SUPPLEMENTAL FIGURES & TABLES

Table S1. ISPY2 investigational regimens

Investigational regimen*	N
TNBC regimens containing immunotherapy	**215**
Paclitaxel + Cemiplimab	29
Paclitaxel Cemiplimab + REGN3767	28
Oral Paclitaxel/Encequidar + dostarlimab	15
Oral Paclitaxel/Encequidar + Carboplatin + Dostarlimab	42
Paclitaxel + Durvalumab + Olaparib	20
Paclitaxel + Pembrolizumab (no AC)**	24
Paclitaxel + pembrolizumab (followed by AC)	34
Paclitaxel + SD-101 + pembrolizumab***	23
TNBC regimens not containing immunotherapy	**423**
Paclitaxel (control)	137
Irinotecan + talazoparib***	31
Paclitaxel + carboplatin + veliparib	35
Paclitaxel + AMG386	46
Paclitaxel + ganetespib	37
Paclitaxel + ganitumab	40
Paclitaxel + MK-2206	25
Paclitaxil + Neratinib	29
Paclitaxel -> AC + Trilaciclib****	10
SGN-LIV1A***	31
Paclitaxel + PLX3397	1
Trastuzumab duocarmazine (SYD985)***	1
HER2+ regimens	**395**
Paclitaxel + Trastuzumab +/- Pertuzumab (control)	189
Oral Paclitaxel + Encequidar + Dostarlimab + Carboplatin + Trastuzumab	4
Oral Paclitaxel + Encequidar + Dostarlimab + Trastuzumab	15
Paclitaxel + AMG 386 + Trastuzumab	19
Paclitaxel + MK-2206 + Trastuzumab	27
Paclitaxel + Neratinib	50
Paclitaxel + Trastuzumab + HER3-DXd	24
Paclitaxel + Pertuzumab + Trastuzumab + Tucatinib	17
Paclitaxel + Trilaciclib + Pertuzumab + Trastuzumab, followed by AC	3
T-DM1 + Pertuzumab***	47

*Paclitaxel was administered IV unless specifically noted
** This arm consisted of 12 weeks of paclitaxel + pembrolizumab. Patients achieving complete response by imaging moved on to surgery without receiving pre-operative doxorubicin + cyclophosphamide
*** These arms did not include a taxane
**** In this arm, investigational therapy was added during AC, rather than during paclitaxel

Table S2. Baseline Clinical T Category and N status associations

Overall Cohort	N	Baseline Clinical Node Status		
		cN0, N = 535[1]	**cN+**, N = 498[1]	p-value[2]
Baseline Clinical T Category Groups	1,033			**<0.001**
cT1-2		446 / 535 (83%)	318 / 498 (64%)	
cT3-4		89 / 535 (17%)	180 / 498 (36%)	
TNBC	**N**	**Baseline Clinical Node Status**		
		cN0, N = 360[1]	**cN+**, N = 278[1]	p-value[2]
Baseline Clinical T Category Groups	638			**<0.001**
cT1-2		298 / 360 (83%)	174 / 278 (63%)	
cT3-4		62 / 360 (17%)	104 / 278 (37%)	
HER2+	**N**	**Baseline Clinical Node Status**		
		cN0, N = 175[1]	**cN+**, N = 220[1]	p-value[2]
Baseline Clinical T Category Groups	395			**<0.001**
cT1-2		148 / 175 (85%)	144 / 220 (65%)	
cT3-4		27 / 175 (15%)	76 / 220 (35%)	

[1]n / N (%)

[2]Pearson's Chi-squared test

Table S3. Baseline Clinical T and N Category associations with pCR

Overall Cohort	N	pCR		p-value[2]
		No, N = 550[1]	**Yes**, N = 483[1]	
Baseline Clinical T Category Groups	1,033			**<0.001**
cT1-2		382 / 764 (50%)	382 / 764 (50%)	
cT3-4		168 / 269 (62%)	101 / 269 (38%)	
Baseline Clinical Node Status	1,033			0.6
cN0		281 / 535 (53%)	254 / 535 (47%)	
cN+		269 / 498 (54%)	229 / 498 (46%)	
TNBC	**N**	**pCR**		**p-value[2]**
		No, N = 356[1]	**Yes**, N = 282[1]	
Baseline Clinical T Category Groups	638			**0.001**
cT1-2		246 / 472 (52%)	226 / 472 (48%)	
cT3-4		110 / 166 (66%)	56 / 166 (34%)	
Baseline Clinical Node Status	638			0.3
cN0		195 / 360 (54%)	165 / 360 (46%)	
cN+		161 / 278 (58%)	117 / 278 (42%)	
HER2+	**N**	**pCR**		**p-value[2]**
		No, N = 194[1]	**Yes**, N = 201[1]	
Baseline Clinical T Category Groups	395			0.089
cT1-2		136 / 292 (47%)	156 / 292 (53%)	
cT3-4		58 / 103 (56%)	45 / 103 (44%)	
Baseline Clinical Node Status	395			>0.9
cN0		86 / 175 (49%)	89 / 175 (51%)	
cN+		108 / 220 (49%)	112 / 220 (51%)	

[1]n / N (%)

