Early Reconstitution of CD6^{+} T Cells after Hematopoietic Cell Transplantation Identifies a Suitable Target for Acute Graft Versus Host Disease Treatment Using Anti-CD6 Monoclonal Antibody Itolizumab

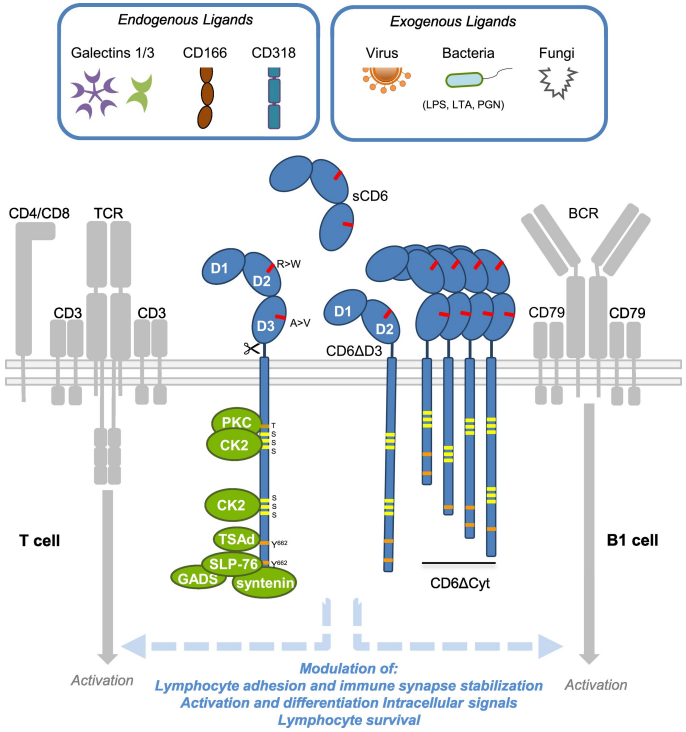
Benedetta Rambaldi, MD, Ph.D. Student

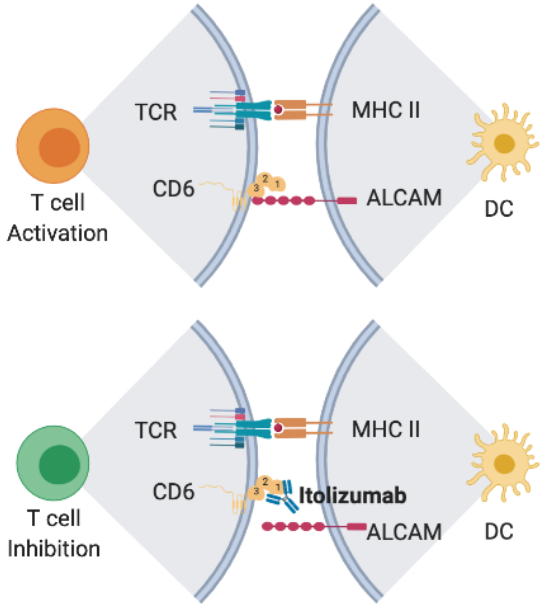
Dana-Farber Cancer Institute, Department of Hematologic Malignancies and Harvard Medical School, Boston, Massachusetts, USA

Disclosures

Equillium: Research Funding

CD6-ALCAM pathway promotes T cell activation





Consuegra-Fernández M et al. Autoimmunity Reviews; 2018

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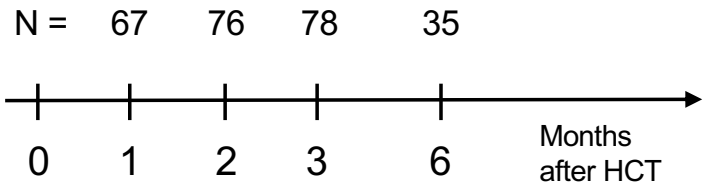
Aims of the study

