Poster 59P

A Multicenter, Retrospective Study to Determine The Prevalence of HER2-Low & Associated Outcomes in Patients Previously Identified with HER2 Negative Locally Advanced (LA) or Metastatic Breast Cancer (mBC) Who Progressed on Systemic Anticancer Therapy: Interim Analysis of iRetroBC-HER2L Study

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Background

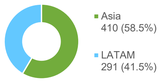
- Breast cancer (BC) is the most diagnosed malignancy among women worldwide, with approximately 2.3 million new cases annually[1]. Human epidermal growth factor receptor 2 (HER2) status is a key biological and predictive marker in BC. Clinically, HER2-positive disease accounts for only 15–20% of cases, whereas HER2-negative BC, defined as immunohistochemistry (IHC) 0, IHC 1+, or IHC 2+ with negative in situ hybridization (ISH), represents approximately 80% of all BC cases[2].
- Tumors classified as HER2-low (IHC 1+ or IHC 2+/ISH−) account for an estimated 45–55% of all BC cases[3]. With the emergence of novel therapies targeting HER2-low disease, accurate identification of this subgroup has become clinically critical. Therefore, understanding the reproducibility of HER2 assessment through rescoring of archived IHC-stained slides or re-staining of stored tissue samples is essential[4].
- Objective: This study aimed to evaluate the prevalence of HER2-low, the concordance between historical and rescored HER2 IHC results, treatment patterns, and clinical outcomes in patients with previously identified HER2-negative locally advanced or metastatic breast cancer (LA/mBC) who progressed on systemic anticancer therapy.

Methods

- This multicenter, non-interventional, retrospective study involved the rescoring of archived HER2 IHC–stained formalin-fixed paraffin-embedded (FFPE) tissue slides from patients diagnosed with HER2-negative LA/ mBC, irrespective of hormone (HR) status.
- Patients were eligible if they had a confirmed diagnosis of HER2-negative LA /mBC from January 2017 to December 2022, had experienced disease progression while receiving any systemic anticancer therapy for advanced disease, and had at least 12 months of follow-up data available in the medical records at the participating site, unless death occurred within the first 12 months after diagnosis.
- The study included patients from eight Asian countries (Hong Kong, India, Indonesia, Malaysia, Philippines, Thailand, Singapore, and Vietnam) and five Latin American (LATAM) countries (Argentina, Brazil, Dominican Republic, Mexico, and Panamá).
- The prevalence of HER2-categories, treatment patterns, and clinical outcomes in patients previously classified as having HER2-negative LA /mBC was described. In addition, the concordance between historical HER2 IHC scores and rescoring archived IHC-stained slides for HER2 was evaluated, reported as percentage agreement, and assessed using Cohen's kappa statistic. The findings presented reflect the interim analysis of the iRetroBC-HER2L Study.

Results

Study Population: 701 patients



HER2 Status Distribution

- HER2-low (IHC 1+ or IHC 2+/ISH−) prevalence: 41.4% (290/701)
- HER2 IHC 0: 49.8% (349/701), comprising:
  - HER2 IHC 0 with membrane staining: 25.2% (88/349)
  - HER2 IHC 0; absent membrane staining: 74.8% (261/349)

HER2-Low by Hormone Receptor (HR) Status

- HR-positive: 41.3% (191/462)
- HR-negative: 35.2% (56/159)

Concordance of HER2 Assessment

- Overall Concordance:
  - Concordance: 81.2%
  - Cohen's κ = 0.62 (95% CI: 0.56–0.68)

Clinical Outcomes

- Median Overall Survival (OS):

HR+/HER2-low	HR−/HER2-low
47.0 months (95% CI: 40.1–64.8)	36.7 months (95% CI: 28.0–NE)

- Median Progression-Free Survival (PFS):

	1st Line Of Treatment (LOT)	2nd LOT	3rd LOT
HR+/HER2-low	15.8 months (95% CI: 12.4–17.6)	7.4 months (95% CI: 5.6–9.2)	5.6 months (95% CI: 4.3–7.4)
HR−/HER2-low	7.4 months (95% CI: 5.5–11.3)	4.4 months (95% CI: 3.4–5.4)	4.9 months (95% CI: 2.3–5.6)

Table 1: Proportion of HER2 expression in HER2-negative LA/mBC, based on rescoring

HER2 rescores	Asia	LATAM	Overall
HER2-low (IHC 1+ or IHC 2+/ISH−), n/ N(%)	175/410 (42.7%)	115/ 291 (39.5%)	290/ 701 (41.4%)
HER2 IHC 0, n/ N (%)	186/410 (45.4%)	163/291 (56.0%)	349/ 701 (49.8%)
Including			
HER2 IHC 0 with membrane staining, n/ N(%)	55/186 (29.6%)	33/163 (20.2%)	88/ 349 (25.2%)
HER2 IHC 0; absent membrane staining, n/ N(%)	131/186 (70.4%)	130/163 (79.8%)	261/ 349 (74.8%)

Table 2: Clinical outcomes across Asia and LATAM and in the overall population according to the HR status

