

## Trial of Letrozole + Palbociclib/Placebo in Metastatic Endometrial Cancer

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. **▲** [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:

NCT02730429

[Recruitment Status](#) ⓘ : Recruiting

[First Posted](#) ⓘ : April 6, 2016

[Last Update Posted](#) ⓘ : April 4, 2017

See [Contacts and Locations](#)

### Sponsor:

Nordic Society for Gynaecologic Oncology

### Collaborators:

European Network of Gynaecological Oncological Trial Groups (ENGOT)

GCIG

North Eastern Germany Society of Gynaecologic Oncology

Multicenter Italian Trials in Ovarian cancer and gynecologic malignancies (MITO)

Grupo Español de Investigación en Cáncer de Ovario

### Information provided by (Responsible Party):

Nordic Society for Gynaecologic Oncology

**Study Details**

[Tabular View](#)

[No Results Posted](#)

[Disclaimer](#)

[How to Read a Study Record](#)

## Study Description

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### Brief Summary:

This randomized double-blind, placebo-controlled phase 2 trial is evaluating superiority of Letrozole-palbociclib combination versus letrozole-placebo combination in ER positive endometrioid adenocarcinoma of endometrium

<a href="#">Condition or disease</a> ⓘ	<a href="#">Intervention/treatment</a> ⓘ	<a href="#">Phase</a> ⓘ
Endometrial Cancer	Drug: Palbociclib/placebo Drug: Letrozole	Phase 2

### Detailed Description:

This multicenter, prospective, randomized, double-blind, placebo-controlled phase 2 study is evaluating the efficacy of letrozole-palbociclib combination against letrozole-placebo combination in women with ER+ advanced or relapsed endometrial cancer.

## Stratification

Patients are stratified according to:

1. Number of prior lines of therapy (primary advanced disease vs. 1st relapse vs.  $\geq 2$  relapses)
2. Measurable vs. evaluable disease
3. Prior use of MPA/Megace

Randomization 1:1 randomization The patients with prior MPA/Megace treatment will be capped to a maximum of 50%.

## Study arms

Patients are randomized to one of the two treatment arms:

- Arm A: (comparator) letrozole-placebo combination therapy until progression.
- Arm B: (experimental arm): Letrozole- palbociclib combination therapy until progression

## Study Design

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**Study Type** ⓘ : Interventional (Clinical Trial)

**Estimated Enrollment** ⓘ : 78 participants

**Allocation:** Randomized

**Intervention Model:** Parallel Assignment

**Intervention Model Description:** randomized, double-blind, placebo-controlled

**Masking:** Double (Participant, Investigator)

**Primary Purpose:** Treatment

**Official Title:** ENGOT-EN3-NSGO/PALEO: A Randomized, Double-blind, Placebo-controlled, Phase II Trial of Palbociclib in Combination With Letrozole Versus Placebo in Combination With Letrozole for Patients With Estrogen Receptor Positive Advanced or Recurrent Endometrial Cancer.

**Actual Study Start Date** ⓘ : February 15, 2017

**Estimated Primary Completion Date** ⓘ : December 2020

**Estimated Study Completion Date** ⓘ : December 2022

### Resource links provided by the National Library of Medicine

[Drug Information](#) available for: [Letrozole](#) [Palbociclib](#)



[U.S. FDA Resources](#)

## Arms and Interventions

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<b>Arm</b> ⓘ	<b>Intervention/treatment</b> ⓘ
Placebo Comparator: Letrozole + placebo letrozole 2.5mg once daily days 1-28 every 28 days shall be administered until progression of disease or unacceptable toxicity. Letrozole is administered as standard of care in both study arms. Placebo for palbociclib once daily days 1-21 every 28 days shall be administered until progression of disease or unacceptable toxicity.	Drug: Letrozole Letrozole is standard of care in both arms
Experimental: Letrozole + palbociclib Palbociclib 125mg once daily days 1-21 every 28 days shall be	Drug: Palbociclib/placebo Palbociclib or a placebo is

administered until progression of disease or unacceptable toxicity.  
letrozole 2.5mg once daily days 1-28 every 28 days shall be administered until progression of disease or unacceptable toxicity.  
Letrozole is administered as standard of care in both study arms.

