



Changes in tumour expression of HER2 and hormone receptors status after neoadjuvant chemotherapy in Japanese breast cancer registry

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Disclosure slide

The authors declare that they have no conflict of interest.

Background

- Recently, neoadjuvant chemotherapy has become a treatment of choice in clinics.
- Clinical trials have demonstrated that each subtype of breast cancer has a different pathological complete response (pCR) rate.
- Estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2) expression status may change (positive to negative and vice versa) after neoadjuvant chemotherapy.

HER2 status in primary tumors and metastatic tumor

**Primary tumor
HER2 positive
N=182**

IHC 3+, FISH +	60
IHC 3+, FISH -	14
IHC 3+, FISH unknown	58
IHC -, FISH +	16
IHC unknown, FISH +	34

**Metastatic lesion
HER2 positive
N=139**

IHC 3+, FISH +	16
IHC 3+, FISH -	0
IHC 3+, FISH unknown	25
IHC -, FISH +	7
IHC unknown, FISH +	91

**Metastatic lesion
HER2 negative
N=43**

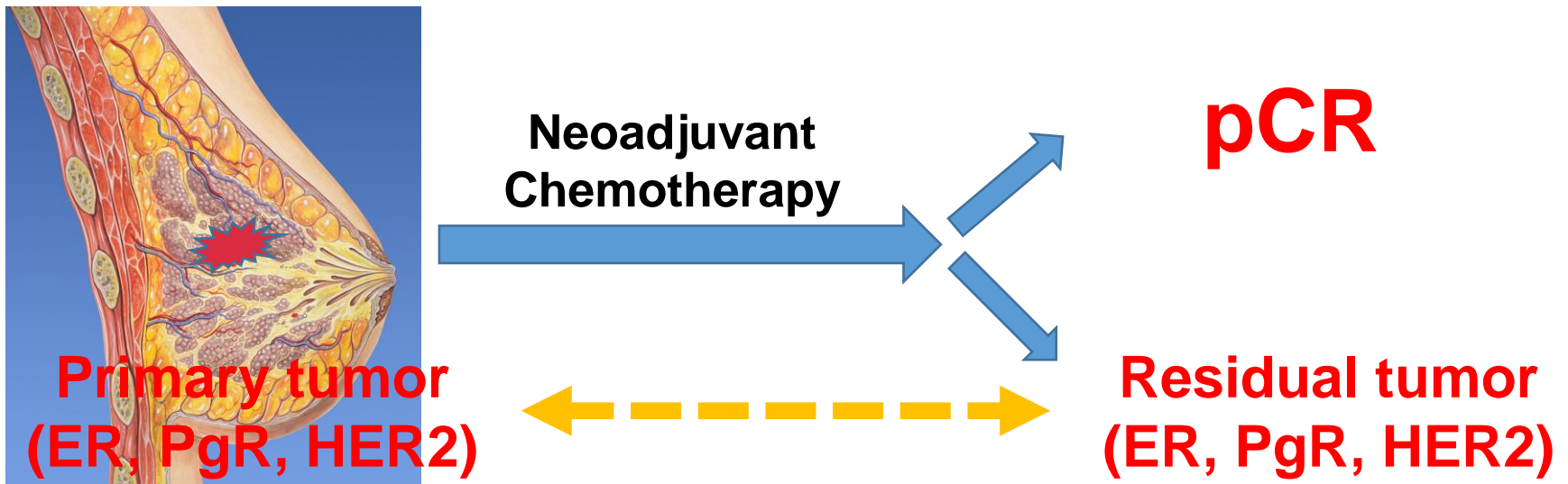
IHC -, FISH -	6
IHC -, FISH unknown	3
IHC unknown, FISH -	34

Discordance rates by clinical factors

Subgroup	HER2 Status		<i>P</i>
	Concordant n = 139	Discordant n = 43	
Trastuzumab			
None	78 (74%)	28 (26%)	0.296
Before biopsy	61 (80%)	15 (20%)	
Timing of metastasis diagnosis			
At presentation	30 (88%)	4 (12%)	0.077
At recurrence	109 (74%)	39 (26%)	
Metastatic location			
Local	53 (72%)	21 (28%)	0.212
Distant	86 (80%)	22 (20%)	
HR status			
Positive	79 (77%)	23 (23%)	0.865
Negative	58 (74%)	20 (26%)	
Unknown	2		
Chemotherapy with or without trastuzumab			
None	36 (90%)	4 (10%)	0.022
Before biopsy	103 (73%)	39 (27%)	

Objectives

- We aimed to investigate the pCR rate in each subtype and the discordance rate of ER, PgR, and HER2 before and after neoadjuvant chemotherapy using the Japanese breast cancer registry.



