A phase Ib study of combination of temsirolimus (ToriselÂ®) and pegylated liposomal doxorubicin (PLD, DoxilÂ®/ CaelyxÂ®) in advanced or recurrent breast, endometrial and ovarian cancer

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

Summary

ID

NL-OMON33331

Source
ToetsingOnline

Brief title
Temsirolimus-PLD

Condition

- Other condition
- Plasma cell neoplasms

Synonym
breast cancer, endometrial cancer, ovarian cancer

Health condition

advanced or recurrent breastcancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,Schering

Intervention

Keyword: Phase I, PLD, Temsirolimus

Outcome measures

Primary outcome

MTD, pharamcokinetic parameters

Secondary outcome

Effectiveness: objective response rate, time to progression

FDG-PET: kwalitative and kwantitative (SUV)

CTC and CEC: numbers

Study description

Background summary

A phase Ib study of combination of temsirolimus (mTOR inhibitor) and PLD (chemotherapeutic) in advanced or recurrent breast, endometrial and ovarian cancer

Study objective

The primary objective of this Phase 1b study is to identify the maximum tolerated dose (MTD) and recommended phase II dose of the combination of temsirolimus and Caelyx® in patients with advanced or therapy refractory breast cancer, endometrial cancer, or ovarian cancer.
The secondary objectives are:
1.To assess the safety and toxicity profile.
2.To assess the pharmacokinetic profile of the combination of temsirolimus and PLD.

3.To assess the anti tumour activity of the combination of temsirolimus and PLD.
4.To assess the early effect on tumor metabolism by FDG-PET (baseline, after 2 and 6 weeks)
5.To assess the effects on regulatory T cells, the IGF pathway and on circulating tumour cells (CTCs) and circulating endothelial cells (CECs).

Study design

This study is an open label, single centre, dose escalation phase I trial. A dose escalating study in a 3 + 3 design will be performed. Twelve additional patients will be treated at MTD dose level. The study will require 18-30 patients, and will be performed in 1 centre.

Intervention

Treatment with temsirolimus and PLD.

Study burden and risks

Toxicity due to treatment with temsirolimus and/or PLD. Complications due to venipuncture (hematoma) or CT-scan (contrast nephropathy, allergic reaction) as well known for these techniques.

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 proven advanced breast cancer, endometrial cancer or ovarian cancer, who are refractory to standard therapies or for whom no standard therapy exists.
•Age >= 18 years
•Patients who have an ECOG status of 0 or 1
•Patients who have a life expectancy of at least 12 weeks
•Negative pregnancy test for female patients of childbearing potential
•Signed informed consent

Exclusion criteria

•Adequate bone marrow: neutrophils >= 1.5 x 109/L, platelets >= 100 x 109/L and haemoglobin >= 5.0 mmol/l
•Adequate renal function: GFR >= 60 ml/min
•Adequate liver function: ALT and AST < 2.5 x ULN, total bilirubin <= 1x ULN
•Fasting level of total cholesterol of no more than 350 mg/dL (9.1 mmol/L) and triglyceride level of no more than 400 mg/L (4.5 mmol/L)
•Left ventricular ejection fraction (LVEF) < 50%
•History of serious cardiac disease
•Active clinically serious bacterial, viral or fungal infections (> grade 2).
•Known history of human immunodeficiency virus (HIV) infection or chronic hepatitis B or C.
•Clinically symptomatic brain or meningeal metastasis. Patients with seizure disorders requiring medication (such as steroids or antiepileptics). Concomitant treatment with strong CYP3A4 inductors (such as rifampicin, St. John*s Wort) or CYP3A4 inhibitors (such as ketoconazole, voriconazole, itraconazole, diltiazem, verapamil, erythromycin) within 2 weeks prior to start.
•Moderate or weak CYP3A4 modifiers should be used concomitantly only after careful assessment of risk-benefit ratio. Concomitant use of carbamazepine, phenobarbital, phenytoin or chronic use of dexamethasone is not allowed. (Table 1)
•Other concomitant anti-cancer therapy (except steroids)
•Concomitant use of streptozocin, mercaptopurine.
•Previous treatment with one of the study drugs.

•Previous treatment with other mTOR inhibitors
•Prior investigational therapy/agents within 4 weeks of start, in case of bevacizumab at least 60 days between bevacizumab discontinuation and first dosing of temsirolimus.
•Surgical treatment or radiation therapy in the past 4 weeks. Palliative radiotherapy at focal sites on the extremities is allowed, also within 4 weeks before start
•Unresolved toxicity CTC >= grade 2 from previous anti-cancer therapy except alopecia.
•Known or suspected allergy to any investigational agent or any agent given in association with this trial.
•Substance abuse, medical, psychological or social conditions that may interfere with the patients participation in the study or evaluation of the study results
•Any condition that is unstable or which could jeopardize the safety of patient and his compliance in the study.
•Antracyclines: > 450 mg/m2 doxorubicin or and > 600 mg/m2 epirubicin
•Medications known to have dysrhythmic potential is not permitted (ie, terfenadine, quinidine, procainamide, disopyramide, sotalol, probucol, bepridil, haloperidol, risperidone, indapamide)
•Usage of coumarin-derivate anticoagulants. Low molecular weight heparin is permitted and advised.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-06-2009
Enrollment:	30
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine

Brand name:	Caelyx
Generic name:	Doxorubicin hydrochloride
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Torisel
Generic name:	temsirolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-03-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-05-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2011
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
EudraCT	EUCTR2009-010290-21-NL
CCMO	NL27117.091.09