An open label, phase 1 study to evaluate the safety, feasibility and immunogenicity of an allogeneic, cell-based vaccine (DCP-001) in high grade serous ovarian cancer patients after primary treatment

Published: 12-10-2020
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This study has been transitioned to CTIS with ID 2024-516781-10-00 check the CTIS register for the current data. Primary objective:• Systemic immunogenicity of the DCP-001 vaccination in high grade serous ovarian (HGSOC) cancer patients.

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

Summary

ID

NL-OMON55212

Source
ToetsingOnline

Brief title
ALISON

Condition

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

Synonym
ovarian cancer, Overian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: DC Prime

Intervention

Keyword: Dendritic cell vaccine, Immunogenicity, Ovarian carcinoma, Phase I

Outcome measures

Primary outcome

To assess whether the DCP-001 vaccine induces a systemic vaccine-specific

immune response.

Secondary outcome

To assess the safety and tolerability of the DCP-001 vaccine in ovarian cancer

patients after primary treatment.

Recurrence Free Survival

Overall survival

Study description

Background summary

Ovarian cancer (OC) is the leading cause of death from gynecological malignancies with a 5-year survival of no more than 40%. Current standard treatment (surgery and chemotherapy) is initially effective, but almost all patients suffer from chemotherapy-resistant relapse. After cytoreductive surgery (complete/suboptimal), most patients remain in a state of microscopic minimal residual disease until relapse.
Recently maintenance therapy has been introduced for these patients with the approval of poly adenosine diphosphate ribose polymerase inhibitors (PARPi) for BReast CAncer gene (BRCA) germline mutated OC patients. PARPi treatment showed beneficial clinical effect in large trials by improving progression free

survival (PFS) and overall survival (OS) in OC patients with deleterious germline BRCA mutations. Approximately, 10-15% of epithelial ovarian cancer patients carry the germline BRCA1/2 mutation, the highest prevalence (20%) is found in the high grade serious subtype. However, it still leaves the majority of OC patients without an effective maintenance therapy. Therefore, new approaches that improve therapeutic outcome for OC patients are urgently needed.

Here, we propose a novel immunotherapeutic approach using an allogeneic cell-based vaccine (DCP-001), consisting of cells expressing common tumor-associated antigens, expressed by OC as well, and having characteristics of dendritic cells (DC), as a novel maintenance therapy in OC. Dendritic cells are professional antigen-presenting cells (APCs) and exquisitely suited to induce anti-tumor immune responses.

Clinical activity of DC-based immunotherapy in OC was recently demonstrated by Cibula et al. (2018) showing an improved OS in relapsed platinum-sensitive OC patients treated with second line chemotherapy (carboplatin/gemcitabine) in combination with DC-based immunotherapy (DCVAC/OvCa) compared to chemotherapy alone. In another study design, DCVAC/OvCa was administered sequentially as maintenance therapy after completing SoC treatment and demonstrated an improved PFS in OC patients. Administration of a vaccine after successful initial treatment has the potential advantage of eradicating residual tumor cells, providing optimal conditions for the immune system to prevent clinical relapse. For the current protocol, we propose the use of a maintenance therapy with the allogeneic cell-based vaccine, DCP-001.

This novel vaccine was developed from an acute myeloid leukemia (AML)-derived cell line that uniquely combines the positive features of allogeneic DC vaccines and expression of multiple tumor associated antigens. Vaccination with DCP-001 in 12 post-remission AML patients prolonged minimal residual disease status and was associated with improved PFS and systemic immunogenicity. Administration of the vaccine was associated with only limited side-effects like fever, injection site reactions, adenopathy, and fatigue. A phase II trial in AML is currently ongoing.

Importantly, the tumor associated antigens (TAAs) expressed by DCP-001 are shared across tumor types, most notably ovarian cancer. These antigens include, but are not limited to, the hallmark OC antigens: WT-1, MUC-1, Survivin, and PRAME. In addition, immune monitoring results from a completed phase I clinical study in AML showed that DCP-001 vaccination also induced immune responses towards TAAs which are not directly expressed by DCP-001 cells itself, like NY-ESO and MAGE-A3, which are two other dominant TAAs in ovarian cancer. Accordingly, pre-clinical studies of DCP-001 with isolated peripheral blood cells of OC patients resulted in potent vaccine-induced T cell responses in general and also specifically against certain OC cell lines. On top of that, DCP-001, when used as relapse vaccine in a humanized mouse model of OC, was capable to suppress tumor growth and lead to tumor regressions.

Taken together, these data support the evaluation of DCP-001 as relapse vaccine in high grade serous ovarian cancer (HGSOC) patients.

Study objective

This study has been transitioned to CTIS with ID 2024-516781-10-00 check the CTIS register for the current data.

Primary objective:
• Systemic immunogenicity of the DCP-001 vaccination in high grade serous ovarian (HGSOC) cancer patients.