[2]Pearson's Chi-squared test

Table S4. Baseline Clinical T and N Category associations with RCB among patients with residual disease

Overall Cohort	N	RCB Class I, N = 147[1]	II, N = 299[1]	III, N = 104[1]	p-value[2]
Baseline Clinical T Category Groups	550				**0.012**
cT1-2		110 / 382 (29%)	210 / 381 (55%)	62 / 381 (16%)	
cT3-4		37 / 168 (22%)	89 / 168 (53%)	42 / 168 (25%)	
Baseline Clinical Node Status	550				**<0.001**
cN0		91 / 280 (32%)	163 / 280 (58%)	27 / 280 (9.6%)	
cN+		56 / 269 (21%)	136 / 269 (51%)	77 / 269 (29%)	
TNBC	**N**	**RCB Class I**, N = 95[1]	**II**, N = 188[1]	**III**, N = 73[1]	**p-value**[2]
Baseline Clinical T Category Groups	356				**0.021**
cT1-2		72 / 246 (29%)	131 / 245 (53%)	43 / 245 (18%)	
cT3-4		23 / 110 (21%)	57 / 110 (52%)	30 / 110 (27%)	
Baseline Clinical Node Status	356				**<0.001**
cN0		61 / 195 (31%)	113 / 194 (58%)	21 / 194 (11%)	
cN+		34 / 161 (21%)	75 / 161 (47%)	52 / 161 (32%)	
HER2+	**N**	**RCB Class I**, N = 52[1]	**II**, N = 111[1]	**III**, N = 31[1]	**p-value**[2]
Baseline Clinical T Category Groups	194				0.3
cT1-2		38 / 136 (28%)	79 / 136 (58%)	19 / 136 (14%)	
cT3-4		14 / 58 (24%)	32 / 58 (55%)	12 / 58 (21%)	
Baseline Clinical Node Status	194				**0.001**
cN0		30 / 86 (35%)	50 / 86 (58%)	6 / 86 (7.0%)	
cN+		22 / 108 (20%)	61 / 108 (56%)	25 / 108 (23%)	

[1]n / N (%)

[2]Cochran-Armitage test

Fig S1A. Factors associated with DRFS on UVA and MVA (TNBC)

Forest Plot: TNBC DRFS Univariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		638	0.99 (0.98, 1.01)	0.33
Baseline Clinical T Category Groups	cT1-2	472	Reference	
	cT3-4	166	2.73 (1.89, 3.94)	<0.001
Baseline Clinical Node Status	cN0	360	Reference	
	cN+	278	1.92 (1.32, 2.77)	<0.001
NAC Immunotherapy	NAC without ICI	423	Reference	
	NAC + ICI	215	0.61 (0.38, 0.97)	0.04
RCB Index		638	2.19 (1.92, 2.50)	<0.001

Forest Plot: TNBC DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		638	0.99 (0.98, 1.01)	0.325
Baseline Clinical T Category Groups	cT1-2	472	Reference	
	cT3-4	166	1.89 (1.28, 2.78)	0.001
Baseline Clinical Node Status	cN0	360	Reference	
	cN+	278	1.03 (0.69, 1.54)	0.883
NAC Immunotherapy	NAC without ICI	423	Reference	
	NAC + ICI	215	0.88 (0.55, 1.42)	0.612
RCB Index		638	2.08 (1.81, 2.39)	<0.001

Fig S1B. Factors associated with DRFS on UVA and MVA (TNBC achieving pCR)

Forest Plot: pCR TNBC DRFS Univariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		282	1.01 (0.96, 1.06)	0.7
Baseline Clinical T Category Groups	cT1-2	226	Reference	
	cT3-4	56	0.67 (0.15, 3.02)	0.6
Baseline Clinical Node Status	cN0	165	Reference	
	cN+	117	1.50 (0.53, 4.28)	0.4
NAC Immunotherapy	NAC without ICI	162	Reference	
	NAC + ICI	120	0.72 (0.22, 2.30)	0.6
RCB Index		282		

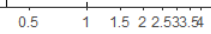
Forest Plot: pCR TNBC DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		282	1.01 (0.96, 1.06)	0.7
Baseline Clinical T Category Groups	cT1-2	226	Reference	
	cT3-4	56	0.62 (0.14, 2.82)	0.5
Baseline Clinical Node Status	cN0	165	Reference	
	cN+	117	1.68 (0.58, 4.87)	0.3
NAC Immunotherapy	NAC without ICI	162	Reference	
	NAC + ICI	120	0.68 (0.21, 2.20)	0.5
RCB Index		282		

Fig S1C. Factors associated with DRFS on UVA and MVA (TNBC with RD)

Forest Plot: RD TNBC DRFS Univariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		356	0.99 (0.97, 1.00)	0.135
Baseline Clinical T Category Groups	cT1-2	246	Reference	
	cT3-4	110	2.75 (1.86, 4.06)	<0.001
Baseline Clinical Node Status	cN0	195	Reference	
	cN+	161	1.91 (1.29, 2.84)	0.001
NAC Immunotherapy	NAC without ICI	261	Reference	
	NAC + ICI	95	0.81 (0.49, 1.36)	0.437
RCB Index		356	2.19 (1.84, 2.62)	<0.001



