Supplemental Online Content

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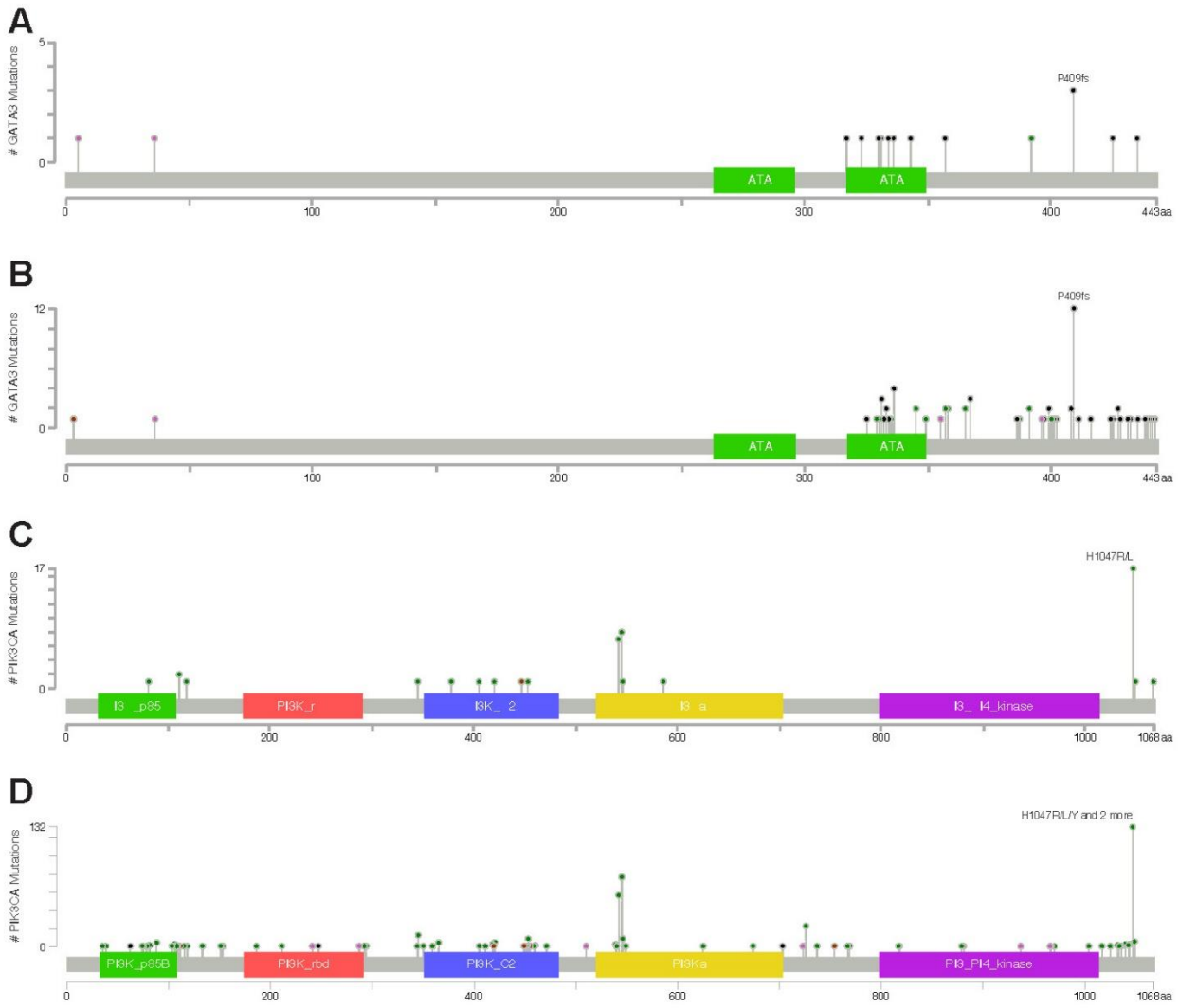
This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Lollipop plots demonstrating the distribution of genomic alterations by their amino acid coordinates in (A) GATA3 in Black patients with mBC, (B) GATA3 in White patients with mBC, (C) PIK3CA in Black patients with mBC, and (D) PIK3CA in White patients with mBC.



eTable 1. Univariate logistic association of clinical characteristics of the population (Black vs. White).

Characteristic	OR	95% C.I.	P>|z|
Lung	1.28	0.87-1.87	0.21
Liver	1.06	0.73-1.53	0.77
Bone	0.87	0.60-1.27	0.47
Node	1.19	0.83-1-71	0.35
Soft tissue	1.05	0.66-1.67	0.83
CNS	1.46	0.81-2.61	0.20
De novo	1.39	0.90-2.15	0.13
ET type			
Fulvestrant	0.99	0.61-1.60	0.97
AI	1.23	0.78-1.94	0.38
Treatment line			
2	0.86	0.48-1.56	0.627
>=3	1.13	0.71-1.78	<0.001

Abbreviations: OR, Odds Ratio; C.I., Confidence Interval; ET, Endocrine Therapy; CNS, central nervous system

eTable 2. Univariate logistic association of single gene alterations in the general population (Black versus White).

Alteration	OR	95% C.I.	P>|z|
PIK3CA SNVs	0.96	0.64-1.43	0.83
ESR1 SNVs	1.03	0.66 – 1.61	0.89
TP53 SNVs	1.24	0.87-1.78	0.24
ARID1A SNVs	0.88	0.37-2.10	0.78
ERBB2 SNVs	1.40	0.61-3.18	0.43
CDKN2A SNVs	5.37	1.49-19.27	0.01
NF1 SNVs	0.26	0.35-1.90	0.18
PTEN SNVs	1.00	0.42-2.39	0.99
CDH1 SNVs	0.60	0.14-2.55	0.49
AKT1 SNVs	1.16	0.45-3.02	0.76
GATA3 SNVs	1.99	1.05-3.75	0.03
SMAD4 SNVs	0.32	0.04-2.40	0.27
RB1 SNVs	0.19	0.03-1.40	0.10
FBXW7 SNVs	1.97	0.22-17.78	0.54
HRAS SNVs	0.87	0.11-6.94	0.90
GNAS SNVs	2.00	0.74-5.42	0.17
BRCA2 SNVs	1.66	0.67-4.06	0.27
KRAS SNVs	1.60	0.65-3.91	0.30
NRAS SNVs	1.58	0.18-13.59	0.68
BRCA1 SNVs	0.74	0.17-3.21	0.69
VHL SNVs	7.91	0.49-127.21	0.14
BRAF SNVs	0.35	0.047-2.63	0.31
APC SNVs	1.77	0.59-5.31	0.31
JAK2 SNVs	3.95	0.36-43.87	0.26
RAF1 SNVs	2.63	0.27-25.48	0.40

