

Identify Patients at Risk of CMV Infection

60 to 80% of post-transplant patients are susceptible to high morbidity and mortality from cytomegalovirus (CMV) infection due to suppressing cell-mediated immunity.

Dextramer[®] CMV Kit enables reliable monitoring of CMV-specific CD8+ T cells in hematopoietic stem cell transplantation (HSCT) recipients for appropriate prophylactic treatment while avoiding potential toxicity from antiviral drugs.

- Quantify CMV-specific CD8+ T cells in blood
- Follow CMV immunity in post-transplant patients
- Predict patients at risk of CMV reactivation.

Guidance for Patient Management

A semi-quantitative assay intended for the identification and enumeration of CMV-specific CD8+ T cells that allows to:

- Measure reconstitution of CMV-specific CD8+ T cells
- Manage patient stratification: Delayed recovery of T cells, high-risk patients¹⁻⁴ (**Figure 1**).
- Guide therapeutic decision-making based on:
 - Cost-effective approach
 - Ensure the optimal treatment
 - Fewer side effects.

Features of Dextramer[®] CMV Kit

- The only available IVD assay** for the enumeration of CMV-specific CD8+ T cells in blood by flow cytometry⁵⁻⁷
- Ready-to-use kit:** Fast, robust, and reproducible assay
- Robust monitoring** of patients' CMV immunity
- Sensitive assessment** of the risk of CMV reactivation⁵⁻⁹
- Regulatory Status:** For in vitro diagnostics use in US and Europe^{8,9}

Patients at Risk of CMV Reactivation

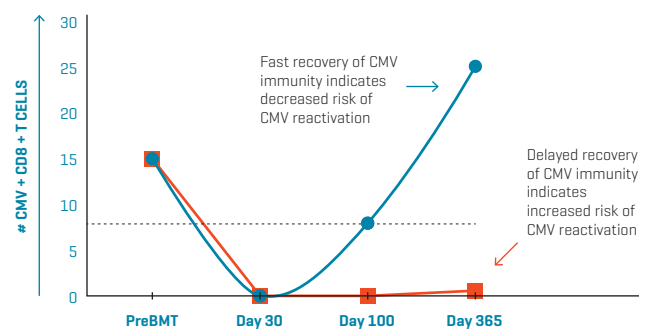


Figure 1. Model for CMV-specific T-cell immune monitoring in two post-transplant patients. The dashed line indicates the threshold for recovery of CMV T-cell immunity.

Dextramer[®] CMV Kit Application

- Use in conjunction with measurement of CMV viral load
- Testing is every other week starting on Day 30 post-transplant



Use of Dextramer[®] CMV Kit in Clinical Data

Clinical Data Support the Use of Dextramer[®] CMV Kit for assessment of CMV-specific immune status and risk of CMV reactivation in HSCT patients following immunosuppression

In a prospective study, 120 allogeneic HSCT patients were followed up for CMV reactivation in the first year post-transplant^{8,9}. The absolute number of CMV-specific CD8+ T cells was monitored in whole blood using Dextramer[®] CMV Kit and flow cytometry.

The number of CMV-specific CD8+ T cells at day 100 post-transplant showed a significant association with the risk of developing CMV reactivation (**Table 1**)^{8,9}.

No. of CMV-specific T cells	CMV Reactivation	
	Yes	No
< 7 cells/ μ L	90%	10%
\geq 7 cells/ μ L	26%	74%

Table 1. The relative risk was 3.4 times higher [95% CI: 1.57 – 7.46] for patients with < 7 cells/ μ L CMV+ CD8+ T cells compared to patients with \geq 7 cells/ μ L CMV+ CD8+ T cells^{8,9}

Dextramer[®] CMV Kit - Product Description

The Dextramer[®] CMV Kit is for in vitro diagnostic (IVD) use in HSCT patients¹⁰.

Europe [CE-IVD]

- 8 Specificities, 7 alleles:
 - HLA-A*0101/VTEHDLLY
 - HLA-A*0201/NLVPMVATV
 - HLA-A*0301/KLGGALQAK
 - HLA-A*2402/QYDPVAALF
 - HLA-B*0702/RPHERNGFTVL
 - HLA-B*0702/TPRVTGGGAM
 - HLA-B*0801/ELRRKMMYM
 - HLA-B*3501/IPSINVHHY
- Negative Control

US [IVD]

- 5 Specificities:
 - HLA-A*0101/VTEHDLLY
 - HLA-A*0201/NLVPMVATV
 - HLA-B*0702/TPRVTGGGAM
 - HLA-B*0801/ELRRKMMYM
 - HLA-B*3501/IPSINVHHY
- Negative Control
- CD3/CD4/CD8 Antibodies included

References

1. Cwynarski, K. *et al.* Direct visualization of cytomegalovirus-specific T cell reconstitution after allogeneic stem cell transplantation. *Blood* [2001] 97:1232.
2. Gratama, J.W. *et al.* Immune monitoring with iTAg MHC Tetramers for prediction of recurrent or persistent cytomegalovirus infection or disease in allogeneic hematopoietic stem cell transplant recipients: a prospective multicenter study. *Blood* [2010] 116:1655.
3. Gratama, J.W. *et al.* Tetramer-based quantification of cytomegalovirus [CMV]-specific CD8+ T lymphocytes in T-cell depleted stem cell grafts and after transplantation may identify patients at risk of progressive CMV infection. *Blood* [2001] 98: 1358.
4. Borchers, S. *et al.* Sequential anti-cytomegalovirus response monitoring may allow prediction of cytomegalovirus reactivation after allogeneic stem cell transplantation. *PLoS One* [2012] 7: e50248.
5. Tario, J.D. *et al.* Dextramer reagents are effective tools for quantifying CMV antigen-specific T cells from peripheral blood samples. *Cytometry B Clin. Cytom.* [2015] 88: 6.
6. Vidal-Castiñeira JR, *et al.* Effect of Type of Dialysis on CMV-Specific CD8+ T Cells in Kidney Transplant Candidates. *Front Immunol.* 2019 Jul 19;10:1680.
7. Chen, G. L. *et al.* Low-Level Cytomegalovirus Antigenemia Promotes Protective Cytomegalovirus Antigen-Specific T Cells after Allogeneic Hematopoietic Cell Transplantation. *Biol Blood Marrow Transplant* [2020] 26[11]:2147–2154.
8. TF1000.07 Dextramer CMV Kit Package Insert US [IVD], Immudex.
9. TF1010.07 Dextramer CMV Kit Package Insert EU [CE-IVD], Immudex.
10. K153538 510(k) premarket notification

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