SELECT: A Phase 2 Adjuvant Trial Evaluating the Impact of Omitting Chemotherapy Based on Patient's Selection for Moderate to High-Anatomical Risk, Low-Genomic Risk, ER-Positive, HER2-Negative Breast Cancer with a Combination Regimen of Ribociclib and Optimized Endocrine Therapy

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Background

Most patients with ER-positive, HER2-negative, node-positive breast cancer are treated with curative intent, which typically involves some combination of surgery, radiation, endocrine therapy (ET) and often chemotherapy. The recent integration of CDK 4/6 inhibitors into adjuvant ET has complicated treatment decision-making for this subtype of breast cancer. These agents have demonstrated substantial benefits in reducing recurrence risk when combined with ET, prompting a reassessment of the role and necessity of chemotherapy in certain patient populations. However, it remains unclear to what extent prior exposure to a course of adjuvant chemotherapy impacts treatment persistence of CDK 4/6 inhibitors. In the Phase 3 NATALEE trial, approximately 90% of participants has received prior chemotherapy, yet 34 % participants prematurely discontinued the CDK 4/6 inhibitor, ribociclib. This finding underscores the significant barrier in maintaining long-term treatment persistence to CDK 4/6 inhibitor therapy and emphasize the need to develop and implement strategies for optimizing treatment regimens to minimize discontinuation rates, especially in patients for whom the benefit of chemotherapy is uncertain.

Table 1. Patient Disposition of NATALEE

Phase III Clinical Trial	Ribociclib + NSAI (%)	NSAI Alone (%)
Prior Chemotherapy	88	88
Discontinuation of Ribociclib	34	-
- Due to AEs	19	-
- Other	15	-
Discontinuation of NSAI	21	24
- Due to AEs	5	4
- Other	17	20
Dose Reduction of Ribociclib Due to AEs	27	-

Methods

Study Design

- This is a Phase 2, two-arm, single center, patient preference clinical trial designed to evaluate the impact of omitting adjuvant chemotherapy on ribociclib treatment persistence in moderate to high-anatomical risk, low-genomic risk (RS ≤ 25), ER-positive, HER2-negative breast cancer participants treated with a combination regimen of ribociclib and optimized endocrine therapy (Figure 1).
- Eligible participants aged ≥18 years, ECOG PS of 0 to 1, with anatomic stage II/III ER-positive, HER2-negative breast cancer (men or premenopausal women with T1-3N1-2 or postmenopausal women with T3N1 or T1-3N2) and RS 0-25 will be included.
- Participants will have the option to decide whether to include adjuvant chemotherapy in their treatment plan. GnRH agonists are used to achieve gonadal suppression in all men and premenopausal women.
  - Arm 1 will receive the combination of ribociclib and optimized ET.
  - Arm 2 will be treated with adjuvant chemotherapy followed by a combination of ribociclib and optimized ET.
- Estimated enrollment is 140 participants (70 each arm). Recruitment is ongoing.
- Clinical trial information: NCT06953882.

Table 2. Key Eligibility Criteria

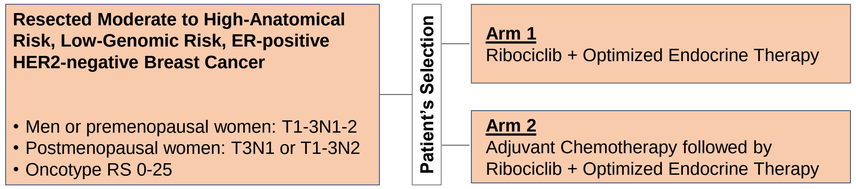
Key Inclusion Criteria

- Female or male age ≥ 18 years old. ECOG 0 -1.
- Complete surgical resection and axillary staging. Radiation therapy should be used according to standard guidelines.
- Postoperative stage (AJCC 8th ed): Men or premenopausal with T1-3N1-2. Postmenopausal with T3N1 or T1-3N2.
- The tumor must be ER-positive (≥ 10%), HER2-negative.
- Oncotype Dx Recurrence Score must be 0 - 25.
- Patients must have adequate organ and marrow function.
- QTc interval at screening < 450 msec. Resting heart rate 50-90 beats per minute.

Key Exclusion Criteria

- Definitive clinical or radiologic evidence of metastatic disease.
- T4 tumors, including inflammatory breast cancer.
- N3 tumors.
- Participants received neoadjuvant chemotherapy or biotherapy.
- Participant has received any CDK4/6 inhibitor.
- Participant has received prior treatment with tamoxifen, raloxifene or AIs for chemoprevention of breast cancer and/or treatment for osteoporosis within the last 2 years prior to registration.
- Participant is concurrently using hormone replacement therapy.
- History of ipsilateral or contralateral invasive breast cancer.
- Clinically significant, uncontrolled heart disease and/or cardiac repolarization abnormality.
- Pregnant or breast-feeding (lactating) women or women who plan to become pregnant or breast-feed during the trial.

Figure 1. Study Design



Objectives

Primary Objectives
To assess the 1-year discontinuation rate of ribociclib in participants chosen to forgo chemotherapy in their treatment.
To assess the 1-year discontinuation rate of ribociclib in participants chosen to include chemotherapy in their treatment.
Secondary Objectives
To evaluate the 3-year invasive disease-free survival (iDFS) in participants in each arm.
To describe patient reported outcomes (PRO) for symptoms, anxiety and depression in participants in each arm.
To describe PRO health-related quality-of-life (QoL) in participants in each arm.
To explore the factors that impact decision on whether to include or omit chemotherapy in participants in each arm.
To evaluate the change in fear of cancer recurrence and decision regret in participants in each arm.
Exploratory Objectives
To evaluate the one-year discontinuation rates of ribociclib between participants in arm 1 and arm 2, documenting and analyzing these metrics within each group before conducting a comparative evaluation.
To evaluate the change in willingness to join a randomized clinical trial for adjuvant treatment in participants in each arm.
To assess adherence to ribociclib in participants in each arm.
To characterize the clinical and biological profile of disease recurrence in participants in each arm.
Offer enrollment for circulating tumor DNA (ctDNA) analyses.

Current Status of the Study

- The Phase 2, single center, patient preference SELECT trial aims to explore the impact of the adjuvant chemotherapy regimens on the discontinuation rates to ribociclib, offering insights into optimizing therapy for ER-positive, HER2-negative node-positive early breast cancer with oncotype RS ≤ 25.
- The study started recruiting in July 2025. As of November 21, 2025, 6 participants have been enrolled.

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Acknowledgement:

Industry sponsor: Novartis
Grant support: BCRF, Ethel Donaghue Trust Project
The authors thank the patients enrolled in the study and their families, the study investigators.

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