

SUPPLEMENTARY TABLE 1

Clinical data of patients from protocol S57123 (UZ Leuven)

Patient ID	Age diagnosis	Gender	Reason of surgery
S57123-001		68 M	volume reduction surgery in emphysema
S57123-002		69 M	volume reduction surgery in emphysema
S57123-003		58 M	peritumoral normal lung tissue from tumorectomy
S57123-004		64 F	volume reduction surgery in emphysema
S57123-005		56 F	peritumoral normal lung tissue from tumorectomy
S57123-006		34 F	peritumoral normal lung tissue from tumorectomy
S57123-007		66 M	peritumoral normal lung tissue from tumorectomy

SUPPLEMENTARY TABLE 2

Clinical data of patients from the UPTIDER program

Patient ID	Age diagnosis	Age death	Molecular subtype primary tumor	Histotype	Grade of tumor at diagnosis*	Stage at diagnosis*
2004	56	61	ER+/PR+/HER2-	Metaplastic-SCC	2	II
2005	53	60	ER+/PR-/HER2-	ILC	2	III
2006	46	60	ER+/PR+/HER2-	NST+ILC	2	I
2008	69	77	ER+/PR+/HER2-	NST	3	II
2009	51	62	ER+/PR+/HER2-	NST	3	II
2010	65	88	ER+/PR+/HER2-	NST	2	II
2011	51	60	ER+/PR+/HER2-	ILC	2	III
2016	49	56	ER+/PR+/HER2-	NST	2	I
2018	47	60	ER+/PR+/HER2-	NST+ILC	2	II

*When the samples were obtained they were both stage IV (which is the case for all UPTIDER patients)

SUPPLEMENTARY TABLE 3

Clinical data comparison between primary metastasized and non-metastasized patients in the CHEMOREL study.

Variables	Contrast	Primary metastasized patients	Non-metastasized patients
Age patients	N Median Average Range	14 63.5 62 [32.0; 88.0]	43 54 56 [36.0; 82.0]
Grade of tumor			
Grade 2	n/N (%)	0/14 (0%)	1/43 (2%)
Grade 3	n/N (%)	14/14 (100%)	42/43 (98%)
Stage (without M* info)			
Stage I	n/N (%)	0/14 (0%)	3/43 (7%)
Stage IIA	n/N (%)	0/14 (0%)	15/43 (35%)
Stage IIB	n/N (%)	5/14 (36%)	8/43 (19%)
Stage IIIA	n/N (%)	1/14 (7%)	14/43 (32%)
Stage IIIB	n/N (%)	5/14 (36%)	0/43 (0%)
Stage IIIC	n/N (%)	3/14 (21%)	3/43 (7%)
ER			
Positive	n/N (%)	14/14 (100%)	42/43 (98%)
Negative	n/N (%)	0/14 (0%)	1/43 (2%)
PR			
Positive	n/N (%)	13/14 (93%)	41/43 (95%)
Negative	n/N (%)	1/14 (7%)	2/43 (5%)
HER2			
Positive	n/N (%)	0/14 (0%)	0/43 (0%)
Negative	n/N (%)	14/14 (100%)	43/43 (100%)

Abbreviations: M*: Metastasis

SUPPLEMENTARY TABLE 4

Clinical information

		N(%)					
		TCGA(n=1220)			METABRIC(n=1904)		
		CPT1A-low (n=610)	CPT1A-high (n=611)	p value	CPT1A-low (n=716)	CPT1A-high (n=683)	p value
Characteristics							
Age	median(range)	57(26, 90)	59(27, 90)	0,04	59.8(21.93, 96.3)	26.72, 85	0,001
Age-group	young(<50)	190	154	0,03	183	132	0,006
	old(>=50)	420	456		533	551	
Menopaus	pre	135	124	0,89	183	132	0,006
	post	379	389		533	551	
	intermediate	25	32		0	0	
	missing	71	66		0	0	
TNM-Stage	1	116	86	p<0.001	280	195	p<0.001
	2	358	339		380	420	
	3	115	161		52	63	
	4	8	14		4	5	
	missing	13	11		0	0	
Stage-group	stage 1-2	474	425	p<0.001	660	615	0,19
	stage 3-4	123	175		56	68	
Subtype	LumA	231	249	0,14	307	213	p<0.001
	LumB	44	153		129	210	
	Her2-enriched	31	43		42	100	
	Basal	116	41		83	52	
	normal	8	19		61	39	
	missing	180	106		94	69	
histologic	: IDC	438	448	0,41	546	545	0,05
	ILC	102	110		41	59	
	others	70	53		129	79	

Uni-multi variate analysis

KM plot and forest plot

cutoff: age(<50,>=50), stage(1-2 vs 3-4), subtype(LumA, LumB, Her2, Basal, Normal)

