Brincidofovir (BCV) Prophylaxis for Herpes Simplex Virus (HSV) and Varicella Zoster Virus (VZV) after Hematopoietic Cell Transplantation (HCT): Clinical Experience at Memorial Sloan Kettering Cancer Center

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Background

• Herpes simplex (HSV) and Varicella zoster (VZV) viruses may cause serious infections in HCT recipients.
• Universal prophylaxis with ACV has been effective in preventing HSV/VZV infections.

Brincidofovir (BCV; CMX001)
• Broad spectrum oral antiviral
• In vitro activity against HSV/VZV
• In clinical development for CMV prevention
• No clinical experience for HSV/VZV prophylaxis

Objective

• Report the MSK experience with BCV for HSV/VZV prophylaxis in HCT treated with open label BCV.

Methods

• Allo-HCT patients treated with open label BCV for ≥14 days for any indication from April/2010 and July/2015 were included in the study.
• HSV or VZV reactivation was defined as positive viral culture or PCR and compatible clinical presentation.

Primary virus treated with BCV

Number of patients

• HSV, ACV resistant (2); disseminated VZV (1)
• BK polyoma virus (1) Human herpes virus 6 (1), John Cunningham virus (1)

Duration of BCV

HSV breakthrough infections

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Transplant type</th>
<th>Indication for BCV</th>
<th>BCV dose</th>
<th>HSV diagnosis from BCV</th>
<th>GvHD</th>
<th>Immunosuppressants at the time of breakthrough infection</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>58</td>
<td>Peripheral blood T-cell depleted</td>
<td>Oral HSV Resistant to ACV</td>
<td>200mg weekly</td>
<td>30 days</td>
<td>Grade III skin</td>
<td>Methylprednisolone 1mg/kg/day Mycophenolate 1mg q12h Sirolimus 1mg PO daily</td>
<td>Clinical resolution of initial lesions. Intermittent positive HSV PCR during treatment- responding to transient increase in BCV dose.</td>
</tr>
<tr>
<td>F</td>
<td>59</td>
<td>Umbilical Cord</td>
<td>CMV viremia, HSV</td>
<td>100mg BIW &gt; 200mg weekly</td>
<td>71 days</td>
<td>Grade II gut</td>
<td>Methylprednisolone 2mg/kg/day Mycophenolate 1mg q 12h Etanercept 25mg</td>
<td>Genital HSV infection during interruption of BCV prophylaxis for severe diarrhea related to GvHD.</td>
</tr>
</tbody>
</table>

Conclusions

• The rate of HSV breakthrough infections was 0.7 cases/1,000 patient-days of BCV prophylaxis. There was no breakthrough VZV among 48 highly immunosuppressed HCT patients.
• Thirty-one (56%) patients received BCV 100mg twice weekly. This dose is currently evaluated in clinical trials for CMV prevention in HCT.
• Interruption of BCV prophylaxis and/or impaired GI absorption likely explain the breakthrough HSV infections in 2 patients.
• Our clinical experience supports BCV as a suitable alternative to acyclovir prophylaxis against HSV/VZV in HCT patients.