Autologous Transplantation of Adult Salivary Gland Stem Cells to Restore Submandibular Gland Function after Radiotherapy

Published: 28-10-2020
Last updated: 09-11-2024

This study has been transitioned to CTIS with ID 2024-512968-57-00 check the CTIS register for the current data. The primary objective of the study is to assess the safety and feasibility of autologous salivary gland stem cell transplantation of the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49128

Source
ToetsingOnline

Brief title
RESTART

Condition

- Other condition

Synonym
Irradiated salivary gland

Health condition

Head and neck cancer

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: - Radiotherapy, - Stem Cell Transplantation, - Submandibular Gland, - Xerostomia

Outcome measures

Primary outcome

The primary objective of the study is to test the safety and the feasibility of autologous salivary gland stem cell transplantation of the submandibular gland.

For safety, the number of adverse events (AE), serious adverse events (SAE) or suspected unexpected adverse reactions (SUSAR) after autologous salivary stem cell transplantation, will be recorded between days 1 to 365. All possible adverse events will be scored according to the definitions of the Common Toxicity Criteria for Adverse Events version 4.0 (CTCAEv4.0).

For feasibility, salivary flow rate of the remaining submandibular gland will be recorded 6 months and 12 months after autologous stem cell transplantation.

Secondary outcome

- Unstimulated whole saliva, paraffin stimulated whole saliva and 5% citric acid stimulated parotid and submandibular/sublingual saliva at 6 and 12 months and then on a yearly basis until 5 years after postoperative (chemo)radiation
- Patient-rated outcome measures including various side effects related to the postoperative (chemo)radiation and Quality of Life (QoL) at 6 and 12 months and then on a yearly basis until 5 years after (chemo)radiation using

internationally validated questionnaires (GRIX, EORTC QLQ-H&N35, EORTC QLQ-C30)

- Locoregional control

- Overall survival and disease free survival

- The rate of water diffusion in remaining submandibular gland derived from

DWI-MRI at 6 and 12 months after postoperative (chemo)radiation.

- The amount of prostate specific membrane antigen (PSMA) in the remaining

submandibular gland derived from PET-CT

Study description

Background summary

The majority of patients with head and neck cancer are treated with radiotherapy, either as single modality or in combination with surgery and/or systemic agents. Despite the beneficial effects of radiotherapy regarding loco-regional tumor control, damage inflicted to surrounding salivary glands cause permanent xerostomia (hyposalivation), which severely hamper the quality of life (QoL) as reported by patients.
In salivary glands, radiation damage is due to sterilization of the tissues* endogenous gland stem cells rendering them incapable to replenish dysfunctional or dead saliva producing cells. Increasing the regenerative potential of salivary glands by stem cell therapy after irradiation should be able to restore salivary gland function.

Study objective

This study has been transitioned to CTIS with ID 2024-512968-57-00 check the CTIS register for the current data.

The primary objective of the study is to assess the safety and feasibility of autologous salivary gland stem cell transplantation of the submandibular gland.

Study design

The study design is a phase I safety and feasibility study to treat head and neck cancer patients with autologous salivary gland stem cell transplantation after postoperative radiotherapy.

Intervention

Autologous transplantation of salivary stem cells (salisphere derived cells) cultured in vitro as obtained from submandibular glands after postoperative radiotherapy.

Study burden and risks

Patients participating in the study follow the normal procedure of primary tumour resection, ipsilateral neck dissection and postoperative radiotherapy (with or without chemotherapy) as indicated by current national standards.
Extra burden of these patients, will be two additional salivary flow measurements, four MRI scans, four PSMA-PET scans and the ultrasound guided injection of submandibular salivary gland stem cells in the remaining submandibular gland.
The additional risk for participating patients might be a mild local infection (<10%) at the site of injection of the salivary stem cells into the remaining submandibular gland after transplantation. Another highly unlikely risk (<0.1%) is a transplanted tumour from the original removed head and neck cancer in the remaining submandibular gland.

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

- Squamous cell carcinoma (SCC) originating from the mucosa of the oral cavity
- Primary resection of tumour including an electively or therapeutic ipsilateral neck dissection (at least levels Ib to III, including the submandibular gland)
- Postoperative radiotherapy or chemoradiation, including prophylactic or therapeutic irradiation of the contralateral side of the neck (where the remaining submandibular gland is), including at least levels Ib to IV), next to irradiation of the tumour bed and ipsilateral neck (current standard)
- Age >= 18 years
- WHO performance 0-2
- Written informed consent

Exclusion criteria

- Primary (definitive) radiotherapy, with or without systemic treatment
- Previous radiotherapy of the head and neck region (re-irradiation)
- Positive microbiological screening for Human Immunodeficiency Virus type 1 and 2, hepatitis B and C virus and Treponema pallidum
- Presence of systemic disease known to affect salivary gland functioning (e.g., Sjögren*s syndrome)
- History within the past five years of malignancies other than:
o basal or squamous cell carcinoma of the skin
o in situ carcinoma of the cervix
- Females who are pregnant or lactating at entry

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-06-2022
Enrollment:	18
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	28-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-02-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-06-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

Haag)

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
EU-CTR	CTIS2024-512968-57-00
EudraCT	EUCTR2020-000966-41-NL
ClinicalTrials.gov	NCT04593589
CCMO	NL75095.000.20