Supplementary Online Content

Schmid P, Zaiss M, Harper-Wynne C, et al. Fulvestrant plus vistusertib vs fulvestrant plus everolimus vs fulvestrant alone for women with hormone receptor–positive metastatic breast cancer: the MANTA phase 2 randomized clinical trial. *JAMA Oncol.* Published online August 29, 2019. doi:10.1001/jamaoncol.2019.2526

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

eTable 1. Treated Patient Demographics and Disease Characteristics at Baseline

		Fulvestrant plus daily vistusertib	Fulvestrant plus intermittent vistusertib	Fulvestrant	Fulvestrant plus everolimus
		(N = 101)	(N = 95)	(N = 66)	(N = 64)
Age (years), median (IQR)		63 (55-70)	64 (55-68)	63 (55-68)	63 (58-72)
Measurable disease					
	Yes	76 (75%)	77 (81%)	50 (76%)	51 (80%)
	No	25 (25%)	18 (19%)	16 (24%)	13 (20%)
Sites of metastatic disease					
	Visceral	64 (63%)	53 (56%)	41 (62%)	44 (69%)
	Bone-only	24 (24%)	21 (22%)	18 (27%)	11 (17%)
	Other[1]	13 (13%)	21 (22%)	7 (11%)	9 (14%)
Number of metastatic					
	1	36 (36%)	30 (32%)	29 (44%)	24 (38%)
	2	30 (30%)	34 (36%)	19 (29%)	20 (31%)
	≥3	35 (35%)	31 (33%)	18 (27%)	19 (30%)
Endocrine resistance					
	Secondary[2]	86 (85%)	83 (87%)	55 (83%)	58 (91%)
	Primary	15 (15%)	12 (13%)	11 (17%)	6 (9%)
Prior lines of therapy for ABC					
	None	38 (38%)	41 (43%)	24 (36%)	24 (38%)
	1	30 (30%)	29 (31%)	25 (38%)	20 (31%)
	≥2	33 (33%)	25 (26%)	17 (26%)	20 (31%)
Number of prior ET for ABC					
	None	44 (44%)	45 (47%)	29 (44%)	27 (42%)
	1	45 (45%)	36 (38%)	27 (41%)	25 (39%)
	≥2	12 (12%)	14 (15%)	10 (15%)	12 (19%)
Prior (neo)adjuvant chemotherapy					
	Yes	63 (62%)	56 (59%)	47 (71%)	38 (59%)
	No	38 (38%)	39 (41%)	19 (29%)	26 (41%)
Prior metastatic chemotherapy					
	Yes	24 (24%)	24 (25%)	13 (20%)	14 (22%)

	No	77 (76%)	71 (75%)	53 (80%)	50 (78%)

ABC = advanced breast cancer; ET = endocrine therapy; IQR = interquartile range.

Summaries are presented as counts and percentages unless otherwise stated.

[1] Other = no visceral metastases, but can have bone metastases in addition to others; including locally advanced breast cancer.

[2] Secondary endocrine resistance is defined as (i) ≥24 months of adjuvant ET before recurrence or (ii) CR or PR or SD for ≥24 weeks with ≥1 ET for MBC; all other patients are classified as primary resistance.

eTable 2. Adverse Events Occurring in ≥10% in the Safety Population; the Safety Population Includes All Patients Who Received at Least One Dose of the Study Drug

	Fulvestrant plus daily vistusertib (N = 92)		Fulvestrant plus intermittent vistusertib (N = 92)		Fulvestrant (N = 56)		Fulvestrant plus everolimus (N= 60)	
	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
Asthenia	34.8	2.2	45.7	5.4	16.1	0	53.3	3.3
Nausea	31.5	0	68.5	3.3	12.5	0	26.7	0
Rash	54.3	20.7	22.8	4.3	0	0	50.0	5.0
Stomatitis	40.2	13.0	29.3	4.3	0	0	60.0	11.7
Diarrhoea	25.0	2.2	35.9	5.4	5.4	0	31.7	1.7
Decreased appetite	16.3	0	32.6	0	5.4	0	30.0	1.7
Vomiting	12.0	1.1	40.2	5.4	0	0	11.7	0
Headache	9.8	1.1	22.8	2.2	12.5	0	18.3	0
Pruritus	23.9	2.2	12.0	3.3	1.8	0	16.7	0
Musculoskeletal pain	9.8	1.1	16.3	2.2	10.7	0	13.3	0
Dry mouth	13.0	0	12.0	0	3.6	0	20.0	0
Skin injury	14.1	1.1	9.8	0	0	0	25.0	0
Infection	15.2	5.4	10.9	1.1	3.6	0	16.7	6.7
Injection site reaction	12.0	1.1	10.9	0	8.9	0	15.0	0
Oral pain	10.9	3.3	12.0	0	0	0	21.7	0
Dysgeusia	5.4	0	16.3	0	3.6	0	18.3	0

Summaries are presented as percentages. Percentages are based on N (the total number of patients with at least one AE [regardless of grade] in the specified arm).