Supplementary Online Content

Sledge GW Jr, Toi M, Neven P, et al. The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor–positive, ERBB2-negative breast cancer that progressed on endocrine therapy—MONARCH 2: a randomized clinical trial. Published online September 29, 2019. *JAMA Oncol*. doi:10.1001/jamaoncol.2019.4782

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

eTable 1. Patient and Disease Baseline Characteristics

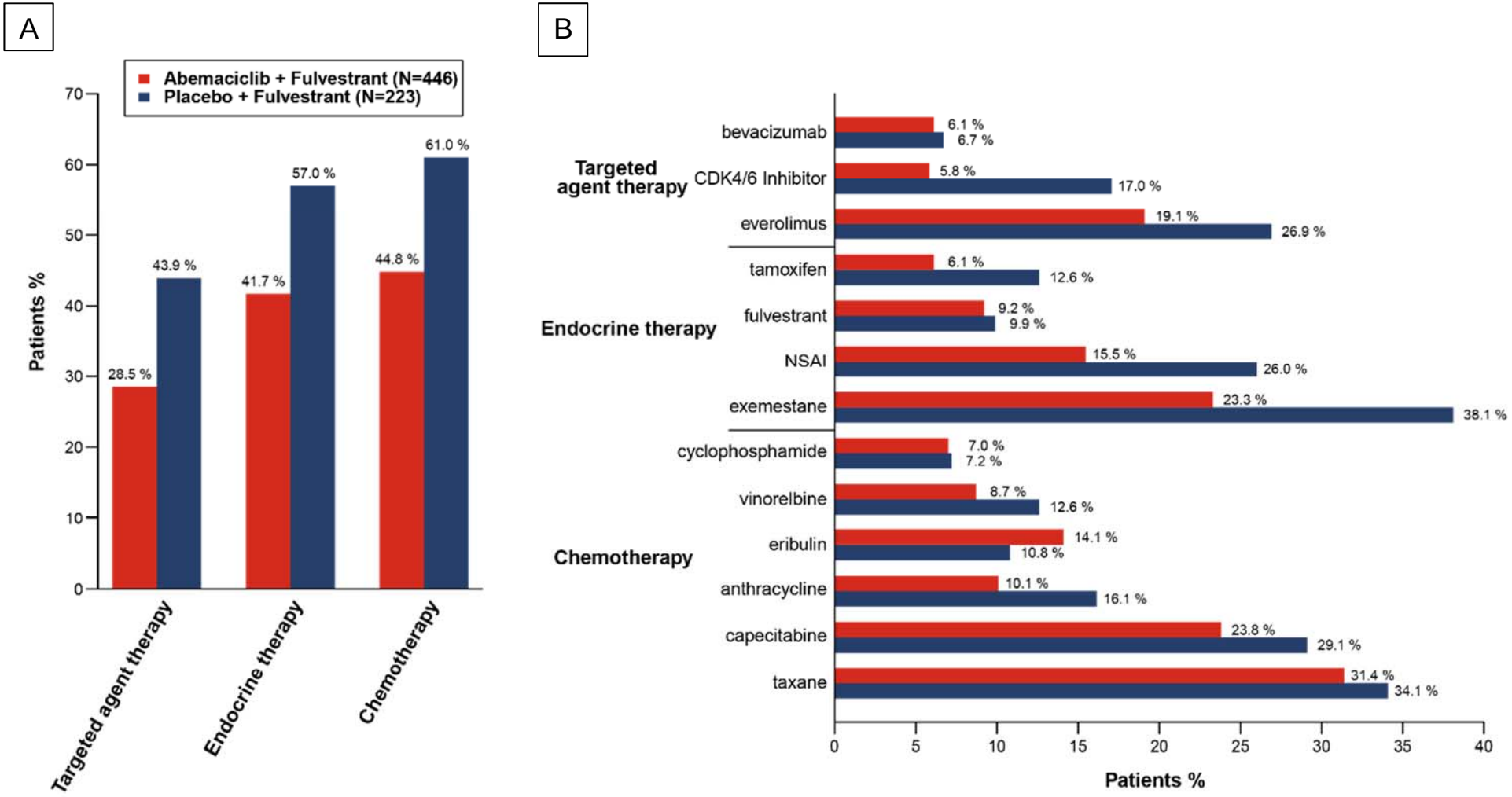
Characteristic	Abemaciclib + Fulvestrant N=446	Placebo + Fulvestrant N=223
Median age, years (range)	59 (32-91)	62 (32-87)
ET resistance[a], No. (%)		
Primary	111 (24.9)	58 (26.0)
Secondary	326 (73.1)	163 (73.1)
Most recent ET[b], No. (%)		
(Neo)adjuvant	263 (59.0)	133 (59.6)
Metastatic	171 (38.3)	85 (38.1)
Prior AI, No. (%)		
Yes	316 (70.9)	149 (66.8)
No	130 (29.1)	74 (33.2)
PgR status[c], No. (%)		
Positive	339 (76.0)	171 (76.7)
Negative	96 (21.5)	44 (19.7)
Metastatic site, No. (%)		
Visceral	245 (54.9)	128 (57.4)
Bone only	123 (27.6)	57 (25.6)
Other	75 (16.8)	38 (17.0)
Measurable disease, No. (%)		
Yes	318 (71.3)	164 (73.5)
No	128 (28.7)	59 (26.5)
Race[d], No. (%)		
Asian	149 (33.4)	65 (29.1)
Caucasian	237 (53.1)	136 (61.0)
Other	29 (6.5)	13 (5.8)
ECOG performance status[e], No. (%)		
0	264 (59.2)	136 (61.0)
1	176 (39.5)	87 (39.0)
Prior chemotherapy for neoadjuvant or adjuvant treatment, No. (%)		
Yes	267 (59.9)	134 (60.1)
No	179 (40.1)	89 (39.9)
Menopausal status, No. (%)		
Pre- or perimenopausal	72 (16.1)	42 (18.8)
Postmenopausal	371 (83.2)	180 (80.7)

