Hyperthermia induced homologous recombination (HR) deficiency in cervical carcinoma

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To investigate whether hyperthermia induces HR-deficiency in cervical tumors and as a feasibility study, secondly to investigate whether it is possible to detect circulating tumor cells before and after hyperthermia.

Ethical review	Approved WMO
Status	Pending
Health condition type	Cervix disorders (excl infections and inflammations)
Study type	Observational invasive

Summary

ID

NL-OMON40739

Source
ToetsingOnline

Brief title
Hyperthermia Cervical Cancer Pilot

Condition

- Cervix disorders (excl infections and inflammations)

Synonym
cervical cancer, Cervical carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Verloskunde en Gynaecologie, subafdeling Gynaecologie en Gynaecologische Oncologie, Erasmus MC, Daniel den Hoed
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: BRCA2, cervical cancer, homologous recombination deficiency, hyperthermia

Outcome measures

Primary outcome

The level of BRCA2 protein as detected by immuno (Western) blotting with anti-BRCA2 antibody before and after hyperthermia as a measure of homologous recombination (HR) deficiency. In parallel, part of the pre-hyperthermia obtained tumor cells will be incubated at 37*C or 41*C in the laboratory, as an ex vivo control experiment in the same patient.

Secondary outcome

The presence of CTC before and after hyperthermia treatment.

Study description

Background summary

Cervical cancer is the third most common type of cancer among women and in advanced cases and recurrent disease the outcome is poor. Therefore, there is an urgent need to enhance the effectiveness of current therapies and to develop new strategies for treating cervical cancer.
Hyperthermia is currently added to radiotherapy in locally advanced cervical cancer and added to chemotherapy in local recurrent disease. Recently it has been demonstrated in vitro that mild hyperthermia (41 - 42.5 °C) leads to degradation of BRCA2. BRCA2 deficiency inhibits homologous recombination (i.e. HR-deficiency), a DNA repair mechanism. Defective HR-deficiency sensitizes cells to double-strand break-inducing therapy like platinum derivates, radiation and poly (ADP-ribose) polymerase (PARP)-1 inhibitors.
Confirmation of these results in human cervical tumor samples will support the current treatment of chemotherapy or radiotherapy combined with hyperthermia by gaining insight into the mechanism of action. Furthermore, it will be a useful model to study the effect of new therapeutic strategies on HR deficiency in cervical tumors.
In several carcinomas including breast and prostate, enumeration of circulating tumor cells (CTC) bears prognostic information. In cervical cancer, it is

unknown whether CTC can be detected, and the role of CTC has not been studied.

Study objective

To investigate whether hyperthermia induces HR-deficiency in cervical tumors and as a feasibility study, secondly to investigate whether it is possible to detect circulating tumor cells before and after hyperthermia.

Study design

Pilot study.

Study burden and risks

Benefit: This is a pilot study to provide proof of principle of a preclinical proven concept of in vitro hyperthermia induced HR-deficiency in cervical tumors and to investigate whether it is possible to identify circulation tumor cells in locally advanced cervical carcinoma. This will be of no benefit for the individual patient on the short term. However, once the concept is confirmed, an intervention trial will be planned, in order to show benefit of hyperthermia-induced HR-deficiency for future patients.
Risks: The patient will undergo two tumor biopsies and 2 venous blood samples will be taken. Since the biopsies are small (4 mm only) and patients with bleeding disorders are excluded, no serious risks are to be expected other than discomfort and minimal blood loss.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Cervical cancer patients with a routine indication for primary treatment combined with hyperthermia
• Tumor lesions amendable for biopsies
• Age >18 years
• Platelets >100 x 10e9/L
• Written informed consent

Exclusion criteria

• Current therapeutically use of anti-coagulant (coumarin, warfarin, heparin or low molecular weight heparin [LMWH]). LMWH if used for prophylaxis is allowed.
• Any psychological condition potentially hampering compliance with the study protocol.
• Patients who are treated in another institution for radiotherapy, with more than 2 hour travel distance.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2014
Enrollment:	15
Type:	Anticipated

Ethics review

Approved WMO

Date:	20-01-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL49462.078.14