1. 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
2. Define the *in vitro* activity of Itolizumab in the regulation of T cell homeostasis in the setting of aGVHD
3. Understanding the Itolizumab mechanisms of action

Study design and patients' clinical characteristics

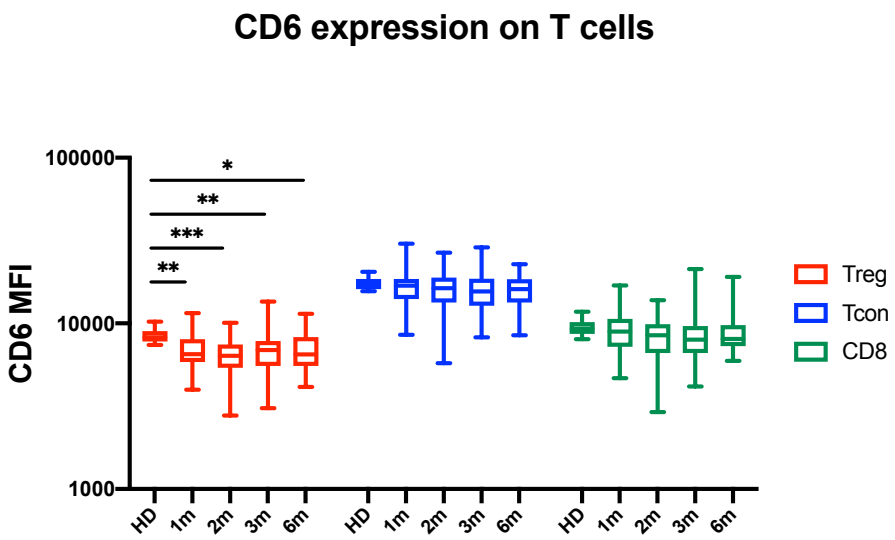
- 95 Patients
- **Conditioning**:
  Fludarabine + Busulfan
- **GVHD prophylaxis**:
  Tacrolimus + Methotrexate

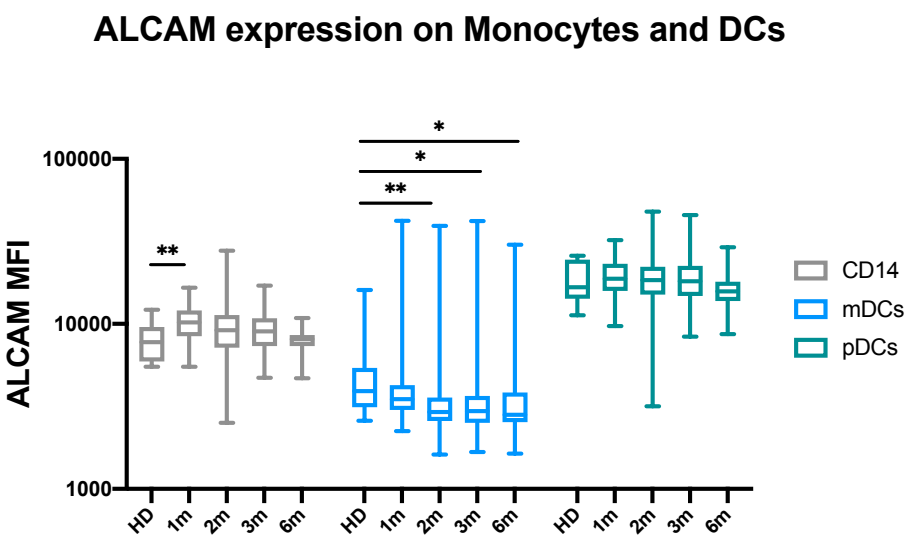
Sample collection for multicolor flowcytometry analysis



