

SUPPLEMENTARY MATERIAL

Manuscript title: MONARCH plus: Abemaciclib Plus Endocrine Therapy in Women With HR+/HER2- Advanced Breast Cancer: The Multinational Randomized Phase 3 Study

Supplementary Table 1. Ethics Committees for MONARCH plus

Supplementary Table 2. Best Overall Response in ITT Population With Measurable Disease

Supplementary Table 3. Laboratory Abnormalities

Supplementary Figure 1. Trial Profile

Supplementary Figure 2. Best Percentage Change From Baseline in Tumor Size in the ITT Population With Measurable Disease in (A) Cohort A and (B) Cohort B

SUPPLEMENTARY TABLES

Supplementary Table 1. Ethics Committees for MONARCH plus

Country and Site Number	Name and Address of Ethics Committee
China	
#110	IRB of The Fifth Medical Center of PLA General Hospital No. 8 East Street, Fengtai District, Beijing, China
#111	Medical Ethics Committee of Fudan University Shanghai Cancer Center No.270, Dong An Road, Shanghai, China
#112	Clinical Medicine Ethics Committee of The First Affiliated Hospital of Bengbu Medical College No.287, Changhuai Road, Bengbu, Anhui, China
#113	Ethic Committee of Beijing Cancer Hospital No.52, Fucheng Road, Haidian District, Beijing, China
#116	Guangdong Provincial People's Hospital Ethics Committee No.106, Zhong Shan Er Road, Guangzhou, Guangdong, China
#118	Ethics Committee of Hubei Cancer Hospital No 116, Zhuodaoquan South Road, Hongshan District, 430079, Wuhan, China
#119	Ethics Committee for Drug Clinical Trials of Huazhong University of Science and Technology Room #12, Level 16, No 2 Jiaoxue Building, Tongji Medical College Jichu Medical College, No.13, Hnagkong Road, Wuhan, China
#120	Harbin Medical University Cancer Hospital Ethics Committee No.150, Haping Road, Harbin, Helongjiang, China
#122	Shanghai General Hospital Institutional Review Board No.100, Haining Road, Shanghai, China
#123	IRB of Liaoning Cancer Hospital/Liaoning Cancer Hospital Building 2 F1 EC Office, No.44, Xiaoheyuan Road, Dadong District, Shenyang, Liaoning, China
#124	IRB of Jilin Province Cancer Hospital F4 Tumor Research Institute EC Office, No.1018, Huguang Road, Chaoyang District, Changchun, Jilin, China
#125	Medical Ethics Committee of Hunan Cancer Hospital 4th floor, Building 15, Hunan Cancer Hospital, No.283, Tongzipo Road, Yuelu District, Changsha, Hunan, China
#126	Tianjin Medical University Cancer Institute and Hospital Ethics Committee Huanhu West Road, North of Ti Yuan, Hexi District, Tianjin, China
#127	Human Research Ethics Committee of The Second Affiliated Hospital of Zhejiang University School of Medicine No.88, Jiefang Road, Hangzhou, Zhejiang, China
#128	Ethics Committee of Jiangsu Cancer Hospital No.42, Baiziting, Nanjing, Jiangsu, China
#129	The First Hospital of China Medical University Ethics Committee No.155, Nanjingbei Street, Heping District, Shenyang, Liaoning, China
#130	Zhejiang Cancer Hospital Institutional Review Board Room 308, Administrative Research Building, Zhejiang Cancer Hospital, No.1, Banshan East Road, Gongshu District, Hangzhou, Zhejiang, China
#131	Ethics Committee for Drug Clinical Trials of Huazhong University of Science and Technology Room #12, Level 16, No 2 Jiaoxue Building, Tongji Medical College Jichu Medical College, No.13, Hnagkong Road, Wuhan, Hubei, China
#133	Medical Ethics Committee of Henan Cancer Hospital Room 113, First Floor, Building 5, Henan Cancer Hospital, No.127, Dongming Road, Zhengzhou, Henan, China

