ASCO CDK Study

Abstract 357: CDK4/6 Inhibitor (CDK4/6i) Dosing Knowledge (CDK) Study: A Pragmatic Randomized Trial of Indicated vs. Titrated CDK4/6i Dosing in Older Adults with HR+/HER2- Metastatic Breast Cancer

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Background

- The maximum tolerated dose (MTD) approach is not always appropriate for targeted therapies, as the optimal biological dose may be lower than the MTD.
- CDK4/6 inhibitors (CDK4/6is) are commonly combined with endocrine therapy (ET) for treatment (tx) of HR+/HER2- metastatic breast cancer (MBC).
- CDK4/6is are often dose-reduced to manage side effects and improve tolerability, without loss of efficacy.
- Benefits of CDK4/6i therapy are similar in younger and older patients (pts); however, toxicity can be worse in older pts.[1, 2]

Primary Objective

The CDK Study (**NCT06377852**), a multicenter, pragmatic, randomized trial, was developed to compare the time to CDK4/6i discontinuation in a titrated dosing approach vs. standard FDA-approved indicated dosing approach of palbociclib (P) or ribociclib (R) in pts aged ≥65 years with HR+/HER2- MBC given in combination with ET.

Trial Design & Methods

Hypothesis:

Titrated dosing will enable older pts to remain on CDK4/6i longer with fewer adverse events as compared to indicated dosing.

Primary Endpoint: Time to CDK4/6i discontinuation

Main Eligibility Criteria: (Figure 1)

- 65 years or older.
- Diagnosed with HR+/HER2- MBC.
- No prior tx with CDK4/6i for metastatic cancer.
- Must have planned tx with CDK4/6i (P or R) plus ET.

Dosing Schedule: (Figure 1)

All participants receive physician's choice of CDK4/6i (P or R) for 21 days in a 28-day cycle plus ET (aromatase inhibitor (AI) or fulvestrant (F)). Subsequent dose reduction and escalation in both arms is per standard-of-care (SOC) management. Encouraged to increase dose in titrated arm if well-tolerated.

Figure 1. CDK Study Schema

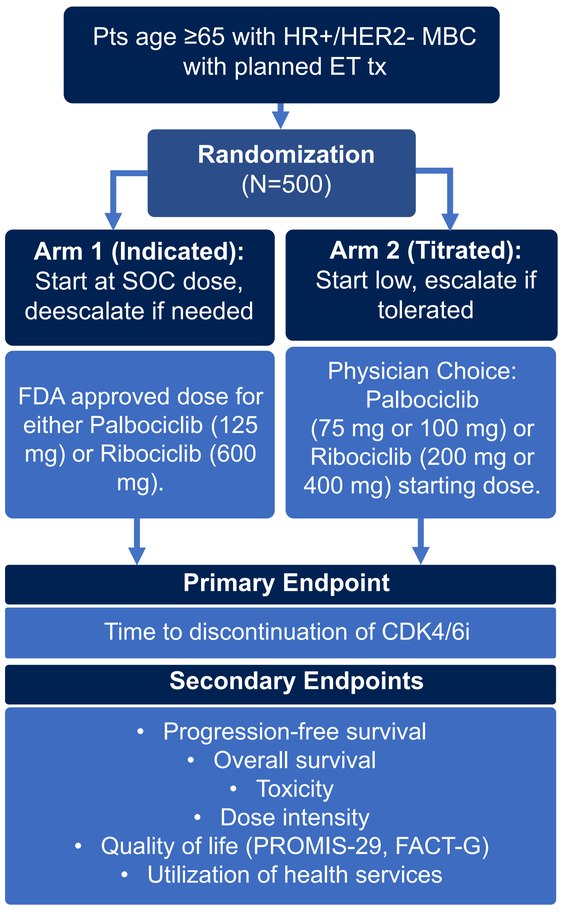
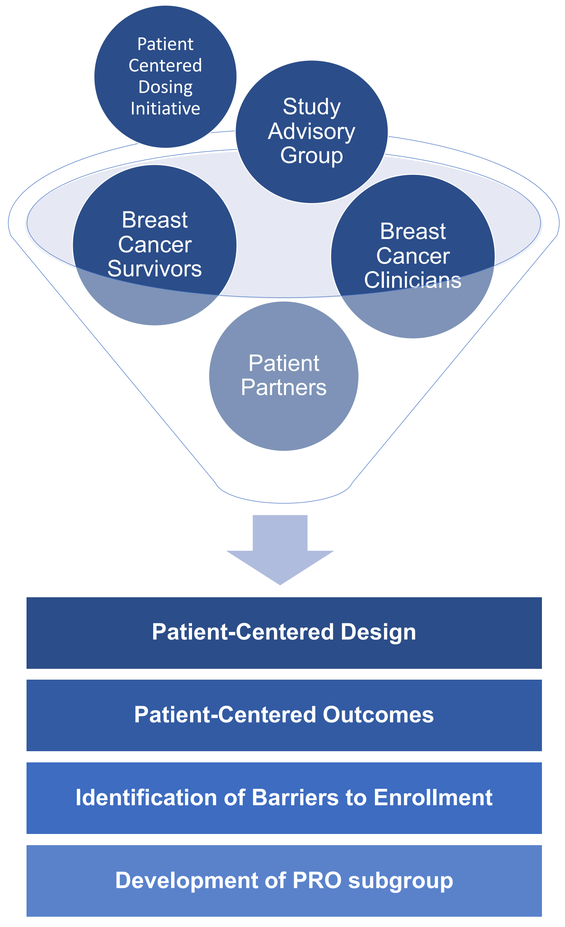


