SUPPLEMENTARY MATERIAL

Supplementary Table 1. Prevalence of underweight, normal weight, overweight and obesity of included patients according to treatment group.

BMI	ABEMACICLIB + ET (N = 757)		PLACEBO + ET (N = 381)	
Mean ± SD	26.4 ± 5.6		26.6 ± 5.7	
Median (Q1-Q3)	25.5 (22.2-29.7)		25.9 (22.5-30.1)	
Underweight	24	3.2%	8	2.1%
Normal	327	43.2%	164	43.0%
Overweight	223	29.5%	113	29.7%
Obese	183	24.2%	96	25.2%

Supplementary Table 2. Univariate and multivariate analysis of PFS according to BMI (<25 and ≥25) in patients treated with abemacicilib + ET vs. placebo + ET.

BMI	PFS rate at 1 year	Median PFS (months)	Unadjusted HR (95% CI)	P Value	Adjusted* HR (95% CI)	P Value
Abemaciclib + ET						
<25	67%	22.0 (17.2-29.1)				
≥25	66%	21.7 (17.1-27.5)	1.03 (0.83-1.27)	0.81	1.0 (0.81-1.25)	0.98
Placebo + ET						
<25	44%	10.8 (7.9-13.7)				
≥ 25	50%	12.7 (9.0-15.4)	0.81 (0.64-1.04)	0.10	0.80 (0.62-1.04)	0.09

*Adjusted for age, ECOG, prior endocrine therapy, prior aromatase inhibitor, menopausal status, numebr of metastatic sites and type of endocrine therapy. BMI: Body mass index, PFS: progression-free survival, HR: Hazard ratio, CI: confidence interval, ET: endocrine therapy

Supplementary Table 3. Adverse events according to BMI (< 25 and ≥25) in patients receiving abemaciclib + ET and placebo + ET*

Adverse event	BMI <25		BMI ≥25		P-value
Group 1: abemaciclib + ET (N = 757), No.	351		406		
Pts with a fatal AE	7	2.0%	12	3.0%	0.49
Pts with treatment withdrawal for toxicity	36	10.3%	54	13.3%	0.20
Pts with diarrhea (any grade)	307	87.5%	337	83.0%	0.08
Pts with diarrhea grade ≥3	41	11.7%	47	11.6%	0.96
Pts with neutropenia (any grade)	179	51.0%	164	40.4%	0.004
Pts with neutropenia grade ≥3	103	29.3%	88	21.7%	0.02
Pts with weight decrease (any grade)	40	11.4%	45	11.1%	0.89
Pts with weight decrease grade ≥3	3	0.9%	2	0.5%	0.67
Group 2: placebo ET (N = 381), No	172		209		
Pts with at least on grade ≥3	41	23.8%	52	24.9%	0.81
Pts with a fatal AE	1	0.6%	3	1.4%	0.63
Pts with treatment withdrawal for toxicity	4	2.3%	8	3.8%	0.56

