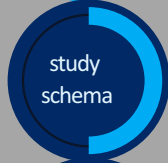


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Although many patients with HR+/HER2- breast cancer may be cured of their disease with optimal local and systemic therapy, a significant number of patients with stage II and III disease will experience disease recurrence. Adjuvant endocrine therapy for breast cancer can be extremely effective, particularly with extension beyond 5 years, however disease recurrence can occur, with risk distributed over the decades following initial diagnosis. Methods to improve the efficacy of endocrine therapy, and delay the onset of resistance, are needed.

HR+ breast cancer biologically may demonstrate features suggestive of sensitivity to CDK4/6 inhibition with agents such as palbociclib. Given the demonstrated activity and safety of palbociclib in the first-line treatment of metastatic HR+/ HER2- breast cancer, supporting FDA approval, there is interest in whether the benefits of CDK4/6 inhibition may translate into the adjuvant setting. The purpose of the PALLAS study is to determine whether the addition of palbociclib to adjuvant endocrine therapy will improve outcomes over endocrine therapy alone for HR+/HER2- early breast cancer. Assessment of a variety of correlative analysis, including evaluation of the effect of palbociclib in genomically defined tumor subgroups, is planned.

**Primary Objective**

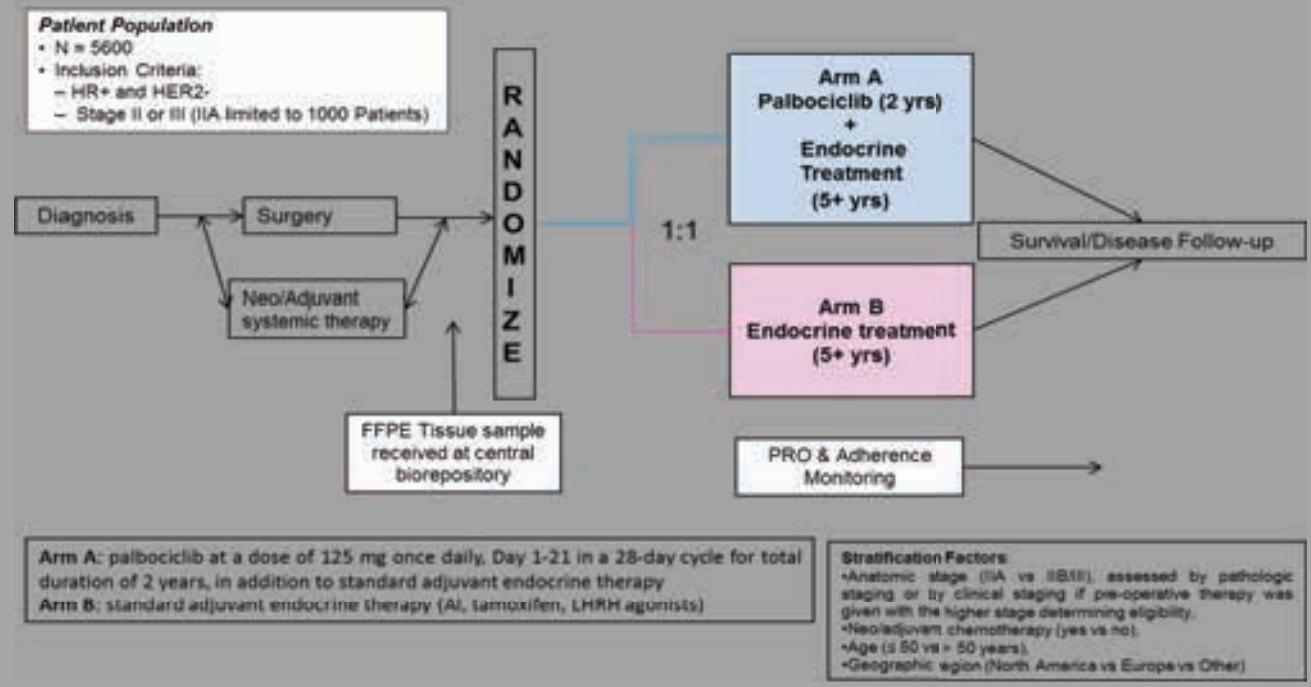
- To compare invasive disease-free survival (iDFS) for the combination of at least 5 years endocrine therapy and 2-year palbociclib treatment versus at least 5 years endocrine therapy alone in patients with histologically confirmed HR+/HER2- invasive early breast cancer (EBC).

**Secondary Objectives**

- To compare the following endpoints: iDFS excluding second primary cancers of non-breast origin, distant recurrence-free survival (DRFS), locoregional recurrences-free survival (LRRFS), and overall survival (OS).
- To compare the safety of 2 years of palbociclib with adjuvant endocrine therapy versus adjuvant endocrine therapy alone.

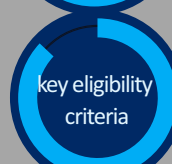
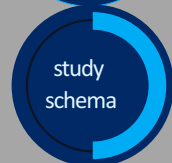
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- rationale/  
objective
- study  
schema
- treatment plan/  
intervention
- key eligibility  
criteria
- follow up



**STUDY SCHEMA**

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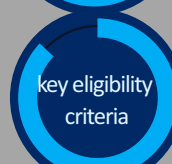
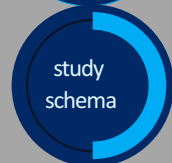
## Study Treatment Overview / Terms and Descriptions

- *IP Treatment* is comprised of palbociclib treatment for 2 years (refer to 6.1.2) for patients randomized into Arm A.
- *Non-IP Treatment* is comprised of standard endocrine therapy for at least 5 years for patients randomized into Arm A and B. Participating Groups and Academic Identifiers: AFT (AFT-05), ABCSG (ABCSG 42), BIG (BIG 14-03), PrECOG (PrE0109), NSABP (B-57-I)  
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Palbociclib is the only *investigational product (IP)* of this trial and will be provided free of charge by the sponsors.

Protocol approved adjuvant endocrine therapy regimens (also referred to as background treatment) are considered *Non-IP* as they represent routine or standard of care treatment for the respective patient population. Endocrine therapy will not be provided by the sponsors and must be selected by the Investigator as part of a standard of care therapy.

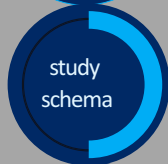
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- Signed informed consent obtained prior to any study specific assessments and procedures.
- Age  $\geq 18$  years (or per national guidelines).
- Premenopausal and postmenopausal women or men with stage II (stage IIA limited to a maximum of 1000 patients) or stage III early invasive breast cancer per AJCC (American Joint Committee on Cancer) Breast Cancer Staging version 7 /UICC (Union for International Cancer Control). Baseline staging to document absence of metastatic disease is not required, however is recommended as determined by institutional practice. If performed, reports of these examinations must be available.
- Patients with multicentric and/or multifocal and/or bilateral early invasive breast cancer whose histopathologically examined tumors all meet pathologic criteria for ER+ and/or PR+ and HER2-

## **KEY ELIGIBILITY CRITERIA**

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