Angiogenic factor expression during fractionated irradiation

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23950

Source
Nationaal Trial Register

Health condition

Adult patients (>18) who will receive standard neoadjuvant chemoradiation for primary oesophageal carcinoma

Sponsors and support

Primary sponsor: VU University Medical Centre, Amsterdam, The Netherlands
Source(s) of monetary or material Support: initiator = sponsor

Intervention

Outcome measures

Primary outcome

The primary parameter is the alteration of the VEGF expression on mRNA level in the tumour before and during the
course of neoadjuvant chemoradiation. In addition, in the bevacizumab treated cohort, the primary parameter is the
activity (phosphorylation) of the VEGF receptor (VEGFR) in the tumour tissue obtained with biopsy and the microvessel

density of the resection material of the tumour

Secondary outcome

(1) Determination of mRNA expression levels of other pro-angiogenic factors than VEGF and factors that may influence
radiosensitivity in the tumour tissue.
(2) Determination of protein expression of pro-angiogenic factors and factors that may influence radiosensitivity in the
tumour tissue with IHC.
(3) Determination of Epstein Barr virus (EBV) status in the tumour tissue.
(4) Quantification of vascular parameters in the tumour tissue to assess on-going angiogenesis.
(5) Measurement of the plasma concentration of pro-angiogenic factors to determine if this correlates with the
expression levels in the tumour tissue.
(6) Determination of the expression level of angioregulatory miRNAs in the tumour tissue to assess whether this is
affected during neoadjuvant chemoradiation.

Study description

Background summary

Evidence is emerging that the effect of radiotherapy might be enhanced by angiostatic drugs. Whereas preclinical results
are promising, clinical trials have shown only moderate effect so far. This is most likely due to suboptimal scheduling;
both modalities have to be precisely dosed and scheduled to gain the optimal effect, with the lowest possible toxicity. Our
results show that fractionated irradiation in vitro and in vivo induces a fast and significant up-regulation of pro-angiogenic
factors. These results indicate that the long term anti-tumour effects of radiotherapy might be enhanced by inhibiting the
pro-angiogenic response induced during the course of radiotherapy. Whether and when this pro-angiogenic response to
radiotherapy occurs in patients remains elusive. Therefore, it is important to determine the time point at which the proangiogenic
response during fractionated radiotherapy develops in patients. Furthermore, it is important to determine
whether this up-regulation can be inhibited by the administration of bevacizumab, a monoclonal antibody against VEGF.
In this way an optimal dose schedule could be designed for the combination treatment of angiostatic drugs and

radiotherapy.

Study objective

This study has 2 primary objectives:
1) To determine the time point of induction of VEGF expression in the tumour tissue of oesophagus carcinomas during
chemoradiation.
2) To determine whether the tumour promoting effects of this induction of VEGF expression can be inhibited by
administration of bevacizumab.

Study design

Before chemoradiation
during chemoradiation
after chemoradiation
surgery

Intervention

Patients will undergo 1 extra endoscopic biopsy to collect tumour tissue. In addition, on four time points blood samples
will be collected. The time point of this biopsy and blood collection depends on the study cohort. The patients in the final
cohort will receive bevacizumab (3mg/kg/wk) starting at the identified time point of induction. Bevacizumab administration
will be discontinued 4 weeks before the surgical resection of the tumour.

Contacts

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Eligibility criteria

Inclusion criteria

(1) Histological confirmation of adenocarcinoma/squamous cell carcinoma of the oesophagus
(2) Patients that will receive standard chemoradiation treatment before surgery for oesophageal carcinoma
(3) Ability to give informed consent
(4) Age 18 years or older
(5) no prior therapy for oesophageal carcinoma

Exclusion criteria

(1) pregnancy
(2) Inflammation of the gastro-intestinal tract
(3) Brain metastasis
(4) Diastolic/ systolic Hypertension (>90/>140 mmHg), not responding to treatment
(5) Arterial thromboembolism in medical history
(6) Surgery within the month prior to start of bevacizumab treatment

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	N/A: single arm study
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-02-2014
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	18-02-2014
Application type:	First submission

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
NTR-new	NL4296
NTR-old	NTR4440
Other	METC VU : 2013/340

Study results