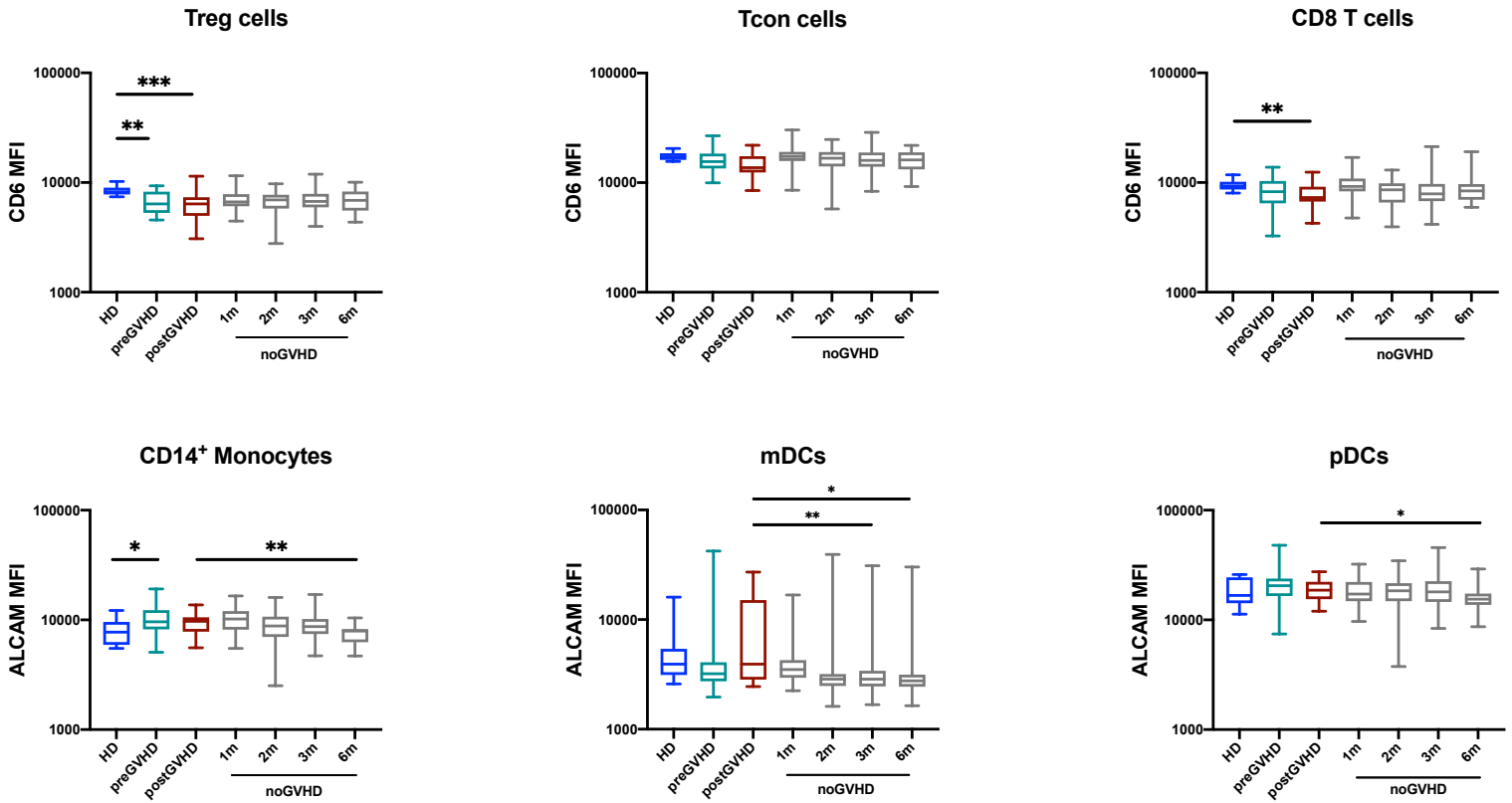
Clinical characteristics	N (%)
Age at HCT, median (range)	61 (19-76)
Pt sex, Male	55 (57.9%)
MUD MRD MMUD	63 (66.3) 26 (27.4) 6 (6.3)
PBSC	93 (98%)
MAC	48 (50.5)
aGVHD I-IV	42 (44.2)
aGVHD II-IV	26 (27.4)
Follow-up (days), median (range)	237 (87-591)

