Using a commercially available assay measuring cytomegalovirus (CMV)-specific CD4+ and CD8+ T-cell immunity by flow cytometry and intracellular cytokine staining to predict clinically significant CMV events

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Background

- CMV infection is a common opportunistic infection associated with significant morbidity, mortality, and risk of allograft loss.
- Early detection of viremia and initiation of treatment prior to disease progression are paramount1,2.
- In the absence of treatment, some patients control CMV infection, including low-level viremia, without progression to disease3.
- Thus, many treatment decisions (e.g. viremia thresholds to initiate treatment or use of secondary prophylaxis) are individualized3-5.
- Given the excessive toxicities and costs of antiviral therapy, there is growing interest in assays that measure CMV-specific T-cell immunity (TCI), which may predict protection against infection3-11.
- CMV-specific CD4+ are necessary to build a pool of memory CMV-specific CD8+ cells, which can rapidly expand into effector CD8+ cells, and potentially control CMV after discontinuation of the antiviral3-11.
- The Viracor® CMV TCI Panel (CMV-TCIP) uses flow cytometry and intracellular cytokine staining (ICS) to measure % of CMV-specific CD4+ and CD8+ T cells (Fig. 1)11,12. Other currently available TCI commercial assays measure only aggregate (CD4+ and CD8+) or CD8+ immune responses9.

Methods

- We included patients who had CMV-TCIP results at Rhode Island Hospital and who subsequently had at least one additional assessment for CMV viremia, between 1/2016 and 2/2018.
- CMV events were defined as rising viremia prompting initiation of treatment and were captured after the most recent CMV-TCIP result. We built CMV-protection relative-operating curves (ROC) for % of CD4+ and CD8+ CMV-specific T-cells.

Results

- We analyzed 17 samples from 13 patients: 10 were SOT (8 kidney, 2 heart) recipients: 7 CMV R+, 3 D+/R-. Two patients had hematologic malignancies. One was immunosuppressed on prednisone and infliximab for autoimmune colitis.
- Four additional samples were excluded because of CMV+ or CD8+ ICS background positivity.
- The % of CMV-specific CD4+ but not CD8+ T-cells was significantly lower in patients who developed clinically significant CMV events, compared to those who did not (Fig. 2A).
- ROC AUC was significant for % of CMV-specific CD4+ and CD8+ T-cells in predicting protection against CMV.

Conclusions

- In this small, single-center, heterogeneous series, the % of CMV-specific CD4+ T-cells, measured by flow cytometry and ICS was predictive of protection against CMV.
- The CMV-TCIP can be a useful, cost-effective test, and merits further validation in larger prospective studies.

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References