

Article

Supplementary Materials: HER2-Low Breast Cancer: Molecular Characteristics and Prognosis

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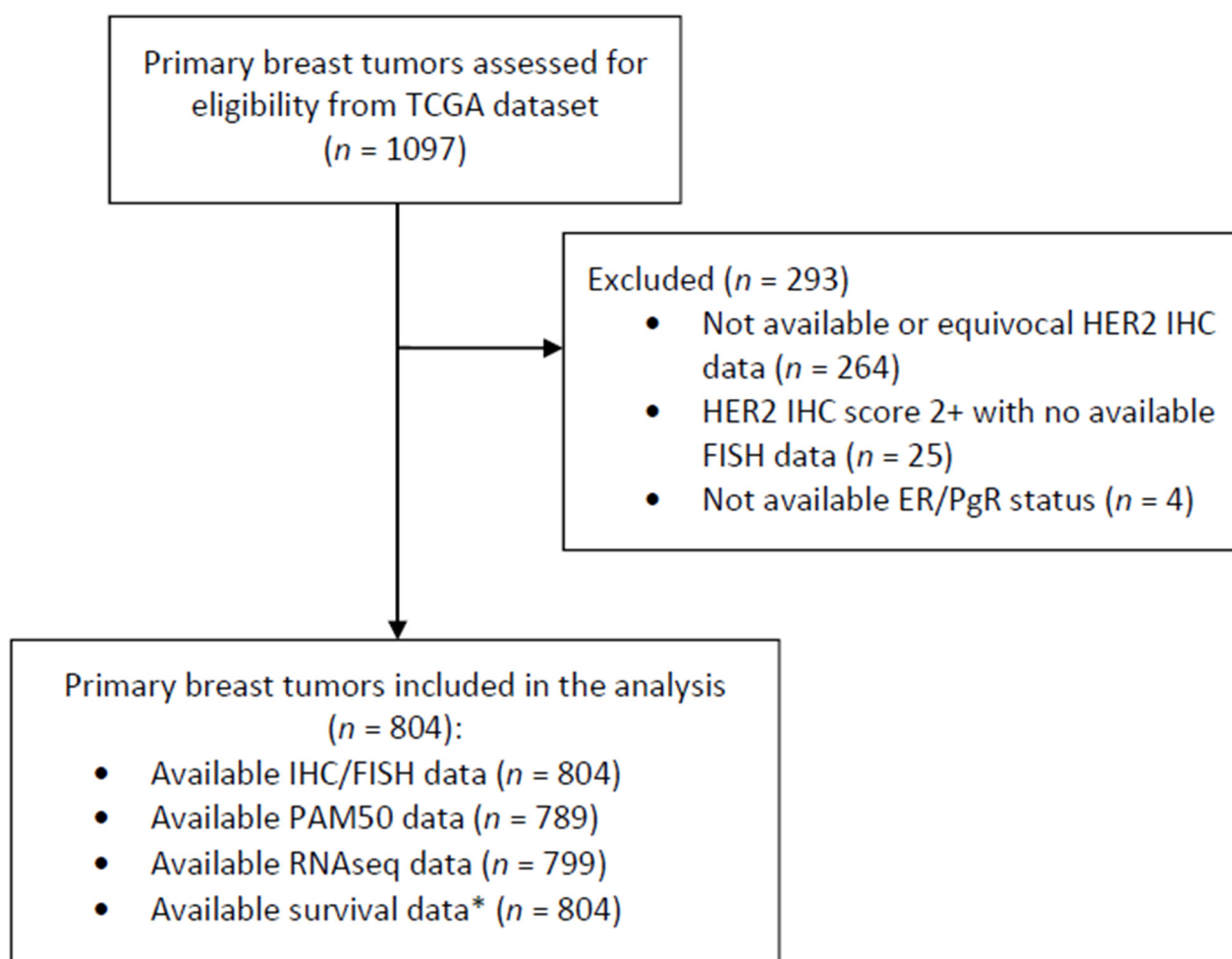


Figure S1. STROBE flow-chart resuming the patient selection process. * Survival data were obtained from the TCGA Pan-Cancer Clinical Data Resource, developed by Liu et al. [15]. Abbreviations: TCGA: The Cancer Genome Atlas, IHC: immunohistochemistry, FISH: fluorescent in situ hybridization, ER: estrogen receptors, PgR: progesterone receptor.

