

Supplementary Table S1: PTEN mutations and their association with PTEN IHC

sample		PTEN mut	coding change	PTEN functional domain	pathogenic	PTEN IHC A	PTEN IHC B	PTEN STATUS A	PTEN STATUS B	PTEN mut vs. IHC A	PTEN mut vs. IHC B
order	ID										
1	BR5-006	p.Phe21Leu	c.59_63delGATTC	phosphatase domain, FS	yes (FS)	N.A.	N.A.	loss	loss	N.A.	N.A.
2	BR5-027	p.Gly20Arg	c.58G>A	phosphatase domain	yes (COSMIC)	no loss	no loss	no loss	no loss	discordant	discordant
3	BR5-036	p.Gly20Val	c.59G>T	phosphatase domain	yes (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
4	BR5-045	p.Cys250Tyr; p.Gly251Ser	c.749G>A; c.751G>A	C2 lipid membrane binding	yes (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
5	BR5-047	p.Asp19Glu	c.57T>G	phosphatase domain	yes (COSMIC)	no loss	no loss	no loss	no loss	discordant	discordant
6	BR5-055	p.Val255Leu	c.763G>T	C2 lipid membrane binding	yes (COSMIC)	loss	loss	loss	loss	concordant	concordant
7	BR5-063	p.Val249Ala	c.746T>C	C2 lipid membrane binding	not reported	no loss	no loss	no loss	no loss	discordant	discordant
8	BR5-073	p.Lys13Thr	c.38A>C	none assigned	yes (COSMIC)	no loss	no loss	no loss	no loss	discordant	discordant
9	BR5-119	p.Arg233*; p.Ile253Asn	c.697C>T; c.756_757insA	C2 lipid membrane binding, Ter & FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
10	BR5-157	p.Arg234Gln ^	c.701G>A	C2 lipid membrane binding	yes (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
11	BR5-215	p.Tyr225*	c.675T>A	C2 lipid membrane binding, Ter	yes (Ter)	loss	loss	loss	loss	concordant	concordant
12	BR5-222	p.Gln17Arg	c.50_51delAA	phosphatase domain, FS	yes (FS)	loss	no loss	loss	no loss	concordant	discordant
13	BR5-231	p.Asp331Glu	c.992_993delAC	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
14	BR5-463	p.Thr319*	c.950_953delTACT	C2 lipid membrane binding, FS	yes (FS)	N.A.	N.A.	loss	loss	N.A.	N.A.
15	BR5-464	p.Pro248Leu	c.743C>T	C2 lipid membrane binding	unknown (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
16	BR5-465	p.Gly230Arg	c.688G>A	C2 lipid membrane binding	yes (COSMIC)	N.A.	N.A.	loss	loss	N.A.	N.A.
17	BR5-474	p.Thr319*	c.950_953delTACT	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
18	BR5-516	p.Glu242*	c.720_721insT	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
19	BR5-547	p.Val317Ser	c.947_948insA	C2 lipid membrane binding, FS	yes (FS)	N.A.	N.A.	loss	loss	N.A.	N.A.
20	BR5-569	p.Leu25Phe	c.75G>C	phosphatase domain	unknown (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
21	BR5-589	p.Arg15*	c.43A>T	phosphatase domain, Ter	yes (Ter)	N.A.	N.A.	loss	loss	N.A.	N.A.
22	BR5-805	p.Ser229*	c.686C>G	C2 lipid membrane binding, Ter	yes (Ter)	N.A.	N.A.	loss	loss	N.A.	N.A.
23	BR5-830	splice site	n.a.	phosphatase domain	possibly pathogenic	loss	no loss	loss	no loss	concordant	discordant
24	BR5-840	p.Pro244Leu	c.731C>T	C2 lipid membrane binding	not reported	no loss	no loss	no loss	no loss	discordant	discordant
25	BR8-221	p.Ser227Cys	c.680C>G	C2 lipid membrane binding	yes (COSMIC)	loss	loss	loss	loss	concordant	concordant
26	BR8-298	splice site	n.a.	C2 lipid membrane binding	possibly pathogenic	loss	loss	loss	loss	concordant	concordant
27	BR8-326	p.Pro213Leu	c.637_637delC	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
28	BR8-351	p.Thr319*	c.950_953delTACT	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
29	BR8-396	p.Thr319Asn	c.954_955insA	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
30	BR8-495	p.Ala328*	c.978_982delCAAAG	C2 lipid membrane binding, FS	yes (FS)	N.A.	N.A.	loss	loss	N.A.	N.A.
31	BR8-548	p.Ile253*	c.756_757insTG	C2 lipid membrane binding, FS	yes (FS)	loss	loss	loss	loss	concordant	concordant
32	BR8-614	p.Val222Met	c.664G>A	C2 lipid membrane binding	yes (COSMIC)	loss	loss	loss	loss	concordant	concordant
33	BR8-620	p.Asp24Gly	c.71A>G	phosphatase domain	yes (COSMIC)	loss	no loss	loss	no loss	concordant	discordant
34	BR8-642	p.Pro248Leu	c.743C>T	C2 lipid membrane binding	unknown (COSMIC)	no loss	no loss	no loss	no loss	discordant	discordant
35	BR8-699	p.Glu7Lys	c.19G>A	none assigned	yes (COSMIC)	N.A.	N.A.	loss	loss	N.A.	N.A.
36	BR8-735	p.Gln17*	c.49C>T	phosphatase domain, Ter	yes (Ter)	no loss	no loss	no loss	no loss	discordant	discordant
37	BR8-741	p.Arg15Lys	c.44G>A	phosphatase domain	yes (COSMIC)	loss	loss	loss	loss	concordant	concordant
38	BR8-774	p.Pro354Ser	c.1060C>T	none assigned	yes (COSMIC)	loss	loss	loss	loss	concordant	concordant

Notes: variant description based on NM_000314.4; FS = frameshift mutation; Ter = nonsense mutations (terminating); N.A. = non informative

Supplementary Table S2. Associations of PTEN status and PIK3CA genotypes with clinicopathological characterist

