

Clinical Updates From San Antonio

HR+/HER2- Breast Cancer: CDK4/6 Inhibitors

This activity is provided by Integrity Continuing Education, Inc.

This program has been supported by an independent educational grant from Gilead Sciences, Inc.

This activity is supported by an educational grant from Lilly.

Phase 3 Outcomes With Adjuvant CDK4/6 Inhibitors Plus Endocrine Therapy for HR+/HER2- Early Breast Cancer

Trial	monarchE	PALLAS
Intervention	ET ± abemaciclib	ET ± palbociclib
Population	HR+, HER2-, N+, high-risk EBC N=5637 (1:1)	HR+, HER2-, high-risk EBC N=5796 (1:1)
Median follow-up, months	42	31
IDFS*	HR 0.66 4-year: 85.8% vs 79.4%	HR 0.96 4-year: 84.2% vs 84.5%
DRFS	HR 0.66 4-year: 88.4% vs 82.5%	HR 1.05 4-year: 86.2% vs 87.8%
OS	HR 0.93 (95% CI 0.75, 1.15)	HR 1.32 4-year: 93.8% vs 95.2%
AEs grade ≥3 (≥5%), %	Neutropenia (19.6% vs 0.8%), diarrhea (7.8% vs 0.2%), infections (5.6% vs 3.0%)	Neutropenia (62% vs 0.4%), leukopenia (30% vs 0.1%)

*Primary endpoint.

AE, adverse event; CDK4/6, cyclin dependent kinase 4/6; CI, confidence interval; DRFS, distant relapse-free survival; EBC, early breast cancer; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; HR+, hormone receptor positive; IDFS, invasive disease-free survival; N+, lymph node positive; OS, overall survival.

Gnant M, et al. *J Clin Oncol*. 2022;40(3):282-293; Harbeck N, et al. *Ann Oncol*. 2022;33(2):227-228; Johnston S, et al. SABCs 2022. Abstract GS1-09; Johnston SRD, et al. *Lancet Oncol*. 2022; Rugo HS, et al. *Ann Oncol*. 2022;33(6):616-627; Toi M, et al. *Oncologist*. 2022.

GS1-09, Abemaciclib Plus Endocrine Therapy for HR+, HER2-, Node-positive, High-risk Early Breast Cancer (monarchE): Results From a Preplanned Overall Survival Interim Analysis, Including 4-Year Efficacy Outcomes

Patients (N=5637)

- HR+, HER2-, N+, high-risk EBC
- Completed definitive locoregional therapy

Cohort 1

- ≥4 pathologic pALN or 1-3 pALN and ≥1 of: tumor histologic grade 3 or tumor size ≥5 cm

Cohort 2

- 1-3 pALN and Ki-67 score ≥20%

Randomization

1:1

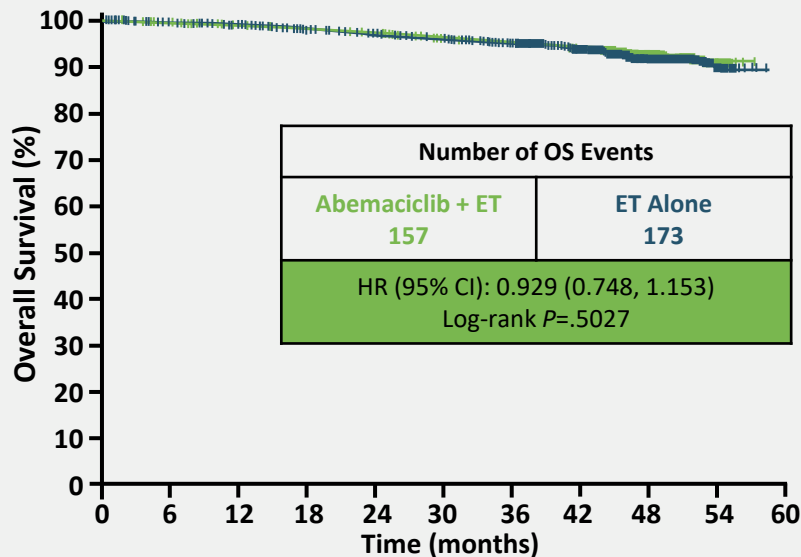
Stratification

- Prior chemo
- Menopausal status
- Region

Abemaciclib 150 mg BID + ET

ET

Johnston S, Toi M, O'Shaughnessy J, Rastogi P, Campone M, Neven P, Huang CS, Huober J, Jaliffe GG, Cicin I, Tolaney SM, Goetz MP, Rugo HS, Senkus E, Testa L, Del Mastro L, Shimizu C, Wei R, Shahir A, Munoz M, San Antonio B, Andre V, Harbeck N, Martín M



BID, twice daily; pALN, positive axillary lymph nodes.