	OR	95% C.I.	P>|z|
STK11 SNVs	0.78	0.09-6.18	0.82
PTPN11 SNVs	7.96	1.11-56.99	0.04
ATM SNVs	0.20	0.03-1.44	0.11
NOTCH1 SNVs	3.95	0.36-43.87	0.26
HRAS SNVs	0.87	0.11-6.94	0.90
RAF1 SNVs	2.63	0.27-25.48	0.40
KIT CNVs	1.51	0.51-4.47	0.45
PDGFRA CNVs	1.53	0.58-4.06	0.39
BRAF CNVs	1.22	0.57-2.63	0.61
ERBB2 CNVs	0.91	0.35-2.34	0.85
CCND1 CNVs	1.65	0.93-2.91	0.08
KRAS CNVs	1.24	0.47-3.23	0.66
AR CNVs	1.05	0.24-4.64	0.95
RAF1 CNVs	0.98	0.34-2.82	0.97
CDK6 CNVs	0.57	0.17-1.85	0.35
PIK3CA CNVs	1.06	0.58-1.95	0.85
EGFR CNVs	1.28	0.71-2.32	0.42
MYC CNVs	1.23	0.69-2.18	0.48
MET CNVs	1.13	0.38-3.26	0.83
CCNE1 CNVs	0.76	0.32-1.80	0.54
CCND2 CNVs	3.36	1.37-8.25	0.008
FGFR2 CNVs	0.56	0.07-4.28	0.57

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval; ET, Endocrine Therapy

eTable 3. Multivariate logistic association in the general population (Black versus White).

Alteration	OR	95% C.I.		P>|z|
GATA3 SNVs				
mut	2.31	1.17	4.54	0.02
CCND2 CNVs				
ampl	4.63	1.79	11.97	0.002
Characteristic				
Treatment line				
2	0.84	0.46	1.53	0.57
3	1.10	0.69	1.75	0.68

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval

eTable 4. Univariate logistic association of pathway alterations in the general population (Black versus White).

Alteration	OR	95% C.I.	P>|z|
PI3K SNVs	0.89	0.61-1.31	0.57
ER SNVs	1.22	0.81-1.84	0.33
P53 SNVs	1.20	0.84-1.71	0.32
RTK SNVs	0.83	0.39-1.76	0.62
Cell Cycle SNVs	0.83	0.32-2.12	0.70
RAS SNVs	1.12	0.56-2.22	0.75
NOTCH SNVs	2.64	0.53-13.23	0.24
RAF SNVs	0.58	0.14-2.45	0.45
WNT SNVs	1.59	0.54-4.72	0.40
RTK CNVs	1.44	0.96-2.15	0.08
RAF CNVs	1.28	0.68-2.43	0.44
Cell Cycle CNVs	1.24	0.79-1.96	0.35
RAS CNVs	1.24	0.47-3.23	0.66
ER CNVs	0.92	0.21-4.04	0.92
PI3K CNVs	1.06	0.58-1.95	0.85
MYC CNVs	1.23	0.69-2.18	0.48

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval; ET, Endocrine Therapy

eTable 5. Univariate logistic association of clinical characteristics in the HR+/HER2- population (Black versus White).

Characteristic	OR	95% C.I.	P>|z|
Lung	1.50	0.94-2.39	0.09
Liver	1.06	0.67-1.67	0.80
Bone	0.93	0.56-1.52	0.76
Node	1.34	0.85-2.10	0.21
Soft tissue	0.79	0.41-1.54	0.50
CNS	1.73	0.78-3.83	0.18
De novo	1.55	0.92-2.63	0.10
ET type			
Fulvestrant	1.06	0.59-1.88	0.85
AI	1.19	0.67-2.11	0.56
Treatment line			
2	0.99	0.51-1.97	>0.99
>= 3	1.10	0.63-1.94	0.73

Abbreviations: OR, Odds Ratio; C.I., Confidence Interval; ET, Endocrine Therapy; CNS, central nervous system; AI, aromatase inhibitor

eTable 6. Univariate logistic association of single genes alterations in the HR+/HER2- population (Black versus White).

Alteration	OR	95% C.I.	P>|z|
PIK3CA SNVs	1.08	0.68-1.71	0.74
ESR1 SNVs	1.16	0.71-1.88	0.55
TP53 SNVs	0.96	0.61-1.53	0.87
ARID1A SNVs	0.93	0.36-2.41	0.88
ERBB2 SNVs	1.55	0.58-4.14	0.38
CDKN2A SNVs	5.07	1.19-21.57	0.03
NF1 SNVs	0.40	0.05-3.05	0.38
PTEN SNVs	1.10	0.38-3.20	0.86
CDH1 SNVs	0.71	0.16-3.05	0.64
AKT1 SNVs	1.18	0.40-3.45	0.76
GATA3 SNVs	2.22	1.13-4.36	0.02
SMAD4 SNVs	0.40	0.05-3.05	0.38
RB1 SNVs	0.26	0.03-1.90	0.18
FBXW7 SNVs	4.14	0.37-46.15	0.25
GNAS SNVs	1.03	0.23-4.54	0.97
BRCA2 SNVs	0.38	0.05-2.89	0.35
KRAS SNVs	1.75	0.65-4.72	0.27
NRAS SNVs	4.14	0.37-46.14	0.25
BRCA1 SNVs	0.58	0.08-4.48	0.60
VHL SNVs	8.30	0.51-133.8	0.14
BRAF SNVs	0.48	0.06-3.63	0.47
APC SNVs	1.93	0.54-6.90	0.31
JAK2 SNVs	4.14	0.37-46.15	0.31
RAF1 SNVs	4.14	0.37-46.15	0.25
PTPN11 SNVs	16.78	1.51-186.98	0.02