administered together with standard of care letrozole  
Drug: Letrozole  
Letrozole is standard of care in both arms

## Outcome Measures

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### Primary Outcome Measures

1. Progression-Free Survival (PFS). Increase in median PFS in experimental arm versus comparator arm [ Time Frame: 26 months ]  
To be measured (in months) and reported

### Secondary Outcome Measures

1. PFS of patients in the sub-populations as described under stratification factors. Increase in median PFS in experimental arm versus comparator arm [ Time Frame: 26 months ]  
To be measured (in months) and reported
2. Overall Response Rate (ORR) according to RECIST [ Time Frame: 26 months ]  
To be measured (in %) and reported
3. Disease Control Rate (DCR) for at least 12 weeks [ Time Frame: 26 months ]  
To be measured (in %) and reported
4. Time to First Subsequent Therapy (TFST) [ Time Frame: 36 months ]  
TFST: time from randomization to first subsequent therapy or death. To be measured (in months) and reported
5. Progression-Free Survival 2 (PFS2) [ Time Frame: 48 months ]  
PFS2: time from randomization to second objective disease progression or death. To be measured (in months) and reported
6. Time to Second Subsequent Therapy (TSST) [ Time Frame: 48 months ]  
TSST: time from randomization to second subsequent therapy or death. To be measured (in months) and reported
7. Patient Reported Outcomes (PROs) like Quality of Life questionnaire EORTC-QLQ-C30 & EORTC-QLQ-EN24 [ Time Frame: 48 months ]  
These are the validated questionnaires to be answered by patients. Results to be reported as descriptive and on a scale of 1-10
8. Number of participants with treatment-related adverse events as assessed by CTCAE v4.0 [ Time Frame: 48 months ]

To be reported on %

9. Compliance in the two treatment arms. [ Time Frame: 48 months ]

Missed dosages in both arm will be reported.

10. Dose reductions/interruptions in the two treatment arms [ Time Frame: 48 months ]

To be reported on %

## Eligibility Criteria

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### Information from the National Library of Medicine



*Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).*

Ages Eligible for Study: 18 Years and older (Adult, Senior)

Sexes Eligible for Study: Female

Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

1. Histological confirmed endometrial cancer of endometrioid type. Mixed tumor histology is allowed if the non-endometrioid component is less than 5%. Tumor must be estrogen receptor positive.
2. Patients may have received adjuvant chemotherapy for stage 1 or 2.
3. Patients may have received any lines of chemotherapy for primary advanced (stage 3-4) or relapsed disease.
4. Patients may have received external beam radiotherapy, brachytherapy, and surgery.
5. Patient may have received maximum one line of endocrine therapy containing MPA/Megace only.
6. Patients must have measureable disease or evaluable disease on CT scan according to RECIST 1.1 outside irradiated field.
7. Patients must give informed consent
8. Patients must have a WHO performance status of 0-1
9. Patients must have an adequate bone-marrow, renal and hepatic function
10. Life expectancy of at least 12 weeks
11. Patients must be fit to receive combination therapy
12. Patient's age >18 years
13. Patient is post-menopausal. Patients under the age of 55 with intact ovaries shall undergo hormonal verification.
14. Patients with preserved reproductive capacity must have a negative pregnancy test ( $\beta$ -HCG test in urine or serum) prior to commencing study treatment