History of the Breast Cancer Registry in the JBCS

- 1975 Inception of the Breast Cancer Registry (BCR)
- 2003 Change of registration System (Web-based)
- Total number in the Registry
 - 1975-2003: 188,265 cases
 - 2004-2011: 255,519 cases
- From 2012
 - Move to National Clinical Database



NCD

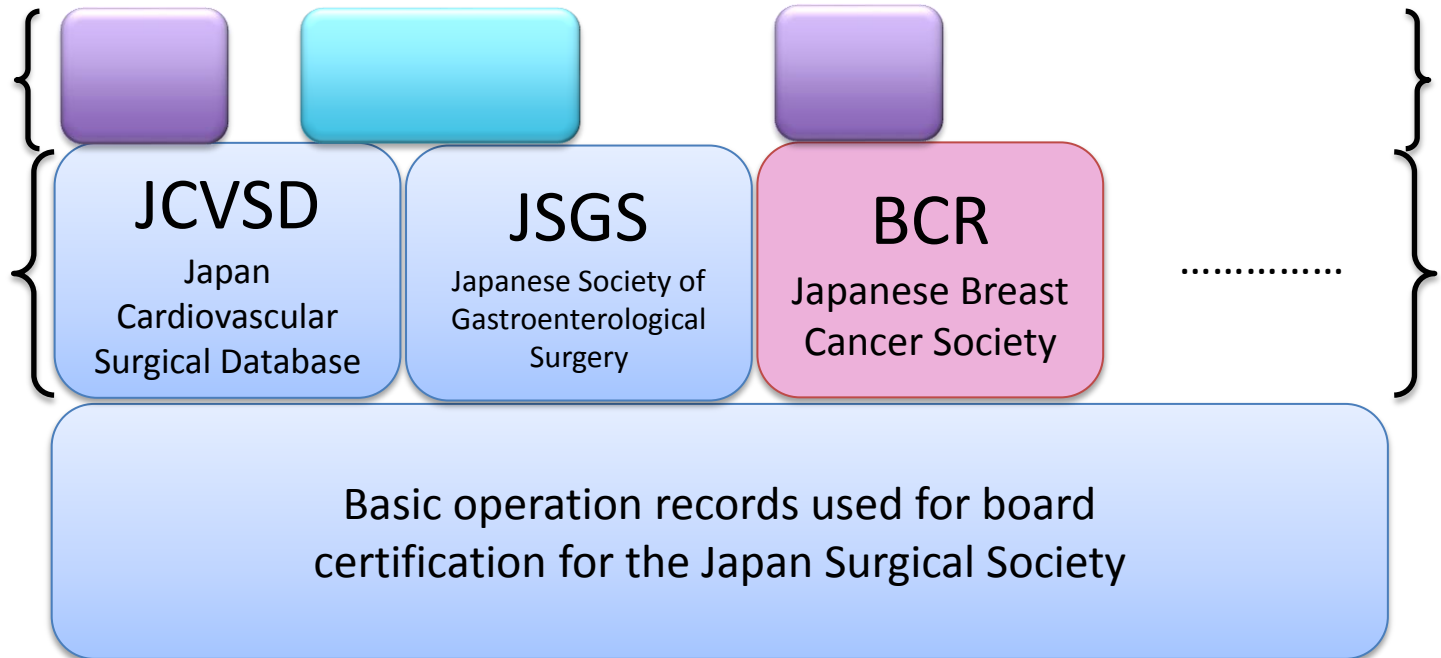
National
Clinical
Database



Number of Units: 4,000
Number of Users: 23,000
Number of Cases: 3,500,000

Clinical research

Clinical records
used for board