	OR	95% C.I.	P>|z|
NOTCH1 SNVs	8.30	0.51-133.80	0.14
KIT CNVs	4.22	1.04-17.16	0.04
PDGFRA CNVs	3.90	1.32-11.48	0.01
BRAF CNVs	0.68	0.16-2.91	0.60
CCND1 CNVs	1.91	1.02-3.57	0.04
KRAS CNVs	1.56	0.45-5.46	0.49
AR CNVs	1.03	0.13-8.31	0.98
RAF1 CNVs	1.31	0.38-4.51	0.67
PIK3CA CNVs	0.68	0.26-1.74	0.42
EGFR CNVs	1.54	0.73-3.23	0.26
MYC CNVs	1.65	0.81-3.38	0.17
MET CNVs	1.18	0.26-5.27	0.83
CCNE1 CNVs	0.35	0.05-2.62	0.54
CCND2 CNVs	4.21	1.03-17.16	0.04

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval

eTable 7. Multivariate logistic association of clinical characteristics and gene alterations in the HR+/HER2- population (Black versus White).

Alteration	OR	95% C.I.		P>|z|
GATA3 SNV				
mut	2.04	1.02	4.08	0.04
PDGFRA CNV				
ampl	3.95	1.33	11.72	0.01
CCND1 CNV				
ampl	1.71	0.90	3.26	0.10

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval

eTable 8. Univariate logistic association of pathway alterations in the HR+/HER2- population (Black versus White).

Alteration	OR	95% C.I.	P>|z|
PI3K SNVs	099	0.64-1.56	0.99
ER SNVs	1.39	0.88-2.19	0.16
P53 SNVs	0.95	0.61-1.51	0.84
RTK SNVs	0.87	0.36-2.08	0.76
Cell Cycle SNVs	0.88	0.31-2.54	0.82
RAS SNVs	1.32	0.60-2.87	0.49
NOTCH SNVs	5.58	0.92-33.85	0.06
RAF SNVs	0.78	0.18-3.37	0.74
WNT SNVs	1.67	0.47-5.87	0.43
RTK CNVs	1.60	0.96-2.66	0.07
RAF CNVs	1.06	0.41-2.75	0.91
Cell Cycle CNVs	1.46	0.82-2.57	0.19
RAS CNVs	1.56	0.45-5.46	0.49
ER CNVs	0.91	0.11-7.28	0.93
PI3K CNVs	0.68	0.26-1.74	0.42
MYC CNVs	1.65	0.81-3.38	0.17

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval

eTable 9. Distribution of pathway alterations in the general population and in the two subgroups (White versus Black).

Alteration	Overall patients N(%)	Black patients N(%)	White patients N(%)	p-value
PI3K SNVs				
WT	789 (65.97)	92 (68.15)	697 (65.69)	0.57
Mutant	407 (34.03)	43(31.85)	364 (34.31)	
ER SNVs				
WT	917 (76.76)	99 (73.33)	818 (77.10)	0.33
Mutant	279 (23.33)	36 (26.67)	243 (22.90)	
P53 SNVs				
WT	677 (56.61)	71 (52.59)	606 (57.12)	0.32
Mutant	519 (43.39)	64 (47.41)	455 (42.88)	
RTK SNVs				
WT	1113 (93.06)	127 (94.07)	986 (92.93)	0.62
Mutant	83 (6.94)	8 (5.93)	75 (7.07)	
CELL CYCLE SNVs				
WT	1144 (95.65)	130 (96.30)	1014 (95.57)	0.70
Mutant	52 (4.35)	5 (3.70)	47 (4.43)	
RAS SNVs				
WT	1115 (93.23)	125 (92.59)	990 (93.31)	0.75
Mutant	81 (6.77)	10 (7.41)	71 (6.69)	
NOTCH SNVs				
WT	1188 (99.33)	133 (98.52)	1055 (99.43)	0.22
Mutant	8 (0.67)	2 (1.48)	6 (0.57)	
RAF SNVs				
WT	1167 (97.58)	133 (98.52)	1034 (97.46)	0.45
Mutant	29 (2.42)	2 (1.48)	127 (2.54)	
WNT SNVs				
WT	1172 (97.99)	131 (97.04)	1041 (98.11)	0.40
Mutant	24 (2.01)	4 (2.96)	20 (1.89)	
MEK SNVs				
WT	1191 (99.58)	135 (100)	1056 (99.53)	0.42
Mutant	5 (0.42)	0 (0)	5 (0.47)	

Alteration	Overall patients N(%)	Black patients N(%)	White patients N(%)	p-value
NRF2 SNVs				
WT	1191 (99.58)	135 (100)	1056 (99.53)	0.42
Mutant	5 (0.42)	0 (0)	5 (0.47)	
RAF CNVs				
WT	1109 (92.73)	123 (91.11)	986 (92.93)	0.44
Mutant	87 (7.27)	12 (8.89)	75 (7.07)	
CELL CYCLE CNVs				
WT	999	109 (80.74)	890 (83.88)	0.35
Mutant	197	26 (19.26)	171 (16.12)	
RAS CNVs				
WT	1159	130 (96.30)	1029 (96.98)	0.66
Mutant	37	5 (3.70)	32 (3.02)	
ER CNVs				
WT	1177	17 (1.60)	1044 (98.40)	0.92
Mutant	19	2 (1.48)	133 (98.52)	
PI3K CNVs				
WT	1086	97 (9.14)	964 (90.86)	0.85
Mutant	110	13 (9.63)	122 (90.37)	
MYC CNVs				
WT	1083	98 (9.24)	963 (90.76)	0.48
Mutant	113	15 (11.11)	120 (88.89)	

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; OR, Odds Ratio; C.I., Confidence Interval; WT, Wild type.

eTable 10. Number of patients who received targeted therapy for PI3K in the White and Black populations.

