



# Study of Efficacy and Safety of LEE011 in Postmenopausal Women With Advanced Breast Cancer.(MONALEESA-2)

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## Main Information

**Primary registry identifying number**

LBCTR2019050229

**Protocol number**

CLEE011A2301

**MOH registration number**

9695/ص

**Study registered at the country of origin**

Yes

**Study registered at the country of origin: Specify**

**Type of registration**

Retrospective

**Type of registration: Justify**

LCTR was recently initiated, original file was previously submitted by Paper

**Date of registration in national regulatory agency**

05/11/2014

**Primary sponsor**

Novartis Pharma Services Inc.

**Primary sponsor: Country of origin**

Novartis Pharmaceuticals

**Date of registration in primary registry**

14/08/2020

**Date of registration in national regulatory agency**

05/11/2014

**Public title**

Study of Efficacy and Safety of LEE011 in Postmenopausal Women With Advanced Breast Cancer.(MONALEESA-2)

**Acronym**

**Scientific title**

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

**Acronym**

**Brief summary of the study: English**

This is a multi-center, randomized, double-blinded, placebo controlled trial. The primary purpose of this study was to assess the efficacy of LEE011, as measured by progression free survival (PFS), in postmenopausal women with HR positive, HER2 negative advanced breast cancer who received no prior treatment for advanced disease.

**Brief summary of the study: Arabic**

وفعاليتها في معالجة Letrozole مع ليتروزول LEE011 دراسة عشوائية مزدوجة التعمية ومضبوطة بدواء وهمي حول سلامة استخدام الدواء والواتي لم يتلقين علاجاً سابقاً للمرض في2النساء بعد انقطاع الطمث المصابات بسرطان ثدي متقدم إيجابي مستقبلات الهرمون وسليبي الهير مراحلها المتقدمة

**Health conditions/problem studied: Specify**

Advanced Breast Cancer

**Interventions: Specify**

•Drug: LEE011  
Ribociclib was administered orally at a dose of 600 mg once daily (three 200 mg capsules).

•Drug: Letrozole



Letrozole 2.5 mg tablets taken orally.

•Drug: LEE011 Placebo

Matching ribociclib placebo was the control drug and was administered orally once daily.

**Key inclusion and exclusion criteria: Inclusion criteria**

- 1.Women with advanced (locoregionally recurrent or metastatic) breast cancer not amenable to curative therapy.
- 2.Patient is postmenopausal. Postmenopausal status is defined either by:
  - Prior bilateral oophorectomy
  - Age  $\geq 60$
  - Age  $< 60$  and amenorrhea for 12 or more months (in the absence of chemotherapy, tamoxifen, toremifen, or ovarian suppression) and FSH and estradiol in the postmenopausal range per local normal range Note: For women with therapy-induced amenorrhea, serial measurements of FSH and/or estradiol are needed to ensure postmenopausal status. Ovarian radiation or treatment with a luteinizing hormone-releasing hormone agonist (LH-RHa) (goserelin acetate or leuprolide acetate) is not permitted for induction of ovarian suppression in this trial.
- 3.No prior systemic anti-cancer therapy for advanced disease.
- 4.Patient has a histologically and/or cytologically confirmed diagnosis of estrogen-receptor positive and/or progesterone receptor positive breast cancer by local laboratory.
- 5.Patient has HER2-negative breast cancer defined as a negative in situ hybridization test or an IHC status of 0, 1+ or 2+. If IHC is 2+, a negative in situ hybridization (FISH, CISH, or SISH) test is required by local laboratory testing.
- 6.Patient must have either:
  - Measurable disease, i.e., at least one measurable lesion as per RECIST 1.1 criteria (Tumor lesions previously irradiated or subjected to other locoregional therapy will only be considered measurable if disease progression at the treated site after completion of therapy is clearly documented).