[a]Percentages do not add up to 100% due to missing values
[b]8 patients (6 abemaciclib arm; 2 placebo) had no prior endocrine therapies.
[c]8 patients in each arm had unknown PgR status.
[d]31 patients in the abemaciclib arm and 9 in the placebo arm had missing race information
[e]One patient (abemaciclib arm) had ECOG performance status of 2.
Abbreviations: AI, aromatase inhibitor; ECOG, Eastern Cooperative Oncology Group; ET, endocrine therapy; N, number of patients in population; No., number of patients; PgR, progesterone receptor

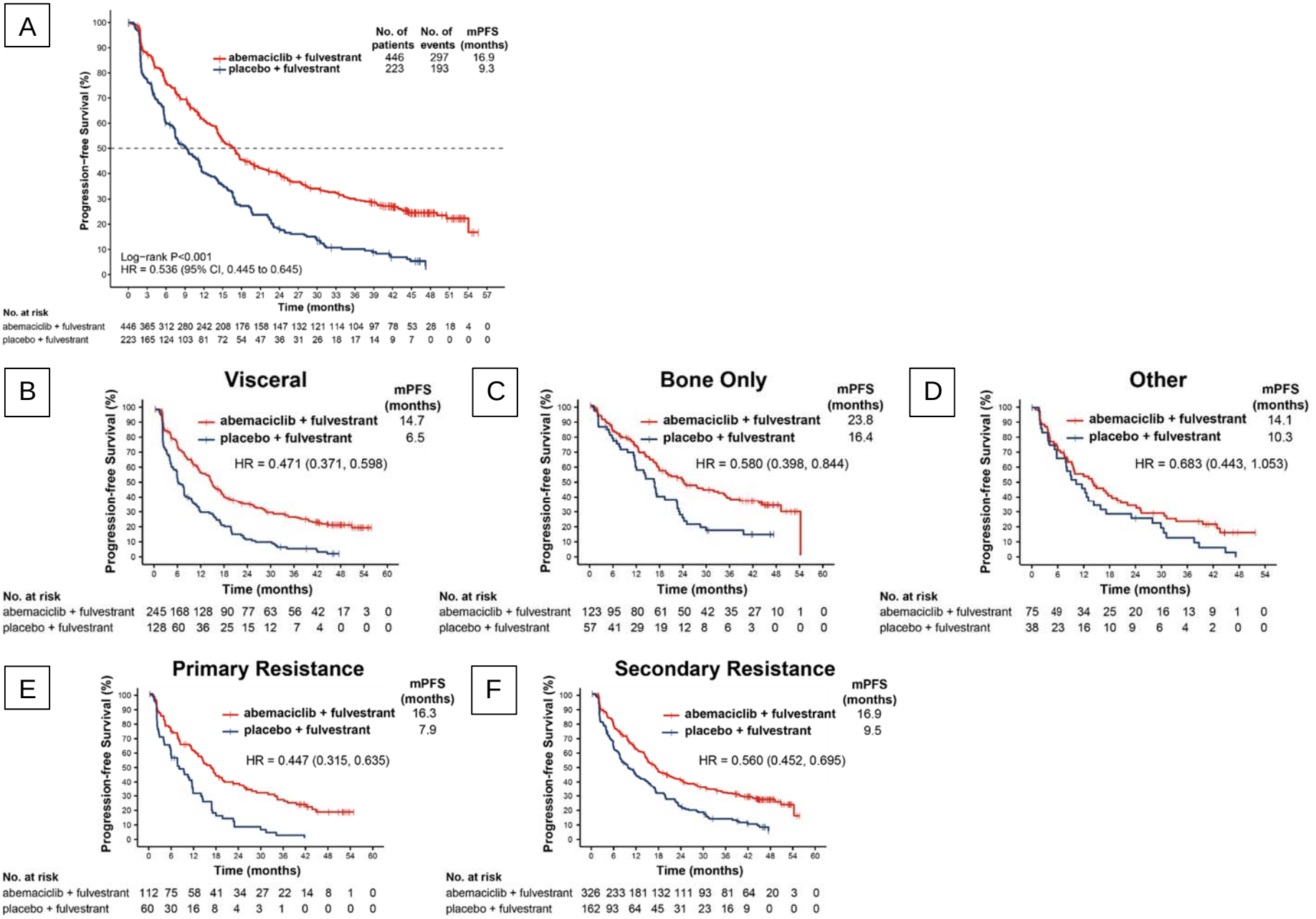
eTable 2. Treatment-emergent Adverse Events

