55P - A Retrospective Study to Investigate the Prevalence and Treatment Outcomes of HER2-low Unresectable/Metastatic Breast Cancer in Taiwan — the RetroBC-HER2L-TW Study

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BACKGROUNDS

- The binary classification of human epidermal growth factor receptor 2 (HER2) has been reassessed following recent clinical trials. The DESTINY-Breast04 trial (NCT03734029) shows promising efficacy in patients with HER2-low [immunohistochemistry (IHC) 1+ or 2+/in situ hybridization- (ISH-)] unresectable/metastatic breast cancer (mBC) using a novel anti-HER2 antibody-drug conjugate—trastuzumab deruxtecan (T-DXd). The evidence highlights the need for HER2-low identification.
- Despite advances in clinical applications, little is known for HER2-low mBC in Taiwan, including the prevalence, current standard of care, and treatment outcomes. The data gap strengthens the needs to better characterize the local patient profile of HER2-low population in Taiwan.
- Here, we describe the prevalence of HER2-low among HER2-negative unresectable/mBC population in Taiwan based on rescored HER2 IHC results. The treatment patterns and clinical outcomes are also presented by retrospectively analyzing the data from medical charts.

OBJECTIVES

Primary Objective
- To understand the prevalence of HER2-low among HER2-negative mBC patients based on the rescored HER2 IHC results

Secondary Objectives
- To describe the real-world treatment patterns in HER2-low mBC patients
- To assess the treatment outcome (time to next treatment [TTNT], overall survival [OS] since the initiation of first-line systemic therapy in HER2-low mBC patients
- To describe the clinical-pathological characteristics of HER2-low mBC patients

Exploratory Objective
- To assess the concordance between historical and rescored HER2 IHC scores

METHODS

Study Population
- Patients diagnosed with HER2-negative (IHC 0, 1+, 2+/ISH-) unresectable/mBC in Jan 2017 to Mar 2020; any hormone status
- Progressed on any systemic anti-cancer therapy (e.g., endocrine therapy, chemotherapy, CDK4/6 inhibitor, immunotherapy, or targeted therapies other than anti-HER2) in the metastatic setting
- Patients who ever had historical HER2 status of IHC 2+/ISH+ or 3+, or HER2 amplified were excluded

Study Design
- Multicenter, retrospective study
- The study consisted of 2 steps as follows:

Step 1: Rescore the archived HER2 IHC slides of HER2-negative mBC patients by a pathologist blinded to historical HER2 scores after a pathologist investigator meeting focusing on 2018 ASCO/CAP guideline. The archived HER2 IHC slides were stained using locally validated HER2 IHC assays.

Step 2: Capture the medical data of patients rescored as HER2-low (IHC 1+, 2+/ISH-) by retrospectively reviewing medical records.

Data included demographics, histopathological features, clinical presentation, treatment and outcomes following advanced BC diagnosis.

RESULTS

Patient Characteristics

- A total of 343 HER2-negative patients were screened; 321 met the eligibility criteria and entered Step 1 — rescoring archived HER2 IHC slides.
- After rescoring, 17 patients were excluded due to changes in IHC scores (IHC 2+/without ISH results or IHC 3+), resulting in a final cohort of 304 HER2-negative patients. Among these, 186 were HER2-low (IHC 1+, IHC 2+/ISH-) and included in Step 2 — extraction of medical data (**Figure 1**).