certification



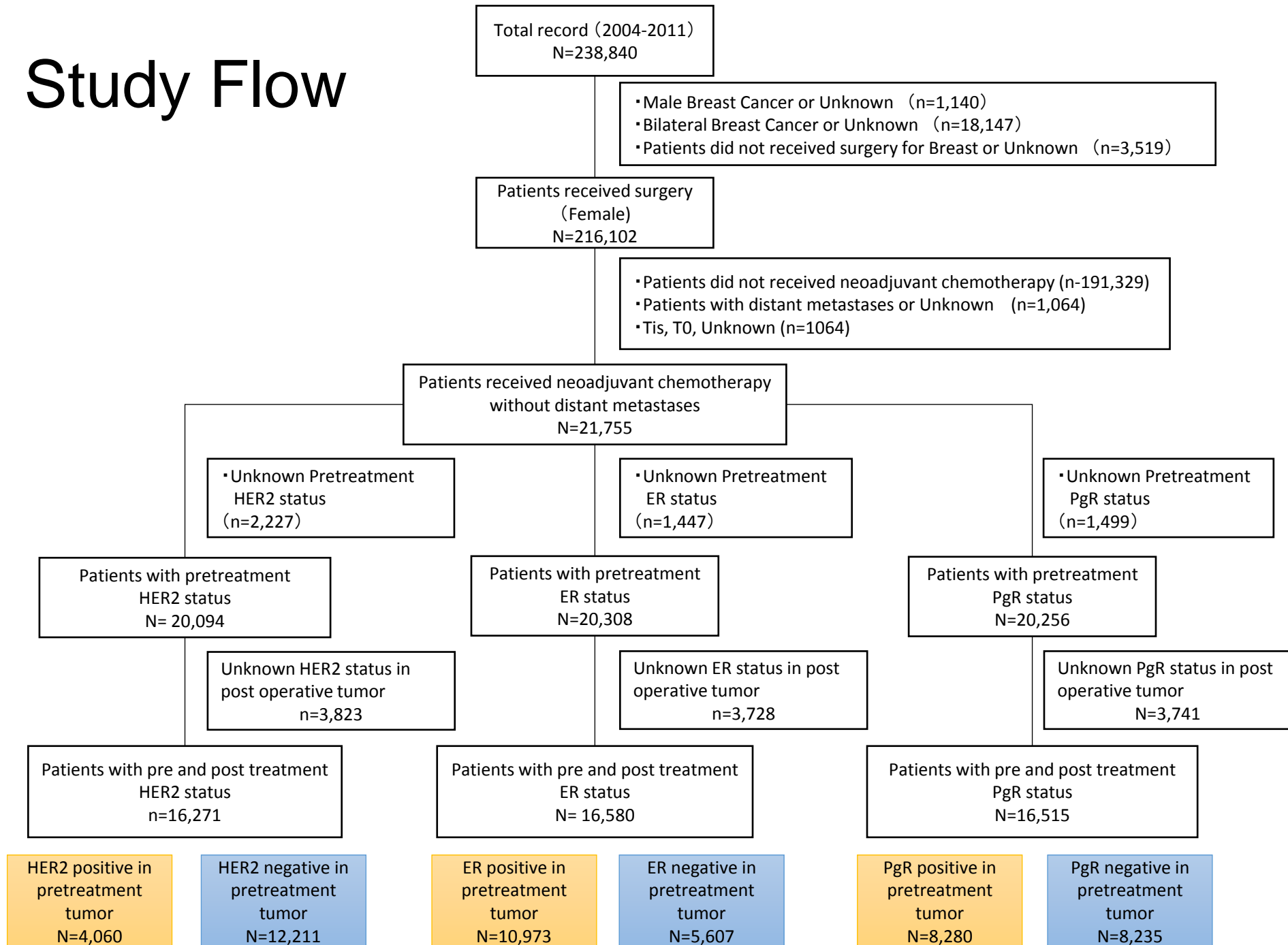
Items collected in the BCR

- More than 50 items (demographic and clinicopathological factors) of newly diagnosed primary breast cancer patients were voluntarily registered to the JBCS through the web-based system from affiliated institutes.
- The TNM classification was registered according to the Unio Internationalis Contra Cancrum (UICC) staging 6th edition.
- The histological classification was registered according to the WHO classification.

