**Results:**

Analysis of the percent coefficient of variation (%CV) for both CD4 and CD8 responses following CMV and SEB stimulated responses in each of five donors, with 2-13 samples evaluated per donor. When evaluating responses, twelve of these had %CVs less than or equal to 25%, and an additional six %CVs were between 25% and 35%. Evaluation of responses from an unselected population (n=350) of patients revealed considerable heterogeneity. Patients demonstrating normal (positive) results for both CD4 and CD8 responses following CMV and SEB stimulated responses was at 31%. An additional 12% of patients had normal CD4 and CD8 SEB responses but negative responses to CMV in both the CD4 and CD8 compartment. Interestingly, a further 11% had positive responses to CD4 SEB, CD8 SEB, and CD8 CMV, but a negative CMV CD4 response. The final 36% of responses were a mix of positive and negative responses and low cell counts.

**Conclusion:** These analyses demonstrate that the functional T cell responses in CMV seropositive donors are stable enough to provide utility in the analysis of patient responses. These patient responses can vary depending on the situation. The use of CMV T cell analysis can provide useful information for physicians in tailoring a CMV prevention plan following treatment.

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**Stability of CMV CD4 and CD8 T Cell Responses in Seropositive Donors and Evaluation of Immunosuppressed Patients**

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Stephanie Fausett BS, Viracor Eurofins, Lee’s Summit, MO

**Introduction:** A frequent complication after transplantation, CMV infection may cause a series of direct and indirect effects that lead to increased incidence of graft rejection, opportunistic infections, and decreased allograft and patient survival. Antiviral therapy is often used to control CMV infections, but presents problems of toxicity, antiviral resistance and excessive costs. Currently, treating physicians are limited in the information and data available to assess a patient’s risk for CMV infection post-transplant.

**Objectives:** Recent studies have shown that measuring a patient’s CMV specific T cell mediated immunity may provide valuable information to physicians for monitoring CMV infection/disease in transplant patients and may aid in determining which patients need antiviral therapy. Questions have been raised about the variability of these responses. The goal of this study is to evaluate the stability of the CMV T cell response in seropositive individuals over time.

**Methods:** Over an 18 month period, five seropositive donors were evaluated for their CMV-specific CD4 and CD8 T cell responses. Briefly, freshly collected whole blood is stimulated with a CMV lysate, pp65 CMV peptide mix, SEB, or left unstimulated. CMV T cell responses are assessed via flow cytometry upon the cellular activation surface marker CD69 in conjunction with IFNg production. Additionally, the spectrum of responses to CMV in both the CD4 and CD8 compartment. Interestingly, a further 11% had positive responses to CD4 SEB, CD8 SEB, and CD8 CMV, but a negative CMV CD4 response. The final 36% of responses were a mix of positive and negative responses and low cell counts.

**Conclusion:** These analyses demonstrate that the functional T cell responses in CMV seropositive donors are stable enough to provide utility in the analysis of patient responses. These patient responses can vary depending on the situation. The use of CMV T cell analysis can provide useful information for physicians in tailoring a CMV prevention plan following treatment.

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**Successful Reduced Intensity Stem Cell Transplant in a Patient with Myeloproliferative Neoplasm/Myelodysplastic (MPN/MDS) Overlap Syndrome Diagnosed with West Nile Virus Encephalitis.**

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West Nile Virus (WNV) infections are associated with high morbidity and mortality rates in transplant recipients. Limited information exists regarding the management of WNV in the peri-transplant period. The optimal duration of time for delaying transplantation remains unclear. We describe the first successful case of a patient diagnosed with WNV encephalitis in the pre-transplant period who subsequently underwent successful reduced intensity conditioning (RIC) HSCT.

Our patient initially presented with low grade fevers, malaise, cough and fatigue a fortnight before planned HSCT for myelodysplastic syndrome (see Figure). Chest X-ray and respiratory tract PCR were negative. As Colorado is endemic for WNV, a WNV nucleic acid amplification test (NAAT) was sent and returned positive. WNV IgM in blood was positive (6.22), WNV IgG was negative (0.70), WNV serum reverse transcriptase polymerase chain reaction (RT-PCR) was negative. A week later he was admitted with high-grade fevers, rigors, retro-orbital headaches and confusion. Exam was unrevealing. Magnetic Resonance Imaging of brain did not show encephalitis. Cerebrospinal fluid IgG was negative (0.7), CSF WNV RNA PCR was negative. One week following discharge both WNV serum IgM (7.45) and WNV IgG (2.21) were positive. Given concerns for possible WNV encephalitis, decision was made to delay HSCT and monitor for neuroinvasive disease.

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**Table 2**

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>CR5, grade 0-1</th>
<th>CR5, grade 2-5</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI</td>
<td>4 (10)</td>
<td>17 (46)</td>
<td>&lt;.001 C</td>
</tr>
<tr>
<td>CLABSI</td>
<td>4 (10)</td>
<td>16 (43)</td>
<td>0.05 C</td>
</tr>
<tr>
<td>Viral infections</td>
<td>25 (61)</td>
<td>30 (81)</td>
<td>0.01 C</td>
</tr>
<tr>
<td>CMV reactivations</td>
<td>15 (37)</td>
<td>11 (30)</td>
<td>0.52 C</td>
</tr>
<tr>
<td>CMV viremia</td>
<td>13 (32)</td>
<td>10 (30)</td>
<td>0.33 C</td>
</tr>
<tr>
<td>BK virusia</td>
<td>10 (24)</td>
<td>17 (46)</td>
<td>0.46 C</td>
</tr>
<tr>
<td>BKV urine infection, needling pre-emptive therapy</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>1.00 C</td>
</tr>
<tr>
<td>Fungal infections</td>
<td>2 (5)</td>
<td>6 (16)</td>
<td>0.14 C</td>
</tr>
</tbody>
</table>

