

Clinical trials of CDK (cyclin-dependent kinase) inhibitor for advanced breast cancer (metastatic) in HR+ HER2-

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1 CDK4/6 inhibitor

Trial	Treatments	Patients	Trials design and methods
palbociclib + exemestane vs capecitabine			
PEARL <i>ongoing</i> [NCT02028507] n=NA follow-up:	Palbociclib, 125 mg, orally once daily on Day 1 to Day 21 followed by 7 days off treatment given as every 28 days cycles in combination with Exemestane, 25 mg, orally once daily (continuously). versus Capecitabine, 1,250 mg/m ² twice daily for 2 weeks followed by a 1 week rest period, given as 3 weeks cycles. Capecitabine can be administered at a dose of 1,000 mg/m ² twice daily for 2 weeks followed by a 1 week of rest period, given as 3 weeks cycles, in	Hormonal Receptor (HR) Positive/HER2 Negative Metastatic Breast Cancer (MBC) Patients With Resistance to Non-steroidal Aromatase Inhibitors	open label HUNGARY
palbociclib + fulvestrant vs fulvestrant alone			
PALOMA 3 , 2015 [NCT01942135] n=347/174 follow-up:	palbociclib (125 mg per day orally for 3 weeks, followed by 1 week off) and fulvestrant (500 mg intramuscularly per standard of care every 14 days for the first three injections and then every 28 days) versus placebo and fulvestrant	women with HR+, HER2 negative metastatic breast cancer whose disease has progressed after prior endocrine therapy	Parallel groups double-blind 17 countries
ribociclib (LEE011)+ fulvestrant vs fulvestrant alone			
MONALEESA-3 <i>ongoing</i> [NCT02422615] n=NA follow-up:	Ribociclib 600mg daily oral (days 1 to 21 in a 28-day Cycle) in combination with fulvestrant 500mg i.m. injections every 28 days (Cycle n Day 1) with 1 additional dose on Day 15 of Cycle 1 versus placebo + fulvestrant 500mg i.m. injections every 28 days (Cycle n Day 1) with 1 additional dose on Day 15 of Cycle 1	post-menopausal women with advanced breast cancer	Parallel groups double-blind
palbociclib + letrozole vs letrozole alone			

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Trial	Treatments	Patients	Trials design and methods
PALOMA-4 <i>ongoing</i> [NCT02297438] n=NA follow-up:	Palbociclib, 125mg, orally once daily on Day 1 to Day 21 of every 28-day cycle followed by 7 days off treatment in combination with Letrozole, 2.5mg, orally once daily (continuously) versus Placebo, 125mg, orally once daily on Day 1 to Day 21 of every 28-day cycle followed by 7 days off treatment in combination with Letrozole, 2.5mg, orally once daily (continuously.)	Asian Postmenopausal Women With ER+/HER2- Advanced Breast Cancer	Parallel groups double-blind china
palbociclib + letrozole vs letrozole alone			
PALOMA-2 , 2016 [NCT01740427] n=666 follow-up:	PD-0332991, 125mg, orally once daily on Day 1 to Day 21 of every 28-day cycle followed by 7 days off treatment in combination with Letrozole, 2.5mg, orally once daily (continuously.) versus Placebo, 125mg, orally once daily on Day 1 to Day 21 of every 28-day cycle followed by 7 days off treatment in combination with Letrozole, 2.5mg, orally once daily (continuously)	postmenopausal women with ER(+)/HER2(-) advanced breast cancer who have not received prior systemic anti cancer therapies for their advanced/metastatic disease	Parallel groups double-blind USA
PALOMA 1/TRIO-18 , 2015 [NCT00721409] n=84/81 follow-up:	continuous oral letrozole 2.5 mg daily plus oral palbociclib 125 mg, given once daily for 3 weeks followed by 1 week off over 28-day cycles versus continuous oral letrozole 2.5 mg daily	postmenopausal women with advanced oestrogen receptor-positive and HER2-negative breast cancer who had not received any systemic treatment for their advanced disease	Parallel groups open-label
ribociclib (LEE011) + letrozole vs letrozole alone			
MONALEESA-2 , 2016 [NCT01958021] n=334/334 follow-up: 18 months	ribociclib (600 mg per day on a 3-weeks-on, 1-week-off schedule) plus letrozole (2.5 mg per day) versus placebo + letrozole	postmenopausal women with HR-positive, HER2-negative recurrent or metastatic breast cancer who had not received previous systemic therapy for advanced disease	Parallel groups double-blind 29 countries
Abemaciclib +nsAI vs nsAI			
MONARCH 3 , 2017 [NCT02246621] n=493 follow-up:	Abemaciclib (LY2835219) + nonsteroidal aromatase inhibitors (nSAI) versus Placebo + NSAI	Postmenopausal Women With Hormone Receptor-Positive, HER2-Negative Locoregionally Recurrent or Metastatic Breast Cancer With No Prior Systemic Therapy in This Disease Setting	Parallel groups double-blind
ribociclib (LEE011) + nsAI/TAM gos vs nsAI/TAM + gos			

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Trial	Treatments	Patients	Trials design and methods
MONALEESA-7 <i>ongoing</i> [NCT02278120] n=NA follow-up:	LEE011 600 mg daily oral (3 weeks on/ 1 week off) in Combination With Tamoxifen and Goserelin or a Non-steroidal Aromatase Inhibitor (NSAI) and Goserelin versus placebo in Combination With Tamoxifen and Goserelin or a Non-steroidal Aromatase Inhibitor (NSAI) and Goserelin	premenopausal women with HR positive, HER2 negative advanced breast cancer	Parallel groups double-blind