Forest Plot: RD TNBC DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		356	0.99 (0.97, 1.01)	0.3
Baseline Clinical T Category Groups	cT1-2	246	Reference	
	cT3-4	110	2.13 (1.41, 3.21)	<0.001
Baseline Clinical Node Status	cN0	195	Reference	
	cN+	161	0.96 (0.62, 1.48)	0.9
NAC Immunotherapy	NAC without ICI	261	Reference	
	NAC + ICI	95	0.94 (0.56, 1.59)	0.8
RCB Index		356	2.06 (1.71, 2.48)	<0.001

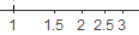
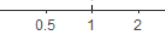


Fig S2A. Factors associated with OS on UVA and MVA (TNBC)

Forest Plot: TNBC OS Univariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		638	0.99 (0.97, 1.01)	0.19
Baseline Clinical T Category Groups	cT1-2	472	Reference	
	cT3-4	166	2.77 (1.81, 4.25)	<0.001
Baseline Clinical Node Status	cN0	360	Reference	
	cN+	278	1.58 (1.03, 2.42)	0.03
NAC Immunotherapy	NAC without ICI	423	Reference	
	NAC + ICI	215	0.56 (0.31, 1.03)	0.06
RCB Index		638	2.36 (2.02, 2.77)	<0.001



Forest Plot: TNBC OS Multivariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		638	0.99 (0.97, 1.01)	0.286
Baseline Clinical T Category Groups	cT1-2	472	Reference	
	cT3-4	166	1.92 (1.22, 3.03)	0.005
Baseline Clinical Node Status	cN0	360	Reference	
	cN+	278	0.76 (0.47, 1.20)	0.237
NAC Immunotherapy	NAC without ICI	423	Reference	
	NAC + ICI	215	0.98 (0.53, 1.81)	0.947
RCB Index		638	2.31 (1.95, 2.74)	<0.001

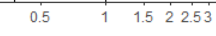


Fig S2B. Factors associated with OS on UVA and MVA (TNBC with RD)

Forest Plot: RD TNBC OS Univariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		356	0.98 (0.96, 1.00)	0.07
Baseline Clinical T Category Groups	cT1-2	246	Reference	
	cT3-4	110	2.70 (1.73, 4.20)	<0.001
Baseline Clinical Node Status	cN0	195	Reference	
	cN+	161	1.49 (0.96, 2.32)	0.08
NAC Immunotherapy	NAC without ICI	261	Reference	
	NAC + ICI	95	0.88 (0.47, 1.64)	0.68
RCB Index		356	2.23 (1.83, 2.73)	<0.001

Forest Plot: RD TNBC OS Multivariate Analysis

Variable		N	Hazard ratio	p
Age at Screening		356	0.99 (0.97, 1.01)	0.188
Baseline Clinical T Category Groups	cT1-2	246	Reference	
	cT3-4	110	2.18 (1.36, 3.49)	0.001
Baseline Clinical Node Status	cN0	195	Reference	
	cN+	161	0.72 (0.44, 1.17)	0.181
NAC Immunotherapy	NAC without ICI	261	Reference	
	NAC + ICI	95	1.11 (0.59, 2.10)	0.744
RCB Index		356	2.17 (1.76, 2.69)	<0.001

Table S5. Factors associated with OS on UVA and MVA (TNBC achieving pCR)

Hazard Ratios from Cox PH model for TNBC: pCR								
			OS Univariate Analysis			OS Multivariate Analysis		
Characteristic	**N**	**Event N**	**HR[1]**	**95% CI[1]**	**p-value[2]**	**HR[1]**	**95% CI[1]**	**p-value[2]**
Age at Screening	282	6	1.03	0.96, 1.11	0.4	1.03	0.96, 1.11	0.4
Baseline Clinical T Category Groups								
cT1-2	226	6	—	—		—	—	
cT3-4	56	0	0.00	0.00, Inf	>0.9	0.00	0.00, Inf	>0.9
Baseline Clinical Node Status								
cN0	165	3	—	—		—	—	
cN+	117	3	1.55	0.31, 7.69	0.6	1.98	0.40, 9.82	0.4
NAC Immunotherapy								
NAC without ICI	162	5	—	—		—	—	
NAC + ICI	120	1	0.43	0.05, 3.76	0.4	0.42	0.05, 3.72	0.4

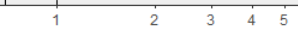
[1]HR = Hazard Ratio, CI = Confidence Interval

[2]Wald Test

Fig S3A. Factors associated with DRFS on UVA and MVA (HER2+)

Forest Plot: HER2+ DRFS Univariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	267	Reference	
	Negative	128	1.50 (0.81, 2.77)	0.2
Baseline Clinical T Category Groups	cT1-2	292	Reference	
	cT3-4	103	2.87 (1.56, 5.27)	<0.001
Baseline Clinical Node Status	cN0	175	Reference	
	cN+	220	1.53 (0.82, 2.86)	0.2
RCB Index		395	1.82 (1.48, 2.24)	<0.001



