Pooled Clinical Trial Data Analyses Comparing the Biology of HER2-low vs HER2-0 Breast Cancer in Patients with Metastatic Breast Cancer Following Treatment with Standard Single Agent Chemotherapy

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Introduction

Observational research suggests that among patients with HER2-negative breast cancer, tumor biology does not vary according to HER2-low vs. HER2-0 expression. Specifically, studies comparing outcomes for patient with HER2-low vs. HER2-0 expressing tumors showed no difference in overall survival (OS) after accounting for patients' clinicopathologic features including hormone receptor (HR) status.[1,2]

We sought to extend existing research regarding potential differential biology associated with HER2-low vs. HER2-0 expression by both

- studying patients treated in historic clinical trials where data was collected to measure associations between protocol defined treatments and outcomes
- evaluating the endpoint of progression-free survival (PFS) in addition to OS

Methods and Materials

We pooled anonymized patient-level clinical trial data from studies within the Medidata Enterprise Data Store and identified 142 women with HER2-negative metastatic breast cancer (MBC) who received treatment with a National Comprehensive Cancer Network recommended single agent chemotherapy in the context of a clinical trial. Using patient-level immunohistochemistry (IHC) results from local testing and reported via electronic case report forms, we categorized patients' HER2 expression as either HER2-low (IHC 1+/2+ and not amplified by in situ hybridization) or HER2-0 (IHC 0). We compared patients' baseline demographic and clinicopathologic features according to HER2 expression. We estimated differences in PFS and OS attributable to HER2 expression after adjusting for patients' baseline demographic and clinicopathologic attributes with Cox proportional hazards regression models and with Kaplan Meier methods.

Results

Twenty percent (28/142) of patients had low levels of HER2 expression. Twenty-five percent (7/28) of HER2-low patients had HR+ disease compared with 17% (19/114) of HER2-0 (p=0.31). For HER2-low vs HER2-0 patients, median PFS was 3.5 vs. 2.9 months (p=0.53) and median OS was 10.7 vs. 12.7 months (p=0.37), respectively.

In adjusted Cox proportional-hazard models, patients with HER2-low tumors had a 22% reduction (non-significant) in hazard of progression or death (HR 0.78, 95% CI: 0.45-1.35) and a 16% elevation (non-significant) in hazard of death compared with patients with HER2-0 tumors (HR 1.16, 95% CI: 0.69-1.95).

Table 1. Cohort Demographic and Clinicopathologic Features, N=142

Patient Attributes	N	HER2-0 n=114	HER2-Low n=28	p-value
Age (median, IQR)	142	50 (42, 61)	50 (40, 55)	0.27
Race (proportion)	138			0.50
White		0.75	0.75	
Black		0.06	0.14	
Asian		0.15	0.11	
Other		0.04	0.00	
Ethnicity (proportion)	138			0.12
Non-Hispanic or Latino		0.90	1.00	
Hispanic or Latino		0.10	0.00	
Hormone Receptor + (proportion)	142	0.17	0.25	0.31
Prior Chemotherapy* (median, IQR)	142	1 (1,2)	1 (0,1)	0.42
ECOG PS=0 (proportion)	138	0.63	0.69	0.58

Legend: ECOG=Eastern Cooperative Oncology Group. *Prior lines of chemotherapy for metastatic disease

Table 2. Multivariable Cox Proportional Hazards Models for PFS and OS Stratified by Hormone Receptor Status, (N=134)

Patient Attributes	PFS*	OS*
	HR, 95% CI	HR, 95% CI
Age (decade)	0.86, 0.72-1.01	0.84, 0.70-1.01
Race		
White	1.00 (referent)	1.00 (referent)
Black	1.57, 0.66-3.73	1.75, 0.84-3.63
Asian	1.33, 0.71-2.51	0.93, 0.47-1.80
Other	2.10, 0.62-7.15	1.69, 0.45-6.38
Ethnicity		
Non-Hispanic or Latino	1.00 (referent)	1.00 (referent)
Hispanic or Latino	1.02, 0.44-2.35	2.10, 0.69-1.95
HER2 Status		
HER2-0	1.00 (referent)	1.00 (referent)
HER2-1+/2+	0.78, 0.45-1.35	1.16, 0.69-1.95
Prior Lines of Chemotherapy		
0	1.00 (referent)	1.00 (referent)
1	1.13, 0.65-1.95	0.82, 0.46-1.46
2	1.00, 0.52-1.93	0.69, 0.35-1.36
3	2.18, 0.45-10.50	0.59, 0.10-3.42
ECOG Performance Status		
0	1.00 (referent)	1.00 (referent)
1	1.57, 1.02-2.43	1.65, 1.07-2.54

Legend: PFS=progression-free survival; OS=overall survival; HR=hazard ratio; HER2=human epidermal group factor receptor 2; ECOG=Eastern Cooperative Oncology Group. *Analyses adjusted for clinical trial membership (coefficients not reported) and stratified by hormone receptor status.

Figure 1. KM Curve of PFS Stratified by HER2-Low vs HER2-0 Expression, N=142

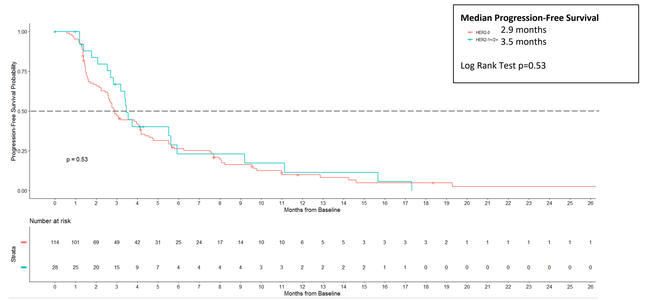
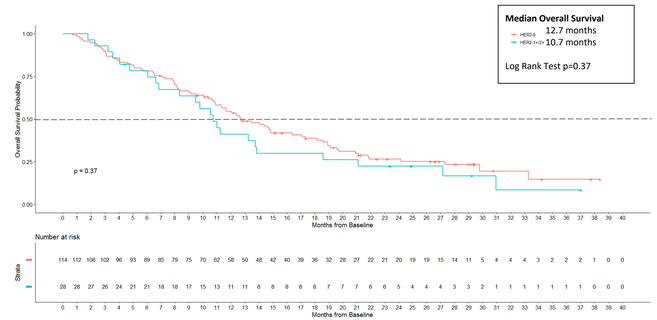


Figure 2. KM Curve of OS Stratified by HER2-Low vs HER2-0 Expression, N=142



Conclusions

Analyses of pooled historic clinical trial data pertaining to women with HER2-negative MBC who were treated with standard single agent chemotherapy in clinical trials revealed no meaningful clinical differences in PFS or OS when assessed by HER2-low vs. HER2-0 status. The results support prior findings from observational research.

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