

HIV-specific CD8⁺ T-cell responses in HIV-1 infected individuals after allo-HSCT Results from the IciStem cohort

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BACKGROUND:

So far the only medical intervention to cure HIV has been allogeneic hematopoietic stem cell transplantation (allo-HSCT). In this study we describe the restoration kinetics of the T-cell compartment including HIV-specific CD8⁺ T-cell responses primed after allo-HSCT in a unique cohort of HIV-positive individuals with hematological malignancies.

PATIENTS:

The IciStem project includes to date 30 HIV-infected patients who received an allogeneic transplant. PBMC samples were available from 16 patients, (4x CCR5Δ32/Δ32, 2x CCR5Δ32/wt).

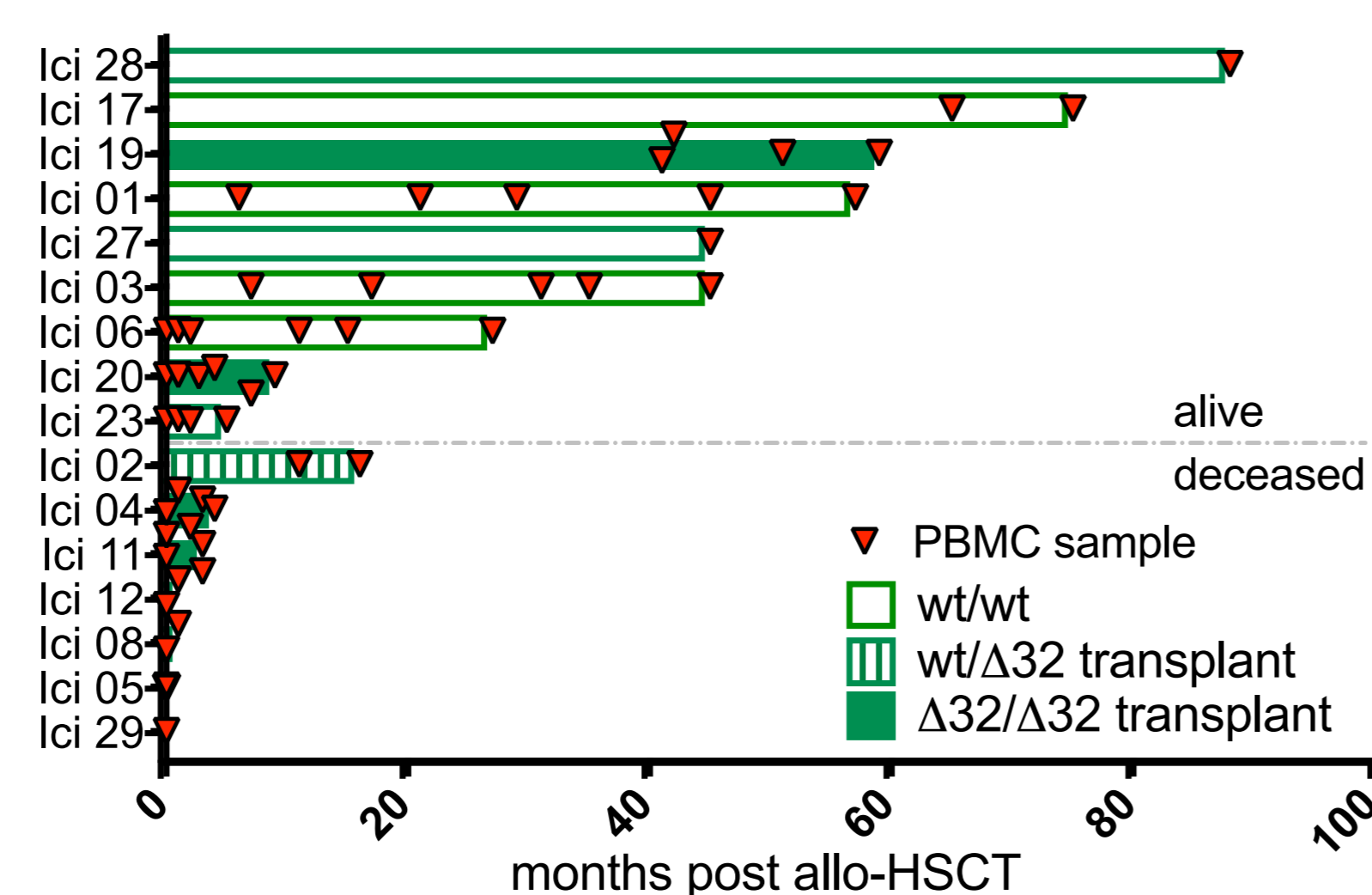


Figure 1: Patient sampling. Bars indicate time of follow-up, triangles sampling.

