Assessment of Potential Mouth/Throat Deposition and Lung Delivery of Suspension- and Solution-Formulated Inhaled Corticosteroid Formulations Delivered by Pressurized Metered Dose Inhaler without and with Valved Holding Chamber Using an Anatomic Adult Upper Airway

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INTRODUCTION / STUDY PURPOSE

• The present laboratory study explored how insertion of a Valved Holding Chamber (VHC) in the pathway between pMDI and the mouth might affect the transfer of particles from inhaler mouthpiece to the airways of the lungs.

• An anatomically correct adult oropharyngeal airway was used in conjunction with simulated patient inhalation, and both suspension and solution corticosteroid pMDIs were assessed.

MATERIALS AND METHODS

Figure 1: Experimental Arrangement Showing Adult Oropharyngeal Inlet; The Same Configuration was Utilized for Evaluation of pMDI Alone or with VHC Present

Table 1: Study Design and Outputs

<table>
<thead>
<tr>
<th>pMDI Product</th>
<th>API/mass per actuation</th>
<th>Formulation Type</th>
<th>VHC Present</th>
<th>Outputs Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flovent 125</td>
<td>FP/125 µg</td>
<td>HFA Suspension</td>
<td>Yes</td>
<td>Carina</td>
</tr>
<tr>
<td>Qvar 100</td>
<td>BDP/100 µg</td>
<td>HFA Solution</td>
<td>No</td>
<td>Carina + Oropharynx</td>
</tr>
</tbody>
</table>

• Following each test, an internally validated HPLC-UV spectrophotometric assay was used to determine the mass of the relevant API recovered at each location.

RESULTS

Figure 2: Particle Deposition in the Oropharynx of the Adult ADAM Airway

• When the VHC was absent, the FP (suspension) formulation was deposited in the oropharyngeal passageway at approximately double the extent to that observed with the BDP (solution) formulation (62% v 29%).

• Significant oropharyngeal airway deposition still occurred, even with the ultrafine HFA solution product, which was greatly reduced when the VHC was present (29% v 3%, p < 0.001).

Figure 3: Particle Deposition on Filter Located at the Distal End of the ADAM Adult Airway

• As expected, the finer aerodynamic particle size distribution of the ultrafine Qvar1 solution aerosol resulted in greater delivery to the filter (‘carina’) compared with the coarser Flovent suspension aerosol (p < 0.001) when the VHC was absent, although the large degree of difference (7% v 36%) is potentially surprising (see Figure 3).

• Filter deposition was increased for both pMDI products when the VHC was present (p < 0.001). The increase was more pronounced with the suspension product; however, an increase was still evident even when used with the solution HFA pMDI.

• The findings for both oropharyngeal and filter deposition in the present study, the view that a VHC might not add value with the solution type of product for oropharyngeal deposition [5], therefore appears to be an overstatement of reality.

CONCLUSIONS

• This laboratory-based pilot study, using a new replicated adult airway, provides new data supporting the fact that finer solution HFA pMDI products are likely to deposit in the oropharynx to a lesser extent and be delivered to the lungs to a greater extent, than suspension HFA pMDIs.

• The combination with a VHC, for either type of product, resulted in significantly less drug deposited in the modelled oropharynx and increased potential for lung delivery.

• Hence the potential value of a VHC, even within an adult population, is demonstrated.

REFERENCES


Drug Delivery to the Lungs 28 December 6 – 8, 2017 Edinburgh, Scotland

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