Sentinel lymph node (SLN) detection in early oral cancer using Gallium-68-Tilmanocept PET/CT

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Ethical review	Approved WMO
Status	Pending
Health condition type	Head and neck therapeutic procedures
Study type	Observational invasive

Summary

ID

NL-OMON55311

Source
ToetsingOnline

Brief title
SEAGATE study

Condition

- Head and neck therapeutic procedures

Synonym
Mouth cancer, occult lymph node metastasis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Oral cavity carcinoma, PET/CT, Sentinel lymph node biopsy

Outcome measures

Primary outcome

The sensitivity and negative predictive value of 68Ga-Tilmanocept PET/CT combined with conventional lymphoscintigraphy for SLNB. Furthermore, the sensitivity and negative predictive value for preoperative 68Ga-Tilmanocept PET/CT alone will be compared with conventional preoperative lymphoscintigraphy alone.

Secondary outcome

To compare the number of 68Ga-Tilmanocept PET-CT detected SLNs with those detected by means of 99mTc-Tilmanocept lymphoscintigraphy on a per-subject basis.

To compare histopathologic assessment (presence or absence of metastasis) of the excised lymph node(s) detected by conventional preoperative 99mTc-Tilmanocept lymphoscintigraphy and intraoperative gammaprobe localization, with the SLNs identified by means of preoperative 68Ga-Tilmanocept PET-CT.

Observing contralateral drainage patterns in lateralized tumors and compare these patterns between of 68Ga-Tilmanocept PET-CT and 99mTc-Tilmanocept lymphoscintigraphy, especially in case of a histopathological positive sentinel node.

To assess pairwise inter-observer agreements between 68Ga-Tilmanocept PET-CT

and 99mTc-Tilmanocept lymphoscintigraphy regarding preoperative SLN detection.

Study description

Background summary

Sentinel lymph node biopsy (SLNB) is a diagnostic staging procedure that is applied in a variety of tumor types, including oral cavity squamous cell carcinoma (OSCC). The procedure aims to identify the first draining lymph node(s) (SLN(s)), which is most likely to harbour metastases. The histopathological status of the SLN reflects the histopathological status of the rest of the nodal basin, and additional treatment of the nodal basin (e.g. surgery) should be performed in case of metastatic involvement of the SLN. Detecting SLNs close to tumor sites is hampered, since the injection site of the radiotracer, around the primary tumor, produces a large hotspot on lymphoscintigraphy possibly hiding SLNs in close proximity of the primary tumor (*shine through* effect). Because of higher resolution 68Ga-Tilmanocept PET/CT-imaging may limit the *shine through* effect and may provide improved anatomic localization of SLNs as compared to conventional lymphoscintigraphy. Therefore, 68Ga-Tilmanocept PET/CT might be more sensitive for detection of SLNs and might improve differentiation between SLNs and second echelon lymph nodes.

Study objective

The primary objective of this study is to assess the diagnostic accuracy, in terms of sensitivity and negative predictive value, of preoperative 68Ga-Tilmanocept PET/CT combined with conventional lymphoscintigraphy for SLN detection. Besides, we aim to compare the diagnostic accuracy of preoperative 68Ga-Tilmanocept PET/CT alone with conventional preoperative lymphoscintigraphy alone.

Study design

1. A pilot study to optimize the 68Ga-Tilmanocept PET/CT imaging protocol and build experience with the outcomes of 68Ga-Tilmanocept PET/CT (10 patients).
2. A prospective cohort study and a within-patient evaluation of 68Ga-Tilmanocept PET/CT for identification of SLNs as compared to conventional lymphoscintigraphy in patients with early-stage OSCC (84 patients).

Intervention

Patients will undergo additional PET/CT imaging following peritumoral injections of 10 MBq 68Ga-Tilmanocept. Results of 68Ga-Tilmanocept PET/CT imaging will be compared to results of conventional lymphoscintigraphy (including SPECT-CT) using 99mTc-Tilmanocept.

Study burden and risks

Patients will undergo additional peritumoral injections and two PET/CT-imaging with a duration of 5 minutes. 68Ga-Tilmanocept PET/CT may identify SLNs more reliable than routinely used lymphoscintigraphy using 99mTc-Tilmanocept. Information obtained from 68Ga-Tilmanocept PET/CT may be helpful in harvesting SLNs. The extra administration of 10 MBq 68Ga-Tilmanocept is considered an acceptable radiation burden to the patient. Adverse reactions after injection of radiolabelled Tilmanocept rarely occur.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. The patient has provided written informed consent authorization before participating in the study.

2. The patient has a diagnosis of primary oral squamous cell carcinoma that is anatomically located in: mucosal lip, buccal mucosa, lower alveolar ridge, upper alveolar ridge, retromolar gingival (retromolar trigone), floor-of-the-mouth, hard palate or oral (mobile) tongue.

3. Clinical TNM-stage is T1-T2 and T3 (only when T3 is assessed based on tumor dimensions of >2 cm and <=4 cm with DOI >10 mm), N0, M0 (see Appendix 6: TNM Staging).

4. Clinical nodal staging (N0) has been confirmed by negative results from ultrasound guided fine needle aspiration cytology within 30 days of the SLN procedure.

5. The patient is a candidate for transoral excision.

6. Patients with prior malignancy of the head and neck area are allowed, provided the patient meets both of the following criteria:
• Underwent potentially curative therapy for all prior head and neck malignancies and is deemed low risk for recurrence; and
• No head and neck malignancy for the past five years and no evidence of recurrence.

7. The patient is >=18 years of age at the time of consent.

8. The patient has an ECOG status of Grade 0 - 2 (see Appendix 7: Performance Status Criteria).

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. The patient has a diagnosis of squamous cell carcinoma of the head and neck in the following anatomical areas: non-mobile base of the tongue, oropharynx, nasopharynx, hy-popharynx, and larynx.

2. The patient is incapacitated.
3. The patient has had a previous allergic reaction after administration of a radionuclide trac-er.
4. The patient has had other nuclear imaging studies, conducted within 2 days (48 hours) of injection.
5. The patient has clinical or radiological evidence of metastatic cancer to the regional lymph nodes.
6. The patient has a history of neck dissection, or gross injury to the neck that would pre-clude reasonable surgical dissection for this trial, or radiotherapy to the neck.
7. The patient is actively receiving systemic cytotoxic chemotherapy.
8. The patient is on immunosuppressive, anti-monocyte, or immunomodulatory therapy.

Study design

Design

Study phase:	3
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2020
Enrollment:	94
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lymphoseek
Generic name:	99m-Technetium-Tilmanocept
Product type:	Medicine
Brand name:	Not applicable

Generic name:	68-Gallium-Tilmanocept

Ethics review

Approved WMO Date:	04-03-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-03-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2019-004914-32-NL
CCMO	NL71558.041.20