Country and Site Number	Name and Address of Ethics Committee
#134	The Fourth Hospital of Hebei Medical University Ethics Committee No.12, Jiankang Road, Shijiazhuang & No.169 Tianshan Street, Shijiazhuang, Hebei, China
#135	Medical Ethic Committee of The Second Hospital of Dalian Medical University No.467, Zhongshan Road, Shahekou District, Dalian, Liaoning, China
#136	Ethics Committee of Nanjing Drum Tower Hospital No.321, Zhongshan Road, Nanjing, Jiangsu, China
#139	Ethics Committee of National Drug Clinical Trial Institution of Fuzhou General Hospital of Nanjing Military Region of the People's Liberation Army No.156, West Erhuan North Road, Fuzhou, Fujian, China
#140	Medical Ethics Committee of The First Affiliated Hospital of Xi'an Jiaotong University First Floor, Science and Education Building, The First Affiliated Hospital of Xi'an Jiaotong University, No.277, Yanta District, Xi'an, Shanxi, China
#141	Affiliated Cancer Hospital of Guangxi Medical University Ethics Committee No.71, Hedi Road, Qingxiu District, Nanning, Guangxi, China
#142	Ethics Committee of the First Affiliated Hospital With Nanjing Medical University No.300, Guangzhou Road, Nanjing, Jiangsu, China
#143	Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University Ethics Committee No.107, Yanjiangxi Road, Guangzhou, China
#144	Ethics Committee of Fujian Cancer Hospital Ethics Office, 3rd floor, Radiotherapy Building, Fujian Cancer Hospital, No.420, Fuma Road, Jin'an District, Fuzhou, Fujian, China
Brazil	
#150	Hospital do Câncer de Barretos/Fundação Pio XII - Rua Antenor Duarte Vilela 1331, Bairro Dr. Paulo Prata, Barretos, Sao Paulo, 14784700, Brazil
#151	USP - Faculdade de Medicina da Universidade de São Paulo - FMUSP Av Dr Arnaldo, 251, Cerqueira César 21º Andar, São Paulo, 01246-000, Brazil
#152	Centro de Referência da Saúde da Mulher - CRSM Av. Brigadeiro Luis Antonio, 683 - 2º Andar, Bela Vista, São Paulo, 01317- 000, Brazil
#153	Faculdade de Medicina de São José do Rio Preto - FAMERP - SP Av Brigadeiro Faria Lima 5544, Sao Jose Rio Preto, Sao Paulo, 15090-000, Brazil
#154	Universidade Regional do Roroeste do Estado do Rio Grande do Sul - Ijuí Rua do Comércio, 3000 - Bairro Universitário, Ijuí, RS, 98700-000, Brazil
#155	Hospital Mãe de Deus/Associação Educadora São Carlos Rua da Costa, 150 - Menino Deus, Comite de Etica Pesquisa da Associação Educadora São Carlos, Porto Alegre, RS, 90470-340, Brazil
India	
#160	Dr. B.L. Kapur Memorial Hospital Ethics Committee Dr. B.L. Kapur Memorial Hospital, Pusa Road, New Delhi, 11005, India
#161	HCG- Central Ethics Committee HCG-Bangalore Institute of Oncology, HCG Towers, Tower 1, 1st Floor, No.8, P. Kalinga Road, Sampangiram Nagar, Bangalore, 560027, Karnataka, India
#162	Ethics Committee, M.S. Ramaiah Medical College and Hospitals MSR Nagar, MSRIT Post, Bangalore, 560054, Karnataka, India
#163	Clinical Research Ethics Committee Medica Superspecialty Hospital, No.127, Mukundpur, E.M. Bypass, Kolkata, 700099, India
#165	Institutional Ethics Committee Tata Memorial Hospital, Dr. E. Borges Marg, Parel, Mumbai, 400012, India

Country and Site Number	Name and Address of Ethics Committee
#167	Ethics Committee Jehangir Clinical Development Centre Pvt. Ltd. Jehangir Hospital Premises, No.32, Sassoon Road, Pune, India
#168	Institutional Review Board Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu, 632004, India
#169	Gujarat Cancer Society and Gujarat Cancer & Research Institute Ethics Committee Civil Hospital Campus, Asarwa, Ahmedabad, 380016, India
South Africa	
#170	PHARMA-ETHICS PO Box 786, Irene, 0062, Gauteng, Republic of South Africa, 123 Amkor Road, Lyttelton Manor Ext 3, Centurion, 0157, South Africa
#172	PHARMA-ETHICS PO Box 786, Irene, 0062, Gauteng, Republic of South Africa, 123 Amkor Road, Lyttelton Manor Ext 3, Centurion, 0157, South Africa
#173	PHARMA-ETHICS PO Box 786, Irene, 0062, Gauteng, Republic of South Africa, 123 Amkor Road, Lyttelton Manor Ext 3, Centurion, 0157, South Africa

Supplementary Table 2. Best Overall Response in ITT Population With Measurable Disease^a