Forest Plot: HER2+ DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	267	Reference	
	Negative	128	3.34 (1.67, 6.70)	<0.001
Baseline Clinical T Category Groups	cT1-2	292	Reference	
	cT3-4	103	2.23 (1.17, 4.24)	0.01
Baseline Clinical Node Status	cN0	175	Reference	
	cN+	220	0.84 (0.43, 1.67)	0.62
RCB Index		395	2.06 (1.62, 2.61)	<0.001

Fig S3B. Factors associated with DRFS on UVA and MVA (HER2+ achieving pCR)

Forest Plot: pCR HER2+ DRFS Univariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	112	Reference	
	Negative	89	3.81 (0.77, 18.88)	0.10
Baseline Clinical T Category Groups	cT1-2	156	Reference	
	cT3-4	45	3.96 (0.99, 15.87)	0.05
Baseline Clinical Node Status	cN0	89	Reference	
	cN+	112	1.39 (0.33, 5.84)	0.65

Forest Plot: pCR HER2+ DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	112	Reference	
	Negative	89	3.26 (0.65, 16.40)	0.2
Baseline Clinical T Category Groups	cT1-2	156	Reference	
	cT3-4	45	3.28 (0.80, 13.49)	0.1
Baseline Clinical Node Status	cN0	89	Reference	
	cN+	112	1.21 (0.29, 5.15)	0.8

Fig S3BC Factors associated with DRFS on UVA and MVA (HER2+ with RD)

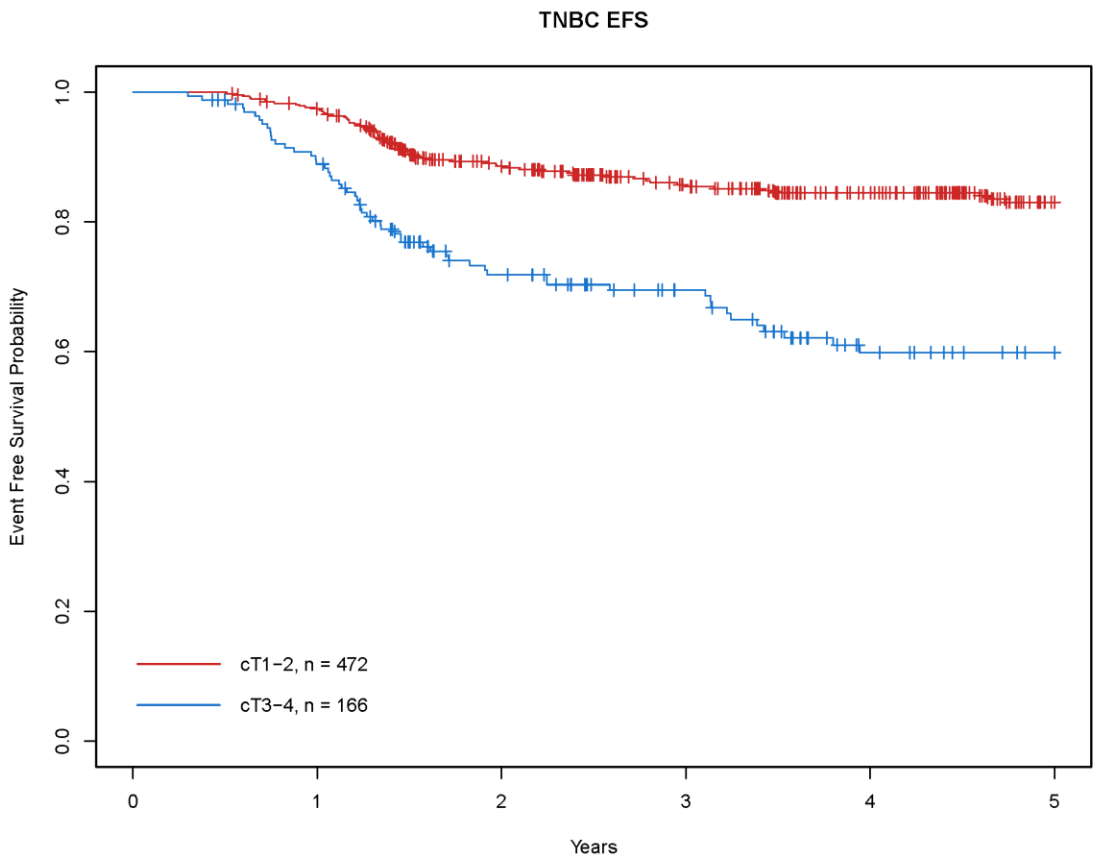
Forest Plot: RD HER2+ DRFS Univariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	155	Reference	
	Negative	39	2.32 (1.13, 4.77)	0.02
Baseline Clinical T Category Groups	cT1-2	136	Reference	
	cT3-4	58	2.35 (1.19, 4.63)	0.01
Baseline Clinical Node Status	cN0	86	Reference	
	cN+	108	1.66 (0.83, 3.32)	0.15
RCB Index		194	1.73 (1.26, 2.36)	<0.001

Forest Plot: RD HER2+ DRFS Multivariate Analysis

Variable		N	Hazard ratio	p
HR Status	Positive	155	Reference	
	Negative	39	3.48 (1.61, 7.49)	0.001
Baseline Clinical T Category Groups	cT1-2	136	Reference	
	cT3-4	58	2.08 (1.01, 4.31)	0.048
Baseline Clinical Node Status	cN0	86	Reference	
	cN+	108	0.81 (0.37, 1.80)	0.608
RCB Index		194	1.92 (1.35, 2.73)	<0.001

