

PRESENTATION: ORAL PRESENTATION (GENERAL SESSION)

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973 – Despatil study: a phase ii trial of de-escalated neoadjuvant chemotherapy for early-stage triple-negative breast cancer guided by tumor-infiltrating lymphocytes and radiologic response

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Introduction: Currently, a four-drug chemotherapy regimen (plus pembrolizumab for stage II–III) is frequently used as a neoadjuvant strategy for triple-negative breast cancer (TNBC). These regimens are associated with high toxicity rates, and, given the heterogeneity of the disease, some patients may achieve favorable outcomes with less intensive treatment strategies. In this context, high levels of tumor-infiltrating lymphocytes (TILs) have been identified as a marker of excellent prognosis. Additionally, radiologic response can assist in treatment decision-making, allowing escalation only for patients with inadequate response, thereby optimizing therapy. The DespaTIL study investigates a biomarker-driven de-escalation approach to neoadjuvant chemotherapy in early-stage TNBC.

Methods: DespaTIL is a multicenter, single-arm, investigator-initiated phase II trial evaluating a de-escalated neoadjuvant chemotherapy strategy in patients with stage I TNBC with any level of TILs, or stage II TNBC with $\geq 50\%$ stromal TILs. All patients receive four cycles of carboplatin and a taxane. Radiologic response is assessed via breast magnetic resonance imaging after cycle 4. Patients achieving a radiologic complete response proceed to surgery. Those without a radiologic complete response are escalated to four additional cycles of anthracycline and cyclophosphamide, with or without pembrolizumab at the physician's discretion. Eligible participants are patients with human epidermal growth factor receptor 2 (HER2)-negative invasive breast carcinoma, estrogen receptor and progesterone receptor expression levels $< 10\%$, and one of the following: (1) clinical stage T1c N0 M0 with any TIL level; or (2) clinical stage T2 N0 M0 with TILs $\geq 50\%$. A total of 40 patients will be enrolled. The primary endpoint is pathologic complete response following four cycles of carboplatin and taxane. Secondary endpoints include the correlation between radiologic and pathologic response, residual cancer burden, event-free survival, overall survival, and subgroup analyses by disease stage. Patient enrollment is expected to begin in the second half of 2026.

Ethics: Research Ethics Committee Approval (CAAE 89541925.0.1001.0087).

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Keywords: triple-negative breast cancers; tumor infiltrating lymphocytes; neoadjuvant therapy; pembrolizumab.