Reconstitution of CMV-specific cell-mediated immunity during letermovir prophylaxis in high-risk hematopoietic cell transplant recipients.

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Background

- Patients who are cytomegalovirus (CMV) seropositive (R+) prior to hematopoietic cell transplant (HCT), have 30% incidence of clinically significant CMV reactivation in the absence of prophylaxis.
- At our institution, letermovir prophylaxis through approximately Day 100 is used in CMV R+ high-risk (HR) HCT recipients
  - Cord blood
  - Haplocord
  - Haploidentical.
- We hypothesized that clinically nonsignificant CMV reactivation during letermovir prophylaxis may lead to reconstitution of CMV specific cell mediated immunity (CMV CMI), which may protect the host against CMV disease after letermovir discontinuation.

Primary Objective

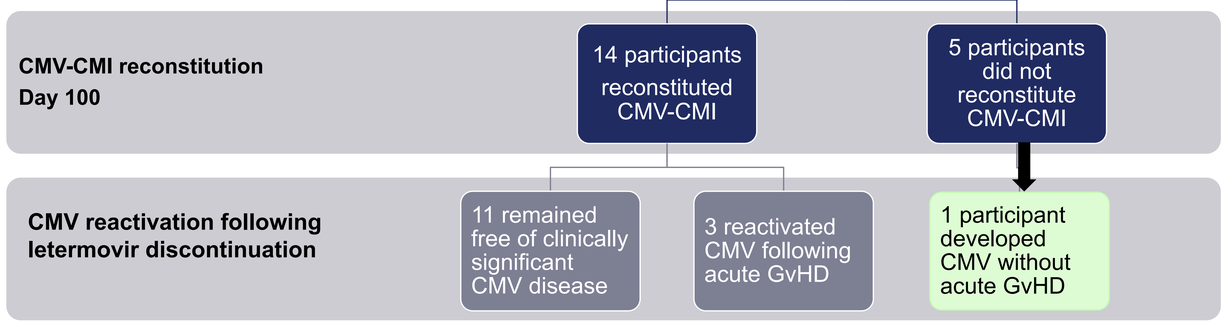
- To determine if CMVR+ HR HCT recipients with evidence of CMV-CMI during letermovir prophylaxis have lower incidence of CMV reactivations during 1st year after HCT compared with those who do not reconstitute CMV-CMI during letermovir prophylaxis.
- To predict the risk of CMV reactivation using CMV specific IL2/IFNg FLUOROSpot in pre transplant setting of patients with hematological malignancies in remission.

Methods

- **Study Design:** Single–center prospective cohort study
  - Blood samples from CMV R+ HR HCT recipients on letermovir were tested by dual color CMV specific IL2/IFNg FLUOROSpot
    - Pre-transplant
    - Days 100,182 and 360
  - Clinical and virologic information were obtained from medical records.

Results High-risk HCT recipients on leteremovir prophylaxis till Day 100

Eligibility criteria for study:
- Pre-HCT CMV CMI defined as ≥20 spot-forming cells/10^6
- CMV-CMI measured at Day 100
- ≥ Day180 follow up



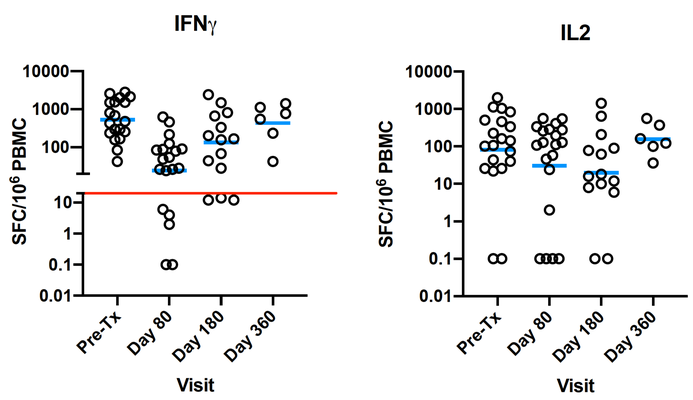


Figure: IFNγ and IL2 FLUOROSpot responses to ex vivo CMV antigenic restimulation. The circles represent results from each of the 19 participants mentioned above. The red horizontal line indicates the threshold for detectable CMV-CMI for this assay, based on responses of CMV seroneg healthy volunteers. The horizontal blue lines indicate geometric means. CMV-CMI progressively reconstituted post-HCT, starting while participants were on Letermovir prophylaxis.

Results

Table: Characteristics

Characteristics of Study Participants	
Median Age (range 22-75 years)	51.5
Sex	
• Male	10
• Female	9
Race	
• Caucasian	9
• Hispanic/Latino/a	9
• Asian	1
Heme Malignancies	
• Acute Myeloid Leukemia	10
• Acute Lymphocytic Leukemia	5
• Aplastic Anemia	1
• Chronic Myeloid Leukemia	1
• Dendritic cell Leukemia	1
• Myelofibrosis	1
GvHD prophylaxis	
• Cyclosporine + MMF	19
Pre-Transplant conditioning	
• Flu/Cy/TBI	8
• Flu/Cy/Thio/TBI	11
HCT	
• Dual Cord	9
• Haplocord	10

Conclusions

- High-risk patient populations can reconstitute CMV CMI while on letermovir.
- Ongoing investigation will help establish predictive parameters for CMV CMI that may allow risk stratification for CMV monitoring and letermovir usage.

Disclosures

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