Optimising paediatric dosing regimens based on a clinical data warehouse

SwissPK_{cdw}

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Background

• For practical and economic reasons, clinical trials to find ideal dosage regimens have generally been restricted to adults in the past and were not followed by trials in children

• Off-label use in children is associated with an increased risk for both severe adverse events due to overdosing, and treatment failure with too low doses
• No common rule to predict the ideal dosage regimen for a child based on available dosing information for adults

• High heterogeneity in dosage recommendations for children
Revision of the Therapeutic Products Act

Art. 67a Provision of information about the use of medicinal products in certain population groups

1. In order to improve safety in the use of medicinal products in paediatrics, the Federal Council may allow for the collection, harmonisation, evaluation and publication of data relating to the prescription, supply and use of medicinal products.

2. The Confederation may arrange for a database to be established and operated by third parties for this purpose. [...]
Harmonisation process

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SwissPK\textsuperscript{cdw} - main goals

1. to develop the \textit{Swiss PharmacoKinetics clinical data warehouse} and online platform \textit{SwissPK\textsuperscript{cdw}} for paediatric pharmacokinetic modelling

2. to develop and provide tools based on open-source and licensed software for pharmacokinetic modelling to predict ideal dosage regimens for paediatric patients based on the data in the CDW

3. to make the CDW, modelling tools and knowledge derived available to the expert community via the SPHN network

National modelling platform to share data, knowledge and expertise
## Drugs to be investigated during this funding period

<table>
<thead>
<tr>
<th>Drug</th>
<th>Consent type</th>
<th>Samples available for genetic analysis</th>
<th>Data type</th>
<th>Number of levels</th>
<th>Number of patients</th>
<th>Number of patients until 2020</th>
<th>Dosage</th>
<th>Time points of plasma levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciclosporin</td>
<td>GC/IC</td>
<td>Yes</td>
<td>Rt</td>
<td>1259</td>
<td>81</td>
<td>100</td>
<td>5mg/kg, q12h</td>
<td>Trough level</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>GC/IC</td>
<td>No</td>
<td>Rt/Pr</td>
<td>2450/NA</td>
<td>300/NA</td>
<td>410/100</td>
<td>5mg/kg/7.5mg/kg, q24h</td>
<td>Peak and trough level</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>GC/IC</td>
<td>Yes</td>
<td>Rt</td>
<td>1226</td>
<td>81</td>
<td>105</td>
<td>0.15mg/kg, q12h</td>
<td>Trough level</td>
</tr>
</tbody>
</table>
Pharmacogenetic

- Pharmacogenetic will play an essential role in the future of personalized medicine

- *SwissPK*\textsuperscript{cdw} will be designed to allow integration of pharmacogenomics data

- we plan to assess the influence of genetic variances on the metabolism of tacrolimus (13 SNPs in the CYP450 enzyme system)

- transfer the results to our CDW/platform for analysis
Outlook beyond the funding period

• Extend population pharmacokinetic modelling to as many drugs as possible in order to
  ✓ optimize dosing of already used drugs in children (off label)
  ✓ increase the number of licensed drugs for pediatric patients
  ✓ support the development of future new potential lifesaving drugs for children with increased efficacy and lower risks of toxicity

• Include the remaining paediatric hubs in Switzerland represented within the SwissPedNet