TEAE ≥10% in either arm	Abemaciclib + Fulvestrant N=441			Placebo + Fulvestrant N=223		
	CTCAE Grade					
	All No. (%)	Grade 3 No. (%)	Grade 4 No. (%)	All No. (%)	Grade 3 No. (%)	Grade 4 No. (%)
Any	435 (98.6)	259 (58.7)	32 (7.3)	203 (91.0)	51 (22.9)	9 (4.0)
Diarrhea	384 (87.1)	64 (14.5)	0	62 (27.8)	1 (0.4)	0
Neutropenia	219 (49.7)	118 (26.8)	13 (2.9)	9 (4.0)	3 (1.3)	1 (0.4)
Nausea	217 (49.2)	12 (2.7)	-	56 (25.1)	5 (2.2)	-
Fatigue	189 (42.9)	18 (4.1)	-	64 (28.7)	2 (0.9)	-
Abdominal pain	164 (37.2)	14 (3.2)	-	37 (16.6)	2 (0.9)	-
Anemia	153 (34.7)	39 (8.8)	1 (0.2)	10 (4.5)	3 (1.3)	0
Leukopenia	146 (33.1)	48 (10.9)	1 (0.2)	4 (1.8)	0	0
Decreased appetite	127 (28.8)	5 (1.1)	0	30 (13.5)	1 (0.4)	0
Vomiting	127 (28.8)	4 (0.9)	0	26 (11.7)	5 (2.2)	0
Headache	106 (24.0)	3 (0.7)	-	36 (16.1)	1 (0.4)	-
Dysgeusia	82 (18.6)	-	-	6 (2.7)	-	-
URTI	82 (18.6)	0	0	17 (7.6)	2 (0.9)	0
Stomatitis	77 (17.5)	1 (0.2)	1 (0.2)	24 (10.8)	0	0
Thrombocytopenia	77 (17.5)	9 (2.0)	6 (1.4)	6 (2.7)	0	1 (0.4)
Alopecia	76 (17.2)	-	-	4 (1.8)	-	-
Cough	73 (16.6)	1 (0.2)	1 (0.2)	29 (13.0)	0	-
ALT increased	70 (15.9)	19 (4.3)	1 (0.2)	12 (5.4)	4 (1.8)	0
Constipation	70 (15.9)	3 (0.7)	0	36 (16.1)	1 (0.4)	0
Arthralgia	69 (15.6)	2 (0.5)	1 (0.2)	33 (14.8)	1(0.4)	-
AST increased	69 (15.6)	12 (2.7)	0	16 (7.2)	7 (3.1)	0
Dizziness	66 (15.0)	3 (0.7)	-	16 (7.2)	0	-
Blood creatinine increased	64 (14.5)	4 (0.9)	0	1 (0.4)	0	0
Pruritus	64 (14.5)	0	-	15 (6.7)	0	-
Oedema peripheral	62 (14.1)	0	-	16 (7.2)	0	-
Pyrexia	59 (13.4)	3 (0.7)	2 (0.5)	16 (7.2)	1 (0.4)	0
Back pain	57 (12.9)	3 (0.7)	-	32 (14.3)	3 (1.3)	-
Dyspnoea	53 (12.0)	11 (2.5)	1 (0.2)	26 (11.7)	3 (1.3)	0
Weight decreased	53 (12.0)	1 (0.2)	-	7 (3.1)	2 (0.9)	-
Muscular weakness	52 (11.8)	6 (1.4)	-	13 (5.8)	0	-
Pain in extremity	52 (11.8)	2 (0.5)	-	9 (4.0)	1 (0.4)	-
Rash	52 (11.8)	5 (1.1)	0	11 (4.9)	0	0
Hot flush	51 (11.6)	0	-	24 (10.8)	0	-
Dry skin	45 (10.2)	0	-	4 (1.8)	0	-
Lymphopenia	45 (10.2)	17 (3.9)	1 (0.2)	2 (0.9)	0	1 (0.4)
UTI	44 (10.0)	4 (0.9)	0	10 (4.5)	1 (0.4)	0