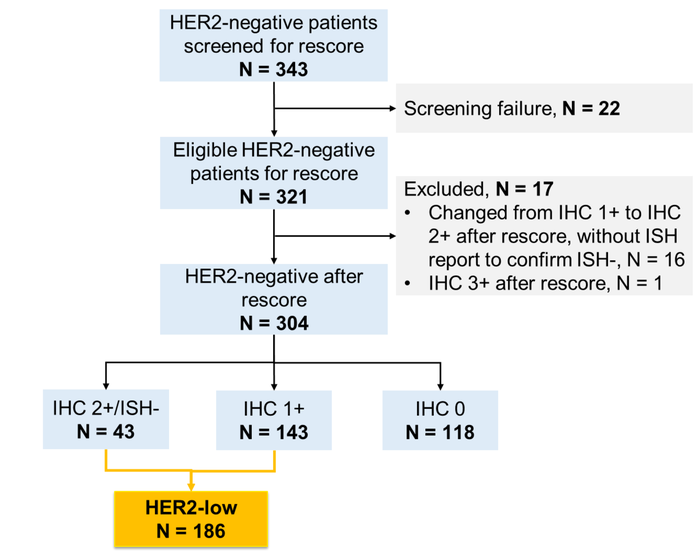

Figure 1. Enrollment status

- Of the 186 HER2-low mBC patients, the majority (78.0%) were HR-positive.
- The HER2-low tumors were predominantly at clinical stages III–IV (59.1%) and invasive ductal carcinomas (60.8%) at initial diagnosis. Common metastatic sites included bone (48.4%) and liver (45.2%), with 18.3% of patients having metastases in three or more locations (**Table 1**).
- Around half of the archived IHC slides were taken from primary tumors (51.6%) and 64.0% were stained using Ventana 4B5 assay.

Table 1. Clinical-pathological characteristics of mBC patients rescored as HER2-low

Variables	HR+/HER2-low N = 145	HR-/HER2-low N = 41	HER2-low N = 186
Age, mean ± SD	55.5 ± 12.01	57.3 ± 13.63	**55.9 ± 12.36**
Stage at initial diagnosis, n (%)			
I	10 (6.9)	3 (7.3)	**13 (7.0)**
II	22 (15.2)	10 (24.4)	**32 (17.2)**
III	16 (11.0)	9 (22.0)	**25 (13.4)**
IV (de novo stage IV)	72 (49.7)	13 (31.7)	**85 (45.7)**
Unknown/not available	25 (17.2)	6 (14.6)	**31 (16.7)**
Histological types, n (%)			
Invasive ductal carcinoma	88 (60.7)	25 (61.0)	**113 (60.8)**
Invasive lobular carcinoma	5 (3.4)	2 (4.9)	**7 (3.8)**
Mucinous carcinoma	1 (0.7)	0 (0.0)	**1 (0.5)**
Metaplastic carcinoma	2 (1.4)	0 (0.0)	**2 (1.1)**
Others	33 (22.8)	7 (17.1)	**40 (21.5)**
Unknown/not available	16 (11.0)	7 (17.1)	**23 (12.4)**
Metastasis, n (%)			
Bone	75 (51.7)	15 (36.6)	**90 (48.4)**
Lung	52 (35.9)	10 (24.4)	**62 (33.3)**
Brain	15 (10.3)	7 (17.1)	**22 (11.8)**
Liver	72 (49.7)	12 (29.3)	**84 (45.2)**
Other	28 (19.3)	8 (19.5)	**36 (19.4)**
Unresectable locally advanced	6 (4.1)	4 (9.8)	**10 (5.4)**
Number of metastatic sites, n (%)			
0	3 (2.1)	7 (17.1)	**10 (5.4)**
1	72 (49.7)	19 (46.3)	**91 (48.9)**
2	41 (28.3)	10 (24.4)	**51 (27.4)**
≥ 3	29 (20.0)	5 (12.2)	**34 (18.3)**
HR-positive, n (%)	145 (100.0)	0 (0.0)	**145 (78.0)**
Biopsy sample collection site (archived HER2 IHC slide), n (%)			
Primary tumor	76 (52.4)	20 (48.8)	**96 (51.6)**
Metastatic sites	69 (47.6)	21 (51.2)	**90 (48.4)**
HER2 IHC assay (archived HER2 IHC slide), n (%)			
Ventana 4B5 assay	91 (62.8)	28 (68.3)	**119 (64.0)**
Dako A0485	50 (34.5)	12 (29.3)	**62 (33.3)**
HercepTest	4 (2.8)	1 (2.4)	**5 (2.7)**

HER2-low Prevalence

- Among 304 HER2-negative patients, the prevalence of HER2-low was 61.2% (95% CI: 55.3 to 66.5%) based on the rescored results.
- Of the rescored results, HER2-low prevalence was slightly higher in samples obtained from metastatic sites than those from primary tumors.
- HER2-low prevalence was numerically higher with non-Ventana 4B5 assays (predominantly Dako A0485) than in the Ventana 4B5 assay (**Figure 2**).
- The prevalence of HER2-low varied across study centers, ranging from 32.5% to 79.2%.