Study design

This is a first phase I study in HGSOC patients with primary disease eligible for SoC treatment with either complete or optimal primary cytoreductive surgery followed by 6 cycles of adjuvant chemotherapy (carboplatin/paclitaxel) or 3 cycles of neoadjuvant chemotherapy (carboplatin/paclitaxel) followed by complete or optimal cytoreductive interval surgery and 3 additional cycles carboplatin/paclitaxel.
In the current study, DCP-001 vaccinations will be scheduled after SoC treatment.
Six doses (4 vaccinations and 2 boosters) of DCP-001 vaccine will be administered to induce an anti-tumor immune response between 6 and 24 weeks after the last cycle carboplatin/paclitaxel. Systemic immune responses are determined by standard immune assays using peripheral blood mononuclear cells (PBMCs) and serum collected before, during and after vaccinations. Progression of disease will be monitored according to standard-of-care follow-up.

Intervention

Patients will receive 6 intradermal vaccinations.

Study burden and risks

Patients in this phase I pilot have received and completed SoC treatment for HGSOC and might experience benefit from this study. The intended goal of the study is to induce a specific anti-cancer immune response. When immunity is induced, the immunotherapy may even prevent recurrence of the disease.
Six vaccinations by intradermal injection are performed with additional vena punctures for immune monitoring. Visits and study related blood collections are aligned to and combined with SoC procedures as much as possible.
Initial clinical data from DCP-001 studies demonstrates that a dosage of at least 25 million cells per vaccination is safe and sufficient for induction of a potent immune response with only limited side-effects like fever, injection site reactions, adenopathy, and fatigue. We will monitor the safety and toxicity of this cancer vaccine in the current trial, using GCP guidelines. Toxicity will be graded according to the NCI CTCAE Version 5.0.

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 HGSOC patients (FIGO stage 3B to IV) who completed primary treatment defined as:

o primary debulking surgery (complete / optimal) and 6 cycles of adjuvant chemotherapy (carboplatin/paclitaxel)

o 3 cycles of neo-adjuvant chemotherapy (more NACT cycles to improve surgical outcome are allowed) followed by interval debulking surgery (complete / optimal) and 3 cycles of adjuvant chemotherapy (carboplatin/paclitaxel)

- Decreased CA125 compared to pre-treatment CA125

- Serum level CA125 < 100 kU/L

- Age >= 18 years

- Signed informed consent form (ICF) in accordance with institutional and regulatory guidelines

Exclusion criteria

- History of a second malignancy except for curatively treated low-stage tumors with a histology that can be differentiated from the epithelial OC type

- Patients must have no ongoing or recent evidence (within the last 5 years) of significant autoimmune disease that required treatment with systemic immunosuppressive treatments which may suggest risk for immune-related adverse events (irAEs).
Note: Patients with autoimmune-related hyperthyroidism, autoimmune-related hypothyroidism who are in remission, or on a stable dose of thyroid-replacement hormone, vitiligo, or psoriasis may be included.

- Patients must have no uncontrolled infection with human immunodeficiency virus, hepatitis B or hepatitis C infection; or diagnosis of immunodeficiency that is related to, or results in chronic infection. Mild cancer-related immunodeficiency (such as immunodeficiency treated with gamma globulin and without chronic or recurrent infection) is allowed.

o Patients with known HIV who have controlled infection (undetectable viral load and CD4 count above 350 either spontaneously or on a stable antiviral regimen) are permitted. For patients with controlled HIV infection, monitoring will be performed per local standards.

o Patients with known hepatitis B (HepBsAg+) who have controlled infection (serum hepatitis B virus DNA PCR that is below the limit of detection AND receiving antiviral therapy for hepatitis B) are permitted. Patients with controlled infections must undergo periodic monitoring of HBV DNA per local standards. Patients must remain on anti-viral therapy for at least 6 months beyond the last dose of trial treatment.

o Patients who are known hepatitis C virus antibody positive (HCV Ab+) who have controlled infection (undetectable HCV RNA by PCR either spontaneously or in response to a successful prior course of anti-HCV therapy) are permitted.

- Liver or renal function abnormalities that are considered to be clinically relevant by the investigator.

- Abnormal blood levels (neutropenia among other things) due to chemotherapy that are considered to be clinically relevant by the investigator.

o If so, blood levels will be repeated in 1-2 weeks, in case blood levels are normalized the patient is allowed to be included in the study. In case of persistent abnormal blood levels the patient will be excluded.

- Use of systemic continuous corticosteroid therapy (e.g. prednisone i.v. or p.o. >7.5 mg / day).

- 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:	Recruitment stopped
Start date (anticipated):	10-06-2021
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DCP-001

Ethics review

Approved WMO Date:	12-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-03-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	22-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-09-2024
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	CTIS2024-516781-10-00
EudraCT	EUCTR2020-003600-13-NL
CCMO	NL74250.000.20