Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1: Post-Progression Treatments received by patients with HR+ HER2-MBC who participated in the seminal 1L and 2L CDK4/6i trials

Trial	CDK4/6i & ET	Study Phase & Line of Treatment	Patient Population	Post Progression Therapy
PALOMA 1 Ref: Finn et al., *Cancer Res* (2016)	Palbociclib (P) Letrozole (L)	II; 1L	Postmenopausal women	50% pts in P+L arm vs. 64% in L arm received ET. 60% pts in P+L arm vs. 66% in L arm received CT.
PALOMA 2 Ref: Rugo et al., Breast Cancer Res and Treat (2019)	Palbociclib (P) Letrozole (L)	III;1L	Postmenopausal women	P+ L delayed initiation of 1ST subsequent CT. ET: most common 1ST PDT in pts on P+L vs. PL + L (60.8% and 58.0%, respectively), followed by CT (36.6% and 34.0%)
MONARCH 3 Ref: Johnston et al. NPJ Breast Cancer 2021.	Abemaciclib (Ab) Anastrozole (A) or Letrozole (L)	III;1L	Postmenopausal women	Most received ET as 1st PDT (n = 132, 40.2% in Ab arm vs n = 88, 53.3% in PL arm), followed by CT (n = 39, 11.9%) in Ab arm vs n = 30, 18.2% in PL arm), targeted therapy (n = 35, 10.7% in Ab arm vs n = 32, 19.4% in PL arm), and other therapies (n = 13, 4.0% in Ab arm vs n = 13, 7.9% in the PL arm).

				F (15.5% in the Ab arm vs 27.9% in the PL arm) and L (11.0% in A arm vs 8.5% in PL arm) were the most common ET administered after progression
MONALEESA 2 Ref: Blackwell et al., *Cancer Res* 2018	Ribociclib (R) Letrozole (L)	III;1L	Postmenopausal women	Most common 1st PDT was single-agent ET in 90 (44.3%) vs 87 (35.4%) pts who discontinued R + L vs PL + L. CT was the most common 2nd PDT in 20 (9.9%) vs 36 (14.6%) pts. CT alone was the 1st PDT after MONALEESA-2 discontinuation in 32 (15.8%) vs 55 (22.4%) pts on R + L vs PL + L.
MONALEESA 7 Ref: Lu et al., Clin Cancer Res 2022	Ribociclib (R) (NSAI; L or A) + goserelin or Tam	III;1L	Pre- and perimenopausal women - Previous ET permitted in (neo)adjuvant setting (CT also permitted in the (neo)adjuvant setting or for advanced BC)	Subsequent antineoplastic therapies following discontinuation balanced between R (77%) and PL (78%) arms. Use of CDK4/6i after discontinuation was higher with PL

				(26%) versus R (13%). Time to 1ST CT was significantly delayed with R versus PL.
PALOMA 3 Ref: Turner et al., Cancer Res 2017	Palbociclib (P) Fulvestrant (F)	III;2L -2: 1 Randomization	Pre and postmenopausal women	Most commonly used post progression tx were capecitabine (n=57 [28.8%]), paclitaxel (n=22 [11.1%]), and exemestane (n=34 [17.2%]). Median time to subsequent CT longer with P + F (252 d) vs. PL + F (132 d). Proportionally fewer pts in P + F vs. PL + F arm discontinued next line tx (33% vs 46%), indicating P does not adversely affect efficacy of PDT
MONARCH 2 Ref: Neven et al., Breast Cancer Research 2021	Abemaciclib (Ab) Fulvestrant (F)	III;2L 2:1 Randomization	-Pre and post Menopausal women	41 (56.9%) pts in Ab +F arm vs. 35 (83.3%) pts in PL+ F arm received PDT. CT received by 60 pts (n = 34, 47.2% vs n = 26, 61.9%) in Ab + F and PL + F

				arms, respectively,) any time PD. ET received by 48 pts (*n* = 26, 36.1%) in Ab + F arm vs *n* = 22, 52.4% in PL+ F arm), while 41 pts received targeted therapy (*n* = 19, 26.4% in Ab + F arm vs *n* = 22, 52.4% in PL + F arm), and 17 received other therapies (*n* = 9, 12.5% pts in Ab + F arm vs *n* = 8, 19% in PL + F arm). Among those who received targeted therapies, 15 received CDK4/6i(s) as PDT (*n* = 5, 6.9% pts in A + F arm vs *n* = 10, 23.8% in PL + F arm).
MONALEESA 3 Ref: Slamon et al. JCO, 2021.	Ribociclib (R) Fulvestrant (F)	III;2L -2:1 Randomization	Men and post menopausal women	Among pts who discontinued study tx, 81.9% and 86.4% received PDT, while 14.0% and 30.0% received a CDK4/6i as any subsequent line in the R vs PL arms, respectively.

				Time to 2nd disease progression prolonged- 34.6 months with F to 50.7 with R+ F(HR = 0.64; 95% CI = 0.49–0.84). Time to CT also delayed (HR = 0.57; 95% CI = 0.42–0.79).
PALOMA 4	Palbociclib (P) Letrozole (L)	III; 1L -1:1 Randomization	Postmenopausal Asian women	N/A

Legend: A- anastrozole; Ab- abemaciclib; BC- breast cancer; CT- chemotherapy; ET-endocrine therapy; pts- patients; 1L- 1st line; 2L- 2nd line; Tx- treatment; NSAI- non-steroidal aromatase inhibitor; TAM- tamoxifen; PD- post discontinuation; PDT- post discontinuation therapy

eTable 2: Hazard Ratios for Overall Survival for Asian vs. Non-Asian Patients Across the CDK4/6i HR+ HER2- Metastatic Breast Cancer Trials in the 1st line metastatic setting

Trial	Hazard Ratio Asian patients	Hazard Ratio Non-Asian patients
PALOMA 1	unknown	0.9 (overall)
PALOMA 2	0.48	0.58
MONARCH 3	0.30	0.69
MONALEESA 2	0.37	0.614
MONALEESA 7	0.40	0.66
PALOMA 3	0.485	0.50
MONARCH 2	0.515	0.620
MONALEESA 3	0.30	0.69
PALOMA 4	0.68	N/A