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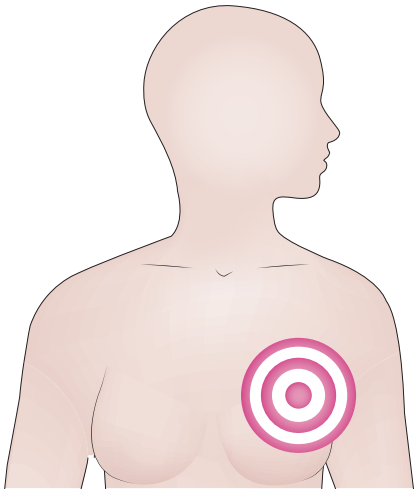
BREAST CANCER

PALOMA-3 confirms that CDK4/6 is a key therapeutic target

Activation of cyclin-dependent kinases 4 and 6 (CDK4/6)—key proteins that upon binding to cyclin D1, promote cell-cycle entry—seems to drive proliferation of breast cancer cells in hormone-receptor positive (HR+) disease. Now, the initial results of the PALOMA-3 trial confirm that the CDK4/6 inhibitor palbociclib, in combination with hormonal therapy, is an effective treatment option for women with HR+ metastatic breast cancer that had progressed on prior endocrine therapy.

Nicholas Turner, lead author of the study, explains the rationale of PALOMA-3, "prior research with derived endocrine-resistant cell lines has suggested that as breast cancers become resistant to endocrine therapy, they remain dependent on CDK4/6." Furthermore, palbociclib, a highly specific CDK4/6 inhibitor, is able to induce responses in HR+ tumours and has a synergistic effect when combined with endocrine therapy, such as fulvestrant. Thus, in this double-blinded phase III trial, the investigators randomized 521 patients with HR+ and HER2-negative advanced-stage breast cancer that had relapsed or progressed during prior endocrine therapy to receive fulvestrant in combination with palbociclib or placebo in a 2:1 ratio.

Patients receiving the combination of fulvestrant and palbociclib had a median progression free survival (PFS) of 9.2 months, more than doubling the PFS of 3.8 months observed in the fulvestrant alone arm. The hazard ratio for disease progression or death was 0.42 (95% CI 0.32–0.56, $P<0.001$). "Palbocicilb was well tolerated; in fact, despite frequent detection of haematological adverse events on blood tests, only a minor increase in symptomatic adverse events was reported, compared to fulvestrant alone," comments Turner.



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Of note, since palbociclib is active after progression on endocrine therapy, its efficacy is being tested in the adjuvant setting, where it might prevent the outgrowth of resistant clones and improve survival. "This study confirms CDK4/6 as a key therapeutic target in breast cancer," concludes Turner, "and palbociclib will likely become a new standard of care for women with HR+ advanced disease."

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