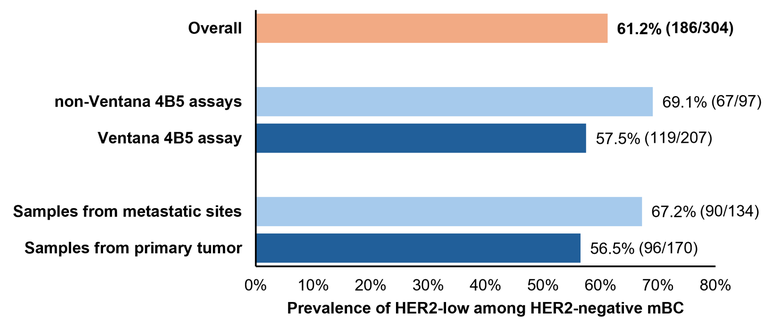

Figure 2. HER2-low prevalence in HER2-negative mBC based on rescored HER2 IHC

Agreement - Historical Scores & Rescores

- The overall percentage agreement (OPA) in HER2 IHC scores between historical and rescored IHC was 90.1% (k [95% CI]: 0.770 [0.708, 0.831]).
- The OPA was numerically greater with non-Ventana 4B5 assays (93.9%; k [95% CI]: 0.886 [0.798, 0.974]) compared to the Ventana 4B5 assay (81.9%; k [95% CI]: 0.720 [0.641, 0.798]).
- When HER2 scores were divided into 2 categories (positive [IHC 1+/IHC 2+] versus negative), the positive agreement was 0.94 and the negative agreement was 0.88.
- The positive and negative agreement was similar between non-Ventana 4B5 assays and Ventana 4B5 assay (**Figure 3**).

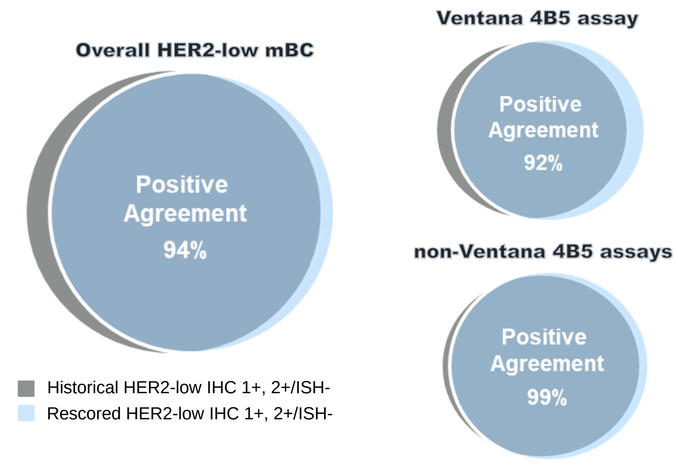

Figure 3. Positive agreement between historical and rescored HER2 IHC

HER2-low mBC Real-world Treatments

- For HR+/HER2-low patients, endocrine therapy was the most frequently used in the first two lines of treatment, while chemotherapies were the most common choice after the second-line treatment.
- For HR-/HER2-low patients, the treatment options were limited, with chemotherapies being the most common treatment choice. Around 50% of them used combination chemotherapy (**Figure 4**).

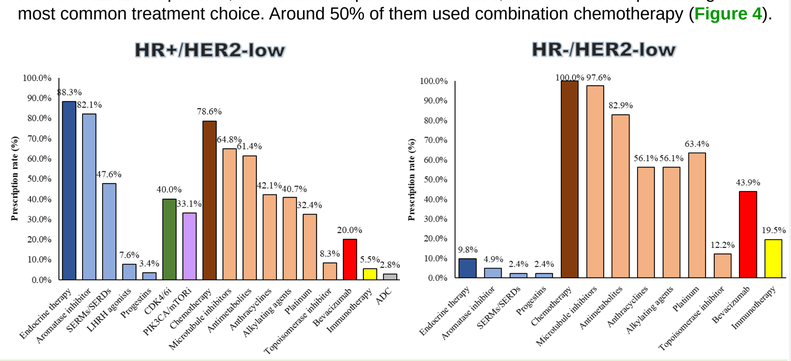

Figure 4. Overall treatment patterns of mBC patients rescored as HER2-low

Time to Next Treatment (TTNT)

- In HER2-low mBC patients, the median first-line, second-line, and third-line TTNT were 6.8, 4.4, and 4.2 months, respectively.
- HR+/HER2-low mBC patients tended to have longer TTNT than HR-/HER2-low mBC patients (**Figure 5**).
- No notable differences in TTNT were observed in patients with HER2 IHC 2+/ISH- vs. HER2 IHC 1+ tumors within both HR-positive and HR-negative cohorts.

