

Supplementary Information

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Serial evaluation of serum thymidine kinase activity is prognostic in women with newly diagnosed metastatic breast cancer

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Supplementary Table S1. Median sTK1 activity levels at baseline and during 1, 3 and 6 months of therapy in all patients and in subgroups based on treatment modality

Treatment group		Baseline Median TK1 level, Du/L (range)	1 month Median TK1 Level, Du/L (range)	3 months Median TK1 Level, Du/L (range)	6 months Median TK1 Level, Du/L (range)
All (n=134)		391 (11-35520)	433 (9-40440)	200 (5-38310)	131 (4-28030)
Chemotherapy (n=64)		420 (12-35520)	874 (21-34510)	759 (20-38310)	387 (14-28030)
Subtype in Chemotherapy treated	ER+ (n=41)	423 (14-35520)	934 (21-34510)	854 (20-38310)	392 (14-28030)
	TNBC (n=22)	435 (12-3379)	804 (92-7660)	646 (87-3476)	283 (33-18360)
Endocrine therapy (n=57)		204 (11-27230)	93 (9-31170)	79 (5-17720)	55 (4-4480)
HER2 directed therapy (n=13)		1037 (16-22740)	913 (47-40440)	197 (47-3709)	107 (21-2523)

Abbreviations: Du/L, Divitum units per Litre; ER+, estrogen receptor positive; TNBC, triple negative breast cancer

Supplementary Table S2. Cox regression analyses of hazard ratios in relation to log10 sTK1 levels in univariable and multivariable models

		PFS			OS		
		HR	CI	P-value	HR	CI	P-value
Baseline	UV	1.58	1.24-2.02	<0.001	1.83	1.35-2.47	<0.001
	MV^a	2.27	1.56-3.30	<0.001	2.97	1.77-4.97	<0.001

PFS, progression-free survival; OS, overall survival; HR, hazard ration; CI, confidence interval; UV, univariable analysis; MV, multivariable analysis

^aAdjusted for age, ECOG (Eastern Cooperative Oncology Group Performance Status), NHG (Nottingham Histological Grade), Subtype, Metastasis-Free Interval, Number of metastatic sites, Site of metastasis (visceral/non-visceral)

Supplementary Table S3. Cox regression analysis evaluating hazard ratios in patients with Log10 changes (decrease versus increase/unchanged) in sTK1 levels from 3 to 6 months, adjusted for sTK1 level at three months and subgroup analyses based on treatment modality (ET versus ChT)

Treatment type	PFS			OS		
	HR	CI	P-value	HR	CI	P-value
All	0.43	0.20-0.90	0.026	0.34	0.16-0.72	0.004
ET	0.24	0.07-0.82	0.023	0.18	0.06-0.51	0.001
ChT	0.37	0.14-0.99	0.049	0.54	0.21-1.39	0.20

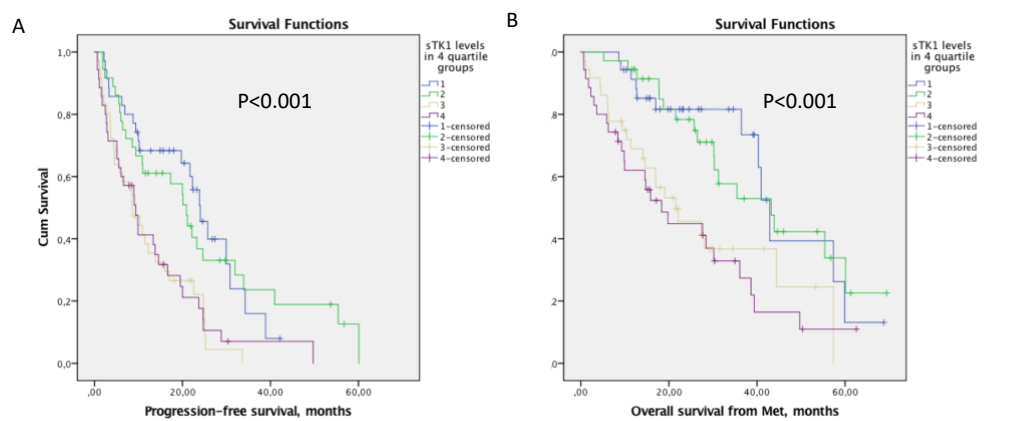
PFS, progression-free survival; OS, overall survival; HR, hazard ration; CI, confidence interval; UV, univariable analysis; MV, multivariable analysis; ET, endocrine therapy; ChT, chemotherapy

Supplementary Table S4. Median sTK1 activity levels at baseline and during 1, 3 and 6 months of therapy based on treatment modality and response evaluation (at 3 and 6 months)

Treatment type	Time point	PD			Non-PD		
		median	range	n	median	range	n
All	BL	560	11-27230	36	227	12-35520	96
	1m	1017	12-31170	36	336	9-40440	96
	3m	693	18-17720	31	181	5-38310	91
	6m	545	27-18360	18	103	4-28030	86
ET	BL	250	11-29230	14	172	13-2352	43
	1m	89	12-31170	14	93	9-1788	43
	3m	89	18-17720	12	78	5-2620	41
	6m	147	27-2281	8	41	4-4480	39
CT	BL	718	83-2677	20	374	12-35520	43
	1m	1258	83-7660	20	733	21-34510	43
	3m	1504	87-3700	18	636	10-38310	42
	6m	1145	125-18360	9	356	14-28030	40

PD, Progressive Disease; non-PD, non Progressive Disease, BL, baseline; ET, endocrine therapy; CT, chemotherapy

Supplementary Figure S1. Progression-free and overall survival in patients with MBC based on quartiles of sTK1 levels at baseline



Supplementary Figure S2: Progression-free (A-B) and overall survival (C-D) in relation to changes in sTK1 levels during therapy from baseline to 3 months based on treatment modality: ET (A, C) versus ChT (B, D)