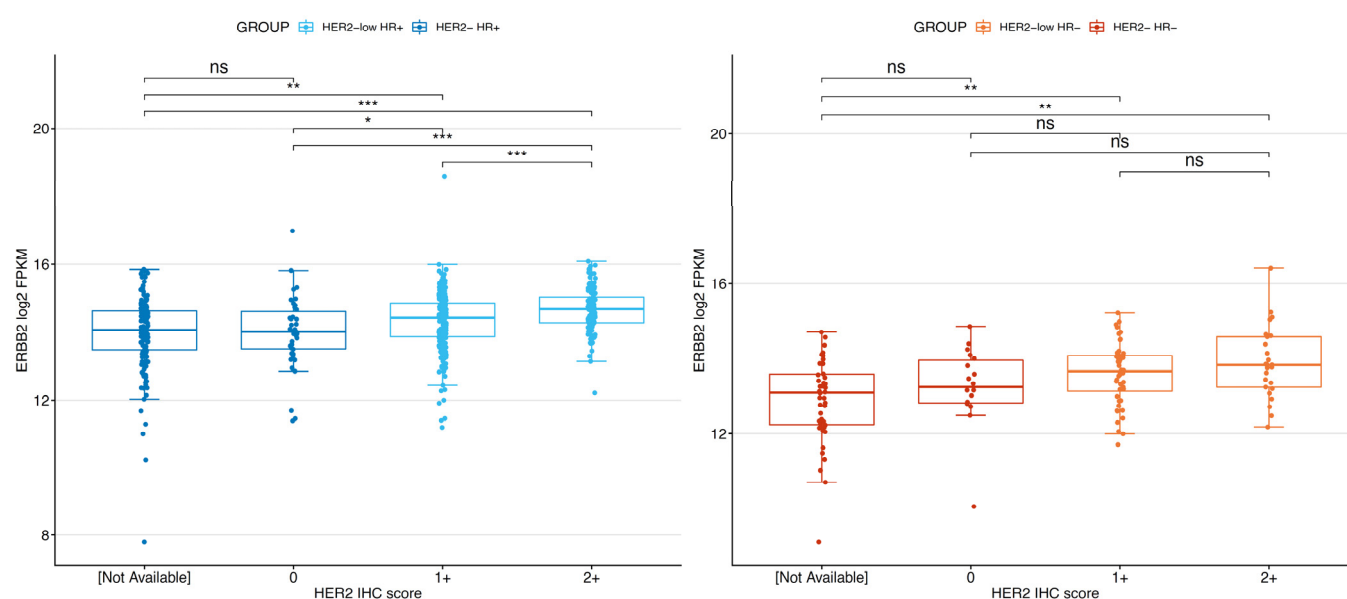


Figure S2. *ERBB2* gene expression levels according to HER2 IHC score in HER2-low/HR+ versus HER2-/HR+ tumors (left plot) and in HER2-low/HR- versus HER2-/HR- tumors (right plot). Statistical differences were assessed using a two-sided Mann–Whitney U-test followed by Benjamin and Hochberg correction for multiple testing. Abbreviations: IHC: immuno-histochemistry, ns = not significant; * = adjusted p -value < 0.05 and ≥ 0.01 ; ** = adjusted p -value < 0.01 and ≥ 0.001 ; *** = adjusted p -value < 0.001 .

