

KANDELA-302: A Phase 3, Global, Open-Label, Randomized Study of the Selective CDK4 Inhibitor BGB-43395 + Letrozole vs CDK4/6 Inhibitors (CDK4/6i) + Letrozole for First-Line (1L) Treatment (Tx) of Advanced or Metastatic HR+/HER2– Breast Cancer (BC)

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Background: HR+/HER2– is the most common advanced/metastatic BC subtype. CDK4/6i + endocrine therapy is a standard 1L Tx, however, resistance and CDK6-related hematologic toxicities often require dose modifications and may limit sustained efficacy. BGB-43395, a potent and selective CDK4 inhibitor, has shown enhanced antitumor activity with reduced CDK6-related hematologic toxicity in preclinical studies. As HR+/HER2– BC is primarily CDK4 driven, the CDK4-selective inhibitor BGB-43395 + aromatase inhibitor (AI) may improve disease control and reduce off-target toxicity, with fewer adverse events vs CDK4/6i + AI.

Study Design: KANDELA-302 (NCT07492641) is an open-label, randomized, global phase 3 study assessing the efficacy and safety of BGB-43395 + letrozole vs investigator's choice of CDK4/6i (abemaciclib, palbociclib, or ribociclib) + letrozole as 1L therapy in patients (pts) with HR+/HER2– advanced/metastatic BC.

Eligible pts (≥18 years) with ECOG PS ≤1, measurable disease per RECIST v1.1 (including evaluable bone-only disease), adequate organ function, and histologically confirmed locally advanced/metastatic HR+/HER2– BC are randomized 1:1 to BGB-43395 400 mg BID + letrozole 2.5 mg QD or investigator's choice of CDK4/6i + letrozole. GnRH agonist Tx is required for premenopausal pts. Stratification factors include visceral metastases, de novo metastatic diagnosis, and investigator's CDK4/6i choice. Key exclusion criteria are prior systemic therapy for advanced/metastatic disease; early recurrence (≤12 months) after (neo)adjuvant ET (±CDK4/6i); and prior CDK4 or CDK2 inhibitors or investigational agents except for oral SERDs.

Approximately 1056 pts are being enrolled across North and South America, Europe, and Asia-Pacific (started May 2026). The primary endpoint is PFS by blinded independent central review (BICR) per RECIST v1.1; key secondary endpoint is OS. Other secondary endpoints include ORR, duration of response and time to response by

BICR, PFS and PFS2 by investigator assessment, clinical benefit rate, safety, and global health status/quality of life.