XIX CONGRESSO NAZIONALE SIES2026
Firenze | 4-6 marzo 2026 Palazzo degli Affari

XIX Congress of the Italian Society of Experimental Hematology ABSTRACT N. P111

Stem Cell Transplantation, immunotherapy and cell therapy

IMPACT OF T CELLS FITNESS ASSESSED BY CYTOFLUORIMETRY IN PATIENTS TREATED WITH CAR-T THERAPY FOR MALIGNANT MATURE B-CELL NEOPLASMS

G. Tancredi[1], M. Franzini[1], E. Orciuolo[1], C. Bono[1], S. Balducci[1], G. Traverso[1], M.L. Del Giudice[1], S. Galimberti[1]

Hematology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy

Introduction: Chimeric Antigen Receptor (CAR) T-cell therapy has revolutionised the management of relapsed or refractory B-cell malignancies, providing unprecedented clinical responses compared with standard therapies. Three CD19-directed CAR-T products—axicabtagene ciloleucel, tisagenlecleucel, and lisocabtagene maraleucel—have been approved based on pivotal phase II and III trials demonstrating significant complete response rates and durable remissions. Nevertheless, despite these advances, the majority of treated patients ultimately relapse, underscoring the need to elucidate mechanisms of resistance and immune dysfunction. Increasing evidence implicates T-cell exhaustion and immunosuppressive tumour microenvironment as major contributors to therapeutic failure. Exhausted T cells are characterised by impaired effector functions, reduced proliferative potential, and sustained expression of multiple inhibitory receptors, including PD-1, TIM-3, LAG-3, and TIGIT. LAG-3 acts mainly through MHC class II engagement, TIGIT through competitive binding to CD155/CD112, and TIM-3 through modulation of TCR signalling via BAT3 and Fyn, each contributing to inhibitory signalling pathways that limit CAR-T efficacy.
Aim: Our study aims to elucidate the contribution of T-cell exhaustion mechanisms to CAR-T cell functionality and clinical response, assessing the expression dynamics of three inhibitory checkpoint receptors—TIGIT, LAG3, and TIM3—on both total T lymphocytes and CAR-T cells. Additionally, we are investigating the distribution of T-cell memory subpopulations, including naïve (Tn), central memory (Tcm), and effector (Te) cells and the possible role of T-regs.
Methods: The dynamic assessment of T-cell exhaustion marker expression is performed in parallel with the monitoring of the maturation curve of the T-cell memory compartment, defined by the differential expression of CCR7 and CD45RA, as well as with the evaluation of regulatory T cells, identified by their characteristic expression of CD25 and CD127. Peripheral blood samples from patients treated with CAR-T cells are analysed at four timepoints—baseline, 72 hours, day 7, and day 10 post-infusion—using a 12-colour flow cytometry panel. The analysis includes the quantitative assessment of inhibitory receptor expression on $CD4^+$, $CD8^+$, and CAR^+T-cell populations and the identification of major T--lymphocyte memory subsets (naïve, central memory, effector memory, and TE) and regulatory T cells.
Conclusions: The results are expected to clarify how exhaustion-related markers evolve during early CAR-T expansion, potentially correlating with treatment response and long-term persistence. Understanding these immunoregulatory pathways may support the development of combinatorial strategies, such as checkpoint blockade, to enhance CAR-T cell efficacy and overcome resistance in hematological malignancies.