Determining prognostic immune markers in patients with ovarian cancer * a prospective explorative cohort study.

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Primary objectiveInvestigate if mMDSC/DC ratio in peripheral blood mononuclear cells (PBMCs) in patients with recurrent EOC before the start of treatment is associated with OS.See page 11 of the research protocol for secundary objectives.

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

Summary

ID

NL-OMON48676

Source
ToetsingOnline

Brief title
IMPrOVE

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
Ovarian cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Lokaal studie budget ovariumcarcinoom

Intervention

Keyword: Biomarkers, Immunity, Ovarian cancer

Outcome measures

Primary outcome

Association between the mMDSC/DC ratio in PBMCs in patients with recurrent EOC before the start of treatment and OS.

Secondary outcome

* Association between the mMDSC/DC ratio in PBMCs in patients with recurrent EOC before the start of treatment and PFS.

* Association between the mMDSC/DC ratio in PBMCs in patients with primary EOC before the start of treatment and PFS/OS.

* Interaction between the mMDSC/DC ratio in PBMCs and EOC groups on PFS/OS.

* Association between mMDSC/DC ratio in PBMCs measured at different time points in patients with primary and recurrent EOC and PFS/OS.

* Composition/counts and function of myeloid cells in PBMCs in patients with primary and recurrent EOC before and during treatment and the association with PFS/OS.

* Influence of the mMDSC/DC ratio and separate immune cell populations on the tumor specific and general immune response.

* Determined, optimized and validated optimal cut-off point for the macrophage/DC ratio and the mMDSC/DC ratio in PBMCs in patients with primary and recurrent EOC for the different chemotherapeutic and immunotherapeutic treatment modalities.

* Immune contexture of primary and recurrent tumors by determination of the

intratumoral immune subset numbers in fresh and archived tumor material and the association with PFS/OS.

* Immune contexture of ascites by determination of the immune subset numbers in ascites fluid of patients with primary and recurrent EOC and the association with PFS/OS.

Study description

Background summary

Survival rates for patients with epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer (EOC) are generally low and numerous studies are currently exploring new, more efficient treatment strategies. EOC is considered to be an immunogenic tumor. Therefore, new (experimental) treatment strategies will focus on the combination of immunotherapy with other therapies like chemotherapy. Two recent studies focussed on immunological aspects of ovarian cancer treatment. Retrospective analyses in these patient cohorts revealed two promising prognostic immune markers. The presence of high numbers of macrophages, and especially monocytic myeloid cell derived suppressor cells (mMDSCs), had a negative impact on overall survival (OS) whereas a high level of dendritic cells (DCs) was associated with higher OS after therapy. Importantly, the ratio of macrophages/DCs and in particular the ratio of mMDSCs/DCs in blood samples of patients at baseline formed an independent prognostic factor for OS after therapy. For each ratio an optimal cut-off point was determined. However, these analyses were performed in a small cohort and have not been validated in an independent cohort. Furthermore, it is not clear whether the ratio of these cells in the circulation are a reflection of the immune contexture within the tumor. Therefore, it is our aim to confirm and validate our earlier observations and to study the immune contexture in tumor tissue within a prospective cohort study of both recurrent and primary EOC patients. These insights not only may help to define a prognostic biomarker for patients with EOC but these ratio*s may also be predictive for the response to immunotherapy since the cells involved are key to suppress or activate tumor-specific T cell reactivity.

See also page 10 of the research protocol.

Study objective

Primary objective

Investigate if mMDSC/DC ratio in peripheral blood mononuclear cells (PBMCs) in patients with recurrent EOC before the start of treatment is associated with OS.

See page 11 of the research protocol for secundary objectives.

Study design

A prospective, explorative cohort study.

Study burden and risks

This study involves the use of blood samples, which are obtained during routine blood sampling. For the patients with (suspicion of) primary EOC, left over tumor material and ascites, obtained during routine surgery, is used in this study. Therefore, the burden and risk associated with participation of these patients is considered very small. For the patients with recurrent EOC, two extra biopsies (before and after systemic therapy) have to be obtained, which can cause some discomfort and, although rarely, complications. Ascites fluid will be collected only if there is an indication for ascites drainage.
Therefore, the burden and risk associated with participation of these patients is considered limited. There are no direct benefits for participating patients.

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

* Patients with (suspicion of) primary or recurrent EOC with an indication for surgery, chemotherapy and/or immunotherapy.
* Age *18 years.
* WHO performance status 0-2.
* Accessible for treatment and follow-up.
* Written informed consent.

Exclusion criteria

* Other active malignancy in past 5 years prior to entry into the study, except for treated non-melanoma skin cancer.
* Any known severe infection like HIV, hepatitis A, B and C.
* Receiving immune suppressive treatment.
* Medical or psychological condition which in the opinion of the investigator would not permit the patient to complete the study or sign meaningful informed consent.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-08-2020

Enrollment:	300
Type:	Actual

Ethics review

Approved WMO Date:	21-06-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
ClinicalTrials.gov	NCTxVOLGT
CCMO	NL66869.058.19