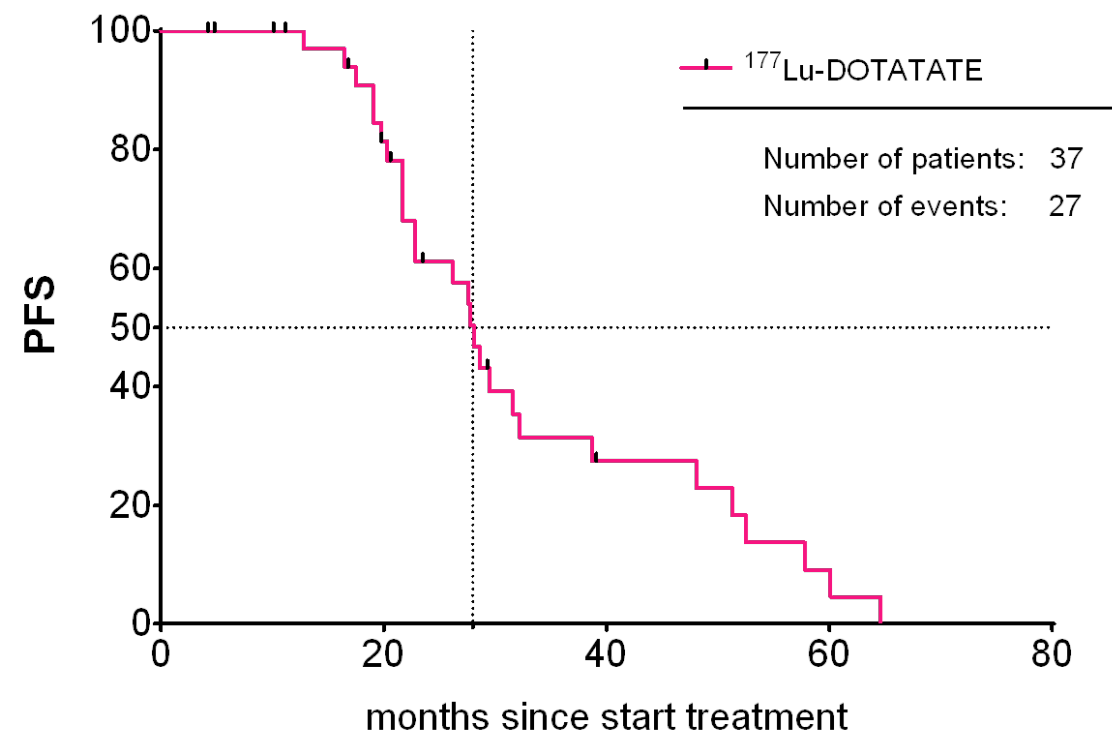
Symptoms, n (%)	
diarrhoea	16 (43)
pain	15 (41)
fatigue	11 (30)
flushes	9 (24)
no symptoms	12 (32)
Previous treatments, n (%)	
SSAs	36 (97)
surgery	27 (73)
targeted therapy	11 (30)
chemotherapy	8 (22)
liver targeted therapy	8 (22)
radiotherapy	4 (11)
interferon	1 (3)



Results

Outcomes:

