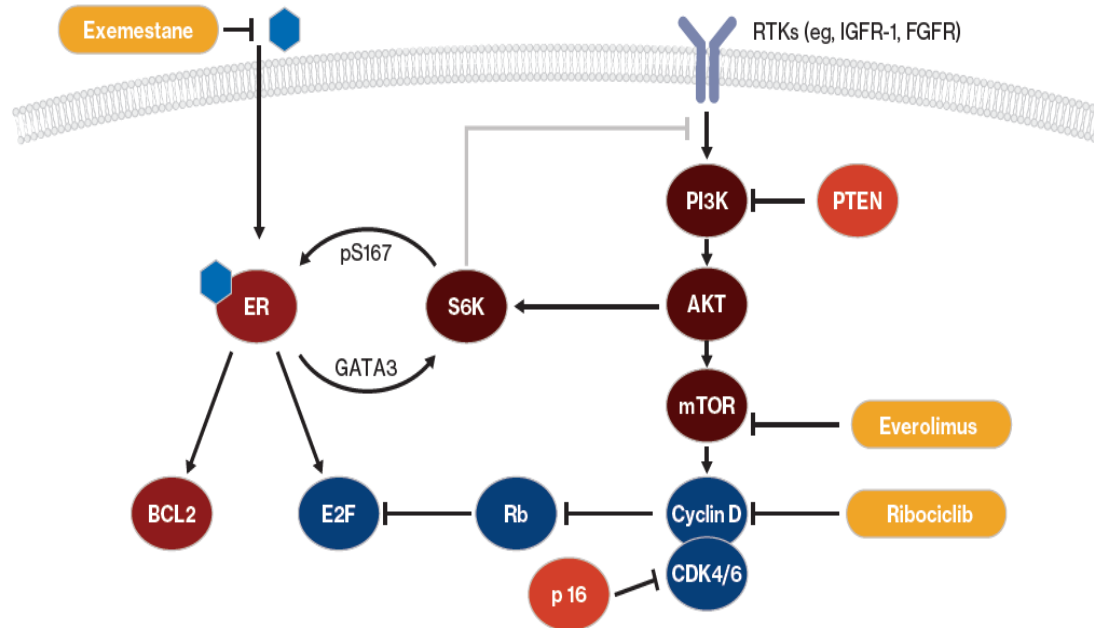
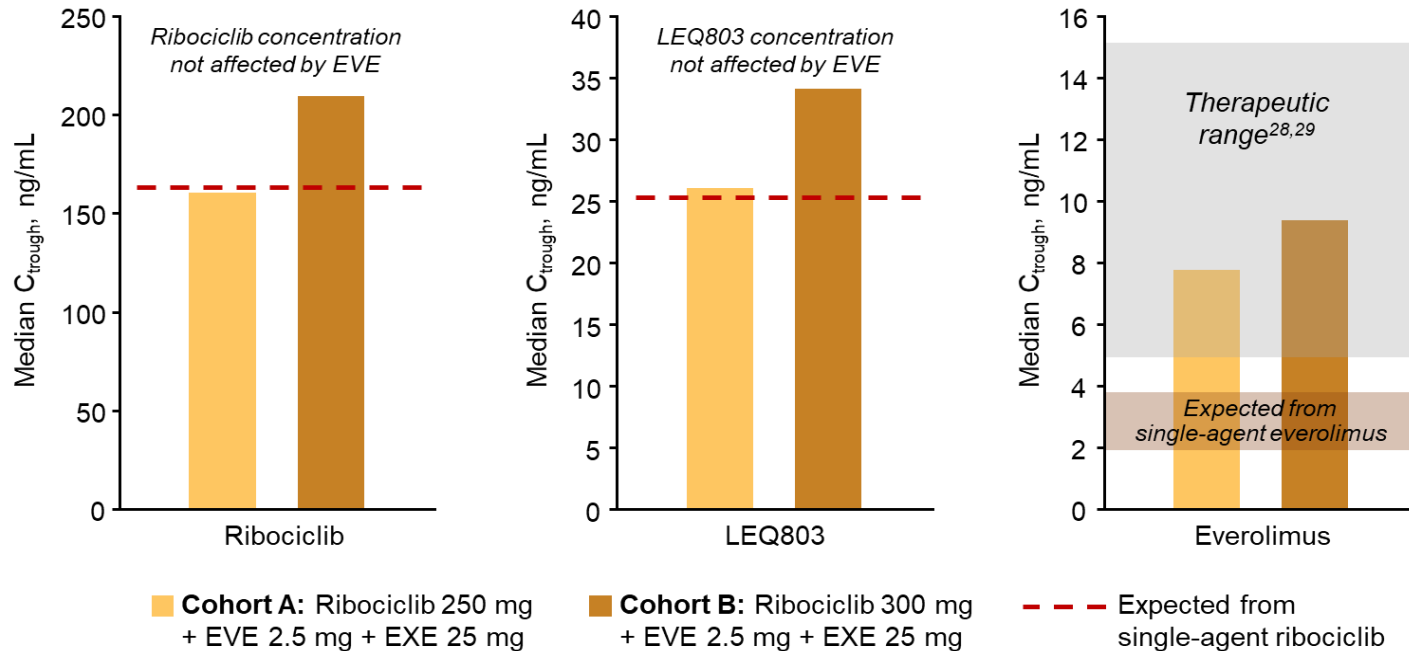


