NEOADJUVANT SINGLE-DOSE TRILACICLIB PRIOR TO COMBINATION CHEMOTHERAPY IN PATIENTS WITH EARLY TRIPLE-NEGATIVE BREAST CANCER: SAFETY, EFFICACY, AND IMMUNE CORRELATE DATA FROM A PHASE 2 STUDY

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INTRODUCTION

• In early-stage high-risk breast cancer (THBC), there is accumulating evidence of a correlation between tumor microenvironment (TME) and breast cancer outcomes. A recent study showed a trend toward increased expression of genes associated with memory T cells from baseline to day 7 in the overall population, suggesting that the TME may influence immune response and treatment outcomes.

METHODS

• In the current study, we aimed to evaluate the relationship between the immune microenvironment of early-stage THBC, as measured in changes in TME-related gene expression, and clinical outcomes.

RESULTS

• Patient disposition and characteristics: 24 patients were enrolled in the study, and 18 patients were evaluable for response. The median age was 55 years (range 33–78), and 71% of patients were White, 21% Black, and 8% Asian. Most patients were women (92%).

• Immunotherapeutic effects of trilaciclib: Compared to the baseline samples, there was a trend toward increased numbers of CD8+ T cells and GZMB+ cells in baseline tumor samples among patients who achieved pCR (Figure 5).

• Gene set enrichment analysis of the top 10 pathways differentially expressed at day 7: There was a trend toward increased expression of genes associated with memory T cells from baseline to day 7, indicating a potential role of trilaciclib in modulating the TME (Figure 6).

• Conclusions: Trilaciclib in combination with AC/T chemotherapy may enhance antitumor immunity by differentially arresting CD8+ T-cell and Treg subsets, leading to a faster recovery of proliferation in CD8+ T cells compared with Tregs (median 19.8 vs 12.6 months; p = 0.0191).

FIGURE 1: PROPOSED IMMUNE MECHANISMS OF ACTION OF TRILACICLIB

TABLE 1: TRAEs RELATED TO ANY STUDY DRUG OCCURRING IN ≥ 20% OF THE PATIENTS

<table>
<thead>
<tr>
<th>TRAE Type</th>
<th>Grade 1/2</th>
<th>Grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>81.7%</td>
<td>18.3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>78.6%</td>
<td>21.4%</td>
</tr>
<tr>
<td>Alopecia</td>
<td>66.7%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Numbness</td>
<td>62.5%</td>
<td>37.5%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>66.7%</td>
<td>33.3%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Trilaciclib in combination with AC/T chemotherapy may enhance antitumor immunity by differentially arresting CD8+ T-cell and Treg subsets, leading to a faster recovery of proliferation in CD8+ T cells compared with Tregs (median 19.8 vs 12.6 months; p = 0.0191).

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REFERENCES