Association of HER2 0 vs HER2 low with median OS in patients with breast cancer and BRCA1, BRCA2, and PALB2 pathogenic mutations

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Background and Objectives

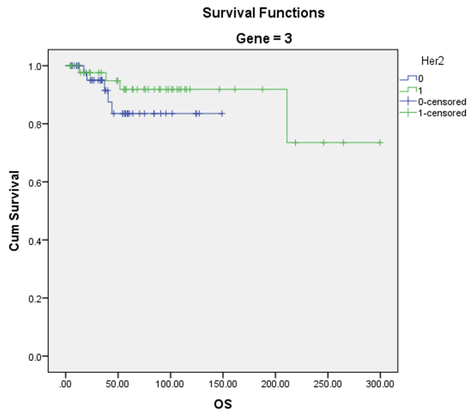
- HER2 0 (HER2 IHC no staining or faint staining in <10% of tumor cells) compared to HER2 low (HER2 IHC 1+ or 2+ and untested or ISH negative) is associated with worse survival in HER2-negative metastatic breast cancer (MBC).
- We explored the impact of HER2 status (0 versus low (1+ or 2+, NOT ultralow)) on survival in patients with HER2-negative breast cancer (HER2-) and germline BRCA1, BRCA2, and PALB2 mutations.

Methods

- We evaluated outcomes among women with HER2- patients with breast cancer treated at MD Anderson Cancer Center from August 1996 to May 2024.
- Patient characteristics were analyzed using descriptive statistics and standard tests of association.
- Cox proportional hazard models evaluated factors associated with overall survival (OS).

Results

Figure 3: Association of HER2 0 v HER2 low with OS in patients with gPALB2



This is the largest dataset evaluating the impact of HER2 expression on survival in patients with HER- breast cancer and germline BRCA1, BRCA2, PALB2 mutations

HER2 0 was associated with worse OS compared to HER2 low in patients with PALB2 mutations.

HER2 0 was associated with better OS compared to HER2 low in patients with BRCA1 and BRCA2, though the association for BRCA2 was not statistically significant.

Future studies should address the impact of targeted therapy and tumor biology in these populations.

Results

Figure 1: Association of HER2 0 v HER2 low with OS in patients with germline BRCA1

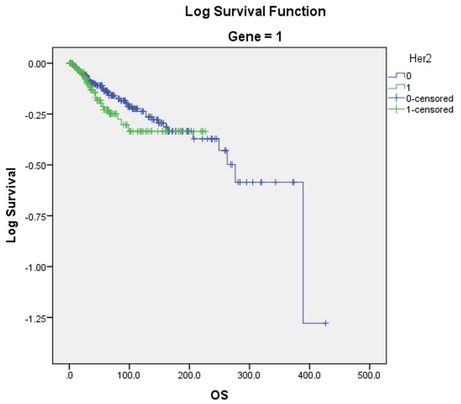
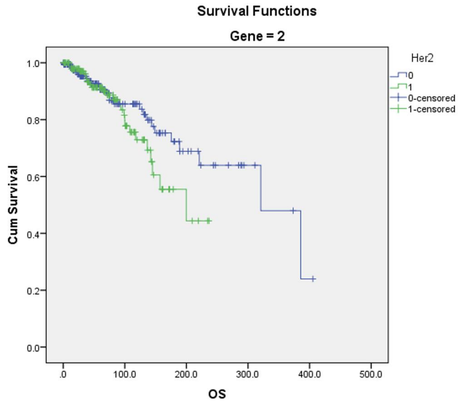


Figure 2: Association of HER2 0 v HER2 low with OS in patients with germline BRCA2



Results

BRCA1 and BRCA2.

- For 752 patients with BRCA1 and 2, median age was 44.5 years (st.dev 11.20). 224 (29.8%) had Stage I disease, 332 (44.1%) Stage II, 144 (19.1%) Stage III, and 42 (5.6%) de novo Stage IV.
- ER was negative in 374 (49.7%), positive in 377 (50.1%). PR was negative in 460 (61.2%) and positive in 289 (38.4%).
- HER2 was 0 in 443 (58.9%), 1+ in 208, 2+ in 101 (13.4%).

BRCA1.

- Among 424 patients with BRCA1, 266 (62.7%) were HER2 0 and 158 HER2 low.
- Among 266 who were HER2 0, 49 died, with OS 81.6%. Among those who were HER2 low, 26 died, with OS 83.5%.
- Median OS was 289.34 months (95% CI 229.66, 548.80) for patients with HER2 0 compared to 175.54 months (95% CI 158.05,193.03) for HER2 low ($p<0.05$). **(Figure 1)**

BRCA2.

- Among 327 patients with BRCA2, 177 (54.1%) were HER2 0 and 150 HER2 low.
- Among 177 who were HER2 0, 26 died with OS 85.3%. Among those with HER2 low, 25 have died with OS 83.3%.
- Median OS was 384.46 months (95% CI 199.54, 441.99) for patients with Her2 0, compared to 172.927 for HER2 low (95% CI 107.98, 291.4) ($p < 0.05$). **(Figure 2)**

PALB2.

- Among 93 patients with PALB2, median age at diagnosis was 49.5 years old (st.dev 10.5). 20 (21.5%) had Stage I, 21 (22.6% Stage II), 18 (19.4%) Stage III, 4 (4.3%) de novo Stage IV disease.
- ER was weakly positive in 4 (4.3%), negative in 28 (30.1%), positive in 61 (65.6%).
- PR was negative in 41 (45.2%), positive in 51 (54.8%).
- 48 (51.6%) were HER2 0, while 45 (48.3) were HER2 low (1+ or 2+).
- Of the 48 patients who were HER2 0, 5 died at last follow-up, with OS 89.6%. Of the 45 patients with HER2 low, 4 died with OS 91.1%.
- Median OS was 130.06 months (95% CI 114.65, 145.465 months) for patients with HER2 0 compared to 261.96 months for HER2 low (95% CI 219.21, 297.89) ($p < 0.05$). **(Figure 3)**

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