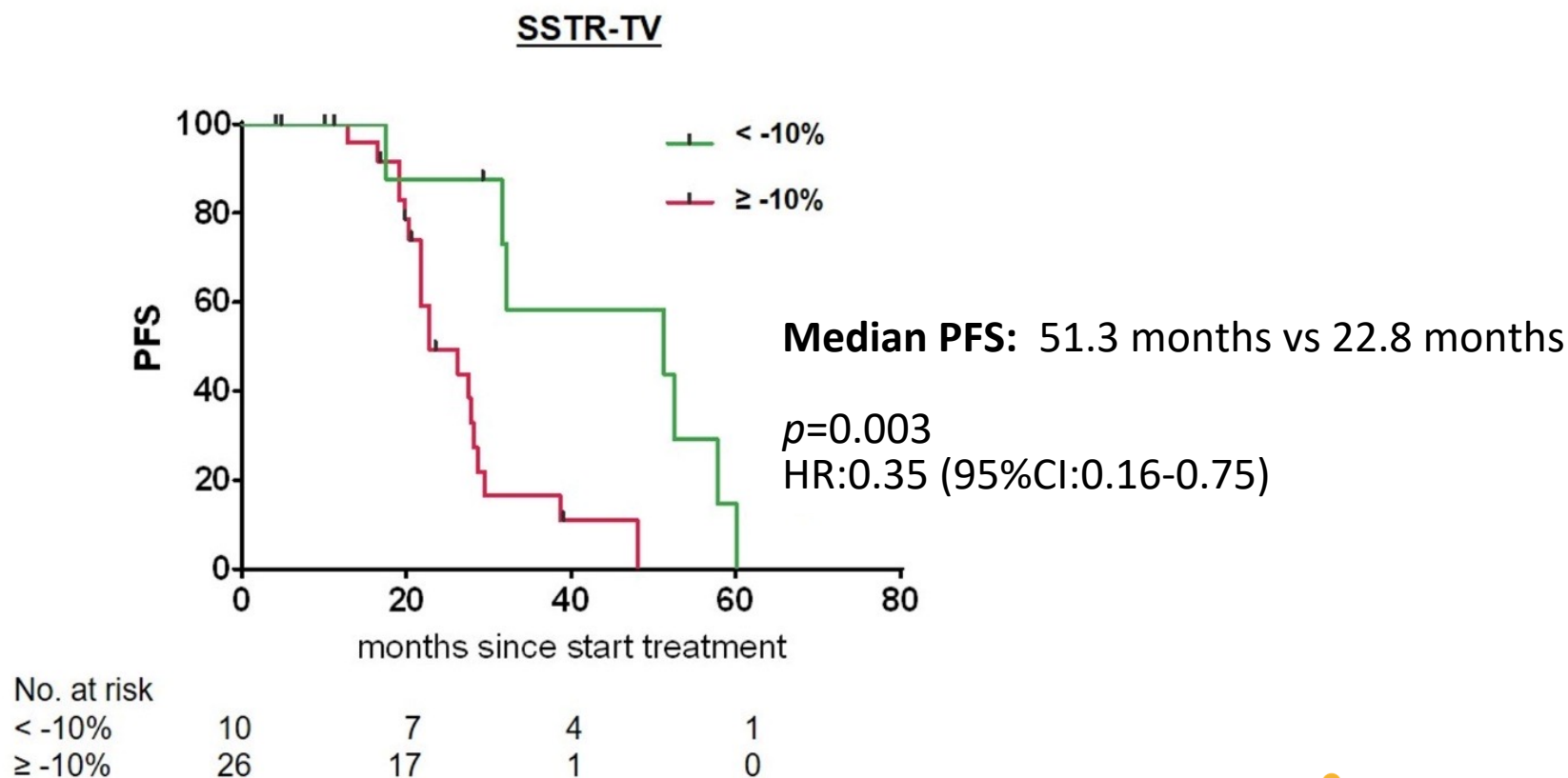
- Median lesion TTP --> Not reached
- 14% (12/84) target lesions progressed (RECIST 1.1) at a median FU time of 57 mo (95%CI: 50-71)
- Median PFS: 28 months
- ORR: 30% (11/37 pt with RECIST 1.1 partial response)



Results

Patient-based analysis of association with imaging parameters:

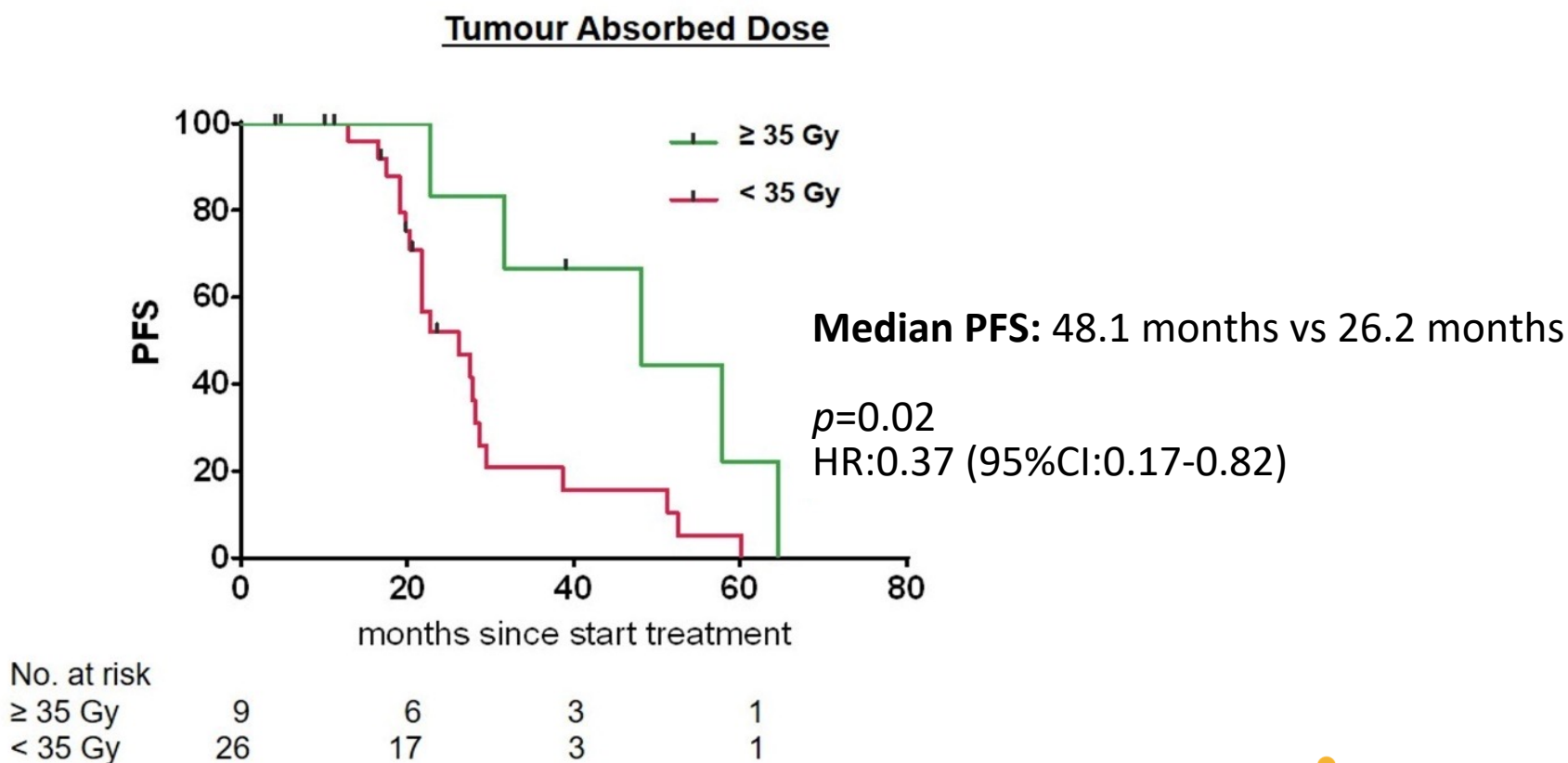
- Decrease of SSTR-TV after C1 from baseline was associated with longer PFS.