Johnston S, et al. SABCs 2022. Abstract GS1-09; Tolaney SM, et al. *J Clin Oncol.* 2022;40(16_suppl):527; Royce M, et al. *J Clin Oncol.* 2022;40(11):1155-1162.

Phase 3 Outcomes With CDK4/6 Inhibitors Plus Fulvestrant for HR+/HER2- Advanced Breast Cancer

Trial	MONARCH 2	PALOMA-3	MONALEESA-3
Intervention	Fulvestrant ± abemaciclib	Fulvestrant ± palbociclib	Fulvestrant ± ribociclib
Population	HR+/HER2- aBC Progression during ET Pre-/perimenopausal N=669 (2:1)	HR+/HER2- aBC Progression on ET N=521 (2:1)	HR+/HER2- aBC ≤1 ET; no chemo N=726 (2:1)
Median follow-up, months	80	44.8	56.3
mPFS*, months	16.4 vs 9.3 HR 0.54; <i>P</i> <.000001	9.5 vs 4.6 HR 0.46; <i>P</i> <.0001	20.5 vs 12.8 HR 0.6; <i>P</i> <.001
mOS, months	45.8 vs 37.3 HR 0.78; <i>P</i> =.016	34.9 vs 28.0 HR 0.81; <i>P</i> =.09	53.7 vs 41.5 HR 0.73
ORR with measurable disease, %	48.1 vs 21.3 OR 3.42; <i>P</i> <.001	24.6 vs 10.9 OR 2.69; <i>P</i> =.0012	40.9 vs 28.7 <i>P</i> =.003
AEs grade ≥3 (≥5%), %	Neutropenia (31 vs 2), diarrhea (15 vs <1), leukopenia (12 vs 0), anemia (10 vs 1)	Neutropenia (65 vs 1), leukopenia (28 vs 1)	Neutropenia (53 vs 0), leukopenia (14 vs 0)

*Primary endpoint.

aBC, advanced breast cancer; mOS, median overall survival; mPFS, median progression-free survival; OR, odds ratio; ORR, objective response rate.
 Cristofanilli M, et al. *Lancet Oncol*. 2016;17(4):425-439; Slamon DJ, et al. *J Clin Oncol*. 2018;36(24):2465-2472; Slamon DJ, et al. *Ann Oncol*. 2021;32(8):1015-1024; Sledge Jr GW, et al. *J Clin Oncol*. 2017;35(25):2875-2884; Sledge Jr GW, et al. *JAMA Oncology*. 2020;6(1):116; Sledge Jr GW, et al. SABCs 2022. Abstract PD13-11; Turner NC, et al. *N Engl J Med*. 2018;379(20):1926-1936.

PD13-11, Final Overall Survival Analysis of Monarch 2 : A Phase 3 Trial of Abemaciclib Plus Fulvestrant in Patients With Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer

Patients (N=669)

- HR+, HER2- aBC
- Pre/peri- or postmenopausal
- ET resistant: relapsed on neoadjuvant or on/within 1 year of adjuvant ET; or progressed on 1L ET
- No chemo and ≤ 1 ET for aBC
- ECOG PS ≤ 1

