Palbociclib combined with aromatase inhibitors in women ≥75 years with oestrogen receptor positive, human epidermal growth factor receptor 2 negative advanced breast cancer: A real-world multicentre UK study

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Background

Breast cancer accounts for 21% of all cancer diagnoses in women aged ≥75 years. The older population is under-represented in clinical trials; thus, real-world data in this patient group is critical to guide management. In this large-scale UK-wide real-world study, we evaluated the tolerability and efficacy of palbociclib combined with an aromatase inhibitor (AI) for first-line treatment of advanced oestrogen receptor positive (ER+ve), human epidermal growth factor receptor 2 negative (HER2-ve) breast cancer in elderly patients.

Methods

14 cancer centres participated in this national retrospective study. Patients aged ≥75 years who received at least one cycle of palbociclib combined with an AI for first-line treatment of advanced ER+ve/HER2-ve breast cancer were eligible. Data included baseline demographics, co-morbidities, metastatic disease burden, toxicities, dose reductions and delays, response to treatment and in-patient secondary care burden. Multivariable Cox regression was used to assess independent predictors of progression-free survival (PFS).

Results

Baseline demographics:

- 276 patients met the eligibility criteria.
- Median age was 78 years (range 75 – 92).
- 19.6% had an ECOG performance status of 2 or more.
- Age-adjusted Charlson Comorbidity Index (ACCI) was used to measure comorbidity burden with higher score reflecting higher comorbidity burden.
- 53.1% of patients had visceral metastases. 33.7% had bone-only disease.
- 88% of patients started palbociclib at the standard dose of 125mg.
- The median duration of treatment was 15.7 months (range 1 – 43.4 months).
- **Figure 1** shows the starting doses of palbociclib and how this relates to baseline ACCI scores.

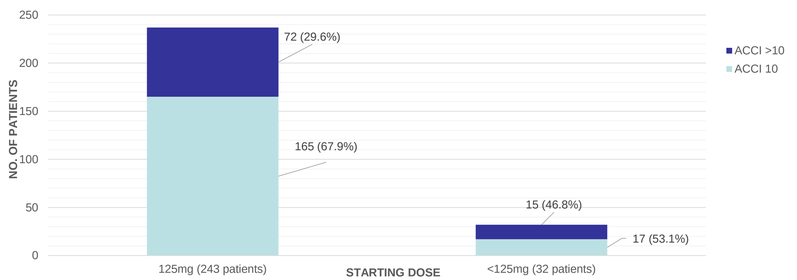

Figure 1. Starting dose of palbociclib and baseline ACCI scores

Results

Toxicity:

- **Table 1** summarises the frequency of treatment-related adverse events and grading as per CTCAE version 5.0 in this real-world population and comparison to adverse events seen in patients aged ≥75 years included in the PALOMA trials.

	Real-world UK data - age ≥75 (n= 276)		PALOMA trials – age ≥75 * (n=83)	
	All grades - n (%)	Grade ≥3 - n (%)	All grades - n (%)	Grade ≥3 - n (%)
Neutropenia	223 (80.8)	128 (46.4)	75 (90.4)	61 (73.5)
Fatigue	148 (53.6)	10 (3.6)	31 (37.3)	6 (7.2)
Anaemia	125 (45.3)	8 (2.9)	36 (43.4)	7 (8.4)
Thrombocytopenia	102 (37.0)	7 (2.5)	21 (25.3)	2 (2.4)
Nausea	61 (22.1)	4 (1.4)	25 (30.1)	0
Stomatitis	59 (21.4)	1 (0.4)	16 (19.3)	0
Anorexia	53 (19.2)	0	23 (27.7)	2 (2.4)
Diarrhoea	51 (18.5)	3 (1.1)	19 (22.9)	0
Transaminitis**	32 (11.6)	4 (1.4)		
Vomiting	24 (8.7)	1 (0.4)	16 (19.3)	0

* Pooled analysis from PALOMA-1,2 and 3 trials by Rugo et al. PALOMA trials used CTCAE version 3.0.
**The frequency of transaminitis was not reported in the pooled analysis of PALOMA trials.

Table 1. Treatment- related adverse events

- 50.7% of patients required a dose reduction. The most common reasons for dose reduction were neutropenia (54.3%), fatigue (21.4%) and thrombocytopenia (5%).
- 59.3% required at least one dose delay. The most common reasons for dose delay were neutropenia (66.3%), infection (10.4%) and fatigue (6.7%).
- 26.1% discontinued treatment due to toxicity. 9.6% of patients required hospital admission due to toxicity. Only 2.2% of patients had febrile neutropenia.

Efficacy:

- **Figure 2** shows the PFS and OS rates at 12 and 24 months.
- The best radiological response was:
  - complete response (CR) in 2%,
  - partial response (PR) in 32.9%,
  - stable disease (SD) in 54.9%.
- The clinical benefit rate (CR+PR+SD) at 24 weeks was 87%.

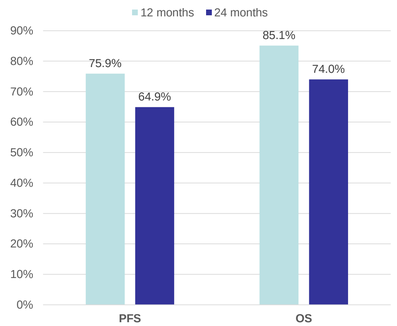

Figure 2. PFS and OS rates at 12 and 24 months

Results

Multivariable Cox regression identified increased ECOG performance status, fewer dose delays, increased ACCI and higher number of metastatic sites to be independent adverse predictors of PFS. Baseline ACCI was an independent predictor of onset and severity of neutropenia. **Figure 3** shows Kaplan-Meier plot of PFS with patients grouped according to whether they had a dose delay or not.

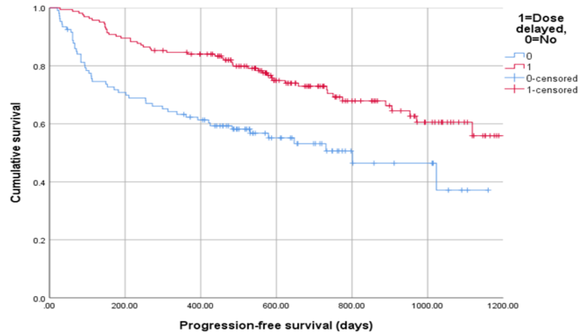

Figure 3. Kaplan-Meier plot of PFS and association with dose delays

Conclusion

This largest known dataset of palbociclib tolerability and efficacy in patients aged ≥75 years shows that this is an effective therapy that is well tolerated and appropriately managed with dose delays/reductions resulting in very low levels of clinically significant toxicity requiring hospital admission. Efficacy outcomes were consistent despite higher rates of treatment discontinuation and dose reduction compared to that seen in trial data. ACCI was found to be an independent significant predictor of PFS as well as the onset and severity of neutropenia which highlights the importance of comorbidity and frailty assessments in decision making in the elderly population.

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-S El Badri has no conflicts of interest to declare.

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