A Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of MORAb-003 (farletuzumab) in Combination with Paclitaxel Therapy in Subjects with Platinum-Resistant or Refractory Relapsed Ovarian Cancer

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To compare the effect of paclitaxel plus MORAb-003 to paclitaxel plus placebo on progression free survival (PFS) as determined by RECIST in subjects who are in a first platinum-resistant or refractory relapse of ovarian cancer.

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

Summary

ID

NL-OMON35492

Source
ToetsingOnline

Brief title
Farletuzumab in Subjects with Ovarian Cancer

Condition

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

Synonym
ovarian cancer

Research involving
Human

Sponsors and support

Primary sponsor: Morphotek Inc
Source(s) of monetary or material Support: Sponsor Morphotek

Intervention

Keyword: Farletuzumab, Ovarian Cancer, paclitaxel, Phase II study

Outcome measures

Primary outcome

radiologic PFS based on Response Evaluation Criteria in Solid Tumors (RECIST)

Secondary outcome

- Overall survival

- PFS based on GCIG criteria

- Overall response rate (based on RECIST)

- Serologic Response (based on Rustin criteria)

Safety endpoints:

• Adverse events (including drug hypersensitivity reactions)

• Clinical laboratory tests (serum chemistry,hematology, urinalysis)

• Tolerability (discontinuations, treatment delays, dose reductions)

• Physical examinations (including vital signs assessment)

• Standard ECG assessments

Standard adverse event (AE) monitoring and grading will be assessed using

National Cancer Institute Common Terminology Criteria for Adverse Events (NCI

CTCAE) Version 3.0, and coded using Medical Dictionary for Regulatory

Activities (MedDRA).

Study description

Background summary

Ovarian cancer is the leading cause of death among women with gynecologic malignancies. According to the American Cancer Society ovarian cancer accounted for an estimated 15,280 deaths in 2007 since the initial presentation is often at advanced stages.1 The prevalence and incidence in Europe and South America are similar. The average lifetime risk for the development of ovarian cancer in women in the United States is 1 in 70. Epithelial ovarian cancers account for nearly 90% of all ovarian malignancies. The standard therapy for advanced ovarian cancer, following maximal cytoreductive surgery, is platinum-based chemotherapy. In women treated with platinum-containing combinations as primary therapy, the response rates are 60% to 80%, with complete response being most common in women who have had adequate surgical therapy. Unfortunately, despite this, the majority of patients eventually die of disease persistence or recurrence, with the abdominal cavity being the most common site of recurrence. Long-term survival remains approximately 15% to 30%.
One of the more promising recent developments was the demonstration that single agent paclitaxel administered weekly can offer an overall response rate of about 21%, with a median duration of remission of 3 months, even though the patient was likely to have been receiving a taxane previously.3 MORAb-003 (farletuzumab) has the potential to be an effective agent against epithelial ovarian cancer, either alone or in combination with other drugs, including taxane .4 MORAb-003 works by a different mechanism from other cancer therapeutics and has been shown to be well tolerated. This study is designed to determine if MORAb-003 in combination with taxane chemotherapy can elicit and prolong a second response in the setting of relapsed platinum-resistant or refractory subjects.

Study objective

To compare the effect of paclitaxel plus MORAb-003 to paclitaxel plus placebo on progression free survival (PFS) as determined by RECIST in subjects who are in a first platinum-resistant or refractory relapse of ovarian cancer.

Study design

This is a multicenter, randomized, double-blind, placebo-controlled, proof-of-concept study. Subjects are randomized in a 2:1 ratio to receive weekly paclitaxel plus MORAb-003 or weekly paclitaxel plus placebo. Stratification factors are 1) intraperitoneal (IP) or intravenous (IV) primary

chemotherapy; 2) geographic regions (North America, Europe and Other Participating Countries). During the treatment period, subjects will be treated with weekly paclitaxel plus MORAb-003 or weekly paclitaxel plus placebo until disease progression, defined by RECIST criteria.
During the follow-up period survival status and additional therapy for ovarian cancer will be captured. Subjects will be contacted monthly for the first 9 months and then every 2 months until death or study termination by Sponsor.

Intervention

MORAb-003 is a humanized IgG1/* monoclonal antibody that binds to the human folate alpha receptor. MORAb-003 is 99.15% humanized. MORAb-003 will be delivered in vials. MORAb-003 (in 0.9% normal saline) will be administered IV at a dose of 2.5 mg/kg, which will be given during cycle 1, cycle 2 and subsequent cycles.

