A Phase II Study of Ovarian Function Suppression And ExemesTane with or without PalbocIclib in PreMenopausal Women with ER positive / HER-2 negative MetAstatic Breast Cancer (FATIMA)

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Main Information

Primary registry identifying number
LBCTR2019020181

Protocol number
AMCI – 001

MOH registration number
2018/2/51295

Study registered at the country of origin
No

Study registered at the country of origin: Specify
Not registered

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
03/01/2019

Primary sponsor
AMCI (Africa Middle East Cancer Intergroup)/Investigator Initiated Research

Primary sponsor: Country of origin
Lebanon

Date of registration in primary registry
05/03/2019

Date of registration in national regulatory agency
03/01/2019

Public title
A Phase II Study of Ovarian Function Suppression And ExemesTane with or without PalbocIclib in PreMenopausal Women with ER positive / HER-2 negative MetAstatic Breast Cancer (FATIMA)

Acronym
FATIMA

Scientific title
A Phase II Study of Ovarian Function Suppression And ExemesTane with or without PalbocIclib in PreMenopausal Women with ER positive / HER-2 negative MetAstatic Breast Cancer

Acronym

Brief summary of the study: English
This is an open label, randomized, multicenter, international phase II study for premenopausal patients with hormone receptor positive, HER2 negative metastatic or locally advanced breast cancer. Randomization will be done in a 1:1 ratio. Patients will be randomized to receive either palbociclib + exemestane + OFS (Arm A) or exemestane +OFS (Arm B).
Treatment will be continued until disease progression, unacceptable toxicities, or withdrawal of consent.

Brief summary of the study: Arabic

هذه دراسة دولية، مفتوحة التسمية، عشوائية، متعددة المراكز وفي المرحلة الثانية لنساء لم يدخلن في سن اليأس ومصابات بسرطان ثدي نقيلي متقدم موضعياً أو إيجابي لمستقبلات . سيتم التوزيع العشوائي2الإستروجين و سلبي لمستقبلات العامل البشري لنمو البشرة – + . سيتم توزيع المرضى عشوائياً لتلقي إما تعطيل وظيفة المبيض+ الإكسيميستان1:1بنسبة) أو تعطيل وظيفة المبيض+ الإكسيميستان (طريقة العلاج1البالبوسيكليب (طريقة العلاج .(2
سيستمر أخذ العلاج إلى حين تفاقم المرض أو الإصابة بتسمم حاد أو سحب الموافقة.

Health conditions/problem studied: Specify

Metastatic Breast Cancer – Oncology

Interventions: Specify

MEDICINAL PRODUCT{S}: Palbociclib

Key inclusion and exclusion criteria: Inclusion criteria

Subjects must meet all the following inclusion criteria to be eligible for enrolment into the study:
1. Adult women (≥ 18 years of age) with metastatic or locally advanced breast cancer (histologically or cytologically proven diagnosis of adenocarcinoma of the breast) not amenable to curative treatment by surgery or radiotherapy.
2. ER positive tumour: Histological or cytological confirmation of estrogen and/or progesterone-receptor positive, as determined by routine IHC. Positivity is defined as ≥1% positive stained cells. The receptor status determined by utilizing an assay consistent with local laboratory standards.
3. HER2 negative breast cancer as confirmed by IHC, SISH or FISH.
4. Premenopausal women : (definition of a real menopause is not a simple task in these relatively young women, owing to the potential effect of prior chemotherapy and /or endocrinal therapy particularly OFS) defined either by:
i. Any age below 40 years , irrespective to E2 level or menstrual history
ii. If the woman had a menstrual period any time within the last 12 months
iii. If the woman has amenorrhea of more than 12 months (in the absence of chemotherapy or ovarian function suppression) that is associated with serum hormone levels that are NOT in the postmenopausal range (either estradiol (E2) < 30 pg/mL and follicle-stimulating hormone (FSH) < 20 mU/mL OR E2 ≥ 30 pg/mL and FSH ≥ 20 mU/mL) [30].
5. Secondary hormonal resistance to tamoxifen or endocrinal sensitive metastatic disease
i. Secondary hormonal resistance is defined as recurrence after 24 months from the start of adjuvant tamoxifen treatment or within 12 months from the end of the 5 years of adjuvant Tamoxifen
ii. Endocrinal sensitive disease is defined as recurrence after 12 months from the end of adjuvant tamoxifen treatment or de novo metastatic disease
6. Measurable disease according to RECIST or bone-only metastases. Previously irradiated lesions are deemed measurable only if progression is documented at the site after completion of radiation.
i. Patients must either have at least one lesion that can be accurately measured;
OR
ii. Patients have bone lesions: lytic or mixed (lytic + sclerotic) in the absence of measurable disease as defined above.
7. ECOG Performance Status 0, 1, & 2.
8. Resolution of all acute toxic effects of prior therapy or surgical procedures to National Cancer Institute (NCI) CTCAE Grade □1 (except alopecia or other toxicities not considered a safety risk for the patient).
9. Adequate organ function as defined by the following criteria:
i. Absolute neutrophil count (ANC) ≥ 1.5 109/L
ii. Platelets > 100 x109/L
iii. Hemoglobin (Hgb) > 9.0g/dL
iv. INR < 2
v. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) < 2.5x ULN (or <5 if hepatic metastases are present)
vi. Total serum bilirubin < 1.5 x ULN (<3 x ULN for patients known to have Gilberts Syndrome)
vii. Serum creatinine < 1.5 x ULN
viii. QTc< 470 msec (based on the mean value of the triplicate ECGs).
10. Written informed consent obtained before any trial related activity and according to local guidelines.