	Cohort A		Cohort B	
	Abemaciclib + NSAI (n=176)	Placebo + NSAI (n=83)	Abemaciclib + fulvestrant (n=80)	Placebo + fulvestrant (n=38)
Best overall response				
Complete response	1.1 (0.0–2.7)	0	0	2.6 (0.0–7.7)
Partial response	64.8 (57.7–71.8)	36.1 (25.8–46.5)	50.0 (39.0–61.0)	7.9 (0.0–16.5)
Stable disease	25.0 (18.6–31.4)	45.8 (35.1–56.5)	42.5 (31.7–53.3)	55.3 (39.5–71.1)
≥6 months	16.5 (11.0–22.0)	25.3 (15.9–34.7)	27.5 (17.7–37.3)	31.6 (16.8–46.4)
Progressive disease	4.5 (1.5–7.6)	15.7 (7.8–23.5)	7.5 (1.7–13.3)	28.9 (14.5–43.4)
Not evaluable	4.5 (1.5–7.6)	2.4 (0.0–5.7)	0	5.3 (0.0–12.4)
Objective response rate	65.9 (58.9–72.9)	36.1 (25.8–46.5)	50.0 (39.0–61.0)	10.5 (0.8–20.3)
Stratified <i>P</i> -value		<0.0001		<0.0001
Disease control rate	90.9 (86.7–95.2)	81.9 (73.6–90.2)	92.5 (86.7–98.3)	65.8 (50.7–80.9)
Stratified <i>P</i> -value		0.0551		0.0004
Clinical benefit rate	82.4 (76.8–88.0)	61.4 (51.0–71.9)	77.5 (68.3–86.7)	42.1 (26.4–57.8)
Stratified <i>P</i> -value		0.0004		0.0001

Abbreviations: ITT, intent-to-treat; NSAI, nonsteroidal aromatase inhibitor.

^aData are % (95% confidence interval), unless otherwise stated.

Supplementary Table 3. Laboratory Abnormalities^a

	Cohort A						Placebo + NSAID					
	Abemaciclib + NSAID						Placebo + NSAID					
	(n=205)						(n=99)					
	N1	Grade 1	Grade 2	Grade 3	Grade 4	Total	N1	Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematology												
laboratory toxicity												
Neutropenia ^b	200	41 (20.5)	93 (46.5)	46 (23.0)	0	180 (90.0)	96	11 (11.5)	7 (7.3)	3 (3.1)	0	21 (21.9)
Leukopenia ^c	201	54 (26.9)	109 (54.2)	21 (10.4)	0	184 (91.5)	96	22 (22.9)	10 (10.4)	1 (1.0)	0	33 (34.4)
Anemia	201	85 (42.3)	68 (33.8)	13 (6.5)	0	166 (82.6)	96	11 (11.5)	11 (11.5)	1 (1.0)	0	23 (24.0)
Thrombocytopenia ^d	200	115 (57.5)	20 (10.0)	6 (3.0)	0	141 (70.5)	95	13 (13.7)	3 (3.2)	1 (1.1)	0	17 (17.9)
Lymphocyte count decreased	200	47 (23.5)	53 (26.5)	12 (6.0)	0	112 (56.0)	96	18 (18.8)	5 (5.2)	0	1 (1.0)	24 (25.0)
Lymphocytopenia ^e	200	0	1 (0.5)	0	0	1 (0.5)	96	0	2 (2.1)	0	0	2 (2.1)
Chemistry												
laboratory tests												
Hypocalcemia	201	29 (14.4)	4 (2.0)	0	0	33 (16.4)	96	10 (10.4)	2 (2.1)	0	0	12 (12.5)
Hypokalemia	201	32 (15.9)	0	12 (6.0)	1 (0.5)	45 (22.4)	96	5 (5.2)	0	1 (1.0)	0	6 (6.3)
Hyponatremia	201	23 (11.4)	0	3 (1.5)	0	26 (12.9)	96	7 (7.3)	0	1 (1.0)	0	8 (8.3)
Hyperkalemia	201	19 (9.5)	1 (0.5)	0	0	20 (10.0)	96	6 (6.3)	3 (3.1)	0	0	9 (9.4)
Hypercalcemia	201	84 (41.8)	1 (0.5)	0	0	85 (42.3)	96	35 (36.5)	0	0	0	35 (36.5)
Hypoalbuminemia	201	5 (2.5)	2 (1.0)	0	0	7 (3.5)	96	1 (1.0)	1 (1.0)	0	0	2 (2.1)
Hypernatremia	201	34 (16.9)	0	0	0	34 (16.9)	96	20 (20.8)	0	0	0	20 (20.8)
Hepatic function tests												
ALP increased	201	40 (19.9)	7 (3.5)	3 (1.5)	0	50 (24.9)	96	24 (25.0)	1 (1.0)	0	0	25 (26.0)
AST increased	201	66 (32.8)	11 (5.5)	7 (3.5)	1 (0.5)	85 (42.3)	96	27 (28.1)	3 (3.1)	1 (1.0)	1 (1.0)	32 (33.3)
ALT increased	201	62 (30.8)	15 (7.5)	7 (3.5)	3 (1.5)	87 (43.3)	96	27 (28.1)	4 (4.2)	2 (2.1)	0	33 (34.4)
Blood bilirubin increased	201	11 (5.5)	1 (0.5)	1 (0.5)	1 (0.5)	14 (7.0)	96	2 (2.1)	0	0	1 (1.0)	3 (3.1)
Renal function tests												
Creatinine increased	201	82 (40.8)	112 (55.7)	5 (2.5)	0	199 (99.0)	95	77 (81.1)	6 (6.3)	0	1 (1.1)	84 (88.4)

