

Società Italiana Ematologia Sperimentale
SIES

XVII CONGRESSO NAZIONALE SIES2022

ROMA

31 marzo, 1-2 aprile

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TARGETING THE CD6-ALCAM T CELL COSTIMULATORY PATHWAY AFTER ALLOGENEIC CELL TRANSPLANTATION FOR ACUTE GRAFT VERSUS HOST DISEASE (aGVHD) TREATMENT USING ANTI-CD6 MONOCLONAL ANTIBODY ITOLIZUMAB

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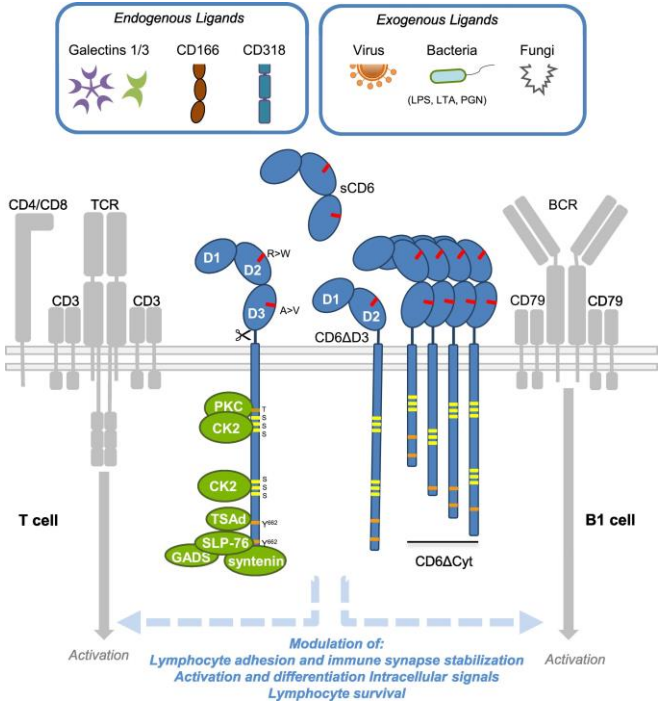
Disclosures of Benedetta Rambaldi

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Equillium	Yes	No	No	No	No	No	Travel grant

CD6-ALCAM pathway promotes T cell activation

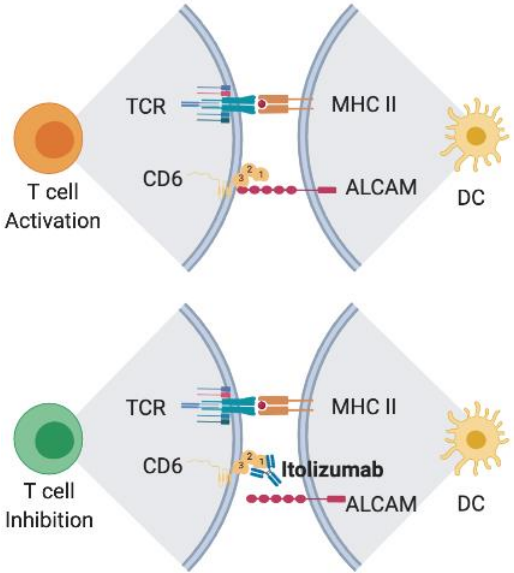


- CD6 is a co-stimulatory receptor expressed on T cells and some B and NK cells
- ALCAM, the ligand of CD6, is expressed on APC, epithelial and endothelial cells
- The CD6-ALCAM pathway promotes T cell activation, proliferation and trafficking playing

Consuegra-Fernández M et al. Autoimmunity Reviews; 2018

Aims of the study

- Characterize the *in vivo* expression of CD6 on T cells and ALCAM on Dendritic cells (DCs) after hematopoietic stem cell transplantation (HCT) in relationship with aGVHD
- Define the in vitro activity of Itolizumab in the regulation of T cell homeostasis in the setting of aGVHD
- Understanding the Itolizumab mechanisms of action



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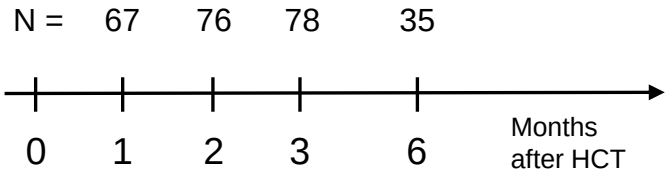
Study design and patients' clinical characteristics