RESULTS:

1. Reconstitution of the T-cell compartment in an HIV-positive cohort after allo-HSCT

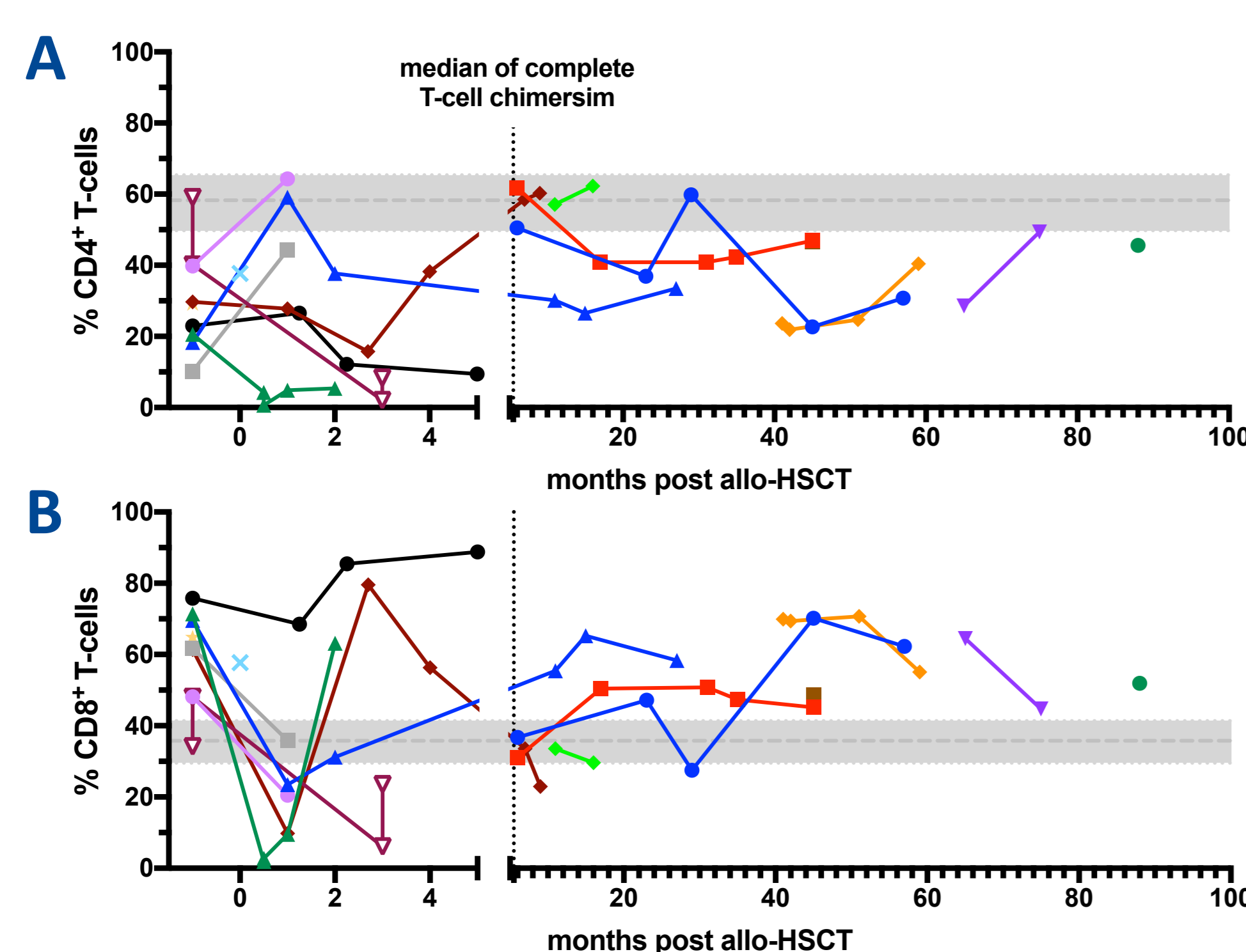


Figure 2: Frequency of CD4⁺ (A) and CD8⁺ (B) T-cells in % of CD3⁺ T-cells. Grey lines show the median and 25% and 75% percentiles in a cohort of healthy controls (n=30).

