Improving Treatment Options for Somatostatin Type 2 Receptor Negative Neuroendocrine Tumor Patients

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23147

Source
Nationaal Trial Register

Brief title
IMPROVE-NET

Health condition

metastasized neuroendocrine tumors (NETs)

Sponsors and support

Primary sponsor: Erasmus MC, Rotterdam, the Netherlands
Source(s) of monetary or material Support: Erasmus MC

Intervention

Outcome measures

Primary outcome

The primary endpoint will be the percentage of patients that will have an uptake of 68Ga-DOTATATE in the tumor equal to or above that of the liver after the 14 days

treatment period.

Secondary outcome

• Safety, as number of adverse events
• Drug levels of valproic acid
• Dosimetric evaluation of intra- and intertumoral SSTR2 expression
• Leucocyte methylation analysis

Study description

Background summary

Somatostatin receptor type 2 (SSTR2) expressions are of eminent importance for the staging and treatment of neuroendocrine tumors (NETs). The clinical benefit obtained by treatment with unlabeled and radiolabeled somatostatin analogues does not apply to the subset of patients with SSTR2-negative tumors. The lack of these anti-tumoral options could be responsible for the inferior outcome of these patients compared to those with SSTR2-positive tumors. Recent in vitro data showed the possibility of upregulating SSTR2 expression in pancreatic NET cells through treatment with epigenetic drugs. Translating these methods into clinic could substantially improve diagnostic and treatment options for SSTR2-negative tumors.
The aim of this prospective proof-of-concept study is to increase the expression of the SSTR2 in SSTR2-negative NET patients to levels amenable for somatostatin analogue treatment through the use of epigenetic drugs.

Study objective

The combined treatment with the epigenetic drugs valproic acid and hydralazine will lead to an increase in SSTR2 expression levels in
patients with metastasized Grade 1 or 2 NETs with low uptake on 68Ga-DOTATATE-PET CT.

Study design

Baseline, 1 & 2 weeks after start of treatment

Intervention

14 days treatment with valproic acid (30mg/kg body weight/day) and hydralazine (150mg / day)

Contacts

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Eligibility criteria

Inclusion criteria

• Age ≥18 years
• Inoperable or metastasized neuroendocrine tumor with well-differentiated histology (grade 1 or 2)
• SSTR2 negativity on 68Ga DOTATATE PET scan, defined as tumor uptake on 68Ga-DOTATATE PET CT below that of the liver

Exclusion criteria

• Hypotension, defined as systolic blood pressure <90mmHg
• Heart failure, defined as NYHA III-IV
• Impaired kidney function, defined as creatinine clearance <50ml/min
• Impaired liver function, defined as bilirubin or liver transaminases >3 times upper normal range
• Uncontrolled hormonal symptoms including severe diarrhea, defined as >5 loose stools / day
• Severe hypoalbuminemia, defined as serum albumin concentration <25g/L
• Epilepsy
• Known allergies / intolerances to valproic acid or hydralazine
• Existing drug treatment which cannot be stopped and interacts or interferes with study drugs
• Inability to provide informed consent
• End of life care

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-05-2019
Enrollment:	10
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	13-05-2019
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7726
Other	METC Erasmus MC : MEC-2019-0031

Study results