Early experience of Duodenal Mucosal Resurfacing treatment for Type 2 Diabetes when expanding from single to multiple sites

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## Disclosures

<table>
<thead>
<tr>
<th>Name</th>
<th>Conflict of Interest</th>
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Bariatric surgery improves glycemia in type 2 diabetes (T2D) independent of weight loss

- Bypass of duodenum assumed key factor

- Bariatric surgery too invasive for managing T2D
Duodenal Mucosal Resurfacing for T2D
DMR appears to improve glycemia in First-in-Human (FIH) study in Chile*

*Unpublished data
Potential use of DMR for T2D

- Patients with insufficient glucose regulation on oral medication
- May prevent the need for insulin therapy
Many “unknowns” still remain

- What is the underlying mechanism of the improved glycemic control?
- How long does this effect remain?
- How safe is the procedure?
Duodenal stenosis (n=3) in Chile FIH study

- All developed < 6 weeks post-DMR
- Resolved by endoscopic dilatation

Underlying causes

- Overlapping ablation zones
- Ablation of non-lifted mucosa
European multicentre study initiated

- Adjusted DMR procedure
  - Ablation proximal $\rightarrow$ distal
  - More extensive mucosal lifting
  - Modified procedure tested in animal lab

- Aim
  - Assess safety and feasibility
Patients

- Age 28-75 years
- T2D ≤ 10 years
- HbA1c 7.5-11.0%
- On oral glucose lowering medication
- BMI 24-40 kg/m²
Step 1: Mucosal lifting

Step 2: Mucosal thermal ablation
After DMR procedure

- Discharge same day or after overnight stay
- Proton Pump Inhibitor from -1 to +4 weeks
- Step-up diet for 2 weeks
Centres and endoscopists

- Single centre study
  - First-in-Human in Chile
  - 39 patients
  - Single endoscopist

- Multi-centre study
  - Amsterdam, Chile, Rome, Brussels, London
  - 27 patients
  - In each centre single endoscopist
### Results

<table>
<thead>
<tr>
<th>Description</th>
<th>Multi-centre study</th>
<th>Single centre study</th>
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<tbody>
<tr>
<td><strong>Patients (n)</strong></td>
<td>27</td>
<td>39</td>
</tr>
<tr>
<td><strong>Age (years) mean &amp; 95% ci</strong></td>
<td>55±9</td>
<td>54±7</td>
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<tr>
<td><strong>HbA1c (%) mean &amp; 95% ci</strong></td>
<td>8.7±1.0</td>
<td>9.5±1.3</td>
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<tr>
<td><strong>Minimal follow-up (months)</strong></td>
<td>5</td>
<td>10</td>
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<tr>
<td><strong>Adverse Events (patients)</strong></td>
<td>52%</td>
<td>82%</td>
</tr>
<tr>
<td><strong>Adverse Events (episodes)</strong></td>
<td>36</td>
<td>85</td>
</tr>
<tr>
<td><strong>Mild / Moderate / Severe (n)</strong></td>
<td>29 / 7 / 0</td>
<td>65 / 17 / 3</td>
</tr>
<tr>
<td>Severe: Duodenal stenosis</td>
<td></td>
<td></td>
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<tr>
<td><strong>Procedure related / unrelated</strong></td>
<td></td>
<td></td>
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<tr>
<td>Related: Mild abdominal pain, nausea, diarrhea, throat pain</td>
<td>36% / 64%</td>
<td>39% / 61%</td>
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<tr>
<td><strong>Procedure time (min) median &amp; IQR</strong></td>
<td>86 (69–118)</td>
<td>91 (78.5–110)</td>
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</table>
• The DMR procedure proved feasible in a multi-centre setting
• Adverse events were generally mild and as expected
• The modified DMR procedure was not associated with duodenal stenosis in 27 patients
• No serious adverse events observed after the DMR procedure
- Procedure time leaves room for improvement
- Complexity of the procedure needs to be reduced
New single-step catheter on its way
Future plans

- Safety and feasibility study new catheter
- RCT comparing DMR procedure with sham
- Establishment durability of effect
- Elucidation of mechanism