A two-part, randomized Phase II, double-blind, multicenter trial assessing the efficacy and safety of pertuzumab in combination with standard chemotherapy vs. placebo plus standard chemotherapy in women with recurrent platinum resistant epithelial ovarian cancer and low HER3 mRNA expression

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PRIMARY OBJECTIVEPart 1: Safety Run-in PhaseThe primary objective for Part 1 of this study is to determine the safety and tolerability of pertuzumab in combination with either topotecan or paclitaxel.Part 2The primary objective for Part 2 of this...

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

Summary

ID

NL-OMON36976

Source
ToetsingOnline

Brief title
PENELOPE

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
ovarian cancer, ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Roche BV

Intervention

Keyword: double blind, Ovarium carcinoma, Pertuzumab plus chemotherapy, Recurrent Platinum Resistant

Outcome measures

Primary outcome

The primary objective for Part 1 of this study is to determine the safety and

tolerability of pertuzumab in combination with either topotecan or paclitaxel.

Part 2

The primary objective for Part 2 of this study is to determine if pertuzumab

plus chemotherapy is superior to placebo plus chemotherapy as measured by PFS.

Secondary outcome

Part 1: Safety Run-in Phase

The secondary objective for Part 1 of this study is to evaluate descriptively

the PFS of pertuzumab in combination with either topotecan or paclitaxel.

Results will be only descriptive.

Part 2

The secondary objectives for Part 2 of this study are to determine if

pertuzumab plus chemotherapy is superior to placebo plus chemotherapy

Study description

Background summary

There is currently no cure for recurrent ovarian cancer, with the outlook particularly poor for platinum-resistant ovarian cancer. Pertuzumab represents a promising new anti-HER2 agent with a novel mechanism of action targeting inhibition of HER2 dimerization. The results of previous clinical trials indicate that pertuzumab has clinical activity in patients with ovarian cancer, particularly in certain subsets of patients, and that pertuzumab may have superior anti-tumor effects when combined with other anticancer treatments such as gemcitabine, particularly in the subset of patients with evidence of HER2-3 signaling, as demonstrated by low HER3 mRNA expression (Amler et al. 2008). Pertuzumab in combination with other chemotherapy agents such as topotecan and paclitaxel may also offer additional benefits over monotherapy.
Paclitaxel or topotecan have been selected as chemotherapeutic combination partners since they are commonly used for treatment of platinum-resistant disease.

Study objective

PRIMARY OBJECTIVE
Part 1: Safety Run-in Phase
The primary objective for Part 1 of this study is to determine the safety and tolerability of pertuzumab in combination with either topotecan or paclitaxel.
Part 2
The primary objective for Part 2 of this study is to determine if pertuzumab plus chemotherapy is superior to placebo plus chemotherapy as measured by PFS.

SECONDARY OBJECTIVES
Part 1: Safety Run-in Phase
The secondary objective for Part 1 of this study is to evaluate descriptively the PFS of pertuzumab in combination with either topotecan or paclitaxel. Results will be only descriptive.
Part 2
The secondary objectives for Part 2 of this study are to determine if pertuzumab plus chemotherapy is superior to placebo plus chemotherapy with respect to:
* OS.
* Objective response rate.
* Biological progression-free interval (PFIBIO).
* Safety and tolerability.

* QoL.

Study design

This is a multicenter trial with two parts; a non-randomized safety run-in Part 1 and a randomized, double-blind Part 2.
Part 1 will be performed to assess safety and tolerability of pertuzumab in a new combination with two chemotherapeutic agents (topotecan or paclitaxel).
Part 2 of the trial is a randomized, double-blind, placebo controlled, two-arm, multicenter, prospective trial of pertuzumab in combination with chemotherapy (topotecan, paclitaxel, or gemcitabine).
A total of approximately 184 patients will be entered into either Part 1 or 2 of the study. Details of the study treatments are given in Section 4.3 of the protocol

Intervention

The patient will receive aditional to the standard treatment a 3 weekly infusion with pertuzumab or placebo. The LEVF will be measured 9 weekly with eiter an ECHO or MUGA. The subject will be asked to complete 4 QoL questionaires on a 9 weekly basis. After the patient has ended the study treatment a 3monthly follow-up visit will be performed.