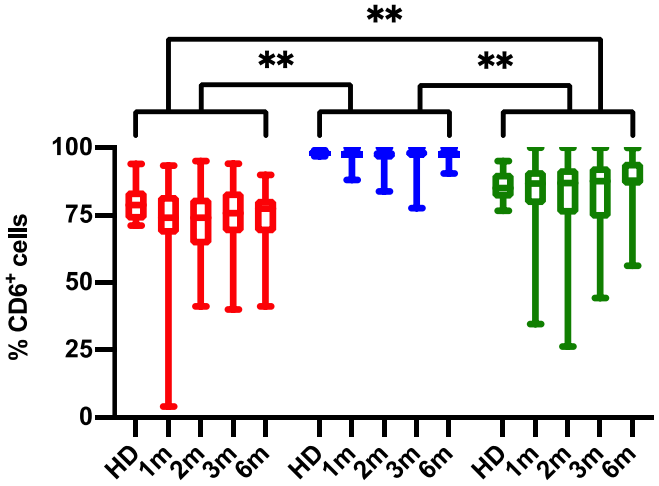
- Single center (DFCI)
- 95 Patients
- **Conditioning**: BuFlu
- **GVHD prophylaxis**: Tac + Mtx

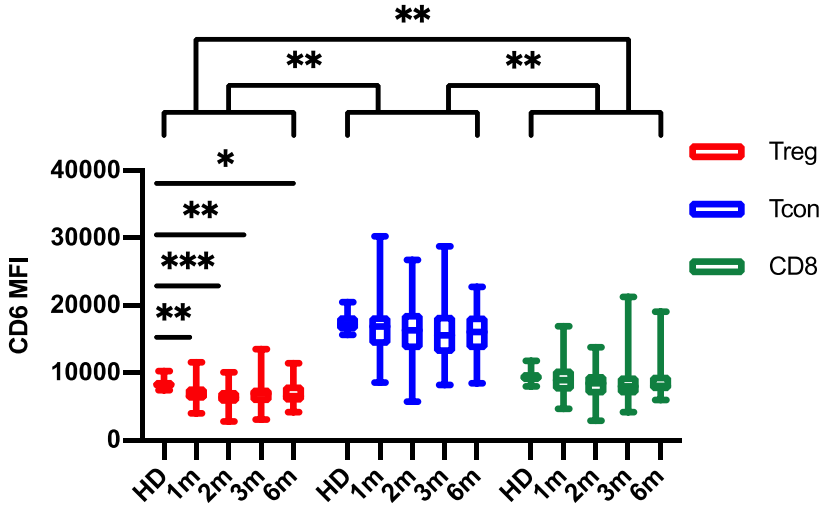
Sample collection for multicolor flowcytometry analysis



Clinical characteristics	N (%)
Age at HCT, median (range)	61 (19-76)
Pt sex, Male	55 (57.9%)
MUD MRD MMUD	63 (66.3) 26 (27.4) 6 (6.3)
PBSC	93 (98%)
MAC	48 (50.5)
aGVHD I-IV	42 (44.2)
aGVHD II-IV	26 (27.4)
Days to aGVHD onset, median (range)	50 (20-294)