PI3K therapy	Black N(%)	White N(%)	Total N(%)
No	16 (94.12)	111 (71.15)	127 (73.41)
Yes	1 (5.88)	45 (28.85)	46 (26.59)
		Fisher's exact	0.04

eTable 11. Number of patients who received a CDK 4/6 inhibitor in the White and Black populations.

Characteristic	Black N(%)	White N(%)	Overall N(%)
CDK 4/6i therapy			
No	19 (26.03)	108 (18.27)	127 (19.13)
Yes	54 (73.97)	483 (81.73)	537 (80.87)
		Fisher's exact	0.12

Abbreviations: CDK 4/6i, CDK4/6 inhibitor

eTable 12. Number of patients who received an mTOR inhibitor in the White and Black populations.

Characteristic	Black N(%)	White N(%)	Overall N(%)
MTOR inhibitor use			
No	55 (76.39)	447 (76.94)	502 (76.88)
Yes	17 (23.61)	134 (23.06)	151 (23.12)
		Fisher's exact	0.88

eTable 13. Differences in A1c between Black and White patients with *PIK3CA* mutations.

	Black	White	P value
Median A1c	6.1	5.5	0.01

A1c value	Black N(%)	White N(%)	P value
<= 6.4%	12 (70.59%)	99 (84.62%)	0.15
> 6.4%	5 (29.41%)	18 (15.38%)	

eTable 14. Univariate Cox regression analysis of clinical characteristics in the Black population.

Characteristic	HR	95% C.I.	P>|z|
Lung	2.19	1.32-3.63	0.002
Liver	2.82	1.71-4.65	<0.001
Bone	1.52	0.88-2.63	0.14
Node	1.02	0.62-1.70	0.92
Soft tissue	1.49	0.80-2.75	0.20
CNS	2.59	1.17-2.74	0.02
De novo	0.85	0.47-1.52	0.58
ET type			
Fulvestrant	0.45	0.24-0.83	0.01
AI	0.27	0.13-0.56	<0.001
Treatment line			
2	1.89	0.83-4.29	0.13
>=3	2.17	1.10-4.27	0.02

Abbreviations: OR, Odds Ratio; C.I., Confidence Interval; ET, Endocrine Therapy; CNS, central nervous system

eTable 15. Univariate Cox regression analysis of single gene alterations in the Black population.

Alteration	HR	95% C.I.	P>|z|
PIK3CA SNVs	1.80	1.06-3.04	0.03
ESR1 SNVs	0.98	0.55-1.76	0.95
TP53 SNVs	1.56	0.94-3.59	0.08
ARID1A SNVs	0.67	0.16-2.74	0.58
ERBB2 SNVs	4.47	1.55-12.88	0.006
CDKN2A SNVs	6.47	1.93-21.65	0.002
NF1 SNVs	42.17	4.39-405.36	0.001
PTEN SNVs	3.39	1.20-9.59	0.02
AKT1 SNVs	3.04	0.93-9.89	0.06
GATA3 SNVs	1.13	0.55-2.29	0.74
FBXW7 SNVs	31.39	3.51-280.89	0.002
HRAS SNVs	9.20	1.20-70.36	0.03
GNAS SNVs	2.03	0.73-5.70	0.18
BRCA2 SNVs	2.25	0.54-9.47	0.27
KRAS SNVs	0.83	0.20-3.41	0.80
NRAS SNVs	2.32	0.32-16.93	0.41
BRCA1 SNVs	4.69	1.13-19.49	0.03
BRAF SNVs	1.24	0.17-8.98	0.83
APC SNVs	0.61	0.08-4.42	0.63
JAK2 SNVs	1.99	0.27-14.47	0.50
STK11 SNVs	1.84	0.25-13.41	0.54
PTPN11 SNVs	4.03	0.55-29.73	0.17
NOTCH1 SNVs	1.36	0.19-9.86	0.76
KIT CNVs	3.84	0.91-16.18	0.07
PDGFRA CNVs	7.49	2.22-25.24	0.001

Alteration	HR	95% C.I.	P>|z|
BRAF CNVs	2.43	0.86-6.88	0.09
ERBB2 CNVs	0.94	0.29-3.01	0.91
CCND1 CNVs	1.95	0.99-3.84	0.05
KRAS CNVs	2.46	0.75-8.06	0.14
AR CNVs	3.98	0.95-16.64	0.06
RAF1 CNVs	1.04	0.25-4.27	0.96
CDK6 CNVs	2.92	0.70-12-10	0.14
PIK3CA CNVs	2.93	1.42-6.06	0.004
EGFR CNVs	2.68	1.26-5.68	0.01
MYC CNVs	3.45	1.70-6.97	0.001
MET CNVs	2.34	0.56-9.73	0.24
CCNE1 CNVs	1.33	0.42-4.26	0.63
CCND2 CNVs	4.30	1.80-10.30	0.001
FGFR2 CNVs	1.70	0.23-12.36	0.60

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy Number Variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 16. Univariate Cox regression analysis of pathway alterations in the Black population.

Alteration	HR	95% C.I.	P>|z|
PI3K SNVs	2.33	1.40-3.89	0.001
ER SNVs	1.06	0.62-1.79	0.84
P53 SNVs	1.64	0.99-2.72	0.06
RTK SNVs	3.65	1.43-9.34	0.007
Cell Cycle SNVs	8.93	3.06-26.08	<0.001
RAS SNVs	1.88	0.75-4.73	0.18
NOTCH SNVs	2.63	0.64-10.87	0.18
RAF SNVs	0.93	0.13-6.74	0.94
WNT SNVs	0.61	0.08-4.43	0.63
RTK CNVs	1.75	1.01-3.04	0.05
RAF CNVs	1.71	0.73-3.99	0.22
Cell Cycle CNVs	2.34	1.35-4.05	0.003
RAS CNVs	2.46	0.75-8.06	0.14
ER CNVs	3.98	0.95-16.64	0.06
PI3K CNVs	2.93	1.42-6.06	0.004
MYC CNVs	3.45	1.70-6.98	0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy Number Variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 17. Univariate Cox regression analysis of clinical characteristics in the HR+/HER2- Black population.