Fig S4. EFS for TNBC according to baseline cT size (top) and RCB class (bottom)



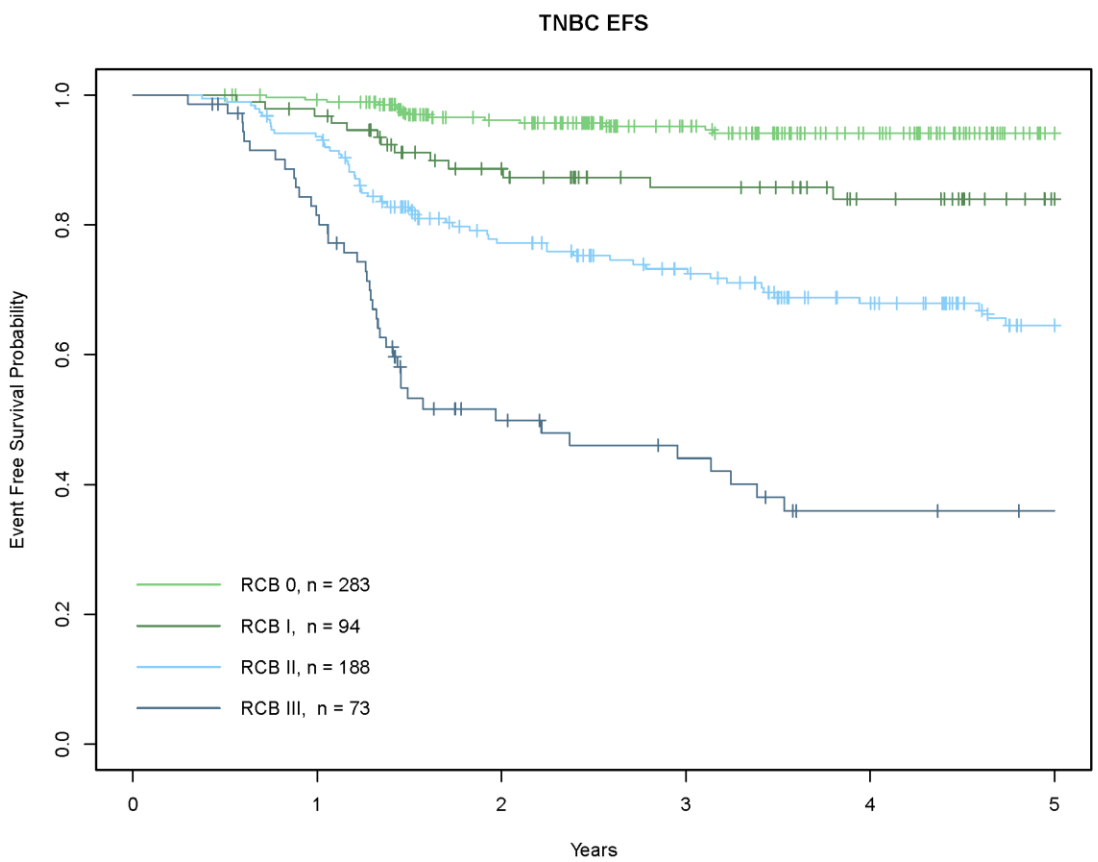
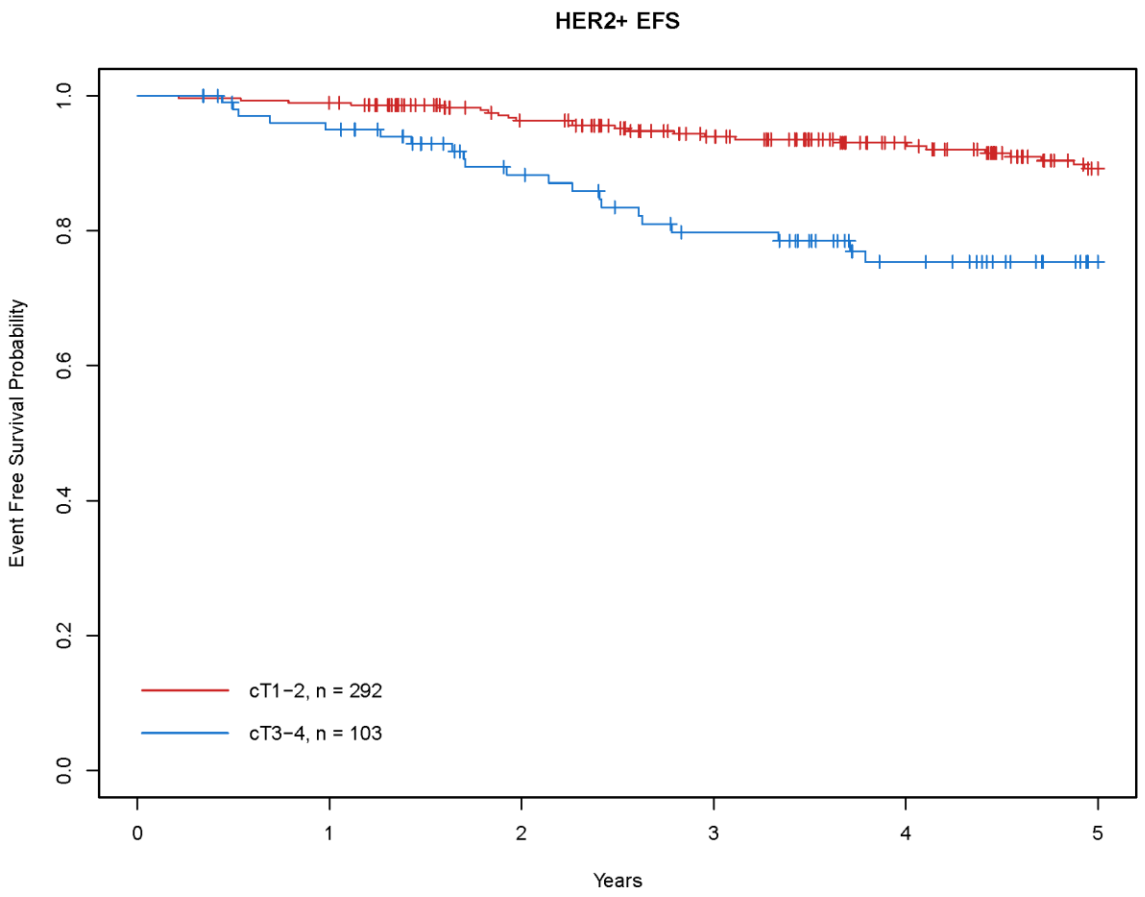


