**EVI1 expression in early-stage breast cancer patients treated with neoadjuvant chemotherapy**

**Background**
Overexpression of the oncogene EVI1 (ecotropic viral integration site 1), a stem cell regulator in hematopoiesis, has been implicated in carcinogenesis, particularly in breast cancer. However, the prognostic importance of EVI1 overexpression in early breast cancer (BC) remains unclear due to low sample sizes of reported outcomes and lack of patient data from controlled clinical trials. The neoadjuvant clinical trial GeparTrio included 1,107 patients, 51% of whom had TNBC. This study aimed to investigate clinical and biological relevance of EVI1 expression in newly diagnosed BC treated with neoadjuvant chemotherapy from the GeparTrio trials.

**Patients and Methods**
EVI1 expression was determined by immunohistochemistry on tissue microarrays of pretherapeutic biopsies of BC patients from GeparTrio trials. EVI1 expression levels were determined using H-score as a cumulative measure of staining intensity and percentage of positive cells. EVI1 protein expression was analyzed as a continuous variable and categorized into low (≤112.16 H-score) or high (>112.16 H-score) based on median cut-off. Logistic regression and Cox proportional hazard models were used to correlate EVI1 expression with pathological complete response (pCR), ypNO, and survival outcomes, respectively. pCR rates were estimated by 2-sided chi-square test. Disease-free survival (DFS) and overall survival (OS) according to EVI1 expression groups were presented by Kaplan-Meier curves and compared with log-rank p-values.

**Results**
A total of 993 breast cancer patients with evaluable immunohistochemical EVI1 H-score and available clinical and follow-up data were included in the analysis (Table 1). Median EVI1 H-score was 112.16 (range 0.5–291.4) in the entire cohort. High EVI1 levels were significantly associated with smaller tumor size (≤2 cm) in the entire cohort and in HR+/HER2- but not in the TNBC subtypes (Table 2).

**Conclusions**
EVI1 did neither influence response to neoadjuvant therapy nor patient survival in the overall cohort. TNBC patients with elevated EVI1 expression showed numerically better pCR and improved survival. Further analyses are needed to verify our findings, especially in the pathological work-up of newly diagnosed TNBC patients.

**References**

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**Table 1: Baseline characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Category</th>
<th>Low, H score (%)</th>
<th>High, H score (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size</td>
<td>ct1-c2</td>
<td>62 (2.8%)</td>
<td>348 (74.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Node status</td>
<td>ct-negative</td>
<td>209 (46.7%)</td>
<td>2 (0.4%)</td>
<td>0.948</td>
</tr>
<tr>
<td></td>
<td>ct-positive</td>
<td>273 (57.7%)</td>
<td>230 (64.8%)</td>
<td>0.376</td>
</tr>
<tr>
<td>Tumor grade</td>
<td>G1</td>
<td>164 (74%)</td>
<td>134 (75%)</td>
<td>0.904</td>
</tr>
<tr>
<td></td>
<td>G2</td>
<td>102 (47.2%)</td>
<td>131 (25.2%)</td>
<td>0.018</td>
</tr>
</tbody>
</table>

**Table 2: Subgroup comparisons**

- **HR+/HER2+**
  - Tumor size: ct1-c2 vs. ct3-c4, median 12 cm vs. 5 cm, p=0.001
  - Node status: ct-negative vs. ct-positive, 209 (46.7%) vs. 273 (57.7%), p=0.376
  - Tumor grade: G1 vs. G2, 164 (74%) vs. 102 (47.2%), p=0.018

- **TNBC**
  - Tumor size: ct1-c2 vs. ct3-c4, median 12 cm vs. 5 cm, p=0.001
  - Node status: ct-negative vs. ct-positive, 209 (46.7%) vs. 273 (57.7%), p=0.376
  - Tumor grade: G1 vs. G2, 164 (74%) vs. 102 (47.2%), p=0.018

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**Figure 1: Flow diagram of patients included in the analysis set**

Patients with available TMA sample for EVI1 immunohistochemistry N=1,107

**Figure 2: Immunohistochemical images of EVI1 expression**

**Figure 3: Correlation of EVI1 expression with therapy response**

**Figure 4: Correlation of EVI1 with DFS (A) and OS (B) within BC subtypes**