Characteristic	HR	95% C.I.	P>|z|
Lung	1.75	0.94-3.25	0.08
Liver	4.14	2.19-7.84	<0.001
Bone	2.32	0.98-5.52	0.06
Node	0.90	0.48-1.68	0.74
Soft tissue	0.93	0.33-2.62	0.89
CNS	3.23	1.35-7.72	0.008
De novo	0.87	0.44-1.72	0.69
Treatment line			
2	1.47	10.57-3.84	0.43
>=3	1.56	0.69-3.48	0.28

Abbreviations: HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system

eTable 18. Univariate Cox regression analysis of single gene alterations in the HR+/HER2- Black population.

Alteration	HR	95% C.I.	P>|z|
PIK3CA SNVs	1.83	0.98-3.41	0.06
ESR1 SNVs	0.92	0.48-1.76	0.80
TP53 SNVs	1.73	0.91-3.27	0.09
ARID1A SNVs	0.34	0.05-2.50	0.29
ERBB2 SNVs	4.83	1.41-16.51	0.01
CDKN2A SNVs	4.05	0.93-17.51	0.06
NF1 SNVs	28.08	2.92-269.97	0.004
PTEN SNVs	3.64	1.09-12.17	0.04
AKT1 SNVs	4.14	1.24-13.84	0.02
GATA3 SNVs	0.99	0.46-2.16	0.99
GNAS SNVs	0.52	0.07-3.94	0.52
KRAS SNVs	0.92	0.22-3.81	0.90
NRAS SNVs	2.42	0.33-17.85	0.39
APC SNVs	1.82	0.25-13.40	0.56
JAK2 SNVs	2.02	0.27-14.86	0.49
PTPN11 SNVs	3.67	0.49-27.47	0.20
NOTCH1 SNVs	1.44	0.20-10.60	0.72
BRAF SNVs	1.34	0.18-9.84	0.77
KIT CNVs	7.79	1.76-34.53	0.007
PDGFRA CNVs	7.04	2.02-24.49	0.002
BRAF CNVs	2.07	0.28-15.43	0.48
CCND1 CNVs	2.89	1.40-5.96	0.004
KRAS CNVs	2.85	0.67-12.18	0.16
AR CNVs	5.10	0.67-38.64	0.11
RAF1 CNVs	0.64	0.09-4.75	0.66

Alteration	HR	95% C.I.	P>|z|
PIK3CA CNVs	2.37	0.84-6.69	0.10
EGFR CNVs	2.96	1.23-7.13	0.01
MYC CNVs	4.26	1.80-10.10	0.001
MET CNVs	2.07	0.28-15.43	0.48
CCND2 CNVs	5.91	1.73-20.19	0.005

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy Number Variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 19. Univariate Cox regression analysis of pathway alterations in the HR+/HER2- Black population.

Alteration	HR	95% C.I.	P>|z|
PI3K SNVs	2.38	1.27-4.44	0.007
ER SNVs	0.93	0.51-1.73	0.83
P53 SNVs	1.84	0.98-3.48	0.06
RTK SNVs	3.69	1.28-10.65	0.02
Cell Cycle SNVs	6.32	1.84-21.70	0.003
RAS SNVs	1.67	0.59-4.73	0.33
NOTCH SNVs	2.75	0.65-11.52	0.17
RAF SNVs	0.96	0.13-6.99	0.96
WNT SNVs	1.82	0.25-13.40	0.56
RTK CNVs	1.90	0.94-3.84	0.07
RAF CNVs	0.99	0.98-4.15	0.99
Cell Cycle CNVs	3.23	1.62-6.44	0.001
RAS CNVs	2.85	0.67-12.18	0.16
ER CNVs	5.10	0.67-38.64	0.11
PI3K CNVs	2.37	0.84-6.69	0.10
MYC CNVs	4.26	1.79-10.1’	0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy Number Variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 20. Multivariate Cox regression analysis of clinical characteristics and single gene alterations in the Black population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	1.38	0.79	2.43	0.25
Liver				
Yes	2.21	1.25	3.92	0.007
CNS				
Yes	1.37	0.55	3.39	0.50
Treatment Line				
2	1.40	0.59	3.35	0.45
>=3	1.67	0.82	3.40	0.16
PIK3CA SNVs				
mut	1.23	0.68	2.22	0.40
MYC CNVs				
ampl	3.97	1.76	8.97	0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy Number Variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system; mut, mutation; ampl, amplification

eTable 21. Multivariate Cox regression analysis of clinical characteristics and pathway alterations in the Black population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	1.49	0.82	2.71	0.19
Liver				
Yes	2.18	1.21	3.93	0.009
CNS				
Yes	1.44	0.58	3.59	0.43
Treatment line				
2	1.57	0.62	4.00	0.34
>=3	1.88	0.90	3.96	0.09
PI3K SNVs	1.55	0.88	2.74	0.13
RTK CNVs	1.52	0.74	3.11	0.25
Cell Cycle CNVs	1.87	0.91	3.84	0.09
MYC CNVs	1.96	0.72	5.30	0.19

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system

eTable 22. Multivariate Cox regression analysis of clinical characteristics and pathway alterations in the HR+/HER2- Black population.

Characteristic	HR	95% conf. interval		P>|z|
Liver				
Yes	3.90	2.01	7.54	<0.001
CNS				
Yes	2.07	0.84	5.07	0.11
PI3K CNVS	2.19	1.14	4.21	0.02
Cell Cycle CNVs	2.00	0.97	4.12	0.06

Abbreviations: CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system

eTable 23. Univariate Cox regression analysis of clinical characteristics in the White population.

	HR	95% C.I.	P>|z|
Lung	1.39	1.15-1.69	0.001
Liver	1.79	1.49-2.15	<0.001
Bone	1.36	1.11-1.68	0.003
Node	1.08	0.90-1.31	0.39
Soft tissue	1.50	1.20-1.89	<0.001
CNS	1.70	1.23-2.34	0.001
De novo	1.21	0.97-1.49	0.09
ET type			
Fulvestrant	0.53	0.43-0.67	<0.001
AI	0.36	0.28-0.47	<0.001
Treatment line			
2	2.01	1.50-2.70	<0.001
>=3	2.86	2.23-3.67	<0.001

Abbreviations: HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system; ET, endocrine therapy; AI, aromatase inhibitor

eTable 24. Univariate Cox regression analysis of single gene alterations in the White population.

