A phase 1b, dose finding, open label study of the safety and tolerability of carboplatin-cyclophosphamide combined with atezolizumab, an antibody that targets programmed death ligand 1 (PD-L1), in patients with advanced breast cancer, ovarian, cervical and endometrial cancer.

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To determine a safe dose combination of carboplatin-cyclophosphamide combined with atezolizumab fixed dose in advanced breast cancer and gynaecologic cancer (ovarian, cervical and endometrial cancer).

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45572

Source
ToetsingOnline

Brief title
PROLOG study

Condition

- Other condition
- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, gynaecological cancer

Health condition

gynaecologische neoplasmata

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Hoffmann-La Roche,Roche

Intervention

Keyword: advanced, breast cancer, gynaecological cancer

Outcome measures

Primary outcome

• To determine a safe dose combination of carboplatin-cyclophosphamide combined with atezolizumab fixed dose in patients with advanced breast cancer and gynecologic cancer (ovarian, cervical and endometrial cancer).

Secondary outcome

• To evaluate the tolerability of carboplatin-cyclophosphamide in combination with atezolizumab;

• To assess preliminary antitumor activity of carboplatin-cyclophosphamide combined with atezolizumab in advanced breast cancer, ovarian, cervical and endometrial cancer.

Study description

Background summary

The Dutch Triple B study is a phase IIB study in advanced TNBC where we test the hypothesis that patients with BRCA-like tumors will benefit from a platinum-alkylating drug combination as first line treatment while patients with non-BRCA like tumors will benefit from a taxane. Besides that, we evaluate whether addition of bevacizumab to either drug schedule can further improve outcome and whether plasma VEGFR-2 levels can predict for benefit of bevacizumab. Because one of the co-primary endpoints of the Triple B study in the meanwhile has been answered by outcomes of the Meridian trial, namely that VEGFR-2 fails as a reliable biomarker for bevacizumab benefit, and because atezolizumab shows promising activity in this particular patient group, we want to replace bevacizumab by atezolizumab in this study.

Study objective

To determine a safe dose combination of carboplatin-cyclophosphamide combined with atezolizumab fixed dose in advanced breast cancer and gynaecologic cancer (ovarian, cervical and endometrial cancer).

Study design

This is a single centre, 3+3, dose finding, open label, phase 1b clinical study of carboplatin and cyclophosphamide, in combination with atezolizumab. The starting dose is carboplatin AUC 5mg/ml*min, cyclophosphamide 600mg/m2 and atezolizumab 840 mg, all administered intravenously (see table 1). One cycle is 28 days. On day 1 carboplatin, cyclophosphamide and atezolizumab will be administered. On day 15 atezolizumab only will be administered. After 6 cycles treatment can be continued with atezolizumab monotherapy, every three weeks as long as the patient experiences clinical benefit in the opinion of the investigator.
Patients will be treated until loss of clinical benefit, unacceptable toxicities, or withdrawal of consent. It is expected that 6-12 patients will be enrolled, depending on safety issues observed.

Intervention

carboplatin AUC 5mg/ml*min, cyclophosphamide 600mg/m2 and atezolizumab 840 mg, all administered intravenously.
One cycle is 28 days.
On day 1 carboplatin, cyclophosphamide and atezolizumab will be administered.
On day 15 atezolizumab only will be administered.
After stop combination therapy patients can continue treatment with atezolizumab monotherapy, 1200 mg flat dose, every three weeks as long as the patient experiences clinical benefit in the opinion of the investigator

Study burden and risks

Patients are at risk for development of carboplatin-, cyclophosphamide-,atezolizumab-related side effects.

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

1.Histological or cytological proof of advanced breast cancer (M1) or gynaecological (cervix (M1, FIGO IVA/IVB), ovarian (after recurrence on carboplatin and/or paclitaxel) or endometrial (T3-T4, FIGO IVA/IVB) cancer) cancer pre-treated with maximally one line of systemic chemotherapy in the advanced setting and any line of hormonal therapy for advanced disease and potentially benefitting from carboplatin-cyclophosphamide and atezolizumab. (prior (neo-) adjuvant chemotherapy is accepted and does not count as one line, since administered in early stage disease);
2. Maximally one line of platinum containing pre-treatment is allowed in either adjuvant or

metastatic setting
3. Men and women >=18 years;
4. Able and willing to give written informed consent;
5. WHO performance status of 0 or 1;
6. Life expectancy >= 3 months, allowing adequate follow up of toxicity evaluation and antitumor activity;
7. Minimal acceptable safety laboratory values

Exclusion criteria

1. Any treatment with investigational drugs within 28 days prior to receiving the first dose of investigational treatment; or 21 days for standard (neo-)adjuvant chemotherapy, hormonal and immunotherapy;
2. Known clinically significant liver disease, including active viral, alcoholic, or other hepatitis, cirrhosis, fatty liver, and inherited liver disease;
3. Known hypersensitivity to Chinese hamster ovary cell products or other recombinant human antibodies.
4. Women who have a positive pregnancy test (urine/serum) and/or who ware breast feeding;
5. Unreliable contraceptive methods

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2017
Enrollment:	12
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:	Endoxan
Generic name:	cyclophophamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MPDL3280A
Generic name:	Atezolizumab

Ethics review

Approved WMO Date:	11-10-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	20-12-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-02-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2017

Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2016-003117-10-NL
ClinicalTrials.gov	NCT02914470
CCMO	NL58580.031.16