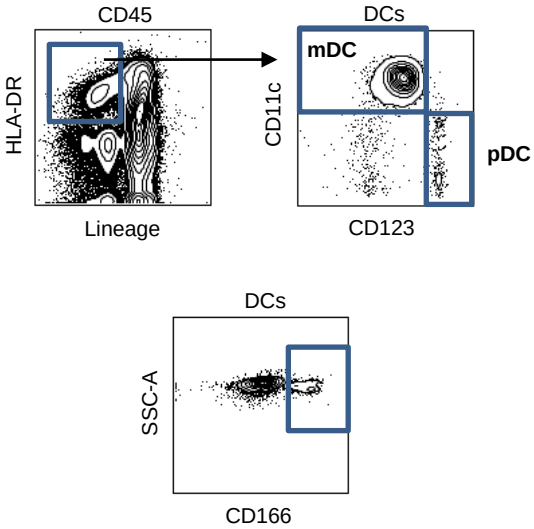
CD6 expression on T cells after HCT

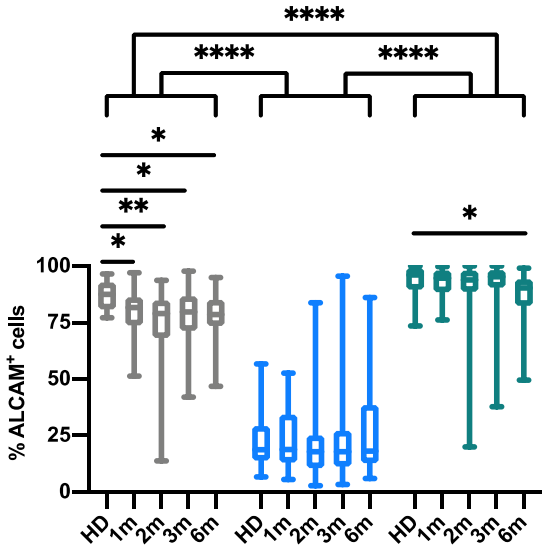


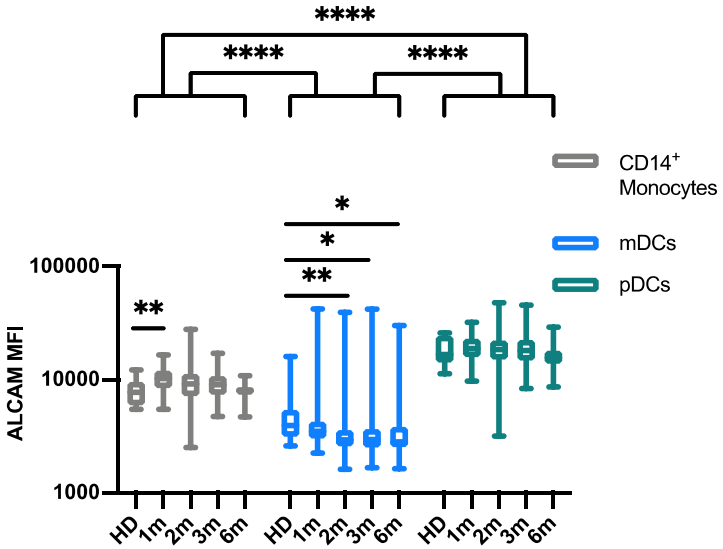


Rambaldi B. et al. under revision

ALCAM expression on APCs after HCT