*Exact test; Chi-square test*

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**Figure 1.** Timeline of West Nile virus infection
He improved with resolution of fever and neurological symptoms and 1.5 months after initial presentation underwent RIC Matched Unrelated Donor (MUD) Allogeneic peripheral blood HSCT. Conditioning regimen involved fludarabine and melphalan. Post-transplant, he was on methotrexate and tacrolimus for graft versus host disease prophylaxis. On Transplant Day + 10, WNV serum IgM was positive at 4.31, WNV IgG positive at 4.12; however, serum WNV RNA PCR were reported negative. He engrafted on Transplant Day + 18, bone marrow biopsy from day + 28 revealed 100% donor cells. At day + 100, there was no evidence of relapse of WNV infection.

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**Successful Treatment of Toxoplasma Induced Hemophagocytic Lymphohistiocytosis (HLH) after Undergoing Allogeneic Stem Cell Transplantation (HSCT)**

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**Introduction:** Toxoplasmosis is a well-known intracellular protozoan parasite with serore prevalence varying geographically. Relatively asymptomatic in healthy individuals, it’s reactivation can be a devastating opportunistic infection in HSCT patients with rare documentation of associated HLH.

**Case:** A 25-year-old woman with Hodgkin lymphoma, refractory to multiple chemotherapies, autologous transplant and Nivolumab, who underwent haploidentical HSCT, was admitted on day + 33 with persistent high-grade fevers. Blood counts were unremarkable, except for eosinophilia. She received broad spectrum antibiotics. PET/CT on day + 36 demonstrated resolution of metabolic activity in multiple lymph nodes, but revealed ‘revved-up’ bone marrow (Image 1). CT-chest (day + 41) demonstrated widespread centrilobular nodules. Blood, urine, enteric cultures, HIV, Histoplasma studies, and respiratory viral panel PCR were negative. Pre-transplant serologies noted a positive toxoplasma IgG. Toxoplasma DNA was detected in blood on day + 41; she received clindamycin, pyrimethamine, and atovaquone due to sulfa allergy but successfully underwent rapid sulfa desensitization. She developed progressive pancytopenia and hypoxemia (day + 43) requiring intubation in the ICU. Ferritin was > 50,000 ng/mL, and triglycerides 931 mg/dL. Bone marrow biopsy showed activated macrophages and hemophagocytosis (Image 2). She met 6/8 criteria described in HLH-2004 trial. She received dexamethasone and tocilizumab for HLH, leading to prompt reversal of HLH physiology within 72 hours of HLH-directed therapy initiation. She was extubated on day + 48. She was discharged on sulfadiazine and pyrimethamine (day + 60) with almost normal ferritin levels and transfusion independency.

**Discussion:** HLH is characterized by cytopenias, extreme systemic inflammatory response, and high mortality. HLH can be triggered by infections, such as toxoplasmosis. Disseminated toxoplasmosis has a high mortality itself (> 60 % treated, and 99% untreated), and HSCT recipients appear to have the highest risk. Early detection and treatment of the underlying infection is essential. Novel drugs, such as Tocilizumab, should be prospectively studied in HLH. In conclusion, HLH after HSCT should be suspected in cases of unexplained inflammatory response and cytopenias after successful engraftment; secondary causes must be explored and promptly treated.

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**Summary of Maribavir (SHP620) Drug – Drug Interactions Based on Accumulated Clinical and Nonclinical Data**

**Ivy Song**, **Kefeng Sun**, **Katarina Ilic**, **Patrick Martin**. 1 Shire, Lexington, MA; 2 Shire, Cambridge, MA

**Introduction:** Maribavir, a potent and orally bioavailable antiviral, is being evaluated in Phase 3 trials for the treatment of cytomegalovirus (CMV) infections in transplant patients. Often numerous concomitant medications are administered to these patients to manage their comorbidities. A thorough evaluation of maribavir potential for drug–drug interactions (DDIs) is warranted and required for the regulatory approval.

**Objectives:** To thoroughly evaluate potential DDIs for maribavir.

**Methods:** Extensive in vitro studies were conducted to evaluate the potential involvement of cytochrome P450s (CYPs), uridine diphosphate glucuronosyltransferases (UGTs) and transporters on the disposition of maribavir, as well as the inhibitory and induction effect of maribavir on these enzymes and transporters. Clinical Phase 1 studies included a human mass-balance study, two probe-cocktail studies, and five DDI studies with ketoconazole, rifampin, antacid, voriconazole, and tacrolimus.

**Results:** Maribavir is metabolized primarily in the liver through CYP3A4 (70–85%) and CYP1A2 (15–30%). Renal clearance is a minor route (< 5%). Maribavir is a substrate of P-gp and UGTs, however, the contribution of glucuronidation to the overall clearance of maribavir is considered low. Maribavir is not a clinically significant inhibitor of CYPs, UGTs, and transporters, except for weak inhibition for CYP2C19, P-gp, and possibly UGT1A1. Maribavir is not a clinically significant inducer for CYP1A2, 2B6, and 3A4. Maribavir’s exposure is increased 46% by ketoconazole and decreased 61% by rifampin and not