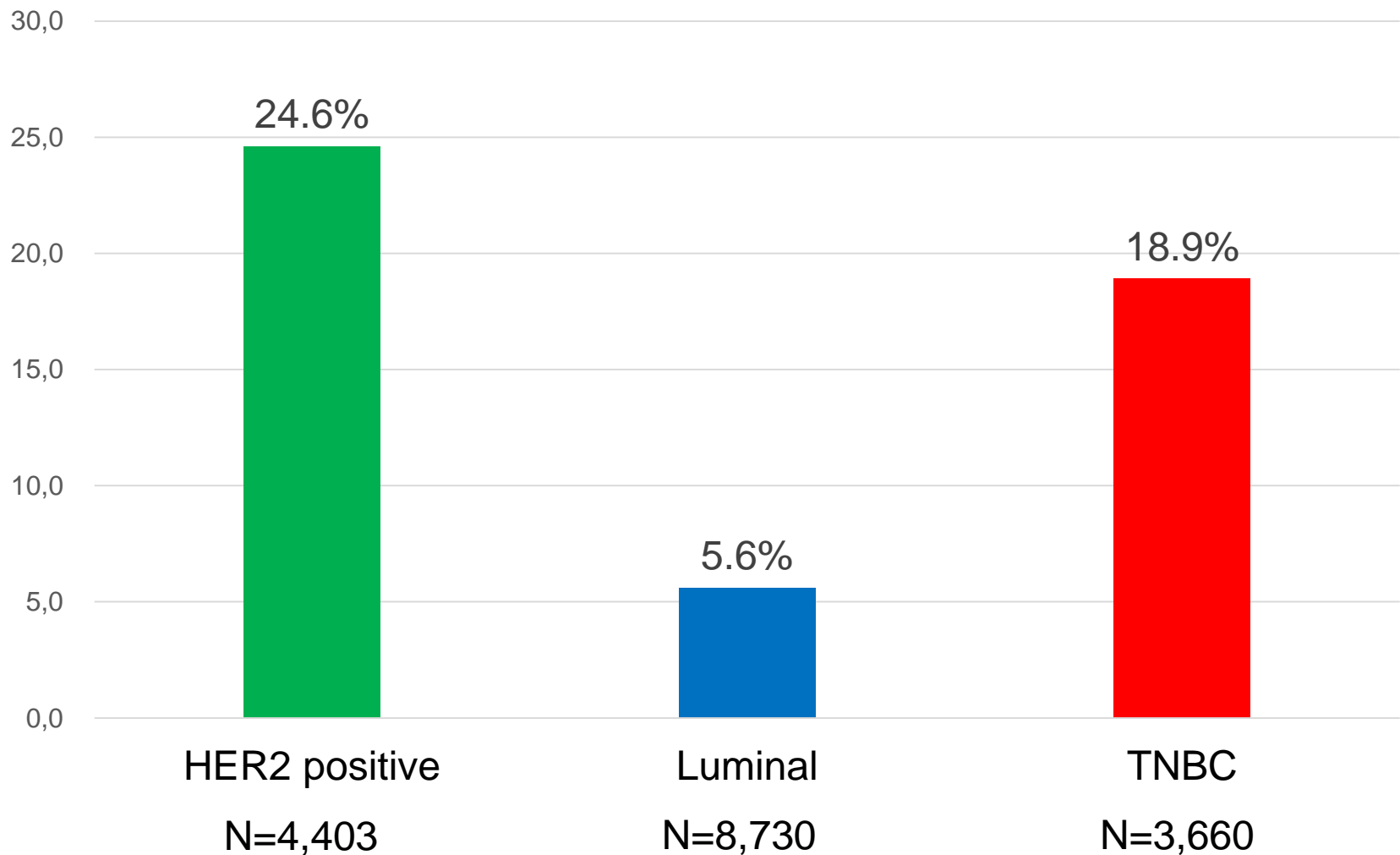
Methods

- After data cleanup, out of a total of 238,840 cases from 2004 to 2011, a total of 21,755 patients without distant metastases who received neoadjuvant chemotherapy between 2004 and 2011 were eligible for analysis (Figure 1).
- Patients with male breast cancer, those with bilateral breast cancer, those who did not receive surgery, and those with Tis and T0 were excluded.
- A pCR was defined as no invasive tumor in the surgical specimen after neoadjuvant chemotherapy.
- HER2 overexpression was evaluated (i.e., immunohistochemically 3+ and/or fluorescence *in situ* hybridization-positive).
- Clinical characteristics that could be viewed as categorical variables were analyzed by Pearson's chi-square and Fisher's exact tests to determine their association with HER2 status.
- A two-sample t-test was used to determine the differences in mean ages between patients with concordant HER2 status and those with discordant status.

