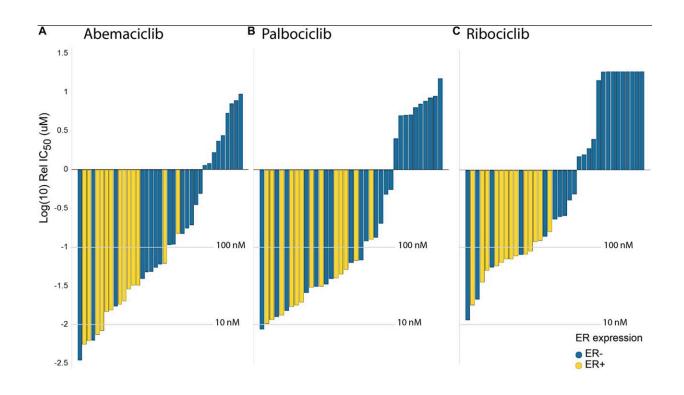


Continuous treatment with abemaciclib leads to sustained and efficient inhibition of breast cancer cell proliferation

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Abemaciclib shows greater potency than palbociclib & ribociclib in breast cancer cells. Credit: Torres-Guzmán et. al.

Worldwide, breast cancer (BC) is the second most common cancer. Pharmacologically targeting cyclin-dependent kinase 4 and 6 (CDK4 & 6) has proven to be a successful therapeutic approach in patients with



estrogen receptor-positive (ER+) breast cancer.

Abemaciclib is the first FDA-approved CDK4 & 6 inhibitor (CDK4 & 6i) approved for the adjuvant treatment of HR+, HER2−, node-positive early breast cancer (EBC) at high risk of recurrence and a Ki-67 score ≥20%. Differences have been observed in both efficacy and severity of neutropenia among the available CDK4 & 6i, generating interest in a possible mechanistic explanation. In their study published in *Oncotarget*, researchers examined the preclinical attributes of abemaciclib and other CDK4 & 6i using biochemical and cell-based assays.

"In vitro, abemaciclib preferentially inhibited CDK4 kinase activity versus CDK6, resulting in inhibition of cell proliferation in a panel of BC <u>cell lines</u> with higher average potency than palbociclib or ribociclib."

Abemaciclib showed activity regardless of HER2 amplification and phosphatidylinositol 3-kinase (PI3KCA) gene mutation status. In human bone marrow progenitor cells, abemaciclib showed lower impact on myeloid maturation than other CDK4 & 6i when tested at unbound concentrations similar to those observed in clinical trials. Continuous abemaciclib treatment provided profound inhibition of cell proliferation, and triggered senescence and apoptosis.

"After continuous dosing with abemaciclib, cells show sustained inhibition of <u>cell proliferation</u> that leads to irreversible effects through apoptosis. These preclinical results support the differentiated safety and efficacy profile of <u>abemaciclib</u> observed in clinical trials."

More information: Raquel Torres-Guzmán et al, Continuous treatment with abemaciclib leads to sustained and efficient inhibition of breast cancer cell proliferation, *Oncotarget* (2022). DOI: 10.18632/oncotarget.28249



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