

EVOLUTION OF CYTOTOXIC AND REGULATORY T CELLS IN BLOOD AND IN TISSUE AFTER NEOADJUVANT TREATMENT IN BREAT CARCINOMA.

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Background

There are more pathological complete responses (pCR) after neoadjuvant treatment in breast cancer with predominance of tumor infiltrating lymphocytes (TILs). The objective is to analyze immunosuppressive (**regulatory T**) and **cytotoxic (CD8+ T) TILs before and after neoadjuvant** treatment and the **pathological response** achieved in breast carcinoma.

Methods

Translational study of 50 breast carcinoma patients with neoadjuvant treatment. Measurement of cytotoxic CD8 + and regulatory T lymphocytes (CD25H or FOXP3 +) was performed in **peripheral blood** (before, during and after treatment), and before (biopsy) and after (surgical specimens) neoadjuvant in **tumor tissue**. The pathological response was assessed according to **Miller & Payne** (M&P: G1: minimal changes, G2: <30%, G3: 30-90%, G4:> 90%, G5: pCR). Peripheral blood lymphocytes were measured by **flow cytometry** (cells/microliter) and lymphocytes from tissue were measured by immunohistochemistry using the **Ladoire classification** (G0: 0 cells in 5f/20x, G1: 1-5, G2: 5-15, G3: > 15).

Results

- Peripheral blood CD8+ T lymphocytes** decreased significantly after treatment in patients with a <30% tumor response (M&P grade 1-2), median of 239 cells/ul in cycle 1 (C1) vs 133 cells/ul in C6, p 0.041. However, they remained constant (200-300 cells/ul) in 30-90% tumor response (M&P grade 3-4) and in pCR (M&P grade 5). Median CD8+ T lymphocytes in M&P grades 1-2 vs 5 were 184 vs 258 cells/ul (p 0.044) in C4, 180 vs 276 cells/ul (p 0.023) in C5 and 133 vs 285 cells/ul (p 0.012) in C6. **FIGURE 1.**
- The percentage of CD8+ T from tissue** in M&P grade 5 is focused on Ladoire grade 3, while M&P grade 1-2 highlights a lower gradation of CD8+ T (Ladoire grade 0-2). **FIGURE 2.**
- There are high levels of **FOXP3+ from tissue** both before and after treatment in M&P grade 1-2. However, a low FOXP3+ percentage is expressed in M&P grade 5, and even that percentage decreases drastically in Ladoire grade 2-3 after treatment. **FIGURE 3.**
- The peripheral blood regulatory T (CD25H) cells** decrease in M&P grade 3-4 and do not vary in M&P grade 1.