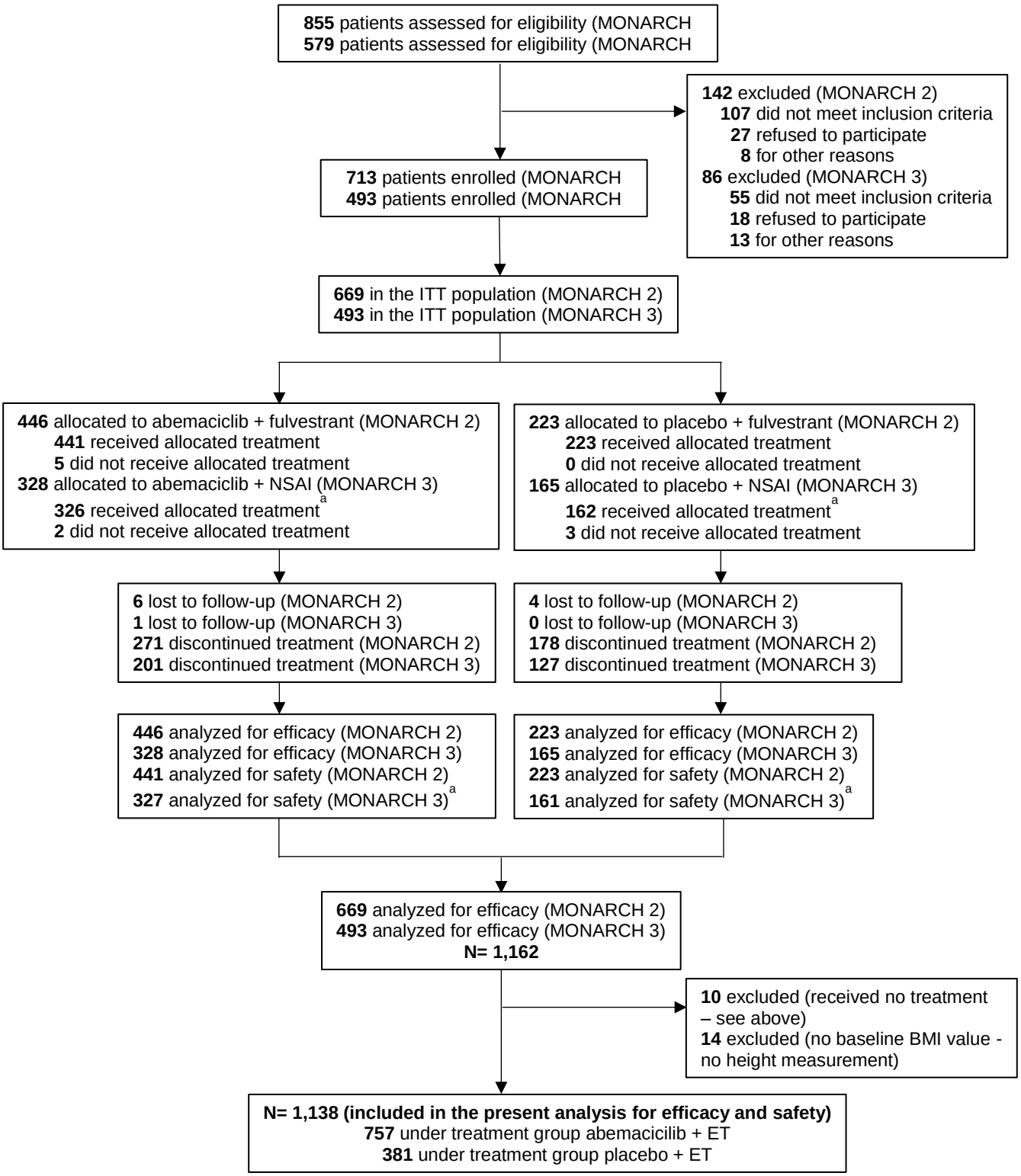
* pts: patients, AE: adverse event, ET: Endocrine therapy, BMI: body mass index

Supplementary Table 4. Dose adjustment, reduction, omission and treatment discontinuation according to BMI in both treatment groups.*

	BMI < 25		BMI ≥ 25		P-value
Group 1: abemaciclib + ET (N = 757), No.		351		406	
Discontinuation of study therapy due to AE	36	10.3%	54	13.3%	0.20
Discontinuation of study therapy from death due to AE	6	1.7%	7	1.7%	1
Discontinuation of any study drug due to AE	69	19.7%	79	19.5%	0.94
Discontinuation of abemaciclib due to AE	34	9.7%	28	6.9%	0.16
Dose adjust of abemaciclib due to AE	214	61.0%	250	61.6%	0.86
Dose reduction of abemaciclib due to AE	156	44.4%	181	44.6%	0.97
Dose omission of abemaciclib due to AE	197	56.1%	222	54.7%	0.69
Dose adjust of study drug due to AE	219	62.4%	253	62.3%	0.98
Dose reduction of study drug due to AE	157	44.7%	181	44.6%	0.97
Dose omission of study drug due to AE	202	57.6%	225	55.4%	0.56
Group 2: placebo + ET (N = 381), No.		172		209	
Discontinuation of study therapy due to AE	4	2.3%	8	3.8%	0.56
Discontinuation of study therapy from death due to AE	-	-	3	1.4%	0.26
Discontinuation of any study drug due to AE	4	2.3%	10	4.8%	0.28
Dose adjust of study drug due to AE	28	16.3%	30	14.4%	0.60
Dose reduction of study drug due to AE	6	3.5%	7	3.4%	1
Dose omission of study drug due to AE	27	15.7%	30	14.4%	0.71

* ET: endocrine therapy, AE: adverse event, BMI: body mass index

Supplementary Figure 1. Flowchart of patient selection and inclusion.