Study burden and risks

Subjects will be randomized to receive paclitaxel plus MORAb-003 or paclitaxel plus placebo in a 2:1 ratio. Paclitaxel 80mg/m2 will be administered intravenously over 1 hour. Body surface area (BSA) will be calculated according to a standard formula in use at the clinical site. BSA should not be rechecked after baseline, unless there is a weight change of at least 10%. MORAb-003 (in 0.9% normal saline) will be administered IV at a dose of 2.5 mg/kg. Placebo will consist of an equivalent volume of normal saline. During Cycle 1 test article (MORAb-003 or placebo) and paclitaxel administration will be weekly on day 1 for 12 weeks. For all subsequent cycles test article (MORAb-003 or placebo) and paclitaxel will be administered in 4-week cycles. Test article (MORAb-003 or placebo) and paclitaxel will be administered on Day 1 of Weeks 1 - 3, and Week 4 will be a rest period. Test article (MORAb-003 or placebo) will be administered prior to paclitaxel.

Please refer to question E4 and flowchart on page 76 of the study protocol for all study procedures.

Please refer to question E9 and the study informed consent for all possible risk and adverse events.

Contacts

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Scientific
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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. Female subjects >=18 years of age.
2. Subjects of childbearing potential must be surgically sterile or consent to use a medically acceptable method of contraception throughout the study period. Contraceptive measures must start either prior to or at screening and continue
throughout the entire study period and for 2 months after the last dose of study drug is administered. Pregnant and/or lactating females are excluded.
3. A diagnosis of non-mucinous epithelial ovarian cancer (EOC), including primary peritoneal and fallopian tube malignancies. Must have measurable disease by CT or MRI scan, assessed within 4 weeks prior to study entry.
4. Must have been treated with surgery for ovarian cancer and received at least one line of platinumbased chemotherapy.
5. At least one of the lines of platinum containing chemotherapy must have included a taxane.
6. Must have relapsed during or within 6 months of platinum-containing chemotherapy.
7. Subjects may have received up to four additional lines of chemotherapy after they developed platinum-resistance.
8. Subjects must be a candidate for repeat weekly paclitaxel.
9. Life expectancy of >=3 months as estimated by the investigator.

10. Other significant medical conditions must be wellcontrolled and stable in the opinion of the investigator for at least 30 days prior to Study Day 1.
11. Karnofsky Performance Status (KPS) > 70%.
12. Subjects must not be receiving total parenteral nutrition (TPN)
13. Laboratory test results within the 30 days prior to Study Day 1 as follows:
ANC count > 1.5x109/L
Platelet count > 100x9/L
Hemoglobin > 8g/dL
Creatinine <1.5xULN (CTCAE grade 1)
Bilirubin < 1.5XULN (CTCAE grade 1)
Asparatate aminotransferase (AST), Alanine Aminotransferase (ALT) and Alkaline Phosphatase <2.5xULN (CTCAE grade 1)
14. Subject must be willing to comply with the protocol and be able to provide written informed consent.

Exclusion criteria

1. Known central nervous system (CNS) tumor involvement.
2. Clinical contraindications to use of paclitaxel
3. Evidence of active invasive malignancy other than ovarian cancer requiring treatment in the past 5 years.
4. Current diagnosis of epithelial ovarian tumor of low malignant potential (borderline carcinomas). Note: EOC with prior diagnosis of a low malignant potential tumor that has been surgically resected is acceptable provided the subject did not receive prior chemotherapy for any ovarian tumor.
5. Clinically significant heart disease (e.g., congestive heart failure of New York Heart Association Class 3 or 4 angina not well controlled by medication, or myocardial infarction within 6 months).
6. ECG demonstrating clinically significant arrhythmias. Note: Subjects with chronic atrial arrhythmia, i.e., atrial fibrillation or paroxysmal supraventricular tachycardia [SVT], are eligible.
7. Active serious systemic disease, including active bacterial or fungal infection.
8. Active viral hepatitis or symptomatic human immunodeficiency virus (HIV) infection. Asymptomatic positive serology is not exclusionary.
9. Breast-feeding, pregnant, or likely to become pregnant during the study.
10. Prior radiation therapy is excluded with the exception that it is allowable only if measurable disease for ovarian cancer is completely outside the radiation portal.
11. Other concurrent immunotherapy (e.g., immunosuppressants or chronic use of systemic corticosteroids with the exception that low-dose corticosteroids).
12. Known allergic reaction to a prior monoclonal antibody therapy or have any documented human anti-human antibody (HAHA).
13. Previous treatment with MORAb-003 (farletuzumab).
14. Prior treatment with any investigational agent within 4 weeks of study entry.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-09-2010
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	farletuzumab
Generic name:	farletuzumab
Product type:	Medicine
Brand name:	paclitaxel
Generic name:	paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	13-07-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	29-10-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-11-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-04-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-05-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-08-2011
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	EUCTR2008-005449-43-NL

Register	ID
CCMO	NL25040.041.09