Breast cancer with a higher proportion of tumor cells staining positive for Her2 is more likely to have pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC).

Maria K. Pomponio BA, Susanna M. Nazarian MD, PhD, Paul J. Zhang MD, PhD, and Julia C. Tchou MD, PhD

Department of Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

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INTRODUCTION

- Neoadjuvant chemotherapy (NAC)- systemic treatment prior to surgical intervention- is commonly employed in early-stage and locally advanced breast cancer to downstage tumor size.
- Achievement of pathologic complete response (pCR- ypT0/is ypN0) following NAC is associated with favorable outcomes in patients with aggressive breast cancer subtypes such as HER2+.
- Prior reports have suggested high gene amplification on the fluorescence in situ hybridization (FISH) assay as a predictive marker for pCR.
- At many institutions, however, immunohistochemistry (IHC) testing is more readily available and FISH is only preformed on equivocal IHC results.
- Given that IHC is often the first-line diagnostic tool for HER2 positivity, we sought to analyze the role of percent staining on the IHC assay (IHC%) as a predictor of pCR following anti-HER2 targeted NAC.

HYPOTHESIS

We propose that women with higher immunohistochemistry percentage (IHC%) staining for the HER2 receptor are more likely to have a pCR following NAC.

METHODS

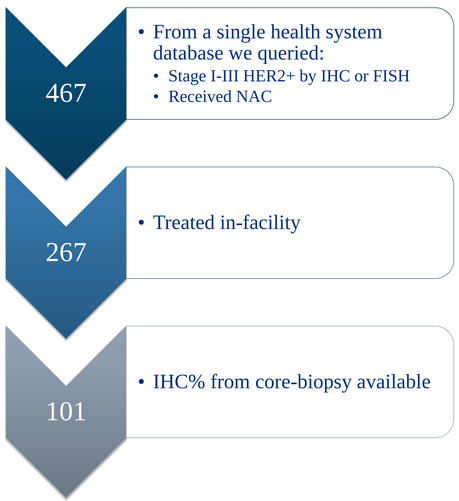

FIGURE 1 - Study schema and patient inclusion/exclusion.

RESULTS

	Total		pCR		non-pCR		P
	101	100%	52	51.5%	49	48.5%	
IHC Protein Staining (%) [2]	90 (60-100)		92.5 (75-100)		80 (30-90)		0.01
IHC group[1,3]							
High	32	31.7%	22	42.3%	10	20.4%	0.02
Low	69	68.3%	30	57.7%	39	79.6%	
FISH Performed[1]							
No	78	77.2%	42	80.8%	36	73.5%	0.39
Yes	23	22.8%	10	19.2%	13	26.5%	
HER2/CEP17 Ratio[2,4]	3.0 (2.3-5.2)		3.0 (2.1-3.5)		3.0 (2.6-5.2)		0.71
Age at diagnosis[2]	51 (41-59)		48.5 (38-55)		54 (44-62)		0.09
Race[1]							
White	65	64.4%	36	69.2%	29	59.2%	0.16
Black	29	28.7%	11	21.2%	18	36.7%	
Asian	7	6.9%	5	9.6%	2	4.1%	
Hormone Receptor Status[1]							
Negative	41	40.6%	26	50.0%	15	30.6%	0.05
Positive	60	59.4%	26	50.0%	34	69.4%	
Clinical Stage[1]							
I	8	7.9%	3	5.8%	5	10.2%	0.62
IIa	26	25.7%	15	28.8%	11	22.4%	
IIb	35	34.7%	16	30.8%	19	38.8%	
III	32	31.7%	18	34.6%	14	28.6%	
NAC Regimen[1]							
Trastuzumab	36	35.6%	14	26.9%	22	44.9%	0.06
Trastuzumab & Pertuzumab	65	64.4%	38	73.1%	27	55.1%	
Surgery[1]							
Lumpectomy	39	38.6%	18	34.6%	21	42.9%	0.40
Mastectomy	62	61.4%	34	65.4%	28	57.1%	

TABLE 1 – Demographic, tumor, and treatment characteristics of patients HER2+ treated with stratified by pathologic response. [1]Chi square test [2]Two-sided ANOVA Test. [3]A logit transformation was used to normalize the percent protein staining on immunohistochemistry test and values corresponding to one SD above the mean comprised the "High IHC%" cohort. This normalized value correlated to a non-normalized IHC% value of 99%. [4]Only 23 patients who underwent FISH assay were included

DISCUSSION

- During multivariate logistic regression analysis, percent IHC% staining remained the only predictor of pCR when assessed as a continuous (OR: 1.016 P=0.02) or categorical variable (OR: 2.39 P=0.07, trending).
- Our results suggest clinical utility of IHC% as a potential biomarker in predicting the benefits of NAC in the treatment of breast cancer.

FUTURE DIRECTIONS

- Given our limited sample size, further investigation to elucidate the mechanisms underlying this observation is warranted.

REFERENCES

1. Schneeweiss A, Chia S, Hegg R, et al. Evaluating the predictive value of biomarkers for efficacy outcomes in response to pertuzumab- and trastuzumab-based therapy: An exploratory analysis of the TRYPHAENA study. *Breast Cancer Res*. 2014;16(4):1-12. doi:10.1186/bcr3690
2. Singer CF, Tan YY, Fitzal F, et al. Pathological complete response to neoadjuvant trastuzumab is dependent on HER2/CEP17 ratio in HER2-amplified early breast cancer. *Clin Cancer Res*. 2017;23(14):3676-3683. doi:10.1158/1078-0432.CCR-16-2373
3. Arnould L, Arveux P, Couturier J, et al. Pathologic complete response to trastuzumab-based neoadjuvant therapy is related to the level of HER-2 amplification. *Clin Cancer Res*. 2007;13(21):6404-6409. doi:10.1158/1078-0432.CCR-06-3022
4. Wu Z, Xu S, Zhou L, et al. Clinical significance of quantitativeHER2gene amplification as related to its predictive value in breast cancer patients in neoadjuvant setting. *Onco Targets Ther*. 2018;11:801-808. doi:10.2147/OTT.S157634
5. Guiu S, Gauthier M, Coudert B, et al. Pathological complete response and survival according to the level of HER-2 amplification after trastuzumab-based neoadjuvant therapy for breast cancer. *Br J Cancer*. 2010;103(9):1335-1342. doi:10.1038/sj.bjc.6605939
6. Kogawa T, Fouad TM, Liu DD, et al. High HER2/Centromeric Probe for Chromosome 17 Fluorescence In Situ Hybridization Ratio Predicts Pathologic Complete Response and Survival Outcome in Patients Receiving Neoadjuvant Systemic Therapy With Trastuzumab for HER2-Overexpressing Locally Advanced Breast Cancer. *Oncologist*. 2015;21(1):21-27. doi:10.1634/theoncologist.2015-0101