Results

Patient-based analysis of association with imaging parameters:

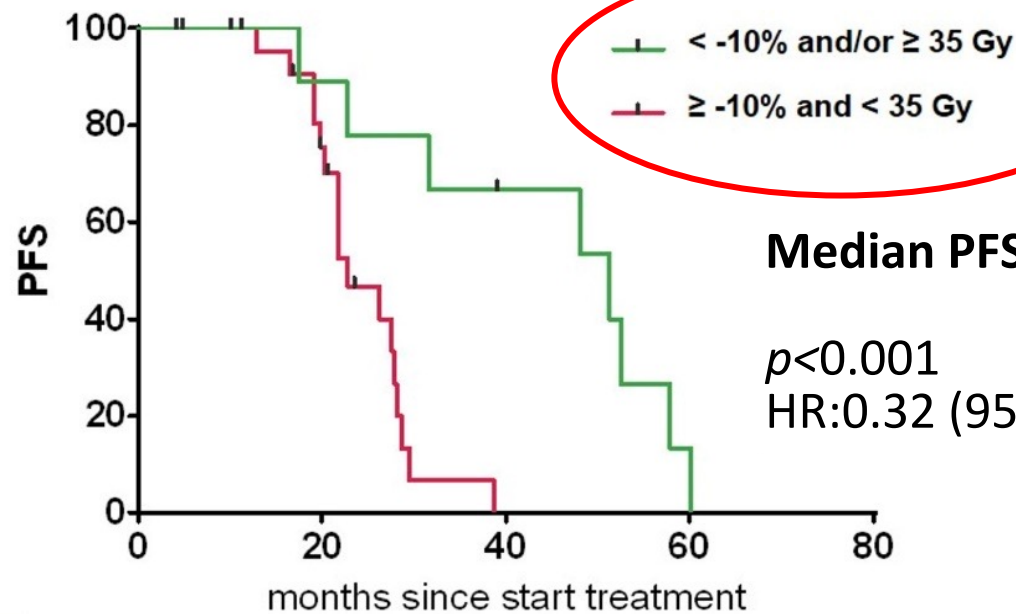
- Minimal absorbed dose received by all target lesions in C1 was associated with longer PFS.



Results

Patient-based analysis of association with imaging parameters:

SSTR-TV and Tumour Absorbed Dose



Results

Patient-based analysis of association with imaging parameters:

- Uptake parameters on ^{68}Ga -DOTATATE PET/CT (baseline and changes after C1) and the average and maximal tumor absorbed dose were not associated with PFS.



Summary and Conclusions

Prospective study, assessing the value of molecular imaging semi-quantitative parameters and tumour absorbed dose in predicting ^{177}Lu -DOTATATE outcome.

High efficacy of PRRT in patients with GEP-NETs, which compares favourably to results from other studies.

Biomarkers predictive of longer PFS, supporting the use of ^{68}Ga -DOTATATE PET/CT for early therapy response assessment and providing basis for treatment strategies focusing on higher administered activities in the early therapy cycles to be explored.



 SYMPOSIUM
BRUSSELS'23
BELNUC

Thank you for your attention!

magdalena.mileva@hubruxelles.be

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