References

PEARL, 0:

PALOMA 3, 2015:

Turner NC, Ro J, Andr F, Loi S, Verma S, Iwata H, Harbeck N, Loibl S, Huang Bartlett C, Zhang K, Giorgetti C, Randolph S, Koehler M, Cristofanilli M Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. *N Engl J Med* 2015 Jul 16;373:209-219 [26030518] [10.1056/NEJMoa1505270](https://doi.org/10.1056/NEJMoa1505270)

Loibl S, Turner NC, Ro J, Cristofanilli M, Iwata H, Im SA, Masuda N, Loi S, Andr F, Harbeck N, Verma S, Folked E, Theall KP, Hoffman J, Zhang K, Bar Palbociclib Combined with Fulvestrant in Premenopausal Women with Advanced Breast Cancer and Prior Progression on Endocrine Therapy: PALOMA-3 Results. *Oncologist* 2017;: [28652278]

Verma S, Bartlett CH, Schnell P, DeMichele AM, Loi S, Ro J, Colleoni M, Iwata H, Harbeck N, Cristofanilli M, Zhang K, Thiele A, Turner NC, Rugo HS Palbociclib in Combination With Fulvestrant in Women With Hormone Receptor-Positive/HER2-Negative Advanced Metastatic Breast Cancer: Detailed Safety Analysis From a Multicenter, Randomized, Placebo-Controlled, Phase III Study (PALOMA-3). *Oncologist* 2016;21:1165-1175 [27368881]

Harbeck N, Iyer S, Turner N, Cristofanilli M, Ro J, Andr F, Loi S, Verma S, Iwata H, Bhattacharyya H, Puyana Theall K, Bartlett CH, Loibl S Quality of life with palbociclib plus fulvestrant in previously treated hormone receptor-positive, HER2-negative metastatic breast cancer: patient-reported outcomes from the PALOMA-3 trial. *Ann Oncol* 2016;27:1047-54 [27029704]

Cristofanilli M, Turner NC, Bondarenko I, Ro J, Im SA, Masuda N, Colleoni M, DeMichele A, Loi S, Verma S, Iwata H, Harbeck N, Zhang K, Theall KP, Jiang Y, Bartlett CH, Koehler M, Slamon D Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. *Lancet Oncol* 2016;17:425-39 [26947331]

MONALEESA-3, 0:

PALOMA-4, 0:

PALOMA-2, 2016:

Finn RS, Martin M, Rugo HS, Jones S, Im SA, Gelmon K, Harbeck N, Lipatov ON, Walshe JM, Moulder S, Gauthier E, Lu DR, Randolph S, Diras V, Slamon DJ Palbociclib and Letrozole in Advanced Breast Cancer. *N Engl J Med* 2016;375:1925-1936 [27959613]

PALOMA 1/TRIO-18, 2015:

Finn RS, Crown JP, Lang I, Boer K, Bondarenko IM, Kulyk SO, Ettl J, Patel R, Pinter T, Schmidt M, Shparyk Y, Thummala AR, Voytko NL, Fowst C, Huang X, Kim ST, Randolph S, Slamon DJ The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. *Lancet Oncol* 2015;16:25-35 [25524798]

Bell T, Crown JP, Lang I, Bhattacharyya H, Zanotti G, Randolph S, Kim S, Huang X, Huang Bartlett C, Finn RS, Slamon D Impact of palbociclib plus letrozole on pain severity and pain interference with daily activities in patients with estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer as first-line treatment. *Curr Med Res Opin* 2016;32:959-65 [26894413]

MONALEESA-2, 2016:

Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Paluch-Shimon S, Campone M, Blackwell KL, Andr F, Winer EP, Janni W, Verma S, Conte P, Arteaga CL, Cameron DA, Petrakova K, Hart LL, Villanueva C, Chan A, Jakobsen E, Nusch A, Burdaeva O, Grischke E Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. *N Engl J Med* 2016 Oct 7;: [27717303] [10.1056/NEJMoa1609709](https://doi.org/10.1056/NEJMoa1609709)

Sonke GS, Hart LL, Campone M, Erdkamp F, Janni W, Verma S, Villanueva C, Jakobsen E, Alba E, Wist E, Favret AM, Bachelot T, Hegg R, Wheatley-Price P, Souami F, Sutradhar S, Miller M, Germa C, Burris HA Ribociclib with letrozole vs letrozole alone in elderly patients with hormone receptor-positive, HER2-negative breast cancer in the randomized MONALEESA-2 trial. *Breast Cancer Res Treat* 2017;: [29058175]

MONARCH 3, 2017:

Sledge GW Jr, Toi M, Neven P, Sohn J, Inoue K, Pivot X, Burdaeva O, Okera M, Masuda N, Kaufman PA, Koh H, Grischke EM, Frenzel M, Lin Y, Barriga S, Smith IC, Bourayou N, Llombart-Cussac A MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2- Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. *J Clin Oncol* 2017;:JCO2017737585 [28580882]

Goetz MP, Toi M, Campone M, Sohn J, Paluch-Shimon S, Huober J, Park IH, Trdan O, Chen SC, Manso L, Freedman OC, Garnica Jaliffe G, Forrester T, Frenzel M, Barriga S, Smith IC, Bourayou N, Di Leo A MONARCH 3: Abemaciclib As Initial Therapy for Advanced Breast Cancer. *J Clin Oncol* 2017;:JCO2017756155 [28968163]

MONALEESA-7, :

2 About TrialResults-center.org

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