Advances in Preterm Birth Prevention, Subcutaneous Versus Intramuscular Dosing of 17 Alpha-hydroxyprogesterone Caproate: Pharmacokinetic Profile, Patient and Practitioner Impact
Objectives

• Incorporate strategies for providing optimal clinical management to women at risk for PTB, based on SMFM, ACOG, and ACNM recommendations

• Define the bioavailability and bioequivalence data regarding subcutaneous administration of 17-OHPC compared with intramuscular administration

• Describe the impact of subcutaneous dosing of 17-OHPC on patient and practitioner parameters
Faculty Information

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Dr. Sibai has nothing to disclose.

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Dr. Smith receives consulting fees from Clovis Oncology, Pfizer Oncology, and Shire and has contracted research with Diawa Pharmaceutical.
Society Guidelines: Progesterone to Prevent Preterm Birth
Pharmacokinetic Properties of 17-OHPC After a Single Dose via Subcutaneous or Intramuscular Administration

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subcutaneous Injection (n=45)</th>
<th>Intramuscular Injection (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$ (ng/mL)</td>
<td>7.9</td>
<td>6.9</td>
</tr>
<tr>
<td>$t_{\text{max}}$ (ng/mL)</td>
<td>48.1</td>
<td>49.7</td>
</tr>
<tr>
<td>AUC 0-168 hrs (ng•h/mL)</td>
<td>813</td>
<td>790</td>
</tr>
<tr>
<td>$t_{\frac{1}{2}}$, h</td>
<td>212</td>
<td>185</td>
</tr>
</tbody>
</table>

## Treatment-emergent Adverse Events (TEAEs)

<table>
<thead>
<tr>
<th>Most Common Treatment Emergent Adverse Events</th>
<th>Subcutaneous Injection (n=57)</th>
<th>Intramuscular Injection (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%) of subjects</td>
<td>Number (%) of subjects</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>22 (37.3)</td>
<td>5 (8.2)</td>
</tr>
<tr>
<td>Headache</td>
<td>9 (15.3)</td>
<td>10 (16.4)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (1.7)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (5.1)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (1.7)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>1 (1.7)</td>
<td>3 (4.9)</td>
</tr>
</tbody>
</table>

Comparison of Pharmacokinetic Properties After Single Dose of Hydroxyprogesterone Caproate in Post-menopausal Women and Pregnant Women

*Note that the higher levels for second and third trimester are due to reaching steady state and having some accumulation from weekly dosing*

<table>
<thead>
<tr>
<th>Group (N)</th>
<th>$C_{\text{max}}$, ng/mL (CV%)</th>
<th>$T_{\text{max}}$, h (range)</th>
<th>AUC $(0-t)$, ng•h/mL (CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-menopausal women IM study arm (n=45)</td>
<td>6.9 (62.9)</td>
<td>49.7 (2-336)</td>
<td>2098 (27.7)</td>
</tr>
<tr>
<td>First trimester pregnant women IM (n=6)</td>
<td>5.0 (1.5)</td>
<td>132 (48-168)</td>
<td>571.4 (195.2)</td>
</tr>
<tr>
<td>Second trimester pregnant women IM (n=8)</td>
<td>12.5 (3.9)</td>
<td>24 (21.6-45.6)</td>
<td>1269.6 (285.0)</td>
</tr>
<tr>
<td>Third trimester pregnant women IM (n=11)</td>
<td>12.3 (4.9)</td>
<td>48 ((24-72)</td>
<td>1268 (511.6)</td>
</tr>
</tbody>
</table>

Auto-Injector

IM Needle (21 gauge)

Sub-cu Needle (27 gauge)
Auto-Injector

- Identify injection location in the back of either upper arm. Disinfect injection site and allow to air dry.
- Place device at a 90 degree angle while supporting patient’s arm. Push down, listen for click, and hold device firmly against arm.
- To ensure full dose, verify window is completely orange before removing device.
### 17-OHPC Subcutaneous/IM Features Comparison Table

<table>
<thead>
<tr>
<th>Product Feature</th>
<th>Subcutaneous 17-OHPC</th>
<th>Intramuscular 17-OHPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Packaging</td>
<td>Pre-filled/single-use</td>
<td>Single-use vials/multi-dose vials</td>
</tr>
<tr>
<td>Location of injection</td>
<td>Back of arm</td>
<td>Buttock</td>
</tr>
<tr>
<td>Needle gauge</td>
<td>27 gauge/0.5” SQ</td>
<td>21 gauge/1.5”</td>
</tr>
<tr>
<td>Duration of injection</td>
<td>15 seconds</td>
<td>≥1 minute</td>
</tr>
<tr>
<td>Needle visibility</td>
<td>Hidden</td>
<td>Viewable</td>
</tr>
<tr>
<td>Safety shield</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Adapted from Krop et al, Clinical Therapeutics 2018; 39(12):2345-2354.