Effects of a novel EP2 and 3 receptor dual agonist (ONO-8055) on lower urinary tract function in normal rats

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Introduction

- Effects of EP2 & 3 dual agonist -
  - Muscle strip studies1: bladder contraction & urethral relaxation
  - LCS rats1: MCC↓, RUR↓, & Pura↓
  - Normal rats: ?

Objectives

To investigate effects of EP2 & 3 agonist (ONO-8055) on LUT function in female normal Wister rats

Materials & Methods

- Experiment 1 (Awake CMG)
  Before and 1, 2, 4 hours after oral administration of vehicle or ONO-8055
- Experiment 2 (Awake Pura)
  Until 2 hours after oral administration of vehicle or ONO-8055

%decrease in Pura = (A/B) x 100²

Results

- Effects of EP2 & 3 dual agonist -

<table>
<thead>
<tr>
<th>Drug</th>
<th>MCC</th>
<th>Pmax</th>
<th>RUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle (n=11)</td>
<td></td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>ONO-8055 0.01 mg/kg (n=7)</td>
<td>*p &lt;0.05 vs. Pre &amp; V</td>
<td></td>
<td>40%</td>
</tr>
<tr>
<td>ONO-8055 0.03 mg/kg (n=7)</td>
<td>*p &lt;0.05 vs. Pre</td>
<td></td>
<td>30%</td>
</tr>
<tr>
<td>ONO-8055 0.1 mg/kg (n=7)</td>
<td>**p &lt;0.05 vs. Pre &amp; V</td>
<td></td>
<td>20%</td>
</tr>
</tbody>
</table>

**References**

2. PLOSOne 2014;9:e93230

Abbreviations

CMG: Cystometry, LCS: Lumbar canal stenosis, LUT: Lower urinary tract, MCC: Maximum cystometric capacity, Pmax: maximal intravesical pressure during voiding, Pura: Intravesical perfusion pressure, RUR: residual urine rate (= residual volume ÷ (voided volume + residual volume) x 100), V: vehicle

Conclusions

- EP2 & 3 receptor dual agonist did not augment bladder contractility.
- Decreases in MCC and Pura were revealed only after administration of the highest dose of ONO-8055.

Interpretation of Results

- Effects of EP2 & 3 dual agonist -

- In LCS rats:
  MCC↓, RUR↓, %Pura↓: 0.003mg/kg~
  EP2 & 3 receptors play a minor role in normal rats while these are more susceptible in LCS rats.
  - No augmenting effects on bladder contractility in normal rats as well as in LCS rats.