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

Subjects presenting with any of the following will not be included in the study:
1. Postmenopausal women. Postmenopausal status is defined by age>40years with amenorrhea of more than 12 months, associated with serum hormonal levels of the postmenopausal range (either estradiol (E2) < 30 pg/mL and follicle-stimulating hormone (FSH) < 20 mU/mL or E2 ≥ 30 pg/mL and FSH ≥ 20 mU/mL) [30], in the absence of chemotherapy, tamoxifen, or OFS.
2. Patients with primary endocrinal resistance, defined as recurrence within 24 months from the start of adjuvant tamoxifen treatment.
3. Symptomatic and/or life threatening visceral metastases
1. Diffuse lymphangitic carcinomatosis.
2. Bulky liver or pulmonary metastases
4. Patients with only non-measurable lesions other than bone metastasis as defined above (e.g., pleural effusion, ascites, etc.).

5. Patients who have received hormonal treatment other than neo/adjuvant tamoxifen ± LHRH agonist for their early breast cancer.
6. Patients who received prior chemotherapy for metastatic or recurrent breast cancer.
7. Another malignancy within 5 years prior to enrolment with the exception of adequately treated in-situ carcinoma of the cervix, uterus, basal or squamous cell carcinoma or non-melanomatous skin cancer.
8. Uncontrolled (clinically or radiologically progressive) CNS metastases, carcinomatous meningitis, or leptomeningeal disease.
9. Major surgery within 3 weeks of first study treatment.
10. Chemotherapy, radiotherapy, or other anti-cancer therapy within 2 weeks before randomization. Patients who previously received radiotherapy to □25% of bone marrow are not eligible independent of when it was received.
11. Current treatment with any anti-cancer therapies for advanced disease; any experimental treatment of another clinical trial; therapeutic doses of anticoagulant.
N.B. Low dose anticoagulants for deep vein thrombosis prophylaxis are allowed.
Low molecular weight heparin is allowed. Aspirin is permitted.
12. Active bleeding diathesis.
13. History of non-compliance to medical regimens. Patients unwilling to or unable to comply with the protocol.
14. Pregnant or breast feeding women or those who are not using effective birth control methods. Adequate contraceptives must be used throughout the trial and for 8 weeks after the last study drug administration. Patients must have a negative serum pregnancy test within 7 days prior to first administration of study drug.
15. Prior hematopoietic stem cell or bone marrow transplantation.
16. Current use of food or drugs known to be potent CYP3A4 inhibitors, drugs known to be potent CYP3A4 inducers, and drugs that are known to prolong the QT interval.
17. Known or possible hypersensitivity to goserelin during the adjuvant setting.
18. Any severe and/or uncontrolled medical conditions such as:
i. Unstable angina pectoris, symptomatic congestive heart failure, myocardial infarction < 6months prior to enrollment, serious uncontrolled cardiac arrhythmia
ii. Uncontrolled diabetes as defined by fasting serum glucose > 3 x ULN
iii. Acute and chronic active infectious disorders (except for Hepatitis B and Hepatitis C positive patients) and non-malignant medical illnesses that are uncontrolled or whose control may be jeopardized by the complications of this study therapy
iv. Known human immunodeficiency virus infection
v. Impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of study drugs (e.g., ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome)

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

Open (masking not used)

