Cancer during pregnancy: short and long term effects on mother and child.

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In 2004, a multidisciplinary team of clinicians and researchers in the UZ Leuven hospital started to collaborate on the rare problem of cancer during pregnancy. The collaboration between gynaecologists, pediatricians, hematologists, farmacologists,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54595

Source
ToetsingOnline

Brief title
Cancer during pregnancy

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Neonatal and perinatal conditions

Synonym
cancer during pregnancy and outcome

Health condition

lange termijn complicaties van moeder en kind

Research involving
Human

Sponsors and support

Primary sponsor: UZ Leuven
Source(s) of monetary or material Support: Fonds Wetenschappelijk Onderzoek (FWO) Vlaanderen;en Nationaal Kanker Plan;België;en European Research Council grant 2016. KWF grant

Intervention

Keyword: cancer, outcome, pharmacokinetics, pregnancy

Outcome measures

Primary outcome

Maternal outcome

Outcome of the child that is exposed to chemo and/or radiotherapy in utero.

Secondary outcome

Obstetric outcome

Differences in diagnosis and therapy, compared to non-pregnant patients

Differences in pharmacokinetics when chemotherapy is administered, compared to

non-pregnant patients

Psychological impact of the diagnosis cancer in pregnancy on the patient and

her partner.

Identify differences in tumor biology and genetic changes in the tumor in

pregnancy-associated cancer, compared to non-pregnancy-associated cancer.

Study description

Background summary

Cancer is the second leading cause of death during the reproductive years and complicates between 0.06% and 0.10% of all pregnancies. In Europe, this number translates into 3000 to 5000 new cases of cancer diagnosis during pregnancy

yearly. As women in developed societies defer childbearing to the third or fourth decade of life, and the incidence of several malignancies rises with increasing age, this rare co-incidence is likely to become more common. The most frequently encountered types of cancer in women of childbearing age are breast cancer, cervical cancer, leukaemia, lymphoma and malignant melanoma. The maternal prognosis is probably similar to non-pregnant women provided the same treatment strategies are applied. These include surgery, chemotherapy and radiotherapy or a combination of these. However, little data exist on the safety and efficacy of chemotherapy and radiotherapy during pregnancy.

Although several reports address the fetal outcome after prenatal exposure to chemotherapy or radiotherapy, we are not aware of any prospective study on this subject. Retrospective data suggest an overall reassuring short term outcome after prenatal exposure to chemotherapy or radiotherapy, however stillbirth, premature birth and low birth weight seem to occur more frequently. Also, neonatal myelosuppression has been reported. Although dose-related cardiotoxicity after anthracycline-exposure in adults or children is a well-known problem, the effects of doxorubicin on the developing fetal heart needs further investigation. On the long term outcome, systematic studies are lacking. The available studies report on a normal physical, neurological, psychological, haematological and immunologic outcome, without an increased occurrence or secondary malignancies, however the children were not examined in a standardized manner.

Study objective

In 2004, a multidisciplinary team of clinicians and researchers in the UZ Leuven hospital started to collaborate on the rare problem of cancer during pregnancy. The collaboration between gynaecologists, pediatricians, hematologists, farmacologists, medical oncologists and gynaecological oncologists resulted in a multicentric, international study, with the main aim to investigate the effect of cancer and cancer treatment during pregnancy on the mother and child*s outcome. Participating countries so far are: Austria, Belgium, Canada, Czech republic, Denmark, France, Greece, Israel, Italy, Lithuania, Mexico, The Netherlands, Norway, Poland, Portugal, Russian Federation, Serbia, Spain, Sweden, United Kingdom, United States (Philadelphia), Switzerland . There is also active collaboration with the German Breast group which registers women diagnosed with breast cancer during pregnancy (www.germanbreastgroup.de).

Study design

PART 1.1A. Registration study *Cancer during pregnancy*
PART 1.1B Effects of prenatal exposure to cancer treatment on fetal growth.
Part 1.2 Measurement of maternal and paternal anxiety and emotional needs when confronted with a cancer diagnosis during pregnancy

PART 1.3 Biobank *cancer in pregnancy*
PART 1.4 Study on the pharmacokinetics of chemotherapeutic agents in pregnant women
PART 2. Long term follow up of children and adolescents in utero exposed to chemotherapy and/or radiotherapy.

