Real world evidence of systemic therapy in hormone receptor positive advanced breast cancer (HR+ ABC) in Australia – ARORA Registry

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Background

- The incorporation of cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) into first line (1L) systemic treatment for patients with HR+ ABC is now standard practice and leads to improved survival.
- Patients routinely seen in clinical practice often differ to those enrolled in trials, such as older age, presence of comorbidities and an ECOG performance status of 2 or higher.
- In an Australian context, there is a paucity of data on the uptake of standard therapies in the treatment of HR+ ABC and their associated toxicities in the real-world setting.

Methods

- Data for patients aged ≥18 years and diagnosed with histologically confirmed metastatic HR+ HER2- breast cancer after 1 Jan 2020 was extracted from ARORA (Advanced Hormone Receptor Positive Breast Cancer Registry in Australia), a prospective multi-site Australian study.
- Prospective data is captured on patient characteristics, disease course, systemic therapy sequencing and treatment outcomes in clinical practice.
- Baseline demographics, clinicopathologic factors and treatment outcomes were analysed with statistical significance denoted as p<0.05.

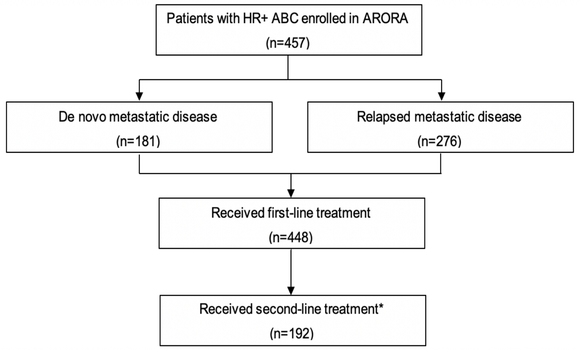


Figure 1. Consort diagram. *At time of database lock on 19 May 2025.

Results

- 457 patients were enrolled from 17 Australian sites.
- Median follow-up time was 38.8 months.
- Median age was 63.6 years (21.9% ≥75 years). 65.6% were ECOG 0-1.
- 2.8% had a BRCA1/2 pathogenic variant.
- 44.2% had liver or lung metastases. 19% had bone-only disease. 2.8% had brain metastases or leptomeningeal disease.

Characteristic	Patients – no. (%) *N* = 274
Treatment for early-stage disease	
Neoadjuvant chemotherapy	25 (9.1%)
Adjuvant chemotherapy	128 (46.7%)
Adjuvant endocrine therapy	206 (75.2%)
Time from end of adjuvant therapy to metastatic diagnosis, months (95% CI)	**12.5 (2.1–21.5)**
Relapse within 12 months	102 (37.2%)
Relapse between 12-24 months	22 (8%)
Relapse after 24 months	82 (29.9%)
Did not receive adjuvant ET	68 (24.8%)

Table 1. Characteristics of patients with relapsed metastatic disease. Two patients have been excluded for lack of data.

First-line treatment

- 9 patients (2%) did not receive any systemic therapy for HR+ ABC.
- Of the 448 patients who received 1L therapy, 338 (75.4%) received CDK4/6i + ET, 68 (15.2%) received ET without a CDK4/6i and 42 (9.4%) received chemotherapy.
- 1L ET without a CDK4/6i tended to be an AI (12.1%) – primarily letrozole (9.4%) – or fulvestrant (1.6%), with or without a GnRH agonist.
- Chemotherapy was often capecitabine-based (3.3%), nab-paclitaxel (2.5%) or an anthracycline plus cyclophosphamide + a taxane (1.2%).

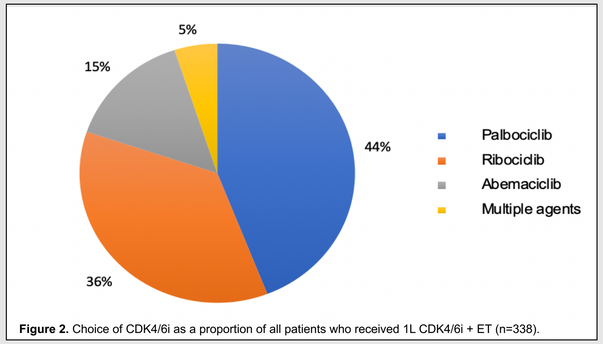


Figure 2. Choice of CDK4/6i as a proportion of all patients who received 1L CDK4/6i + ET (n=338).

Compared to 1L CDK4/6i + ET, those who received **1L ET without CDK4/6i**:
- Were older (mean 74.8 vs 62.2 years, 60.3% vs 16.3% ≥75, p<0.001).
- Had poorer performance status (44.1% vs 8.9% ECOG ≥2, p<0.001).
- Had more co-morbidities (76.5% vs 38.8% Charlson index ≥3, p<0.001).

Conversely, those who received **1L chemotherapy**:
- Were younger (mean 56.1 vs 62.2 years, 4.8% vs 16.3% ≥75, p<0.001).
- Had fewer co-morbidities (19% vs 38.8% Charlson index ≥3, p=0.015).
- Were more likely to have a BRCA1/2 mutation (9.5% vs 2.7%, p=0.031).
- Were more likely to have liver metastases (47.6% vs 18.9%, p<0.001).