Fig S5. EFS for HER2+ according to baseline cT size (top) and RCB class (bottom)



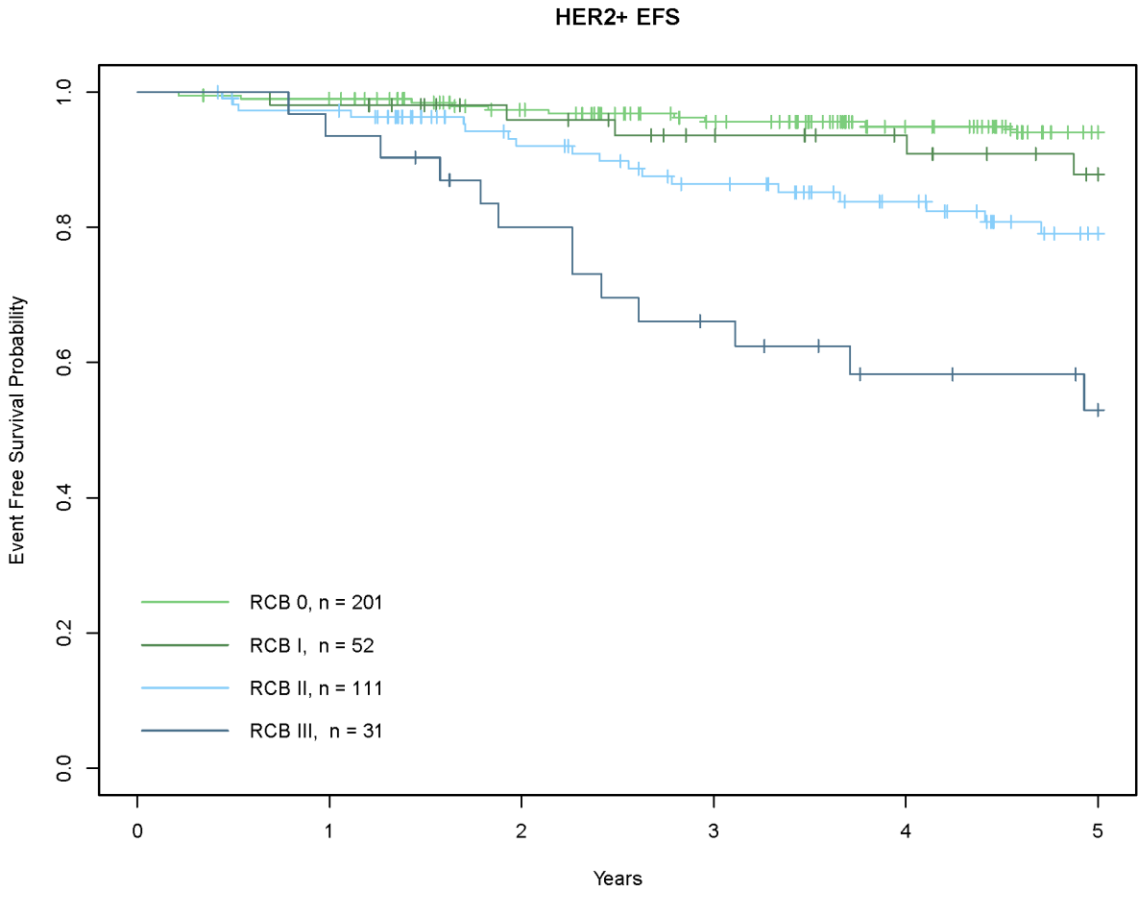


Table S6. Factors associated with OS on UVA and MVA according to response to NAST (HER2+)

