Phase I study of radiotherapy dose escalation on the 18F-FDG-PET avid region of the primary tumor in locally advanced oropharynx and oral cavity tumors eligible for concurrent chemoradiation.

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Primary objective:• To determine the maximum tolerated dose of radiation to the FDG-PET avid subvolume within the GTV of the primary tumor. Secondary objectives:• To determine the incidence and severity of acute and late toxicity of dose escalation...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON33780

Source
ToetsingOnline

Brief title
18F-FDG-PET based radiotherapy dose escalation

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Cancer of the mouth and throat, oropharynx/oral cavity carcinoma`s

Research involving

Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 18F-FDG-PET, Dose escalation, Head and neck tumors, Radiotherapy

Outcome measures

Primary outcome

• Primary end-point:

Maximum tolerated dose (MTD) is defined as the dose where dose limiting

toxicity exceeds 10%

The recommended phase II dose (RPTD) is one dose level below the (MTD)

Secondary outcome

• Secondary end-points:

- CTCAE toxicity scales v 3.0 for acute toxicity (within 3 months after end of

treatment) and late toxicity (after minimum 6 months after end of treatment)

- Loco-regional control, overall and cause specific survival and cause of death

after 2 years

- Localisation of all recurrences with respect to the different dose levels

administered (PTV57.75, PTV70 nodes, PTV70 primary outside the PTV-PET,

PTV-PET).

- Dose to critical organs before and after replanning of the dose escalation

volume. Volume change of PTV-PET after deformation.

Study description

Background summary

Local relapse remains an important problem in advanced head and neck tumors (1,2), most recurrences occur in the primary tumor/high dose area (3). Several studies have suggested that dose escalation can improve local control (4,5) and consequently overall survival (1,6). IMRT with Simultaneous integrated boost (SIB) makes dose escalation possible while keeping the dose to the organs at risk acceptable (7). Fluoro-2-deoxy-D-glucose positron emission tomography (18F-FDG-PET) is of interest for delineating radioresistant subvolumes (8). Volume change during radiation therapy can be tracked with implanted gold markers (9). A replanning after 3 weeks of radiotherapy will be performed. In the second plan, it is only allowed to adjust the GTV-PET based on the deformation of implanted gold markers.

References:
1. Posner MR, Herschock DM, Blajman CR, et al. Cisplatinum and Fluorouracil alone or with Docetaxel in head and neck cancer. New Eng J Med 2007, 357;17:1705-1715.
2. Knegjens JL, Pameijer FA, Balm AJ, et al. Tumor Volume as Outcome Predictor in Chemoradiation for Advanced Head and Neck Cancer. Int J Radiat Oncol Biol Phys 2007, 69;S410-S411
3. Dawson LA, Anzai Y, Marsh L, et al. Patterns of local-regional recurrence following parotid-sparing conformal head and neck cancer. Int J Radiat Oncol Biol Phys 2000, 46;1117-1126
4. Eisbruch A, Dawson LA, Kim HM, et al. Conformal and intensity modulated irradiation of head and neck cancer: the potential for improved target irradiation, salivary gland function, and quality of life. Acta Otorhinolaryngol Belg 1999, 53;3:271-5.
5. Levendag PC, Nowak PJCM, van der Sangen MJC, et al. Local tumor control in radiation therapy of cancers in the head and neck. Am J Clin Oncol 1996, 19;5:469-477.
6. Wadsley JC and Bentzen SM. Investigation of relationship between change in locoregional control and change in overall survival in randomized controlled trials of modified radiotherapy in head and neck cancer. Int J Radiat Oncol Biol Phys 2004, 60;5:1405-1409.
7. Madani I, Duthoy W, Derie C, et al. Positron emission tomography-guided, focal dose escalation using intensity-modulated radiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys 2007, 68;1:126-135.
8. Ragendran JG, Mankoff DA, O`Sullivan F, et al. Hypoxia and glucose metabolism in malignant tumors: evaluation by [18F]Fluoromisonidazole and [18F]Fluorodeoxyglucose positron emission tomography imaging. Clin Cancer Res 2004, 10;2245-2252.
9. Hamming-Vrieze O, Kranen SR, van Beek S et al. Evaluation of tumor

variability in head-and-neck cancer patients over the course of radiotherapy with implanted gold markers. Poster 241, ESTRO 27, Goteburg 2008.

Study objective

Primary objective:
• To determine the maximum tolerated dose of radiation to the FDG-PET avid subvolume within the GTV of the primary tumor.
Secondary objectives:
• To determine the incidence and severity of acute and late toxicity of dose escalation according to the CTCAE toxicity scales v3.0
• To document tumor response (loco-regional control, overall and cause specific survival and cause of death).
• To analyse pattern of failures
• To determine the effect of replanning of the PTV-PET after 3 weeks of radiotherapy

Study design

A single centre, phase I, radiation dose escalation trial using time-to-event continual reassessment strategy

Intervention

Schedule of events:

Prepartations: Week 1: Week 2: Week 3: Week 4: Week 5:
Week 6: Week 7: 4 months: Recurrence:
MRI diagnostic 5x RT 5x RT 5x
RT 5x RT 5x RT 5x RT 5x RT
MRI MRI mask
OON + markers CDDP CT masker
CDDP
CDDP CT mask
CT mask
PET-CT mask
(OON: Investigation under anesthesia, RT = radiotherapy, CDDP = Cisplatinum 100 mg/m² i.v., MRI/CT mask: scan with radiotherapy mask).

All patients receive a radiochemotherapy treatment with dose escalation in the PET positive region of the primary tumor according to these dose levels:
Dose level 0
Dose level I Dose level II Dose level III Dose level IV
PTV-PET primary tumor 35x2.0 (70.0) 35x2.1 (73.5) 35x2.2 (77)
35x2.3 (80.5) 35x2.4 (84)

A replanning after 3 weeks of radiotherapy will be performed. In the second plan, it is only allowed to adjust the GTV-PET based on the deformation of implanted gold markers.

Study burden and risks

No additional pretreatment investigations have to be done since patients with large inoperable oropharynx or oral cavity tumors scheduled for radio-chemotherapy, already undergo a PET scan and investigation under anesthesia with implantation of gold markers, to aid tumor delineation. During treatment, patients participating in this study, have to undergo an extra planning CT scan after three weeks of radiation therapy. Furthermore, if residual disease or a local recurrence is suspected, an additional MRI and CT in old treatment mask should be done to visualize the recurrence in reference to the markers. Otherwise, no extra investigations or visits are necessary. In conclusion, one additional CT scan is negligible relative to the treatment with external radiation therapy. Only patients with a local recurrence undergo a second additional CT scan and a MRI in treatment mask.

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

• Histology proven squamous cell carcinoma of the oral cavity and oropharynx.
• TNM stage III/IV, functional inoperable, > 30 cc primary tumor volume
• Eligible and scheduled for concurrent cisplatin-based chemoradiation with curative intent (RADPLAT, cisplatinum 100mg/m² w1,4 and 7)

Exclusion criteria

Radiotherapy hypersensitivity
Pregnancy

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2009
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	13-01-2010
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	NL25816.031.08