Supplemental Figure 1. ER, PI3K/mTOR, and CDK4/6 Pathways in HR+ Breast Cancer



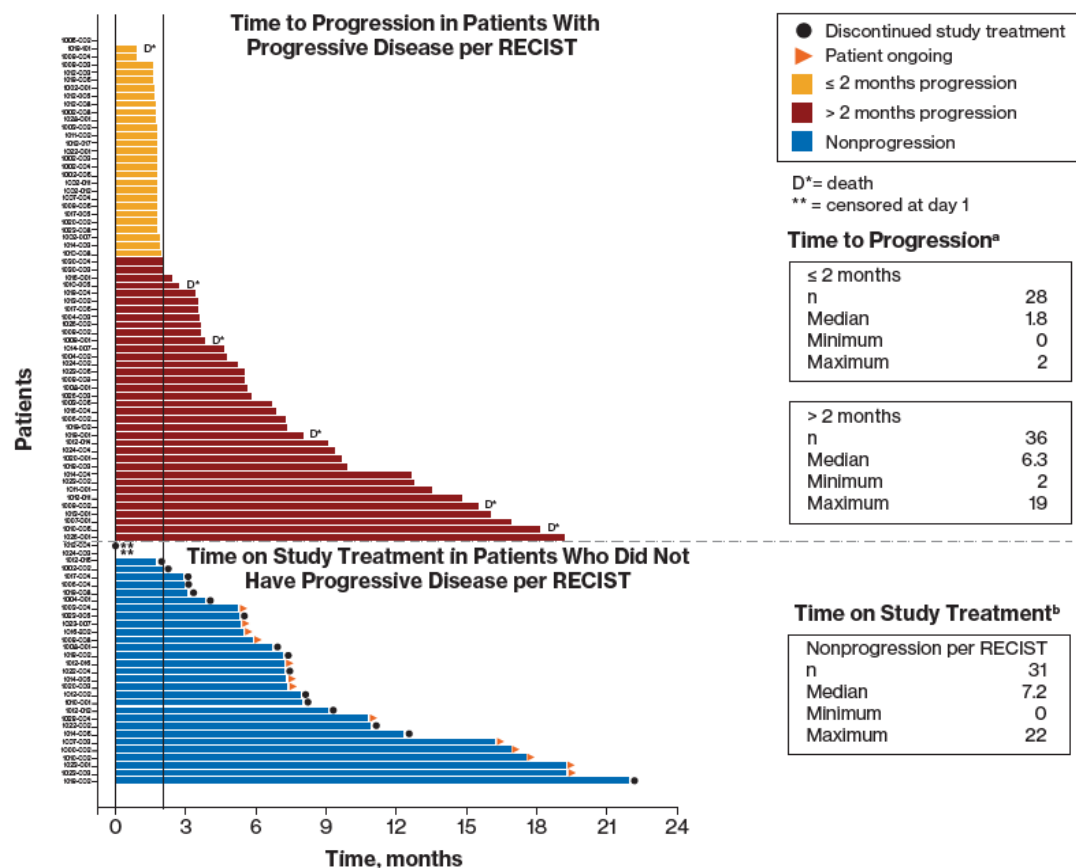
AKT, protein kinase B; CDK, cyclin-dependent kinase; ER, estrogen receptor; FGFR, fibroblast growth factor receptor; IGFR, insulin-like growth factor receptor; mTOR, mechanistic target of rapamycin; mTORi, mTOR inhibitor; PI3K, phosphatidylinositol 3-kinase; Rb, retinoblastoma; RTK, receptor tyrosine kinase.

Supplemental Figure 2. Median C_{trough} From Cycle 1 Day 15 in Cohorts A and B for (A) Ribociclib, (B) Ribociclib Metabolite LEQ803, and (C) EVE 2.5 mg. Red dotted line denotes expected C_{trough} from single-agent data for a ribociclib dose of 280 mg based on results from a previous study.²⁷ Light burgundy shading denotes expected C_{trough} for an EVE dose of 2.5 mg on the basis of the dose proportionality of exposure observed in single-agent studies.