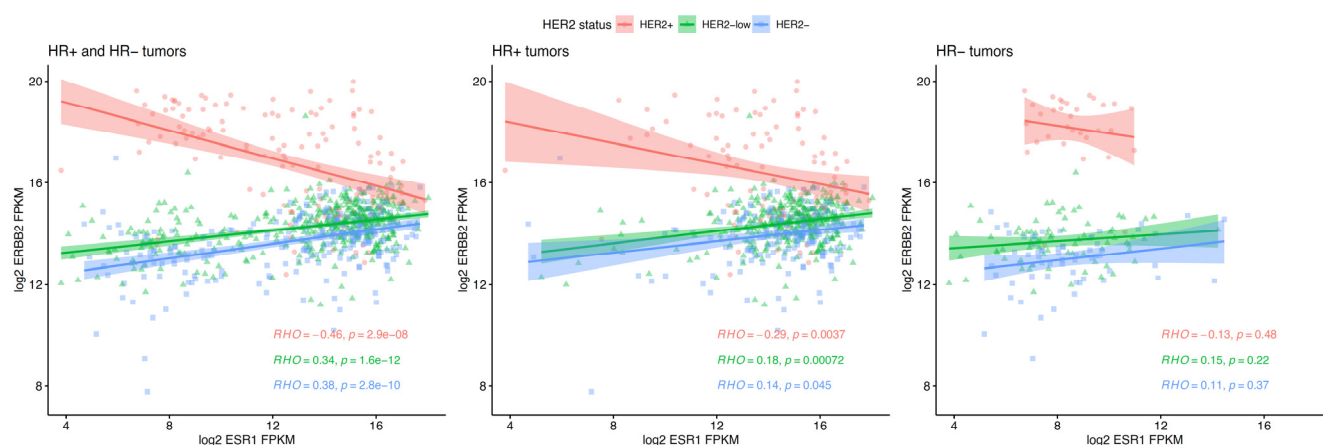


Figure S3. Correlation between *ERBB2* and *ESR1* gene expression levels according to HER2 status (i.e., positive, low and negative) in the whole population, in the HR+ and HR- subgroups. RHO is the Spearman correlation (color-coded according to HER2 status). Red, green, and blue colored regions indicate the 95% confidence interval for each regression line. Abbreviations: HR: hormone receptor.

Table S1. Primary breast tumors included in the present study ($n = 804$).

GROUP	her2_ihc_score	her2_fish_status	her2_status_by_ihc	er_status_by_ihc	pr_status_by_ihc	N
HER2-/HR-	[Not Available]	[Not Evaluated]	Negative	Negative	Negative	42
HER2-/HR-	0	[Not Evaluated]	Negative	Negative	Negative	13
HER2-/HR-	[Not Available]	Negative	Negative	Negative	Negative	4
HER2-/HR-	0	Negative	Negative	Negative	Negative	5
HER2-/HR+	[Not Available]	[Not Evaluated]	Negative	Positive	Indeterminate	1
HER2-/HR+	[Not Available]	[Not Evaluated]	Negative	Positive	Negative	24
HER2-/HR+	0	[Not Evaluated]	Negative	Positive	Negative	5
HER2-/HR+	[Not Available]	Negative	Negative	Positive	Negative	5
HER2-/HR+	0	Negative	Negative	Positive	Negative	1
HER2-/HR+	[Not Available]	[Not Evaluated]	Negative	Negative	Positive	4