Upon allo-HSCT CD8⁺ T-cell frequencies dropped whereas CD4⁺ T-cell frequencies partially increased. About two months after allo-HSCT, CD4⁺ T-cell frequencies dropped again with a concomitant rise of CD8⁺ T-cell frequencies.

2. The early months post allo-HSCT are marked by high levels of T-cell activation and exhaustion

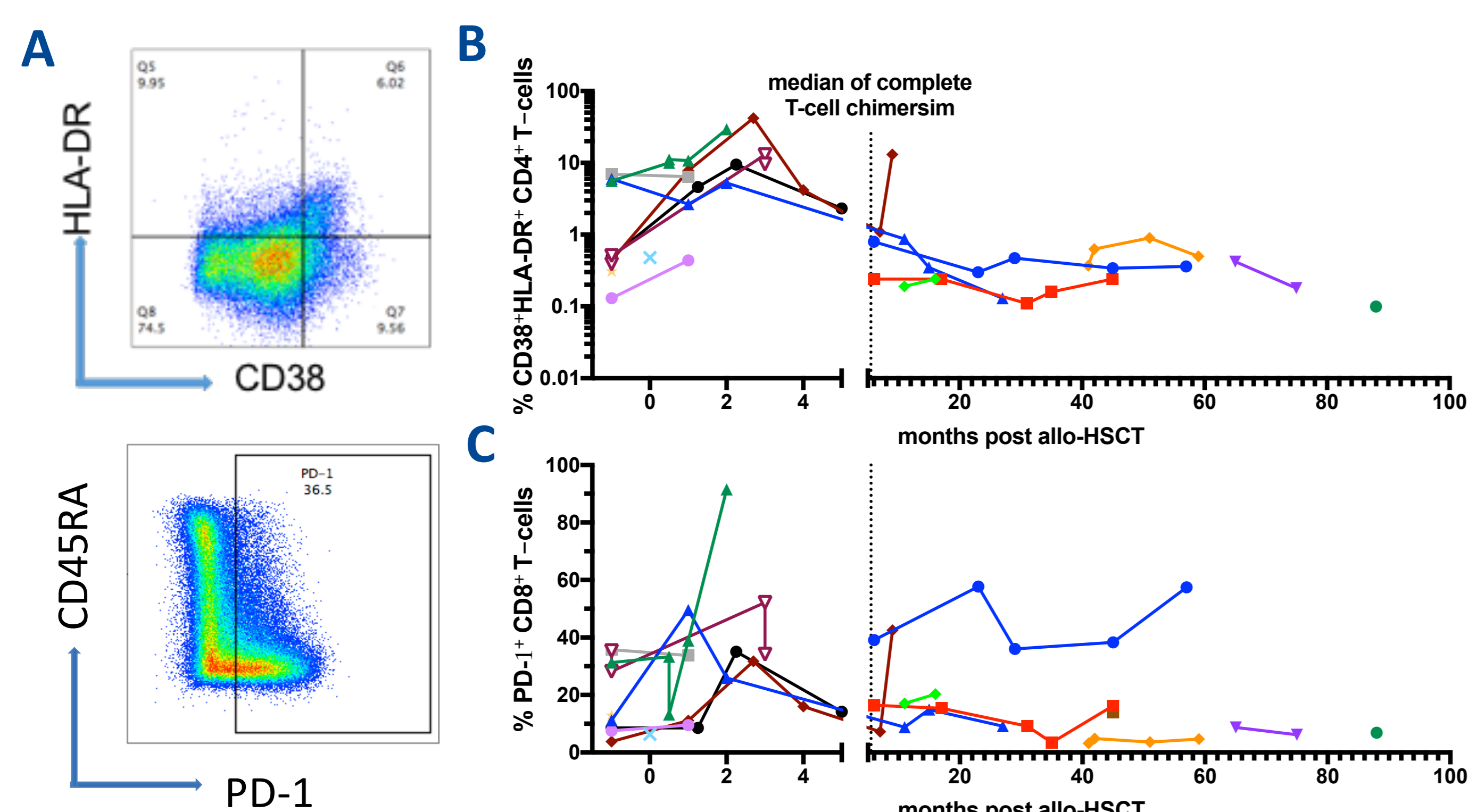


Figure 3: Representative FACS plots (A) and frequency of CD38⁺HLA-DR⁺ CD4⁺ T-cells (B) and PD-1⁺ CD8⁺ T-cells (C) in % of CD3⁺ T-cells.