CD6 and ALCAM expression after HCT

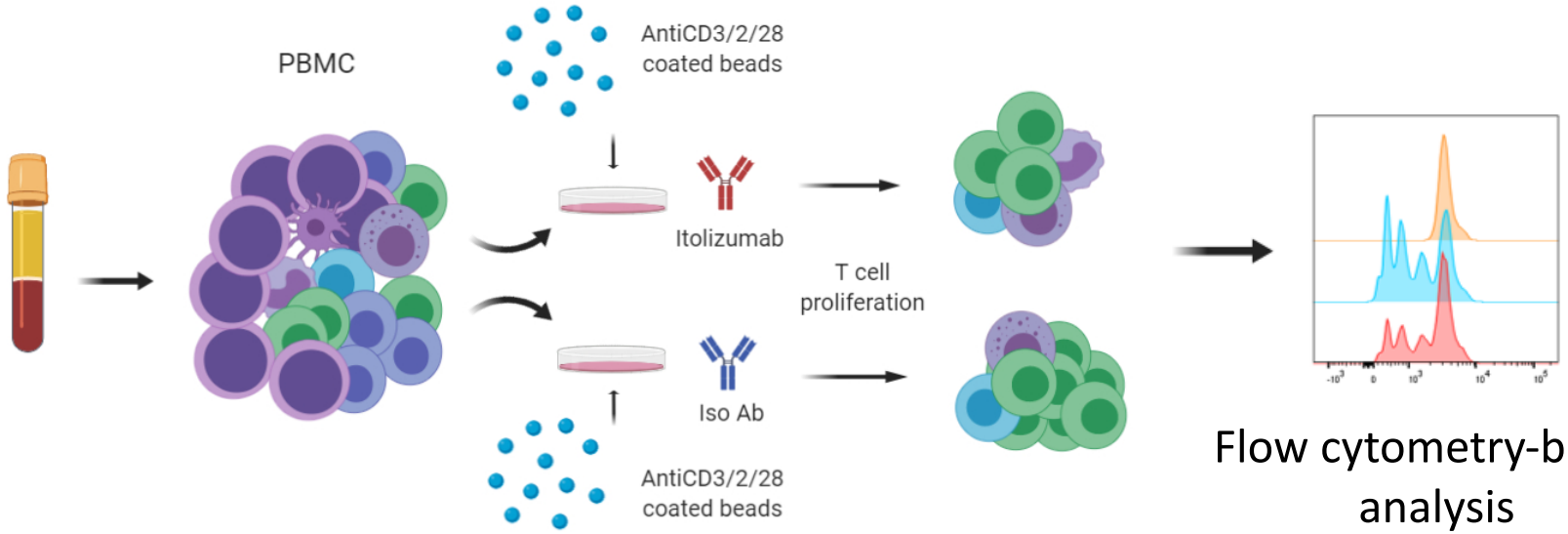




The expression of CD6 and ALCAM is preserved during aGVHD



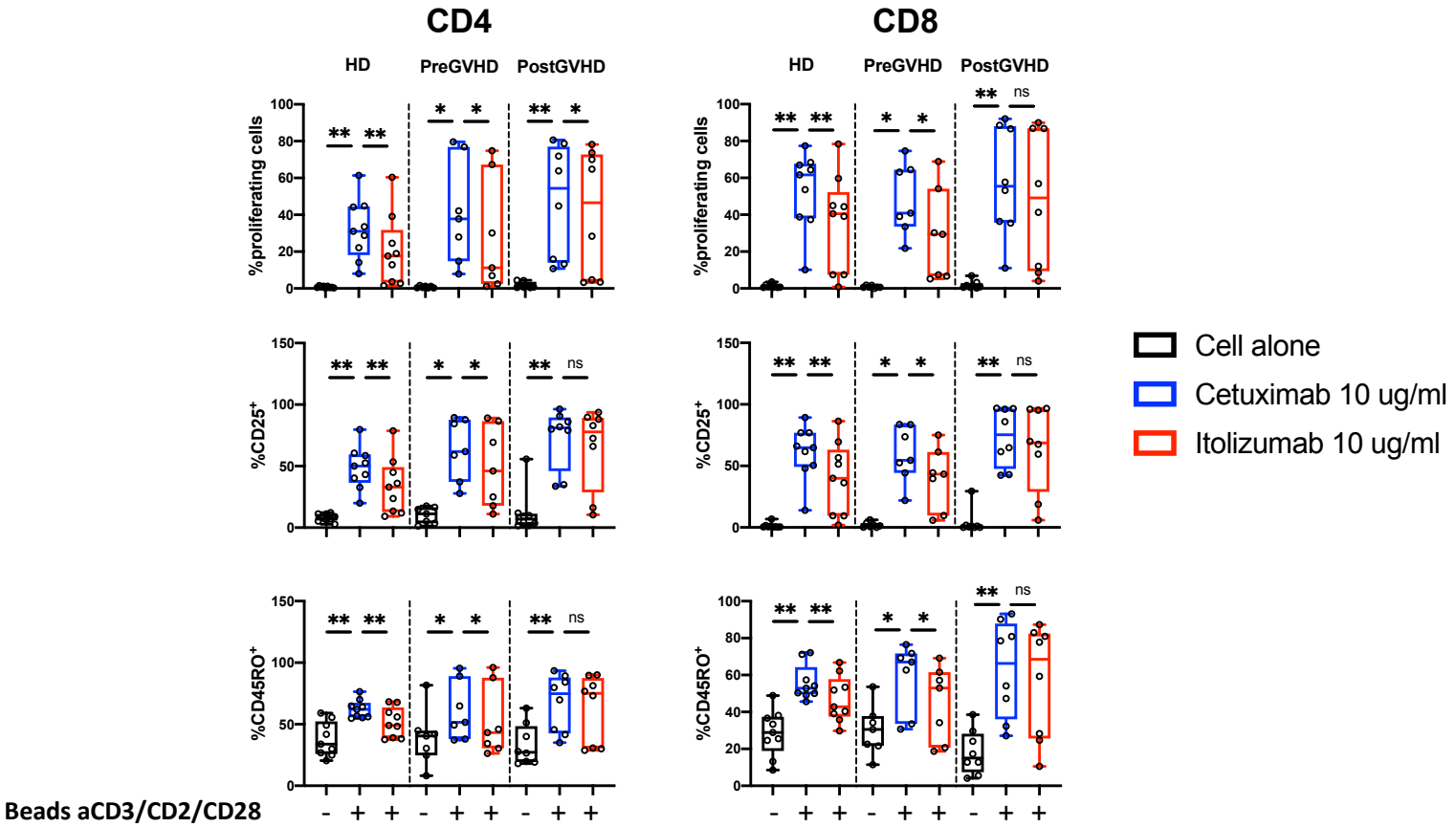
In vitro activity of Itolizumab in aGVHD setting



Flow cytometry-based analysis

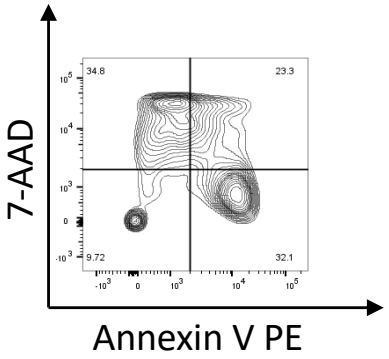
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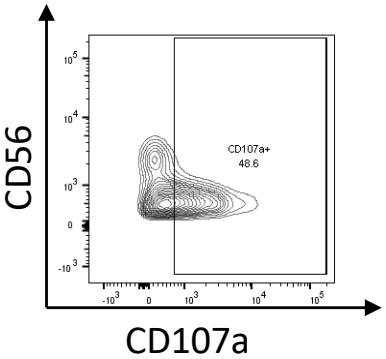
Itolizumab inhibits T cells in aGVHD setting

