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Original Research

Palbociclib plus endocrine therapy in older women with HR+/HER2− advanced breast cancer: a pooled analysis of randomised PALOMA clinical studies

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Abstract ***Aim:*** Because incidence of breast cancer and comorbidities increase with age, it is important to determine treatment benefit in elderly patients. We evaluated outcomes with palbociclib plus endocrine therapy in patients aged ≥65 years.
Methods: Data were pooled from three randomised studies (NCT00721409,

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NCT01740427 and NCT01942135) of women with HR+/HER2− advanced breast cancer (ABC). In PALOMA-1 (open-label) and PALOMA-2 (double-blind, placebo-controlled), treatment-naïve patients received palbociclib plus letrozole or letrozole alone. In PALOMA-3 (double-blind, placebo-controlled), patients with endocrine-resistant disease received palbociclib plus fulvestrant or fulvestrant alone.

Results: Among 528 patients treated with palbociclib plus letrozole and 347 treated with palbociclib plus fulvestrant, 218 (41.3%) and 86 (24.8%), respectively, were aged ≥65 years. Versus endocrine therapy alone, median progression-free survival was significantly improved in patients aged 65–74 years (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.45–0.97; $P = 0.016$) and ≥75 years (HR, 0.31; 95% CI, 0.16–0.61; $P<0.001$) receiving palbociclib plus letrozole and in patients aged 65–74 years (HR, 0.27; 95% CI, 0.16–0.48; $P<0.001$) receiving palbociclib plus fulvestrant; few patients aged ≥75 years received palbociclib plus fulvestrant (HR, 0.59; 95% CI, 0.19–1.8; $P = 0.18$). Patient-reported functioning and quality of life was maintained. No clinically relevant differences in palbociclib exposure were observed between age groups. Although myelosuppression was more common among patients aged ≥75 years, incidence of grade ≥III myelosuppression was similar across age groups, and febrile neutropenia was uncommon (≤2.4%); no new safety concerns were identified in older patients.

Conclusions: Palbociclib plus endocrine therapy is an effective, well-tolerated treatment for older patients with ABC.

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1. Introduction

Hormone receptor–positive (HR+)/human epidermal growth factor receptor 2–negative (HER2−) breast cancer is the most common subtype in patients aged ≥65 years, and its incidence increases with age [1]. Older patients with breast cancer have more comorbidities than younger patients, and increasing age and comorbid disease have been shown to have a negative impact on survival [2]. The potential for drug–drug interactions is also a concern because of polypharmacy in older patients treated for comorbid conditions [3]. Furthermore, functional capacity, cognition and social psychological factors affect treatment decisions in older patients [4]. Therefore, the treatment and management of older breast cancer patients require particular attention to the balance between efficacy, safety and health-related quality of life (HRQoL) [3]. Because of these concerns, older patients with breast cancer often may not receive appropriate treatment [5]. In particular, women aged >75 years often receive less aggressive treatments and have poorer survival rates [5]. Thus, there is a need to examine the efficacy and safety of novel therapies in older breast cancer patients [5].

Palbociclib (IBRANCE®) is a first-in-class oral inhibitor of cyclin-dependent kinases 4 and 6 that blocks G1-to S-phase progression [6–8]. In the Palbociclib Ongoing Trials in the Management of Breast Cancer (PALOMA) clinical trial program, palbociclib combined with endocrine therapy significantly improved progression-free survival (PFS) in patients with treatment-naive (PALOMA-1 and PALOMA-2) and previously treated HR+/HER2− advanced breast cancer [ABC] (PALOMA-3) [9–12]. Median PFS exceeded 2 years in patients receiving palbociclib plus letrozole [12] and was twice as long as the control group in endocrine-resistant patients receiving palbociclib plus fulvestrant [11]. Consequently, the United States Food and Drug Administration approved palbociclib in combination with an aromatase inhibitor (as initial endocrine-based therapy in postmenopausal women) and fulvestrant (after disease progression following endocrine therapy) for treatment of HR+/HER2− ABC [13,14]. Given the importance of endocrine therapy for older women with ABC, we conducted an exploratory pooled analysis of outcomes in older patients with HR+/HER2− ABC enrolled in three PALOMA studies.

2. Methods

2.1. Study design and patients

Data from PALOMA-1 (NCT00721409), PALOMA-2 (NCT01740427) and PALOMA-3 (NCT01942135) were included (Fig. 1). Eligible patients were postmenopausal women aged ≥18 years with locally recurrent or metastatic ER+/HER2− breast cancer (PALOMA-1 and PALOMA-2) or women of any menopausal status aged ≥18 years with HR+/HER2− ABC whose disease progressed on prior endocrine therapy. Additional study design details and eligibility criteria for each study have been published (Supplementary Fig. 1) [9–12].

2.2. Treatments

Patients were randomised 1:1 to receive palbociclib plus letrozole or letrozole alone (PALOMA-1); 2:1 to receive palbociclib plus letrozole or placebo plus letrozole (PALOMA-2) or 2:1 to receive palbociclib plus fulvestrant or placebo plus fulvestrant (PALOMA-3). All

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