HER2-/HR+	[Not Available]	Negative	Negative	Negative	Positive	1
HER2-/HR+	[Not Available]	[Not Evaluated]	Negative	Positive	Positive	98
HER2-/HR+	0	[Not Evaluated]	Negative	Positive	Positive	25
HER2-/HR+	[Not Available]	Negative	Negative	Positive	Positive	21
HER2-/HR+	0	Negative	Negative	Positive	Positive	12
HER2+/HR+	3+	Positive	Positive	Indeterminate (considered positive as column "er_status_ihc_Percent_positive" = 20 29%)	Negative	1
HER2+/HR+	3+	Negative	Equivocal	Positive	Negative	1
HER2+/HR+	2+	Positive	Equivocal	Positive	Negative	5
HER2+/HR+	3+	[Not Evaluated]	Positive	Positive	Negative	6
HER2+/HR+	3+	Negative	Positive	Positive	Negative	1
HER2+/HR+	[Not Available]	Positive	Positive	Positive	Negative	2
HER2+/HR+	2+	Positive	Positive	Positive	Negative	3
HER2+/HR+	3+	Positive	Positive	Positive	Negative	5
HER2+/HR+	2+	Positive	Equivocal	Negative	Positive	1
HER2+/HR+	3+	[Not Evaluated]	Positive	Negative	Positive	1
HER2+/HR+	2+	Positive	Equivocal	Positive	Positive	11
HER2+/HR+	3+	Negative	Indeterminate	Positive	Positive	1
HER2+/HR+	2+	Positive	Indeterminate	Positive	Positive	2
HER2+/HR+	3+	[Not Evaluated]	Negative	Positive	Positive	1
HER2+/HR+	3+	[Not Available]	Positive	Positive	Positive	3
HER2+/HR+	3+	[Not Evaluated]	Positive	Positive	Positive	28
HER2+/HR+	3+	Negative	Positive	Positive	Positive	1
HER2+/HR+	[Not Available]	Positive	Positive	Positive	Positive	4
HER2+/HR+	2+	Positive	Positive	Positive	Positive	12
HER2+/HR+	3+	Positive	Positive	Positive	Positive	12
HER2+/HR-	3+	[Not Evaluated]	[Not Evaluated]	Negative	Negative	1
HER2+/HR-	2+	Positive	Equivocal	Negative	Negative	2
HER2+/HR-	3+	[Not Evaluated]	Negative	Negative	Negative	1
HER2+/HR-	3+	[Not Evaluated]	Positive	Negative	Negative	21
HER2+/HR-	3+	Negative	Positive	Negative	Negative	1
HER2+/HR-	[Not Available]	Positive	Positive	Negative	Negative	1
HER2+/HR-	3+	Positive	Positive	Negative	Negative	5
HER2-low/HR-	1+	Negative	Equivocal	Negative	Negative	1
HER2-low/HR-	2+	Negative	Equivocal	Negative	Negative	24
HER2-low/HR-	1+	[Not Available]	Negative	Negative	Negative	2
HER2-low/HR-	1+	[Not Evaluated]	Negative	Negative	Negative	33
HER2-low/HR-	1+	Negative	Negative	Negative	Negative	9
HER2-low/HR-	1+	Positive	Negative	Negative	Negative	2
HER2-low/HR-	1+	[Not Evaluated]	Positive	Negative	Negative	2
HER2-low/HR-	2+	Negative	Positive	Negative	Negative	1
HER2-low/HR+	1+	[Not Evaluated]	Negative	Positive	Indeterminate	1
HER2-low/HR+	2+	Negative	Equivocal	Positive	Negative	11
HER2-low/HR+	1+	[Not Evaluated]	Negative	Positive	Negative	17
HER2-low/HR+	1+	Negative	Negative	Positive	Negative	8
HER2-low/HR+	1+	Positive	Negative	Positive	Negative	1
HER2-low/HR+	1+	[Not Evaluated]	Positive	Positive	Negative	2
HER2-low/HR+	1+	Negative	Equivocal	Negative	Positive	1
HER2-low/HR+	2+	Negative	Equivocal	Negative	Positive	2
HER2-low/HR+	1+	[Not Evaluated]	Negative	Negative	Positive	3
HER2-low/HR+	1+	Negative	Equivocal	Positive	Positive	2
HER2-low/HR+	2+	Negative	Equivocal	Positive	Positive	92
HER2-low/HR+	1+	[Not Evaluated]	Indeterminate	Positive	Positive	1

HER2-low/HR+	2+	Negative	Indeterminate	Positive	Positive	2
HER2-low/HR+	1+	[Not Evaluated]	Negative	Positive	Positive	125
HER2-low/HR+	1+	Negative	Negative	Positive	Positive	55
HER2-low/HR+	2+	Negative	Negative	Positive	Positive	1
HER2-low/HR+	1+	[Not Evaluated]	Positive	Positive	Positive	7
HER2-low/HR+	2+	Negative	Positive	Positive	Positive	5

Table S2. Treatments received by all subjects and according to breast cancer subtype, as available in the TCGA dataset [13].

	All Subjects N (%)	Available Treatment Data N (%)	Anti-HER2 Treatment N
All	804 (100)	628 (78.1)	59
HER2-low/HR+	336	279	0
HER2-low/HR−	74	61	1
HER2+/HR−	32	23	16
HER2+/HR+	101	75	40
HER2−/HR+	197	144	2
HER2−/HR−	64	46	0