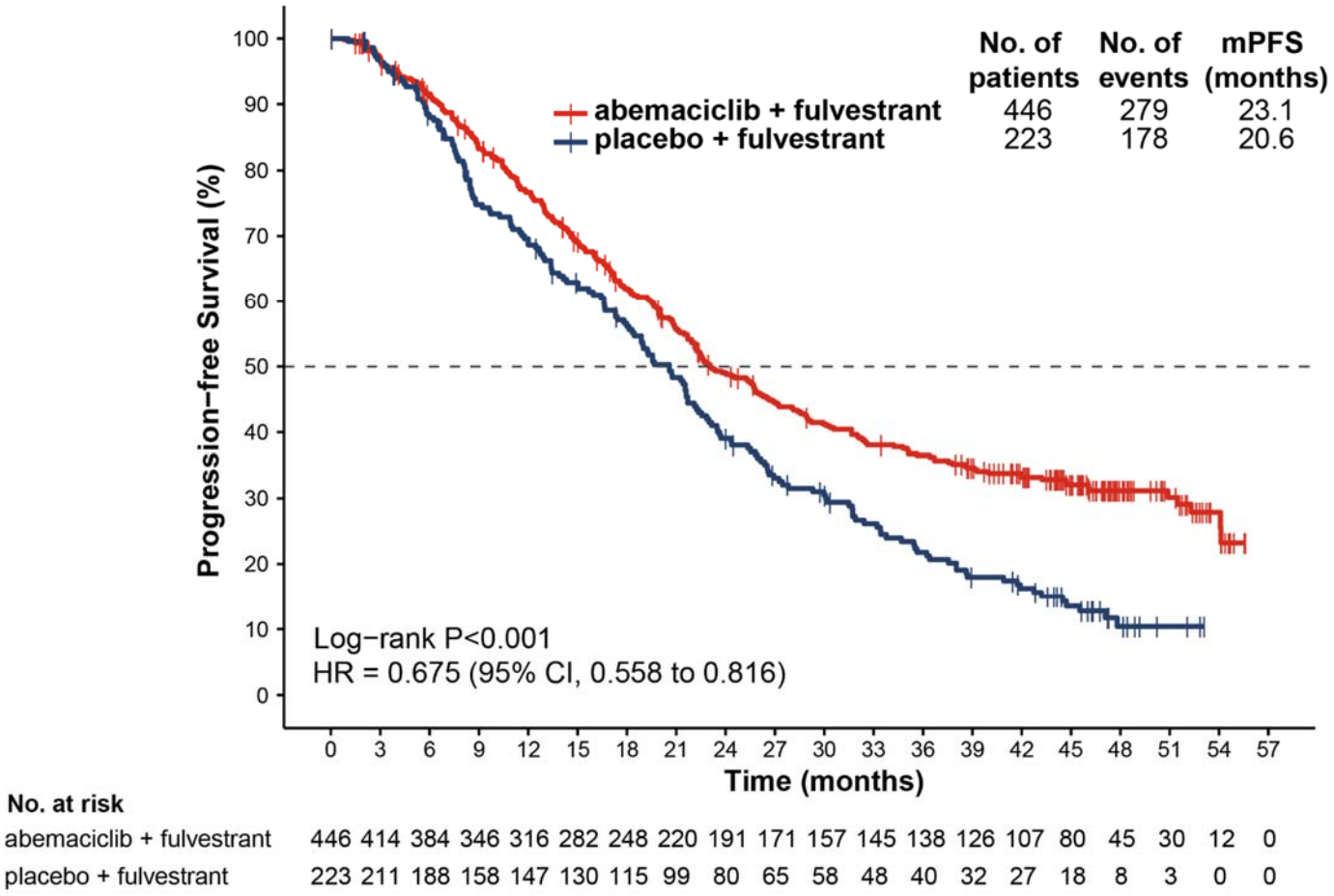
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; N, number of patients in population; No., number of patients; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection



eFigure 1: Post Discontinuation Therapy
Panel A reports selected subsequent systemic therapies. Panel B indicates selected subsequent regimens. Subsequent systemic therapies were received by 281 (63.0%) patients in abemaciclib arm and 180 (80.7%) in the placebo arm; percentages were calculated using number patients receiving each therapy out of the number of randomized patients in each treatment arm.

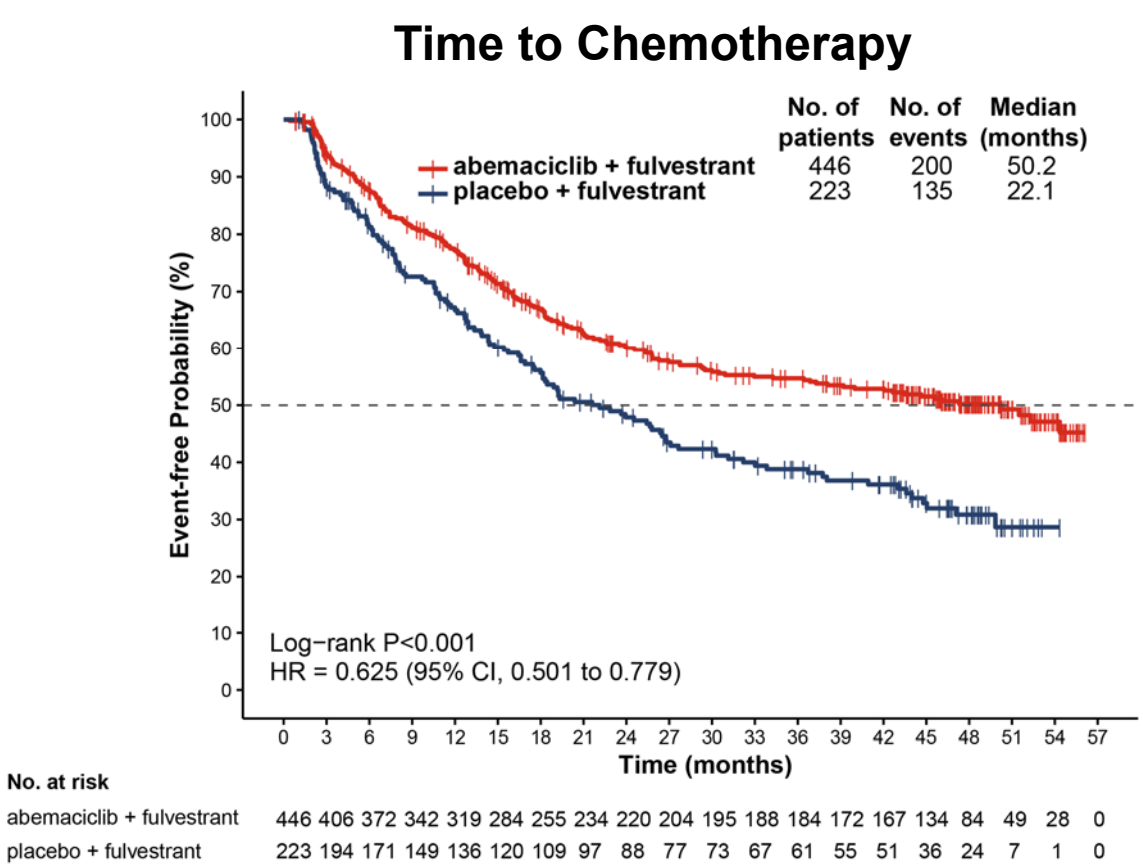


eFigure 2: Kaplan-Meier Plots of Updated Progression-free Survival
Panel A, updated PFS in the ITT population. Panel B-D, updated PFS by metastatic site. Panel E-F, updated PFS by resistance to endocrine therapy.
HR, hazard ratio; ITT, intent-to-treat; mPFS, median PFS; No, number; P, p-value; PFS, progression-free survival



