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

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BACKGROUND & AIM

- Approximately a half of breast tumors traditionally classified as HER2-negative exhibit HER2-low expression (IHC 1+ or 2+ and IHC 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

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.

<table>
<thead>
<tr>
<th>Primary BC phenotype</th>
<th>HER2-0</th>
<th>HER2-LOW</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR+/HER2-</td>
<td>33 (31.4%)</td>
<td>72 (68.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>TN</td>
<td>83 (53.2%)</td>
<td>73 (46.8%)</td>
<td></td>
</tr>
</tbody>
</table>

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

HER2 expression evolution from primary BC to residual disease

<table>
<thead>
<tr>
<th>HER2 status</th>
<th>HER2-0</th>
<th>HER2-LOW</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2-0</td>
<td>17.5%</td>
<td>14.8%</td>
<td></td>
</tr>
<tr>
<td>HER2+</td>
<td>24.1%</td>
<td>8.9%</td>
<td></td>
</tr>
<tr>
<td>HER2+</td>
<td>32.0%</td>
<td>2.4%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

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).

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