

Supplementary Table 1. Patient characteristics, adverse events and best response (patients with HR+ BC from trials NCT03595540 and NCT03340935).

Pt. no	Age	BMI at enrollment (kg/m ²)	Stage and HER2 status	type of ET and other therapies	Adjuvant (A) vs. palliative (P) therapy	Site of metastasis	No of FMD cycles	Reduced/non-administered FMD cycles	Adverse events	Best response
1	51	34.4	IV; HER2-neg	FULV+PALB	P	lymph nodes	10*	1 reduced cycle (4d)	none	SD
2	46	34.8	IV; HER2-pos	exemestane+rastuzumab; pertuzumab	P	liver, lung, lymph nodes	6	none	diarrhea (G2)	SD
3	62	25.3	IV; HER2-neg	letrozole	P	pleura	13	4 reduced cycles (3-4d) and 1 non-administered cycle	none	SD
4	55	26.4	IIB; HER2-neg	exemestane	A	N/A	4*	2 reduced cycles (3-4d)	diarrhea (G2)	NED
5	37	22.1	IA; HER2-neg	exemestane+GnRH agonist	A	N/A	9	1 reduced cycle (4d)	none	NED
6	54	32.3	IIB; HER2-neg	letrozole	A	N/A	14	none	headache (G1); fatigue (G2) hypotension (G2)	NED
7	52	19.6	IV; HER2-neg	exemestane	P	bone	12	1 reduced cycle (4d)	headache (G1)	SD
8	48	22.2	IIB; HER2-neg	exemestane+GnRH agonist	A	N/A	12	none	headache (G1); tinnitus (G1)	NED
9	54	25.2	IIA; HER2-neg	exemestane	A	N/A	3	none	headache (G1)	NED
10	54	22.4	IA; HER2-neg	letrozole	A	N/A	5	none	headache (G1)	NED
11	46	22.3	IA; HER2-neg	letrozole+GnRH agonist	A	N/A	11	4 reduced cycles (4d)	fatigue (G2); headache(G1)	NED
12	49	23	IIB; HER2-pos	exemestane+rastuzumab+GnRH agonist	A	N/A	5	none	none	NED
13	42	26.2	IA; HER2-neg	exemestane+GnRH agonist	A	N/A	5	none	none	NED
14	56	22.9	IIB	exemestane	A	N/A	7	none	abdominal pain (G1)	NED
15	43	33.4	IV	FULV+abemaciclib	P	skin, lung, bone, lymph nodes	1*	none	none	SD
16	42	21.9	IIB	exemestane+GnRH agonist	A	N/A	5	1 reduced cycle (3d)	none	NED
17	45	30.4	IIB	TMX+ GnRH agonist	A	N/A	6	none	fatigue (G1); hypotension (G2); headache (G1)	NED
18	57	25	IV	letrozole	A	N/A	4*	none	none	SD
19	44	30.4	IIA	TMX+ GnRH agonist	A	N/A	6	none	fatigue (G1); headache (G1)	NED

20	50	25.4	IA	TMX+ GnRH agonist	A	N/A	3	1 reduced cycle (3d); 1 cycle not administered	none	NED
21	58	21.3	IB	letrozole	A	N/A	9	1 reduced cycle (4d)	fatigue (G1)	NED
22	48	42.1	IIB	exemestane+ GnRH agonist	A	N/A	7	none	none	NED
23	62	27.6	IIIC	exemestane	A	N/A	4	none	headache (G1)	NED
24	50	24.5	IB	exemestane+ GnRH agonist	A	N/A	1	none	headache (G1), fatigue (G1)	NED
25	67	21.1	IV	exemestane+ everolimus	P	bone	2	N/A	fatigue (G2)	PR
26	52	26.44	IV	FULV+PALB	P	bone	8	N/A	fatigue (G2), headache (G1)	CR
27	50	21.77	IV	FULV+PALB+ GnRH agonist	P	bone, liver	8	N/A	fatigue (G2), headache (G1), vomiting (G1)	CR
28	53	23.84	IV	FULV	P	bone, liver, lymph nodes	4	N/A	fatigue (G3), vomiting (G2), rash (G1)	SD
29	52	23.98	IV	FULV+PALB	P	lung, liver, bone, lymph nodes	5	N/A	fatigue (G1), nausea (G1), vomiting (G1), tachycardia (G1)	SD
30	50	23.16	IV	TMX	P	lung, bone, lymph nodes	5	N/A	Fatigue (G1), headache (G1)	SD
31	43	21.72	IV	FULV+ GnRH agonist	P	bone	2	N/A	fatigue (G1), nausea (G1), dizziness (G1), vomiting (G1), headache (G1)	PD
32	44	29.4	IA	TMX+ GnRH agonist	A	N/A	8	N/A	fatigue (G2), nausea (G1), headache (G1), vomiting (G1)	NED
33	61	33.12	IIB	letrozole	A	N/A	5	N/A	fatigue (G2)	NED
34	50	26.9	IIB	TMX	A	N/A	8	N/A	fatigue (G2), constipation (G1), hot flushes (G1)	NED
35	73	20.82	IA	letrozole	A	N/A	7	N/A	nausea (G1), fatigue (G1), headache (G1)	N/A
36	55	21.13	IIA	letrozole	A	N/A	4	N/A	fatigue (G1), headache (G1), dizziness (G1), muscle cramps (G1)	N/A

