Induction of neo*antigen specific cytotoxic T cells by autologous tumor lysate-loaded specialized cross*presenting dendritic cells in epithelial ovarian cancer patients treated with neoadjuvant chemotherapy, the NEODOC study

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This study has been transitioned to CTIS with ID 2024-512353-24-01 check the CTIS register for the current data. The primary objective of this study is to show immunological efficacy of autologous tumor-lysate loaded XP-DC in epithelial ovarian...

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

Summary

ID

NL-OMON54480

Source
ToetsingOnline

Brief title
NEOadjuvant Dendritic cell vaccination for Ovarian Cancer (NEODOC)

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
epithelial ovarian cancer, high grade serous ovarian cancer, ovarian cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: Dendritic cells, Immunotherapy, Ovarian cancer, Therapeutic vaccination

Outcome measures

Primary outcome

The primary endpoint of the study is the immune response enhanced or induced by autologous tumor lysate-loaded XP-DC in epithelial ovarian cancer patients.

Secondary outcome

Secondary endpoints are

- the safety and feasibility of tumor lysate-loaded XP-DC vaccinations. Safety will be evaluated by adverse events, WHO/ECOG performance status, physical examinations and laboratory tests. Toxicity will be assessed according to CTCAE version 4.3;

- changes in the immunological landscape in tumor material and mutational status after chemotherapy combined with vaccination with DC vaccines;

- clinical efficacy (number with pathological response to chemotherapy, number with complete interval debulking, progression free survival, overall survival;

Study description

Background summary

Epithelial ovarian cancer (EOC) is the deadliest gynaecological malignancy worldwide. Despite intensified treatment, 5-year overall survival rates only improved modestly over the last 20 years and remain low at around 30% for advanced disease in the Netherlands. To this day, results from trials with the checkpoint inhibitors, that have revolutionized treatment in other cancer types, have been disappointing in EOC. Therefore, novel effective therapies are long awaited.
Recently, we showed that naturally circulating blood-derived dendritic cells (nDC) are potent in inducing cytotoxic immune responses and tumor regression in cancer patients. However, there is even a more specialized DC subset, referred to as XP-DC or cDC1. XP-DC have shown their superiority in preclinical models in inducing cytotoxic T cell responses to cancer after uptake of necrotic tumor cell material, a phenomenon called cross priming. XP-DC are hypothesized to be ideal to induce cytotoxic immune responses against the scarce neoantigens present in EOC tumors. Since tumor lysates are the easiest source of personalized neoantigens we propose to vaccinate EOC patients with XP-DC loaded with autologous whole tumor lysate.

Study objective

This study has been transitioned to CTIS with ID 2024-512353-24-01 check the CTIS register for the current data.

The primary objective of this study is to show immunological efficacy of autologous tumor-lysate loaded XP-DC in epithelial ovarian cancer patients undergoing (neo-)adjuvant chemotherapy. The secondary objectives are the safety and feasibility of autologous tumor lysate-loaded XP-DC vaccinations, clinical efficacy (number with pathological response to chemotherapy, number with complete interval debulking, number progression-free survival and overall survival), changes in the immunological landscape and mutational status after, chemotherapy combined with XP-DC vaccination.

Study design

This study is a single arm, single center, exploratory, phase I/II study.

Intervention

Patients are treated with standard (neo-)adjuvant chemotherapy and debulking surgery. On day 14 of every 21 days cycle of chemotherapy (6 cycles in total), autologous whole tumor lysate-loaded XP-DC will be administered.

Study burden and risks

Based on the experience with nDC inoculations in patients with melanoma, prostate cancer and endometrial cancer, we expect that the XP-DC will be well tolerated by EOC patients. Common and expected side effects of nDC vaccination are usually mild and include flu-like symptoms and local reaction at injection site, both not greater than Common Terminology Criteria for Adverse Events (CTCAE) grade 2. The side effects are completely reversible within 24-48 hours. Because of this the risk classification in relation to the chance of adverse events and the severity of the expected adverse events is defined as being negligible.

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

• Age over 18 years old

• Histologically confirmed primary epithelial ovarian cancer
• Not amenable by primary debulking surgery and in need of neoadjuvant chemotherapy and interval debulking
• High-grade serous histology
• FIGO stage IIIb, IIIc, IVa or IVb if only lymph nodes <= 1cm above the diaphragm or in the groins
• Extensive abdominal spread of tumor
• WHO/ECOG performance status 0-1

Exclusion criteria

• Recurrent ovarian cancer
• History of any second malignancy, with the exception of adequately treated basal cell carcinoma, cervical cancer > 5 years ago or early stage breast cancer >10 years ago.
• Any serious clinical condition that may interfere with the safe administration of DC vaccinations or renders patient ineligible for combined carboplatin-paclitaxel chemotherapies
• Active infection of Hepatitis B, C, HIV and syphilis or any other serious active infection
• Known allergy to shell fish
• Auto immune disease (exception: vitiligo is permitted)
• Chronic treatment with systemic immunosuppressive drugs (i.e. more than 10 mg prednisolone equivalent)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-03-2023
Enrollment:	10

Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	07-02-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-02-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-05-2024
Application type:	Amendment
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
EU-CTR	CTIS2024-512353-24-01
EudraCT	EUCTR2021-000714-42-NL
CCMO	NL75563.000.22