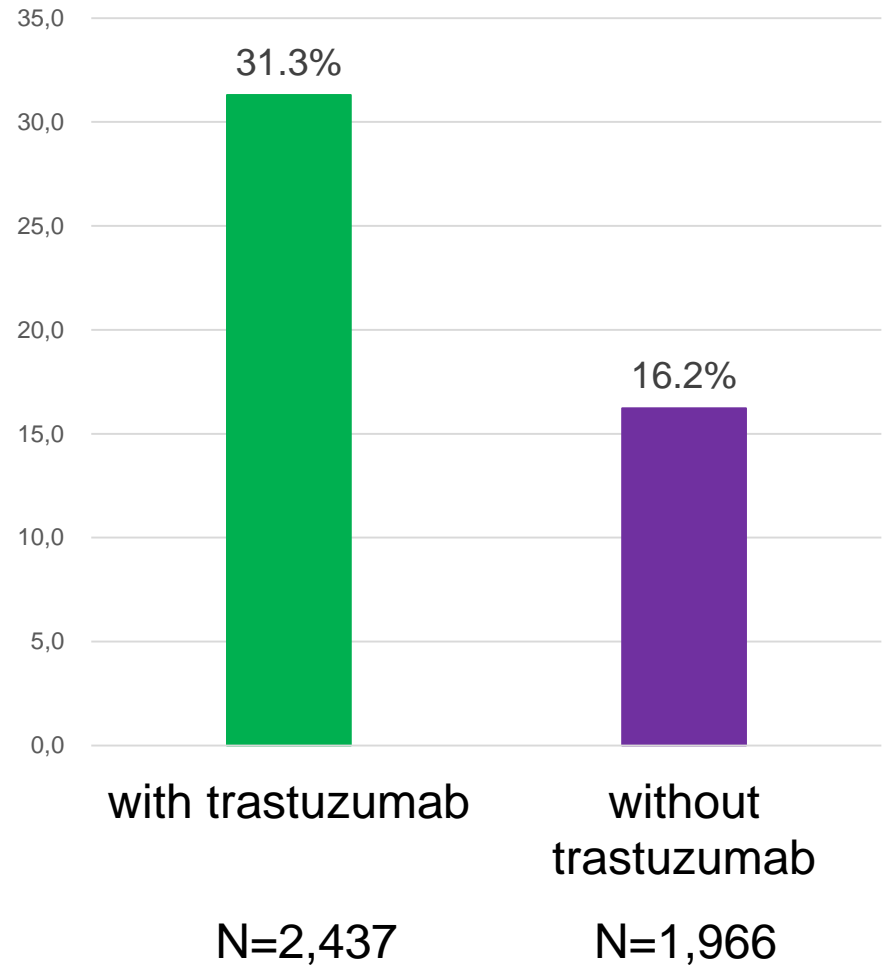
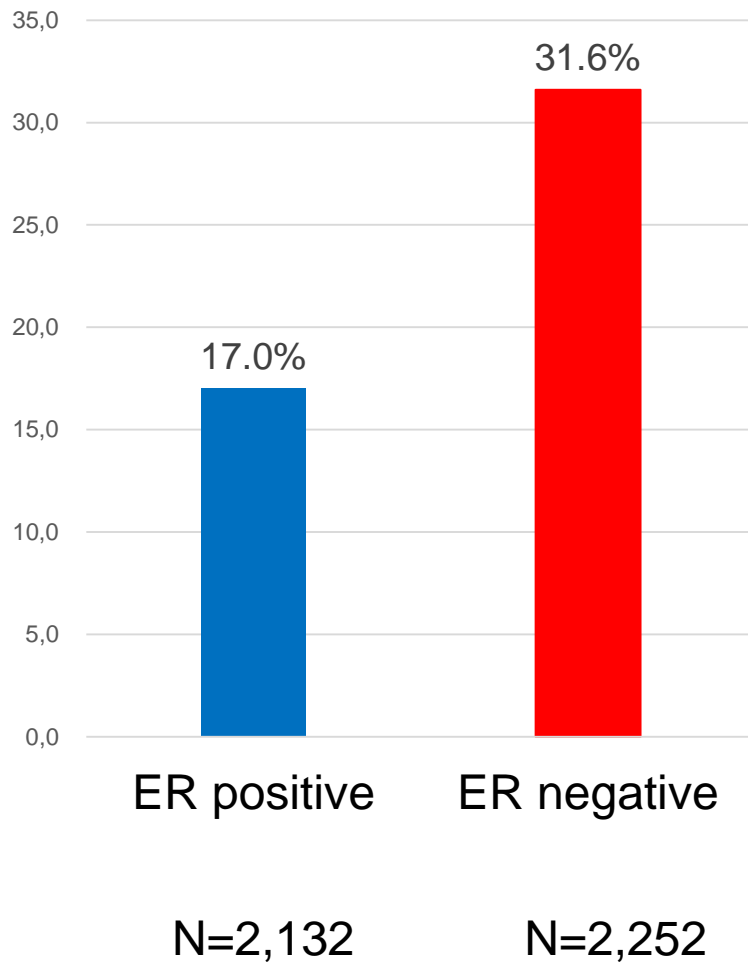
Study Flow