	Asia	LATAM	Overall
HR+			
Overall Survival (months) median (95% CI), N	NE (85.4, NE), 278	36.3 (29.9, 39.3), 150	55.6 (46.0, 66.1), 428
Progression Free Survival (months) median (95% CI), N			
1st LOT	16.7 (12.4, 20.1), 224	12.4 (9.4, 14.5), 128	14.3 (11.9, 16.8), 352
2nd LOT	8.5 (6.7, 10.0), 220	4.4 (3.9, 5.5), 132	6.5 (5.6, 7.7), 352
3rd LOT	7.4 (5.2, 10.2), 164	4.3 (3.5, 5.5), 99	5.6 (4.6, 6.4), 264
HR-			
Overall Survival (months) median (95% CI), N	47.6 (34.8, NE), 77	23.2 (18.6, 28.6), 79	30.0 (25.9, 38.0), 156
Progression Free Survival (months) median (95% CI), N			
1st LOT	9.6 (7.4, 12.6), 70	6.8 (5.7, 8.2), 78	7.7 (6.8, 9.4), 148
2nd LOT	5.4 (4.4, 6.1), 69	3.0 (2.3, 4.2), 75	4.4 (3.6, 5.0), 144
3rd LOT	5.4 (4.6, 8.3), 50	2.3 (1.6, 3.1), 47	3.3 (2.3, 4.9), 90

Treatment Patterns of HER2-Low Patients*

1st LOT

HR-positive (n=187/191)	HR-negative (n=56/56)
• Primarily endocrine therapy (ET): 64.2% (n=120); most commonly aromatase inhibitor: 46.5% (n=87) • Followed by chemotherapy: 48.7% (n=91); most commonly paclitaxel / nab-paclitaxel: 24.1% (n=45) • Combination therapy: ET+ chemotherapy: 6.4% (n=12) • Mean (SD) treatment duration: 13.3 (12.8) months	• Mainly chemotherapy: 98.2% (n=55), most commonly paclitaxel / nab-paclitaxel: 60.7% (n=34) • Mean (SD) treatment duration: 5.6 (4.1) months

2nd LOT

HR-positive (n=181/191)	HR-negative (n=55/56)
• Primarily ET: 63.0% (n=114), mainly aromatase inhibitor: 32.0% (n=58) • Followed by chemotherapy: 37.6% (n=68), mainly paclitaxel / nab-paclitaxel: 11.0% (n= 20) • Combination therapy: ET+ chemotherapy: 3.9% (n=7) • Mean (SD) treatment duration: 7.7 (8.3) months	• Main treatments were chemotherapy: 80.0% (n=44), mainly capecitabine: 34.5% (n=19) • Mean (SD) treatment duration: 4.3 (5.8) months

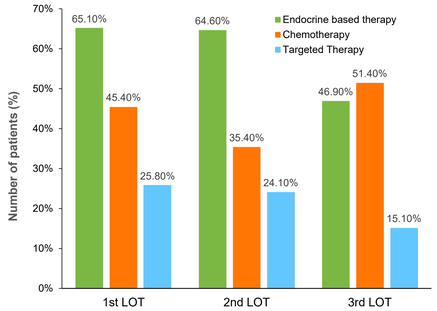
3rd LOT

HR-positive (n=125/191)	HR-negative (n=44/56)
• Chemotherapy: 49.6% (n=62), mainly paclitaxel / nab-paclitaxel: 13.6% (n=17) • Followed by ET: 47.2% (n=59), mainly aromatase inhibitor: 20.0% (n=25) • Combination therapy: ET+ chemotherapy: 2.4% (n=3) • Mean (SD) treatment duration: 6.1 (6.8) months	• Mainly chemotherapy: 90.9% (n=40), mainly capecitabine: 36.4% (n=16) • Mean (SD) treatment duration: 3.9 (3.8) months

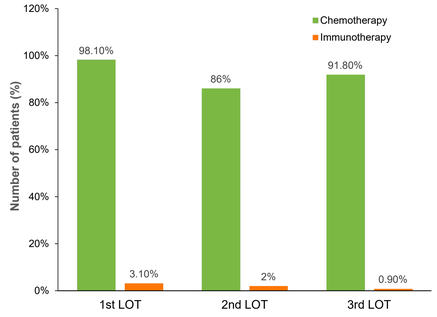
*Patients may receive more than one type of therapy as part of their treatment plan

Figure 1: Treatment Patterns among the overall population according to HR status

A) Treatment Patterns Among the Overall Population with HR+ BC



B) Treatment Patterns Among the Overall Population with HR- BC



Conclusions

- HER2-low expression was identified in approximately 41% of HER2-negative LA/mBC patients, with an additional 25.2% showing HER2 membrane staining.
- Substantial concordance between historical and rescored HER2 assessment supports the use of archived IHC material for HER2-low classification.
- Real-world treatment outcomes were worse than those reported in clinical trials, emphasizing the importance of optimized treatment strategies.

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Conflict of interest

The presenter declares no conflicts of interest

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