TCGA						
category						
variable	HR	95%CI	p-value	n	groups	
CPT1A	1,74	1.29-2.29	0,0002	1218(200)	median	
age	1,47	1.07-2.01	0,0200	1218(200)	<50 vs. >=50	
stage	1,85	1.34-2.55	0,0002	1218(200)	1-2 vs. 3-4	
subtype	0,79	0.34-1.81	0,5750	934(164)	LumA vs. Normal	
	1,33	0.56-3.16	0,5116		LumB vs. Normal	
	2,18	0.87-5.44	0,0949		Her2 vs. Normal	
	0,97	0.40-2.33	0,937		Basal vs. Normal	

*univariate analysis, model, OS=CPT1A/age/stage/subtype

variable	HR	95%CI	p-value	n	groups	
CPT1A	1,73	1.20-2.51	0,004	915(156)	median	
age	1,70	1.17-2.47	0,0050		<50 vs. >=50	
stage	2,48	1.77-3.49	<0.001		1-2 vs. 3-4	
subtype	0,72	0.31-1.67	0,4400		LumA vs. Normal	
	0,90	0.38-2.17	0,8200		LumB vs. Normal	
	1,97	0.78-4.96	0,1500		Her2 vs. Normal	
	1,29	0.53-3.19	0,57		Basal vs. Normal	

*multivariate analysis: model, OS=CPT1A+age+stage+subtype

METABRIC						
category						
variable	HR	95%CI	p-value	n	groups	
CPT1A	1,48	1.31-1.67	<.0001	1904(1103)	median	
age	1,68	1.43-1.98	<.0001	1904(1103)	<50 vs. >=50	
stage	2,30	1.84-2.89	<.0001	1390(783)	1-2 vs. 3-4	
subtype	0,86	0.67-1.11	0,2444	1699(1009)	LumA vs. Normal	
	1,30	1.01-1.67	0,0396		LumB vs. Normal	
	1,47	1.12-1.94	0,0059		Her2 vs. Normal	
	1,16	0.87-1.56	0,306		Basal vs. Normal	

*univariate analysis

variable	HR	95%CI	p-value	n	groups	
CPT1A	1,22	1.05-1.43	0,009	1227(710)	median	
age	1,60	1.31-1.97	<.0001		<50 vs. >=50	
stage	1,92	1.50-2.47	<.0001		1-2 vs. 3-4	
subtype	0,87	0.64-1.19	0,3786		LumA vs. Normal	
	1,12	0.81-1.54	0,4995		LumB vs. Normal	
	1,43	1.01-2.02	0,0457		Her2 vs. Normal	
	1,18	0.82-1.70	0,3612		Basal vs. Normal	

*multivariate analysis: model, OS=CPT1A+age+stage+subtype

*still sig after correct for menopausal

TCGA						
continuous						
variable	HR	95%CI	p-value	n	groups	
CPT1A	1,01	1.00-1.02	0,0087	1218(200)	continuous	
age	1,47	1.07-2.01	0,0200	1218(200)	<50 vs. >=50	
stage	1,93	1.58-2.34	<.0001	1196(188)	1,2,3,4	
subtype	0,79	0.34-1.81	0,5800	934(164)	LumA vs. Normal	
	1,33	0.56-3.16	0,51		LumB vs. Normal	
	2,18	0.87-5.44	0,09		Her2 vs. Normal	
	0,96	0.40-2.33	0,94		Basal vs. Normal	

*univariate analysis

variable	HR	95%CI	p-value	n	groups	
CPT1A	1,01	1.00-1.02	0,025	915(156)	continuous	
age	1,68	1.02-1.05	0,0056		<50 vs. >=50	
stage	2,02	1.68-2.58	<0.001		1,2,3,4	
subtype	0,67	0.28-1.51	0,3508		LumA vs. Normal	
	0,82	0.34-1.98	0,7016		LumB vs. Normal	
	1,74	0.74-4.67	0,2402		Her2 vs. Normal	
	1,12	0.46-2.74	0,7997		Basal vs. Normal	

*multivariate analysis: model, OS=CPT1A+age+stage+subtype

METABRIC						
continuous						
variable	HR	95%CI	p-value	n	groups	
CPT1A	1,51	1.34-1.71	<.0001	1904(1103)	continuous	
age	1,68	1.43-1.98	<.0001	1904(1103)	<50 vs. >=50	
stage	1,81	1.62-2.03	<.0001	1403(792)	0,1,2,3,4	
subtype	0,86	0.67-1.11	0,2444	1699(1009)	LumA vs. Normal	
	1,30	1.01-1.67	0,0396		LumB vs. Normal	
	1,47	1.12-1.94	0,0059		Her2 vs. Normal	
	1,16	0.87-1.56	0,306		Basal vs. Normal	

*univariate analysis

variable	HR	95%CI	p-value	n	groups	
CPT1A	1,17	0.99-1.37	0,058	1227(710)	continuous	
age	1,61	1.32-1.98	<.0001		<50 vs. >=50	
stage	1,90	1.48-2.43	<.0001		1,2,3,4	
subtype	0,88	0.64-1.19	0,4001		LumA vs. Normal	
	1,12	0.81-1.54	0,4881		LumB vs. Normal	
	1,44	1.02-2.05	0,0399		Her2 vs. Normal	
	1,18	0.82-1.70	0,3601		Basal vs. Normal	

