immunotherapy of cancer

PATHOLOGICAL COMPLETE RESPONSE AND CHANGES RELATED TO T INFILTRATING LYMPHO CYTES AND REGULATORY T CELLS IN TISSUE AND PERIPHERAL BLOOD AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CARCINOMA

L. De La Cruz Merino1, A. Barco Sánchez2, J. Ibáñez Martínez3, A. Nieto García4, A. Vallejo Benítez3, F. Henao Carrasco1, V. Sánchez Margalet2

1Clinical Oncology, Hospital Universitario Virgen Macarena, Seville, SPAIN
2Biochemistry, Hospital Universitario Virgen Macarena, Seville, SPAIN
3Pathology, Hospital Universitario Virgen Macarena, Seville, SPAIN
4Public Health, Universidad de Sevilla, Seville, SPAIN

Aim: Some clinical trials in breast cancer have reported impressive outcomes related to laboratory immune findings in the neoadjuvant setting. In this context, tumor infiltrating lymphocytes (TILs) and regulatory T cells (Tregs) in tissue specimens and in peripheral blood are being tested as two emerging prognostic and predictive factors. We designed a protocol to analyze immune profile before, during and after neoadjuvant chemotherapy (CT) in breast cancer in blood and tissue, and their eventual relation with pathological complete response (pCR).

Methods: From March 2011 to February 2014, 47 patients (18 her2+ / 29 her2-) with T2-4 N0-3 breast carcinoma treated with neoadjuvant CT in the Breast Cancer Unit of the Hospital Universitario Virgen Macarena (Seville, Spain) were included in the study. CD3+, CD8+, CD8-16-56+ and FOXP3+ cell infiltrates were detected by immunohistochemistry before and after CT in tissue specimens. Blood samples were collected in EDTA-K3 tubes before every cycle to determine the immunophenotype profile. Cell populations were determined by flow cytometry analysis of whole blood, including the study of CD3-CD4-CD25low and CD3-CD4-CD25high (regulatory) T cells.

Results: By February 2014, 47 patients were operated. pCR or near pCR (grade 4/5 Miller&Payne) was attained in 20 patients (42.6%). pCR was achieved in 66.6% (12/18) of tumors overexpressing her2 and treated with CT plus trastuzumab, and in only 27.5% (8/29) of the her2- population. Absence and/or disappearance of Tregs in tissue (Black grading system = 0) was more frequent after neoadjuvant CT (11.11 vs 62.2%). Furthermore, average whole blood CD3-CD4-CD25high (regulatory) T cells were 126.36 before and 91.19 after neoadjuvant CT (p 0.010). Overall Tregs diminished in the pCR and non pCR groups without statistically significant differences.

Conclusions: Neoadjuvant CT decreases Tregs immunosuppressive infiltrates in tissue and CD3-CD4-CD25high (regulatory) T cells in peripheral blood in all the population. Although differences among subgroups (pCR/non-pCR and her-/her2+) were not statistically significant, these data support the role of Tregs as an interesting biomarker with eventual therapeutic implications in breast carcinoma.

Disclosure: All authors have declared no conflicts of interest.