The aim of part 1.1A, Registration study, is to record the incidence and maternal (obstetrical and oncological) outcome of cancer occurring during pregnancy. To record the short and long term neonatal outcome. And to record the incidence and prognosis of women with cancer diagnosed in the first year postpartum. This study will provide insight in the effect of cancer and cancer treatment during pregnancy on the mother and child*s outcome.
The aim of part 1.1B The aim is to study the pathophysiology of IUGR which is associated with cancer treatment during pregnancy.Maternal blood samplings at approximately 32 weeks of gestation will be taken to determine levels of circulating hormones, factors of angiogenesis and inflammation. Placental and umbilical cord biopsies will be collected to examine the morphology and markers of angiogenesis, inflammation, apoptosis and proliferation

In part 1.2, on psychological impact we aim to identify maternal and paternal emotional needs when cancer is diagnosed during pregnancy. And to identify the maternal (and paternal) attitude with regard to oncologic treatment during pregnancy. We developed a questionnaire on maternal anxieties when cancer is diagnosed during pregnancy. In future we hope to establish guidelines on how to emotionally and mentally support the mother and her partner when cancer is diagnosed during pregnancy. These guidelines should form the basis for the counseling and psychological treatment of these patients.

In part 1.3, a Biobank is collected, to identify differences in tumor biology and genetic changes in the tumor in pregnancy-associated cancer, compared to non-pregnancy-associated cancer. The study hopes to compare 2 subgroups within pregnancy-associated cancer; women diagnosed with cancer during pregnancy, and women diagnosed with cancer in the first year postpartum. Permission for storage of blood -and tissue samples for further research will be requested. Samples that are aimed for are: blood samples, plasma samples, tumour samples, placenta samples and cord blood samples. Collected samples will be registered in a central database and will be available for future research on cancer in preganancy.

In part 1.4 on Pharmacokinetics, we aim to investigate the difference in pharmacokinetics of cytotoxic drugs and the therapy related toxicity, compared between pregnant and non-pregnant patients. And to correlate these results with outcome (disease free and overall survival, as registered in part I). Pharmacokinetic parameters will be compared between pregnant and non-pregnant women including terminal elimination half-life, apparent volume of distribution and (whole body) clearance. (limited sampling will be applied) Supplemental blood samples will be taken after the course for determination of total blood

count.

In part II, the long term follow up of the children exposed to chemotherapy and/or radiotherapy in utero the study investigates differences in: general health issues, incidence and prevalence of secondary malignancies, neurologic, cardiologic and sexual development.
At the ages of 6 months, 18 months, 3 years, 6 years, 9 years, 12 years, 15 years and 18 years, the children will be invited to the hospital for a physical, neurologic and cardiac evaluation..

Study burden and risks

Burden for registration study part 1.1A: none. The treating physician will be contacted for information. Risk: none
For part 1.1B: 2 maternal blood samples will be drawn, shortly after delivary. These will be combined with standard of care blood samples. There is no risk or burden from umbilical or placental biopsies

Burden for the psychological questionnaire (part 1.2): to fill in the questionnaire once, will take around 10-15minutes. No risks.

Burden for pharmacokinetics study 1.4: during 1 chemotherapy cycle, 5x 1 blood sample, either through venapunction or using the existing peripheral or central line. Risk of hematoma.

Burden for the children (part 2): 8x half a day (at the ages of 6 months, 18 months, 3, 6, 9, 12, 15 and 18 years), No risks or invasive procedures involved.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

All women with a histological proven diagnosis of cancer during pregnancy or in the first year postpartum are eligible (all types of malignancy).
Patients are at least 18 years of age.
Signed and written informed consent.
Patients do not need to participate in all parts of the study, they are allowed to opt for some or all parts of the study.
- Registration study part: for all patients who are confronted with cancer in pregnancy or in the first year postpartum, irrespective of outcome of pregnancy (e.g. termination, spontaneous abortion or successful delivery) or treatment modality during pregnancy. Patients may be included retrospectively and prospectively in the registration part of the study
- The study of pharmacokinetics is only applicable to women undergoing chemotherapy during pregnancy. Patients must have adequate bone marrow, renal, hepatic and pulmonary function. WHO performance of 0 or 1.
-Patients are invited to fill in the psychological questionnaire (quantification of psychological distress), irrespective of the cancer type or pregnancy term. Also women who receive no active therapy are eligible for the questionnaire.
- Long term follow up of the children who were exposed to chemotherapy and/or radiotherapy in utero is proposed to the parents after the delivery.
-Control group of children who were born preterm on maternal indication, and control group of a term born children of healthy mothers without cancer during pregnancy

Exclusion criteria

Mentally disabled or significantly altered mental status that would limit the understanding and giving of informed consent.
Patients that are not able to read and understand the patient informed consent form, due to language.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-07-2014
Enrollment:	1080
Type:	Actual

Ethics review

Approved WMO Date:	26-05-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	15-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-07-2023
Application type:	Amendment
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
Other	https://clinicaltrials.gov/NCT00330447 S25470 UZ Leuven, Belgie
CCMO	NL43546.078.13