OR

- If no measurable disease is present, then at least one predominantly lytic bone lesion must be present (Patients with no measurable disease and only one predominantly lytic bone lesion that has been previously irradiated are eligible if there is documented evidence of disease progression of the bone lesion after irradiation).

7.Patient has an Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1

**Key inclusion and exclusion criteria: Gender**

Female

**Key inclusion and exclusion criteria: Specify gender**

**Key inclusion and exclusion criteria: Age minimum**

18

**Key inclusion and exclusion criteria: Age maximum**

99

**Key inclusion and exclusion criteria: Exclusion criteria**

- 1.Patient who received any CDK4/6 inhibitor.
- 2.Patient who received any prior systemic anti-cancer therapy (including hormonal therapy and chemotherapy) for advanced breast cancer

Note:

- Patients who received (neo) adjuvant therapy for breast cancer are eligible. If the prior neo (adjuvant) therapy included letrozole or anastrozole the disease free interval must be greater than 12 months from the completion of treatment until randomization.
- Patients who received  $\leq 14$  days of letrozole or anastrozole for advanced disease prior to randomization are eligible.
- Any prior (neo) adjuvant anti-cancer therapy must be stopped at least 5 half-lives or 7 days, whichever is longer, before randomization

3.Patient is concurrently using other anti-cancer therapy.

4.Patient has a concurrent malignancy or malignancy within 3 years of randomization, with the exception of adequately treated, basal or squamous cell carcinoma, non-melanomatous skin cancer or curatively resected cervical cancer.

5.Patient has active cardiac disease or a history of cardiac dysfunction including any of the following:

- History of angina pectoris, symptomatic pericarditis, or myocardial infarction within 12 months prior to study entry
- History of documented congestive heart failure (New York Heart Association functional classification III-IV)
- Documented cardiomyopathy
- Patient has a Left Ventricular Ejection Fraction (LVEF)  $< 50\%$  as determined by Multiple Gated acquisition (MUGA) scan or echocardiogram (ECHO)
- History of any cardiac arrhythmias, e.g., ventricular, supraventricular, nodal arrhythmias, or conduction abnormality in the previous 12 months.
- On screening, any of the following cardiac parameters:

bradycardia (heart rate  $< 50$  at rest), tachycardia (heart rate  $> 90$  at rest), PR interval  $> 220$  msec, QRS interval  $> 109$  msec, or QTcF  $> 450$  msec.

- Systolic blood pressure  $> 160$  or  $< 90$  mmHg



6. Patient is currently receiving any of the following medications and cannot be discontinued 7 days prior start if the treatment:

- That are known strong inducers or inhibitors of CYP3A4.
- That have a known risk to prolong the QT interval or induce Torsades de Pointes.
- That have a narrow therapeutic window and are predominantly metabolized through CYP3A4.
- Herbal preparations/medications

**Type of study**

Interventional

**Type of intervention**

Pharmaceutical

**Type of intervention: Specify type**

N/A

**Trial scope**

Therapy

**Trial scope: Specify scope**

N/A

**Study design: Allocation**

Randomized controlled trial

**Study design: Masking**

Blinded (masking used)

**Study design: Control**

Placebo

**Study phase**

3

**Study design: Purpose**

Treatment

**Study design: Specify purpose**

N/A

**Study design: Assignment**

Parallel

**Study design: Specify assignment**

N/A

**IMP has market authorization**

Yes, Lebanon and Worldwide

**IMP has market authorization: Specify**

Lebanon and Worldwide

**Name of IMP**

Ribociclib

**Year of authorization**

2017

**Month of authorization**

8

**Type of IMP**

Others

**Pharmaceutical class**

Orally bioavailable, highly selective small molecule inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6).

**Therapeutic indication**

postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who received no prior therapy for advanced disease.