Activation- and exhaustion-markers peaked few weeks after allo-HSCT.

METHODS:

T-cell frequencies, differentiation pattern as well as HIV co-receptors, activation-, proliferation-, exhaustion- and migration-markers were characterized via flow cytometry. To estimate breadth and quality of the HIV-specific T-cell responses, multiparameter ex vivo intracellular cytokine staining (ICS) was performed using HIV Gag, Pol and Nef and CMV-peptide pools.

3. HIV-specific immune responses are weak but recur after allo-HSCT

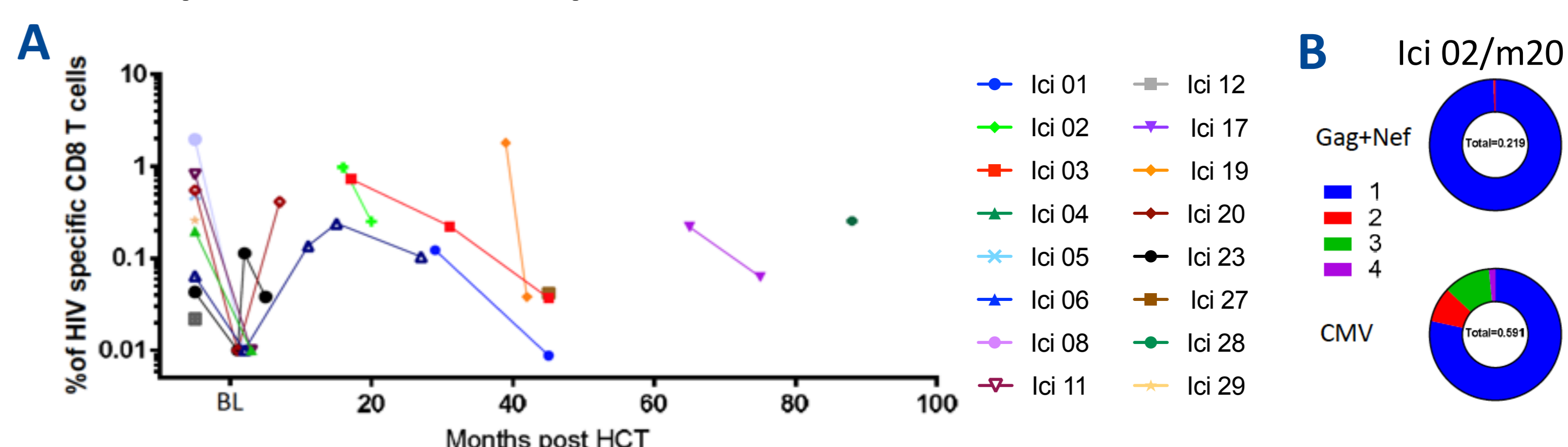


Figure 4: Frequency of HIV-specific CD8⁺ T-cells. Responses against Pol, Nef and Gag derived peptide pools (A). Number of cytokines produced after restimulation with Gag- and Nef- versus CMV derived peptide pools (B).

HIV-specific CD8⁺ T-cell responses disappeared directly after HSCT and reemerged during the reconstitution period after allo-HSCT coinciding with the expansion of allogeneic CD8⁺ T-cells. This HIV-specific CD8⁺ T-cell response had limited functionality compared to CMV-specific CD8⁺ T cell responses.