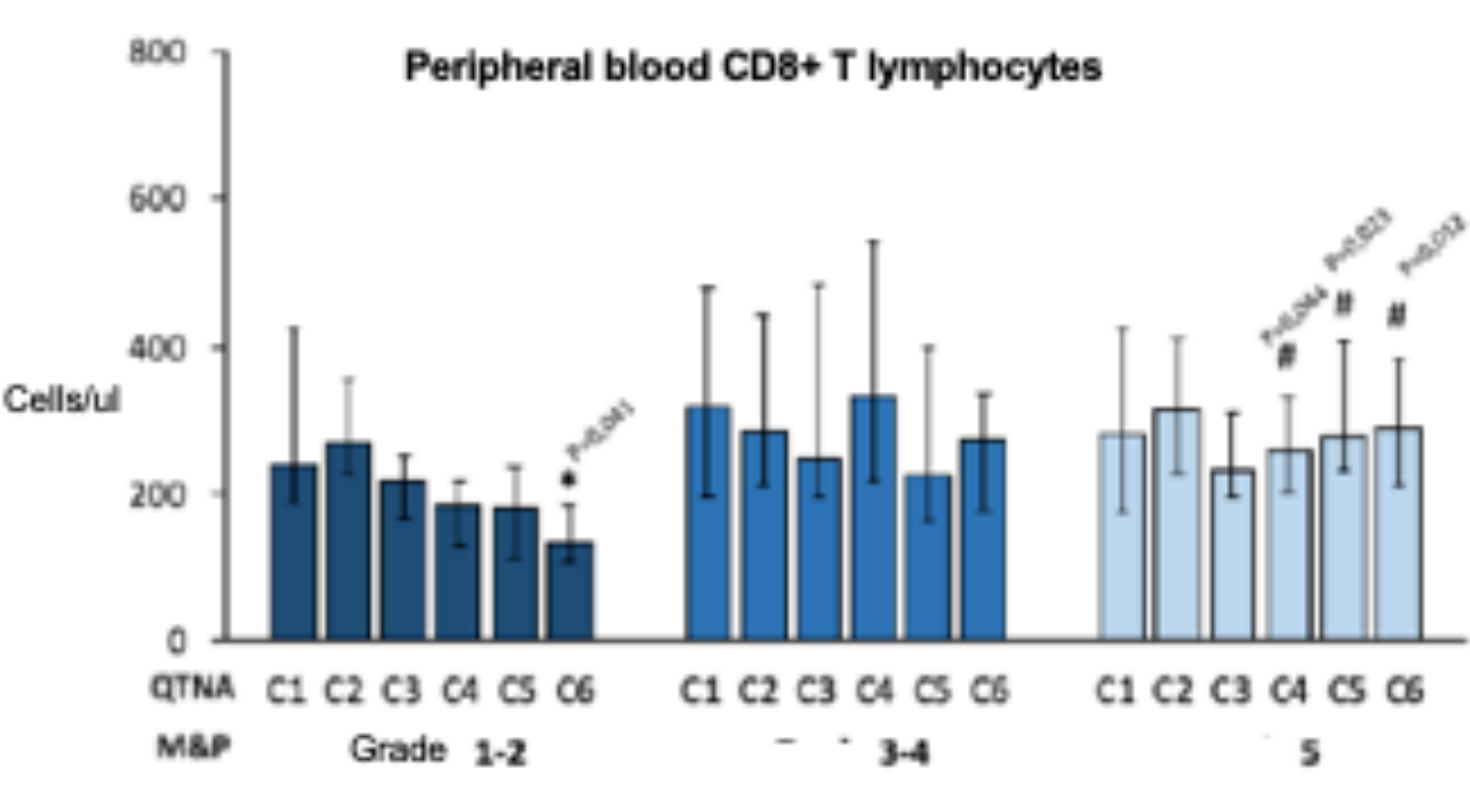


Figure 1. Peripheral blood CD8+ T lymphocytes before, during and after neoadjuvant treatment and pathological response achieved (M&P). *p G1-2 (C1 vs C6). #p C4, C5, C6 (G1-2 vs G5).

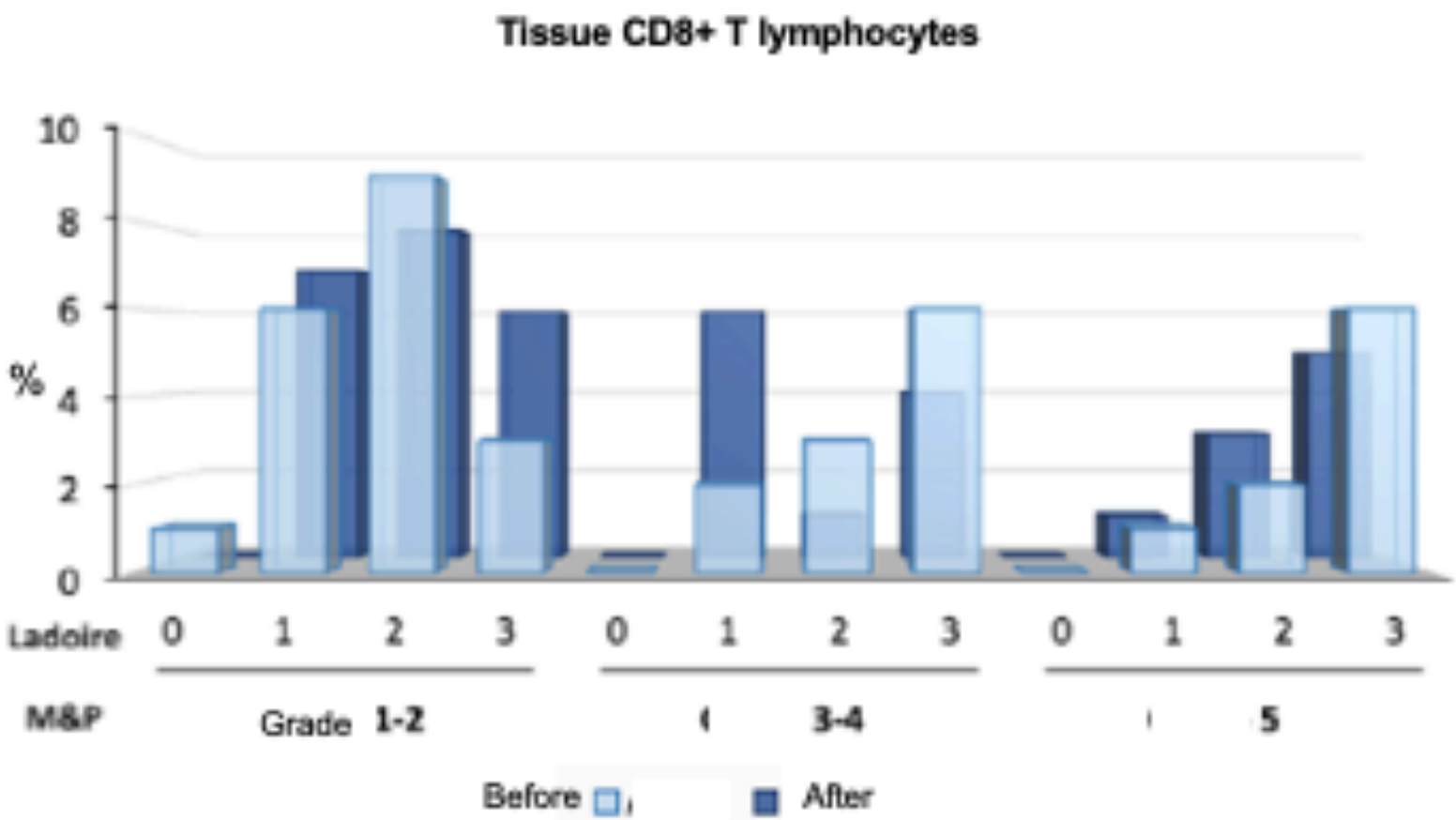


Figure 2. % Tissue CD8+ T lymphocytes (Ladoire 0-3) before and after neoadjuvant treatment and pathological response achieved (M&P).

