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A randomized phase III trial for evaluating the efficacy of adjuvant abemaciclib in patients with locoregional recurrence of hormone receptor-positive, HER2-negative breast cancer: JCOG2313 (AURA study)

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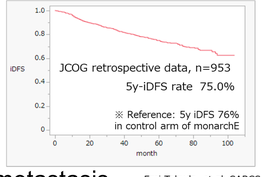
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OBJECTIVE

To evaluate whether adding abemaciclib to endocrine therapy improves invasive disease-free survival in patients with hormone receptor (HR)-positive, HER2-negative breast cancer after curative treatment for locoregional recurrence.

BACKGROUND

- Locoregional recurrence (LRR) occurs in 3–16% of breast cancer patients despite curative initial treatment. LRR includes ipsilateral breast tumor recurrence (IBTR), chest wall recurrence, and regional lymph node recurrence (Non-IBTR).
- In a multicenter retrospective study by JCOG Breast Cancer Study Group, the 5-year invasive disease-free survival (iDFS) after LRR was 76%. Among patients who relapsed after LRR, 63% developed distant metastasis.



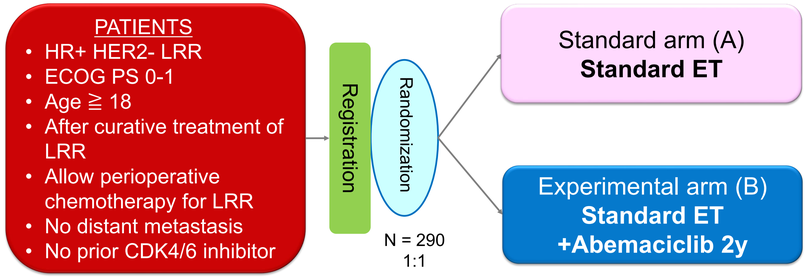
Emi Tokuda, et al. SABCS2024.

- There is a major evidence gap regarding optimal systemic therapy after LRR resulting in substantial variability in clinical practice.
- Abemaciclib improves outcomes in high-risk primary HR+/HER2– breast cancer (monarchE), but its role in the LRR setting is unknown.
- The POLAR trial evaluates palbociclib in isolated LRR, however, no prospective study has evaluated abemaciclib for LRR.
- To address this unmet need, **JCOG2313 (AURA) is a multicenter, open-label, randomized phase III trial evaluating endocrine therapy (ET) ± abemaciclib after curative treatment of HR+/HER2– LRR.**

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STUDY OVERVIEW

➢ Study design



- ✓ Planned enrollment: 290 patients
- ✓ Randomization (1:1):
  - ∗ Arm A: Endocrine therapy (tamoxifen or aromatase inhibitor ± ovarian function suppression)
  - ∗ Arm B: Endocrine therapy + abemaciclib for 2 years
- ✓ Adjustment factors:
  1: Site of LRR (IBTR only vs other LRR ± IBTR)
  2: Endocrine resistance (LRR occurring within 2 years of initiating prior adjuvant ET)
  3: Perioperative chemotherapy for LRR (yes/no)
  4: Institution
- ✓ Primary Endpoint: iDFS
- ✓ Secondary Endpoints: Distant relapse-free survival (DRFS), breast cancer-specific survival (BCSS), overall survival (OS), and adverse events (CTCAE v5.0)

➢ Trial information

- ✓ Registration: NCT07190443, jRCTs031240666
- ✓ Participating sites: 51 in Japan
- ✓ Accrual start: February 2025
- ✓ Accrual: 4 years; Follow-up: 5 years

➢ Key eligibility criteria

Inclusion criteria	◆ **First LRR of HR+/HER2- after curative therapy** ◆ **Curative local therapy completed for all LRR lesions** ◆ Age ≥18, ECOG PS 0–1, Adequate organ function ◆ **Perioperative chemotherapy for LRR allowed** ◆ **No new ET for LRR**, or **initiated ≤ 91 days before registration**
Exclusion criteria	◆ Active concurrent malignancy ◆ **Distant metastasis** present at registration ◆ **Prior CDK4/6 inhibitor** ◆ **Bilateral breast cancer** (synchronous / metachronous)

➢ Statistical analysis

- ✓ Primary analysis: iDFS compared between arms using a stratified log-rank test; HR and 95% confidence interval are estimated via stratified Cox proportional hazards model
- ✓ Sample size: 290 patients (HR=0.59 assumed; 5-year iDFS 76%→85%); requires 72 events for 70% power (one-sided α=0.05)
- ✓ Secondary endpoints: DRFS, BCSS, OS analyzed with unstratified log-rank test and Cox model; safety assessed using CTCAE v5.0
- ✓ Analysis populations: ITT for efficacy; safety population includes all treated patients
- ✓ Two interim analyses are planned; JCOG Data Center performs data management

SIGNIFICANCE

- ✓ Findings from adding abemaciclib may clarify optimal management and guide future approaches to HR+/HER2– LRR.

DISCLOSURES

- ✓ No external funding was received for this study.
- ✓ The trial is conducted under the Japan Clinical Oncology Group (JCOG).