A randomized double-blind, placebo-controlled study of LEE011 in combination with letrozole for the treatment of postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who received no prior therapy for advanced disease (CLEE011A2301)

Published: 07-01-2014
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Primary objective: Progression free survival (PFS) of treatment with letrozole plus LEE011 compared to treatment with letrozole plus placebo .Secondary objectives: Overall survival (OS), overall response rate (OR), overall clinical benefit rate,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON55670

Source
ToetsingOnline

Brief title
CLEE011A2301 - MONALEESA-2

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
advanced breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: advanced, breast cancer, LEE011, letrozole

Outcome measures

Primary outcome

Progression free survival.

Secondary outcome

Overall survival, response, clinical benefit, ECOG performance status,

side-effects, result quality of life questinnaires.

Study description

Background summary

The purpose of this study is to characterize the anti-proliferative activity of LEE011 600 mg when combined with letrozole 2.5 mg in postmenopausal women with advanced HR+, HER2-negative breast cancer.
Hormone dependence is a fundamental hallmark of the majority of breast cancers, and tumor growth can be inhibited either by deprivation of circulating estrogens or by antagonising the effect of these hormones on their receptors. For postmenopausal women with breast cancer, aromatase inhibitors are an important treatment option. Letrozole is an aromatase inhibitor. In breast cancer, genetic alterations such as amplifications and deletions occur at high frequencies, and are closely related to poor clinical outcome. One such region of amplification is with Cyclin D1, which plays a crucial role as a cell cycle regulator, promoting progression through the G1-S phase, following complex formation with CDK4/6 and phosphorylation of the retinoblastoma (rb) protein.

LEE011 is a highly soluble, potent, selective inhibitor of CDK4/6 kinases. LEE011 inhibits CDK4/6 specific phosphorylation of pRb, thereby halting cell cycle progression in the G1 phase.

Study objective

Primary objective: Progression free survival (PFS) of treatment with letrozole plus LEE011 compared to treatment with letrozole plus placebo .
Secondary objectives: Overall survival (OS), overall response rate (OR), overall clinical benefit rate, time to deterioration of ECOG performance status, safety and tolerability, quality of life.

Study design

Randomized double blind placebo controlled phase III study. Approximately 650 patients.
Randomization (1:1) to treatment in cycles of 4 weeks with
• letrozole 2.5 mg QD continuously plus LEE011 600 mg QD during the 1st 3 weeks of a cycle
• letrozole 2.5 mg QD continuously plus placebo during the 1st 3 weeks of a cycle
Treatment duration until disease progression or unacceptable side-effects.
Follow-up for survival.

Intervention

Treatment with letrozole with or without LEE.

Study burden and risks

Risk: Adverse events of study medication.
Burden:
Visits cycle 1 day 1 and 15, next cycles day 1 only. Duration approx. 2-4 h.
Each visit fasting blood draw(s) 15-30 mL/occasion and collection of urine
Optional Blood draw for PK during cycle 1 day 15, pre-dose and 2 h post-dose and optional blood draw for biomarker research during screening and day 15
ECG cycle 1 day 15, cycle 2 day 1, cycel 3 day 1, cycle 6 day 1, cycle 9 day 1 and end of study pre-dose and 2 hrs post-dose. Pre dose during cycle 4 day 1, cycle 5 day 1, cycle 7 day 1 and cycle 8 day 1
MUGA-scan of echocardiogram during screening
Quality of life questionnaires (3x)(every 8-12 weeks)
Daily completion of diary
Tumor measurements (CT- or MRI-scans during the first 18 months every 8 weeks and thereafter conform standard treatment (every 12 weeks).
Optional tumor biopsy at screening and disease progression.
In case the subjects discontinues the study medication prior to disease

progression: follow-up until progression with tumor measurements every 8-12 weeks.

Contacts

Public
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Women >=18 years old, with advanced breast cancer.
• No prior therapy for advanced disease
• Postmenopausal. See protocol page 34 for details.
• Confirmed diagnosis of estrogen-receptor positive and/or progesterone receptor positive, HER2 negative breast cancer.
• Measurable disease or at least one predominantly lytic bone lesion.
• ECOG performance status 0 or 1.
• Adequate bone marrow and organ function (based on central

lab)

Exclusion criteria

• Received any CDK4/6 inhibitor.
• Any prior systemic anti-cancer therapy (including hormonal therapy and chemotherapy) for advanced breast cancer. See protocol page 45 for details.
• Known history of HIV infection (testing not mandatory).
• Patient has CNS metastases
• Active cardiac disease or a history of cardiac dysfunction. See protocol page 46 for details.
• Prohibited medication. See protocol page 36 for details.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-06-2014
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Femara
Generic name:	letrozole

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	LEE011
Generic name:	LEE011
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-01-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-04-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-06-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-07-2014
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	25-08-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-05-2015
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	19-08-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-08-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2016
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	03-08-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-02-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-03-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-10-2017
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	10-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-04-2020
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	02-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-12-2021
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	EUCTR2013-003084-61-NL
ClinicalTrials.gov	NCT01958021
CCMO	NL46891.031.13