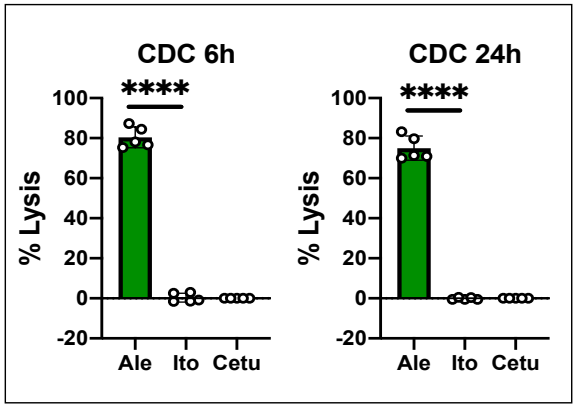


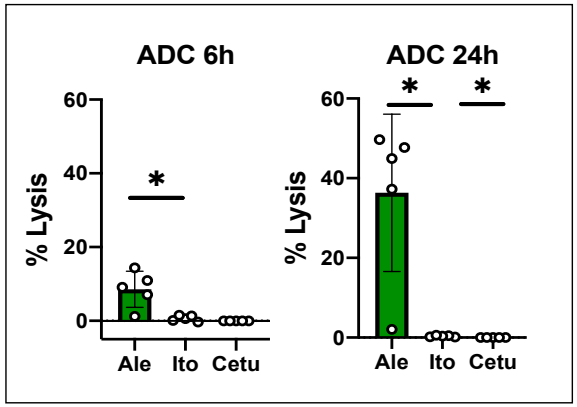
Itolizumab does not mediate CDC, ADC or ADCC

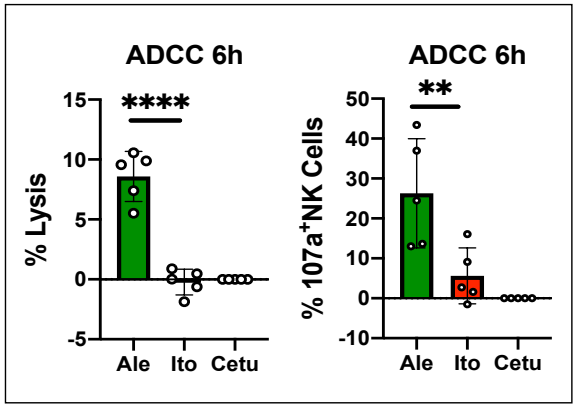
- Itolizumab
- Alemtuzumab (CTR+)
- Cetuximab (CTR-)