*multivariate analysis: model, OS=CPT1A+age+stage+subtype

*still sig after correct for menopausal

SUPPLEMENTARY TABLE 5

Primers used to analyze mRNA levels

Target organism	Target gene	Sequence 5' – 3'
Human	<i>RPL19</i>	Fwd: ATTGGTCTCATTGGGGTCTAAC Rev: AGTATGCTCAGGCTTCAGAAGA
Human	<i>CPT1A</i>	Fwd: GCACCTCCGTAGCTGACTC Rev: GAGTGACCGTGAAGTGAAGG
Human	<i>ICAM1</i>	Fwd: GGCTGGAGCTGTTTGAGAAC Rev: CTGTGGGGTTCAACCTCTG
Human	<i>PTPN13</i>	Fwd: TTCTCTGCAGACCTCCACCT Rev: TCTTCTCCACTCCCACTGCT
Human	<i>TNFAIP2</i>	Fwd: GAAGTCTGGCTGAGGTCTGG Rev: CTCCAGAAGGAGTGCAGGAC
Human	<i>MMP9</i>	Fwd: TTGACAGCGACAAGAAGTGG Rev: GCCATTCACGTCGTCTTAT
Human	<i>JAG1</i>	Fwd: TGCTACAACCGTGCCAGTGACT Rev: TCAGGTGTGTCGTTGGAAGCCA
Mouse	<i>Cpt1a</i>	Fwd: CAGAGGATGGACACTGTAAAGG Rev: AGTATGCTCAGGCTTCAGAAGA
Mouse	<i>Rpl19</i>	Fwd: CAGGCATATGGGCATAGGGAA Rev: TGCCTTCAGCTTGTGGATGT
Mouse	<i>Icam1</i>	Fwd: AGCACCTCCCCACCTACTTT Rev: AGCTTGACGACCCCTTCTAA
Mouse	<i>Ptpn13</i>	Fwd: GAACACCTCGACTGTGCTGA Rev: GGACGCTGGTATTCACACCT
Mouse	<i>Tnfaip2</i>	Fwd: AAAAAGGACCAGCCCAGATT Rev: TACAGAGCTCCACCTTGCT
Mouse	<i>Mmp9</i>	Fwd: TGAATCAGCTGGCTTTTGTG Rev: GTGGATAGCTCGGTGGTGT
Mouse	<i>Fabp5</i>	Fwd: GACGACTGTGTTCTCTTGTAAAC Rev: TGTTATCGTGCTCTCCTTCCCG
Mouse	<i>Sfpb</i>	Fwd: TGTGCCAAGAGTGTGAGGAT Rev: CAGGGGCAGGTAGACATCAA
Mouse	<i>Sfpc</i>	Fwd: GATGAGAAGGCGTTTGAGGT Rev: GATGAGAAGGCGTTTGAGGT
Mouse	<i>Abca3</i>	Fwd: GGTCTGATGGAGAGTCCAC Rev: GGAGCAGGAACGCTGAGAT
Mouse	<i>Acsl4</i>	Fwd: CCTTTGGCTCATGTGCTGGAAC Rev: GCCATAAGTGTGGGTTTCAGTAC
Mouse	<i>Kat2a</i>	Fwd: CACGGAATCGTCTTCTGTGCC Rev: CGTACTCGTCAGCATAGGTGAG
Mouse	<i>Kat2b</i>	Fwd: CCTCTTACCTGCGTCCACAAA Rev: TCTCCAAGGAGCCTTCAACCAC
Mouse	<i>Noa1</i>	Fwd: GAGCGGCATAAAATTCTGCACCG Rev: CACTGACACAGCAGTAGAGGCT
Mouse	<i>Kat5</i>	Fwd: TGAGCGTGAAGGACATCAGTGG Rev: TTAAGTCCAGCCGCTCGTGAGT
Mouse	<i>Kat6a</i>	Fwd: CGGTCAAACCTGCCACCAATTC Rev: CTAACACCTCCGTGGTCTCAGA
Mouse	<i>Kat6b</i>	Fwd: GCTGTGGTTTCTGAGGAAGAGC Rev: TGCCTACTGCTAACTCTGGACG
Mouse	<i>Ep300</i>	Fwd: GTGATGACCCTTCCCAACCTCA Rev: CTCGTGGTGAAGGACACAGATC
Mouse	<i>Crebbp</i>	Fwd: CACCATCTGTGGCTACTCCTCA Rev: GGTTCAGCACTGGTCACAGAG
Mouse	<i>Kat7</i>	Fwd: AGGAAAAGGTGGCTGAAGTCAAGG Rev: GTCAGGTTTTCCAAGAGAGGCTC
Mouse	<i>Kat8</i>	Fwd: CAGCAGAAGTGATCCAGTCTCG Rev: TTGGTCAGTGCGAGTCGGTTCT