Rationale

This study addresses a key research priority of the Cancer and Aging Research Group, National Cancer Institute, National Institute on Aging, and the Institute of Medicine: the assessment of cancer therapy in older adults. [1,2] Palbociclib is a novel drug with the potential to change the treatment of metastatic breast cancer— a disease of aging. The combination of palbociclib and endocrine therapy (letrozole or fulvestrant) is associated with an improvement in progression-free survival (PFS) compared to endocrine therapy alone. [3,4] However, a small proportion of patients enrolled in these studies were age 75 and older. The pivotal trial of palbociclib reported in the package insert notes that only 37 patients (44%) were ≥65 years of age and 8 patients (10%) were ≥75 years of age.

The goal of this study is to fill this gap in knowledge by utilizing a phase II design to examine the tolerability of palbociclib and endocrine therapy among older adults age 70 and older with estrogen receptor positive, HER2 negative breast tumors. A comprehensive cancer-specific geriatric assessment which includes an evaluation of functional status, other medical conditions, cognitive function, nutritional status, social support, psychological state, and a review of medications will be included, as well as an assessment of adherence.
Objective

**Primary**
- To estimate the safety and tolerability (adverse event rate) of the combination of palbociclib and letrozole or fulvestrant in adults age 70 or older with ER-positive, HER2-negative metastatic breast cancer.

**Secondary**
- To describe the full toxicity profile including all grade $\geq 2$ adverse events (per CTCAE version [v.] 5.0)
- To describe rates of dose reductions, dose holds, and hospitalizations.
- To estimate median time to treatment failure, including PFS and OS.
- To estimate the rate of adherence to palbociclib, letrozole and fulvestrant.
Alliance A171601: A Phase II Trial Assessing the Tolerability of Palbociclib in Combination with Letrozole or Fulvestrant in Patients Aged 70 and Older with Estrogen Receptor-positive, HER2-Negative Metastatic Breast Cancer

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City of Hope National Medical Center

Rationale
Objective
Study Schema
Treatment Plan
Eligibility Criteria
Follow Up

Please use the headings above to navigate through the different sections of the poster

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Study Schema

1 cycle = 28 days

Registration

TREATMENT

Palbociclib
125 mg a day
(Once daily orally on days 1-21 of each 28 day cycle)
and
Letrozole or Fulvestrant
(Per treating investigator discretion)
Dosing per packet insert in each 28 day cycle

Continue protocol treatment until unacceptable toxicity, disease progression, or patient withdrawal
### Treatment Plan

#### Palbociclib plus Letrozole

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palbociclib</td>
<td>1 capsule every day</td>
<td>1 capsule every day</td>
<td>1 capsule every day</td>
<td>No capsule</td>
<td>1 capsule every day for 21 days, then 7 days no capsules</td>
</tr>
<tr>
<td>Letrozole</td>
<td>1 pill every day</td>
<td>1 pill every day</td>
<td>1 pill every day</td>
<td>1 pill every day</td>
<td>1 pill every day for 28 days</td>
</tr>
</tbody>
</table>

#### Palbociclib plus Fulvestrant

<table>
<thead>
<tr>
<th></th>
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</tr>
<tr>
<td>Fulvestrant</td>
<td>Injection on Day 1</td>
<td>No injection</td>
<td>Injection on Day 15</td>
<td>No injection</td>
<td>Injection on Day 1 of every 28-day cycle</td>
</tr>
</tbody>
</table>

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Key Eligibility Criteria

- ER-positive, HER2-negative metastatic breast cancer. Histologic confirmation is required.
- Measurable disease or non-measurable disease
- Planning to begin endocrine therapy for metastatic disease. One prior line of endocrine therapy or chemotherapy for metastatic disease is allowed.
- No prior therapy with a CDK inhibitor
- Resolution of all acute toxic effects of prior therapy or surgical procedures to CTCAE Grade ≤ 1 (except alopecia)
- No untreated brain metastases. Patients with treated brain metastases must have completed treatment with steroids.
- No second malignancies other than non-melanoma skin cancers or cervical carcinoma in situ
- No active infection requiring treatment with antibiotics
- Must be able to swallow and retain oral medication
- Patient Age: ≥ 70 years
- Patients must be able to read and comprehend English or Spanish.
- Chronic concomitant treatment with strong inhibitors or inducers of CYP3A is strongly discouraged on this study.
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