Dextramer® CMV Kit used in Clinical Study Shows that Early Presence of CMV-specific T Cells Impacts CMV Reactivation Risk after Allo-HCST Transplantation

Tassi, E. *et al.* Cytomegalovirus-specific T cells restricted for shared and donor human leukocyte antigens differentially impact cytomegalovirus reactivation risk after allogeneic hematopoietic stem cell transplantion. Haematologica 2023. 108, 1530-1543. https://doi.org/10.3324/haematol.2022.280685

Background

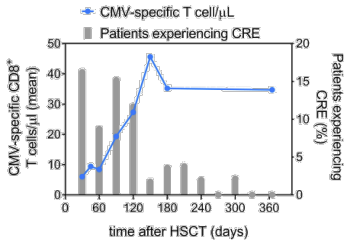
Reactivation of CMV is an important cause of morbidity and mortality in allogeneic hematopoietic stem cell transplantation (HSCT) recipients. Reconstitution of CMV immunity after immunosuppressive therapy post-transplantation is vital to prevent viral infection in CMV seropositive recipients. This prospective study reports the use of the Dextramer® CMV kit to examine the numbers of circulating CD8⁺ T-cells restricted for shared, host or donor-specific HLA over time after HSCT and how they relate to risk of CMV reactivation.

Results

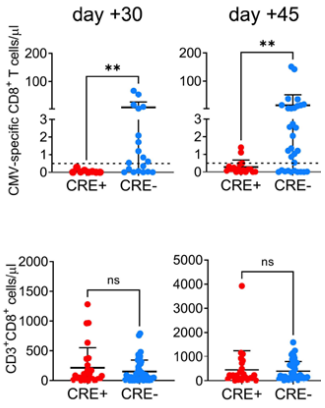
- CMV-related clinically relevant events (CRE) happen most frequently within 90-120 days after HSCT when the amount of CMV specific CD8⁺ T cells are low (**Fig. 1A**).
- Enumeration of CMV-specific T cells using the Dextramer® CMV kit confirmed that the presence of CMV-specific CD8⁺ cells is a reliable early predictor of protection against viral reactivation (**Fig. 1B-C**). The prediction by CMV-specific T cells is earlier than the same prediction can be made with functional assays (IFN-γ ELISpot).
- The Dextramer® CMV kit was also used to analyze the fate of both host and donor T cells according to their HLA restriction. Immunosuppressive therapy had permanently wiped-out recipient host-restricted T cells that didn't recover. Shared restricted CMV-specific donor derived T cells displayed a more differentiated phenotype and persisted longer time than donor-restricted counterparts (**Fig. 1D-E**).

Fig.1. Detected CMV-specific Dex⁺CD8⁺ T cells predict risk of CMV reactivation

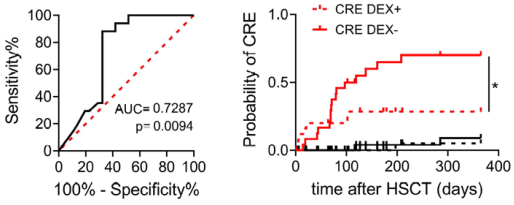
A CMV-specific immune response and CRE events



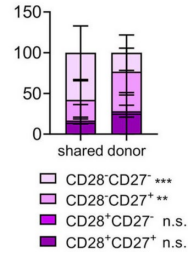
B Quantification of CMV-specific CD8⁺ T cells in patients with or without CRE events



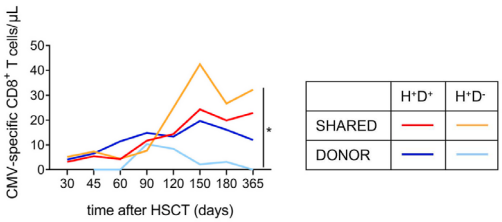
C ROC and Competitive Risk analysis of protective effect of at least 0.5 CMV-specific CD8⁺ T cells/µl at 45 days after HSCT



D Differentiation phenotype of CD8⁺ CRE Dextramer⁺ T cells restricted for shared or donor-specific HLA



E Development of circulating CMV-specific CD8⁺ T cell populations over time according to HLA type



Conclusions

- Monitoring CMV-specific T cells in peripheral blood with the Dextramer® CMV kit (IVD) allows for reliable early risk stratification of HSCT patients for timely antiviral treatment.
- This study illustrates how Dextramer® reagents can be used in clinical studies for sensitive enumeration and phenotypic characterization of antigen-specific immune cells over long periods of time.

CONTACT IMMUDEX
customer@immudex.com
IMMUDEX.COM