		PTEN mutations			PIK3CA mutations			PTEN IHC Approach A ▶	PTEN IHC status			PTEN status*			PTEN final status / PIK3CA mut					Approach B ▶	PTEN IHC status			PTEN status*			PTEN final status / PIK3CA mut					
		Mutant	Wild type	p-value	Mutant	Wild type	p-value		loss	no loss	p-value	loss	no loss	p-value	PTEN loss / PIK3CA no mut	PTEN loss/PIK3CA MUT	PTEN no loss / PIK3CA no mut	PTEN no loss/PIK3CA MUT	p-value		loss	no loss	p-value	loss	no loss	p-value	PTEN loss / PIK3CA no mut	PTEN loss/PIK3CA MUT	PTEN no loss / PIK3CA no mut	PTEN no loss/PIK3CA MUT	p-value	
Age (median cutoff)	≤50 >50	12 (31.6) 26 (68.4)	380 (41.2) 543 (58.8)	0.238	100 (35.2) 184 (64.8)	292 (43.1) 385 (56.9)	0.023	170 (41.0) 245 (59.0)	342 (40.6) 500 (59.4)	0.906	172 (40.7) 251 (59.3)	342 (40.6) 500 (59.4)	0.988	114 (45.4) 137 (54.6)	25 (30.5) 57 (69.5)	178 (41.8) 248 (58.2)	75 (37.1) 127 (62.9)	0.068		113 (41.5) 159 (58.5)	399 (40.5) 586 (59.5)	0.758	115 (41.1) 165 (58.9)	399 (40.5) 586 (59.5)	0.865	80 (47.6) 88 (52.4)	16 (31.4) 35 (68.6)	212 (41.7) 297 (58.3)	84 (36.1) 149 (63.9)	0.059		
Menopausal status	Premenopausal Postmenopausal	27 (71.1) 11 (28.9)	502 (54.4) 421 (45.6)	0.043	163 (57.4) 121 (42.6)	366 (54.1) 311 (45.9)	0.343	226 (54.5) 189 (45.5)	473 (56.2) 369 (43.8)	0.564	232 (54.8) 191 (45.2)	473 (56.2) 369 (43.8)	0.653	123 (49.0) 128 (51.0)	54 (65.9) 28 (34.1)	243 (57.0) 183 (43.0)	109 (54.0) 93 (46.0)	0.039		150 (55.1) 122 (44.9)	549 (55.7) 436 (44.3)	0.863	156 (55.7) 124 (44.3)	549 (55.7) 436 (44.3)	0.995	83 (49.4) 85 (50.6)	33 (64.7) 18 (35.3)	283 (55.6) 226 (44.4)	130 (55.8) 103 (44.2)	0.241		
Breast surgery	MRM Breast conserving surgery	20 (52.6) 18 (47.4)	451 (48.9) 472 (51.1)	0.649	151 (53.2) 133 (46.8)	320 (47.3) 357 (52.7)	0.095	206 (49.6) 209 (50.4)	435 (51.7) 407 (48.3)	0.5	209 (49.4) 214 (50.6)	435 (51.7) 407 (48.3)	0.449	119 (47.4) 132 (52.6)	40 (48.8) 42 (51.2)	201 (47.2) 225 (52.8)	111 (55.0) 91 (45.0)	0.298		140 (51.5) 137 (48.9)	501 (50.9) 484 (49.1)	0.859	143 (51.1) 137 (48.9)	501 (50.9) 484 (49.1)	0.951	81 (48.2) 87 (51.8)	27 (52.9) 24 (47.1)	239 (47.0) 270 (53.0)	124 (53.2) 109 (46.8)	0.412		
ERPgR status (centrally assessed)	Negative Positive	5 (13.2) 33 (86.8)	154 (16.8) 762 (83.2)	0.554	29 (10.2) 254 (89.8)	130 (19.4) 541 (80.6)	0.001	111 (26.7) 304 (73.3)	79 (9.5) 755 (90.5)	<0.001	112 (26.5) 311 (73.5)	79 (9.5) 755 (90.5)	<0.001	80 (31.9) 171 (68.1)	19 (23.2) 63 (76.8)	50 (11.9) 370 (88.1)	10 (5.0) 191 (95.0)	<0.001		72 (26.5) 200 (73.5)	118 (12.1) 859 (87.9)	<0.001	73 (26.1) 207 (73.9)	118 (12.1) 859 (87.9)	<0.001	54 (32.1) 114 (67.9)	12 (23.5) 39 (76.5)	76 (15.1) 427 (84.9)	17 (7.3) 215 (92.7)	<0.001		
ERPgR status (locally assessed)	Negative Positive	8 (21.1) 30 (78.9)	186 (20.2) 737 (79.8)	0.892	33 (11.6) 251 (88.4)	161 (23.8) 516 (76.2)	<0.001	133 (32.0) 282 (68.0)	94 (11.2) 748 (88.8)	<0.001	135 (31.9) 288 (68.1)	94 (11.2) 748 (88.8)	<0.001	99 (39.4) 152 (60.6)	19 (23.2) 63 (76.8)	62 (14.6) 364 (85.4)	14 (6.9) 188 (93.1)	<0.001		85 (31.3) 187 (68.8)	142 (14.4) 843 (85.6)	<0.001	87 (31.1) 193 (68.9)	142 (14.4) 843 (85.6)	<0.001	69 (41.1) 99 (58.9)	12 (23.5) 39 (76.5)	92 (18.1) 417 (81.9)	21 (9.0) 212 (91.0)	<0.001		