Randomization

2:1

Primary Endpoint

- PFS

Secondary Endpoints

- OS, response, CBR, safety

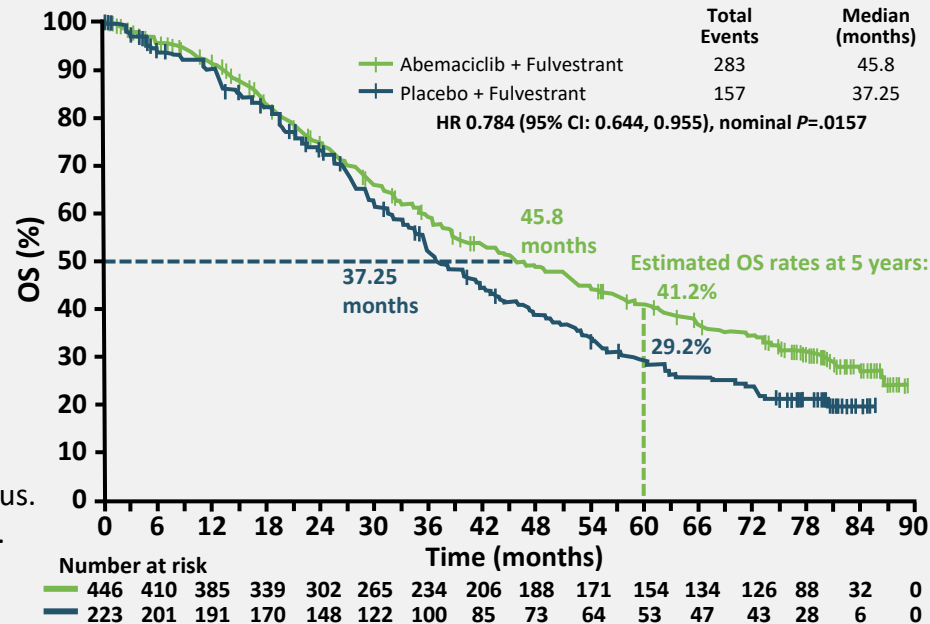
Stratification

- Metastatic site
- ET resistance

Abemaciclib 150 mg BID
Fulvestrant 500mg

Placebo BID
Fulvestrant 500 mg

Sledge Jr GW, Toi M, Neven P, Sohn JH, Inoue K, Pivot X, Okera M, Masuda N, Kaufman PA, Koh H, Grischke E-M, Conte P, Andre V, Bian Y, Shahir A, van Hal G, Llombart-Cussac A



1L, first line; CBR, clinical benefit rate; ECOG, Eastern Cooperative Oncology Group; mBC, metastatic breast cancer; PS, performance status. Neven P, et al. *J Clin Oncol*. 2018;36(15_suppl):1002.; Sledge GW, et al. *JAMA Oncology*. 2020;6(1):116; Sledge Jr GW, et al. SABCs 2022. Abstract PD13-11.

GS3-06, Palbociclib After CDK4/6i and Endocrine Therapy (PACE): A Randomized Phase II Study of Fulvestrant, Palbociclib, and Avelumab for Endocrine Pretreated ER+/HER2-Metastatic Breast Cancer

Patients (N=220)

- HR+, HER2- mBC
- Progression on CDK4/6i
- ≤1 prior lines of chemotherapy

Randomization
1:2:1

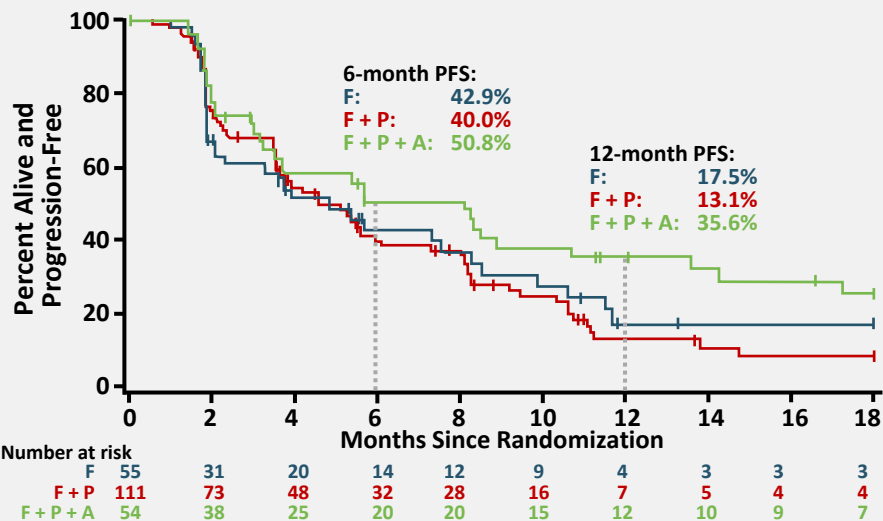
Fulvestrant (F)

F + palbociclib (P)

F + P + avelumab (A)

Oliveira M, Pominchuk D, Nowecki Z, Hamilton E, Kulyaba Y, Andabekov T, Hotko Y, Melkadze T, Nemsadze G, Neven P, Semegen Y, Vladimirov V, Zamagni C, Denys H, Forget F, Horvath Z, Nesterova A, Bennett M, Kirova B, Klinowska T, Lindemann JPO, Lissa D, Mathewson A, Morrow CJ, Traugottova Z, van Zyl R, Arkania E

	Patients	PFS Events	Median PFS, months (90% CI)	HR vs F (90% CI)	P-value
F	55	34	4.8 (2.1, 8.2)	—	—
F + P	111	79	4.6 (3.6, 5.9)	1.11 (0.74, 1.66)	P=.62
F + P + A	54	35	8.1 (3.2, 10.7)	0.75 (0.47, 1.20)	P=.23



CDK4/6i, cyclin dependent kinase 4/6 inhibitor.

Mayer EL, et al. *J Clin Oncol*. 2018;36(15_suppl):TPS1104;

Mayer EL, et al. SABCS 2022. Abstract GS3-06.