**Therapeutic benefit**

increase OS & PFS

**Study model**

N/A

**Study model: Explain model**

N/A

**Study model: Specify model**

N/A

**Time perspective**

N/A

**Time perspective: Explain time perspective**



**Time perspective: Specify perspective**

N/A

N/A

**Target follow-up duration**

**Target follow-up duration: Unit**

**Number of groups/cohorts**

**Biospecimen retention**

Samples with DNA\*\*

**Biospecimen description**

Samples with circulating tumor DNA will be done, in addition to safety Labs ( CBC, chemistry ) sent to central lab : Covance located in Switzerland.

**Target sample size**

15

**Actual enrollment target size**

15

**Date of first enrollment: Type**

Actual

**Date of first enrollment: Date**

29/04/2014

**Date of study closure: Type**

Actual

**Date of study closure: Date**

20/12/2021

**Recruitment status**

Complete

**Recruitment status: Specify**

**Date of completion**

12/02/2015

**IPD sharing statement plan**

Yes

**IPD sharing statement description**

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent expert panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data is currently available according to the process described on [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com).

URL: <http://www.clinicalstudydatarequest.com>

**Additional data URL**

<https://clinicaltrials.gov/ct2/show/record/NCT01958021?id=CLEE011A2301&rank=1>

**Admin comments**

**Trial status**

Approved



## Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinicaltrials.gov	NCT01958021

## Sources of Monetary or Material Support

Name
Novartis Pharma Services Inc.

## Secondary Sponsors

No Sponsors

## Contact for Public/Scientific Queries

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Public	Fadi El Karak	Beirut	Lebanon	03-061621	felkarak@yahoo.com	Bellevue Medical Center
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## Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Dr Joseph Kattan	Hematology Oncology	Approved
Hammoud Hospital University Medical Center	Dr Fadi Farhat	Hematology Oncology	Approved
Bellevue Medical Center	Dr Fadi El Karak	Hematology Oncology	Approved
American University of Beirut Medical Center	Dr Ziad Salem	Hematology Oncology	Approved

## Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	05/09/2014	Fuad Ziyadeh	fz05@aub.edu.lb	+961 (0) 1 350 000 ext:5445
Hotel Dieu de France	20/09/2013	Nancy Alam	nancy.alam@usj.edu.lb	+961 (0) 1 421000 ext 2335
Bellevue Medical Center	20/02/2014	Ghassan Maalouf	gmaalouf@bmc.com.lb	+961 (0) 1 682666 ext 7600
Hammoud Hospital University Medical Center	30/10/2013	Ahmad Zaatari	zaatari@hammoudhospital.com	+961 (0) 7 723111 ext 1160



Countries of Recruitment	
Name	
Lebanon	
Argentina	
Australia	
Austria	
Belgium	
Brazil	
Canada	
Denmark	
Finland	
France	
Germany	
Hungary	
Ireland	
Italy	
Netherlands	
Norway	
Singapore	
Spain	
Sweden	
Turkey	
United Kingdom	
United States of America	



## Health Conditions or Problems Studied

Condition	Code	Keyword
Advanced Breast Cancer	Malignant neoplasm of breast (C50)	ABC

## Interventions

Intervention	Description	Keyword
Physical Exam, Vital signs, ECG, Echocardiography, Urinalysis, Serum/ urine pregnancy test, lab test, completion of QoL questionnaires	Physical Exam, Vital signs, ECG, Echocardiography, Urinalysis, Serum/ urine pregnancy test, lab test, completion of QoL questionnaires	ICF, Lab, IMP, radiology

## Primary Outcomes

Name	Time Points	Measure
Progression Free Survival	20 months	PFS up to approximately 20 months

## Key Secondary Outcomes

Name	Time Points	Measure
•Overall Response Rate (ORR)	20 months	20 months
Overall survival	65 months	65 months





## Trial Results

**Summary results**

**Study results globally**

**Date of posting of results summaries**

**Date of first journal publication of results**

**Results URL link**

**Baseline characteristics**

**Participant flow**

**Adverse events**

**Outcome measures**

**URL to protocol files**