Prognostic Impact of HER2-Low Expression in Hormone Receptor Positive Early Breast Cancer

Raz Mutai[1], Tamar Barkan [1], Assaf Moore [1,2], Michal Sarfaty [1,2], Tzippy Shochat [3], Rinat Yerushalmi[1,2], Salomon M. Stemmer [1,2], Hadar Goldvaser [4,5]

[1]Davidoff Cancer Center, Rabin Medical Center, Petah Tikva, Israel , [2] Sackler Faculty of Medicine, Tel Aviv University, Israel, [3] Statistical consulting unit, Rabin Medical Center, Petah Tikva, Israel.

[4]The Oncology Institute, Shaare Zedek Medical Center, Jerusalem, Israel . [5] Faculty of Medicine, Hebrew University, Jerusalem, Israel.

Background

- Recent data suggest that human epidermal growth factor receptor 2 (HER2)-low breast cancer may represent a distinct entity.
- We aimed to compare disease characteristics and outcomes between HER2-low and HER2-0 in estrogen receptor (ER) positive, early-stage breast cancer.

Methods

- A single center retrospective study comprising all women with ER positive, HER2 negative early breast cancer, for whom an Oncotype DX test was performed between 2005-2012.
- Women were grouped to HER2-low (immunohistochemistry +1 or +2 and in situ hybridization not amplified) or HER2-0.
- Clinico-pathological features and Oncotype recurrence score (RS) were collected.
- Data on overall-survival (OS), disease-free survival (DFS) and distant disease-free survival (DDFS) were evaluated according to HER2 expression status.

Results

- 608 women were included, of which 304 women had HER2-0 and 304 had HER2-low disease.
- Lobular subtype was significantly more common in HER-0 compared to HER2-low disease (17% vs. 8%, p=0.005).
- The prevalence of other clinic-pathological characteristics were comparable between both groups (Table 1).
- HER2 expression was not associated with long-term prognosis in whole population (Fig 1)
- For high genomic risk (RS>25), HER2-low expression was associated with significantly favorable OS (HR=0.31, 95% CI 0.11-0.78, p=0.01), DFS (HR= 0.40, 95% CI 0.20-0.82, p=0.01) and DDFS (HR=0.26, 95% CI 0.11-0.63, P=0.002) compared to women with HER2-0 (Fig 3).
- For genomic risk (RS≤25) HER2 expression did not affect long-term prognosis (Fig 2)

Corresponding author: Hadar Goldvaser, hadar7g@gmail.com

Table 1- Patients Clinicopathologic Characteristics at Baseline

Characteristic	HER2-0 (n=304)	HER2-Low (n=304)	P-Value
Median age (range)-yr.	61 (34-84)	60 (35-85)	0.36
Ethnicity			0.58
Ashkenazi Jews	151 (52%)	133 (47%)	
Sephardi Jews	119 (40%)	120 (43%)	
Arab	5 (2%)	6 (2%)	
Other	17 (6%)	23 (8%)	
Postmenopausal	234 (80%)	220 (76%)	0.32
T ≤2 cm	226 (74%)	242 (80%)	0.12
T >2 cm	78 (26%)	61 (20%)	
Node negative	257 (85%)	245 (81%)	0.23
Grade 1	43 (18%)	42 (16%)	0.83
Grade 2	154 (64%)	174 (66%)	
Grade 3	43 (18%)	46 (18%)	
Ki67% < 20%	150 (70%)	161 (71%)	0.36
Histologic type[2]			*0.005*
IDC	232 (76%)	259 (86%)	
ILC	51 (17%)	25 (8%)	
Other	21 (7%)	19 (6%)	
ER intensityw	4 (1%)	6 (2%)	0.103
ER intensity iintermediate	76 (25%)	55 (18%)	
ER intensity strong	224 (74%)	243 (80%)	
PR positive	260 (86%)	262 (86%)	0.90
LVI present	20 (7%)	14 (5%)	0.37
Oncotype DX RS ≤ 25	252(83%)	245 (81%)	0.52
25>Oncotype DX RS	52 (17%)	59 (19%)	

Conclusions

- The prognostic impact of HER2-low expression in early-stage luminal disease **varies across the genomic risk.**
- Significant **favorable outcomes** of HER2-low expression compared to HER2-0 in women with **high genomic risk** were observed.

Fig. 1: A-Overall Survival B- Disease Free Survival - All Study population

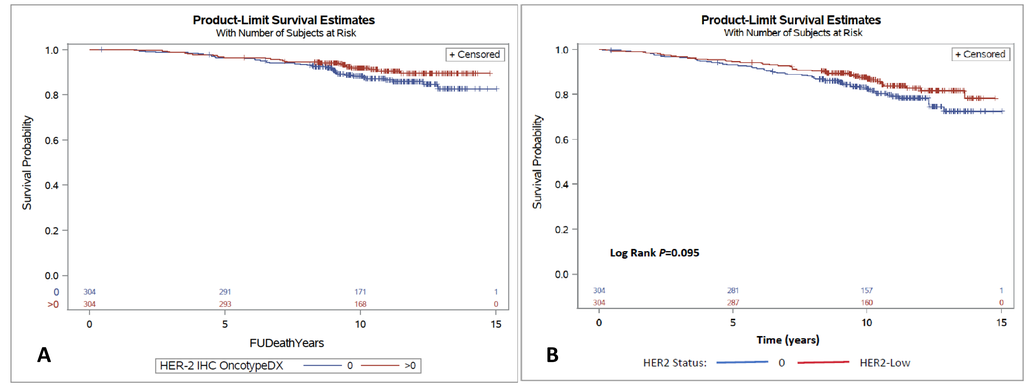

Fig. 2: A-Overall Survival B- Disease Free Survival - Low Genomic Risk- RS 0-25

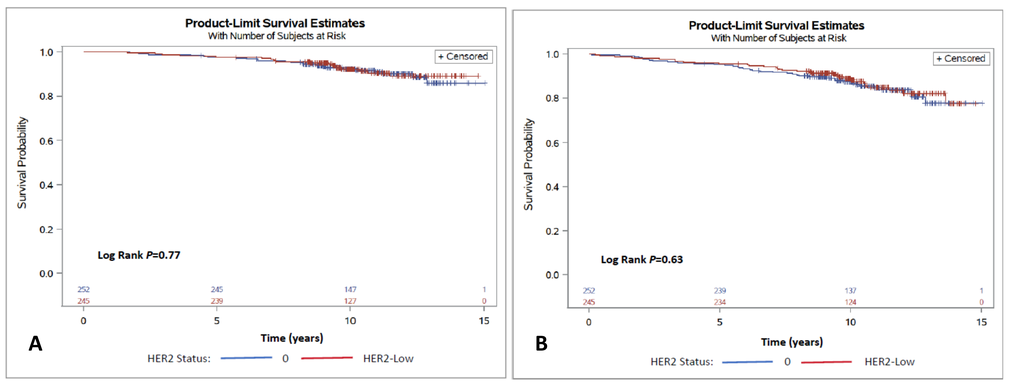

Fig. 3: A-Overall Survival B- Disease Free Survival High Genomic Risk- RS >25