Reason for patients stopping first-line treatment	CDK4/6i + ET *N* = 338	ET without a CDK4/6i *N* = 68	Chemotherapy *N* = 42	P value a. CDK4/6i + ET vs ET without a CDK4/6i b. CDK4/6i + ET vs chemotherapy
Progressive disease	117 (34.6%)	26 (38.2%)	19 (45.2%)	a. 0.57 b. 0.18
Toxicity	61 (18%)	1 (1.5%)	5 (11.9%)	a. 0.0081 b. 0.33
Patient request	11 (3.3%)	8 (11.8%)	1 (2.4%)	a. 0.0046 b. 0.76

Table 2. Reasons for stopping first-line treatment of HR+ ABC.

Toxicity	Palbociclib + ET *N* = 149	Ribociclib + ET *N* = 122	Abemaciclib + ET *N* = 50	P value
No toxicity	41 (27.5%)	24 (19.7%)	8 (16%)	0.14
Any toxicity	105 (70.5%)	97 (79.5%)	42 (84%)	0.076
Neutropaenia	69 (46.3%)	50 (41%)	10 (20%)	0.003
Anaemia	10 (6.7%)	13 (10.7%)	9 (18%)	0.082
Thrombocytopaenia	11 (7.4%)	5 (4.1%)	2 (4%)	0.44
Diarrhoea	10 (6.7%)	12 (9.8%)	30 (60%)	<0.001
Nausea/vomiting	27 (18.1%)	34 (27.9%)	11 (22%)	0.16
Neuropathy	2 (1.3%)	4 (3.3%)	0 (0%)	0.2
Skin	3 (2%)	11 (9%)	2 (4%)	0.029
Stomatitis	7 (4.7%)	1 (0.8%)	0 (0%)	0.033
Pneumonitis	1 (0.7%)	(0.8%)	1 (2%)	0.74
Hepatotoxicity	1 (0.7%)	7 (5.7%)	3 (6%)	0.023
Cardiotoxicity	0 (0%)	6 (5%)	0 (0%)	0.0027
Fatigue	15 (10%)	10 (8%)	6 (12%)	0.73

Table 3. Toxicities experienced by patients who received first-line combination therapy with CDK4/6 inhibitors. 17 patients were excluded due to occurrence of switching between multiple agents.

First-line progression-free survival (PFS)

- Median PFS for all patients was 27.8 months (95% CI 24.2-33.9).
- **Median PFS on 1L CDK4/6i + ET was 32.1 months** (95% CI 26.5-41.6). This was longest with palbociclib (37.1 months), followed by ribociclib (34.2 months) and abemaciclib (18.4 months).
- In comparison, median PFS on ET without CDK4/6i was 21.9 months (HR 1.39, 95% CI 0.93-2.09, p=0.11).
- In comparison, median PFS on chemotherapy was 12 months (HR 2.74, 95% CI 1.80-4.15, p<0.001).

Second-line (2L) treatment

- At time of database lock, 187 of 335 patients (55.8%) had moved to 2L.
- Of these, 74 (39.6%) received chemotherapy with a median duration of treatment of 4.83 months (95% CI 4.04–5.88). 63 (33.7%) received ET without a CDK4/6i with a median duration of treatment of 3.91 months (95% CI 3.22–7.13).

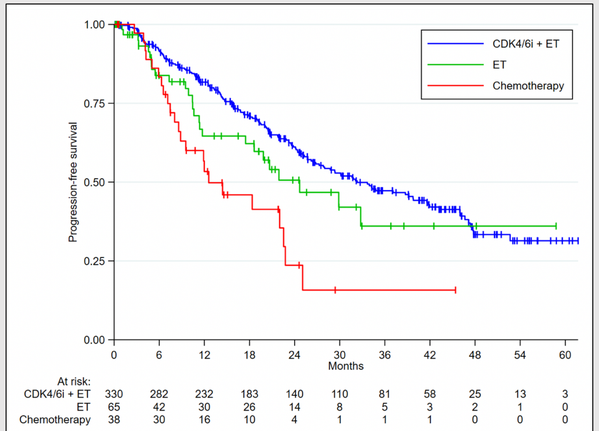


Figure 3. Progression-free survival by first-line treatment for HR+ ABC.

Conclusion

- While CDK4/6i + ET is recommended as 1L treatment of HR+ ABC, three-quarters of routinely treated patients received this combination in an Australian context.
- A substantial minority of patients received ET without a CDK4/6i or chemotherapy alone.
- Age, ECOG, co-morbidity burden and presence of visceral disease remain major determinants of treatment choice.
- Real-world CDK4/6i toxicity profiles are consistent with trial data.
- In the 1L setting, median PFS is highest with CDK4/6i + ET and real-world outcomes appear to be consistent with trial data.
- In the 2L setting, chemotherapy is preferred in over a third of patients. However, this was prior to newer agents such as capivasertib being accessible to patients.
- Overall survival data is immature.

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