Exploratory study of neo-adjuvant treatment with carboplatin, paclitaxel and pembrolizumab in primary stage IV serous ovarian cancer

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

Summary

ID

NL-OMON54749

Source
ToetsingOnline

Brief title
Neo Pembro

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
ovarian cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut

Source(s) of monetary or material Support: Merck Sharp & Dohme,Merck Sharp & Dohme (MSD)

Intervention

Keyword: chemotherapy, gynaecological cancer, neoadjuvant, primary stage 4

Outcome measures

Primary outcome

Primary objective: The primary objective of this study is to determine the immune-activating capacity of treatment with pembrolizumab and carboplatin/paclitaxel in the neo-adjuvant setting of primary stage IV ovarian cancer as measured by the alteration in magnitude and breadth of the tumor specific T cell response during therapy in peripheral blood.

Secondary outcome

Secondary objectives of this study are:

- To evaluate the safety of the carboplatin-paclitaxel-pembrolizumab treatment

- To evaluate the tolerability of the carboplatin-paclitaxel-pembrolizumab treatment based on adverse events according to CTCAE version 4.03

- To assess the tumor response based on RECIST 1.1 and serum CA-125 levels

- To assess the efficacy of the treatment based on the result of the debulking surgery (no viable invasive tumor left in the resection specimen)

- To evaluate the feasibility of the carboplatin-paclitaxel-pembrolizumab treatment

- To evaluate Overall survival (OS, time from start chemotherapy to death from any cause)

- To evaluate Disease free Survival (DFS, time from start chemotherapy to tumor

progression)

Study description

Background summary

Long-term survival in stage IV serous ovarian, peritoneal, and fallopian tube cancer is poor and has not significantly improved over the last decades. Standard treatment consists of debulking surgery and six courses of carboplatin and paclitaxel. Nevertheless, the disease recurs in >90% of women, usually within two years.

Since early observations that the presence of infiltrating T cells is associated with improved outcome, ovarian cancer is linked to a potential benefit of immunotherapy.10 More recently, T cell checkpoint blockade with anti-PD1 and anti-PDL1 have shown promising activity in platinum resistant ovarian cancer with objective and durable responses in 10-20% of patients.This finding raises the question whether anti-PD1 could also play a role in first line treatment of ovarian cancer.

To fully use the power of T cell checkpoint inhibition, sufficient TCR stimulation is required. Importantly, the amount of antigen that can provide this signal will correlate with tumor load, and because of this adjuvant immunotherapy may work most efficiently, when initiated prior to surgery. In addition, we postulate that antigen retrieval will increase after induction treatment with cytotoxic therapy.
To address these questions, we propose a feasibility study in patients with FIGO stage IV serous ovarian, peritoneal, or fallopian tube cancer in which we evaluate pembrolizumab added to standard treatment for its capacity to induce and broaden T cell responses against neo-antigens.

Study objective

The primary objective of this study is to determine the immune-activating capacity of treatment with pembrolizumab and carboplatin/paclitaxel in the neo-adjuvant setting of primary stage IV ovarian cancer as measured by the alteration in magnitude and breadth of the tumor specific T cell response during therapy in peripheral blood.

Study design

- Three cycles carboplatin/paclitaxel. Pembrolizumab will be added from cycle 2.
- Debulking surgery (standard)
- Three cycles carboplatin/paclitaxel/pembrolizumab

- 7 cycles mono therapy pembrolizumab

Protocol version 2.1 dated 15 January2020:
Patients with germline or somatic BRCA1 / 2 mutations will be treated with PARPi according to the local guideline when indicated. This oral therapy is added to the standard treatment, and therefore also to the current study protocol.

Study burden and risks

The patient may experience additional side effects from the addition of pembrolizumab to the standard chemotherapy schedule.
The patient may also experience physical discomfort with some of the procedures performed during the study such as blood sampling, the IV line en tumor biopsy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

1. Written informed consent for the trial.
2. Diagnosis of primary high-grade serous ovarian, peritoneal, or fallopian tube cancer. Stage IV disease should ideally be cytologically or histologically proven
3. Age >= 18 years on day of signing informed consent.
4. Willing and able to provide three tumor biopsies (1 FFPE, 2 fresh frozen) prior to start of treatment
5. Performance status of 0 or 1 on the ECOG Performance Scale.
6. Adequate organ function as defined in Table 1 of the protocol
7. Female subject of childbearing potential should have a negative urine or serum pregnancy within 72 hours prior to receiving the first dose of study medication. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.

Exclusion criteria

1. previously received treatment for ovarian, peritoneal, or fallopian tube cancer.
2. known additional malignancy, unless treated with curative intent without chemotherapy at least five years ago. In situ cancers, basal cell carcinoma of the skin or squamous cell carcinoma of the skin that have undergone potentially curative therapy within the past five years may also be eligible.
3. currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks of the first dose of treatment.
4. a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment.
5. A known history of active TB (Bacillus Tuberculosis)
6. Hypersensitivity to pembrolizumab or any of its excipients.
7. Has had a prior anti-cancer monoclonal antibody (mAb) within 4 weeks prior to study

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2017
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin Hospira
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Olaparib
Generic name:	AZD2281
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel Hospira
Generic name:	Paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zejula
Generic name:	Niraparib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-06-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-06-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-10-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	24-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	29-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2016-004700-56-NL
ClinicalTrials.gov	NCT03126812

Register	ID
CCMO	NL59444.031.16