Does stimulation of salivary glands by oral intake increase uptake and toxicity of PSMA-ligands?

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To determine if stimulated salivation during the biodistribution of PSMA-ligands causes a significant increase in the accumulation in salivary glands

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Prostatic disorders (excl infections and inflammations)
Study type	Observational invasive

Summary

ID

NL-OMON49260

Source
ToetsingOnline

Brief title
Stimulation of salivary glands with intake

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
dry mouth, xerostomia

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF subsidie

Intervention

Keyword: PET/CT, prostate, PSMA, salivary glands

Outcome measures

Primary outcome

The accumulation of systemically administered PSMA-ligands in salivary glands

on PET/CT.

Secondary outcome

To screen for potential influence of oral intake on the biodistribution of

PSMA-ligands on PET/CT in other organs and tumour.

Study description

Background summary

Many pharmaceuticals can damage salivary glands, and this can lead to a dry mouth (xerostomia) with detrimental effect on quality of life. Systemically administered pharmaceuticals reach the salivary glands via blood supply and diffusion, and their accumulation can be further augmented by active or passive transporters. This also applies to radiopharmaceuticals used in radionuclide therapy (RNT). Radiolabelled ligands to the prostate-specific membrane antigen (PSMA) are increasingly used to treat metastatic prostate cancer. The currently applied Lutetium-177-PSMA-617 ligand (Lu-PSMA) shows very high uptake in salivary glands, which is explained by the high perfusion of salivary glands and the abundant expression of the PSMA receptor on their acinar and ductal seromucous cells. As a result, salivary glands are inadvertently exposed to high radiation doses in Lu-PSMA treatment, with xerostomia as a known dose-limiting factor.

Salivation is stimulated during intake, and this is known to induce an increase in salivary gland perfusion of up to 10-20x baseline values. It is therefore possible that salivary gland stimulation during the biodistribution phase of PSMA-ligands leads to increased delivery and binding in salivary glands. If this is the case, intake and activation of salivation should be avoided during the administration and biodistribution of therapeutic doses of Lu-PSMA. This is currently not advised in clinical protocols, with a potential risk on avoidable toxicity and reduced quality of life.

The hypothesis is that stimulation of salivation during the biodistribution phase of PSMA-ligands leads to increased accumulation in salivary glands. The uptake of PSMA-ligands can be assessed with quantitative PET/CT imaging using the diagnostic radiopharmaceutical 18Fluor-DCFPyl (F-PSMA) or 68Gallium-PSMA (Ga-PSMA). The biodistribution of current PSMA-ligands is very fast, a significant part of administered PSMA-ligand binds its target within the first 10 minutes. Salivation representative for normal intake can be stimulated for 10 minutes by continuous intake, chewing and swallowing of food that contains sugar, fat and acids. An increase in PSMA-ligand uptake in salivary glands due to intake will predict a similar unwanted effect for treatment with Lu-PSMA.

Study objective

To determine if stimulated salivation during the biodistribution of PSMA-ligands causes a significant increase in the accumulation in salivary glands

Study design

Single center prospective interventional phase II study.

Study burden and risks

Participation in this study has no significant risks. Participation does not induce a delay in diagnosis or treatment, and imaging results have no impact on the diagnosis or treatment of the prostate cancer. Patients will receive 1 additional PSMA PET/CT scan, with a total procedure duration of 1,5 hour and an estimated radiation dose of 6-7 mSv. This dose is well within the range of normal diagnostic procedures and does not induce a significant risk in this population with prostate cancer.

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

- Received PSMA PET/CT on clinical indication (< 1 month before study scan)
- Salivary glands and lacrimal glands visible in the baseline PSMA PET/CT scan

Exclusion criteria

- Poor quality of the baseline PSMA PET/CT scan
- Planned start or changes in treatment between the baseline scan and study scan.
- Age <18y
- Inability to provide informed consent
- Diabetes Mellitus
- Vegan diet
- Claustrophobia
- History of disease or treatment involving the salivary glands, like malignant or benign tumour, sialoadenitis, stone, surgery, SLE, RT to head-neck, etc

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-08-2020
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	11-06-2020
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL71902.031.20