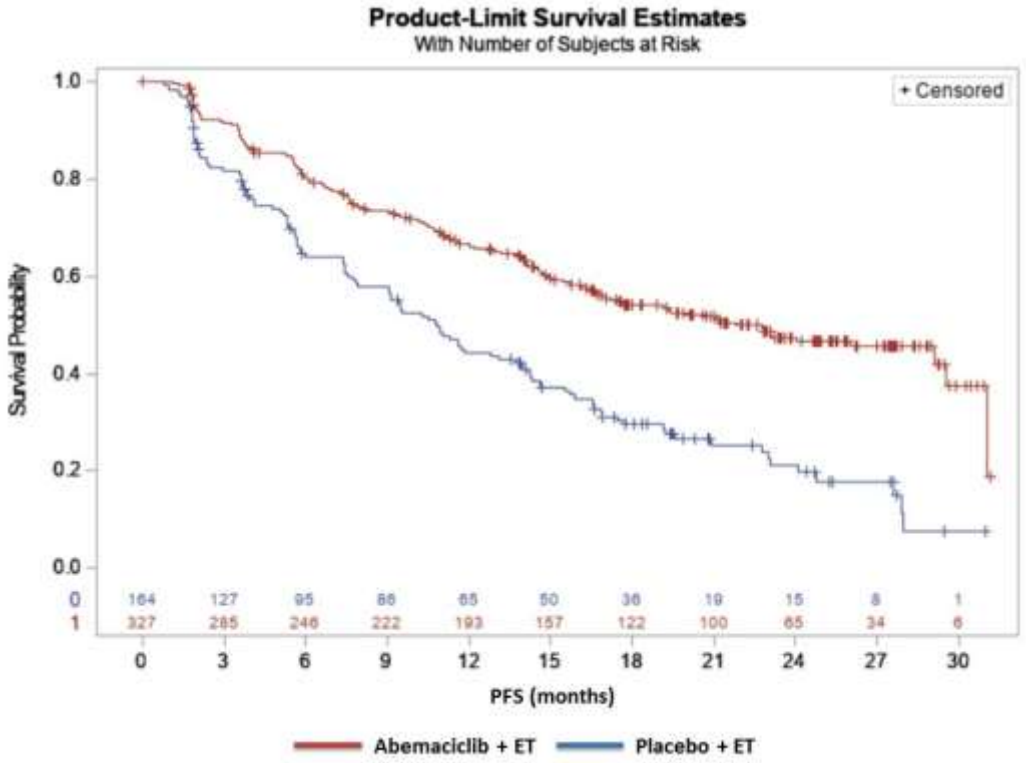


[a] In MONARCH 3, during Cycle 1 a single patient who was randomized to placebo received abemaciclib, and this patient is included in the abemaciclib safety population.

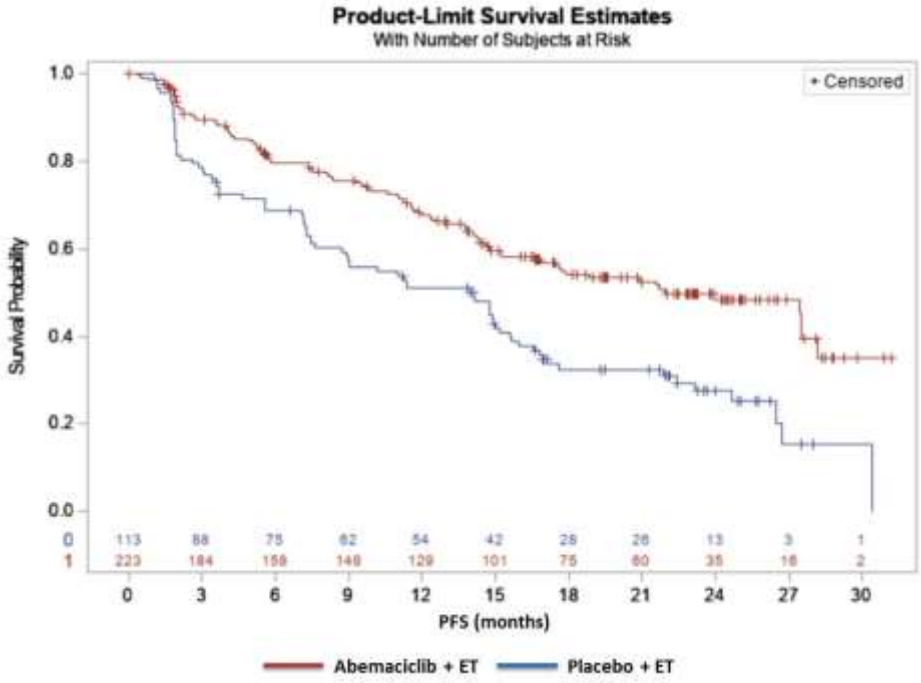
Legends: ITT, intent-to-treat; NSAI, nonsteroidal aromatase inhibitor, ET: endocrine therapy