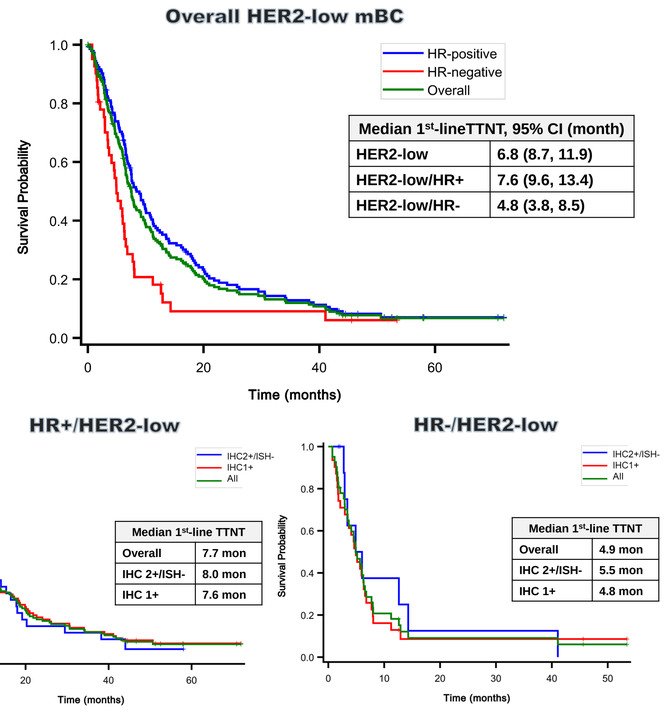

Figure 5. First-line TTNT of mBC patients rescored as HER2-low

Overall Survival (OS)

- The median OS (mOS) for HER2-low mBC patients was 33.1 months (95% CI: 27.2 to 40.0 months), and was longer in HR+/HER2-low patients than HR-/HER2-low patients.
- In the HR+/HER2-low cohort, the mOS was numerically longer in IHC 2+/ISH- (N = 33) versus IHC 1+ patients (N = 112).
- In the HR-/HER2-low cohort, no difference in OS was observed between IHC 2+/ISH- (N = 10) and IHC 1+ patients (N = 31) (**Figure 6**).

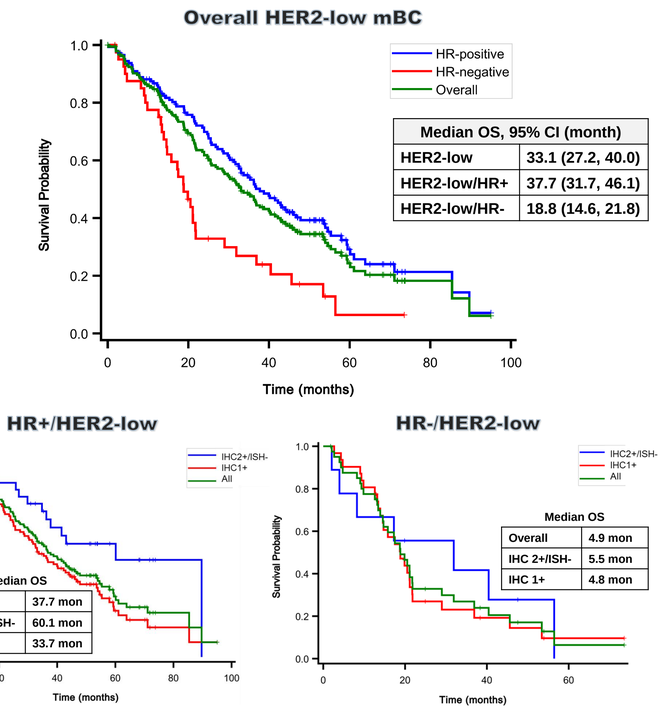

Figure 6. OS of mBC patients rescored as HER2-low

CONCLUSIONS

- This study is the first real-world investigation into the prevalence and treatment outcomes of rescored HER2-low mBC patients in Taiwan.
- Based on rescored IHC results, study results suggest that up to two-thirds of HER2-negative mBC patients in Taiwan were HER2-low patients who may benefit from T-DXd, and reinforce the importance of accurately identifying HER2-low patients.
- A re-evaluation of HER2 status may benefit HER2-negative patients to identify HER2 IHC 1+ and HER2 IHC 2+ patients who are therapeutic targets for T-DXd, especially for HR- patients who have lower TTNT and OS.

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