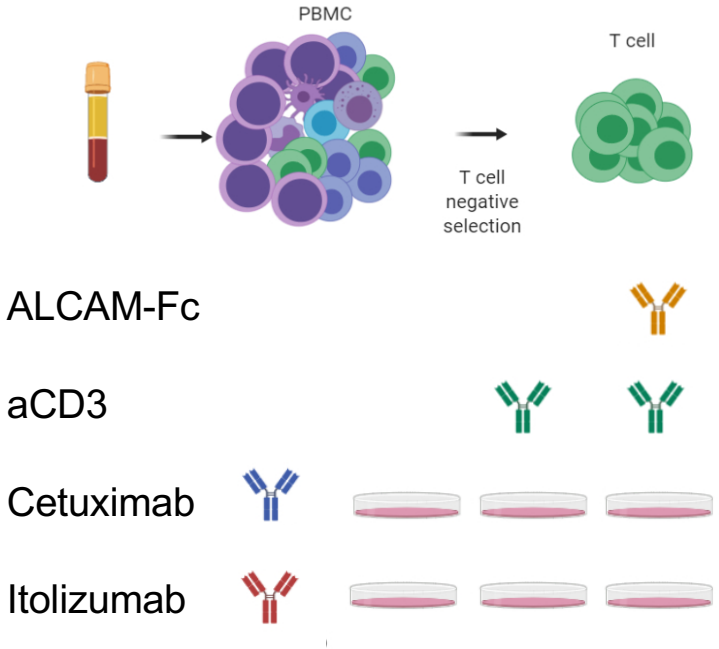




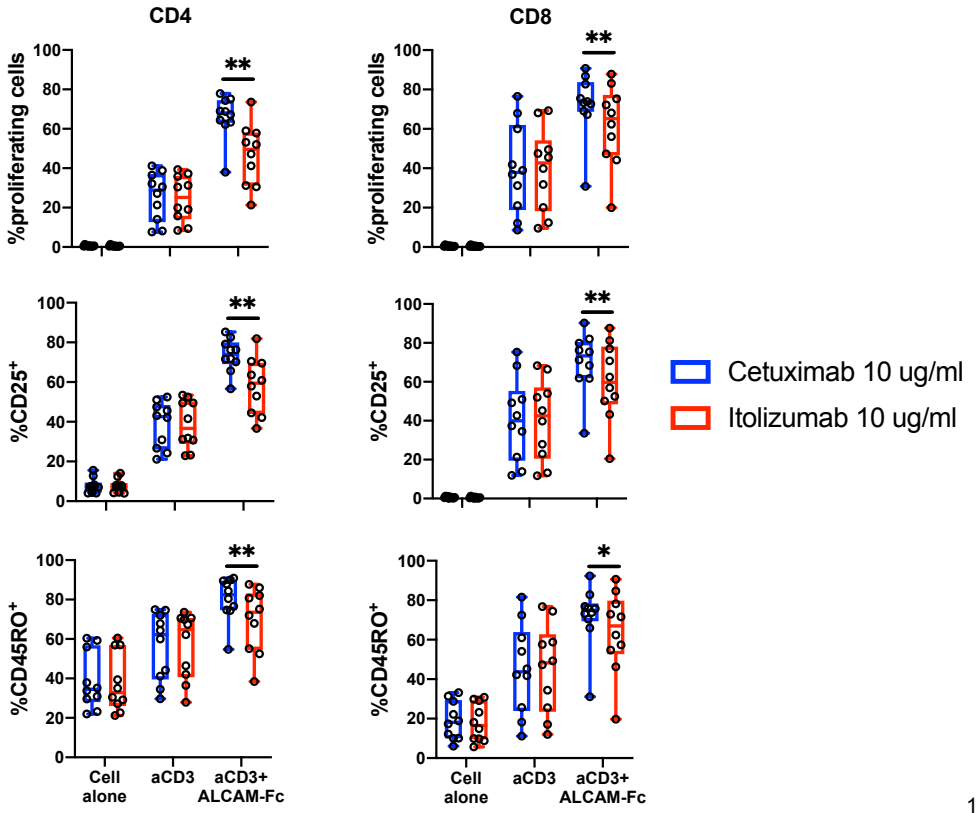




Itolizumab activity is dependent to the presence of ALCAM in the system



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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)

Acknowledgment

Ritz' Laboratory,
Dana-Farber Cancer Institute
Carol Reynolds
Sharmila Chamling Rai
Takeru Asano
Yohei Arihara
Jerome Ritz

Department of Data Science,
Dana-Farber Cancer Institute
Haesook Kim

BMT Unit
Dana-Farber Cancer Institute
John Koreth
Mahasweta Gooptu
Corey Cutler
Sarah Nikiforow
Vincent T. Ho
Joseph H. Antin
Rizwan Romee
Robert J. Soiffer

Equillium
Cherie Ng
Jeanette Ampudia
Stephen Connelly

DIMET Ph.D. Program
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