HER2 status (centrally assessed)	Negative Positive	34 (89.5) 4 (10.5)	721 (78.6) 196 (21.4)	0.107	241 (84.9) 43 (15.1)	514 (76.6) 157 (23.4)	0.004	347 (83.6) 68 (16.4)	645 (77.2) 191 (22.8)	0.008	354 (83.7) 69 (16.3)	645 (77.2) 191 (22.8)	0.007	204 (81.3) 47 (18.7)	72 (87.8) 10 (12.2)	310 (73.8) 110 (26.2)	169 (83.7) 33 (16.3)	0.003		239 (87.9) 33 (12.1)	753 (76.9) 226 (23.1)	<0.001	246 (87.9) 34 (12.1)	753 (76.9) 226 (23.1)	<0.001	145 (86.3) 23 (13.7)	46 (90.2) 39 (76.4)	369 (73.6) 134 (26.6)	195 (83.7) 38 (16.3)	<0.001		
HER2 status (locally assessed)	Negative Positive	32 (84.2) 6 (15.8)	689 (75.1) 229 (24.9)	0.199	230 (81.6) 52 (18.4)	491 (72.8) 183 (27.2)	0.004	315 (76.1) 101 (23.9)	627 (74.9) 210 (25.1)	0.65	321 (76.1) 101 (23.9)	627 (74.9) 210 (25.1)	0.653	188 (74.9) 63 (25.1)	62 (76.5) 19 (23.5)	303 (71.6) 120 (28.4)	168 (83.6) 33 (16.4)	0.014		221 (81.5) 52 (18.6)	721 (73.6) 259 (26.4)	0.007	227 (81.4) 52 (18.6)	721 (73.6) 259 (26.4)	0.008	137 (81.5) 10 (20.0)	40 (80.0) 152 (30.0)	354 (70.0) 152 (30.0)	190 (81.9) 42 (18.1)	0.001		
Tumor size	≤2 2-5 >5	15 (39.5) 16 (42.1) 7 (18.4)	374 (40.5) 484 (52.4) 65 (7.0)	0.029	119 (41.9) 143 (50.4) 22 (7.7)	270 (39.9) 357 (52.7) 50 (7.4)	0.797	167 (40.2) 210 (50.6) 40 (9.5)	346 (41.1) 438 (52.0) 58 (6.9)	0.362	170 (40.2) 213 (50.4) 40 (9.5)	346 (41.1) 438 (52.0) 58 (6.9)	0.272	96 (38.2) 134 (53.4) 21 (8.4)	34 (41.5) 42 (51.2) 6 (7.3)	174 (40.8) 223 (52.3) 101 (50.0)	85 (42.1) 505 (51.3) 16 (7.9)	0.971		104 (38.2) 143 (52.6) 25 (9.2)	409 (41.5) 505 (51.3) 71 (7.2)	0.421	107 (38.2) 146 (52.1) 12 (1.7)	409 (41.5) 505 (51.3) 71 (7.2)	0.319	60 (35.7) 96 (57.1) 6 (11.8)	19 (37.3) 26 (51.0) 38 (75.3)	210 (41.3) 261 (51.3) 11 (1.6)	100 (42.9) 117 (50.2) 16 (6.9)	0.685		
Number of positive nodes	0-3 ≥4	26 (68.4) 12 (31.6)	657 (71.2) 266 (28.8)	0.713	206 (72.5) 78 (27.5)	477 (70.5) 300 (29.5)	0.517	289 (69.6) 126 (30.4)	577 (68.5) 265 (31.5)	0.689	294 (69.5) 129 (30.5)	577 (68.5) 265 (31.5)	0.724	191 (76.1) 60 (23.9)	53 (64.6) 29 (35.4)	286 (67.1) 140 (32.9)	153 (75.7) 49 (24.3)	0.018		186 (68.4) 86 (31.6)	680 (69.0) 305 (31.0)	0.837	191 (68.2) 89 (31.8)	680 (69.0) 305 (31.0)	0.793	126 (75.0) 42 (25.0)	32 (62.7) 19 (37.3)	351 (69.0) 158 (31.0)	174 (74.7) 59 (25.3)	0.135		
Histological grade	I II III	1 (2.6) 19 (50.0) 18 (47.4)	73 (8.0) 399 (43.6) 444 (48.5)	0.429	36 (12.7) 137 (48.4) 110 (38.9)	38 (5.7) 281 (41.9) 352 (52.5)	<0.001	22 (5.3) 163 (39.5) 228 (55.2)	72 (8.6) 410 (49.0) 355 (42.4)	<0.001	22 (5.2) 166 (39.4) 233 (55.3)	72 (8.6) 410 (49.0) 355 (42.4)	<0.001	7 (2.8) 88 (35.3) 154 (61.8)	10 (12.2) 38 (46.3) 34 (41.5)	31 (7.3) 193 (47.5) 198 (46.9)	26 (12.9) 99 (49.3) 76 (37.8)	<0.001		14 (5.0) 106 (39.1) 151 (55.7)	80 (8.2) 467 (47.7) 432 (44.1)	0.002	14 (5.0) 109 (39.1) 156 (55.9)	80 (8.2) 467 (47.7) 432 (44.1)	0.002	4 (2.4) 58 (34.7) 105 (62.9)	7 (13.7) 23 (45.1) 21 (41.2)	34 (6.7) 223 (44.2) 247 (49.0)	29 (12.5) 114 (49.1) 89 (38.4)	<0.001		
Histological type	Invasive ductal Mixed Invasive lobular Other	27 (71.1) 5 (13.2) 2 (5.3) 4 (10.5)	794 (86.0) 73 (7.9) 25 (2.7) 31 (3.4)	0.042	232 (81.7) 32 (11.3) 12 (4.2) 8 (2.8)	589 (87.0) 46 (6.8) 15 (2.2) 27 (4.0)	0.026	273 (84.0) 26 (8.0) 6 (1.8) 20 (6.2)	541 (86.1) 51 (8.1) 21 (3.3) 15 (2.4)	0.018	280 (84.1) 27 (8.1) 6 (1.8) 20 (6.0)	541 (86.1) 51 (8.1) 21 (3.3) 15 (2.4)	0.021	210 (83.7) 19 (7.6) 6 (2.4) 16 (6.4)	70 (85.4) 8 (9.8) 9 (2.1) 4 (4.9)	379 (89.0) 27 (6.3) 12 (5.9) 11 (2.6)	162 (80.2) 24 (11.9) 12 (5.9) 4 (2.0)	0.002		173 (82.0) 17 (8.1) 7 (3.3) 14 (6.6)	641 (86.4) 60 (8.1) 20 (2.7) 21 (2.8)	0.07	180 (82.2) 18 (8.2) 7 (3.2) 14 (6.4)	641 (86.4) 60 (8.1) 20 (2.7) 21 (2.8)	0.094	135 (80.4) 13 (7.7) 7 (4.2) 13 (7.7)	45 (88.2) 5 (9.8) 8 (16.0) 1 (2.0)	454 (89.2) 33 (6.5) 12 (5.2) 14 (2.8)	187 (80.3) 27 (11.6) 12 (5.2) 7 (3.0)	0.001		
