A novel intranasal (IN) epinephrine spray (neffy) is presented in comparator clinical trials to compare the PK and PD parameters of this novel route of administration to EpiPen and other auto-injectors. PK and PD parameters of neffy are also compared to manual intramuscular (IM) injection,4,5 the corresponding differences in pharmacodynamic (PD) parameters have not been assessed.

Although recent studies have demonstrated that there are pharmacokinetic (PK) differences among EpiPen/other auto-injectors and IN injection,6,7 the corresponding differences in pharmacodynamic (PD) parameters have not been assessed.

A novel intranasal (IN) epinephrine spray (neffy, ARS Pharmaceuticals, Inc) is being developed as a potential alternative to IM epinephrine administration. PK and PD parameters of this novel route of administration are being explored.

Table 1. Summary of Individual Studies Included in the Integrated Pharmacodynamic Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Number of Participants</th>
<th>Age (years)</th>
<th>Sex (male/female)</th>
<th>Weight (kg)</th>
<th>SBP Baseline (mmHg)</th>
<th>SBP Maximal Change (mmHg)</th>
<th>DBP Baseline (mmHg)</th>
<th>DBP Maximal Change (mmHg)</th>
<th>Pulse Rate Baseline (bpm)</th>
<th>Pulse Rate Maximal Change (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>neffy 0.3 mg</td>
<td>20</td>
<td>19-54</td>
<td>14/6</td>
<td>68.5</td>
<td>100</td>
<td>50</td>
<td>80</td>
<td>10</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>Study 2</td>
<td>EpiPen 0.3 mg</td>
<td>20</td>
<td>19-54</td>
<td>14/6</td>
<td>68.5</td>
<td>100</td>
<td>50</td>
<td>80</td>
<td>10</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>Study 3</td>
<td>Symjepi 0.3 mg</td>
<td>20</td>
<td>19-54</td>
<td>14/6</td>
<td>68.5</td>
<td>100</td>
<td>50</td>
<td>80</td>
<td>10</td>
<td>60</td>
<td>10</td>
</tr>
</tbody>
</table>

RESULTS

Values After Administration

- The epinephrine concentration-versus-time curve indicated that the highest mean concentration occurred after administration followed by Symjepi, 0.3 mg IM, and neffy (Figure 1).
- The differences in the speed of absorption between different injection routes of administration were noted across all treatments (Figures 3 and 4).
- The PK/PD relationship between change from baseline SBP and Cmax for both EpiPen and Symjepi appears to be less well defined. While there does appear to be a positive relationship between change from baseline SBP and Cmax for EpiPen, the overall PK/PD response following neffy is more complex (Figures 3 and 4).

CONCLUSIONS

1 mg IN resulted in Cmax levels that were similar to those observed following IM injection, 0.3 mg IN and lower than those observed following EpiPen and Symjepi.

REFERENCES