

supplemenatry table 1

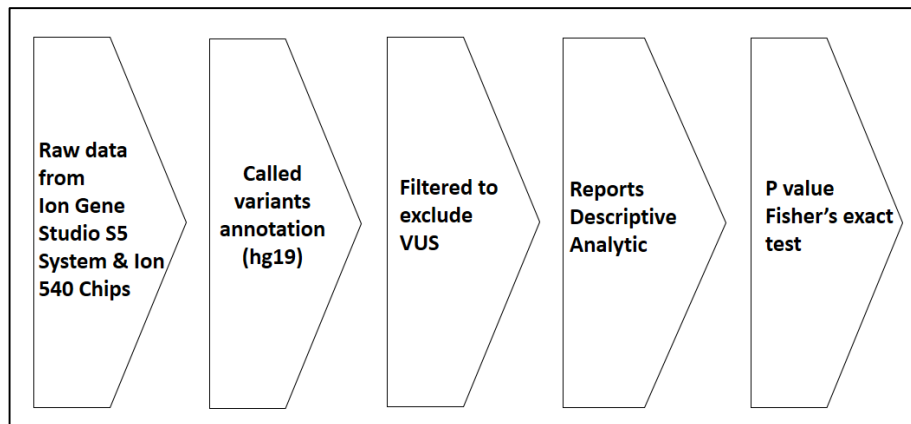
Hotspot genes				Full length genes			Copy number genes	
AKT1	ESR1	KIT	PDGFRB	ARID1A	FBXW7	PTEN	AKT1	FGFR4
AKT2	EZH2	KNSTRN	PIK3CB	ATM	MLH1	RAD50	AKT2	FLT3
AKT3	FGFR1	KRAS	PIK3CA	ATR	MRE11	RAD51	AKT3	IGF1R
ALK	FGFR2	MAGOH	PPP2R1A	ATRX	MSH6	RAD51B	ALK	KIT
AR	FGFR3	MAP2K1	PTPN11	BAP1	MSH2	RAD51C	AXL	KRAS
ARAF	FGFR4	MAP2K2	RAC1	BRCA1	NBN	RAD51D	AR	MDM2
AXL	FLT3	MAP2K4	RAF1	BRCA2	NF1	RNF43	BRAF	MDM4
BRAF	FOXL2	MAPK1	RET	CDK12	NF2	RB1	CCND1	MET
BTK	GATA2	MAX	RHEB	CDKN1B	NOTCH1	SETD2	CCND2	MYC
CBL	GNA11	MDM4	RHOA	CDKN2A	NOTCH2	SLX4	CCND3	MYCL
CCND1	GNAQ	MED12	ROS1	CDKN2B	NOTCH3	SMARCA	CCNE1	MYCN
CDK4	GNAS	MET	SF3B1	CHEK1	PALB2	SMARCB	CDK2	NTRK1
CDK6	H3F3A	MTOR	SMAD4	CREBBP	PIK3R1	STK11	CDK4	NTRK2
CHEK2	HIST1H3	MYC	SMO	FANCA	PMS2	TP53	CDK6	NTRK3
CSF1R	HNF1A	MYCN	SPOP	FANCD2	POLE	TSC1	EGFR	PDGFRA
CTNNB1	HRAS	MYD88	SRC	FANCI	PTCH1	TSC2	ERBB2	PDGFRB
DDR2	IDH1	NFE2L2	STAT3				ESR1	PIK3CB
EGFR	IDH2	NRAS	TERT				FGF19	PIK3CA
ERBB2	JAK1	NTRK1	TOP1				FGF3	PPARG
ERBB3	JAK2	NTRK2	U2AF1				FGFR1	RICTOR
ERBB4	JAK3	NTRK3	XPO1				FGFR2	TERT
ERCC2	KDR	PDGFRA					FGFR3	

Gene fusion		
AKT2	FGFR2	NUTM1
ALK	FGFR3	PDGFRA
AR	FGR	PDGFRB
AXL	FLT3	PIK3CA
BRCA1	JAK2	PRKACA
BRCA2	KRAS	PRKACB
BRAF	MDM4	PTEN
CDKN2A	MET	PPARG
EGFR	MYB	RAD51B
ERBB2	MYBL1	RAF1
ERBB4	NF1	RB1
ERG	NOTCH1	RELA
ESR1	NOTCH4	RET
ETV1	NRG1	ROS1
ETV4	NTRK1	RSPO2
ETV5	NTRK2	RSPO3
FGFR1	NTRK3	TERT

Supplementary information

Supplementary table 1.

Supplementary figure 1. Pipeline for data analysis of target sequencing. VUS, variants with unknown significance.

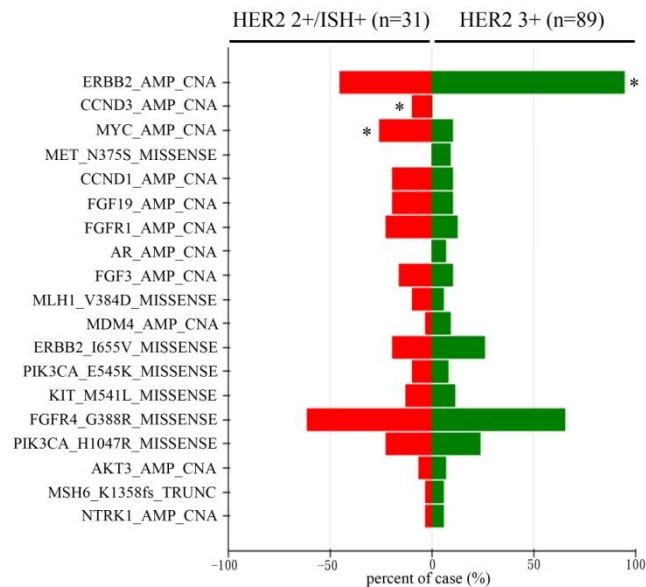


Supplementary table 2. Actionable genes alterations across the level of HER2 expression.

