Angiogenic factor expression during fractionated irradiation

No registrations found.

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

Summary

ID

NL-OMON23950

Source NTR

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 upregulation 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 presention offects of this induction of VECE expression

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

Public

De Boelelaan 1117 H.M.W. Verheul Amsterdam 1081 HV The Netherlands +31 (0)20 4444321/300 **Scientific**

De Boelelaan 1117 H.M.W. Verheul Amsterdam 1081 HV The Netherlands +31 (0)20 4444321/300

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:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

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

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Ethics review

Positive opinionDate:18-02Application type:First

18-02-2014 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

RegisterIDNTR-newNL4296NTR-oldNTR4440OtherMETC VU : 2013/340

Study results