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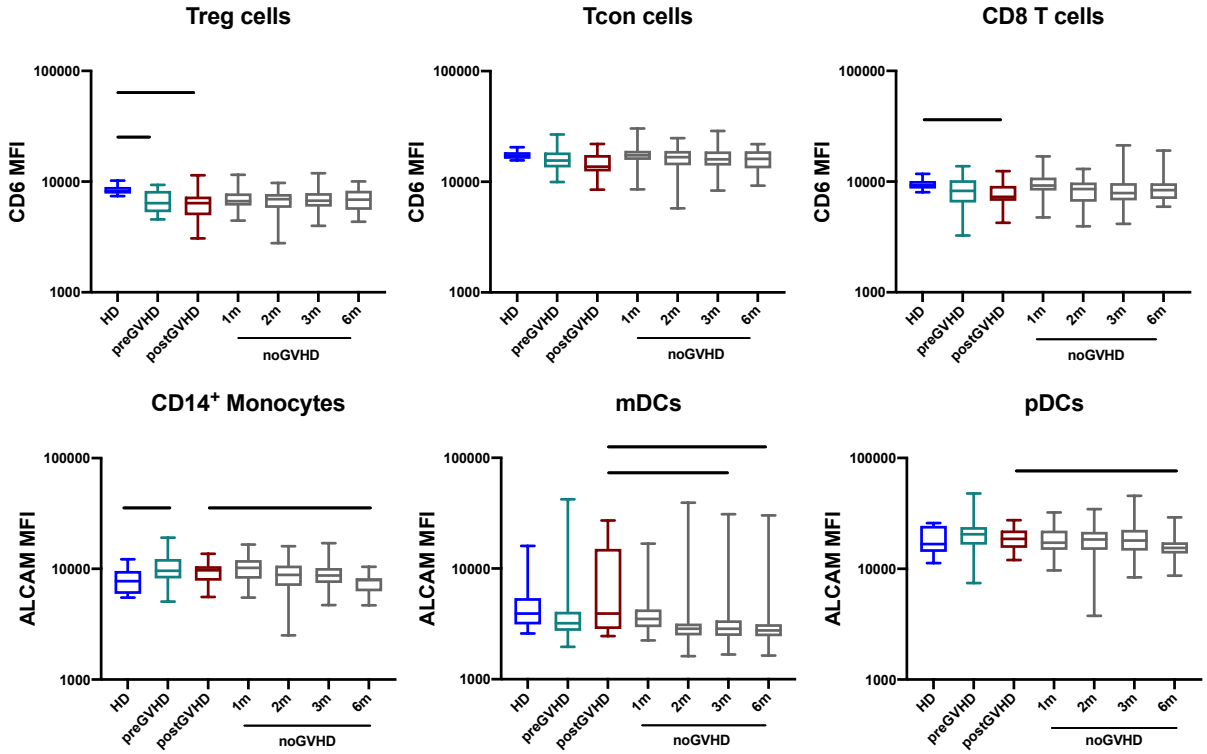
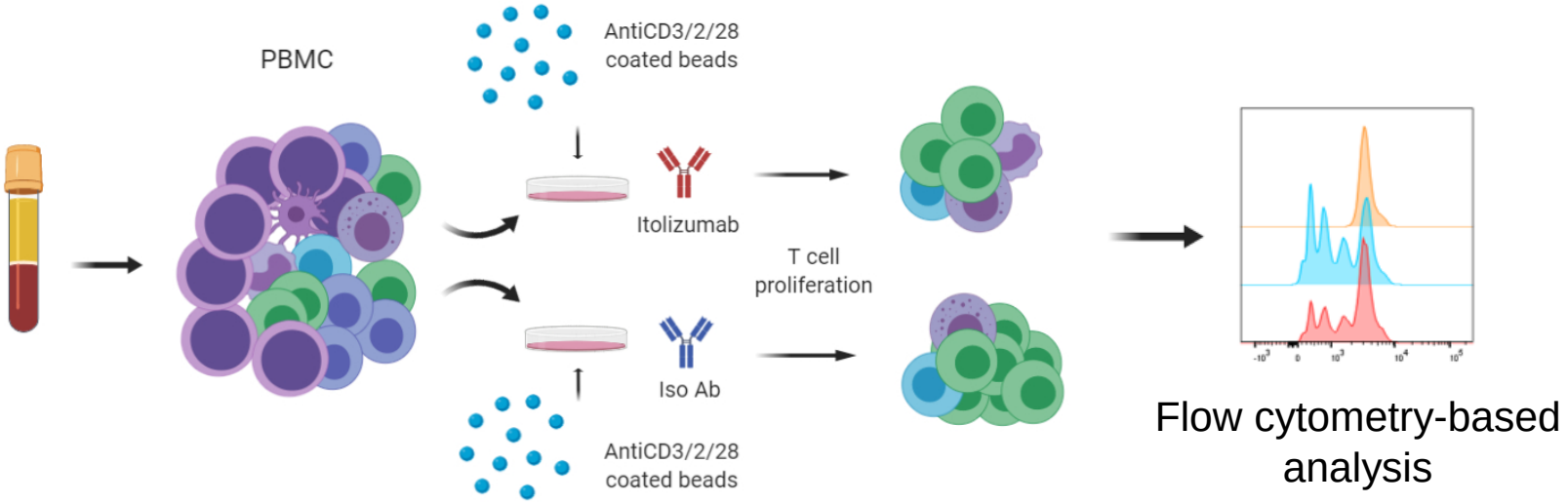
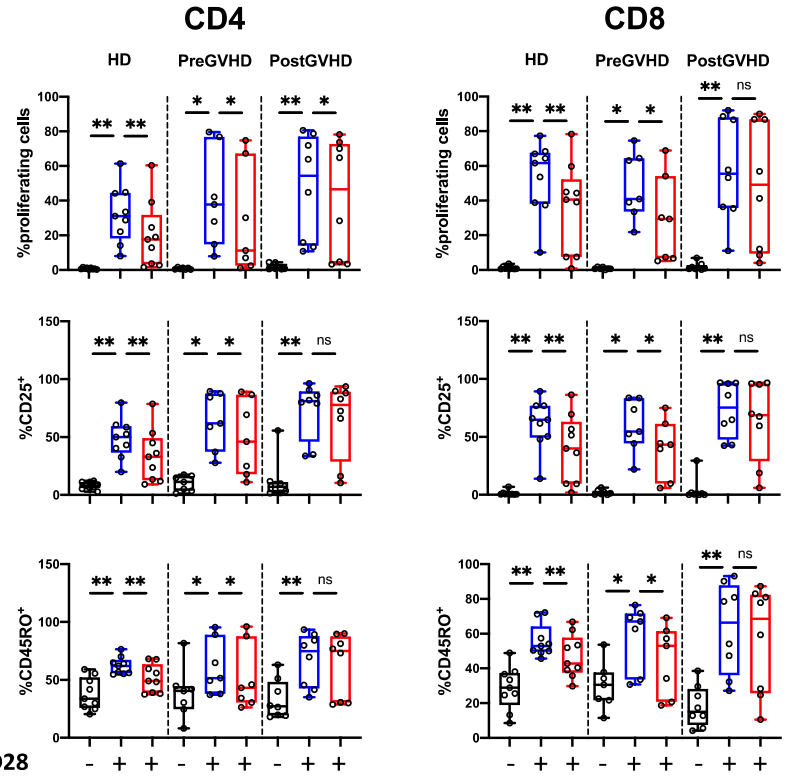
CD6 and ALCAM expression is preserved during aGVHD