Study design: Control

Active

Study phase

2

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

USA

Name of IMP

MEDICINAL PRODUCT{S}: Palbociclib

Year of authorization

2015

Month of authorization

1

Type of IMP

Others

Pharmaceutical class

Cyclin-dependent kinase (CDK) inhibitor

Therapeutic indication

Metastatic Breast Cancer – Oncology

Therapeutic benefit

There is a strong in-vitro and clinical evidence suggesting that the dual inhibition of CDK 4/6 and ER signaling is a highly effective therapeutic strategy in HR+ MBC. With the unprecedented success of palbociclib in PALOMA-1 trial, several phase 2 and 3 trials are underway to evaluate this agent (and other CDK4/6 inhibitors as well) in the different clinical scenarios of HR+ breast cancer [28].The vast majority of these trials –if not all– are testing these novel agents in postmenopausal patients, which would render the clinical experience of these agents restricted to postmenopausal women (median age was 62 years in PALOMA-1 trial)
The scarcity of clinical trials addressing endocrinal therapy in premenopausal women with MBC is, at least in part, related to the fact that the majority of women in western countries are diagnosed with breast cancer during their postmenopausal life. However the situation is rather different in many countries, including those in the Middle East region, where the median age of women diagnosed with breast cancer is below 50 years, and where approximately 50% of these patients are still menstruating.
This study will be the first to explore the therapeutic effects of palbociclib when combined with exemestane and ovarian function suppression (OFS) in premenopausal with hormone receptor positive and HER2 negative MBC, and how it will compare to the classic approach of using OFS plus an aromatase inhibitor.

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

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

None retained

Biospecimen description

No exportation of biological samples.

Target sample size

160

Actual enrollment target size

160

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

15/03/2019

Date of study closure: Type

Anticipated

Date of study closure: Date

15/09/2021

Recruitment status

Not recruiting

Recruitment status: Specify

Date of completion

IPD sharing statement plan

Yes

IPD sharing statement description

Yes (Sharing Individual Participant Data)
Presentation in a conference proceedings in mid-2019. Full publication in January 2020

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

No Numbers

Sources of Monetary or Material Support

No Sources

Secondary Sponsors

No Sponsors

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Marwan Ghosn	Center Sehnaoui, 894 Blvd Alfred Naccache, 5th Floor, Clinic Professor Marwan GHOSN, Achrafieh, Beirut	Lebanon	00961 1 613395 / 1 613396	marwanghosnmd@yahoo.com	Hotel Dieu de France Hospital
Scientific	Loay El Kassem	Egypt	Egypt	00201003022907	loay.kassem@cairocure.com	AMCI

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu de France Hospital, Beirut	Marwan Ghosn	Hematology/Oncology	Approved
Hammoud Hospital University Medical Center, Saida	Fadi Farhat	Hematology/Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	29/11/2018	Marwan Ghosn	drghosn@sodetel.net.lb	+9613226842
Hammoud Hospital University Medical Center	03/10/2018	Fadi Farhat	drfadi.trials@gmail.com	+9613753155

Countries of Recruitment

Name
Lebanon
Egypt
Algeria
South Africa

Health Conditions or Problems Studied

Condition	Code	Keyword
Breast Cancer	2-Propanol (T51.2)	Not applicable

Interventions

Intervention	Description	Keyword
MEDICINAL PRODUCT{S}: Palbociclib	MEDICINAL PRODUCT{S}: Palbociclib	Not applicable

Primary Outcomes

Name	Time Points	Measure
Progression Free Survival (PFS)* as assessed by the Investigator.	Primary Endpoint: - Progression Free Survival (PFS)* as assessed by the Investigator. *PFS will be defined as the time from randomization to the time of disease progression or death for both treatment arms.	Primary Endpoint: - Progression Free Survival (PFS)* as assessed by the Investigator. *PFS will be defined as the time from randomization to the time of disease progression or death for both treatment arms.

Key Secondary Outcomes

Name	Time Points	Measure
Objective Response (OR): Complete Response (CR) or Partial Response (PR).	Objective Response (OR): Complete Response (CR) or Partial Response (PR).	Objective Response (OR): Complete Response (CR) or Partial Response (PR).
Clinical benefit Rate (CBR): Complete Response + Partial Response + Stable Disease (SD) for □ 24 weeks	Clinical benefit Rate (CBR): Complete Response + Partial Response + Stable Disease (SD) for □ 24 weeks	Clinical benefit Rate (CBR): Complete Response + Partial Response + Stable Disease (SD) for □ 24 weeks
Overall Survival (OS)	Overall Survival (OS)	Overall Survival (OS)
Overall treatment safety: Type, incidence and severity of adverse events (as graded by the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v4.0)	Overall treatment safety: Type, incidence and severity of adverse events (as graded by the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v4.0)	Overall treatment safety: Type, incidence and severity of adverse events (as graded by the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v4.0)

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