Figure 2. Patient and Stakeholder Engagement



Pragmatic Design to Reflect SOC for an Aging Population:

- **Measurement:** Clinician determined progression
- **Endpoint:** Time to CDK4/6i discontinuation.
- **Follow Up:** Relaxed timing; telehealth visits permitted; labs and scans anywhere
- **Setting:** ~50% of centers are community practices
- **Delivery:** Both arms are commonly given in SOC setting
- **Eligibility:** Few exclusion criteria
- **Adherence:** Allowing patients to adhere based on tolerance
- **Geriatric Assessment:** PROMIS-29, MOS-SS, PHQ-2, BMI

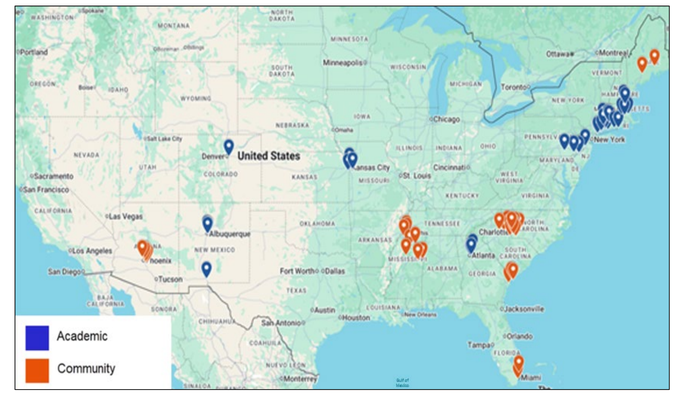
Statistical Methods:

- Randomization is stratified by CDK4/6i (P vs. R), age (65-74 vs. >75 yrs), and ET (AI vs. F).
- The primary analysis will estimate the hazard ratio (HR) comparing time to discontinuation (TTD) in the two arms using a stratified Cox proportional hazards model. The null hypothesis will be rejected if the 2-sided p-value for the HR is <0.05. A sample size of 500 was based on 80% power to detect a HR of 0.75.

Patient Advocate Engagement Goals

- Ensure relevance to patients with MBC
- Enhance communication through recruitment materials
- Support patient retention and enrollment

Figure 3. Map of Participating Clinical Centers as of October 2025 (N=86)



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