In this study, we report the dissociation kinetics of bictegravir and other INSTIs.

Figure 1. Structure of Bictegravir (BIC) and other INSTIs

Methods

Methods (cont’d)

Table 2. Apparent Association Half-life of INSTIs from Wild-type and G140S/Q148H HIV-1 Integrase-DNA Complexes

<table>
<thead>
<tr>
<th>INSTI</th>
<th>Association t1/2 (min)</th>
<th>p-value vs BIC Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIC</td>
<td>5.4 ± 2.8</td>
<td>0.017</td>
</tr>
<tr>
<td>DTG</td>
<td>15 ± 3</td>
<td>0.001</td>
</tr>
<tr>
<td>RAL</td>
<td>30 ± 4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>EVG</td>
<td>40 ± 5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Figure 3. Bictegravir Dissociation Half-life from WT and G140S/Q148H HIV-1 Integrase-DNA Complexes

Conclusions

Bictegravir has the longest measured dissociation half-life from wild-type HIV-1 IN-DNA complexes compared to DTG, RAL, and EVG.

The Exponential Decay Method of analysis results in an overestimation of dissociation half-life compared to the exponential binding method. The Exponential Binding Method is a modification of the Exponential Decay Method and involves an initial exponential decline in the signal followed by a gradual exponential increase in the signal. This method provides a more accurate estimation of the dissociation half-life.

References

1. Lazard et al., “Discovery of Bictegravir (GS-9883): A Novel, Unboosted, Once-Daily HIV-1 Integrase Strand Transfer Inhibitor (INSTI) with Improved Pharmacokinetic and In Vivo Resistance Profile,” ASM Microbe, June 19, 2016, Boston, MA, Poster #413.
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