Imaging of tumour microenvironment in patients with oropharyngeal head and neck squamous cell carcinoma using RGD PET/CT imaging.

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The aim of this study is to assess differences in tumour microenvironment between HPV+ and HPV- oropharyngeal HNSCC using [68Ga]Ga-RGD2 PET/CT and perfusion CT.

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON47965

Source
ToetsingOnline

Brief title
PIVOT study - RGD PET Imaging of Vasculature in Oropharyngeal Tumours

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
mouth- and throat cavity tumours, Oropharyngeal squamous cell carcinomas

Research involving
Human

Sponsors and support

Primary sponsor: Radiologie en Nucleaire Geneeskunde

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: HPV, Oropharyngeal carcinoma, PET imaging, tumour vasculature

Outcome measures

Primary outcome

The primary objective of this study is to assess the differences in [68Ga]Ga-RGD2 uptake and quantitative CT perfusion parameters between HPV+ oropharyngeal HNSCC tumours and HPV- oropharyngeal HNSCC tumours in patients who will be treated with chemoradiotherapy. Furthermore, the changes in [68Ga]Ga-RGD2 uptake and CT perfusion parameters in tumours before and during chemoradiotherapy will be investigated.

Secondary outcome

To explore the correlation between the PET/CT and CT perfusion scans and locoregional control at one year follow-up.

Study description

Background summary

The incidence of Human Papilloma Virus positive (HPV+) oropharyngeal Head and Neck Squamous Cell Carcinoma (HNSCC) is rising and it has become evident that this type of cancer represents a subgroup of HNSCC that is characterized by a more favourable prognosis, mediated by a distinct tumour microenvironment, compared to patients with HPV negative (HPV-) tumours (five year overall survival of approximately 80% versus approximately 45%). However, the exact mechanisms underlying this improved treatment outcome and the potential role of the tumour microenvironment are not fully understood yet. A distinctive factor may include changes in endothelial activation during the cancer associated response. Endothelial activation is characterized by the expression of αvβ3 integrins and the role of this integrin in angiogenesis makes it a relevant target for molecular imaging. Imaging of αvβ3 integrin expression may allow us

to obtain more insight in the differences in tumour microenvironment between HPV+ and HPV- oropharyngeal HNSCC. Therefore, this technique may have the potential to predict response to treatment and might allow us to investigate the possibility to steer treatment decisions in future clinical trials.

Study objective

The aim of this study is to assess differences in tumour microenvironment between HPV+ and HPV- oropharyngeal HNSCC using [68Ga]Ga-RGD2 PET/CT and perfusion CT.

Study design

This is a non-randomized, non-blinded, prospective proof-of-concept study in patients with a T1-T4N0-3 oropharyngeal squamous cell carcinoma of at least 1 cm in diameter, who will be treated with chemoradiotherapy (CRT) as per standard of care. Dynamic [68Ga]Ga-RGD2 PET/CT scans and CT perfusion scans of the tumour lesion will be performed at baseline and in the second week of chemoradiation treatment to investigate the changes in tracer uptake and perfusion CT during treatment. Furthermore, the differences in tracer uptake and perfusion CT between HPV+ and HPV- tumours will be assessed.

Study burden and risks

Toxicity tests have been performed in mice and no adverse events were seen. Previous studies with [68Ga]Ga-RGD2 (n=22) in our department showed no adverse events. The risks associated with the radiolabeled peptide injection are negligible. Only those patients who meet the inclusion criteria (normal kidney function) are included. The combination of two [68Ga]Ga-RGD2 PET/CTs and perfusion CTs will cause a radiation dose equivalent below 15 mSv to the patient. The additional radiation dose due to participating in this study is negligible as compared to the radiation dose obtained during standard of care chemoradiation therapy: The additional dose falls within the daily error margin of the therapeutic fractionated radiotherapy (RT) dose. Therefore, participation to this study will not cause a significant change in risk. Since routine diagnostic and treatment are not influenced by the outcome of this study, the patient will not directly benefit from participation in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with a histologically proven OHNSCC;
- P-16 immunohistochemical analysis to determine HPV status of the tumour;
- A primary tumour lesion with a diameter of at least 1.0 cm concluded from a diagnostic CT, MRI or FDG PET/CT scan within 4 weeks prior to intake;
- Planned chemoradiotherapy as primary treatment;
- Age of at least 18 years;
- Ability to provide written informed consent.

Exclusion criteria

- Contra-indication for (PET/)CT: Pregnancy; Breast-feeding; Severe claustrophobia.
- Contra-indication for administration of iodine-containing contrast agents.
- Other serious illness, e.g. history of malignancies
- Estimated creatinine clearance <= 30 mL/min according to the Cockcroft-Gault formula

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-11-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	Ga-68-DOTA-E-(cRGDfK)2

Ethics review

Approved WMO Date:	04-06-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-08-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-12-2019
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2019-001843-37-NL
CCMO	NL69928.091.19