EARLY AND LONG-LASTING ALTERATION OF NAÏVE CD45RA(+)FOXP3(LOW) REGULATORY T-CELL RECONSTITUTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION

Evidence indicates that inadequate or abnormal immune reconstitution of regulatory T cells (Tregs) may increase the risk of graft-versus-host disease (GvHD) following allogeneic hematopoietic stem cell transplantation (HSCT). Within the Treg population, naïve and effector subsets can be distinguished based on CD45RA and Foxp3 expression. This study aimed to assess the immune reconstitution of Treg subsets after allogeneic HSCT.

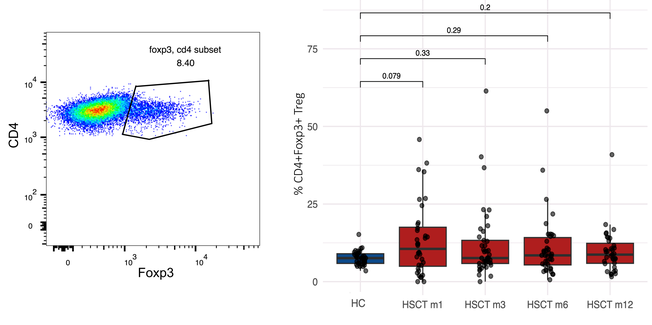
METHODS

Peripheral blood mononuclear cells were collected from **healthy controls** (HC, n=31) and patients following **allogeneic HSCT** (n=53) at 1,3,6,12 months post transplant at the Geneva University Hospitals.

Among CD4+ T cells, the proportion of total (Foxp3+), naïve (CD45RA+Foxp3(low)) and effector (CD45RA-Foxp3(high)) **regulatory T cells** were assessed by flow cytometry.

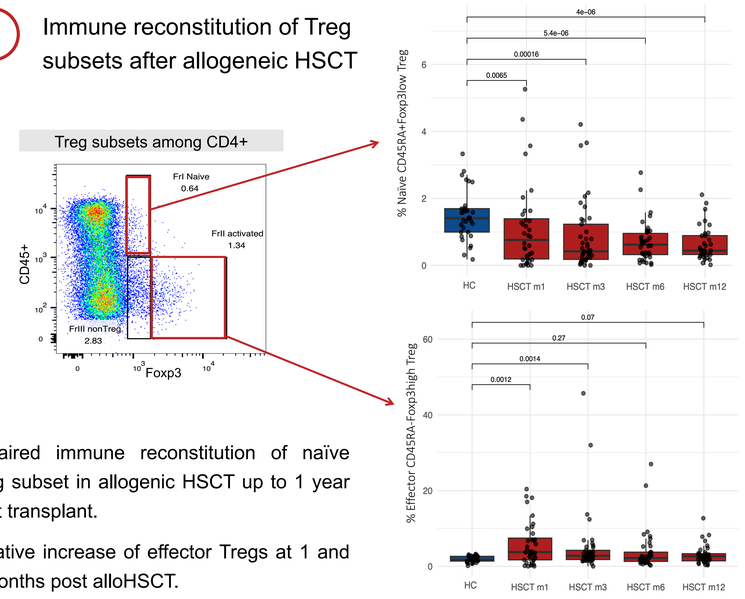
RESULTS

1 Proportion of Total Treg cells among allogenic HSCT



No difference in percentages of total CD4+Foxp3+ Treg population between HC and allogeneic HSCT recipients at all time points studied.

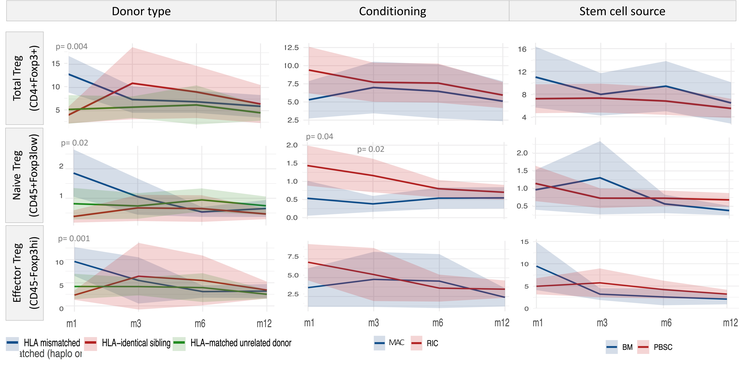
2 Immune reconstitution of Treg subsets after allogeneic HSCT



Impaired immune reconstitution of naïve Treg subset in allogenic HSCT up to 1 year post transplant.

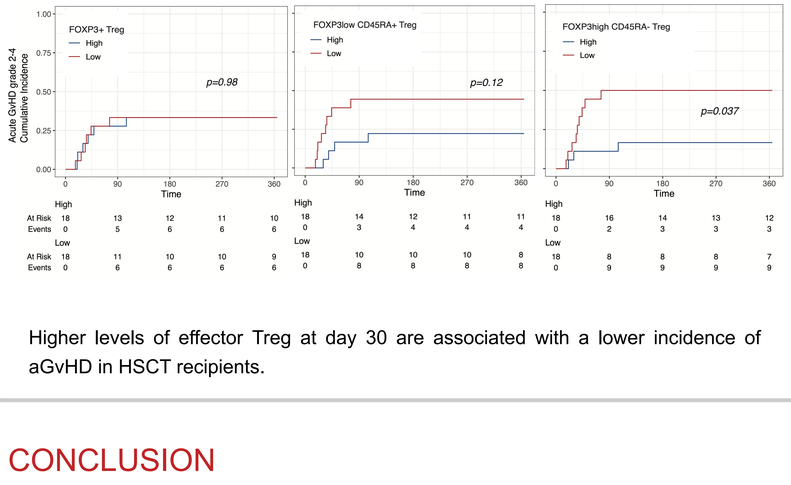
Relative increase of effector Tregs at 1 and 3 months post alloHSCT.

3 Impact of transplant characteristics on immune reconstitution of Treg subsets



Recipients of HLA-mismatched grafts (i.e. haplo or mismatched unrelated donors) display higher percentages of total, naïve and effector Treg at 1 month after alloHSCT.
RIC is associated with higher proportion of Naïve Treg at 1 and 3 months after alloHSCT.
No significant impact of stem cell source on Treg subsets immune reconstitution.

4 Impact of immune reconstitution of Treg subsets on incidence of aGvHD



Higher levels of effector Treg at day 30 are associated with a lower incidence of aGvHD in HSCT recipients.

CONCLUSION

The analysis provides a detailed characterization of the immune-reconstitution of Treg subsets after allogeneic HSCT and reveals an early and long lasting impairment in naïve Treg reconstitution.

The work also suggests a potential relationship between effector Treg subset and the incidence of aGvHD.

REFERENCES

Gating strategy based on Makoto Miyara et al., “Functional Delineation and Differentiation Dynamics of Human CD4+ T Cells Expressing the FoxP3 Transcription Factor”, *Immunity* (Vol.30, Issue 6), 2009

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