Background: Cell cycle inhibition is a proven target for novel cancer therapeutics. Palbociclib (P) is an orally active inhibitor of CDK4/6, and arrests the cell cycle at the G1-S transition. P in combination with endocrine therapy (ET) has demonstrated efficacy in phase II and III randomized trials for patients with newly diagnosed and recurrent hormone receptor positive/HER2 negative (HR+/HER2-) metastatic breast cancer (MBC), and is approved in these settings. Given confirmed benefits of P and ET for MBC, the PALLAS study was designed to determine if the addition of P to adjuvant ET improves outcomes over ET alone in HR+/HER2- early breast cancer.

Trial design: PALLAS is an international open-label phase III trial randomizing (1:1) patients (pts) to 2 years of P (125 mg daily, 21 days on 7 days off in a 28-day cycle) combined with at least 5 years of provider choice ET (AI, tamoxifen, +/- LHHR agonist), versus ET alone. The primary objective of the study is to compare invasive disease-free survival (iDFS) for the combination of P and ET, versus ET alone. Secondary objectives include comparison of iDFS excluding cancer of non-breast origin, DRFS, LRRFS, OS, as well as safety. The principal objective of the translational investigations is to determine the predictive or prognostic utility of defined genomic subgroups with respect to iDFS and OS. Additional objectives include evaluation of cDNA and tissue biomarkers predictive of benefit or resistance, pharmacogenomics, adherence, and patient-reported QOL. Eligible pts are pre- or post-menopausal women or men with stage II-III, HR+/HER2- breast cancer. Patients may have already initiated ET, but must be randomized within 12 months of diagnosis and 6 months of initiation of adjuvant ET. Trial sample size is 4600 pts and stage IIA pts will be capped at a total accrual of 1000 pts. Interim analyses for safety, futility/efficacy and sample size re-estimation are planned. PALLAS opened in 9/2015 and accrual is ongoing. Contact information: emayer@partners.org.


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