Supplementary Figure 2. A) PFS in normal weight patients receiving abemaciclib + ET vs placebo + ET. Abemaciclib patients had a longer PFS (21.9 vs. 10.8 months), for a hazard ratio of 0.48 (95% CI, 0.38-0.61; p-value <0.001). B) PFS in overweight patients receiving abemacicilib + ET vs placebo +ET. Abemaciclib patients had a longer PFS (22.0 vs. 14.0 months), for a hazard ratio of 0.54 (95% CI, 0.40 -0.73; p value < 0.001). C) PFS in obese patients receiving abemaciclib + ET vs placebo + ET. Abemaciclib patients had a longer PFS (20.2 vs. 11.6 months), for a hazard ratio of 0.70 (95% CI, 0.50-0.97; p-value 0.03).

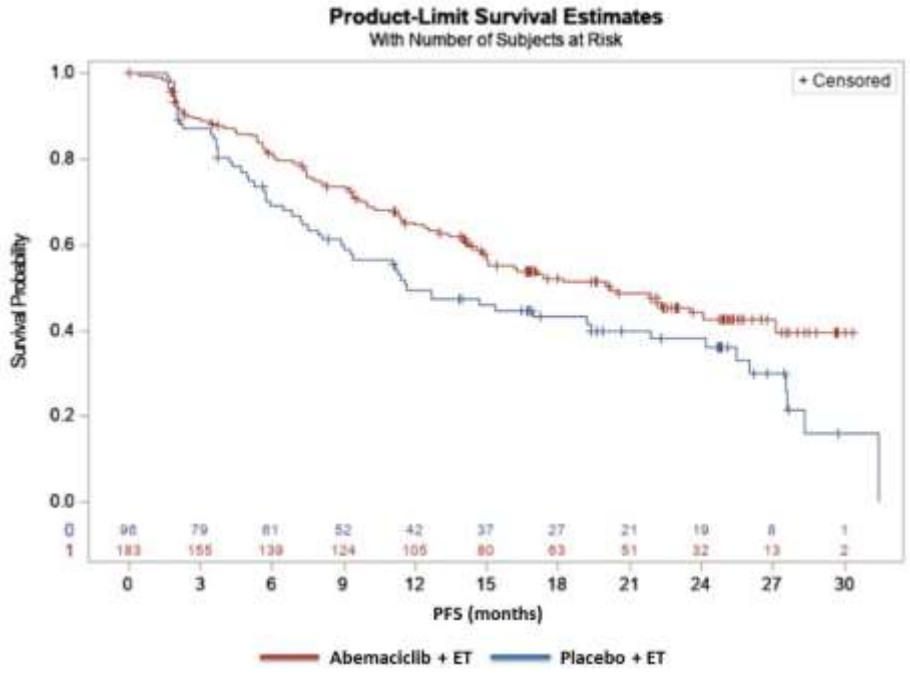
A



B


Product-Limit Survival Estimates
With Number of Subjects at Risk
+ Censored
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0 113 88 75 62 54 42 28 26 13 3 1
1 223 184 159 148 129 101 75 60 35 16 2
0 3 6 9 12 15 18 21 24 27 30
PFS (months)
Abemaciclib + ET
Placebo + ET

C


Product-Limit Survival Estimates
With Number of Subjects at Risk
+ Censored
Survival Probability
1.0
0.8
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0 96 79 61 52 42 37 27 21 19 8 1
1 183 155 139 124 105 80 63 51 32 13 2
0 3 6 9 12 15 18 21 24 27 30
PFS (months)
Abemaciclib + ET
Placebo + ET

Supplementary Figure 3. Association of weight loss and progression-free survival in patients receiving abemaciclib + ET vs placebo + ET. In the abemaciclib arm, there was no difference in PFS between the two weight change classes: p=0.55. In the placebo arm, there was also no difference in PFS between the two weight change classes: p=0.95.