EW-7197 Eluting Nanofiber-covered Stent to Prevent Granulation Tissue Formation in a Canine Urethral Model

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Introduction

- **Nanofiber covered stent**
  - Nanofibers fabricated by electrospinning formed a homogenous
  - Steady release of drug without an initial burst
  - Period of drug release can be prolonged by adding nanofiber layers


Esophageal stent for delivery of an Anticancer Drug
Introduction

Specific aims / Hypothesis

➢ To evaluate EW-7197 eluting nanofiber-covered stent (NFCS) for suppressing granulation tissue formation after stent placement in a canine urethral model.
Materials and Methods

- **Stent**
  - EW7197-eluting nanofiber-covered stent
  - Drug: 1000 ug

- **Animals**
  - Proximal and distal urethra of 6 male mongrel dogs
  - Weight: 20 – 25 kg

- **Stent placement in 6 dogs**
  - Group A (3 dogs) – Nanofiber covered stent (control group)
  - Group B (3 dogs) – EW7197-eluting nanofiber covered stent (drug group)

Sacrifice 8 wks
Stent placement
Follow-up RGU
4 wks
8 wks
10 mm in diameter, 20 mm long
10 Fr delivery system
Materials and Methods

- Analysis of retrograde urethrography
  - Luminal diameters at three different levels
  - Before and after stent placement and 4 and 8 weeks after
Materials and Methods

- Hematoxylin and Eosin (H&E) staining
  - Number of epithelial layers (number)
  - Thickness of papillary projection (mm)
  - Thickness of submucosal fibrosis (mm)
  - Degree of Inflammatory cell infiltration

- Masson’s trichrome (MT staining)
  - Degree of collagen deposition
Results

In vitro release study
### Results

#### Retrograde urethrogram

<table>
<thead>
<tr>
<th></th>
<th>1 month follow-up</th>
<th></th>
<th>2 months follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proximal</td>
<td>Distal</td>
<td>Proximal</td>
<td>Distal</td>
</tr>
<tr>
<td><strong>CS group</strong></td>
<td>7.36 ± 1.231</td>
<td>6.62 ± 0.5</td>
<td>6.68 ± 0.39</td>
<td>6.20 ± 1.05</td>
</tr>
<tr>
<td><strong>DS group</strong></td>
<td>9.20 ± 0.42</td>
<td>8.31 ± 0.67</td>
<td>8.60 ± 0.37</td>
<td>7.72 ± 0.58</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>$^P$-value</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.205</td>
<td>0.008</td>
<td>0.223</td>
</tr>
</tbody>
</table>

$^P$-value $< 0.001$ 0.002 $< 0.001$ 0.015

Note. Data are mean ± standard deviation. CS; control stent, DS; drug stent

*Control and drug groups were compared.

$^P$The proximal and the distal urethra were compared.
Results

Histological finding

* CS and DS groups were compared in the proximal urethra.
§ CS and DS groups were compared in the distal urethra.
€ Proximal and distal urethra were compared in the CS group.
¥ Proximal and distal urethra were compared in the DS group.

Thickness of papillary projection

- Proximal
- Distal

<table>
<thead>
<tr>
<th></th>
<th>CS group</th>
<th>DS group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean 95% CI (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X 50</td>
<td><img src="image1" alt="Proximal urethra of CS group" /></td>
<td><img src="image2" alt="Proximal urethra of DS group" /></td>
</tr>
</tbody>
</table>
Results

Histological finding

<table>
<thead>
<tr>
<th>Thickness of submucosal fibrosis</th>
</tr>
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<tbody>
<tr>
<td>Proximal</td>
</tr>
<tr>
<td>Distal</td>
</tr>
<tr>
<td>*  p &lt; 0.001</td>
</tr>
<tr>
<td>§  p &lt; 0.001</td>
</tr>
<tr>
<td>€  p = 0.805</td>
</tr>
<tr>
<td>¥  p = 0.553</td>
</tr>
</tbody>
</table>

* CS and DS groups were compared in the proximal urethra.
§ CS and DS groups were compared in the distal urethra.
€ Proximal and distal urethra were compared in the CS group.
¥ Proximal and distal urethra were compared in the DS group.
Results

Histologic finding

Proximal urethra of CS group

Proximal urethra of DS group

Number of epithelial layer

![Bar graph showing number of epithelial layers in CS and DS groups.]

- **Proximal**
- **Distal**

- * $p < 0.001$
- § $p = 0.002$
- € $p = 0.136$
- ¥ $p = 0.487$

* CS and DS groups were compared in the proximal urethra.
§ CS and DS groups were compared in the distal urethra.
€ Proximal and distal urethra were compared in the CS group.
¥ Proximal and distal urethra were compared in the DS group.
## Results

### Histologic finding

<table>
<thead>
<tr>
<th>Degree of inflammatory cell infiltration</th>
<th>CS group</th>
<th>DS group</th>
</tr>
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<tr>
<td>Mean 95% CI (grade from 1 to 5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CS and DS groups were compared in the proximal urethra. * $p = 0.506$

§ CS and DS groups were compared in the distal urethra. § $p = 0.742$

€ Proximal and distal urethra were compared in the CS group. € $p = 0.387$

¥ Proximal and distal urethra were compared in the DS group. ¥ $p = 0.634$
Results

Histologic finding

Proximal urethra of CS group

Proximal urethra of DS group

Degree of collagen deposition

Mean 95% CI (grade from 1 to 5)

<table>
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* CS and DS groups were compared in the proximal urethra.  
§ CS and DS groups were compared in the distal urethra.  
€ Proximal and distal urethra were compared in the CS group.  
¥ Proximal and distal urethra were compared in the DS group.

* p < 0.001  
§ p < 0.001  
€ p = 0.864  
¥ p = 0.620
Conclusion

- EW-7197 eluting NFCS is effective and safe for suppressing granulation tissue formation after stent placement in a canine urethral model.

- The promising results in this study warrant further studies on this drug for broader applications for stents in other parts of the organs.