Volumetric Absorptive Microsampling (VAMS™) for blood collection in clinical studies of padsevonil

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Disclosures

- UCB Pharma-sponsored.
- H Chanteux, C Otoul, and C Rospo are employees of UCB Pharma.
- D Sciberras was an employee of UCB Pharma at the time of the analyses.
- G Lelij and B Van Den Steen are contractors for UCB Pharma.

Disclaimer

- Padsevonil is a pipeline compound in clinical development.
- The clinical significance of nonclinical findings discussed in this presentation is not known.
- The presentation may contain information about unapproved indications and/or use and/or products.
- Licenses may vary by country – please always refer to the Prescribing Information in your country before prescribing any drug.

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Agenda

- **Background information**
  - Volumetric Absorptive Microsampling (VAMS™)

- **Methodology**
  - Implementation

- **Results**
  - Bioanalytical validation
  - Bridging of clinical data

- **Conclusions**
Background information

Volumetric Absorptive Microsampling (VAMS™)

Novel technique

Enable accurate collection of small (10 µL) blood volumes

- Mitra® microsampler (Neoteryx LLC, Torrance, CA) is an absorbent polymeric tip
- Blood is collected by dipping the Mitra® microsampler into a blood bead after skin prick
- After blood collection, Mitra® is air-dried and stored at room temperature

Image source: Neoteryx LLC
Volumetric Absorptive Microsampling (VAMS)
Background information

Volumetric Absorptive Microsampling (VAMS™)

Added value of Mitra® for collection of PK samples in clinical studies

- Decreased patient burden
  - Less invasive technique (pediatric application) compared to venous method
  - Low blood volume (10µL) ↔ conventional blood sampling (1mL)

- Reduced operational burden improving logistical feasibility
  - Storage and shipment at room temperature – No need for freeze-thaw cycles
  - No need for centrifugation, plasma separation, and aliquoting

- Flexibility in collection of PK data in Phase 2/3 studies
  - Home sampling possible → sparse PK sampling not limited to time window during clinical visit
Methodology

Implementation of Mitra® in a global drug development program

Padsevonil (PSL) is a drug in development (Phase 2b/Phase 3) for the treatment of patients with epilepsy and drug-resistant focal seizures.

- Feasibility assessment
- Bioanalytical validation (FDA & EMA)
- Bridging with plasma data obtained in healthy volunteers and in patients
Results

Bioanalytical validation

The bioanalytical method was demonstrated to be accurate, precise, and selective for quantification of PSL over a clinically relevant concentration range (2-2000 ng/mL)

Accuracy and precision of PSL intra-run and inter-run in Mitra® (N=18)

<table>
<thead>
<tr>
<th>Nominal PSL concentration</th>
<th>2.0 ng/mL</th>
<th>6.0 ng/mL</th>
<th>1000 ng/mL</th>
<th>1600 ng/mL</th>
<th>2000 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean intra-run precision, %CV</td>
<td>13.3</td>
<td>7.1</td>
<td>5.3</td>
<td>5.5</td>
<td>5.8</td>
</tr>
<tr>
<td>Mean intra-run bias, %</td>
<td>−7.0</td>
<td>0.4</td>
<td>1.5</td>
<td>1.3</td>
<td>3.7</td>
</tr>
<tr>
<td>Inter-run precision, %CV</td>
<td>13.2</td>
<td>6.9</td>
<td>5.7</td>
<td>5.9</td>
<td>6.2</td>
</tr>
<tr>
<td>Inter-run bias, %</td>
<td>−7.0</td>
<td>0.5</td>
<td>2.0</td>
<td>1.3</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Haematocrit effect on PSL (N=6)

<table>
<thead>
<tr>
<th>Concentration</th>
<th>6.0 ng/mL</th>
<th>1000 ng/mL</th>
<th>1600 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematocrit</td>
<td>30%</td>
<td>50%</td>
<td>70%</td>
</tr>
<tr>
<td>Precision, %CV</td>
<td>14.7</td>
<td>3.5</td>
<td>9.1</td>
</tr>
<tr>
<td>Bias, %</td>
<td>15.3</td>
<td>9.5</td>
<td>7.5</td>
</tr>
</tbody>
</table>
Results

Bridging of clinical data

Mitra® blood vs plasma concentrations following oral administration of PSL

Healthy participants (UP0057; N=28)

- Parameter estimates – R2
- Intercept = 2.3231
- Slope = 0.6478
- R-square = 0.9614

Patients with epilepsy (UP0070; N=14)

- Parameter estimates – R2
- Intercept = −12.93
- Slope = 0.7641
- R-square = 0.8725
Results

Bridging of clinical data

Bland-Altman plot comparing results from Mitra® and venous plasma sampling following oral administration of PSL in patients with epilepsy (UP0070; N=14)

Blood PSL exposure was ~34% lower than plasma exposure

This is in close agreement with the measured *in vitro* blood to plasma ratio of PSL (0.7)
Results

Bridging of clinical data

Analysis of variance of PK parameters of Mitra® vs venous sampling following single dose (100 mg) administration of PSL in healthy participants (UP0057; N=28)

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>Venous geometric mean (95% CI)</th>
<th>Mitra® geometric mean (95% CI)</th>
<th>Ratio (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$, ng/mL</td>
<td>459 (408, 517)</td>
<td>315 (280, 355)</td>
<td>0.687 (0.597, 0.790)</td>
</tr>
<tr>
<td>AUC$_{(0-12 \text{ h})}$, h*ng/mL</td>
<td>1780 (1560, 2040)</td>
<td>1130 (983, 1290)</td>
<td>0.632 (0.538, 0.741)</td>
</tr>
</tbody>
</table>

Blood PSL exposure was ~34% lower than plasma exposure
This is in close agreement with the measured *in vitro* blood to plasma ratio of PSL (0.7)
Conclusions

Volumetric Absorptive Microsampling (VAMS™)

VAMS™ is a novel technology for collection of PK samples

- Reduced blood sampling volumes, ease of collection, transportation and storage compared with conventional plasma sampling

Bioanalytical method for quantification of PSL using VAMS™ has been successfully validated

PK data obtained with VAMS™ have been bridged with plasma in both healthy study participants and patients with epilepsy

UCB Pharma has implemented the use of VAMS™ (Mitra®) for collection of PK samples in global development studies

PK, pharmacokinetic; PSL, padsevonil.
Questions?
Thanks!