eFigure 3: Kaplan-Meier Plot of Time to Second Disease Progression (PFS2)
PFS2 was defined as the time from randomization to the discontinuation date of next-line (first line of post discontinuation treatment), or starting date of the second line of post discontinuation treatment or death from any cause, whichever was earlier. CI, confidence interval; HR, hazard ratio; mPFS, median PFS; No., number; P, p-value

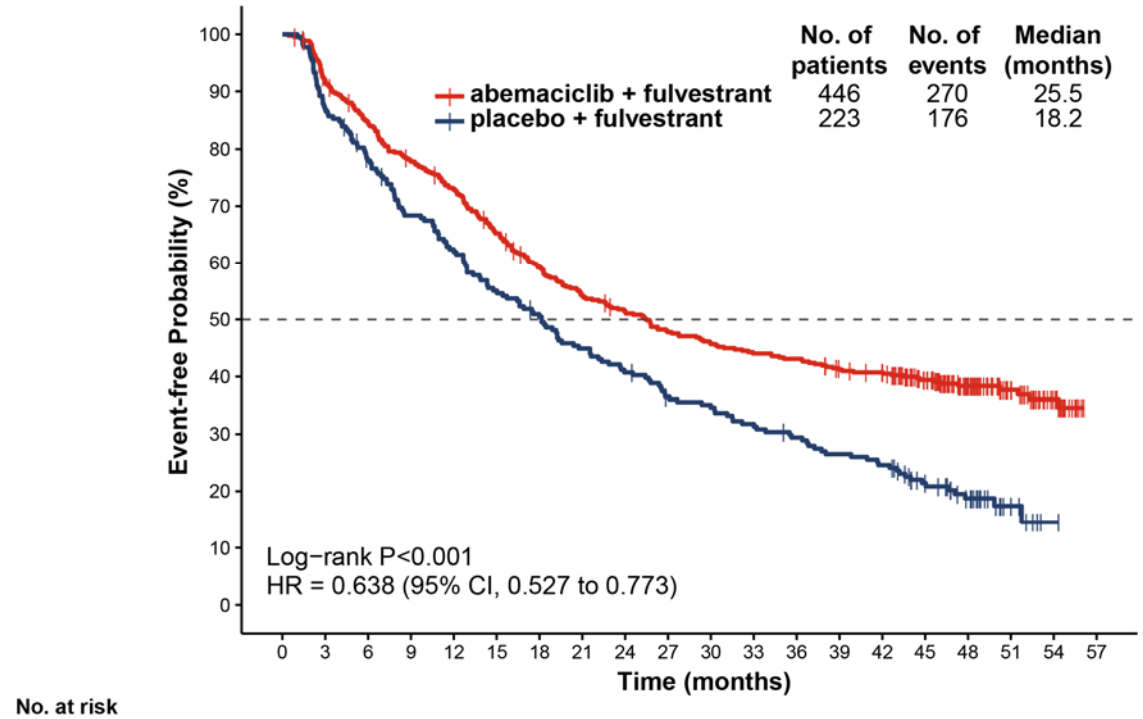
A



No. at risk

abemaciclib + fulvestrant	446	406	372	342	319	284	255	234	220	204	195	188	184	172	167	134	84	49	28	0
placebo + fulvestrant	223	194	171	149	136	120	109	97	88	77	73	67	61	55	51	36	24	7	1	0

B



No. at risk

abemaciclib + fulvestrant	446	406	372	342	319	284	255	234	220	204	195	188	184	172	167	134	84	49	28	0
placebo + fulvestrant	223	194	171	149	136	120	109	97	88	77	73	67	61	55	51	36	24	7	1	0

eFigure 4: Kaplan-Meier Plots of Time to Chemotherapy (TTC) and Chemotherapy-free Survival (CFS)
Panel A, TTC was defined as the time from randomization to initiation on first post discontinuation chemotherapy (censoring pts who died prior to initiation of chemotherapy). Panel B, CFS was defined as the time from randomization to initiation of first post discontinuation chemotherapy or death. CI, confidence interval; HR, hazard ratio; No., number; P, p-value