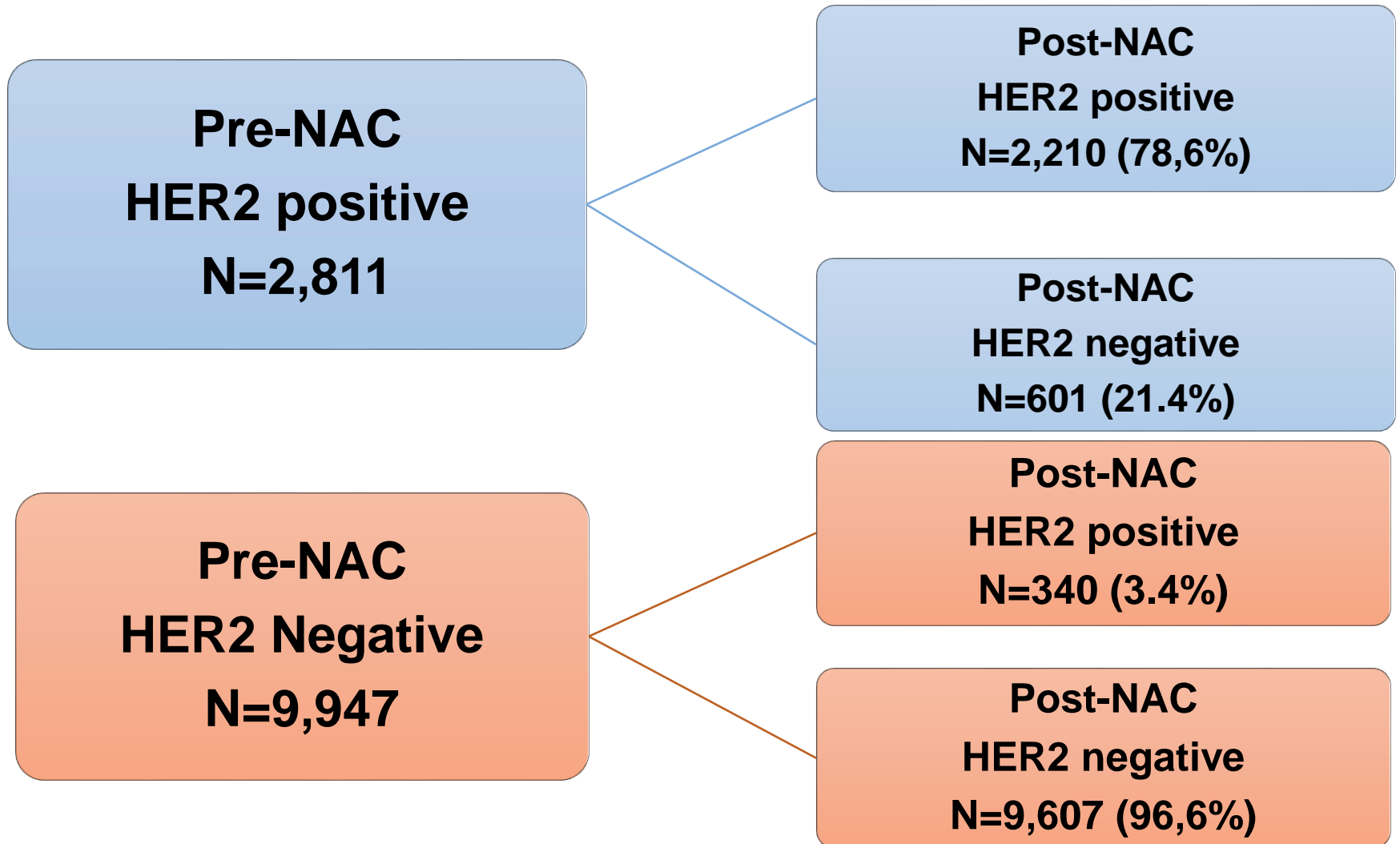
pCR rate in each subtype (HER2 positive, Luminal, TNBC)



pCR rate in HER2 positive tumors



HER2 status in Primary tumor between Pre and Post Neoadjuvant therapy



Change in HER2 status of the primary tumor after neoadjuvant therapy

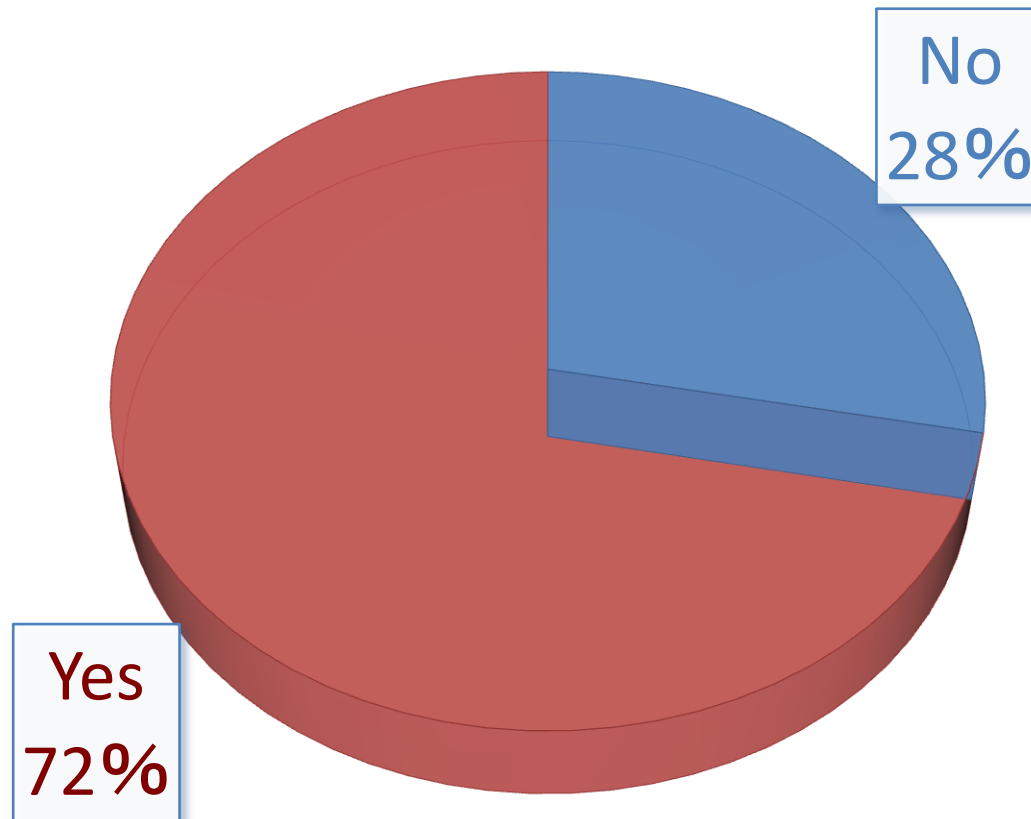
Before neoadjuvant therapy		After neoadjuvant therapy	
HER2 status	n	HER2 status	n
HER2 positive	2,811	HER2 positive	2,210 (78.6%)
		HER2 negative	601 (21.4%)
HER2 negative	9,947	HER2 positive	340 (3.4%)
		HER2 negative	9,607 (96.6%)
Immunohistochemical analysis			
HER2 3+	3,548	HER2 3+	2,913 (82.1%)
		HER2 0, 1+, 2+	635 (17.9%)
HER2 0, 1+, 2+	12,305	HER2 3+	283 (2.3%)
		HER2 0, 1+, 2+	12,022 (97.7%)
FISH analysis			
FISH positive	375	FISH positive	344 (91.7%)
		FISH negative	31 (8.3%)
FISH negative	915	FISH positive	49 (4.3%)
		FISH negative	876 (95.7%)