Alteration	HR	95% C.I.	P>|z|
PIK3CA SNVs	1.26	1.04-1.53	0.020
ESR1 SNVs	1.89	1.54-2.32	<0.001
TP53 SNVs	1.96	1.63-2.35	<0.001
ARID1A SNVs	0.88	0.57-1.35	0.55
ERBB2 SNVs	1.29	0.82-2.02	0.26
CDKN2A SNVs	0.78	0.19-3.12	0.72
NF1 SNVs	1.73	2.08-2.77	0.02
PTEN SNVs	1.81	1.20-2.74	0.005
CDH1 SNVs	1.59	0.91-2.76	0.10
AKT1 SNVs	1.31	0.83-2.08	0.24
GATA3 SNVs	1.27	0.85-1.90	0.24
SMAD4 SNVs	1.70	1.05-2.75	0.03
RB1 SNVs	2.31	1.57-3.39	<0.001
FBXW7 SNVs	0.96	0.24-3.85	0.95
HRAS SNVs	5.23	2.59-10.56	<0.001
GNAS SNVs	1.40	0.75-2.61	0.30
BRCA2 SNVs	1.20	0.73-1.97	0.48
IDH1 SNVS	0.94	0.23-3.76	0.93
KRAS SNVs	0.81	0.44-1.47	0.48
NRAS SNVs	0.37	0.52-2.61	0.32
BRCA1 SNVs	0.79	0.38-1.68	0.55
FGFR1 SNVs	3.13	1.17-8.40	0.02
BRAF SNVs	1.65	0.91-2.99	0.10
FGFR2 SNVs	2.15	1.15-4.03	0.02
RHOA SNVs	1.85	0.76-4.47	0.17

Alteration	HR	95% C.I.	P>|z|
APC SNVs	1.37	0.76-2.50	0.30
JAK2 SNVs	0.56	0.08-4.01	0.57
RAF1 SNVs	0.60	0.08-4.27	0.61
STK11 SNVs	1.35	0.56-3.25	0.51
PTPN11 SNVs	0.49	0.07-3.46	0.47
ATM SNVs	0.79	0.45-1.37	0.40
KIT SNVs	8.51	1.19-60.95	0.03
RET SNVs	0.89	0.22-3.59	0.87
EGFR SNVs	1.35	0.56-3.26	0.51
TERT SNVs	27.81	3.78-204.56	0.001
IDH2 SNVs	1.13	0.42-3.03	0.80
MAPK1 SNVs	1.31	0.18-9.33	0.79
TCS1 SNVs	1.22	0.30-4.90	0.78
ARAF SNVs	7.90	1.96-31.85	0.004
PDGFRA SNVs	0.44	0.06-3.13	0.41
NFE2L2 SNVs	0.85	0.21-3.42	0.82
MPL SNVs	1.12	0.16-8.01	0.91
HNF1A SNVs	0.94	0.13-6.72	0.95
NOTCH1 SNVs	6.26	0.88-44.78	0.07
MAP2K2 SNVs	47.48	6.39-352.98	<0.001
KIT CNVs	2.26	1.24-4.11	0.008
PDGFRA CNVs	1.86	1.07-3.24	0.03
BRAF CNVs	2.86	2.00-4.09	<0.001
ERBB2 CNVs	0.89	0.55-1.44	0.63
CDK4 CNVs	1.56	0.86-2.84	0.14
CCND1 CNVs	2.27	1.69-3.05	<0.001

Alteration	HR	95% C.I.	P>|z|
KRAS CNVs	2.35	1.53-3.61	<0.001
AR CNVs	2.01	1.07-3.76	0.03
RAF1 CNVs	2.18	1.38-3.45	0.001
CDK6 CNVs	1.84	1.21-2.81	0.004
PIK3CA CNVs	2.57	1.94-3.40	<0.001
EGFR CNVs	2.17	1.63-2.89	<0.001
MYC CNVs	2.01	1.22-3.31	0.006
MET CNVs	1.18	0.26-5.27	0.83
CCNE1 CNVs	2.03	1.42-2.89	<0.001
CCND2 CNVs	2.30	1.23-4.32	0.009
FGFR2 CNVs	3.99	2.24-7.11	<0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 25. Univariate Cox regression analysis of pathways alterations in the White population.

Alteration	HR	95% C.I.	P>|z|
PI3K SNVs	1.33	1.10-1.60	0.003
ER SNVs	1.70	1.39-2.08	<0.001
P53 SNVs	1.86	1.55-2.24	<0.001
RTK SNVs	1.43	1.04-1.96	0.03
Cell Cycle SNVs	1.96	1.37-2.88	<0.001
RAS SNVs	1.31	0.93-1.83	0.12
NOTCH SNVs	1.34	0.43-4.17	0.61
RAF SNVs	1.63	0.96-2.79	0.07
WNT SNVs	1.34	0.74-2.44	0.34
MEK SNVs	2.45	0.78-7.63	0.12
NRF2 SNVs	0.85	0.21-3.42	0.82
RTK CNVs	1.73	1.40-2.13	<0.001
RAF CNVs	2.73	2.01-3.70	<0.001
Cell Cycle CNVs	2.13	1.70-2.67	<0.001
RAS CNVs	2.35	1.53-3.61	<0.001
ER CNVs	2.05	1.12-3.73	0.02
PI3K CNVs	2.57	1.94-3.40	<0.001
MYC CNVs	2.50	1.91-3.30	<0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 26. Univariate Cox regression analysis of clinical characteristics in the HR+/HER2- White population.

Characteristic	HR	95% C.I.	P>|z|
Lung	1.28	1.01-1.62	0.04
Liver	2.14	1.73-2.66	<0.001
Bone	1.64	1.23-2.18	0.001
Node	0.98	0.78-1.23	0.87
Soft tissue	1.60	1.20-2.12	0.001
CNS	2.03	1.32-3.13	0.001
De novo	1.39	1.08-1.79	0.01
Treatment line			
2	2.22	1.53-3.21	<0.001
>=3	3.86	2.81-5.30	<0.001

Abbreviations: HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system; ET, endocrine therapy; AI, aromatase inhibitor

eTable 27. Univariate Cox regression analysis of single gene alterations in the HR+/HER2- White population.

