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PALLAS: A randomized phase III trial of adjuvant palbociclib with endocrine therapy versus endocrine therapy alone for HR+/HER2- early breast cancer

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Background

Palbociclib (P) added to endocrine therapy (ET) improves progression-free survival in hormone receptor positive (HR+)/HER-2 negative (HER2-) metastatic breast cancer. The global PALLAS trial (NCT02513394) was designed to determine if the addition of two years of P to adjuvant ET improves invasive disease-free survival (iDFS) over ET alone in patients (pts) with HR+/HER2- early-stage breast cancer.

Methods

In this phase III open-label trial, pts with stage II-III HR+/HER2- breast cancer were randomized to receive either 2 years of P with adjuvant ET, or ET alone. Eligible pts were within 12 months of diagnosis and 6 months of initiating adjuvant ET. The primary objective was to compare invasive disease-free survival (iDFS) between arms; secondary objectives include other recurrence endpoints and safety, as well as quality of life, adherence, and translational science. The study had 85% power to detect a 25% improvement in iDFS (0.75 hazard ratio [HR]). Interim analyses (IA) were predefined in the protocol; IA2 was triggered when 67% of events were observed.

Results

5,760 pts (median age 52 years) were randomized and included in the analysis; 1,013 (17.6%) had stage IIA disease and 4,729 (82.1%) stages IIB/III. 4,754 (82.5%) had received prior chemotherapy. At IA2, after a median follow-up of 23.7 months (351 events), iDFS was similar between the two arms, with 3-year iDFS of 88.2% for P and ET, and 88.5% for ET alone (HR 0.93, 95% confidence interval 0.76-1.15), crossing a pre-specified futility boundary. No benefit from P was observed within clinicopathologic subgroups. Grade 3 or 4 neutropenia was more common with P (61.3% vs 0.4%) but febrile neutropenia was uncommon (1.0%). Other all-grade toxicities occurring more often with P included leukopenia, fatigue, thrombocytopenia, anemia, upper respiratory tract infection, and alopecia. 42.2% of pts discontinued P prior to the planned 2 year duration, primarily due to adverse events.

Conclusions

Within the PALLAS trial, at IA2, two years of adjuvant palbociclib with ET did not improve iDFS compared to ET alone. Ongoing long-term follow-up and additional clinical and translational analyses will explore the effect of P in this patient population.

Clinical trial identification

NCT02513394.

Legal entity responsible for the study

Alliance Foundation Trials, LLC; Austrian Breast and Colorectal Cancer Study Group (ABCSG).

Funding

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Disclosure

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