BACKGROUND
Palbociclib is a first-in-class, selective, small-molecule inhibitor of cyclin-dependent kinases (CDKs) 4 and 6, with demonstrated activity in estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2–) metastatic breast cancer (MBC).

METHODS
Study Design and Treatment
Patients with ER+/HER2– MBC were randomized 2:1 (palbociclib:placebo) after having completed 12 weeks of prior endocrine therapy. Patients were then randomized to either placebo plus letrozole or palbociclib plus placebo. Treatment duration was a minimum of 22 weeks. Safety monitoring was performed weekly during the first cycle, every 4 weeks during cycles 2 through 4, and every 6 weeks thereafter.

Eligibility Criteria
Enrollment criteria included ER+/HER2– MBC (locoregionally recurrent or metastatic disease inoperable with intent, but at study entry, were required to be treatment-naive for advanced/metastatic breast cancer).

RESULTS
Overall, 666 postmenopausal women with ER+/HER2– ABC previously untreated for advanced/metastatic disease were enrolled, 222 in the placebo plus letrozole arm and 444 in the palbociclib plus letrozole arm. Median (range) of follow-up was 24.1 (5.1–34.4) months. The primary endpoint of the study was investigator-assessed PFS. Key secondary endpoints included objective response (OR), clinical benefit rate (CBR), and duration of response (DOR), as well as a safety assessment between the treatment arms.

The incidence of all-causality treatment-emergent AEs (TEAEs) for all grades was similar among the treatment arms. The most common TEAEs were arthralgia (36.9%–38.2%), and leukopenia (28.7%–30.7%; Table 1). Across all subgroups receiving palbociclib plus letrozole, regardless of receiving or not receiving prior (neo)adjuvant endocrine therapy or prior chemotherapy, the incidence of TEAEs was similar. TEAEs of special interest included grade 3–5 neutropenia (1.6%–2.1%) and grade 3–5 leukopenia (5.2%–8.2%).

Efficacy
Median PFS was similar for patients pretreated with endocrine therapy or prior chemotherapy (13.7 months and 17.0 months, respectively; Table 3). The primary endpoint of the study was investigator-assessed PFS. Key secondary endpoints included objective response (OR), clinical benefit rate (CBR), and duration of response (DOR), as well as a safety assessment between the treatment arms.

CONCLUSIONS
Regardles of prior (neo)adjuvant treatment, palbociclib plus letrozole significantly prolonged PFS vs placebo plus letrozole and demonstrated consistent efficacy in both pretreated and never treated populations of patients with ER+/HER2– ABC in a first-line setting.

REFERENCES

ACKNOWLEDGMENTS AND DISCLOSURES
The authors disclosed no conflicts of interest. This study was funded by Palatin Pharmaceuticals Inc. and Pfizer Inc. The current authors were all involved in the study conception and design, acquisition of data, analysis and interpretation of data, and in writing the manuscript. R.S. Finn was the study sponsor and principal investigator for this study. A. Tjulandin was the chair of the Data Monitoring Committee for this study.