Proton Image-guided Radiation Assignment for Therapeutic Escalation via Selection of locally advanced head and neck cancer patients

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To assess the safety & feasibility of image-guided mid-treatment hyper-fractioned dose-escalation with proton therapy for the treatment of locally advanced HPV-negative squamous cell oropharyngeal cancer

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

Summary

ID

NL-OMON56786

Source
ToetsingOnline

Brief title
PIRATES

Condition

- Other condition

Synonym
Head and neck cancer

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: Ministerie van OC&W

Intervention

Keyword: Dose-escalation, Head and neck cancer, Hyperfractionation, Radiotherapy

Outcome measures

Primary outcome

The number of dose limiting toxicity (DLT) events, defined as grade *4 mucositis, grade *4 ulceration, grade *4 dermatitis, grade *4 aspiration, grade *4 osteonecrosis and grade >=3 myelopathy

Secondary outcome

- Percentage of patients completing radiotherapy regimen (meaning completion of treatment with a maximum of 2 fraction interruption)
- Percentage of patients completing the complete chemotherapy regimen
- Rates of grade >=3 mucositis, dermatitis, aspiration, dysphagia, hearing impaired, xerostomia, weight loss, trismus, hoarseness, oropharyngeal pain at 6 months after chemoradiation (according to CTCAEv5).
- Preliminary tumor response rates measured on the standard follow-up MRI scan
- Preliminary disease-free, overall survival and time-weighted locoregional control analyses

Study description

Background summary

Patients with HPV-negative locally advanced head and neck squamous cell carcinoma (HNSCC) have poor survival (3- and 5-year overall survival (OS): 53% and 42%, resp.) and local-regional control rates (~30%) despite multimodality treatment. Recurrent or residual tumor predominantly originates in the regions that receive the highest radiotherapy dose (i.e., CTV70). Hence, higher radiation doses to the tumor have potential improve the cure rates for these patients. Introduced in the Netherlands in 2018, proton therapy can reduce radiation dose to the normal tissue surrounding the tumor, and thus toxicities, while delivering the same dose to the tumor tissues. Yet, proton therapy remains to be deployed to achieve higher tumor doses with similar (or even lower) normal tissue dose compared to conventional photon therapy. For this study we propose a novel design to achieve tumor radiation dose-escalation with proton therapy plus standard of care concomitant chemotherapy, in combination with mid-treatment image-guided tumor boost dose adaptation, hybrid hyper-fraction and selective critical structure sparing to prevent toxicities (arising from both the high- and intermediate- dose regions) and improve locoregional control.

Study objective

To assess the safety & feasibility of image-guided mid-treatment hyper-fractioned dose-escalation with proton therapy for the treatment of locally advanced HPV-negative squamous cell oropharyngeal cancer

Study design

Single arm Bayesian Phase I intervention study

Intervention

Radiation dose escalation of the prescribed dose to the gross tumor volume (80.5Gy)

Study burden and risks

Participants will receive a higher radiotherapy dose to the gross tumor volume. To minimize the risk of toxicities within target volumes receiving the highest dose, a hybrid hyper-fractionated fractionation schedule is used, meaning that participants are irradiated twice per day in week 5-7 of treatment (note, treatment in week 1-4 are according to current clinical standard). Moreover, dose escalation is only applied tumor tissue that is detectable at the end of week 4 of treatment, which means that patients will undergo an additional MRI scan in week 4 during treatment to define the remaining tumor volume.
The PIRATES treatment strategy is designed to minimize the risk of (life-threatening) toxicities. Specifically, previous randomized studies have demonstrated that these toxicities were not observed after full-treatment

hyper-fractionation schedules to a total dose of around 80 Gy. By integrating this approach with adaptive proton therapy, the risk is considered minimal. Moreover, the target population is locally advanced OPC patients that are at high-risk of treatment failure at the primary tumor site and pathologic lymph nodes. The potential benefit of hybrid hyper-fractionated dose escalation with protons for these patients is improved locoregional tumor control without enhancing severe toxicity.

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

- Biopsy proven diagnosis of squamous cell carcinoma originating in the oropharynx.
- Routine staging procedures, including CT of the head and neck region and

chest, head and neck FDG-PET/CT and MRI (treatment planning allowed), and endoscopic evaluation when indicated.
- Negative for p16
- Locally advanced disease, specifically meeting all following criteria:
o Stage III-IV
o T-stage 2-4
o All N-stages (N0-3)
o M0
- Eligible for primary concurrent chemoradiation using conventionally fractionated radiotherapy 70 Gy combined with weekly cisplatin
- Eastern Cooperative Oncology Group (ECOG) performance score <=2
- Age >=18 years
- Written informed consent

Exclusion criteria

- Definitive resection of their primary tumor or nodal disease, except for incisional or excisional biopsies.
- Radiation therapy in the head and neck area in the past
- No detectable tumor anymore at both the primary site and lymph nodes at week 4 in treatment, because there will not be a volume to boost.
- Unable or unwilling to give written, informed consent
- Contra-indications for chemotherapy. This is at the discretion of the treating medical oncologist.
- Unable to tolerate intravenous contrast for both CT and MRI, having an estimated GFR < 60 ml/min/1.73 m2 or any contraindications to gadolinium-based contrast agents.
- Any evidence of iron overload on pre-imaging laboratory studies.
- Other serious illnesses or medical conditions present at entry in the study, including (but not limited to): immunodeficiency virus (HIV) infection or other conditions of persistent immunodeficiency, neurologic or psychiatric disorders, active disseminated intravascular coagulation, unstable cardiac disease despite treatment or uncontrolled diabetes mellitus.
- Women who are pregnant or breast feeding

Study design

Design

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

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	19-04-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL85823.042.23