Adjuvant hormonotherapy	No Yes	7 (18.9) 30 (81.1)	203 (22.0) 720 (78.0)	0.657	38 (13.4) 246 (86.6)	172 (25.4) 504 (74.6)	<0.001	138 (33.3) 276 (66.7)	119 (14.1) 723 (85.9)	<0.001	140 (33.2) 282 (66.8)	119 (14.1) 723 (85.9)	<0.001	99 (39.6) 151 (60.4)	21 (25.6) 61 (74.4)	73 (17.1) 353 (82.9)	17 (8.4) 185 (91.6)	<0.001		91 (33.3) 180 (66.4)	166 (16.9) 819 (83.1)	<0.001	93 (33.3) 186 (66.7)	166 (16.9) 819 (83.1)	<0.001	71 (42.5) 96 (57.5)	13 (25.5) 38 (74.5)	101 (19.8) 408 (80.2)	25 (10.7) 208 (89.3)	<0.001		
Adjuvant radiotherapy	No Yes	10 (27.8) 26 (72.2)	216 (23.9) 689 (76.1)	0.59	73 (26.1) 207 (73.9)	153 (23.1) 508 (76.9)	0.337	95 (23.1) 316 (76.9)	208 (25.3) 615 (74.7)	0.406	97 (23.2) 322 (76.8)	208 (25.3) 615 (74.7)	0.411	61 (24.6) 187 (75.4)	15 (18.5) 66 (81.5)	92 (22.3) 321 (77.7)	58 (29.1) 141 (70.9)	0.176		59 (21.9) 210 (78.1)	244 (25.3) 721 (74.7)	0.259	61 (22.0) 216 (78.0)	244 (25.3) 721 (74.7)	0.266	38 (23.0) 127 (77.0)	10 (19.6) 41 (80.4)	115 (23.2) 381 (76.8)	63 (27.5) 166 (72.5)	0.503		
Herceptin	No Yes	31 (81.6) 7 (18.4)	696 (75.4) 227 (24.6)	0.385	232 (81.7) 52 (18.3)	495 (73.1) 182 (26.9)	0.005	315 (75.9) 100 (24.1)	633 (75.2) 209 (24.8)	0.779	321 (75.9) 102 (24.1)	633 (75.2) 209 (24.8)	0.783	187 (74.5) 64 (25.5)	63 (76.8) 19 (23.2)	308 (72.3) 118 (27.7)	169 (83.7) 33 (16.3)	0.02		222 (81.6) 50 (18.4)	726 (73.7) 259 (26.3)	0.007	228 (81.4) 52 (18.6)	726 (73.7) 259 (26.3)	0.008	137 (81.5) 31 (18.5)	41 (80.4) 10 (19.6)	358 (70.3) 151 (29.7)	191 (82.0) 42 (18.0)	0.001		
Subtypes (centrally assessed)	HER2-Enriched LUMA LumB LuminalHER2 TNBC	65 (7.3) 19 (50.0) 10 (26.3) 4 (10.5) 5 (13.2)	67 (7.2) 331 (37.2) 273 (30.7) 131 (14.7) 89 (10.0)	0.25	9 (3.3) 124 (45.1) 88 (32.0) 34 (12.4) 20 (7.3)	56 (8.6) 226 (34.7) 195 (29.9) 101 (15.5) 74 (11.3)	0.001	33 (8.1) 141 (34.6) 122 (29.4) 35 (8.6) 78 (19.2)	51 (6.4) 349 (44.1) 224 (28.3) 140 (17.7) 28 (3.5)	<0.001	33 (8.0) 145 (34.9) 122 (29.4) 36 (8.7) 79 (19.0)	51 (6.4) 349 (44.1) 224 (28.3) 140 (17.7) 28 (3.5)	<0.001	25 (10.0) 70 (28.1) 77 (30.9) 22 (8.8) 55 (22.1)	3 (3.8) 31 (38.8) 23 (28.8) 7 (8.8) 16 (20.0)	31 (7.7) 93 (47.7) 65 (33.3) 19 (9.6) 19 (4.7)	6 (3.1) 101 (50.0) 118 (58.3) 27 (13.8) 4 (2.1)	<0.001		17 (6.3) 92 (34.2) 91 (32.9) 16 (5.9) 55 (20.2)	67 (7.2) 398 (42.8) 255 (27.4) 159 (17.1) 51 (5.5)	<0.001	17 (6.1) 96 (34.7) 91 (32.9) 17 (6.1) 56 (20.2)	67 (7.2) 398 (42.8) 255 (27.4) 159 (17.1) 51 (5.5)	<0.001	13 (7.7) 45 (26.8) 59 (35.1) 10 (6.0) 10 (20.0)	2 (4.0) 181 (37.4) 136 (28.1) 3 (6.0) 91 (88.8)	43 (8.9) 104 (46.2) 73 (32.4) 31 (18.8) 33 (6.8)	7 (3.1) 104 (46.2) 73 (32.4) 31 (18.8) 10 (4.4)	<0.001		
Subtypes (locally assessed)	HER2-En LumAB LumHER2 TNBC	2 (5.3) 26 (68.4) 4 (10.5) 6 (15.8)	80 (8.7) 586 (63.8) 149 (16.2) 104 (11.3)	0.572	18 (6.4) 225 (54.3) 34 (12.1) 13 (4.6)	64 (9.5) 395 (58.5) 119 (17.6) 97 (14.4)	<0.001	42 (10.1) 225 (54.3) 57 (13.8) 90 (21.7)	61 (7.3) 397 (71.2) 1																							

