Use of Cytomegalovirus T-Cell Immunity Panel (TCIP) to Predict the Risk of Recurrent Cytomegalovirus Infection in Solid Transplant Patients and Guide Appropriate Management

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Background

- Cytomegalovirus infection (CMV) is the most common opportunistic infection in solid organ transplant recipients (SOTR).
- Given significant morbidity and mortality of CMV infections, prevention of recurrent infection is essential.
- Predicting recurrent disease and determining who would benefit from secondary antiviral prophylaxis is currently poorly defined.
- CMV-specific T-cell assays are promising tools in determining presence of CMV immunity and may predict who should receive secondary prophylaxis.
- CMV T-Cell Immunity Panel (CMV-TCIP, Eurofins-Viracor, Lenexa, KS) is a commercially available assay that measures CMV-specific CD4+ and CD8+ T-cells responses.
- The goal was to evaluate the ability of commercially available CMV-TCIP in predicting the risk of CMV relapse.

Methods

- All data were collected after IRB approval approval. Data was collected primarily from the Northwestern Medicine Enterprise Data Warehouse with supplemental primary chart review by the lead author.
- CMV T-Cell Immunity Panel (CMV-TCIP, Viracor Eurofins, Lenexa, KS) was collected at the discretion of the TID attending caring for the patient; protocol suggested getting a CMV-TCIP around time of first negative test.
  - Use of 2° prophylaxis was at the discretion of the TID attending; in general <1 month if felt to be positive and ~3 months if negative. Was not protocol driven.
- Included patients: Solid transplant patients >18 years old, treated for detectable CMV viremia, completed CMV-TCIP before and after anti-viral treatment.
- Relapse was defined as detectable CMV viremia.
- Analysis was completed for total patient population and subgroup of patients with CMV-TCIP tests ± 21 days of first CMV viral load <137 IU/mL (CMV VL).
  - Subgroup was created to capture CMV-TCIP tests closer to completion of CMV treatment and hence better predict relapse rates.
- Descriptive and Cohen's Kappa statistics were used to assess association of relapse with assay results.

Results

	Total Patients N = 74	Complete Data Subgroup* N = 44 (59.5%)
Sex		
Female	38 (51.4%)	24 (54.5%)
Race		
White	56 (75.7%)	34 (77.2%)
Black	12 (16.2%)	5 (11.4%)
Asian	5 (6.8%)	5 (11.4%)
American Indian/Alaska Native	1 (1.4%)	0 (0%)
Transplant Type		
Liver	9 (12.2%)	6 (13.6%)
Lung	20 (27.0%)	13 (29.6%)
Kidney	24 (32.4%)	18 (41.0%)
Heart	13 (17.6%)	2 (4.5%)
SPK	4 (5.4%)	2 (4.5%)
SLK	2 (2.7%)	2 (4.5%)
Heart/Kidney	1 (1.3%)	0 (0%)
Liver/Kidney	1 (1.3%)	1 (2.3%)
CMV IgG Status		
D+/R+	18 (24.3%)	11 (25.0%)
D-/R-	2 (2.7%)	2 (4.5%)
D+/R-	45 (60.8%)	23 (52.3%)
D-/R+	9 (12.2%)	8 (18.2%)
Median Time CMV+ From Transplant	346 days	350 days
Average Absolute Lymphocyte Count at Time of TCIP Collection (Range)	1.03 K/UL (0.1 - 3.7 K/UL)	0.91 K/UL (0.1 - 2.9 K/UL)
Secondary Prophylaxis		
Yes	60 (81.1%)	38 (86.4%)
Duration of Secondary Prophylaxis (Median [Range])	71 days (0 - 614 days)	55 days (0 - 270 days)
2° Prophylaxis ≤ 30 days	6 patients	5 patients
2° Prophylaxis 31-90 days	30 patients	25 patients
TCIP Results^		
Positive CD4+ / Positive CD8+	31 (41.9%)	15 (34.1%)
Positive CD4+ / Negative CD8+	3 (4.1%)	1 (2.3%)
Negative CD4+ / Positive CD8+	29 (39.2%)	20 (45.4%)
Negative CD4+ / Negative CD8+	11 (14.8%)	8 (18.2%)

Table 1: Patient Demographics

* Patients with CMV-TCIP tests completed ± 21 days of the first negative CMV VL (<137 IU/mL)
^ Values representing presence or absence of either CD4+ or CD8+ T-cell immunity

	Total Patients N = 74	Complete Data Subgroup* N = 44
Total Relapses		
Yes	26 (35.1%)	17 (38.6%)
Relapse in Patients with Negative CD4+ T-Cell Immunity	17 (23.0%) OR 2.053, 95% CI [0.765, 5.507], P=0.153	12 (27.3%) OR 1.65, 95% CI [0.452, 6.026], P=0.449
Relapse in Patients with Negative CD8+ T-Cell Immunity	6 (8.1%) OR 1.5, 95% CI [0.458, 4.915], P=0.503	3 (6.8%) OR 0.75, 95% CI [0.160, 3.506], P=0.715
Relapse in Patients with Negative CD4+ or CD8+ T-Cell Immunity	19 (25.7%) OR 2.714, 95% CI [0.964, 7.641], P=0.059	13 (29.5%) OR 2.234, 95% CI [0.574, 8.692], P=0.246

Table 2: CMV T-Cell Immunity Results and Association with Relapse of Disease

- 74 patients were included in the total population (Table 1).
- 2° prophylaxis was given to 60 (81.1%) of total patients for a mean of 86 days (0-614 days) after the first negative CMV VL.
- Overall, 34 (45.9%) patients had positive CD4+ and 60 (81.1%) had positive $CD8^+$ CMV-TCIP values. 31 (41.9%) patients were positive for both cell types.
  - About ¾ of relapses occurred in patients with negative CD4+ or $CD8^+$ CMV-TCIP values (80.7% in total population, 82.3% in complete data population).
  - Relapse was less common in patients with positive CD4+ or $CD8^+$ CMV-TCIP values (14.1% and 33.3% respectively).
  - Patients with relapse had an average absolute lymphocyte count of 1.04 K/UL.
- 26 (35.1%) SOTRs had relapse of which 9 with positive $CD4^+$ and 20 with positive $CD8^+$ CMV-TCIP values (5 positive for both cell types).
- No association between specific test results and risk of relapse in the overall study population or the subgroup (Table 2).

Discussion

- Studies have shown that detectable CMV-specific immunity and higher absolute lymphocyte counts are associated with a lower risk of relapse and may be useful in determining need for 2° prophylaxis.
  - This would translate to more personalized therapies and could reduce antiviral adverse effects such as myelotoxicity and cost to the patient.
- Relapse occurred in about a quarter of patients with negative CMV-TCIP values and about 12% of those with positive values.
  - Although this study did not find a significant predictive value of CMV- TCIP, it highlights the potential of such assays.
- Limitations included lack of controlled CMV-TCIP use given retrospective study design, small sample size, variable severity of CMV infections, variable use of 2° prophylaxis & subsequent relapses.

Conclusion

CMV-TCIP did not predict CMV relapse after initial infection and treatment. More studies of CMV-TCIP are needed to assess the utility of this assay for this indication.

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