Hazard Ratios from Cox PH model for HER2+: all patients								
		OS Univariate Analysis				OS Multivariate Analysis		
Characteristic	**N**	**Event N**	**HR[1]**	**95% CI[1]**	**p-value[2]**	**HR[1]**	**95% CI[1]**	**p-value[2]**
HR Status								
Positive	267	13	—	—		—	—	
Negative	128	9	1.45	0.62, 3.40	0.4	3.99	1.50, 10.6	**0.006**
Baseline Clinical T Category Groups								
cT1-2	292	11	—	—		—	—	
cT3-4	103	11	3.42	1.48, 7.90	**0.004**	2.31	0.94, 5.66	0.066
Baseline Clinical Node Status								
cN0	175	9	—	—		—	—	
cN+	220	13	1.43	0.61, 3.35	0.4	0.65	0.25, 1.68	0.4
RCB Index	395	22	2.07	1.55, 2.78	**<0.001**	2.46	1.72, 3.51	**<0.001**

Hazard Ratios from Cox PH model for HER2+: Non-pCR								
		OS Univariate Analysis				OS Multivariate Analysis		
Characteristic	**N**	**Event N**	**HR[1]**	**95% CI[1]**	**p-value[2]**	**HR[1]**	**95% CI[1]**	**p-value[2]**
HR Status								
Positive	155	13	—	—		—	—	
Negative	39	6	2.00	0.75, 5.33	0.2	3.38	1.16, 9.83	**0.025**
Baseline Clinical T Category Groups								
cT1-2	136	10	—	—		—	—	
cT3-4	58	9	2.51	1.02, 6.20	**0.046**	1.87	0.71, 4.93	0.2
Baseline Clinical Node Status								
cN0	86	7	—	—		—	—	
cN+	108	12	1.82	0.72, 4.65	0.2	0.79	0.27, 2.30	0.7
RCB Index	194	19	1.99	1.30, 3.02	**0.001**	2.25	1.36, 3.73	**0.002**

Hazard Ratios from Cox PH model for HER2+: pCR								
		OS Univariate Analysis				OS Multivariate Analysis		
Characteristic	**N**	**Event N**	**HR[1]**	**95% CI[1]**	**p-value[2]**	**HR[1]**	**95% CI[1]**	**p-value[2]**
HR Status								
Positive	112	0	—	—		—	—	
Negative	89	3	737,040,794	0.00, Inf	>0.9	606,546,375	0.00, Inf	>0.9
Baseline Clinical T Category Groups								
cT1-2	156	1	—	—		—	—	
cT3-4	45	2	8.37	0.76, 92.8	0.083	7.49	0.66, 85.1	0.10
Baseline Clinical Node Status								
cN0	89	2	—	—		—	—	
cN+	112	1	0.46	0.04, 5.07	0.5	0.34	0.03, 3.86	0.4

[1]HR = Hazard Ratio, CI = Confidence Interval

[2]Wald Test

Table S7. UVA and MVA including treatment arms as a co-variate (TNBC)

Hazard Ratios from Cox PH model for all TNBC								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
Age at Screening	638	129	0.99	0.98, 1.01	0.3	0.99	0.97, 1.00	0.15
Clinical T Category Groups								
cT1-2	472	72	—	—		—	—	
cT3-4	166	57	2.67	1.88, 3.77	<0.001	1.97	1.36, 2.84	<0.001
Clinical Node Status								
cN0	360	56	—	—		—	—	
cN+	278	73	1.87	1.32, 2.65	<0.001	1.06	0.72, 1.54	0.8
NAC Arms								
Control	137	33	—	—		—	—	
Experimental with immunotherapy	215	24	0.59	0.35, 0.99	0.047	1.07	0.62, 1.85	0.8
Experimental without immunotherapy	286	72	1.04	0.69, 1.57	0.9	1.46	0.95, 2.23	0.083
RCB Index	638	129	2.14	1.90, 2.42	<0.001	2.06	1.81, 2.35	<0.001
Hazard Ratios from Cox PH model for TNBC achieving pCR								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
Age at Screening	282	14	1.01	0.96, 1.06	0.7	1.01	0.96, 1.06	0.6
Clinical T Category Groups								
cT1-2	226	12	—	—		—	—	
cT3-4	56	2	0.67	0.15, 3.02	0.6	0.63	0.14, 2.87	0.6
Clinical Node Status								
cN0	165	7	—	—		—	—	
cN+	117	7	1.5	0.53, 4.28	0.4	1.66	0.57, 4.82	0.4
NAC Arms								
Control	47	2	—	—		—	—	
Experimental with immunotherapy	120	4	0.99	0.18, 5.44	>0.9	0.94	0.17, 5.20	>0.9
Experimental without immunotherapy	115	8	1.54	0.33, 7.24	0.6	1.52	0.32, 7.23	0.6
Hazard Ratios from Cox PH model for TNBC not achieving pCR								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
Age at Screening	356	115	0.99	0.97, 1.00	0.094	0.99	0.97, 1.00	0.09
Clinical T Category Groups								
cT1-2	246	60	—	—		—	—	
cT3-4	110	55	2.63	1.82, 3.80	<0.001	2.19	1.49, 3.22	<0.001
Clinical Node Status								
cN0	195	49	—	—		—	—	
cN+	161	66	1.87	1.29, 2.70	<0.001	1.03	0.69, 1.54	0.9
NAC Arms								
Control	90	31	—	—		—	—	
Experimental with immunotherapy	95	20	0.84	0.48, 1.49	0.6	1.13	0.63, 2.01	0.7
Experimental without immunotherapy	171	64	1.15	0.75, 1.76	0.5	1.46	0.93, 2.27	0.1
RCB Index	356	115	2.02	1.71, 2.38	<0.001	1.92	1.62, 2.28	<0.001
[1]HR = Hazard Ratio, CI = Confidence Interval								
[2]Wald Test								