Supplementary Table S3: Hazard ratios (95% CI) estimated from Cox regression for each of the clinico-pathological variables in the entire cohort, N=1265.

Parameter	DISEASE-FREE SURVIVAL (DFS)					OVERALL SURVIVAL (OS)				
	N patients	N events	HR	95% CI	Wald's p	N patients	N events	HR	95% CI	Wald's p
Adjuvant HT										
Yes vs. No	1005 vs. 259	123 vs. 50	0.58	0.41-0.80	0.001	1005 vs. 259	65 vs. 36	0.43	0.28-0.64	<0.001
Adjuvant RT										
Yes vs. No	937 vs. 305	135 vs. 36	1.21	0.84-1.74	0.32	937 vs. 305	77 vs. 24	1.03	0.65-1.62	0.91
Age										
>50 vs. ≤50	751 vs. 514	112 vs. 62	1.25	0.92-1.70	0.16	751 vs. 514	69 vs. 33	1.46	0.96-2.20	0.076
Breast surgery										
Other vs. MRM	621 vs. 644	64 vs. 110	0.58	0.43-0.79	0.001	621 vs. 644	38 vs. 64	0.6	0.40-0.90	0.013
Herceptin										
Yes vs. No	311 vs. 954	44 vs. 130	1.04	0.74-1.47	0.81	311 vs. 954	25 vs. 77	0.98	0.62-1.54	0.93
Histological grade										
I-II vs. III	670 vs. 588	73 vs. 101	0.6	0.44-0.81	0.001	670 vs. 588	33 vs. 69	0.4	0.26-0.61	<0.001
Histological type					0.53					0.27
Mixed vs. Invasive ductal	27 vs. 821	5 vs. 122	1.27	0.52-3.11	0.6	27 vs. 821	4 vs. 74	1.7	0.62-4.66	0.3
Invasive lobular vs. Invasive ductal	78 vs. 821	11 vs. 122	0.91	0.49-1.69	0.77	78 vs. 821	0 vs. 74	0.54	0.20-1.47	0.23
Other vs. Invasive ductal	35 vs. 821	2 vs. 122	0.38	0.09-1.54	0.18	35 vs. 821	1 vs. 74	0.32	0.04-2.28	0.25
Menopausal status										
Postmenopausal vs. Premenopausal	705 vs. 560	102 vs. 72	1.13	0.83-1.52	0.43	705 vs. 560	65 vs. 37	1.42	0.95-2.12	0.091
Number of positive nodes										
0-3 vs. ≥4	871 vs. 394	83 vs. 91	0.38	0.28-0.52	<0.001	871 vs. 394	49 vs. 53	0.4	0.27-0.59	<0.001
Subtypes local					0.69					0.34
HER2-Enriched vs. TNBC	104 vs. 122	14 vs. 20	0.79	0.40-1.56	0.49	104 vs. 122	10 vs. 14	0.79	0.35-1.79	0.58
Luminal-HER2 vs. TNBC	207 vs. 122	30 vs. 20	0.85	0.48-1.50	0.58	207 vs. 122	16 vs. 14	0.64	0.31-1.30	0.21
Luminal A/B* vs. TNBC	827 vs. 122	108 vs. 20	0.75	0.47-1.22	0.25	827 vs. 122	60 vs. 14	0.6	0.33-1.07	0.083
Subtypes central					0.12					0.1
HER2-Enriched vs. TNBC	84 vs. 107	9 vs. 14	0.8	0.35-1.85	0.6	84 vs. 107	6 vs. 12	0.61	0.23-1.64	0.33
Luminal-HER2 vs. TNBC	176 vs. 107	30 vs. 14	1.33	0.70-2.50	0.38	176 vs. 107	18 vs. 12	0.91	0.44-1.89	0.8
Luminal A vs. TNBC	494 vs. 107	56 vs. 14	0.84	0.47-1.51	0.56	494 vs. 107	28 vs. 12	0.49	0.25-0.97	0.04
Luminal B vs. TNBC	346 vs. 107	58 vs. 14	1.28	0.72-2.30	0.4	346 vs. 107	35 vs. 12	0.88	0.46-1.69	0.7
Tumor size					0.002					0.008
2-5 vs. ≤2	651 vs. 516	98 vs. 54	1.49	1.07-2.07	0.019	651 vs. 516	55 vs. 32	1.4	0.91-2.17	0.13
>5 vs. ≤2	98 vs. 516	22 vs. 54	2.37	1.44-3.89	0.001	98 vs. 516	15 vs. 32	2.59	1.40-4.79	0.002
Ki67 percent			1.005	1000-1.010	0.068			1.011	1.005-1.017	<0.001
TILs (10% increments)			0.8	0.70-0.93	0.003			0.91	0.78-1.06	0.22

