HER2-LOW BREAST CANCER: EVOLUTION FROM PRIMARY TUMOR TO RESIDUAL DISEASE AFTER NEOADJUVANT TREATMENT

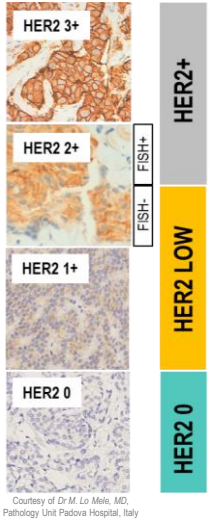
Federica Miglietta[1,2](federica.miglietta@iov.veneto.it), **Gaia Griguolo[1,2]**, **Michele Bottosso[1,2]**, **Tommaso Giarratano[2]**, **Marcello Lo Mele[3]**, **Matteo Fassan[4]**, **Matilde Cacciatore[5]**, **Elisa Genovesi[1,2]**, **Debora De Bartolo[4]**, **Grazia Vernaci[1,2]**, **Ottavia Amato[1,2]**, **Francesca Porra[1,2]**, **PierFranco Conte[1,2]**, **Valentina Guarneri[1,2]**, **Maria Vittoria Dieci[1,2]**.

1 Department of Surgery, Oncology and Gastroenterology (DISCOG), University of Padova, Italy; 2 Medical Oncology 2, Istituto Oncologico Veneto IOV-IRCCS, Padova, Italy; 3 Surgical Pathology Unit, University Hospital of Padua, Italy; 4 Department of Medicine, Surgical Pathology & Cytopathology Unit, University of Padua, Italy; 5 Department of Pathology and Molecular Genetics, Treviso General Hospital, Italy

BACKGROUND & AIM

- Approximately a half of breast tumors traditionally classified as HER2-negative exhibit HER2-low expression (IHC 1+ or 2+ and ISH negative).
- We recently described a high instability of HER2-low expression from primary breast cancer (BC) to relapse. *(Miglietta et al, ESMO Breast Cancer 2021).*
- **Aim: to track the evolution of HER2-low expression from primary BC to residual disease (RD) after neoadjuvant treatment.**

METHODS



Patients

446 patients undergoing neoadjuvant treatment with available baseline tumor tissue and matched samples of RD (in case of no-pCR) were included.

HER2 evaluation

- HER2 expression was evaluated according to ASCO/CAP recommendations in place at the time of diagnosis *(Wolff et al 2007; Wolff et al 2013; Wolff et al 2018).*
- Cases diagnosed between 2007 and 2013 were reviewed to comply with the 10% cutoff of IHC for HER2-positivity.
- **HER2-negative cases were further classified as HER2-0 (IHC 0) or HER2-low (IHC 1+ or 2+ and ISH neg.).**

RESULTS

Patients' characteristics

Age, median	50.2 (Q1-Q3: 42.7-60.2)		
Hystology	Ductal	397	89.0%
	Lobular	28	6.3%
	Other/NA	21	4.7%
Grading	1	4	0.9%
	2	89	20.0%
	3	316	70.9%
	NA	37	8.2%
Clinical TNM	I	21	4.7%
	II	259	58.1%
	III	159	35.7%
	NA	7	1.5%
Primary BC phenotype	HR+/HER2-	105	23.5%
	TN	156	35.0%
	HER2+	185	41.5%
Neoadj. CT	Anthra-Tax	354	79.4%
	Tax	68	15.2%
	Anthra	9	2.0%
	Other/NA	15	3.4%
Neoadj. anti-HER2	Trastuzumab	160	35.9%
Pathologic response	pCR	155	34.8%
	RD	291	65.2%

Table I ***patients' characteristics.*** *(Abbr: CT, chemotherapy; anthra, anthracycline; tax, taxane; NA; not available).*

HER2 expression in primary BC and residual disease according to BC phenotype

HER2-low cases were significantly enriched in the HR-pos/HER2-neg vs triple-neg subgroup.

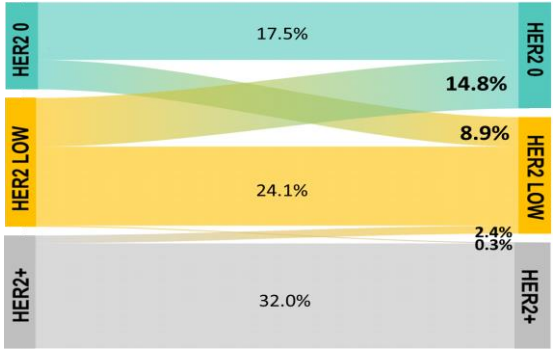
Primary BC phenotype	HER2-0	HER2-LOW	p
HR+/HER2-	33 (31.4%)	72 (68.6%)	0.001
TN	83 (53.2%)	73(46.8%)	

Table II ***HER2 expression distribution in primary BC (HER2-neg cohort).***

RD phenotype	HER2-0	HER2-LOW	p
HR+/HER2-	36 (34.6%)	68 (65.4%)	<0.001
TN	58 (62.4%)	35 (37.6%)	

Table III ***HER2 expression distribution in residual disease (HER2-neg cohort).***

HER2 expression evolution from primary BC to residual disease



- **Total rate of HER2 discordance: 26.4%, mostly driven by cases switching either to or from HER2-low.**
- Among HR-pos/HER2-neg patients with HER2-low expression on RD, 23% had an estimated high risk of relapse according to the residual proliferative cancer burden (RPCB class 3).

Figure 1 ***HER2 expression evolution from primary BC to residual disease after neoadjuvant treatment.***

CONCLUSIONS

HER2-low expression showed high instability from primary BC to RD after neoadjuvant treatment. HER2-low expression on RD may guide personalized adjuvant treatment for high-risk patients in the context of clinical trials with novel anti-HER2 drugs.

COI & FUNDINGS

First author does not have any COI to declare. *Funding: DOR funding from the University of Padova (VG, MVD, GG, PFC); Fondazione AIRC under 5 per mille 2019 (PFC and MF).*