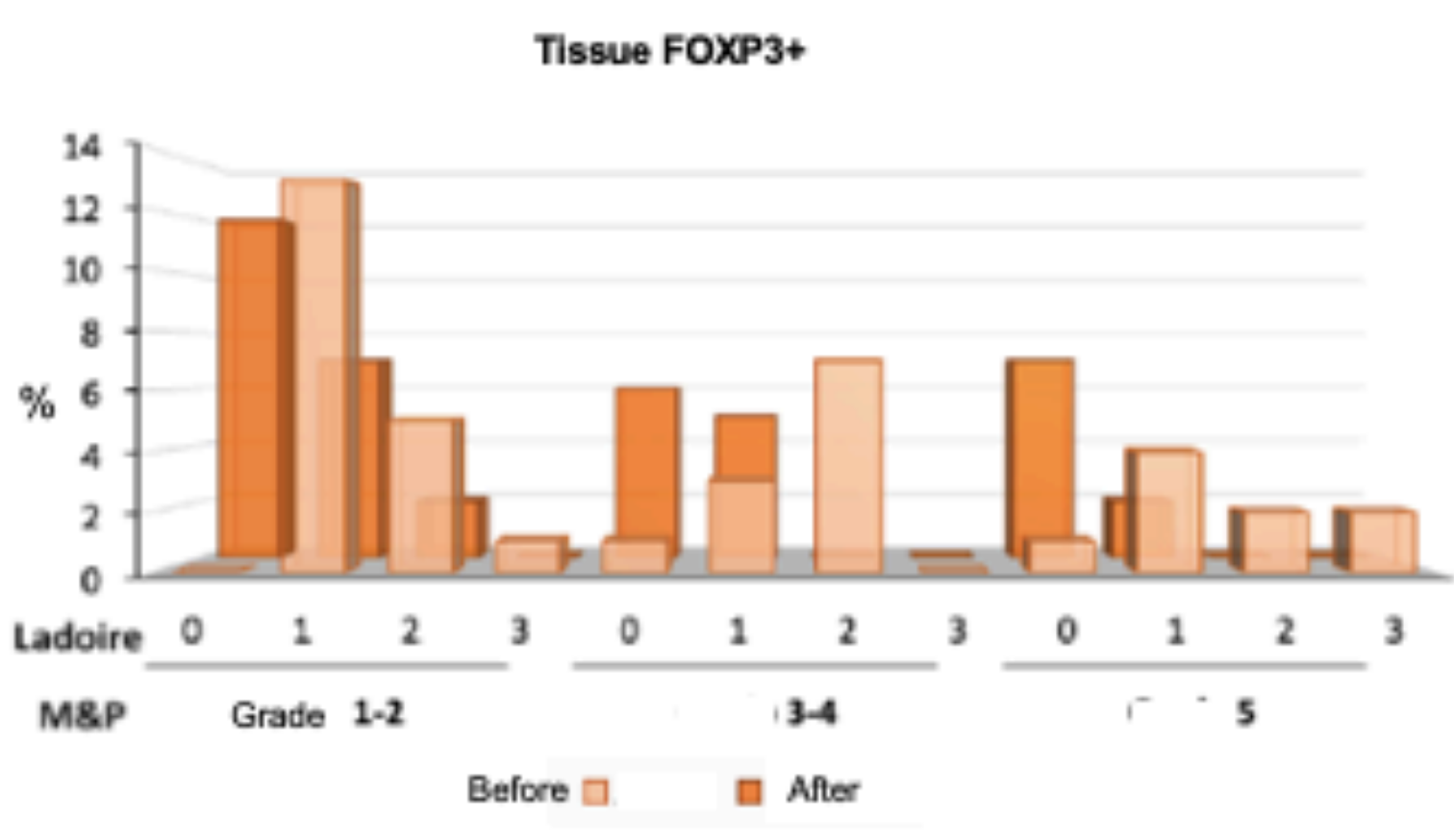


Figure 3. % Tissue FOXP3+ (Ladoire 0-3) before and after neoadjuvant treatment and pathological response achieved (M&P).

Conclusions

- There is a significant descent of CD8+ T cells in non-pCR patients, while remaining elevated in pCR.
- There are more FOXP3+ T cells in non-pCR.
- CD8+ T and regulatory T cells are potential predictive biomarkers in breast carcinoma.