In vitro activity of Itolizumab in aGVHD setting



Itolizumab inhibits T cells in aGVHD setting



- Cell alone
- Cetuximab
- Itolizumab

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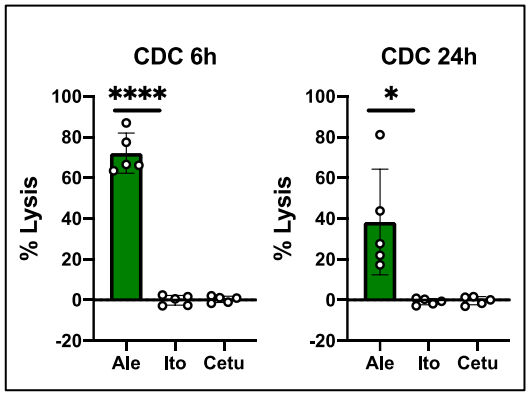
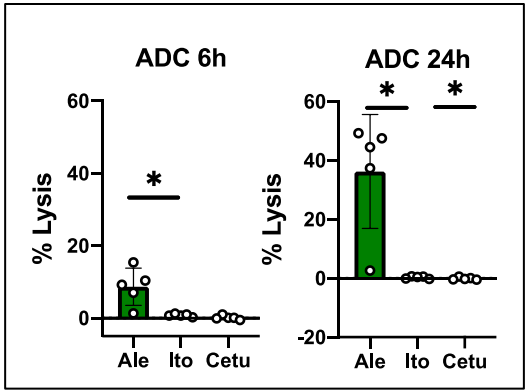
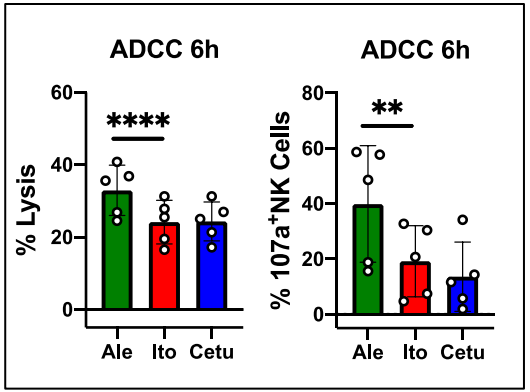
Itolizumab does not mediate CDC, ADC or ADCC







- Alemtuzumab (CTR+)
- Itolizumab
- Cetuximab (CTR-)