## Exclusion Criteria:

1. Non-endometrioid adenocarcinomas, sarcomas, small cell carcinoma with neuroendocrine differentiation or non-epithelial cancers.
2. Previous anti-cancer endocrine therapy other than MPA/Megace. This means that eg. tamoxifen is not allowed prior to study entry.
3. Concurrent cancer therapy
4. Previous treatment with Palbociclib or other CDK inhibitors.
5. Concurrent treatment with an investigational anticancer agent or participation in another anticancer clinical trial within 21 days before entering into study.
6. Treatment within 21 days prior to randomization with any investigational drug, radiotherapy,
7. Major injuries or surgery within the past 21 days prior to start of study treatment with incomplete wound healing and/or planned surgery during the on-treatment study period.
8. Previous malignant disease, except patients with other malignant disease, for which the patient has been disease-free for at least three years. Concurrent other malignant disease except for curatively treated carcinoma in situ of the cervix or basal cell carcinoma of the skin.
9. Active infection or other serious underlying medical condition, which might prevent the patient from receiving treatment or to be followed.
10. Evidence of significant medical illness, abnormal laboratory finding or psychiatric illness/social situation that would, in the Investigator's judgment, makes the patient inappropriate for this study.
11. Known uncontrolled hypersensitivity to the investigational drugs.
12. History of major thromboembolic event defined as:
13. History of a cerebral vascular accident, transient ischemic attack or subarachnoid hemorrhage within the past 3 months.
14. History of clinically significant hemorrhage in the past 3 months.
15. Uncontrolled and/or symptomatic CNS metastasis or leptomeningeal carcinomatosis (dexamethasone/prednisone therapy will be allowed if administered as stable dose for at least one month prior randomization).
16. Significant cardiovascular diseases, including uncontrolled hypertension, uncontrolled clinically relevant cardiac arrhythmia, unstable angina or myocardial infarction within 6 months prior to randomization, congestive heart failure > NYHA III, severe peripheral vascular disease, clinically significant pericardial effusion.
17. Pregnancy or breastfeeding. Patients with preserved reproductive capacity, unwilling to use a medically acceptable method of contraception for the duration of the trial and for 3 months afterwards.
18. Active or chronic hepatitis C and/or B infection
19. Persistence of clinically relevant grade 3-4 therapy related toxicity from previous chemo and/or radiotherapy
20. Known hypersensitivity to the trial drugs, or to their excipients.
21. Gastrointestinal disorders or abnormalities that would interfere with absorption of the study drug
22. Unable or unwilling to swallow tablets/capsules

## Contacts and Locations

Go to

**Information from the National Library of Medicine**



*To learn more about this study, you or your doctor may contact the study research staff*

using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT02730429**

## Contacts

Contact: Mansoor R Mirza, MD +4535453311 [mansoor@rh.regionh.dk](mailto:mansoor@rh.regionh.dk)

Contact: Pernille Strøm, RN [Pernille.Stroem@regionh.dk](mailto:Pernille.Stroem@regionh.dk)

## Locations

### Denmark

#### NSGO

#### Recruiting

Copenhagen, Sjaelland, Denmark, 2100

Contact: Pernille Strøm, RN [pernille.stroem@regionh.dk](mailto:pernille.stroem@regionh.dk)

## Sponsors and Collaborators

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Grupo Español de Investigación en Cáncer de Ovario

## Investigators

Study Chair: Mansoor R Mirza, MD NSGO

## More Information

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Responsible Party: Nordic Society for Gynaecologic Oncology

ClinicalTrials.gov Identifier: [NCT02730429](#) [History of Changes](#)

Other Study ID Numbers: ENGOT-EN3-NSGO/PALEO

First Posted: April 6, 2016 [Key Record Dates](#)

Last Update Posted: April 4, 2017

Last Verified: April 2017

### Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Yes

Plan Description: As all endpoints are matured, the individual participant data will be shared.

Studies a U.S. FDA-regulated Drug Product: No

Studies a U.S. FDA-regulated Device Product: No

### Additional relevant MeSH terms:

Endometrial Neoplasms

Antineoplastic Agents

Uterine Neoplasms

Aromatase Inhibitors

Genital Neoplasms, Female

Steroid Synthesis Inhibitors

Urogenital Neoplasms

Enzyme Inhibitors

Neoplasms by Site  
Neoplasms  
Uterine Diseases  
Genital Diseases, Female  
Letrozole  
Palbociclib

Molecular Mechanisms of Pharmacological Action  
Estrogen Antagonists  
Hormone Antagonists  
Hormones, Hormone Substitutes, and Hormone  
Antagonists  
Physiological Effects of Drugs  
Protein Kinase Inhibitors