Clinical characterization and outcome of a HER2-low metastatic breast cancer (mBC) cohort receiving first line treatment (1L) with ET +/- CDK 4/6 inhibitor (CDKi)

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Background

- About 50% of BC presented with a HER2-low expression, defined as HER2 immunohistochemistry score of 1+ or 2+ with negative in situ hybridization assay.
- No anti-HER2 agents are currently approved in Europe for this subgroup, nevertheless new antibody-drug conjugate showed meaningful activity.[1]
- **This study aimed to investigate the clinical relevance of HER2 low status as a independent prognostic factor in mBC and its potential utility in predictive 1L outcome.**

Methodology

A retrospective analysis was conducted on a consecutive series of 322 luminal mBC patients (pts) without Her2 iperexpression, receiving 1L endocrine therapy (ET) or ET in combination with a CDKi (ET+CDKi) at the Oncology Department of Udine and Aviano (Italy) from 2008 to 2019. Association analysis were investigated through Fisher-exact test. The prognostic impact of HER2-low was investigated through Cox regression, and differences in progression free survival (PFS) and overall survival (OS) were tested by log-rank.

	N°of pts	% of pts
Age		
< 45	22	5.7
45 -60	118	30.5
> 60	247	63.8
Histotype		
ductal	231	75.0
lobular	73	23.7
other	4	1.3
PS		
0-1	223	77.7
≥2	64	22.3
Stage IV de novo		
Yes	110	34.4
No	210	65.2
Ormono-sensitive		
Yes	94	39
No	147	61
Menopausal status		
Pre	38	11.9
Post	282	22.1
Sites of metastasis		
Bone only	134	41.7
Visceral and nodal	187	58.3
Nr of sites of metastasis		
< 3	248	77
≥3	74	23
Tipe of 1L treatment		
ET	238	73.9
ET + CDK4/6 i	84	26.1

Table 1. Patients' clinical and pathologic characteristics

Results

In the total series, 247 pts (63.8%) were aged >65, 282 (88.1%) were post-menopausal, 110 pts (34.3%) had de novo metastatic disease, 121 pts (37.7%) had visceral disease, 74 pts (23%) had ≥3 sites of involvement. As 1L, 238 pts (73,9%) received ET while 84 pts (26,1%) were treated with ET+CDKi (Table1)

As expected, in the total series HER2-negative (i.e HER2 score 0) BC were 212 (65,8%) while HER2-low were 110 (34,2%), no association with visceral disease, number of sites of disease, and menopausal status was detected (p>0.05). By univariate analysis, **HER2-low was not associated with prognosis neither in terms of PFS** (HR 0.98, P=0.91, 95% CI 0.76-1.26 Figure1) **nor OS** (HR 1.01, P=0.932, 95% CI 0.76-1.34 Figure 2).

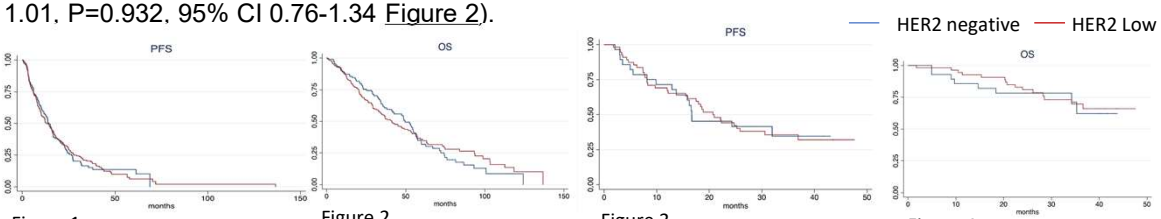

Figure 1 Figure 2 Figure 3 Figure 4

Interestingly, **in the subgroup of pts treated with ET+CDKi, HER2 low had no statistically significant impact on PFS** (HR 0.98, P=0.96, 95% CI 0.55-1.76 Figure 3) **or OS** (HR 0.89, P=0.79, 95% CI 0.38-2.10 Figure 4), similarly in the population treated with ET (PFS: HR 0.98, P=0.94, 95% CI 0.74-1.31 and OS: HR 1.04, P=0.79, 95% CI 0.76-1.41).

Conclusion

In the present exploratory study, patients with HER2-low and HER2 negative luminal mBC showed a comparable outcome when treated with ET or ET+CDK4/6i. Further prospective studies are needed to explore this novel subgroup.

[1] Modi S, Park H, Murthy RK, et al. Antitumor activity and safety of trastuzumab deruxtecan in patients with HER2-low–expressing advanced breast cancer: results from a phase Ib study. *J Clin Oncol*. 2020;38(17):1887-1896. doi:10.1200/JCO.19.02318

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