Guided by light: Optimizing surgical excision of oral cancer using real-time fluorescence imaging

Published: 16-11-2020
Last updated: 17-01-2025

This study has been transitioned to CTIS with ID 2024-512824-13-01 check the CTIS register for the current data. The overarching goal of this study is to improve adequate resection of oral cancer. We will perform a clinical trial to determine the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON49733

Source
ToetsingOnline

Brief title
Guided by Light

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer, squamous cell carcinoma of the oral cavity

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: cRGD-ZW800-1, fluorescence imaging, head and neck cancer, image-guided surgery

Outcome measures

Primary outcome

1) To determine the TBR of cRGD-ZW800-1 in patients with oral cancer;

2) To determine if using FLI can increase the rate of adequate (i.e. >5mm

clear) tumor resection margins.

Secondary outcome

1) To determine the recommended dosage of cRGD-ZW800-1 for intraoperative

imaging of oral cancer.

2) To determine the sensitivity, specificity, positive and negative predictive

values of FLI

3) To-determine colocalization of FLI with immunochemistry on pathology slides

4) To determine the percentage of extra tissue resection based on FLI-driven

frozen sections

5) To determine if FLI significantly increases operation time

6) To determine if lymph node metastases can be identified using FLI

Study description

Background summary

Head and neck cancer (HNC) is the 9th most common tumor worldwide, a third of them arising in the oral cavity. Complete tumor resection of oral cancer is the most important surrogate marker for survival. Precise margin delineation is imperative in the delicate head and neck region where wider resections inevitably lead to increased morbidity and loss of functionality.

In current practice, intraoperative assessment of the tumor-free margin is dependent on visual appearance and palpation of the tumor. We have reported inadequate surgical margins in up to 85% of patients with oral cancer, which is unacceptable. Therefore, new intraoperative visualization techniques are required to assess tumor margins in real-time and to guide surgical removal of oral cancer with adequate tumor-free margins while retaining maximal functionality.
Fluorescence imaging (FLI) using near-infrared light has recently emerged as a revolutionary technique to provide real-time visualization of tumor tissue, enabling image-guided surgery. Tumor-specific fluorescent targeting agents are systemically injected preoperatively and real-time FLI is performed using a dedicated intraoperative camera system. In this study, we will test the use of cRGD-ZW800-1, a tumor-specific agent that targets integrins, for intraoperative detection and margin delineation of oral cancer. Overexpression of a wide range of integrin receptors is reported in HNC.
The overarching goal of this two-staged clinical trial is to improve adequate resection of oral cancer.

Study objective

This study has been transitioned to CTIS with ID 2024-512824-13-01 check the CTIS register for the current data.

The overarching goal of this study is to improve adequate resection of oral cancer. We will perform a clinical trial to determine the optimal dose of cRGD-ZW800-1 and to investigate the feasibility of intraoperative FLI to adequately assess tumor margins in patients with oral cancer.

Primary Objective:
To improve adequate resection of oral cancer using fluorescent imaging technology.
1. WP I: To determine the recommended dose for the highest tumor-to-background ratio (TBR) of at least >2.0 using cRGD-ZW800-1 in oral cancer;
2. WP II: To increase the rate of adequate (i.e. >5mm clear) tumor resection margins

Study design

This proposal describes a two-staged clinical trial to investigate the feasibility of intraoperative FLI to adequately assess tumor margins in patients with oral cancer using cRGD-ZW800-1. In WP-I, I will determine the preferred dose of the agent for imaging of margins in oral cancer. The signal-to-noise ratio will be determined in dose group A (n=7). After an interim evaluation of this ratio, the second dose group B (n=7) will receive either a higher or a lower dosage of the tracer. After inclusion of all patients (n=14), the dose with the highest intraoperative signal-to-noise ratio

will be selected.

In WP-II, I will then add an expansion cohort (n=14) to the group of patients that had received the selected dose in WP-I. In this group of 21 patients, I then determine if FLI can improve the rate of adequate surgical resection margins. As secondary research questions I will assess sensitivity, specificity, positive and negative predictive values of FLI; colocalization with immunohistochemistry; change in surgical management; incremental operation time; and FLI of excised cervical lymph nodes.

Amendment (October 2023): After the first 7 inclusions in dose group A (0.05 mg/kg), it was decided to de-escalate to 0.01 mg/kg based on the very strong signal. After including 3 patients with this dose, it was concluded during an interim analysis that 0.01 mg/kg showed insufficient fluorescent signal, and that it was not sensible to give this dose to another 4 patients. It was decided to proceed with an intermediate dose, namely 0.025 mg/kg. The next 7 patients (dose group B) received this dose, which was found to be the ideal dose after the completion of WP-1. Therefore, the extension cohort in WP-2 (n=14) received/are receiving 0.025 mg/kg.

I will measure fluorescence signal during the operation. Next, the surgeon will perform the operation without using FLI. After the resection, I will perform FLI of the specimen surface and surgical wound bed and mark any fluorescent areas. Together with the pathologist, the surgeon then performs intraoperative assessment (IOA) of the resection margins. If inadequate, a limited extra resection of tissue is performed. Meanwhile, if I find fluorescent areas in the wound bed, I will take frozen sections. Only if these show tumor cells, the surgeon performs a limited extra resection. Postoperatively, I will perform FLI of all tissues in a black box scanner and I correlate integrin-specific targeting to immunohistochemistry.

Intervention

Injection of cRGD-ZW800-1 within 48 hours before imaging/surgery

Study burden and risks

Patient burden:

1) Consideration to join scientific research at an emotionally heavy time of diagnosis and treatment of cancer;
2) Administration of single-dose of fluorescent tracer;
3) Additional measurements of vital functions, ECG and laboratory testing after administration;
4) Minimal risk of allergic reaction to fluorescent tracer;
5) Expected extension of operating time of 10-15 minutes;

Potential patient benefit:

Small chance of higher surgical success rate.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients with biopsy-proven squamous cell carcinoma of the oral cavity, eligible for surgical resection of the primary tumor;
2. Patients >= 18 years of age;
3. Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

1. Previous surgery, chemotherapy or radiotherapy to the oral cavity;
2. History of a clinically significant allergy or anaphylactic reactions to any of the components of the agent.
3. Patients pregnant or breastfeeding, lack of effective contraception in male or female patients with reproductive potential;
4. Patients with renal insufficiency (eGFR<60);
5. Patients with a previous kidney transplantation in the medical history;
6. Patients using medications that may significantly impair renal function (i.e. NSAIDs, particularly COX-2 inhibitors);
7. Immuno-compromised patients who do not have the ability to respond normally to an infection due to an impaired on weakened immune system, caused by either a pre-existing disease or concomitant medications;
8. Any condition that the investigator, anesthesiologist or head- and neck surgeon considers to be potentially jeopardizing to the patient's wellbeing or the study objectives.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-07-2022
Enrollment:	31
Type:	Actual

Medical products/devices used

Registration:	No

Product type:	Medicine
Brand name:	cRGD-ZW800-1
Generic name:	n.a.

Ethics review

Approved WMO Date:	16-11-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-12-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	CTIS2024-512824-13-01
EudraCT	EUCTR2019-003416-30-NL
ClinicalTrials.gov	NCT04191460
CCMO	NL71347.078.20