A radical Chemoradiation schedule with hypofractionated radiotherapy plus capecitabine for esophageal cancer patients that are unfit for the standard chemoradiation; a phase II study

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

Summary

ID

NL-OMON57178

Source
ToetsingOnline

Brief title
CRADLE

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: de betrokken afdelingen (medische oncologie en radiotherapie) financieren extra kosten

Intervention

Keyword: chemoradiation, esophageal cancer, unfit patients

Outcome measures

Primary outcome

feasibility of this regime (grade 3 toxicity and compliance)

Secondary outcome

locoregional control and survival

Study description

Background summary

Technically irresectable or medically inoperable patients in a curable stage of disease of esophageal cancer are referred for curatively intended chemoradiation. The standard chemoradiation schedule consists of 50,4 Gy with 6x weekly Carboplatin and Paclitaxel. This schedule has a curative intent (3-years OS = 40%) but leads to grade III toxicity in about one third of the patients, with an excess in toxicity in older patients. This standard CRT regime is often considered too heavy for old or unfit patients. For patients considered not eligible for the standard chemoradiation, a palliative radiotherapy only schedule remains. The Dutch national radiation guideline suggests for unfit patients a high dose hypo fractionated scheme of 50 Gy in 16 fractions, which is considered feasible in this patient group. However, radiation only for esophageal cancer should be considered as palliative. The combination of radiation with sensitizing chemotherapy has proven to change the intend from palliative to curative. Capecitabine, an oral drug which metabolizes in the body to the active drug 5-FU, is a well-known radiosensitzer, with a mild toxicity profile, which can be adapted quickly and easy according to the encountered toxicity.

Study objective

Objective of the study is to investigate if a mild sensitizing drug (oral capecitabine) combined with a high dose hypofractionated radiation regime to the esophageal region is feasible in this unfit patient group. If feasible, in a consecutive study the the added value of capecitabine to the standard radiotherapy will be investigated with locoregional tumorcontrol as primairy endpoint and survival as secondary endpoint.

Study design

Observational study radiotherapy of 16 fractions of 3.125 Gy radiotherapy combined with twice daily oral capecitabine 825 mg\m2.

Intervention

addition of capecitabine twice daily to the standard radiotherapy

Study burden and risks

The burden of participation is considered small since it only consists of twice daily intake of tablets. The risk of toxicity can be an excess in fatique, diarrhoea, swallowing pain and hematological disturbances, but is considered small since this schedule is part of standard treatment in patients with bladder cancer and rectal cancer, with acceptable toxicity and good compliance.

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

- Age of 18 years or older - WHO performance score 0-3 - Biopsy proven carcinoma of the esophagus - cT1-T4aN0-3M0, including patients with M1 disease based on pathologic nodes at supraclavicular or truncus coeliacus level - The multidisciplinary team rejects surgical treatment - The radiation oncologist and medical oncologist consider patient not eligible for the standard chemoradiation, with at least one of the following characteristics: WHO performance 3, age of > 80 year, metabolic disorders excluding Carboplatin or Paclitaxel, mainly wheelchair bounded, evidence of interstitial lung disease or active, non-infectious pneumonitis, or a Charlson index of 3 or more.

Exclusion criteria

- Previous irradiation overlapping with the intend fields
- Stent in situ
- Serum DPD deficiency
- Prior intravenous chemotherapy for esophageal cancer
- An active infection requiring systemic therapy
- Has known psychiatric disorders or substance abuse disorders that would interfere with cooperation in the trial
- Inability, or serious suspicion of inability to administer the prescribed doses of capecitabine
- Is pregnant or breast feeding

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):	14-07-2021
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xeloda
Generic name:	Capecitabine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-04-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 25277
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2020-006164-85-NL
CCMO	NL75846.029.21