Abbreviations: CR: complete response; PR: partial response; SD: stable disease; NED no evidence of disease; PD: progression of disease.

Pts. 1-24 are from trial NCT03595540; Pts. 25-36 are from trial NCT03340935.

*The patient dropped out for personal reasons.

Supplementary Table 2. Complete blood counts and metabolic panel post-FMD (within 48h from the end of a FMD cycle) in patients with HR+ BC treated with ET and periodic FMD (trial NCT03595540).

Blood test	Pt.#3	Pt.#5	Pt.#6	Pt.#7	Pt.#14	Pt.#24
hemoglobin (g/dl; 12-16)	13.4	13.4	13.8	13.9	14.3	14.0
hematocrit (%; 35-47)	41.6	38.0	42.2	40.7	43.5	41.0
mean corpuscular volume (fl; 79-98)	90.3	83.7	91.2	88.0	89.8	91.9
white blood cells ($10^3/\mu\text{l}$; 4.5-9.8)	5.15	3.87	3.94	2.7	4.2	4.80
neutrophils ($10^3/\mu\text{l}$; 1.8-7.8)	2.24	2.32	1.78	1.2	2.3	2.1
lymphocytes ($10^3/\mu\text{l}$; 1.1-4.8)	2.52	1.21	1.63	1.2	1.3	1.9
platelets ($10^3/\mu\text{l}$; 130-430)	214	180	267	163	208	347
creatinine (mg/dl; 0.51-0.95)	0.67	0.8	0.74	0.75	0.8	0.8
blood urea nitrogen (mg/dl; 21-54)	n.a.	n.a.	33	38	22	29
sodium (mmol/l; 135-150)	139	143	141	139	140	141
potassium (mmol/l; 3.5-5.0)	4.5	4.4	n.a.	4.6	3.8	4.4
phosphorus (mg/dl; 2.5-4.5)	3.7	4.3	n.a.	4.0	2.6	3.9
magnesium (mg/dl; 1.9-2.5)	2.0	2.0	2.2	2.14	2.1	2.1
albumin (g/l; 34-50)	45	52.5	47.3	n.a.	47.6	45.9

Abbreviations: n.a.: not available.

Supplementary Table 3. QPCR primer list

Gene name	FW/REV primer	primer sequence
Human ACTB	FW	CGGGAAATCGTGCCTGACATTAAG
	REV	TGATCTCCTTCTGCATCCTGTCGG
Human TFF1	FW	TTTGGAGCAGAGAGGAGGCAATG
	REV	ACCACAATTCTGTCTTTCACGGGG
Human E2F1	FW	ATGTTTTCCCTGTGCCCTGAG
	REV	ATCTGTGGTGAGGGATGAGG
Human E2F2	FW	CTCTCTGAGCTTCAAGCACCTG
	REV	CTTGACGGCAATCACTGTCTGC
Human CCNE1	FW	TGTGTCCTGGATGTTGACTGCC
	REV	CTCTATGTGCGCACCCTGATACC
Human CCND1	FW	GCCTCTAAGATGAAGGAGAC
	REV	CCATTTGCAGCAGCTC
Human EGR1	FW	GCAGAGTCTTTTCCTGAC
	REV	TTGGTCATGCTCACTAGG
Human PTEN	FW	GGCTAAGTGAAGATGACAA
	REV	GTTACTCCCTTTTTGTCTCT
Human TFF1	FW	TTTGGAGCAGAGAGGAGGCAATG
	REV	ACCACAATTCTGTCTTTCACGGGG
Human GREB	FW	CTTGGTTTCTCTGGGAATTG
	REV	TTCCAACAGATTAAGGTCC
mouse Actb	FW	GATGTATGAAGGCTTTGGTC
	REV	TGTGCACTTTTATTGGTCTC
mouse Egr1	FW	CAGAGTCCTTTTCTGACATC
	REV	GAGAAGCGGCCAGTATAG
mouse Pten	FW	AACTTGCAATCCTCAGTTTG
	REV	CTACTTTGATATCACCACACAC
mouse Tff1	FW	CTCAAGAAGAAGAATGTCCC
	REV	CTCTTTTAATTCTCAGGCCG