**D38**

**Pharmacokinetics of tiotropium in patients aged 6–11 years with moderate asthma following administration via the Respimat® inhaler**

Ashish Sharma1, Sabrina Wiebe1, Stanley Szefler1, René Aalbers3, Eckard Hamelmann4, Stanley Goldstein5, Michael Engel6, Petra Moroni-Zentgraf7, Christian Vogelberg8

1Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany  
2Children’s Hospital Colorado; University of Colorado Denver School of Medicine, Denver, United States of America  
3Martini Hospital, Van Swietenplein 1, Groningen, Netherlands  
4Evangelisches Krankenhaus Bielefeld GmbH, Malvenstrasse 12, Bielefeld, Germany  
5Goldstein Stanley Asthma Care of Long Island, Rockville Centre, New York, United States of America  
6Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany  
7Boehringer Ingelheim Pty Ltd, Sydney, Australia  
8University Hospital Carl Gustav Carus, Technical University of Dresden, Dresden, Germany

**Introduction**

Tiotropium Respimat® has been demonstrated to be efficacious and well tolerated as add-on to maintenance inhaled corticosteroids (ICS) ± additional controller therapy in children aged 6–11 years with moderate and severe asthma. The pharmacokinetic (PK) properties of tiotropium have been reported in adult and adolescent patients, but the PK of tiotropium in children with moderate persistent asthma requires elucidation. We studied single- and multiple-dose PK characteristics of tiotropium in patients aged 6–11 years with moderate persistent asthma (NCT01383499).

**Methods**

PK parameters of tiotropium were evaluated in plasma and urine samples using a subset of patients in a Phase II, randomized, double-blind, placebo-controlled, incomplete crossover trial of tiotropium; additionally, some patients who were not part of the subset consented to the 24-hour urine collection resulting in more urine data than plasma data. Overall, 24 patients were included who received tiotropium at 2.5 μg, or 5 μg as two puffs delivered by the Respimat® inhaler once daily in the evening, added on to at least ICS (leukotriene modifiers were permitted throughout the trial). PK were determined after the first dose (first treatment only) and after 4 weeks of dosing.

**Results**

Tiotropium was rapidly absorbed following oral inhalation with a median t\text{max,ss} following multiple dosing over 4 weeks ranging between 4.1 and 4.7 minutes for the two dose groups. An average of 3.17–4.32% of the nominal dose was excreted unchanged in the urine over 24 hours post-single dose. At steady state, urinary excretion was 1.7 to 3.2-fold higher than post-single dose, and renal clearance was 278–358 mL/minute. Tiotropium exposure increased in an approximately dose proportional manner. PK parameters after multiple dosing are presented in Table 1.

**Table 1. PK parameters after multiple dosing of tiotropium delivered by the Respimat® inhaler in children aged 6–11 years with moderate asthma**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Tiotropium Respimat 2.5 μg</th>
<th>Tiotropium Respimat 5 μg</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC\text{0–1,ss}</td>
<td>pg.h/mL</td>
<td>3</td>
<td>2.08</td>
</tr>
<tr>
<td>C\text{max,ss}</td>
<td>pg/mL</td>
<td>6</td>
<td>2.42</td>
</tr>
<tr>
<td>C\text{pre,ss}</td>
<td>pg/mL</td>
<td>3</td>
<td>1.82</td>
</tr>
</tbody>
</table>
### Conclusion

These data establish the PK of tiotropium Respimat® following administration of a single dose and at steady state in children aged 6–11 years with moderate asthma. Overall, the pattern of absorption, exposure and clearance at steady state was comparable in this age group to that previously published for adolescents and adults.