TRILACICLIB, AN INTRAVENOUS CYCLIN-DEPENDENT KINASE 4/6 INHIBITOR, ENHANCES ANTITUMOR RESPONSES BY MODULATING T CELLS

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Introduction

- Administering trilaciclib (COSELA™, G1 Therapeutics, Inc.), an intravenous myelosuppressive therapy prior to chemotherapy results in the transient arrest of cyclin-dependent kinase (CDK) 4/6-dependent hematopoietic stem and progenitor cells and immature cells in the G1 phase of the cell cycle, thus protecting these cells from chemotherapy-induced damage.1
- Trilaciclib has also been shown to favorably alter the tumor microenvironment via modulation of processes within the cancer-immunity cycle (Figure 1).2

Methods

- Peripheral blood mononuclear cells (PBMCs) were isolated from 6 healthy human donors and activated with α-activated CD8+ T cells following the addition of trilaciclib.3
- Flow cytometric analysis was performed on immunophenotypically defined cell populations using CD8, CD45RA, and MHC-I expression.

Results

- Compared with the control, the addition of trilaciclib increased the expression of MHC class I and II and PD-L1 on the tumor cell surface (Figure 2A) and resulted in the increased secretion of IFN-γ (Figure 2B).4
- Administering trilaciclib resulted in an enrichment of T cm cells and decreased Simpson clonality in peripheral blood, suggesting enhanced antigen presentation and activation of T cells.5

Conclusions

- Data showed a trend of increased CD8+ T cm cells in trilaciclib populations spot exposure to trilaciclib.
- Increased differentiation into memory T cells was observed irrespective of when trilaciclib was added post activation.

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References