Regimen	**Control**	**Experimental + IO**	**Experimental without IO**
ABT 888 + Carboplatin	0	0	35
AMG 386 +/- Trastuzumab	0	0	46
Cemiplimab	0	29	0
Cemiplimab + REGN3767	0	28	0
Durvalumab + Olaparib	0	20	0
Encequidar + Dostarlimab + Carboplatin+/- Trastuzumab	0	42	0
Encequidar + Dostarlimab +/- Trastuzumab	0	15	0
Ganetespib	0	0	37
Irinotecan + Talazoparib	0	0	31
MK-2206 +/- Trastuzumab	0	0	25
Neratinib	0	0	29
Paclitaxel	137	0	0
Paclitaxel + Ganitumab	0	0	40
Pembrolizumab	0	24	0
Pembrolizumab 8-Cycle + AC	0	34	0
PLX3397	0	0	1
SD-101 + Pembrolizumab	0	23	0
SGN-LIV1A	0	0	31
SYD985	0	0	1
Trilaciclib + AC	0	0	10
		Total	638

Table S8. UVA and MVA including treatment arms as a co-variate (HER2+)

Hazard Ratios from Cox PH model for all HER2+								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
HR Status								
Positive	267	31	—	—		—	—	
Negative	128	19	1.34	0.76, 2.37	0.3	2.68	1.40, 5.12	0.003
Clinical T Category Groups								
cT1-2	292	29	—	—		—	—	
cT3-4	103	21	2.53	1.44, 4.44	0.001	2.1	1.15, 3.81	0.015
Clinical Node Status								
cN0	175	22	—	—		—	—	
cN+	220	28	1.18	0.67, 2.06	0.6	0.68	0.37, 1.25	0.2
NAC Arms								
Control	189	20	—	—		—	—	
Experimental	206	30	1.37	0.78, 2.42	0.3	1.1	0.62, 1.95	0.7
RCB Index	395	50	1.7	1.41, 2.05	<0.001	1.92	1.54, 2.39	<0.001
Hazard Ratios from Cox PH model for HER2+ achieving pCR								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
HR Status								
Positive	112	3	—	—		—	—	
Negative	89	7	2.94	0.76, 11.4	0.12	2.65	0.68, 10.4	0.2
Clinical T Category Groups								
cT1-2	156	6	—	—		—	—	
cT3-4	45	4	2.66	0.75, 9.45	0.13	2.26	0.62, 8.23	0.2
Clinical Node Status								
cN0	89	4	—	—		—	—	
cN+	112	6	1.27	0.36, 4.50	0.7	1.17	0.33, 4.19	0.8
NAC Arms								
Control	108	5	—	—		—	—	
Experimental	93	5	1.1	0.32, 3.81	0.9	1.09	0.32, 3.79	0.9
Hazard Ratios from Cox PH model for HER2+ not achieving pCR								
	EFS Univariate Analysis					EFS Multivariate Analysis		
Characteristic	N	Event N	HR[1]	95% CI[1]	p-value[2]	HR[1]	95% CI[1]	p-value[2]
HR Status								
Positive	155	28	—	—		—	—	
Negative	39	12	2.08	1.05, 4.10	0.035	2.78	1.34, 5.74	0.006
Clinical T Category Groups								
cT1-2	136	23	—	—		—	—	
cT3-4	58	17	2.24	1.20, 4.21	0.012	2.18	1.10, 4.32	0.026
Clinical Node Status								
cN0	86	18	—	—		—	—	
cN+	108	22	1.19	0.64, 2.23	0.6	0.62	0.30, 1.28	0.2
NAC Arms								
Control	81	15	—	—		—	—	
Experimental	113	25	1.26	0.66, 2.39	0.5	1.08	0.56, 2.06	0.8
RCB Index	194	40	1.49	1.12, 1.99	0.007	1.7	1.22, 2.35	0.001
[1]HR = Hazard Ratio, CI = Confidence Interval								
[2]Wald Test								

Regimen	Control	Experimental
AMG 386 +/- Trastuzumab	0	19
Encequidar + Dostarlimab + Carboplatin+/- Trastuzumab	0	4
Encequidar + Dostarlimab +/- Trastuzumab	0	15
MK-2206 +/- Trastuzumab	0	27
Neratinib	0	50
Paclitaxel + Trastuzumab	27	0
Patritumab + Trastuzumab	0	24
Pertuzumab + Trastuzumab	162	0
Pertuzumab + Trastuzumab + Tucatinib	0	17
T-DM1 + Pertuzumab	0	47
Trilaciclib + Pertuzumab + Trastuzumab + AC	0	3
	Total	395