Early identification of patients who benefit from palbociclib in addition to letrozole

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To evaluate in a feasibility study whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON46198

Source
ToetsingOnline

Brief title
Palbociclib and FES PET

Condition

- Metastases

Synonym
Metastatic breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Pfizer,Pfizer Oncology

Intervention

Keyword: FES PET, Palbociclib

Outcome measures

Primary outcome

The relation between low uptake on FES-PET to response per lesion, as measured by RECIST 1.1 criteria in case of measurable disease (1). In case of non-measurable bone lesions, progression is defined as an increase in SUV on FDG-PET per lesion compared to baseline.

It is hypothesized that lesions with a low uptake on FES-PET will not respond to letrozole plus palbociclib. When in at least 85% of the lesions with no response on treatment, also a low uptake (tumor SUV of <1.5) on baseline FES-PET is observed, we consider that FES-PET can be evaluated in further, larger studies as a potential predictive biomarker.

Secondary outcome

Descriptive analysis of quantitative FES-uptake and correlation with progression free survival.

Descriptive analysis of circulating tumor DNA and correlation with FES-PET results and progression free survival.

Predictive value of change in FDG uptake per lesion (baseline compared to 2 week scan) for response after 8 weeks (measured by CT or FDG PET in case of bone lesions).

Per patient analysis of response on CT related to change on FDG PET (baseline-2 weeks) and FES uptake at baseline

Study description

Background summary

As ER expression predicts response to palbociclib in metastatic breast cancer patients we hypothesize that lesions with low uptake on FES-PET will not respond to the combination of letrozole plus palbociclib. Furthermore as toxicity to treatment is seen within 2 weeks after initiating treatment we also hypothesize that an early metabolic response, measured as change in FDG uptake after 2 weeks treatment compared to baseline, can predict 8 week CT response to palbociclib in combination with letrozole.
The purpose is to evaluate whether non invasive in vivo imaging of ER presence in metastatic breast cancer patient by means of FES-PET, as well an early metabolic response on FDG PET, can be related to treatment response to palbociclib plus letrozole.

We hypothesize that this study will lead to a prospective independent biomarker for patient selection in future studies. Optimal selection of patients is of great relevance in view of avoiding unnecessary toxicities and financial burden.

Study objective

To evaluate in a feasibility study whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment.

Study design

We will perform this single center, feasibility study in 30 patients with ER positive metastatic breast cancer, eligible for letrozole and palbociclib therapy. This study will be executed in the University Medical Center Groningen, the Netherlands. All patients will be treated with letrozole 2.5mg daily continuously throughout a 28-day cycle. This is combined with palbociclib 125 mg daily for 21 consecutive days followed by 7 days off treatment. The primary objective of the study is to evaluate whether low uptake on FES-PET at baseline can predict non-response to letrozole plus palbociclib treatment per metastatic lesion. A FES-PET will be performed at baseline, and a FDG-PET will be performed to evaluate response at 2 weeks. AFter 8 weeks response evaluations will be performed with an CT scan and in case of bone metastases an FDG PET will be added. Patients will be treated with combination therapy until progression or unacceptable toxicity is encountered.

Intervention

1 FES PET
1 FDG PET
palbociclib

Study burden and risks

Currently the combination with palbociclib and letrozole has been approved by the FDA and EMA as initial endocrine-based therapy for postmenopausal women with ER positive HER2 negative advanced breast cancer. This is based on improved progression free survival with 10 months compared to endocrine therapy alone in both first and second line hormonal treatment for ER-positive metastatic breast cancer. Therefore, in this study, all patients will receive a effective treatment combination, that they do not have standard access to in the Netherlands yet. In addition to the standard control visits to the clinic, three extra visits will be performed as part of the study: for screening and for the FES-PET scan and early FDG PET scan after 2 weeks. The PET scan will induce an extra radiation burden of 11.1 mSv. In the future, this study may potentially contribute to improved selection of patients for this combination treatment. This is of relevance in view of optimal treatment for individual patients, avoiding unnecessary toxicity and financial burden.

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. Patients with ER positive (i.e. >1% staining), HER2 negative metastatic breast cancer
2. Post-menopausal status
3. Adequate bone marrow and organ function
4. ECOG performance 0-2
5. Signed written informed consent
6. Able to comply with the protocol
7. Age >=18 years

Exclusion criteria

1. Life expectancy < 3 months
2. Evidence of central nervous system metastases
3. Presence of life-threatening visceral metastases
4. Prior use of CDK4/6 inhibitor
5. Use of estrogen receptor ligands including estrogens, fulvestrant or tamoxifen <6 weeks before study entry.
6. Use of other anticancer therapy < 2 weeks prior to start with palbociclib
7. Concurrent malignancy
8. Active cardiac disease or a history of cardiac dysfunction

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2016
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	18F-FDG
Generic name:	18F-FDG
Product type:	Medicine
Brand name:	18F-FES
Generic name:	18F-FES
Product type:	Medicine
Brand name:	palbociclib
Generic name:	palbociclib

Ethics review

Approved WMO Date:	29-03-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-08-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-07-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-07-2017

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTRNL2015004231-1-NL
CCMO	NL56265.042.16