Discordance rates by clinical factors

		Post treatment HER2 status (N=2,811)				p-value
		Negative		Positive		Fisher's exact tests
		N	%	N	%	
Pretreatment ER status	Negative	169	13.0	1,130	86.9	<.0001
	Positive	427	28.4	1,075	71.5	
Pretreatment PgR status	Negative	263	14.9	1,501	85.0	<.0001
	Positive	330	32.0	701	67.9	
Menopausal status	Pre	245	22.4	846	77.5	0.4462
	Post	337	20.5	1,301	79.4	
	Unknown	19	23.1	63	76.8	
Neoadjuvant Trastuzumab	No	259	18.1	1,167	81.8	<.0001
	Yes	342	24.6	1,043	75.3	
Rate of Residual tumor	less than 50%	265	22.3	923	77.6	0.345
	more than 50%	313	20.8	1,192	79.2	

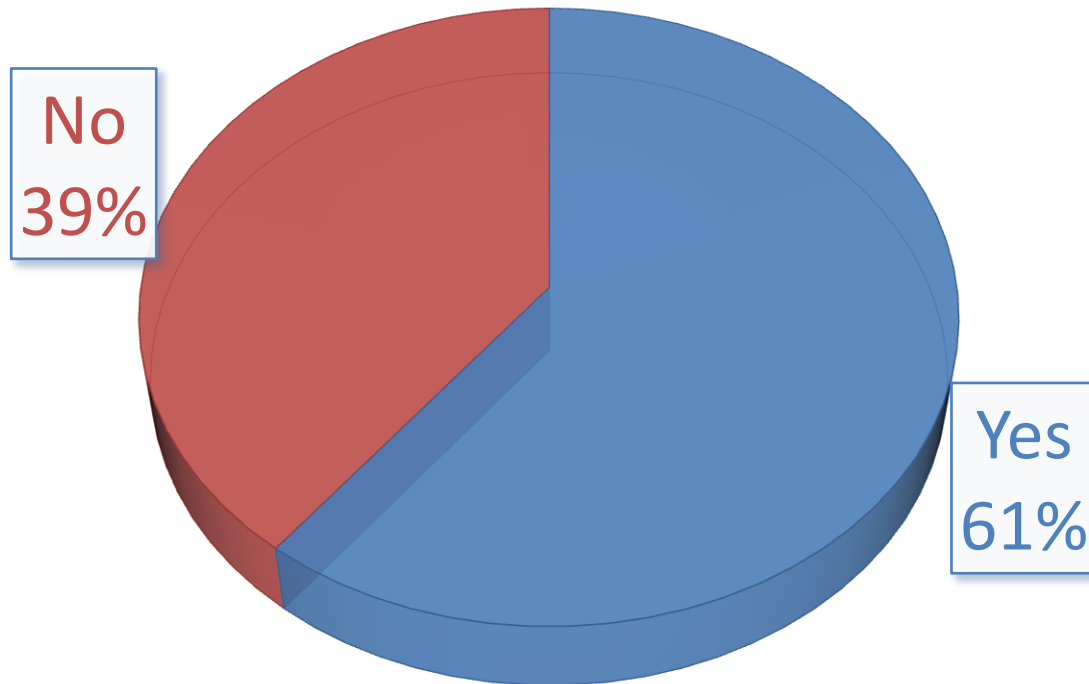
Of 342 patients whose tumors converted from HER2-positive to HER2-negative, who received neoadjuvant trastuzumab.

Did patients receive adjuvant trastuzumab?



