Preliminary Results of RETREAT
(Renal Denervation with Ultrasound After Failed Radiofrequency Denervation)

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There are many potential reasons why renal denervation may fail:

- Renal denervation may not work at all
- Changes in medication
  - before the procedure
  - during follow-up
- Patient specific factors
  - type of medication
  - race
- Procedural technical issues
  - not enough or incomplete ablations
  - ablation not circumferential
- Technology not good enough to destroy all renal nerves in all patients
Renal Denervation with Ultrasound

• As with RF energy, renal denervation is achieved by inducing thermal necrosis
• Ultrasound energy passes through fluids and generates frictional heating in soft tissues
• Unlike RF, no direct tissue contact required
  - Stability is less of an issue
Ultrasound: Recor Medical

- Ultrasound transducer mounted inside of a low pressure balloon
- Cooled water in the balloon protects the endothelium against heat
- 30 seconds of circumferential heating
REDUCE:
Office Systolic Blood Pressure (93% Responder Rate)

Source: Company Data
Purpose of RETREAT

• To evaluate the effect of renal denervation with ultrasound (Recor system) after failed denervation with radiofrequency (Syplicity)
RETREAT

• Physician initiated prospective multi-center study
• No funding
• N = 30
• Enrolment clashed with
  - the publication of HTN-3
  - stop of reimbursement for renal denervation in Germany
  - decline in referrals for renal denervation
  - new treatment modalities for hypertension
• Enrolment was very low and almost stopped
• Study results are not conclusive ....
  - .... but still some interesting observations
RETREAT

Inclusion Criteria

- First renal denervation with Symplicity \( \geq 12 \) months prior to study participation
- "Non-responder"
  - \( \text{BP} \downarrow < 10\text{mmHg} \) or
  - \( \text{BP} \) still high (> 160mmHg)
- Systolic Office BP \( \geq 140\text{mmHg} \)
- Optimal medical therapy
  - 3 or more antihypertensive drugs including one diuretic, all at max. tolerated dose
- Secondary hypertension was ruled out
RETREAT Endpoints

• Primary Endpoints:
  - change in office and ambulatory blood pressure 12 months after the procedure
  - decrease in antihypertensive medication

• Secondary Endpoint:
  - Freedom from adverse events
RETREAT
Examination schedule

• Baseline:
  - OBP, ABPM
  - Blood test: Creatinine
  - MRI/angiographic evaluation to rule out renal artery abnormalities

• Follow up after 1, 3, 6 and 12 months:
  - OBP, ABPM
  - Changes in medication
  - Adverse events

• Renal duplex ultrasound after 6 months
• Creatinine after 6 and 12 months
Prior Renal Denervation Procedure with Radiofrequency

- Radiofrequency RDN with the Medtronic Symplicity Catheter
- Both renal arteries were treated in each patient
  - Circumferential ablation
  - 10-20 (14.5) ablations per patient
- No adverse events occurred during the procedure
- OBP after 6 months
  - Decrease of less than 10mmHg and/or
  - OBP >160 mmHg
RETREAT Procedure

- N = 8
- Ultrasound Renal Denervation with the Recor Paradise System
- 2-3 (2.3) ablations per artery
- Technical success in all patients
- No device related adverse events
- One false occurred in one patient
- No changes in Creatinine levels
Office Blood Pressure

<table>
<thead>
<tr>
<th>Follow up</th>
<th>Mean OBP</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>171/87mmHg</td>
<td>9</td>
</tr>
<tr>
<td>1 month</td>
<td>150/80mmHg</td>
<td>3</td>
</tr>
<tr>
<td>3 months</td>
<td>154/84mmHg</td>
<td>6</td>
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<tr>
<td>6 months</td>
<td>175/89mmHg</td>
<td>7</td>
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<tr>
<td>12 months</td>
<td>171/94mmHg</td>
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Ambulatory Blood Pressure

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<tr>
<th>Follow up</th>
<th>Mean ABP</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>158/87mmHg</td>
<td>9</td>
</tr>
<tr>
<td>1 month</td>
<td>143/77mmHg</td>
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<tr>
<td>3 months</td>
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<tr>
<td>6 months</td>
<td>152/82mmHg</td>
<td>6</td>
</tr>
<tr>
<td>12 months</td>
<td>154/78mmHg</td>
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</tr>
</tbody>
</table>
Conclusions

• Enrolment in this trial has been too slow due to a number of reasons
• Renal denervation with ultrasound (Recor system) after prior denervation with radiofrequency seems to be safe
• After an initial decrease of BP after one month we observed an increase in blood pressure which has not been seen in other renal denervation studies
• Renal denervation with ultrasound (Recor system) may be effective in patients with resistant hypertension who failed to respond to renal denervation with the Symplicity system
• The study is too small to draw valid conclusions
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