CONCLUSIONS:

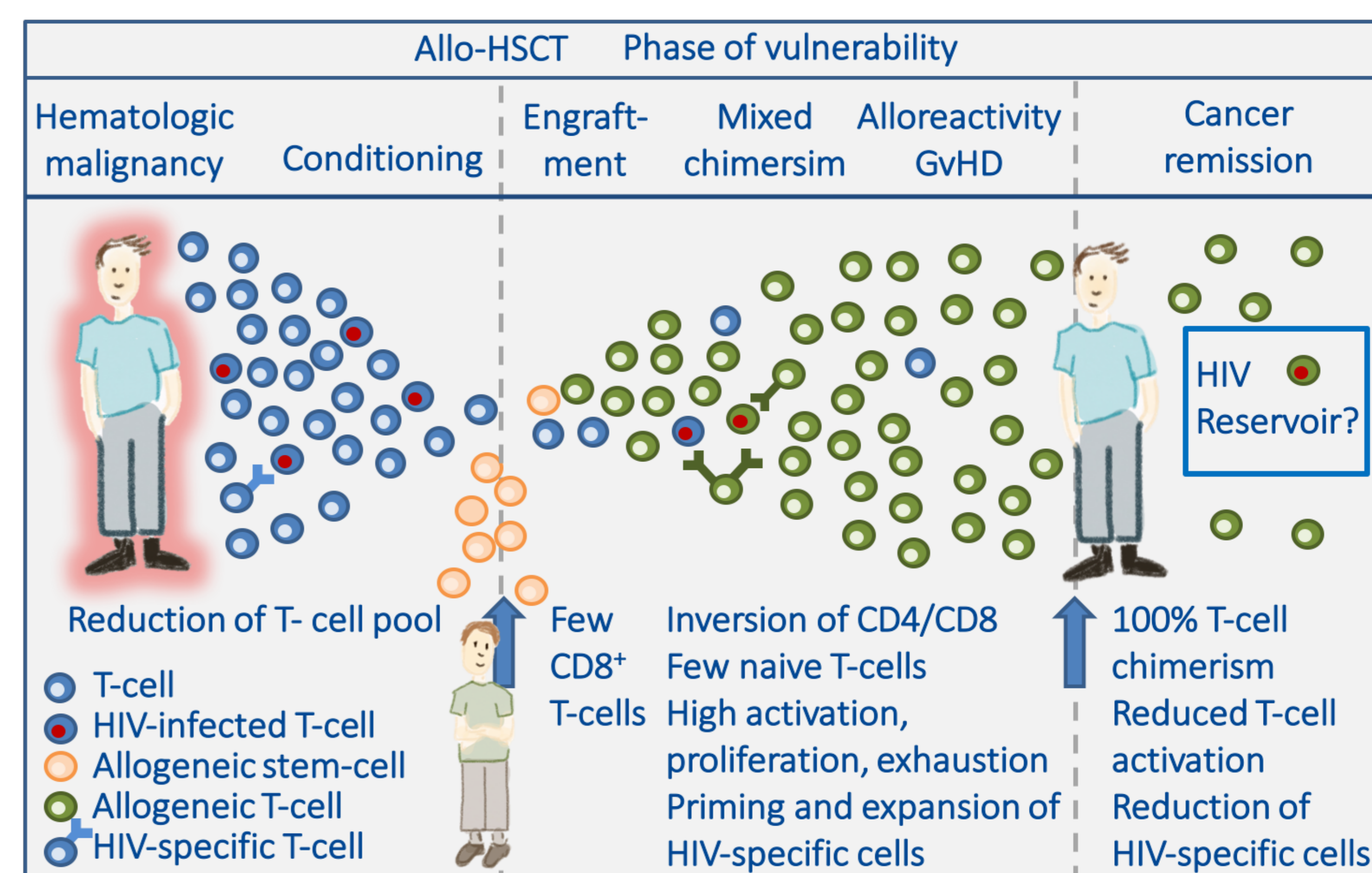


Figure 5: Timeline of hematological events and T-cell reconstitution pre and post allo-HSCT in an HIV-infected cohort.

Immune reconstitution in the study participants was slow and heterogeneous after allo-HSCT and accompanied by the *de novo* development of weak HIV-specific T-cell responses. There is an initial short phase of high T-cell activation that may constitute a window of vulnerability for the reseeding of viral reservoirs. Our findings point out the importance of maintaining ART during the first months after allo-HSCT.

ACKNOWLEDGEMENTS:

We thank the patients and donors for their participation. This project is funded by amfAR. JSzW and JME receive funding from the DZIF and are members of the EHVA consortium. (email: j.eberhard@uke.de)