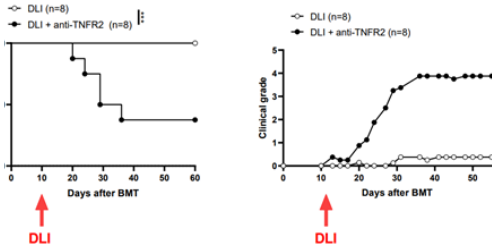
MODULATION OF TNF-TNFR2 TO PROMOTE ALLOREACTIVITY AND ANTI-LEUKEMIA RESPONSE DURING BLOOD MALIGNANCY RELAPSE

Use of an anti-TNFR2 mAb to target Treg cells as a treatment for blood malignancy relapse, used either directly in grafted patients or to enhance donor lymphocyte infusion strategies.

PRESENTATION

Blood malignancy such as chronic myeloid leukemia (CML) and lymphomas are pathologies dealing with a high relapse rate. Allogeneic hematopoietic stem cell transplantation (Allo-HCT) and Donor lymphocyte injections (DLI) are among potential strategies to treat or prevent relapse, however, response rate generally remains low. Treg cells play a key role in the fine tuning of the immune responses in alloHCT. Cell therapy using Treg infusions to prevent graft-versus-host disease (GVHD) showed very promising results in the clinic. Conversely, ex vivo Treg depletion from DLI has been shown to enhance the graft-versus-leukemia (GVL) effect in patients who relapsed after alloHCT without previously developing GVHD. Using an anti-TNFR2 mAb, the team provided proof of concept that an anti-TNFR2 treatment can mediate a potent GVL/GVT effect in different experimental models of hematological malignancy relapse after alloSCT through inhibition of Treg population. These results pave the way toward a novel immune checkpoint therapy to modulate alloreactivity after allo-HCT through the TNF/TNFR2 signaling pathway and, more widely, open new perspectives to amplify anti-tumor responses in solid cancers by directly targeting Tregs and tumor cells through their TNFR2 expression.



Graft versus Leukemia (GvL) - TNFR2 Monoclonal antibody - Donor lymphocytes infusion (DLI) - Treg lymphocytes - Alloreactivity

APPLICATIONS

- Enhancement of alloreactivity through Tregs depletion for the treatment of hematological malignancy relapse after alloHCT or DLI
- TNFR2-expressing tumor cell depletion

DEVELOPMENT PHASE

- In vivo POC in a mice model using anti-TNFR2 blocking mAb showing abolition of the protective effect of Treg after allo-HCT and the development of a potent GVL/GVT effect
- Clinical data on samples from post-transplant patients with leukemia relapse or GVHD, showing that regulatory T cells preferentially overexpress TNFR2 compared to effector T cells

COMPETITIVE ADVANTAGES

- Validation of a new indication for the blockade of the TNF/TNFR2 pathway, as TNFR2 blockade has never been tested to trigger an allogeneic immune response
- A technologically much simpler method to deplete Tregs compared to other ex-vivo cell sorting method

INTELLECTUAL PROPERTY

WO2017220711A1

PUBLICATIONS

- Moatti et al. 2021
- Leclerc et al. 2016

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Ref. project : 326