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The Impact of Pre- and Week 2 and Week 4 Post-transplant CMV-Specific Elispot Assay on CMV Reactivation in CMV-seropositive Allogeneic Hematopoietic Cell Transplant (allo-HCT) Recipients

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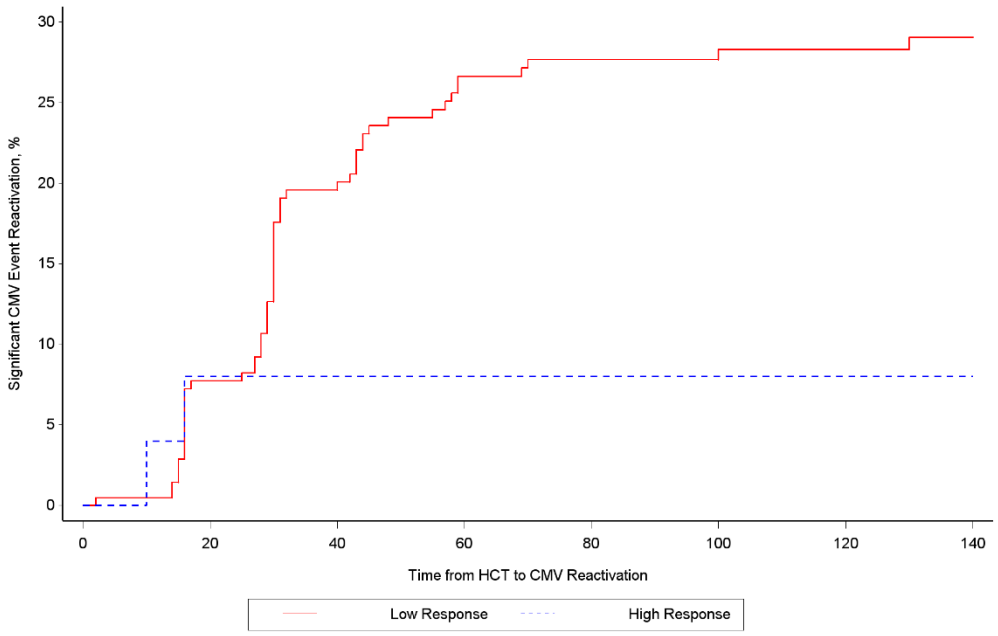
Background: CMV infection causes significant morbidity and mortality in allo-HCT. CMV cell-mediated immunity (CMI), assessed by engrafted T cell production of IFN-γ, is a major mechanism to control CMV replication. The potential role of pre- and post-transplant CMI and its impact on CMV replication and survival is not well understood.

Material/methods: This is an ongoing multi-center (13 sites), prospective, observational study of adult CMV seropositive allo-HCT recipients. T cell responses were serially monitored pre-transplant (screening), and every 2 weeks post-HCT up to 26 weeks with an ELISPOT assay that uses CMV-specific IE-1 and pp65 antigens (T-SPOT.*CMV*, Oxford Diagnostics Laboratories®, Memphis, TN). The changes in spot counts (SPCs) at 4 weeks post-HCT from screening for both antigens and its impact on first CMV reactivation were assessed. Additionally, week 2 pp65 >100 was correlated with the occurrence of first CMV reactivation.

Results: Of 244 enrolled patients, 236 patients had a week 2 visit while 151 subjects had both a screening and week 4 visit. Majority of the 244 enrolled patients are white (73%), males (56%), and median age of 56 years (22 – 80). More patients (46%) had unrelated and 36% had matched HCT, and 55% had a CMV seropositive donor. Changes in SPCs between screening and week 4 post-HCT were associated with first CMV reactivation occurring post-week 4 were assessed. Using a positive change for SPCs for both IE1 and pp65 (SPCs at week 4 > SPCs pre-transplant), a negative predictive value (NPV) for the development of first CMV reactivation was 80.0% and 83.7%, respectively. The NPV for the development of CMV reactivation at week 2 and week 4 pp65 SPCs >100 were 92.0% and 91.3%, respectively, during the 26 week study period (Figure).

Conclusions: Assessment of CMV-specific CMI at screening and 4 weeks post-HCT may prove useful for determining the likelihood of protection against CMV reactivation. Interestingly, a single time point at 2 weeks post-transplant, demonstrated a 92% NPV for the development of CMV reactivation throughout the course of the study. These data suggest the utility of a single measurement but need further validation.

KM Plot – Time from HCT to CMV reactivation stratified by pp65 > 100 (high response) vs. pp65 ≤ 100 (low response); log-rank p-value = 0.044.


Significant CMV Event Reactivation, %
30
25
20
15
10
5
0
0
20
40
60
80
100
120
140
Time from HCT to CMV Reactivation
Low Response
High Response