Alteration	HR	95% C.I.	P>|z|
PIK3CA SNVs	1.24	0.99-1.55	0.06
ESR1 SNVs	2.06	1.64-2.59	<0.001
TP53 SNVs	1.77	1.43-2.20	<0.001
ARID1A SNVs	0.88	0.55-1.40	0.58
ERBB2 SNVs	1.83	1.09-3.08	0.02
CDKN2A SNVs	0.84	0.21-3.38	0.81
NF1 SNVs	2.51	1.49-4.22	0.001
PTEN SNVs	1.96	1.18-3.25	0.009
CDH1 SNVs	1.60	0.89-2.86	0.11
AKT1 SNVs	1.36	0.82-2.24	0.24
GATA3 SNVs	1.31	0.85-1.99	0.22
SMAD4 SNVs	2.07	1.21-3.54	0.008
RB1 SNVs	2.02	1.29-3.18	0.002
FBXW7 SNVs	0.86	0.12-6.13	0.88
HRAS SNVs	4.99	2.35-10.61	<0.001
GNAS SNVs	1.27	0.60-2.69	0.53
BRCA2 SNVs	1.16	0.65-2.07	0.60
IDH1 SNVS	0.61	0.09-4.35	0.62
KRAS SNVs	0.70	0.35-1.41	0.31
BRCA1 SNVs	0.71	0.27-1.91	0.50
FGFR1 SNVs	3.24	1.20-8.71	0.02
BRAF SNVs	1.83	0.97-3.44	0.06
FGFR2 SNVs	2.04	1.01-4.11	0.05
RHOA SNVs	1.54	0.57-4.14	0.39
APC SNVs	1.39	0.69-2.81	0.36

Alteration	HR	95% C.I.	P>|z|
JAK2 SNVs	0.56	0.08-3.97	0.56
RAF1 SNVs	0.64	0.09-4.55	0.65
STK11 SNVs	1.08	0.35-3.36	0.90
PTPN11 SNVs	1.11	0.16-7.92	0.92
ATM SNVs	0.71	0.35-1.43	0.33
KIT SNVs	9.28	1.29-66.81	0.03
RET SNVs	0.90	0.23-3.64	0.89
EGFR SNVs	0.85	0.21-3.41	0.82
TERT SNVs	30.06	4.00-225.62	0.001
IDH2 SNVs	0.61	0.15-2.47	0.492
MAPK1 SNVs	1.36	0.19-9.72	0.76
TCS1 SNVs	1.24	0.31-5.01	0.75
ARAF SNVs	8.31	2.05-33.69	0.003
PDGFRA SNVs	0.42	0.06-3.02	0.39
NFE2L2 SNVs	0.84	0.21-3.37	0.80
MPL SNVs	1.11	0.16-7.92	0.92
HNF1A SNVs	0.94	0.13-6.72	0.95
MAP2K2 SNVs	42.67	5.66-321.73	<0.001
BRAF SNVs	1.83	0.97-3.44	0.06
KIT CNVs	2.77	1.03-7.47	0.04
PDGFRA CNVs	2.21	1.04-4.68	0.04
BRAF CNVs	2.04	1.17-3.56	0.01
ERBB2 CNVs	2.55	1.05-6.17	0.04
CDK4 CNVs	1.30	0.58-2.92	0.52
CCND1 CNVs	2.13	1.51-2.99	<0.001
KRAS CNVs	1.82	0.99-3.32	0.05

Alteration	HR	95% C.I.	P>|z|
AR CNVs	2.63	1.17-5.90	0.02
RAF1 CNVs	2.61	1.53-4.47	0.001
CDK6 CNVs	1.22	0.65-2.28	0.54
PIK3CA CNVs	2.17	1.51-3.10	<0.001
EGFR CNVs	1.80	1.24-2.61	0.002
MYC CNVs	2.71	1.93-3.81	<0.001
MET CNVs	1.18	0.52-2.64	0.69
CCNE1 CNVs	2.14	1.27-3.59	0.004
CCND2 CNVs	1.67	0.62-4.48	0.31
FGFR2 CNVs	4.07	2.01-8.28	<0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 28. Univariate Cox regression analysis of pathway alterations in the HR+/HER2- White population.

Alteration	HR	95% C.I.	P>|z|
PI3K SNVs	1.33	1.07-1.65	0.01
ER SNVs	1.87	1.50-2.34	<0.001
P53 SNVs	1.65	1.33-2.05	<0.001
RTK SNVs	1.60	1.11-2.30	0.01
Cell Cycle SNVs	1.74	1.13-2.68	0.01
RAS SNVs	1.61	1.10-2.34	0.01
NOTCH SNVs	0.76	0.11-5.44	0.79
RAF SNVs	1.80	1.03-3.13	0.04
WNT SNVs	1.38	0.67-3.72	0.40
MEK SNVs	2.64	0.66-10.69	0.17
NRF2 SNVs	0.84	0.21-3.37	0.80
RTK CNVs	1.68	1.29-2.19	<0.001
RAF CNVs	2.35	1.55-3.57	<0.001
Cell Cycle CNVs	1.86	1.40-2.48	<0.001
RAS CNVs	1.82	0.99-3.32	0.05
ER CNVs	2.43	1.08-5.46	0.03
PI3K CNVs	2.17	1.51-3.10	<0.001
MYC CNVs	2.71	1.93-3.81	<0.001

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval

eTable 29. Multivariate Cox regression analysis of clinical characteristics and single gene alterations in the White population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	1.17	0.95	1.45	0.13
Liver				
Yes	1.49	1.21	1.83	<0.001
Bone				
Yes	1.29	1.01	1.65	0.04
Soft tissue				
Yes	1.52	1.18	1.96	0.001
CNS				
Yes	1.47	1.03	2.11	0.03
Treatment line				
2	1.80	1.32	2.46	<0.001
3	2.39	1.84	3.11	<0.001
PIK3CA SNVs				
mut	0.96	0.77	1.20	0.75
ESR1 SNVs				
mut	1.39	1.10	1.76	0.007
TP53 SNVs				
mut	1.79	1.46	2.19	<0.001
NF1 SNVs				
mut	1.17	0.68	2.00	0.58
PTEN SNVs				
mut	1.24	0.77	2.02	0.38

