

## P1309 DYSREGULATED EXPRESSIONS OF INHIBITORY CHECKPOINT MOLECULES AND THEIR LIGANDS ON T-CELLS AND BLASTS IN AML RELAPSES AFTER STEM CELL TRANSPLANTATION (SCT)

**Topic:** 21. Stem cell transplantation - Experimental

Sophia Bohlscheid<sup>1</sup>, Giuliano Filippini Velazquez<sup>2</sup>, Hazal Aslan<sup>1</sup>, Tobias Baudrexler<sup>1</sup>, Helga Schmetzer<sup>1</sup>, Christoph Schmid<sup>2</sup>

<sup>1</sup> Medical Department III, Department for Hematopoietic Cell Transplantation, Munich University Hospital, Munich, Germany; <sup>2</sup> Department of Hematology and Oncology, Section for Stem Cell Transplantation, Augsburg University Hospital, Augsburg, Germany

### Background:

Upregulation of inhibitory checkpoint molecules (ICM) on T-cells and their ligands on leukemic blasts may be a mechanism of acute myeloid leukaemia (AML) relapse after allogeneic stem cell transplantation (SCT).

**Aims:** Better understanding of relapse biology could improve treatment efficacy.

### Methods:

We examined peripheral blood (PB) and bone marrow (BM) samples of 5 AML patients (PTs) relapsing after SCT, and PB of 5 healthy individuals (H), including 2 stem cells donors. ICM (PD-1, CTLA-4) expressions on T-cells and their ligands (CD86, PD-L1, PD-L2) on leukemic blasts were assessed through flow cytometry. PTs' PB was cultivated with and without "KitM" (GM-CSF+PGE-1) to generate leukemia-derived dendritic cells (DC<sub>leu</sub>), followed by MLC, enriched by PTs' or donors' T-cells. After MLC, immune activation and functionality (degranulation, intracellular cytokine production, blast lysis) was assessed.

### Results:

1. Whilst all patients showed high expressions of PD-1 on their T-Cells, additional overexpression of CTLA-4 was negatively correlated with responses to relapse treatment. Expression of ICM was low on T-cells from 4/5 healthy individuals (*Figure 1*).

### 2. Influence of KitM on ICM/ligand expressions on T-cells/blasts

- ICM/ligand expressions on uncultured T-cells/blasts: In contrast to H, PTs presented high co-expressions of CTLA-4 and PD-1 on PB T-cells (*Figure 1*). In addition, PTs showed high frequencies of PB/BM blasts co-expressing CD86.
- DC/DC<sub>leu</sub> in PB: Generation of DC<sub>leu</sub> in AML as well as generation of DC in H was successful with KitM pretreated PB vs. Control.
- ICM co-expression on T-cells after MLC with KitM pretreated PB: MLC of KitM treated PB enriched with unstimulated PTs T-cells resulted in reduced frequencies of ICM-positive T-cells in 3/5 PTs, and increased frequencies of activated (leukemia specific) T-cells in 3/5 PTs. Beyond, blast lysis was improved in 4/5 samples treated with KitM. Both findings were not observed when PB cells were cultivated in the absence of KitM.

---

**Copyright Information:** (Online) ISSN: 2572-9241

© 2022 the Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

**Abstract Book Citations:** Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at <https://journals.lww.com/hemasphere/pages/default.aspx>.

**Disclaimer:** Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.

### 3. Possible impact of ICM profiles on clinical outcome in a particular case

PT1 suffered from early relapse both after 1<sup>st</sup> and 2<sup>nd</sup> SCT from her healthy father. A role of ICM in relapse mechanisms was suggested by CTLA-4/PD-1 expression on her T-cells and CD86 expression on AML blasts. In addition, >90% of the healthy father's T-cells expressed CTLA-4/PD-1, which might have contributed to treatment failure. In contrast, T-cells from PT1's mother presented with low ICM levels (*Figure 1*), suggesting that the mother might have been a better donor. Stimulation of PT1's PB cells with KitM generated DC<sub>leu</sub>, decreased ICM-expressions and increased T-cell activity. KitM pretreated samples also revealed improved blast lysis after MLC.

Image:

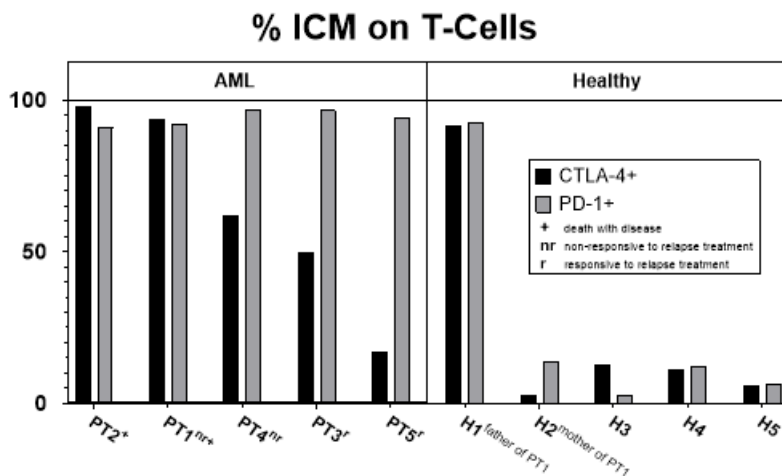


Figure 1: % Expressions of CTLA-4 and PD-1 on T-Cells in uncultivated PB of AML Patients and Healthy Individuals

**Summary/Conclusion:** T-cells and blasts of AML PTs relapsing after SCT uniformly co-expressed ICM and their ligands, which could be a reason for inferior immune responses. High aberrant ICM-expressions, in particular CTLA-4, on donor T-cells could be responsible for relapse after SCT by inactivating antileukemic immune reactions. Hence, checkpoint-inhibitory antibodies might represent a specific therapeutic option in these patients. Further, interactions between ICM-expressions on healthy (fresh) donor T-cells could have an impact in therapy responses and should be evaluated in donor selection. Finally, generation of DC<sub>leu</sub> by treatment with KitM triggers immune responses in MLC alongside with reduced ICM-expressions on T-cells, possibly reducing their inhibitory effects and therefore improving antileukemic responses.

Copyright Information: (Online) ISSN: 2572-9241

© 2022 the Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

Abstract Book Citations: Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at <https://journals.lww.com/hemasphere/pages/default.aspx>.

Disclaimer: Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.