p53 synthetic long peptides vaccine with cyclophosphamide for ovarian cancer, a phase II trial.

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Primary objectives:- To improve the clinical effectiveness of the p53 synthetic long peptides vaccine by pre-administration of cyclophosphamide.- To evaluate the immunogenicity of a p53 synthetic long peptide vaccine when preceded by administration...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON31732

Source
ToetsingOnline

Brief title
ISA-p53-CTX

Condition

- Reproductive neoplasms female malignant and unspecified
- Ovarian and fallopian tube disorders

Synonym
ovarian cancer, ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ISA Pharmaceuticals,KWF

Kankerbestrijding;ISA Pharmaceuticals

Intervention

Keyword: immunotherapy, ovarian cancer, p53, peptide

Outcome measures

Primary outcome

Clinical response after treatment with the p53 synthetic long peptides vaccine preceded by administration of cyclophosphamide will be evaluated by serum CA-125 levels and tumour volume with CT-scan.

Immunogenicity of the vaccine when preceded by cyclophosphamide, will be determined by assessment of the induction and frequency of p53-specific T cells following vaccination by proliferation and IFN-γ ELISPOT.

The effect of addition of cyclophosphamide to the regimen will be determined by comparing the responses elicited in the present study with those from the previous study for all endpoints.

Secondary outcome

Safety of the vaccine preceded by cyclophosphamide will be assessed by monitoring the incidence and severity of adverse events using Common Terminology Criteria for Adverse Events v3.0.

Study description

Background summary

Ovarian cancer is considered a silent lady killer. Due to the absence of specific symptoms, the majority of patients present with advanced stage disease. Although the incidence of ovarian cancer is low, the mortality rate is high. The standard treatment consists of a combination of surgery and platinum based chemotherapy. Despite this treatment, 80% of the patients die within 5 years after the diagnosis has been made.
Progress in the fight against ovarian cancer has been hampered by the lack of highly effective therapy to permanently eradicate disseminated intraperitoneal metastases, present in most patients at the time of diagnosis. In order to improve the poor outcome for ovarian cancer patients old and new treatment modalities, such as targeted or biologic agents and immunotherapy should be combined. Recent data show the importance of the immune response in the course of ovarian cancer as well as the negative influence of Tregs. The availability of new potent immunization strategies urge further exploration of immunotherapy as adjuvant treatment modality in ovarian cancer patients.

Study objective

Primary objectives:
- To improve the clinical effectiveness of the p53 synthetic long peptides vaccine by pre-administration of cyclophosphamide.
- To evaluate the immunogenicity of a p53 synthetic long peptide vaccine when preceded by administration of cyclophosphamide.

Secondary objective:
To evaluate the safety of the p53 synthetic long peptide vaccine when preceded by administration of cyclophosphamide.

Study design

This is an uncontrolled, mono-centre, phase II study, investigating the clinical effectiveness, immunogenicity and safety of four vaccinations with the p53 synthetic long peptide vaccine, with each vaccination preceded by administration of cyclophosphamide i.v.

Intervention

The vaccine consists of 10 synthetic p53 peptides in dimethylsulfoxide (DMSO) / phosphate buffer 20mM (PBS) / Montanide ISA51 (20/30/50 v/v/v-%). The vaccine will be administered by subcutaneous injection at a dose of 300 µg per peptide. Patients will be vaccinated four times at three week intervals. Vaccinations are given in four different sites: left upper arm, left thigh, right upper arm, right thigh.

Cyclophosphamide will be administered intravenously, in a dose of 300mg/m2, two

days prior to each peptide vaccination.

Study burden and risks

Burden and risks:
Based on the results from the previous phase I/II study with the p53 synthetic long peptides vaccine, little toxicity is anticipated from peptide vaccination.
The peptide components in the vaccine are designed to be non-toxic. Experienced toxicity so far using this vaccine was local pain, redness, pruritis and swelling of the local skin, grade I/II according to the Common Terminology Criteria for Adverse Events.
Cyclophosphamide may cause nausea and vomiting as a side effect of treatment. Premedication for nausea will be administered prior to infusion of the drug.
With the specified dose, hematologic toxicity is not expected.
Anemia caused by blood sampling may occur, but is not expected as this was not observed in the previous phase I/II study (with a higher total volume of blood taken).
At two times during the study a skin biopsy will be taken from the vaccination site under local anesthesia, where after the wound is closed with stitches.

Benefit and group relatedness:
Immunotherapy is one of the novel therapeutic strategies under investigation in ovarian cancer. In theory, immunotherapy directed at tumor specific antigens, administered after standard therapy, provides an ideal tool to consolidate anti-tumor effects of standard therapy, and to delay and possibly prevent progression of disease.
There are indications that chemotherapy after vaccination might be more effective in patients who showed an immunological response after vaccination.

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

-Written informed consent.
-Histological proven epithelial ovarian carcinoma
-At least 4 weeks after termination of the last course of chemotherapy.
-Rising CA-125 serum levels after *first line* treatment and no measurable disease according to the RECIST (Response Evaluation Criteria in Solid Tumours) criteria,
or
Rising CA-125 serum levels after *first line* treatment with measurable disease according to the RECIST (Response Evaluation Criteria in Solid Tumours) criteria, but not willing or otherwise not fit to receive *second line* chemotherapy.
-18 years or older, and an life expectancy of at least 3 months
-Performance status 0 to 2 (WHO scale).
-Adequate hepatic, renal, and bone marrow function as defined:
ASAT <100 U/l; ALAT <113 U/l; PT 9-12 seconds; APTT 23-33 seconds; creatinine < 135 µmol/l; WBC > 3.0 x 109/L; platelets > 100 x 109/L; hemoglobin > 6.0 mmol/l.

Exclusion criteria

-Pregnancy and / or breast feeding.
-(A)symptomatic cystitis
-Other malignancies (previous or current), except basal or squamous cell carcinoma of the skin.
-Immunosuppressive agents, except for topical and inhalation corticosteroids.
-Prior therapy with a biological response modifier.
-Participation in any other trial with an investigational drug.
-Any other major disease that may interfere with the conduct of the study (e.g. uncontrolled hypertension, severe and/or unstable heart disease, neurological and psychiatric disorders).
-Signs or symptoms of CNS metastases.

-Known substance abuse (drug or alcohol).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-10-2008
Enrollment:	19
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Endoxan
Generic name:	cyclophosphamide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-02-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-07-2008

Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2007-007734-19-NL
CCMO	NL21308.000.07