Study burden and risks

Most assessments are "standard of care" when chemotherapy is given. Study specific assessments are ICF, MUGA, infusion with pertuzummab or placebo, QoL questionaires, 3 monthly follow-up

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. Signed written informed consent approved by the relevant IEC/IRB.;2. Female patients aged 18 years or older.;3. Low HER3 mRNA expression levels (concentration ratio equal or lower than 2.81, as assessed by qRT-PCR on a cobas z480 instrument).;4. Histologically or cytologically confirmed and documented epithelial ovarian cancer that is platinum-resistant or refractory (defined as progression within 6 months from completion of a minimum of 4 platinum therapy cycles or progression during platinum therapy).;5. At least one measurable lesion and/or non measurable disease according to RECIST version 1.1, or cancer antigen-125 (CA-125) assessable disease according to Gynecologic Center Intergroup (GCIG) criteria. The following histological types are eligible:;* Adenocarcinoma not otherwise specified. ;* Clear cell adenocarcinoma. ;* Endometrioid adenocarcinoma. ;* Malignant Brenner's tumor.;* Mixed epithelial carcinoma including malignant mixed Müllerian tumors.;* Mucinous adenocarcinoma. ;* Serous adenocarcinoma. ;* Transitional cell carcinoma. ;* Undifferentiated carcinoma.;6. Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2. ;7. LVEF greater than or equal to 55%.;8. Negative serum pregnancy test in women of childbearing potential (WOCBP; premenopausal or less than 12 months of amenorrhea post-menopause, and who have not undergone surgical sterilization).;9. For WOCBP who are sexually active, agreement to use a highly effective, non hormonal form of contraception or two effective forms of non hormonal contraception during and for at least 6 months post trial treatment (a highly effective non-hormonal form of contraception, such as surgical sterilization, or two effective non-hormonal forms of contraception, such as a barrier method of contraception in conjunction with spermicidal jelly).

Exclusion criteria

1. Non-epithelial tumors. ;2. Ovarian tumors with low malignant potential (i.e. borderline tumors). ;3. History of other malignancy within the last 5 years, except for carcinoma in situ of the cervix or basal cell carcinoma, except for tumors with a negligible risk for metastasis or

death, such as adequately controlled basal-cell carcinoma or squamous-cell carcinoma of the skin or carcinoma in situ of the cervix or breast.;4. Serious uncontrolled concomitant disease that would contraindicate the use of any of the investigational drugs used in this study or that would put the patient at high risk for treatment-related complications.;5. Previous treatment with more than 2 chemotherapy regimens, . If a patient has previously been treated with topotecan, paclitaxel, or gemcitabine as second-line therapy, the patient will not be retreated with the same agent.;6. Any prior radiotherapy to the pelvis or abdomen.;7. History or evidence on physical/neurological examination of central nervous system disease unrelated to cancer, unless adequately treated with standard medical therapy (e.g. uncontrolled seizures). ;8. Pre-exisiting peripheral neuropathy * CTC grade 2.;9. Inadequate organ function, evidenced by the following laboratory results:;* Absolute neutrophil count <1,500 cells/mm3.;* Platelet count <100,000 cells/mm3.;* Hemoglobin <9 g/dL.;* Total bilirubin greater than 1.5 ×upper limit of normal (ULN) (unless the patient has documented Gilbert*s syndrome).;* Serum alkaline phosphatase, aspartate aminotransferase (AST; SGOT) or alanine aminotransferase (ALT; SGPT) >2.5 × ULN (or > 5 × ULN in the presence of liver metastases);* Serum creatinine >2.0 mg/dL or >177 *mol/L.;* International normalized ratio (INR) and activated partial thromboplastin time (aPTT) or partial thromboplastin time (PTT) >1.5 × ULN (unless on therapeutic anti-coagulation).;10. Uncontrolled hypertension (systolic >150 mm Hg and/or diastolic >100 mm Hg) or clinically significant (i.e. active) cardiovascular disease: cerebrovascular accident (CVA)/stroke or myocardial infarction within 6 months prior to first study medication, unstable angina, congestive heart failure (CHF) of New York Heart Association (NYHA) Grade II or higher, or serious cardiac arrhythmia requiring medication.;11. Current known infection with HIV, HBV, or HCV.;12. Dyspnea at rest due to complications of advanced malignancy, or other disease requiring continuous oxygen therapy.;13. Major surgical procedure or significant traumatic injury within 28 days prior to first study drug administration or anticipation of need for major surgery during the course of study treatment.;14. Receipt of intravenous antibiotics for infection within 14 days prior to first study drug administration.;15. Current chronic daily treatment with corticosteroids (dose equivalent to or greater than 10 mg/day methylprednisolone), excluding inhaled steroids.;16. Known hypersensitivity to any of the trial drugs or excipients.;17. History of receiving any investigational treatment within 28 days prior to first study drug administration, including prior enrollment into Part 1 of the trial. ;18. Concurrent participation in any clinical trial.;19. Assessed by the investigator to be unable or unwilling to comply with the requirements of the protocol.

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):	09-04-2013
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Perjeta
Generic name:	pertuzumab

Ethics review

Approved WMO Date:	17-01-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-02-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	Alle Roche studies worden, zodra er patiënten inzitten, publiek gemaakt op www.rochetrials.com. Via het protocolnummer kan de studie worden gevonden. Het EUDRACT nummer is: 2011-005975-17
EudraCT	EUCTR2011-005975-17-NL
CCMO	NL42341.091.12