Title:

Predictive factors for pathologic complete response and disease-free survival after neoadjuvant chemotherapy with trastuzumab: a multicenter retrospective observational study in patients with HER2-positive primary breast cancer (JBCRG-C03 study)

Abstract:

BACKGROUND:

Addition of trastuzumab to neoadjuvant chemotherapy (NAC) improved pathologic complete response (pCR) rate in HER2-positive breast cancer. Although recent trials have shown favorable prognosis with NAC plus trastuzumab, clinicopathological factors to predict the outcome have not been fully understood. The aim of this study was to investigate the survival after NAC with trastuzumab and to explore the predictive factors.

PATIENTS AND METHODS:

This is a multicenter retrospective observational study. Patients with HER2-positive primary breast cancer treated with NAC plus trastuzumab from 2001 to 2010 were identified from the institutional database. Primary end point was disease-free survival (DFS). pCR was defined as ypT0/is+ypN0. Kaplan-Meier method was used to estimate DFS. Logistic regression and proportional hazard analysis were used to identify clinicopathological factors to predict pCR and DFS, respectively.

RESULTS:

733 patients were included in the analysis (whole dataset). 425 were ER/PgR-negative (HR- dataset) and 306 were ER/PgR-positive (HR+ dataset). Radiation therapy was performed in 90% of lumpectomy and 31% of mastectomy. Hormonal therapy was performed in 84% of HR+ dataset. pCR rate was 45% in whole dataset, 60% in HR- dataset, and 34% in HR+ dataset. Table 1 showed the result of multivariate analysis for pCR in whole dataset. When HR+ and HR- dataset were analyzed separately, no definitive predictors for pCR were identified in multivariate analysis. Although the patients with pCR showed a significantly favorable prognosis than those without pCR at 3 years DFS, in whole dataset (93% vs 83%, $p<0.0001$) and HR- dataset (94% vs 80%, $p<0.0001$), there was no significant difference in HR+ dataset (89% vs 86%, $p=0.10$). Different predictors were selected for DFS when multivariate analysis was conducted separately between HR- and HR+ dataset (Table 2).

CONCLUSIONS:

In this observational study, we clarified predictors for pCR and DFS in HER2-positive patients treated with neoadjuvant trastuzumab containing therapy based on tumor

subtype. Our results may help us to predict the prognosis more precisely and to simulate the disease course.

Table 1) Multivariate logistic regression analysis for pCR in whole dataset

	OR	95%CI	p-value
Post-menopause vs Pre-menopause	1.50	(1.05—2.15)	0.026*
cT1—2 vs cT3—4	1.72	(1.16—2.59)	0.008*
ER/PgR-negative vs ER/PgR-positive	3.32	(2.30—4.82)	<0.0001*
Grade 3 vs Grade 1—2	1.28	(0.89—1.84)	0.183

Table 2) Multivariate proportional hazard analysis for DFS

Factors†	HR	95%CI	p-value
Whole dataset			
Pre-menopause vs Post-menopause	1.61	(1.04—2.52)	0.033*
cN2—3 vs cN0	3.06	(1.58—6.24)	0.001*
cN1 vs cN0	2.26	(1.23—4.41)	0.007*
Grade 3 vs Grade 1—2	1.87	(1.20—2.97)	0.006*
non-pCR vs pCR	1.90	(1.18—3.13)	0.008*
HR- dataset			
Pre-menopause vs Post-menopause	1.7	(1.01—2.85)	0.046*
cT3—4 vs cT1—2	1.86	(1.09—3.17)	0.024*
non-pCR vs pCR	3.28	(1.90—5.87)	<0.0001*
HR+ dataset			
cN2—3 vs cN0	5.01	(1.79—16.19)	0.002*
cN1 vs cN0	3.50	(1.40—10.61)	0.006*
Grade 3 vs Grade 1—2	2.95	(1.52—5.87)	0.001*

† Only factors with statistical significance