HR, Hazard ratio; MRM, Modified Radical Mastectomy; *Ki67 was not assessed locally

Supplementary Table S4: Hazard ratios (95% CIs) estimated from univariate Cox regression with respect to DFS and OS (PTEN IHC approach A).

	DISEASE-FREE SURVIVAL (DFS)				OVERALL SURVIVAL (OS)			
	N events / N patients	HR	95% CI	p-value	N events / N patients	HR	95% CI	p-value
	Entire cohort (N=1265)				Entire cohort (N=1265)			
PTEN IHC status								
Loss vs. no loss	74/415 vs. 98/842	1.63	1.21-2.21	0.001	50/415 vs. 51/842	2.11	1.43-3.12	<0.001
PTEN status ¹								
Loss vs. no loss	76/423 vs. 98/842	1.65	1.22-2.23	0.001	51/423 vs. 51/842	2.12	1.44-3.12	<0.001
PIK3CA mutations								
Non mutant vs. mutant	107/677 vs. 33/284	1.42	0.96-2.09	0.08	63/677 vs. 20/284	1.35	0.82-2.34	0.24
PTEN status/ PIK3CA mutations (ref. Category: PTEN no loss/PIK3CA non-mutant)				0.001				0.002
PTEN loss/PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	54/251 vs. 53/426	1.88	1.29-2.75	0.001	35/251 vs. 28/426	2.28	1.39-3.75	0.001
PTEN loss/PIK3CA mut vs. PTEN no loss/PIK3CA non-mutant	13/82 vs. 53/426	1.34	0.73-2.45	0.35	9/82 vs/ 28/426	1.78	0.84-3.76	0.13
PTEN no loss/PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	20/202 vs. 53/426	0.77	0.46-1.29	0.32	11/202 vs. 28/426	0.81	0.40-1.63	0.56
PTEN status/ PIK3CA mutations (ref. Category: PTEN loss/PIK3CA non-mutant)								
PTEN loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	13/82 vs. 54/251	0.71	0.39-1.30	0.27	9/82 vs. 35/251	0.78	0.37-1.62	0.5
PTEN no loss/ PIK3CA non-mutant vs. PTEN loss/PIK3CA non-mutant	53/426 vs. 54/251	0.53	0.36-0.78	0.001	28/426 vs. 35/251	0.44	0.27-0.72	0.001
PTEN no loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	20/202 vs. 54/251	0.41	0.24-0.68	<0.001	11/202 vs. 35/251	0.36	0.18-0.70	0.003
	HER2(+) cohort (N=211) ²				HER2(+) cohort (N=211) ²			
PTEN IHC status								
Loss vs. no loss	9/57 vs. 18/153	1.37	0.62-3.06	0.44	6/57 vs. 10/153	1.73	0.63-4.78	0.29
PTEN status ¹								
Loss vs. no loss	10/58 vs. 18/153	1.52	0.70-3.29	0.29	6/58 vs. 10/153	1.7	0.62-4.70	0.3
PIK3CA mutations ³								
Non mutant vs. mutant	20/132 vs. 1/31	3.38	0.62-18.4	0.16	11/132 vs. 1/31	1.88	0.32-11.02	0.49
PTEN status/ PIK3CA mutations ³				0.21				
PTEN loss/PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	9/40 vs. 11/92	2.02	0.82-4.98	0.13	5/40 vs. 6/92	2.07	0.61-7.04	0.25
PTEN loss/PIK3CA mut vs. PTEN no loss/PIK3CA non-mutant	1/7 vs. 11/92	1.81	0.31-10.74	0.51	1/7 vs. 6/92	3.43	0.50-23.38	0.21
PTEN no loss/PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	0/24 vs. 11/92	0.16	0.01-3.05	0.22	0/24 vs. 6/92	2.28	0.01-6.19	0.42

HR: hazard ratio; CI, confidence interval

¹loss: loss by IHC and/ or PTEN mutant, no-loss: no-loss by IHC; ²patients with concordant local/central HER2 status treated with trastuzumab; ³firth’s correction was used for the estimation of HRs (95% CIs)

Supplementary Table S5: Hazard ratios (95% CI) estimated from Cox regression multivariate analysis using backwards selection with respect to OS (PTEN IHC approach A).

	Categories	N patients	N events	HR	95% CI		p-value
Entire Cohort (N=919)							
Model 1							
Hormonotherapy	Yes vs. No	711 vs. 208	51 vs. 30	0.49	0.27	0.86	0.014
Number of positive lymph nodes	0-3 vs. ≥4	655 vs. 264	41 vs. 40	0.33	0.21	0.52	<.0001
Histological grade	I-II vs. III	468 vs. 451	24 vs. 57	0.47	0.28	0.80	0.005
Subtypes (central assesement)	TNBC vs. Luminal HER2	93 vs. 134	11 vs. 15	0.57	0.24	1.34	0.194
	HER2-enriched vs. Luminal HER2	65 vs. 134	5 vs. 15	0.28	0.10	0.83	0.021
	Luminal A vs. Luminal HER2	346 vs. 134	18 vs. 15	0.49	0.24	1.00	0.051
	Luminal B vs. Luminal HER2	281 vs. 134	32 vs. 15	0.88	0.47	1.64	0.690
PTEN status*	Loss vs. no-loss	326 vs. 593	43 vs. 38	2.07	1.30	3.31	0.002
TILSs (10% increments)				0.79	0.64	0.96	0.020
Model 2							
Hormonotherapy	Yes vs. No	711 vs. 208	51 vs. 30	0.49	0.28	0.87	0.015
Number of positive lymph nodes	0-3 vs. ≥4	655 vs. 264	41 vs. 40	0.34	0.21	0.53	<.0001
Histological grade	I-II vs. III	468 vs. 451	24 vs. 57	0.47	0.28	0.80	0.005
Subtypes (central assesement)	TNBC vs. Luminal HER2	93 vs. 134	11 vs. 15	0.57	0.24	1.34	0.196
	HER2-enriched vs. Luminal HER2	65 vs. 134	5 vs. 15	0.29	0.10	0.83	0.022
	Luminal A vs. Luminal HER2	346 vs. 134	18 vs. 15	0.49	0.24	1.01	0.054
	Luminal B vs. Luminal HER2	281 vs. 134	32 vs. 15	0.88	0.47	1.65	0.699
PTEN status/ PIK3CA mutations (ref. Category: PTEN no loss/PIK3CA non-mutant)							
	PTEN loss/ PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	246 vs. 399	34 vs. 28	2.05	1.20	3.48	0.008
	PTEN loss/ PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	80 vs. 399	9 vs. 28	1.96	0.91	4.19	0.085
	PTEN no loss/ PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	194 vs. 399	10 vs. 28	0.92	0.44	1.90	0.812
PTEN status/ PIK3CA mutations (ref. Category: PTEN loss/PIK3CA non-mutant)							
	PTEN loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	80 vs. 246	9 vs. 34	0.96	0.45	2.01	0.904
	PTEN no loss/ PIK3CA non-mutant vs. PTEN loss/PIK3CA non-mutant	399 vs. 246	28 vs. 34	0.49	0.29	0.83	0.008
	PTEN no loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	194 vs. 246	10 vs. 34	0.45	0.21	0.94	0.033
TILS (10% increments)				0.79	0.64	0.96	0.020
HER2(+) cohort (N=162)							
Model 1							
PTEN status*	Loss vs. no-loss	47 vs. 115	6 vs. 6	2.47	0.80	7.66	0.118
TILs (10% increments)				0.26	0.08	0.81	0.021

HR, Hazard ratio; MRM, Modified Radical Mastectomy; *loss: loss by IHC and/ or PTEN mutant, no-loss: no-loss by IHC

