Human rhinovirus detection in the lower respiratory tract of hematopoietic cell transplant recipients: association with mortality

Sachiko Seo,1,2 Alpana Waghmare,1,3,4 Emily M Scott,5 Hu Xie,6 Jane M Kuypers,1,7 Robert C. Hackman,1 Angela P. Campbell,1,3,4,* Su-Mi Choi,8 Wendy M. Leisenring,6 Keith R. Jerome,1,7 Janet A. Englund1,3,4 and Michael Boeckh1,6,9

1Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; 2Department of Hematology and Oncology, National Cancer Research Center East, Chiba, Japan; 3Department of Pediatrics, University of Washington, Seattle, WA, USA; 4Pediatric Infectious Disease Division, Seattle Children's Hospital, WA, USA; 5School of Medicine, University of Washington, Seattle, WA, USA; 6Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; 7Department of Laboratory Medicine, University of Washington, Seattle, WA, USA; 8Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea and 9Department of Medicine, University of Washington, Seattle, WA, USA

*Present affiliation: Centers for Disease Control and Prevention, Atlanta, GA, USA

©2017 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2016.153767

Received: August 1, 2016.
Accepted: January 31, 2017.
Correspondence: mboeckh@fredhutch.org
### Supplemental Table 1. Risk factors for mortality from all causes or respiratory failure by day 90 after HRV LRI (N=128)

<table>
<thead>
<tr>
<th></th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Overall mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocyte count at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 300 cells/μL</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≤ 300 cells/μL</td>
<td>2.70</td>
<td>1.49-4.7 6</td>
</tr>
<tr>
<td>Monocyte count at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 300 cells/μL</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≤ 300 cells/μL</td>
<td>2.44</td>
<td>1.33-4.5 5</td>
</tr>
<tr>
<td>LRI symptoms at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3.03</td>
<td>1.37-6.7 4</td>
</tr>
<tr>
<td>Oxygen use at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.94</td>
<td>1.54-5.6 2</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>10.3</td>
<td>4.82-22. 0</td>
</tr>
<tr>
<td>Steroid dose before diagnosis*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&lt; 1 mg/kg</td>
<td>0.82</td>
<td>0.41-1.6 4</td>
</tr>
<tr>
<td>≥ 1 mg/kg</td>
<td>3.69</td>
<td>1.93-7.0 3</td>
</tr>
<tr>
<td>Steroid dose after diagnosis*#</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&lt; 1 mg/kg</td>
<td>1.39</td>
<td>0.64-3.0 0</td>
</tr>
<tr>
<td>Steroid dose before diagnosis*</td>
<td>1</td>
<td>2.39-10.</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---</td>
<td>----------</td>
</tr>
<tr>
<td>≥ 1 mg/kg</td>
<td>4.92</td>
<td>0.95-1.0</td>
</tr>
</tbody>
</table>

| Ct value at diagnosis †       | 0.99 | 0.95-1.0 | 0.70 |

**Mortality from respiratory failure**

**Lymphocyte count at diagnosis**

| > 300 cells/μL | 1.00 | 1.00 |
| ≤ 300 cells/μL | 2.50 | 1.30-4.7 | 0.006 | 1.87 | 0.93-3.7 | 5 | 0.08 |

**Monocyte count at diagnosis**

| > 300 cells/μL | 1.00 | 1.00 |
| ≤ 300 cells/μL | 2.44 | 1.22-4.7 | 0.012 | 1.12 | 0.54-2.3 | 4 | 0.75 |

**LRI symptoms at diagnosis**

| No | 1.00 | 1.00 |
| Yes | 4.28 | 1.52-12. | 0 | 2.40 | 0.70-8.2 | 6 | 0.16 |

**Oxygen use at diagnosis**

| No | 1.00 | 1.00 |
| Yes | 2.72 | 1.31-5.6 | 0.007 | 2.09 | 0.89-4.9 | 3 | 0.09 |

| Mechanical ventilation | 10.3 | 4.47-23. | <0.001 |

**Steroid dose after diagnosis#**

| No | 1.00 | 1.00 |
| < 1 mg/kg | 1.68 | 0.66-4.3 | 0.28 |

<p>| ≥ 1 mg/kg | 4.65 | 2.18-9.9 | &lt;0.001 | 2.25 | 1.11-4.5 | 8 | 0.025 |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>2.90-16.4</th>
<th>&lt;0.001</th>
<th>2.77</th>
<th>1.39-5.5</th>
<th>0.004</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 mg/kg</td>
<td>6.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ct value at diagnosis †</td>
<td>0.99</td>
<td>0.94-1.0</td>
<td>0.68</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Peak steroid dose was recorded from the period within two weeks prior to LRI.

* Peak steroid dose after LRI diagnosis was recorded from within two weeks after the diagnosis. These variables are analyzed as time-dependent.

† This analysis was performed as a continuous variable.

All variables in Table 1 were used for the univariable analysis. Only variables with p < 0.05 are shown in this table. Ct value was shown regardless of p values.

**Abbreviations; HRV: human rhinovirus, LRI: lower respiratory tract infection, Ct: cycle threshold**