Subtype	Actionable gene	Mean	SD	Min	Max
IHC2+/ISH+ (31)* (Mean: 1.97 SD: 7.80 Min: 0 Max: 9)	AKT2	0.03	0.18	0	1
	BRCA1	0.29	1.01	0	4
	BRCA2	0.29	0.64	0	2
	ERBB2	0.65	0.66	0	2
	ERBB3	0.03	0.18	0	1
	PIK3CA	0.61	0.67	0	2
	MDM2	0.06	0.25	0	1
IHC3+ (89)* (Mean: 1.92 SD: 1.19 Min: 0 Max: 8)	AKT2	0.01	0.11	0	1
	BRCA1	0.11	0.68	0	5
	BRCA2	0.12	0.36	0	2
	ERBB2	1.21 [#]	0.46	0	2
	ERBB3	0.02	0.15	0	1
	PIK3CA	0.42	0.52	0	2
MDM2	0.02	0.15	0	1	

*Subtype (Subject number); #, p<0.001 vs IHC2+/ISH+

Supplementary figure 2. CoBar plots of the 20 most commonly mutated alterations between HER2 IHC2+/ISH+ (n=31) and IHC3+ (n=89) groups. Asterisk indicates a *p* value less than 0.05.



Supplementary figure 3. The prevalence of *ERBB2_CNA*, *CCND3_CNA*, *MYC-CNA*, and *FGF3_CNA* presence in breast cancer samples obtained from TCGA (A) and METABRIC (B) datasets. The prevalence of *ERBB2_CNA*, *CCND3_CNA*, *MYC-CNA*, and *FGF3_CNA* found in TCGA dataset is 14%, 3%, 19%, 15%, respectively. The prevalence of *ERBB2_CNA*, *CCND3_CNA*, *MYC-CNA*, and *FGF3_CNA* found in METABRIC dataset is 18%, 2%, 25%, 16%, respectively.

A. TCGA dataset



B. METABRIC dataset



Supplementary table 3. Mutation types across non_pCR and pCR in HER2 (+) breast cancer

	Mutation Type	Mean	SD	Min	Max
Non_pCR (21)* (Mean: 8.10 SD: 10.60 Min: 1 Max: 53)	CNA	2.76	2.30	0	8
	Expr control	0.29	1.31	0	6
	Frameshift insertion	0.05	0.22	0	1
	Fusion	0.10	0.44	0	2
	Gene expression	0	0	0	0

	Inframe	0	0	0	0
	Missense	4.38	8.89	1	43
	Nonframeshift deletion	0	0	0	0
	Truncation	0.52	1.03	0	4
pCR (19)*	CNA	2.05	1.99	1	9
(Mean: 7.58	Expr control	0	0	0	0
SD: 10.10	Frameshift insertion	0.05	0.23	0	1
Min: 2	Fusion	0.11	0.46	0	2
Max: 48)	Gene expression	0	0	0	0
	Inframe	0	0	0	0
	Missense	4.05	9.74	0	44
	Nonframeshift deletion	0.05	0.23	0	1
	Truncation	1.26	1.10	0	3

Non_pCR, non_pathological complete response; pCR, pathological complete response

*Subtype (Sample number)

Supplementary table 4. Actionable genes across non_pCR and pCR in HER2 (+) breast cancer

Group	Actionable gene	Mean	SD
Non_pCR (21)* (Mean: 2.29 SD: 1.49 Min: 1 Max: 8)	AKT2	0.05	0.22
	BRCA1	0.24	1.09
	BRCA2	0.24	0.44
	ERBB2	1	0.45
	ERBB3	0	0
	PIK3CA	0.67	0.48
pCR (19)* (Mean: 2.16 SD: 1.86 Min: 1 Max: 9)	MDM2	0.10	0.30
	AKT2	0.05	0.23
	BRCA1	0.26	0.93
	BRCA2	0.26	0.56
	ERBB2	1	0.33
	ERBB3	0.16	0.37
	PIK3CA	0.42	0.51
	MDM2	0	0

Non_pCR, non_pathological complete response; pCR, pathological complete response

*Subtype (Sample number)

Supplementary table 5. Comparisons of actionable genes across non_pCR and pCR.

Chromosome	Type	ALT	gene symbol	Non-pCR			pCR			p-value
				# variant (+)	# total subjects	SF(%)	# variant (+)	# total subjects	SF(%)	
17	CNA	AMP	ERBB2	15	21	71.4	18	19	94.7	0.053
8	CNA	AMP	FGFR1	4	21	19.0	0	19	0	0.045
3	MISSENSE	H1047R	PIK3CA	8	21	38.1	2	19	10.5	0.044

ALT, alteration; AMP, amplification; Chrom, chromosome; CNA, copy number amplification; SF, sample frequency. #, number.

Supplementary figure 4. Oncoplot of comparisons of actionable genes across non_pCR and pCR.