Cohort B												
Abemaciclib + fulvestrant (n=104)							Placebo + fulvestrant (n=53)					
	N1	Grade 1	Grade 2	Grade 3	Grade 4	Total	N1	Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematology laboratory toxicity												
Neutropenia ^b	104	17 (16.3)	51 (49.0)	25 (24.0)	0	93 (89.4)	53	6 (11.3)	4 (7.5)	0	0	10 (18.9)
Leukopenia ^c	104	24 (23.1)	56 (53.8)	19 (18.3)	0	99 (95.2)	53	10 (18.9)	2 (3.8)	2 (3.8)	0	14 (26.4)
Anemia	104	43 (41.3)	44 (42.3)	8 (7.7)	0	95 (91.3)	53	11 (20.8)	2 (3.8)	1 (1.9)	0	14 (26.4)
Thrombocytopenia ^d	103	57 (55.3)	7 (6.8)	1 (1.0)	0	65 (63.1)	52	3 (5.8)	3 (5.8)	0	0	6 (11.5)
Lymphocytopenia ^e	104	26 (25.0)	26 (25.0)	11 (10.6)	0	63 (60.6)	53	4 (7.5)	4 (7.5)	1 (1.9)	0	9 (17.0)
Chemistry laboratory tests												
Hypocalcemia	104	22 (21.2)	1 (1.0)	0	0	23 (22.1)	53	7 (13.2)	1 (1.9)	0	0	8 (15.1)
Hypokalemia	104	16 (15.4)	0	1 (1.0)	0	17 (16.3)	53	4 (7.5)	0	0	0	4 (7.5)
Hyponatremia	104	11 (10.6)	0	1 (1.0)	0	12 (11.5)	53	3 (5.7)	0	0	0	3 (5.7)
Hyperkalemia	104	6 (5.8)	0	1 (1.0)	0	7 (6.7)	53	3 (5.7)	1 (1.9)	0	0	4 (7.5)
Hypercalcemia	104	23 (22.1)	1 (1.0)	0	0	24 (23.1)	53	13 (24.5)	0	0	0	13 (24.5)
Hypoalbuminemia	104	1 (1.0)	0	0	0	1 (1.0)	53	1 (1.9)	1 (1.9)	0	0	2 (3.8)
Hypernatremia	104	20 (19.2)	0	0	0	20 (19.2)	53	6 (11.3)	0	0	0	6 (11.3)
Hepatic function tests												
ALP increased	104	12 (11.5)	2 (1.9)	1 (1.0)	0	15 (14.4)	53	6 (11.3)	5 (9.4)	0	0	11 (20.8)
AST increased	104	37 (35.6)	3 (2.9)	1 (1.0)	2 (1.9)	43 (41.3)	53	12 (22.6)	2 (3.8)	0	0	14 (26.4)
ALT increased	104	38 (36.5)	6 (5.8)	6 (5.8)	1 (1.0)	51 (49.0)	53	18 (34.0)	1 (1.9)	0	0	19 (35.8)
Blood bilirubin increased	104	4 (3.8)	1 (1.0)	0	0	5 (4.8)	53	2 (3.8)	1 (1.9)	0	1 (1.9)	4 (7.5)
Renal function tests												
Creatinine increased	104	43 (41.3)	60 (57.7)	1 (1.0)	0	104 (100)	53	37 (69.8)	2 (3.8)	0	0	39 (73.6)

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; N1, number of patients with at least a baseline result and 1 postbaseline result; NSAI, nonsteroidal aromatase inhibitor.

^aData are No. (%).

