HR+, HER2- Metastatic Breast Cancer:
Treatment Paradigm for Patients Who Progress on 1L Standard of Care

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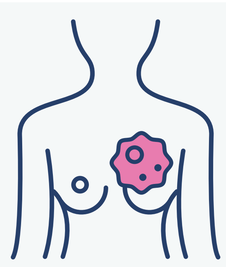
Standard of care for metastatic disease

For many patients with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2-) metastatic breast cancer (MBC), the current 1L standard of care includes **endocrine therapy (ET) + cyclin-dependent kinase 4/6 inhibitor (CDK4/6i)**[1,2]

Although treatment with ET + CDK4/6i has led to improvements in patient outcomes, patients with metastatic disease inevitably experience **disease progression**. Progression is often due to **resistance mechanisms**[3,4]

Unmet needs for patients who progress on 1L treatment

For these patients, no consensus on the optimal 2L treatment strategy has been reached[1-3]



HR+, HER2- MBC with progression on ET ± CDK4/6i

2L treatment options

ET
AIs | SERDs | SERMs

Targeted therapy
AKTi | CDK4/6i | mTORi | PARPi | PI3Ki

Non-targeted therapy
ADCs | Chemotherapy

The choice and efficacy of each 2L treatment may be impacted by various factors, including treatment history, duration of response to previous ET, breast cancer disease characteristics, presence of actionable biomarkers, risk of organ failure, and patient preference[1]

Clinical research to support treatment decisions in the 2L setting

For patients with HR+, HER2- MBC who have progressed after 1L ET + CDK4/6i, treatment with a subsequent line of therapy has resulted in a shorter median progression-free survival (mPFS) when compared with patients who had no prior therapy.[5-11] Treatment outcomes for 2L therapies are poor and remain an area of unmet need. Clinical research is ongoing

Trial	Treatment After Prior ET + CDK4/6i	Hazard Ratio (95% CI)	mPFS (mo)
Phase 3			
CAPItello-291[12]	Capivasertib + ET vs. PBO + ET	0.59 (0.48-0.72)	5.5 vs. 2.6
EMERALD[a,13]	Elacestrant vs. ET, all patients	0.69 (0.54-0.88)	2.79 vs.1.91
	Elacestrant vs. ET, patients with *ESR1*-mutated tumors	0.52 (0.36-0.74)	4.14 vs. 1.87
Phase 2			
MAINTAIN[8]	Ribociclib + ET vs. PBO + ET	0.57 (0.39-0.85)	5.29 vs. 2.76
SERENA-2[14]	Camizestrant (75 mg) vs. ET	0.49 (0.31-0.75)[b]	5.5 vs. 2.1
	Camizestrant (150 mg) vs. ET	0.68 (0.44-1.04)[b]	3.8 vs. 2.1
ELAINE 1[15]	Lasofoxifene vs. ET, patients with *ESR1*-mutated tumors	0.70 (0.43-1.13)	5.6 vs. 3.7

[a]Patients received at least 6 mo of prior CDK4/6i in the metastatic setting.
[b]Hazard ratios adjusted for liver/lung metastases. SERENA-2 reports hazard ratios with 90% CI.
These data are intended to provide a summary of ongoing clinical trials in this setting and are not intended to make any cross-trial comparisons.

The current lack of consensus for treatment after progression on an ET + CDK4/6i is a gap in the management of patients with HR+, HER2- MBC; additional treatment strategies are desired to support patients in the 2L metastatic setting[3]

1L=first line; 2L=second line; ADC=antibody drug conjugate; AI=aromatase inhibitor; AKTi=serine/threonine protein kinase inhibitor; mTOR=mammalian target of rapamycin; PARPi=poly (ADP-ribose) polymerase inhibitor; PBO=placebo; PI3Ki=phosphoinositide 3-kinase inhibitor; SERD=selective estrogen receptor degrader; SERM=selective estrogen receptor modulator.

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