Utilization of the QuantiFERON-Cytomegalovirus Assay to Guide Duration of Antiviral Prophylaxis in CMV-Mismatched Solid Organ Transplant Recipients

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Background

- Cytomegalovirus is the most common viral infection affecting solid organ transplant (SOT) recipients. CMV seronegative recipients of organs from seropositive donors (D+/R-) are at highest risk for CMV disease.
- Antiviral prophylaxis is the preferred method for prevention. However, the duration of prophylaxis varies among institutions, ranging from 3 to 12 months, depending on degree of immunosuppression and type of organ transplanted. Antiviral prophylaxis is also associated with high cost and toxicity.
- Ideally, an optimized risk stratification of SOT recipients would guide duration of antiviral prophylaxis at the individual patient level.
- An investigational interferon gamma (IFN-γ) release assay (IGRA), the QuantiFERON-CMV (QFT-CMV; Qiagen, Germantown, MD), detects an IFN-γ CD8 T-cell response specific to CMV antigens in whole blood.
- Our aim is to evaluate QFT-CMV assay as indirect evidence for the development of CMV-specific immunity in CMV D+/R- SOT patients receiving anti-CMV prophylaxis.

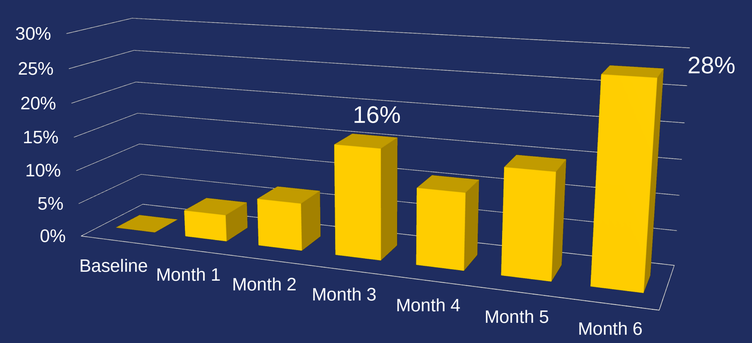
Patients

Variable	N=31
Age in years, median (IQR)	56 (48 – 63)
Male, N (%)	21 (68%)
Transplant type, N (%)	- Kidney 14 (45%) - Liver 8 (26%) - Heart 4 (13%) - Lung 2 (6%) - Pancreas 1 (4%) - Combined 2 (6%)
Induction Immunosuppression N (%)	- Methylprednisolone 20 (65%) - Thymoglobulin 9 (29%) - Basiliximab 8 (26%) - Alemtuzumab 6 (19%) - Other 2 (6%)
Maintenance Immunosuppression N (%)	- Prednisone 26 (84%) - Mycophenolate 29 (94%) - Tacrolimus 30 (97%) - Azathioprine 2 (6%) - Cyclosporine 1 (4%)
CMV prophylaxis N (%)	28 (90%)
CMV disease, N (%)	6 (19.4%) - All had negative QFT-CMV prior to diagnosis
Relapse, N (%)	3/6 (50%) - All relapses had negative QFT-CMV prior to diagnosis

Methods

- Written informed consent was obtained from CMV D+/R- adult SOT recipients
- A whole blood sample obtained within 1 week of transplantation served as the baseline QFT-CMV result. Subsequently, QFT-CMV testing was performed monthly for 6 months post-transplantation.
- Patients were monitored for development of CMV disease for 1 year post-transplant. Definitions for active CMV infection and CMV disease are based on criteria recommended by the American Society of Transplantation.
- The QFT-CMV assay was performed per manufacturer instructions. Whole blood was collected into 3 (1 mL each) QTB-CMV specific collection tubes (i.e., mitogen control, nil control, and CMV-antigen). Tubes were shaken, incubated for 16 to 24 hours at 37°C and centrifuged to harvest plasma. Plasma was tested to measure the amount of IFN-γ using the QFT-CMV ELISA. The optical density (OD) of each well was measured using a microplate reader and results were analyzed using the QFT-CMV analysis software (v3.03).
- CMV antigen-nil values of 0.2 IU/mL or greater were considered positive, as recommended by the manufacturer.

Figure 1. Percent Positive QFT-CMV Tests by Month



Conclusions

- The proportion of patients positive by the QFT-CMV assay increased over the 6 month period post transplant.
  - Up to 28% at 6 months
- This reflects a higher likelihood of a protective immune response against CMV when immunosuppression is reduced.
- **All 6 patients who developed CMV disease had a negative QFT-CMV result prior to CMV diagnosis.**
- **CMV disease did not occur in patients with a positive CMV-QFT result**
- This assay may signal the optimal time to discontinue antiviral prophylaxis.
- Follow-up of all enrolled patients for up to 1 year post-transplant is ongoing to monitor for development of CMV disease.

References

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