Hyperthermia Induced Synthetic Lethality in Tumour Biopsies from Women with Cervical Cancer

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This study is part of a larger project funded by the KWF-Dutch Cancer Society (UvA 2015-7820) to establish a new cancer treatment based on a combination of PARP1-inhibition with hyperthermia and radiotherapy and/or cisplatin.Objective of this study...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON47845

Source
ToetsingOnline

Brief title
Hyperthermia in Cervical Cancer Biopsies

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
cervical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: KWF-Kankerbestrijding (project UVA 2015_7820)

Intervention

Keyword: cervical cancer, hyperthermia, radiotherapy, synthetic lethality

Outcome measures

Primary outcome

Tumour specimens will be used for a variety of in vitro and in vivo to

investigate synthetic lethality caused by hyperthermia plus targeted DNA-repair

inhibitors, i.e. PARP1-inhibitors, in combination with radiotherapy and

cisplatin. Several laboratory parameters for treatment response

Secondary outcome

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Study description

Background summary

Cervical cancer is the 4th most common cause of cancer death in women worldwide. In The Netherlands the 5 year survival rate is 65% and has only marginally improved in the last 25 years despite more effective combined radiotherapy with cisplatin, or radiotherapy with hyperthermia. More effective treatment strategies are urgently needed.
Repair of DNA damage is an important cause of resistance to radiotherapy or cisplatin treatment in cancer cells. Targeting DNA repair mechanisms offers the possibility to sensitize tumour cells to cytotoxic treatments. Earlier, we discovered two different molecular mechanisms by which hyperthermia gives a tumour selective sensitization to radiotherapy and cisplatin: (1) Down-regulation of the DNA repair protein BRCA2, one of the key proteins of homologous recombination (HR) repair, and (2) down-regulation of HPV-E6 and restoration of p53 in HPV-positive cervical cancer cells, both in vitro and in animals. Translation of these promising results to patients requires further studies on optimal combination in terms of tumour response and toxicity. Combination of hyperthermia with experimental targeted inhibitors of DNA-repair, such as PARP1, will lead to so-called synthetic lethality that will further sensitize tumour specific damage from radiotherapy and/or cisplatin. Before we wish to start a clinical study, additional pre-clinical studies are

needed.

Study objective

This study is part of a larger project funded by the KWF-Dutch Cancer Society (UvA 2015-7820) to establish a new cancer treatment based on a combination of PARP1-inhibition with hyperthermia and radiotherapy and/or cisplatin.

Objective of this study: Collection of human cervical cancer biopsies for in vitro and in vivo studies of hyperthermia induced synthetic lethality.

Study design

Prospective cohort study.

All women with newly diagnosed cervical cancer who will have a standard gynaecological investigation under general anaesthesia will be asked for this study. During this investigation, usually including a standard diagnostic biopsy, an extra tumour biopsy will be obtained for this study.

Study burden and risks

The major burden to the patient is the risk of tumour bleeding directly after taking the biopsy.
Cervical cancers are easily bleeding tumours; many patients present with vaginal bleeding as the first sign of cervical cancer. Tumour bleeding may be provoked by any tumour manipulation, such as taking a biopsy. Such a bleeding is usually minor, mostly stops spontaneously, or can be stopped by simple haemostasis, coagulation, or a vaginal gauzes.
Fistula formation and infection can theoretically be caused by a biopsy, although these risks are more likely to be related to extensive tumour invasion and necrosis.

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

* Adult women with cervical cancer (>18 years)
* who will have an investigation under general anesthesia (or: under spinal anesthesia),
* and who have given written informed consent for extra biopsies for research.

Exclusion criteria

* Women * 18 years,
* Or who will not have an investigation under general anesthesia for whatever reason,
* Unwilling or unable to give written informed consent, either because of mental limitations or because of a language barrier.

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-12-2017
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	26-05-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2019
Application type:	Amendment
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

No registrations found.

In other registers

Register	ID
CCMO	NL57465.018.16