HER2-low metastatic breast cancer: management and prognosis of a new breast cancer entity in a real world setting

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Background

HER2-low (i.e. HER2 IHC 1+ or 2+ in the absence of HER2 gene amplification) breast cancer (BC) is a new entity accounting for 45 to 55% of breast cancer. Patients are managed as HER2- patients however, some dedicated treatments are emerging including antibody drug conjugated

Few data are available on this subtype regarding prognosis and response to treatment in the metastatic setting. We aimed at evaluating the prognosis of patients with HER2 low MBC in a real world setting.

ESME database and Flowchart

ESME-MBC is a unique French national multicenter cohort of metastatic breast cancer (MBC) patients. It retrospectively collects real-world data using clinical trial-like methodology (NCT03275311). We included patients treated between the 1 January 2008 to 31 December 2016.

22463 patients included in ESME-MBC database

↓

19271 overall population with HER2 status

HER2 neg (n=15698) | HER2 pos (n=3573)

↓

15698 patients with "HER2 negative" MBC

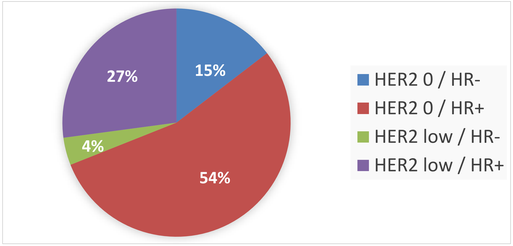
HER2 0 (n=10783)	**HER2 low (n=4915)**
2451 HER2 0 / HR-	704 HER2 low / HR-
8332 HER2 0 / HR+	4211 HER2 low / HR+

↓

15054 analysis population

HER2 0 (n=10383)	**HER2 low (n=4671)**
2195 HER2 0 / HR-	588 HER2 low / HR-
8188 HER2 0 / HR+	4083 HER2 low / HR+

Distribution of HER2-low status in the HER2 - population

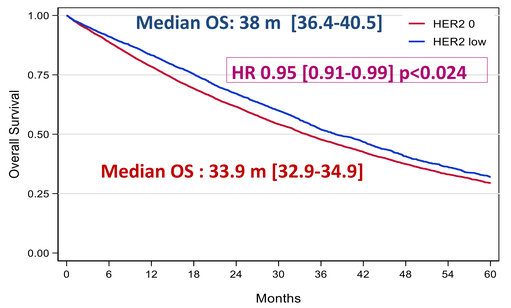


Patients and MBC characteristics

At MBC diagnosis	Total	HER2 0	HER2 low	
				p-value
Age (n=15054)	(N = 15054)	(N = 10383)	(N = 4671)	**<0.0001**
Median	60.0	60.0	61.0	
Range	(22.0;103.0)	(22.0;96.0)	(22.0;103.0)	
Menopausal (n=14913)				**<0.0001**
No	4395 (29.5%)	3148 (30.6%)	1247 (27.0%)	
Yes	10518 (70.5%)	7148 (69.4%)	3370 (73.0%)	
Missing	141	87	54	
De novo mBC (n=15044)				**<0.0001**
No	10413 (69.2%)	7485 (72.2%)	2928 (62.7%)	
Yes	4631 (30.8%)	2889 (27.8%)	1742 (37.3%)	
Missing	10	9	1	
HR Status (n=15054)				**NS**
Negative	2783 (18.5%)	2195 (21.1%)	588 (12.6%)	
Positive	12271 (81.5%)	8188 (78.9%)	4083 (87.4%)	
Missing	152	97	55	
Histological grade (n=12876)				**NS**
Grade I/II	8598 (66.8%)	5788 (65.8%)	2810 (68.8%)	
Grade III	4278 (33.2%)	3003 (34.2%)	1275 (31.2%)	
Missing	2178	1592	586	
Metastatic sites (n=15054)				
CNS	857 (5.7%)	628 (6.0%)	229 (4.9%)	**0.0050**
Lung	3649 (24.2%)	2479 (23.9%)	1170 (25.0%)	**NS**
Bone metastases	9134 (60.7%)	6172 (59.4%)	2962 (63.4%)	**<0.0001**
Bone metastases only	4189 (27.8%)	2903 (28.0%)	1286 (27.5%)	**NS**
Liver metastases	3975 (26.4%)	2697 (26.0%)	1278 (27.4%)	**NS**

OS of HER2 low MBC (Kaplan Meier, adjusted)

Median follow-up: 49.5 months [48.6; 50.4]

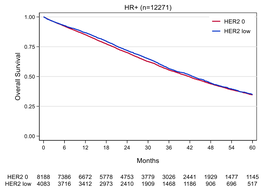


HER2 0	10383	9003	7778	6505	5235	4099	3254	2610	2060	1572	1215
HER2 low	4671	4170	3741	3206	2562	2006	1539	1237	942	726	536

The survival medians were estimated by the Kaplan-Meier method and adjusted Hazard Ratios by multivariable Cox model including age, type and number of metastases, de novo disease, period of care and HR status.

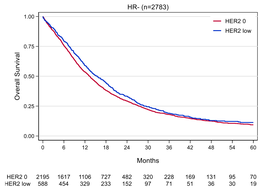
OS of HER2 low MBC according to HR status (Kaplan Meier, adjusted)

HR+



HER2 0	8188	7386	6672	5778	4753	3779	3026	2441	1929	1477	1145
HER2 low	4083	3716	3412	2973	2410	1909	1468	1186	906	696	517

HR-



HER2 0	2195	1617	1106	727	482	320	228	169	131	95	70
HER2 low	588	454	329	233	152	97	71	51	36	30	19

	Subtype	N	OS (median)	Adjusted HR	p-value
HR+	HER2 low	4,083	43.0 [41.5-44.4]	1	
	HER2 0	8,188	41.8 [40.5-42.8]	0.97 [0.92-1.02]	**0.173**
Triple negative	HER2 low	588	15.6 [13.5-17.4]	1	
	HER2 0	2,195	13.3 [12.6-14.0]	0.90 [0.81-1.00]	**0.093**

The survival medians were estimated by the Kaplan-Meier method and adjusted Hazard Ratios by multivariable Cox model including age, type and number of metastases, de novo disease, period of care and HR status.

Conclusion

This study is one of the largest cohorts of HER2 low MBC patients to date in a real world setting.

HER2 low patients may have a distinct outcome from HER2 0 pts, particularly in the triple negative sub group of metastatic breast cancer.

Dedicated clinical trials and treatments are under evaluation for this new entity and may change the treatment landscape.

Centers

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Disclosure

JS Frenel has disclosure with Pfizer, Lilly, Astra Zeneca, Novartis, GSK, Roche, Daiichi Sankyo, Clovis Oncology