C_{trough} , predose trough concentration; EVE, everolimus; EXE, exemestane.

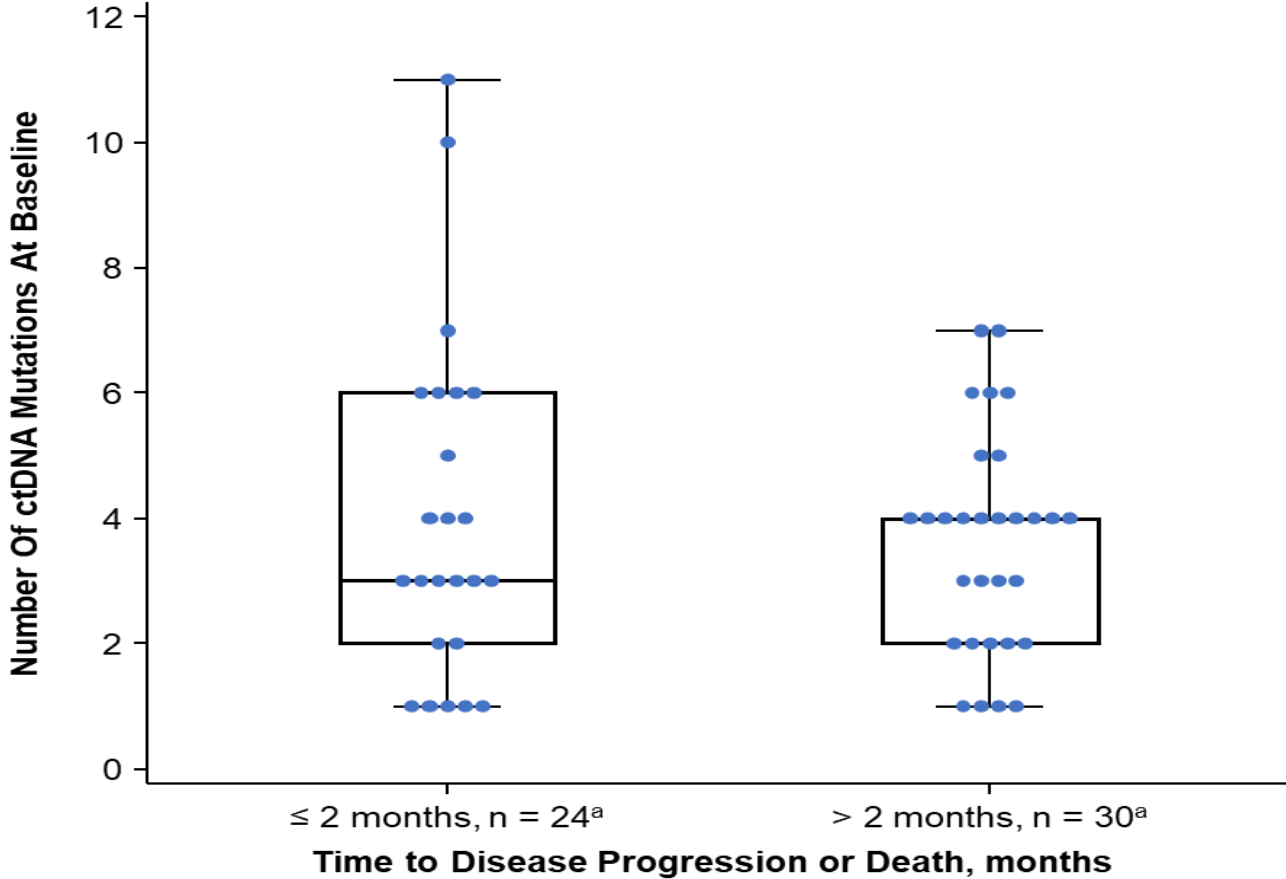
Supplemental Figure 3. Time to Progression or Time on Study Treatment



^a First tumor assessment was at 2 months (8 weeks).

^b Discontinuation due to reasons other than progressive disease (PD) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Among 31 patients who did not have PD per RECIST 1.1, 17 discontinued study treatment: physician decision (n = 7), AE (n = 3), stable disease per RECIST 1.1 at last evaluation or unknown with PD as clinical reason for discontinuation (n = 5), and other (n = 2). Patients 1012-004 and 1024-003 were censored at day 1 due to no postbaseline RECIST data.

Supplemental Figure 4. Baseline ctDNA Mutations and Time to Disease Progression or Death



^a Patients with baseline ctDNA data.