Characteristic	HR	95% C.I.		P>|z|
SMAD4 SNVs				
mut	1.34	0.76	2.37	0.31
RB1 SNVs				
mut	1.04	0.65	1.65	0.88
KIT CNVs				
ampl	1.46	0.43	4.92	0.54
AR CNVs				
ampl	0.72	0.32	1.63	0.43
PDGFRA CNVs				
ampl	0.61	0.20	1.87	0.39
BRAF CNVs				
ampl	2.39	1.37	4.18	0.002
CCND1 CNVs				
ampl	1.43	0.99	2.06	0.06
KRAS CNVs				
ampl	0.99	0.57	1.72	0.99
RAF1 CNVs				
ampl	1.37	0.68	2.79	0.38
CDK6 CNVs				
ampl	1.36	0.81	2.29	0.24
PIK3CA CNVs				
ampl	1.35	0.93	1.96	0.11
EGFR CNVs				
ampl	1.21	0.81	1.81	0.35
MYC CNVs				
ampl	1.49	1.03	2.16	0.03

Characteristic	HR	95% C.I.		P>|z|
MET CNVs				
ampl	0.52	0.23	1.18	0.12
CCNE1 CNVs				
ampl	0.97	0.60	1.58	0.90
CCND2 CNVs				
ampl	0.96	0.39	2.38	0.93

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system; mut, mutation; ampl, amplification

eTable 30. Multivariate Cox regression analysis of clinical characteristics and single gene alterations in the HR+/HER2- White population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	1.01	0.78	1.31	0.93
Liver				
Yes	1.79	1.40	2.28	<0.001
Bone				
Yes	1.35	0.97	1.87	0.07
Soft tissue				
Yes	1.63	1.19	2.23	0.002
CNS				
Yes	2.14	1.33	3.45	0.002
De Novo	1.25	0.95	1.65	0.11
Treatment line				
2	1.68	1.13	2.49	0.01
>=3	2.67	1.91	3.75	<0.001
ESR1 SNVs				
mut	1.42	1.09	1.85	0.01
ERBB2 SNVs				
mut	1.31	0.69	2.50	0.40
TP53 SNVs				
mut	1.53	1.20	1.94	0.001
NF1 SNVs				
mut	1.90	1.06	3.41	0.03
PTEN SNVs				
mut	1.45	0.81	2.62	0.21

Characteristic	HR	95% C.I.	P>|z|	
SMAD4 SNVs				
mut	1.43	0.74	2.75	0.28
RB1 SNVs				
mut	0.87	0.50	1.51	0.62
BRAF CNVs				
ampl	1.22	0.56	2.64	0.61
CCND1 CNVs				
ampl	1.54	1.03	2.30	0.04
RAF1 SNVs				
ampl	1.21	0.55	2.67	0.64
PIK3CA CNVs				
ampl	1.4	0.88	2.23	0.15
EGFR CNVs				
ampl	0.92	0.56	1.52	0.75
MYC CNVs				
ampl	2.04	1.30	3.20	0.002
CCNE1 CNVs				
ampl	0.78	0.40	1.52	0.46

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system; mut, mutation; ampl, amplification

eTable 31. Multivariate Cox regression analysis of clinical characteristics and pathway alterations in the White population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	1.15	0.94	1.42	0.17
Liver				
Yes	1.48	1.21	1.81	<0.001
Bone				
Yes	1.28	1.01	1.64	0.04
Soft tissue				
Yes	1.49	1.16	1.90	0.002
CNS				
Yes	1.42	1.00	2.03	0.05
Treatment line				
2	1.90	1.40	2.59	<0.001
3	2.49	1.92	3.22	<0.001
PI3K SNVs	1.06	0.86	1.31	0.58
ER SNVs	1.22	0.97	1.54	0.09
P53 SNs	1.73	1.41	2.12	<0.001
Cell Cycle SNVs	1.07	0.70	1.64	0.76
RTK SNVs	1.30	0.92	1.86	0.14
RAS SBVs	1.02	0.70	1.48	0.93
RTK CNVs	0.99	0.74	1.31	0.93
RAF CNVs	1.65	1.08	2.54	0.02
Cell Cycle CNVs	1.30	0.97	1.73	0.07
RAS CNVs	0.91	0.55	1.52	0.72
ER CNVs	0.88	0.43	1.82	0.74
PI3K CNVs	1.52	1.07	2.15	0.02
MYC CNVs	1.36	0.94	1.97	0.10

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system

eTable 32. Multivariate Cox regression analysis of clinical characteristics and pathway alterations in the HR+/HER2- White population.

Characteristic	HR	95% C.I.		P>|z|
Lung				
Yes	0.97	0.75	1.27	0.85
Liver				
Yes	1.82	1.42	2.31	<0.001
Bone				
Yes	1.43	1.03	2.00	0.03
Soft tissue				
Yes	1.55	1.14	2.12	0.005
CNS				
Yes	2.011	1.24	3.22	0.004
De Novo	1.17	0.90	1.54	0.24
Treatment line				
2	1.85	1.25	2.73	0.002
>=3	3.00	2.15	4.19	<0.001
PIK3K SNVs	1.07	0.83	1.36	0.61
ER SNVs	1.22	0.94	1.57	0.14
P53 SNVs	1.47	1.16	1.86	0.001
RTK SNVs	0.97	0.69	1.35	0.84
Cell Cycle SNVs	1.00	0.60	1.65	0.99
RAS SNVs	1.25	0.82	1.90	0.30
RAF SNVs	0.96	0.50	1.85	0.90
RAF CNVs	1.08	0.59	1.99	0.79
Cell Cycle CNVs	1.15	0.81	1.63	0.43
PI3K CNVs	1.60	1.04	2.45	0.03
MYC CNVs	1.93	1.24	2.99	0.003

Abbreviations: SNVs, Single Nucleotide Variants; CNVs, Copy number variants; HR, Hazard Ratio; C.I., Confidence Interval; CNS, Central nervous system