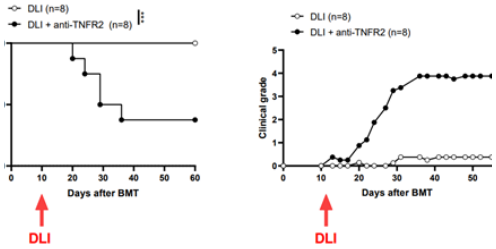
# MODULATION OF TNF-TNFR2 TO PROMOTE ALLOREACTIVITY AND ANTI-LEUKEMIA RESPONSE DURING BLOOD MALIGNANCY RELAPSE

**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


## CONTACT


+33 (0)1 44 23 21 50

industriels@erganeo.com


Ref. project : 326