340 patients whose tumors converted from
HER2-negative to HER2-positive

Did patients receive adjuvant trastuzumab?

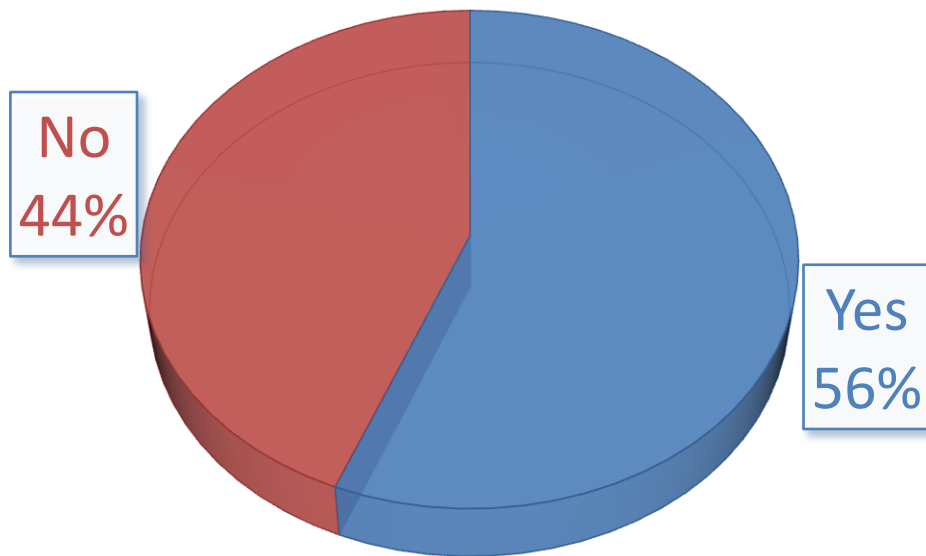


ER and PgR status in Primary tumor between Pre and Post Neoadjuvant therapy

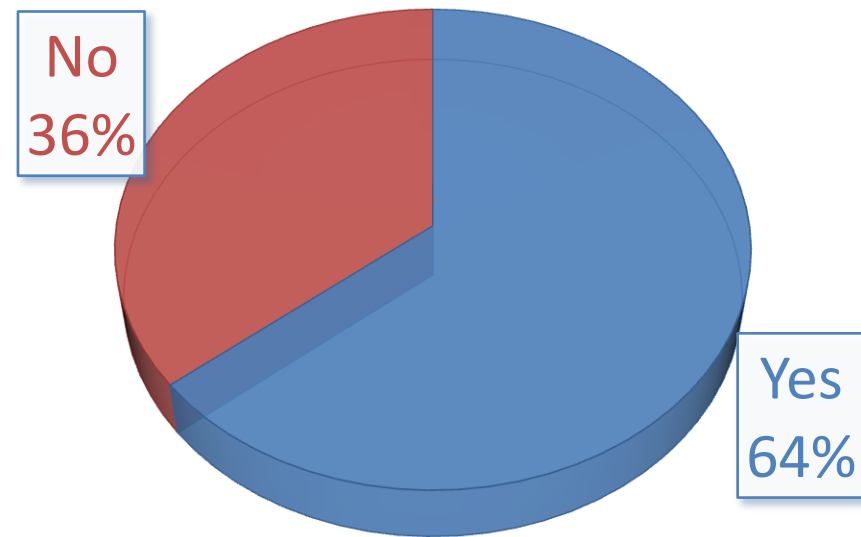
Primary tumor			Residual tumor	
ER status	n		ER status	n
Positive	10,973		Positive	10,474 (95.5%)
			Negative	499 (4.5%)
Negative	5,607		Positive	519 (9.3%)
			Negative	5,088 (90.7%)
PgR status				
Positive	8,280		Positive	6,735 (81.3%)
			Negative	1545 (18.7%)
Negative	8,235		Positive	766 (9.3%)
			Negative	7,469 (90.7%)

Did patients receive adjuvant Endocrine therapy?

Patients whose tumors converted from
ER-positive to ER-negative
(N=499)



Patients whose tumors converted
from
ER-negative to ER-positive
(N=519)



Conclusions

- Our findings demonstrate that although pCR rates in the real world have the same differences with regard to subtypes and trastuzumab treatment that are seen in clinical trials.
- The pCR rate in the real world are also lower than those in clinical trials.
- HER2 status does not always carry over from the original tumor to residual tumors. More than 20% of patients with residual tumors after neoadjuvant therapy showed loss of HER2 expression.
- Our data strongly support the need for retest ER, PgR, HER2 of surgical sample after neoadjuvant therapy in order to accurately determine appropriate use of targeted therapy.
- Additional research should be conducted on biology and treatment in breast cancer patients whose tumors lose HER2 expression after neoadjuvant chemotherapy.

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NCD

National
Clinical
Database



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K A K E N H I