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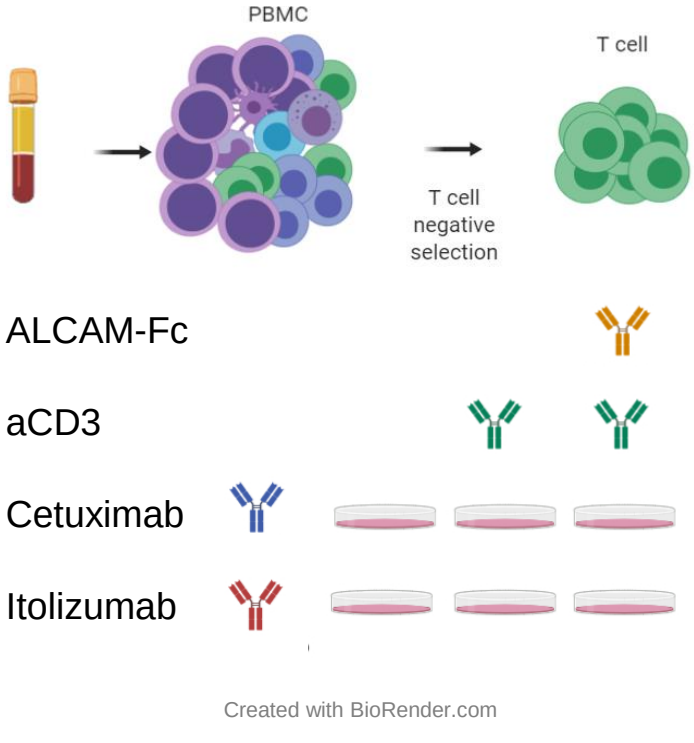
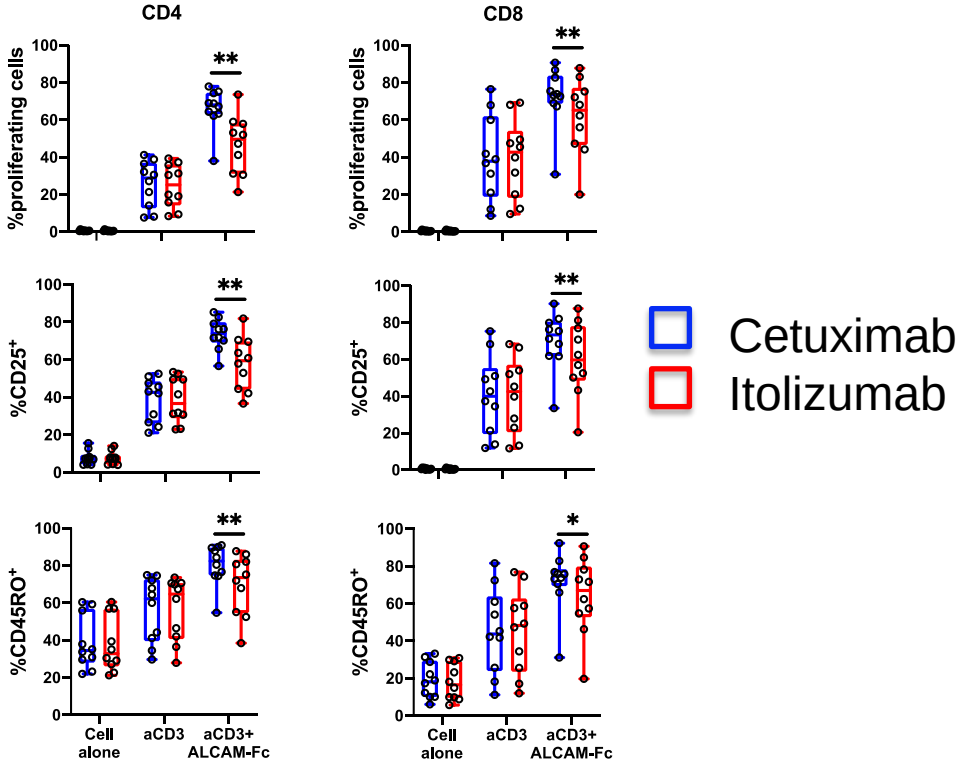
Itolizumab activity is dependent of ALCAM presence





Conclusions

- CD6+ T cells reconstitute rapidly after HCT (Tcon>CD8>Treg)
- ALCAM is expressed on majority of Monocyte and DCs after HCT
- Both CD6 and ALCAM expression on T cells and DCs respectively are preserved during aGVHD occurrence
- *In vitro*, Itolizumab inhibits T cell proliferation and activation in patients with aGVHD
- *In vitro*, Itolizumab abrogates the augmented ALCAM-Fc mediated T cell proliferation

- A phase I/II study using Itolizumab as first line treatment in combination with steroids for patients with aGVHD is currently ongoing (NCT03763318) and a phase III study will be soon launched in the US and in Europe too.

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