Durvalumab and Olaparib in Metastatic or recurrent Endometrial Cancer

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20492

Source
NTR

Brief title
DOMEC

Health condition

Advanced (recurrent, refractory or metastatic) Endometrial cancer or carcinosarcoma of the uterus

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: Sponsor LUMC, partial funding by LUMC and co-founding by AstraZeneca

Intervention

Outcome measures

Primary outcome

Progression free survival

Secondary outcome

• Objective response rate (ORR) according to RECIST 1.1 criteria
• Overall survival (OS)
• Adverse events assessed by NCI Common Terminology Criteria for adverse Events (CTCAE) version 5.0
• Predictive biomarkers

Optional endpoints:
• Baseline functional homologous recombination deficiency-assay
• Immunological effects of PARP-1 inhibition measured by tests for T cell and APC functionality and predictive biomarkers for PD-L1 blocking in blood

Study description

Background summary

The DOMEC trial is designed as a DGOG, prospective, multi-center, phase II study for 55 patients with advanced (recurrent, refractory or metastatic) endometrial cancer, including carcinosarcoma of the uterus. Patients must have had one prior platinum-based chemotherapeutic regimen or not be able/willing to get chemotherapy. The aim is to investigate the efficacy of the combination therapy of olaparib tablets 300mg twice daily and durvalumab 1500mg i.v. every 4 weeks in terms of progression free survival. Secondary objectives are to investigate objective response rate, overall survival, safety and predictive biomarkers.

Study objective

The combination of PARP and PD-L1 inhibition has a synergistic effect and will result in progression free survival improvement.

Study design

Baseline assessment exists of medical history including toxicity assessment, blood chemistry, hematological screening, dipstick urinalysis, a pregnancy test (in women of child-bearing potential), ECG, imaging (e.g. CT thorax/abdomen or MRI) and complete physical examination (incl. height, weight, WHO performance status and vital signs). Optionally, extra tumor biopsy will be performed for RAD51 testing (only at baseline) and at baseline, 6 and 12 weeks extra bloodsamples for immunomonitoring (50cc). Every 4 weeks during and at the end of therapy physical examination, blood chemistry and hematology will be performed by the subject’s own oncologist. Imaging will be repeated every three months. Every three months after last dose WHO, hematology and chemistry and tumor assessment will be reported.

Intervention

olaparib tablets 300mg twice daily orally and durvalumab 1500mg by IV infusion every 4

weeks

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Eligibility criteria

Inclusion criteria

To be included into the DOMEC-trial, patients must be (1) at least 18 years old, (2) have a WHO performance score of 0-1, (3) weight more than 30kg and (4) have histologically confirmed diagnosis of EC or carcinosarcoma of the uterus. There must be (5) a documented progressive disease (metastatic or locally advanced) according to RECIST 1.1 criteria. (6) Disease must be not amendable to local therapy, chemotherapy and hormonal therapy (or patient is not able/willing to get chemotherapy). (7) Organ system function should be adequate, defined as adequate bone marrow function (Haemoglobin ≥ 10.0 g/dL, Absolute neutrophil count (ANC) ≥ 1.5 x 10^9 /L, Platelet count ≥ 100 x 10^9 /L), liver function (Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN), Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) ≤ 2.5 x ULN (in case of lever metastases ≤ 5x ULN) and kidney function (creatinine clearance ≥51 mL/min calculated according to Cockcroft-Gault or 24 hour urine clearance). (8) Life expectancy must be at least 16 weeks.

Exclusion criteria

Patients with (1) history of leptomeningeal carcinomatosis, symptomatic brain metastases (uncontrolled despite of corticosteroids) or spinal cord compression are not eligible. Other exclusion criteria are (2) severe concomitant diseases; (3) active or prior documented autoimmune or inflammatory disorders; (4) active primary immunodeficiency; (5) active infections including tuberculosis, HIV, hepatitis B or C or (6) other malignant disease (except adequately treated non-melanoma skin cancer, lentigo maligna or carcinoma in situ without

evidence of disease). (7) Prior treatment with PARP, PD1 or PD-L1 inhibitor; (8) QTc interval or family history of long QT syndrome; (9) severe psychiatric illness; (10) irreversible grade ≥2 toxicity from previous anti-cancer therapy; (11) major surgery in the last 2 weeks; (12) prior allogeneic bone marrow transplantation or double umbilical cord blood transplantation; (13) inability to swallow oral medication; (14) concurrent treatment with another investigational agent during the conduct of the trial or (15) expected or known intolerance to olaparib or durvalumab will prohibit inclusion; as well as (16) pregnancy or breast feeding.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2019
Enrollment:	55
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	07-03-2019
Application type:	First submission

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
NTR-new	NL7569
Other	METC LUMC : P19.019

Study results