Variables entered in backwards selection:

Entire cohort: age (≤50, >50), breast surgery (Breast conserving surgery, Modified Radical Mastectomy), centrally assessed subtypes (Luminal A/B, HER2-enriched, Luminal-HER2, TNBC), tumor size (≤2, 2-5, >5), histological grade (I-II, III), number of positive nodes (0-3, ≥4), hormonotherapy (no, yes), TILs (10% increments), PIK3CA mutational status and PTEN final status (model 1) or PTEN status/PIK3CA combined variable (model 2).
HER2(+) cohort: age (≤50, >50), breast surgery (Breast conserving surgery, Modified Radical Mastectomy), HER2 subtype (centrally and/or locally), tumor size (≤2, 2-5, >5), histological grade (I-II, III), number of positive nodes (0-3, ≥4), hormonotherapy (no, yes), TILs (10% increments), PIK3CA mutational status, PTEN final status

Supplementary Table S6: Hazard ratios (95% CIs) estimated from univariate Cox regression with respect to DFS and OS (PTEN IHC approach B).

	DISEASE-FREE SURVIVAL (DFS)				OVERALL SURVIVAL (OS)			
	N patients / N events	HR	95% CI	p-value	N patients / N events	HR	95% CI	p-value
	<i>Entire cohort</i>				<i>Entire cohort</i>			
PTEN IHC status								
Loss vs. no loss	48/272 vs. 124/985	1.49	1.07-2.08	0.018	34/272 vs. 67/985	1.94	1.28-2.93	0.002
PTEN status*								
Loss vs. no loss	50/280 vs. 124/985	1.51	1.09-2.10	0.013	35/280 vs. 67/985	1.94	1.29-2.92	0.002
PIK3CA mutations								
Non mutant vs. mutant	107/677 vs. 33/284	1.42	0.96-2.09	0.08	63/677 vs. 20/284	1.35	0.82-2.34	0.240
PTEN status/ PIK3CA mutations (ref. Category: PTEN no loss/PIK3CA non-mutant)				0.001				0.004
PTEN loss/PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	37/168 vs. 70/509	1.74	1.17-2.59	0.007	26/168 vs. 37/509	2.29	1.39-3.79	0.001
PTEN loss/PIK3CA mut vs. PTEN no loss/PIK3CA non-mutant	7/51 vs. 70/509	1.03	0.47-2.24	0.94	5/51 vs. 37/509	1.4	0.55-3.57	0.477
PTEN no loss/PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	26/233 vs. 70/509	0.79	0.50-1.23	0.29	15/233 vs. 37/509	0.87	0.48-1.59	0.655
PTEN status/ PIK3CA mutations (ref. Category: PTEN loss/PIK3CA non-mutant)								
PTEN loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	7/51 vs. 37/168	0.59	0.26-1.33	0.2	5/51 vs. 26/168	0.61	0.24-1.59	0.310
PTEN no loss/ PIK3CA non-mutant vs. PTEN loss/PIK3CA non-mutant	70/509 vs. 37/168	0.58	0.39-0.86	0.007	37/509 vs. 26/168	0.44	0.26-0.72	0.001
PTEN no loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	26/233 vs. 37/168	0.45	0.27-0.75	0.002	15/233 vs. 26/168	0.38	0.20-0.71	0.003
	<i>HER2(+) cohort (N=211)²</i>				<i>HER2(+) cohort (N=211)²</i>			
PTEN IHC status								
Loss vs. no loss	4/23 vs. 23/187	1.46	0.51-4.22	0.49	3/23 vs. 13/187	2.05	0.58-7.20	0.260
PTEN status¹								
Loss vs. no loss	5/24 vs. 23/187	1.79	0.68-4.72	0.24	3/24 vs. 13/187	1.96	0.56-6.86	0.300
PIK3CA mutations³								
Non mutant vs. mutant	20/132 vs. 1/31	3.38	0.62-18.4	0.16	11/132 vs. 1/31	1.88	0.32-11.02	0.490
PTEN status/ PIK3CA mutations^{3,4}								
PTEN loss/PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	5/17 vs. 15/115	2.67	0.97-7.33	0.056	3/17 vs. 8/115	3.25	0.87-12.20	0.080
PTEN no loss/PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	1/28 vs. 15/115	0.38	0.07-2.18	0.28	1/28 vs. 8/115	0.71	0.11-4.48	0.720

HR: hazard ratio; CI, confidence interval

¹loss: loss by IHC and/ or PTEN mutant, no-loss: no-loss by IHC; ²patients with concordant local/central HER2 status treated with trastuzumab;

³firth's correction was used for the estimation of HRs (95% CIs); ⁴PTEN loss/PIK3CA mutant category was excluded due to the very small number of patients (N=3) and 0 events.

Supplementary Table S7: Hazard ratios (95% CI) estimated from Cox regression **multivariate analysis** using backwards selection with respect to DFS and OS (**PTEN IHC approach B**).