^bCTCAE term neutrophil count decreased.

^cCTCAE term white blood cell count decreased.

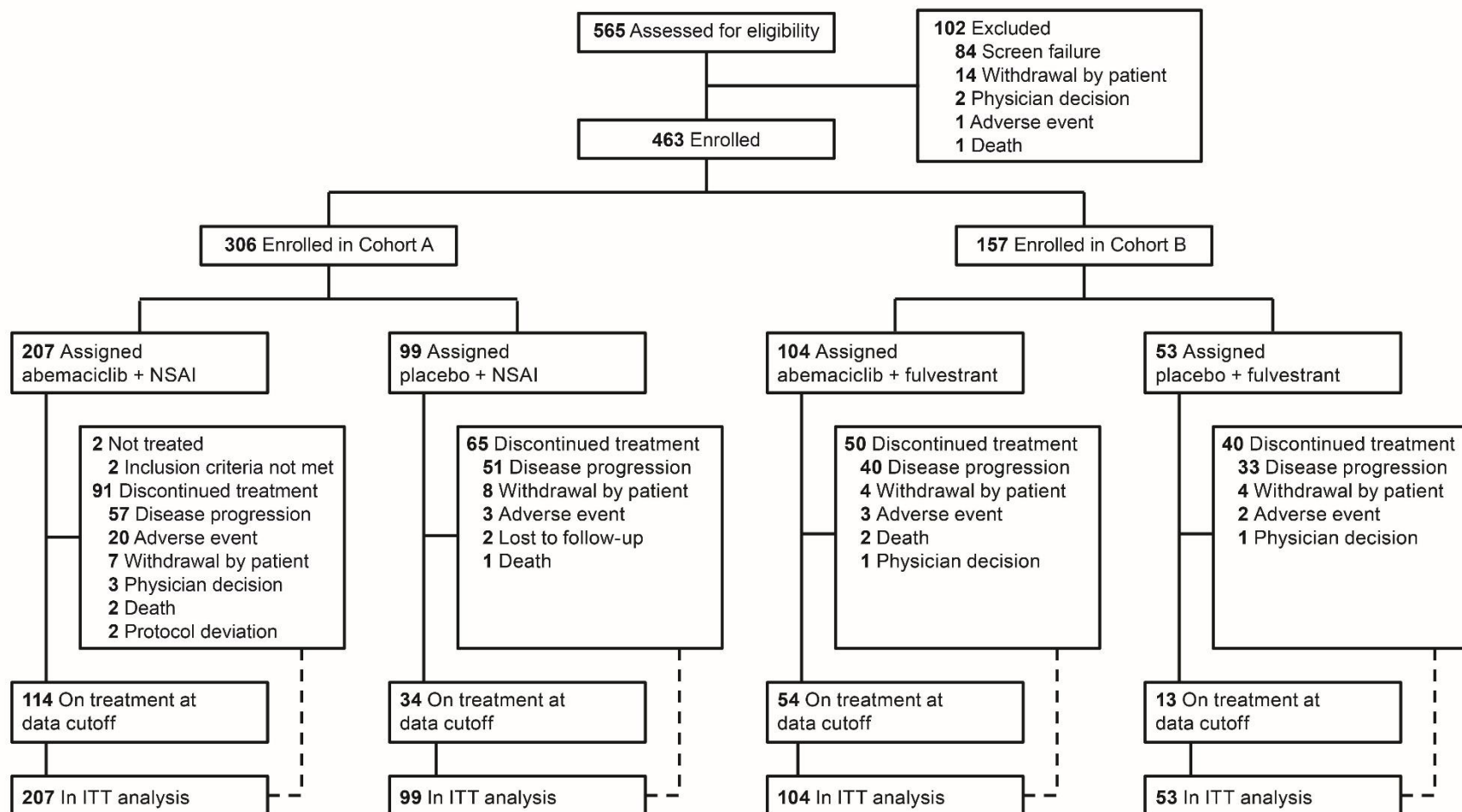
^dCTCAE term platelet count decreased.

^eCTCAE term lymphocyte count decreased.

SUPPLEMENTARY FIGURES

Supplementary Figure 1. Trial Profile.

ITT, intent-to-treat; NSAID, nonsteroidal aromatase inhibitor



Supplementary Figure 2. Best Percentage Change From Baseline in Tumor Size in the ITT Population With Measurable Disease in (A) Cohort A and (B) Cohort B.

CR, complete response; ITT, intent-to-treat; NSAI, nonsteroidal aromatase inhibitor; PD, progressive disease; PR, partial response; SD, stable disease.

