Preliminary Data from 13 Liver Transplantation Patients who Received Brincidofovir (BCV) for Adenovirus (AdV) Infection

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ABSTRACT

Brincidofovir (BCV), a nucleotide analog with broad-spectrum in vitro antiviral activity against double-stranded DNA viruses, including orthopoxvirus, polyomavirus, human adenovirus, and BK virus, and human immuno-deficiency virus (HIV), is being evaluated for the treatment of severe adenovirus infections in patients with underlying conditions. NIBL 350 was an open-label, multicenter, expanded-access study—safety/tolerability. The rate of AdV infection in liver transplantation patients varies from 3.5%–38%, with a median age of 21 months (range: 6 months, 13 years), and 9 (69%) were male. Three patients (all female) were<8 years of age, and 10 (75%) were<12 years of age. Of note, patients had numerous comorbidities causing an increased risk of AdV infection. AdV VL was not available for all patients. The median baseline AdV VL was 2.9 log10 copies/mL (range: 1.2–3.9). In patients followed for 12 weeks, 1 died. In 1 patient (out of 13 patients), treatment was discontinued because of a BCV-related adverse event (AE) (diarrhea). No BCV-related clinical hepatobiliary AEs were reported, which were not related to study drug but rather to the underlying condition. Treatment-related AEs of diarrhea (n=2) and leukopenia (n=1) were possible BCV-related AEs. Most common AEs included AST –5 (–691, +81) U/L, bilirubin –0.05 mg/dL (–15.5, +4.1 mg/dL), and creatinine +0.1 mg/dL (–0.9, +2.5 mg/dL).

RESULTS

Baseline characteristics

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yrs)</th>
<th>Race</th>
<th>Gender</th>
<th>Time from transplant to first dose (days)</th>
<th>Baseline AdV VL (log10 copies/mL)</th>
<th>Time to nadir AdV VL (days)</th>
<th>Baseline disease status</th>
<th>Prior CMX therapy</th>
<th>BCV treatment duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>Male</td>
<td>White</td>
<td>15</td>
<td>2.7</td>
<td>20</td>
<td>Clinical disease</td>
<td>No</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>Male</td>
<td>White</td>
<td>28</td>
<td>2.7</td>
<td>20</td>
<td>Clinical disease</td>
<td>Yes</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>Male</td>
<td>White</td>
<td>12</td>
<td>2.9</td>
<td>20</td>
<td>Clinical disease</td>
<td>No</td>
<td>12</td>
</tr>
</tbody>
</table>

Change from baseline in serum creatinine is shown in Figure 3. AdV, adenovirus; ALT, alanine transaminase; AST, aspartate transaminase; GFR, glomerular filtration rate; LLOQ, lower limit of quantification; log10, base 10 logarithm; SOT, solid organ transplantation; TND, time to nadir; VHD, veno-occlusive disease.

OBJECTIVE

To present preliminary virologic response, survival, and tolerability data from liver transplantation recipients who have received BCV for AdV infection.

METHODS

Pediatric and adult patients who underwent isolated liver transplantation or multi-organ transplantation, including liver transplantation, were identified from studies of NIBL 350—safety/tolerability and NIBL 300—safety/tolerability. The rate of AdV infection in liver transplantation patients varies from 3.5%–38%, with a median age of 21 months (range: 6 months, 13 years), and 9 (69%) were male. Three patients (all female) were<8 years of age, and 10 (75%) were<12 years of age. Of note, patients had numerous comorbidities causing an increased risk of AdV infection. AdV VL was not available for all patients. The median baseline AdV VL was 2.9 log10 copies/mL (range: 1.2–3.9). In patients followed for 12 weeks, 1 died. In 1 patient (out of 13 patients), treatment was discontinued because of a BCV-related adverse event (diarrhea). No BCV-related clinical hepatobiliary AEs were reported, which were not related to study drug but rather to the underlying condition. Treatment-related AEs of diarrhea (n=2) and leukopenia (n=1) were possible BCV-related AEs. Most common AEs included AST –5 (–691, +81) U/L, bilirubin –0.05 mg/dL (–15.5, +4.1 mg/dL), and creatinine +0.1 mg/dL (–0.9, +2.5 mg/dL).

CONCLUSIONS

Although uncontrolled, the preliminary data from these 13 liver transplant patients with AdV infection treated with BCV may reduce AdV viral load and may be associated with improved survival (Figure 2).

In particular, 7 of 8 patients with disseminated AdV disease survived, with a median reduction in AdV viral load of >3.2 log10, which is encouraging.

Survival in this predominantly pediatric liver transplant cohort with AdV compares favorably to published data up to 50% mortality.1

No BCV-related clinical hepatobiliary AEs were reported in these patients.

These data support the continued study of BCV for the treatment of AdV infection in SOT, including liver transplantation.

REFERENCES


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DISCLOSURES

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