		DISEASE-FREE SURVIVAL (DFS)						OVERALL SURVIVAL (OS)					
Categories		N patients	N events	HR	95% CI		p-value	N patients	N events	HR	95% CI		p-value
		Entire Cohort (N=919)						Entire Cohort (N=919)					
Model 1													
Breast surgery	Other vs. MRM	470 vs. 449	54 vs. 80	0.77	0.54	1.10	0.144	470 vs. 449	31 vs. 50	0.71	0.45	1.13	0.148
Hormonotherapy	Yes vs. No	711 vs. 208	95 vs. 39	0.50	0.31	0.81	0.005	711 vs. 208	51 vs. 30	0.47	0.26	0.84	0.011
Number of positive lymph nodes	0-3 vs. ≥4	655 vs. 264	69 vs. 65	0.39	0.27	0.55	<.0001	655 vs. 264	41 vs. 40	0.37	0.23	0.58	<.0001
Histological grade	I-II vs. III	468 vs. 451	52 vs. 82	0.59	0.40	0.87	0.007	468 vs. 451	24 vs. 57	0.46	0.27	0.79	0.004
Subtypes (central assesement)	TNBC vs. Luminal HER2	93 vs. 134	13 vs. 24	0.50	0.24	1.06	0.072	93 vs. 134	11 vs. 15	0.60	0.25	1.41	0.239
	HER2-enriched vs. Luminal HER2	65 vs. 134	7 vs. 24	0.28	0.12	0.69	0.006	65 vs. 134	5 vs. 15	0.29	0.10	0.84	0.023
	Luminal A vs. Luminal HER2	346 vs. 134	41 vs. 24	0.60	0.35	1.03	0.062	346 vs. 134	18 vs. 15	0.48	0.23	1.00	0.051
	Luminal B vs. Luminal HER2	281 vs. 134	49 vs. 24	0.83	0.50	1.37	0.455	281 vs. 134	32 vs. 15	0.84	0.45	1.59	0.595
PTEN status*	Loss vs. no-loss	216 vs. 703	42 vs. 92	1.58	1.07	2.33	0.022	216 vs. 703	30 vs. 51	1.84	1.13	3.01	0.015
TILSs (10% increments)				0.72	0.60	0.87	0.001			0.79	0.64	0.96	0.018
Model 2													
Breast surgery	Other vs. MRM	470 vs. 449	54 vs. 80	0.76	0.54	1.09	0.140	(not retained in the model)					
Hormonotherapy	Yes vs. No	711 vs. 208	95 vs. 39	0.53	0.33	0.85	0.009	711 vs. 208	51 vs. 30	0.48	0.27	0.86	0.013
Number of positive lymph nodes	0-3 vs. ≥4	655 vs. 264	69 vs. 65	0.39	0.27	0.56	<.0001	655 vs. 264	41 vs. 40	0.34	0.22	0.53	<.0001
Histological grade	I-II vs. III	468 vs. 451	52 vs. 82	0.60	0.41	0.89	0.010	468 vs. 451	24 vs. 57	0.47	0.28	0.80	0.005
Subtypes (central assesement)	TNBC vs. Luminal HER2	93 vs. 134	13 vs. 24	0.51	0.24	1.07	0.075	93 vs. 134	11 vs. 15	0.59	0.25	1.41	0.235
	HER2-enriched vs. Luminal HER2	65 vs. 134	7 vs. 24	0.28	0.12	0.70	0.006	65 vs. 134	5 vs. 15	0.30	0.10	0.87	0.027
	Luminal A vs. Luminal HER2	346 vs. 134	41 vs. 24	0.61	0.36	1.04	0.070	346 vs. 134	18 vs. 15	0.49	0.23	1.01	0.054
	Luminal B vs. Luminal HER2	281 vs. 134	49 vs. 24	0.83	0.50	1.37	0.469	281 vs. 134	32 vs. 15	0.86	0.45	1.62	0.632
PTEN status/ PIK3CA mutations (ref. Category: PTEN no loss/PIK3CA non-mutant)													
	PTEN loss/ PIK3CA non-mutant vs. PTEN no loss/PIK3CA non-mutant	166 vs. 479	36 vs. 68	1.669	1.082	2.575	0.021	166 vs. 479	25 vs. 37	1.94	1.12	3.37	0.018
	PTEN loss/ PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	50 vs. 479	6 vs. 68	0.939	0.404	2.18	0.884	50 vs. 479	5 vs. 37	1.56	0.61	4.03	0.355
	PTEN no loss/ PIK3CA mutant vs. PTEN no loss/PIK3CA non-mutant	224 vs. 479	24 vs. 68	0.806	0.503	1.292	0.371	224 vs. 479	14 vs. 37	1.00	0.54	1.87	0.997
PTEN status/ PIK3CA mutations (ref. Category: PTEN loss/PIK3CA non-mutant)													
	PTEN loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	50 vs. 166	6 vs. 36	0.56	0.24	1.35	0.197	50 vs. 166	5 vs. 25	0.81	0.30	2.13	0.663
	PTEN no loss/ PIK3CA non-mutant vs. PTEN loss/PIK3CA non-mutant	479 vs. 166	68 vs. 36	0.60	0.39	0.92	0.021	479 vs. 166	37 vs. 25	0.52	0.30	0.89	0.018
	PTEN no loss/ PIK3CA mutant vs. PTEN loss/PIK3CA non-mutant	224 vs. 166	24 vs. 36	0.48	0.28	0.83	0.009	224 vs. 166	14 vs. 25	0.52	0.26	1.04	0.062
TILS (10% increments)				0.72	0.60	0.87	0.001			0.78	0.64	0.96	0.017
		HER2(+) cohort (N=162)						HER2(+) cohort (N=162)					
Model 1													
Number of positive lymph nodes	0-3 vs. ≥4	108 vs. 54	10 vs. 11	0.42	0.18	0.99	0.049	(not retained in the model)					
PTEN status*	Loss vs. no-loss	20 vs. 142	5 vs. 16	3.06	1.12	8.38	0.030	20 vs. 142	3 vs. 9	3.40	0.92	12.61	0.067
TILS (10% increments)				0.41	0.22	0.77	0.006			0.25	0.08	0.75	0.013

HR, Hazard ratio; MRM, Modified Radical Mastectomy; *loss: loss by IHC and/ or PTEN mutant, no-loss: no-loss by IHC

Variables entered in backwards selection:

Entire cohort: age (≤50, >50), breast surgery (Breast conserving surgery, Modified Radical Mastectomy), centrally assessed subtypes (Luminal A/B, HER2-enriched, Luminal-HER2, TNBC), tumor size (≤2, 2-5, >5), histological grade (I-II, III), number of positive nodes (0-3, ≥4), hormonotherapy (no, yes), TILs (10% increments), PIK3CA mutational status and PTEN final status (model 1) or PTEN status/PIK3CA combined variable (model 2).

HER2(+) cohort: age (≤50, >50), breast surgery (Breast conserving surgery, Modified Radical Mastectomy), HER2 subtype (centrally and/or locally), tumor size (≤2, 2-5, >5), histological grade (I-II, III), number of positive nodes (0-3, ≥4), hormonotherapy (no, yes), TILs (10% increments), PIK3CA mutational status, PTEN final status