Ovarian cancer treatment with a liposome formulated mRNA Vaccine in combination with neo-adjuvant chemotherapy

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To induce a vaccine specific immune response, hereby we hope to introduce the possibility of a new treatment to improve patient outcome and survival.

Ethical review	Not approved
Status	Will not start
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON46832

Source
ToetsingOnline

Brief title
OLIVIA

Condition

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

Synonym
Ovariancancer/ ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: BioNTech RNA Pharmaceuticals GmbH,KWF-subsidie en BioNtech RNA Pharmaceuticals GmbH

Intervention

Keyword: Ovarian carcinoma, Phase I, Therapeutic immunization

Outcome measures

Primary outcome

To assess whether the RNA-LPX OC vaccine induces a vaccine-specific immune response (systemic & local)

Secondary outcome

To assess the safety and tolerability of intravenous RNA-LPX OC vaccination in combination with carboplatin and paclitaxel by monitoring and evaluation of adverse events.

Study description

Background summary

Advanced stage serous ovarian cancer (OC) is the leading cause of death from gynaecological malignancies with a 5-year survival of no more than 40%. Current treatment (surgery and chemotherapy) is initially effective, but almost all patients suffer from chemotherapy-resistant relapse. Moreover, despite adjustment of chemotherapeutic schedules and the introduction of innovative targeted drugs, survival and quality of life have barely improved. A promising new approach that may improve outcome for these patients is immunotherapy. In particular, immune checkpoint inhibition (CPI) therapy targeting e.g. PD-L1 or PD-1 have improved patient survival rates across malignancies, with some responses also observed in ovarian cancer patients. Nevertheless, response to CPIs is almost always dependent on a pre-existing anti-cancer immune response, frequently absent in ovarian cancer patients.

In order to increase/ induce an anti-tumor response an optimized liposomal formulated RNA vaccine targeting tumor-associated antigens (TAA) is developed. This vaccine protects RNA from degradation by plasma RNAses and shows an almost 100% targeted accumulation of RNA in the spleen suggesting a direct delivery to

dendritic cells. Here, we therefore propose to increase/induce an anti-tumor immune response in patients with ovarian cancer while receiving neoadjuvant chemotherapy by use of the RNA lipoplex (LPX) OC vaccine.

The simultaneous treatment with vaccinations and neoadjuvant chemotherapy provides a tumor immune environment where immune defences are decreased. Thereby enhancing the effectiveness of a vaccine induced immune response. Making it a perfect setting for the induction of a tumor specific immune response, with the ultimate aim of moving towards combination therapy of chemotherapy/vaccination with checkpoint inhibition for these patients.

Study objective

To induce a vaccine specific immune response, hereby we hope to introduce the possibility of a new treatment to improve patient outcome and survival.

Study design

A GMP-grade RNA vaccine targeting serous OC antigens will be used to induce a systemic immune response and more importantly tumor accumulation of vaccine-induced T cells. Patients with primary epithelial ovarian carcinoma will receive eight vaccinations, in the same period they will receive three cycles of neoadjuvant chemotherapy (standard treatment).

Data collected for analyzing vaccine-specific immune response (systemic and local) is obtained before and after vaccinations by:
- Collection of PBMCs for immune monitoring by venous blood collection wil occur before vaccination (120mL) and a leukapheresis is planned after final vaccination.
- collection of tumor material by biopsy before vaccination and surgery after vaccination (standard care).

We will need to include at least 10 patients to determine the primary outcome (vaccine specific immune response)

Intervention

Intravenous administration of the vaccine (8 times)

Study burden and risks

Participating patients in this phase I trial have an active disease and might experience a direct benefit from this study. The ultimately intended benefit is to induce a specific anti-cancer immune response which leads to eradication of the malignant lesions, to less invasive surgery and fewer complications. When long-lasting immunity is induced, the immunotherapy may also prevent recurrence

of the disease.

For this study 14 hospital visits are required, including 2 overnight hospitalizations. Visits will be scheduled at the same day as regular visits as much as possible. Vaccination by means of intravenous injection is performed eight times with additional venapunctures for biomonitoring. Initial clinical data from naked RNA studies has demonstrated that a dosage of 100 ug total RNA is safe and sufficient for induction of a potent immune response. In order to minimize the amount of additional venapunctures they will be combined with blood sample collections for standard treatment where possible. Additional study procedures not included in standard patient care are: 1 leukapheresis and 1 image guided tumor biopsy.

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

- Primary epithelial OC patients whom are treated with neoadjuvant chemotherapy, carboplatin/paclitaxel, and subsequent surgery.
- Age * 18 years
- Signed informed consent in accordance with institutional and regulatory guidelines
- Life expectancy * 5 months
- Adequate access of the tumor for image guided biopsy
- Adequate(according to the instiutional standards) hematology, liver and kidney function to undergo chemotherapy with carboplatin and paclitaxel

Exclusion criteria

or any other systemic intercurrent disease or condition that might affect the immunocompetence of the patient, or treatment with systemic highly immunosuppressive therapy (e.g. transplant recipients or patients who underwent a splenectomy)
- Use of systemic continuous corticosteroid therapy (e.g. prednisone i.v. or p.o. > 7,5 mg / day).
- Neurological toxicity > grade 1 at screening
- History of a second malignancy except curatively treated low-stage tumors with a histology that can be differentiated from the serous OC type
- Pregnancy
- Participation in a trial with another investigational drug within 30 days prior to the enrolment in this trial
- Any condition that in the opinion of the investigator could interfere with the conduct of the trial.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	RNA lipoplex OC vaccin

Ethics review

Approved WMO

Date:	02-02-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Not approved

Date:	25-04-2018
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	EUCTR2017-004585-10-NL
CCMO	NL62905.000.18