Six Month Results of First-in-Human Sympathetic Renal Artery Denervation Using a Next Generation Multi-Electrode Renal Artery Denervation System in Patients with Drug-Resistant Hypertension

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Next Generation EnligHTN Product Description

- Proven ablation catheter
  - Consistent, predictable 4 lesion ablation pattern
  - Non-occluding, Nitinol basket design
  - 8F compatible
- Simultaneous 60 second ablation
- Diagnostic mode designed to assess electrode apposition prior to ablation
- Report Summary tracks electrode activation time and average temperature for each electrode
- Touch-screen pole-mounted generator

<table>
<thead>
<tr>
<th>Default Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time</strong></td>
</tr>
<tr>
<td>60 seconds simultaneous</td>
</tr>
<tr>
<td><strong>Impedance</strong></td>
</tr>
<tr>
<td>100-400 Ω</td>
</tr>
<tr>
<td><strong>Maximum Power</strong></td>
</tr>
<tr>
<td>8 Watts</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
</tr>
<tr>
<td>70 degrees C</td>
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</tbody>
</table>
EnligHTN Procedure Proctoring

- Initial basket positioning proximal to the bifurcation
- Expand basket and perform generator diagnostic check for electrode contact (≥ 2°C temp rise required)
- Simultaneous ablation - 60 seconds per basket set
- For a second set of ablations the basket is collapsed, pulled back 1 cm, rotated ~45 degrees and expanded, contact is checked and ablation sequence repeated
- Manually de-activate any electrodes that do not reach >50 degrees C by 20 seconds
## EnligHTN III: FIH Next Generation Study

<table>
<thead>
<tr>
<th><strong>Objective</strong></th>
<th>To establish initial safety and efficacy of the EnligHTN™ Next Generation Renal Denervation System utilizing simultaneous ablations.</th>
</tr>
</thead>
</table>
| **Design & Sample Size** | Prospective, multi-center, single arm, FIH study; similar study design & population as EnligHTN I  
  - Up to 50 subjects – drug-resistant hypertension  
  - 6 international sites (Australia & New Zealand) |
| **Primary Endpoints** | Primary Efficacy: Reduction of Office SBP at 6 months  
  Primary Safety: Adverse events at six (6) months  
  Secondary: Reduction in ABP, renal function, renal safety |
| **Follow-Up Schedule** | 30 days, 3, 6, 12, 18 and 24 months post procedure |
| **Milestones** | 1\textsuperscript{st} Enrollment: Q2 2013  
  1/3 Month results: Presented at TCT Oct 2013, RHC, Trends  
  6 Month results: presented at EuroPCR May 2014 |
EnligHTN III Key Inclusion / Exclusion Criteria

**Inclusion Criteria**
- Patient written informed consent
- Willing / able to comply with follow-up schedule
- ≥ 18 and ≤ 80 years old
- Appropriate renal artery anatomy
- Office systolic BP ≥ 160 mmHg
- Ambulatory systolic BP > 135 mmHg during screening period (daytime mean)
- Stable use of ≥ 3 antihypertensive medications concurrently at maximally tolerated doses for a minimum of 14 days prior to enrollment of which:
  - one is a diuretic, or
  - patient was on diuretic previously but documented to be diuretic intolerant

**Exclusion Criteria**
- Prior renal artery intervention or evidence of renal artery disease (diameter stenosis > 30%)
- Multiple main renal arteries in either kidney or main renal arteries < 4 mm in diameter or < 20 mm in length
- eGFR < 45 mL/min/1.73m² (MDRD formula)
- Type 1 Diabetes Mellitus
- Secondary cause of hypertension
- Hemodynamically significant valvular heart disease
EnligHTN III – Study Design

Enrollment N=65

Screening Period

Renal Denervation Eligible N=39

Not Eligible N=26

Observation Arm N=0

24-Month Follow-up
Current Status:
N=39/39 1-Month Follow-ups Complete
N=38/38 3-Month Follow-ups Complete
N=37/38 6-Month Follow-ups Complete

1-Month Follow-up

Primary Objectives: Safety (Adverse Events) and Efficacy (Office BP) at 6-Months Post-Procedure
## EnligHTN III – Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± Std (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td>63.49 ± 8.75 (39)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.92 ± 5.17 (38)</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>15/39 (38.5%)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>6/39 (15.4%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>23/39 (59.0%)</td>
</tr>
<tr>
<td>Diabetes Type II</td>
<td>13/39 (33.3%)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>5/39 (12.8%)</td>
</tr>
<tr>
<td>eGFR (mL/min per 1.73m²)</td>
<td>73.97 ± 16.78 (38)</td>
</tr>
<tr>
<td>Serum Creatinine (umol/L)</td>
<td>88.90 ± 19.39 (39)</td>
</tr>
<tr>
<td>Cystatin C (mg/L)</td>
<td>1.03 ± 0.30 (37)</td>
</tr>
<tr>
<td>Urine Albumin-to-Creatinine Ratio (mg/g)</td>
<td>306.53 ± 841.90 (36)</td>
</tr>
<tr>
<td>Number of Anti-Hypertensive Medications</td>
<td>4.67 ± 1.11 (39)</td>
</tr>
<tr>
<td>Average Office Systolic BP (mmHg)</td>
<td>174.23 ± 12.71 (39)</td>
</tr>
<tr>
<td>Average Office Diastolic BP (mmHg)</td>
<td>92.90 ± 14.99 (39)</td>
</tr>
<tr>
<td>Average 24 Hour Ambulatory Systolic BP (mmHg)</td>
<td>154.85 ± 15.63 (39)</td>
</tr>
<tr>
<td>Average 24 Hour Ambulatory Diastolic BP (mmHg)</td>
<td>82.08 ± 12.25 (39)</td>
</tr>
<tr>
<td>Average Office Heart Rate (BPM)</td>
<td>67.67 ± 15.58 (39)</td>
</tr>
</tbody>
</table>
EnligHTN III – Procedural Success and Ablation Time

100% of subjects that underwent the procedure received renal denervation in both arteries.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± Std (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablations performed: Left renal artery</td>
<td>8.00 ± 0.69 (39)</td>
</tr>
<tr>
<td>Ablations performed: Right renal artery</td>
<td>7.85 ± 0.49 (39)</td>
</tr>
<tr>
<td>Total ablations performed</td>
<td>15.85 ± 1.01 (39)</td>
</tr>
<tr>
<td>Total ablation sets</td>
<td>4.33 ± 0.62 (39)</td>
</tr>
<tr>
<td>Ablation catheter insertion to removal time (min)</td>
<td>22.38 ± 11.78 (39)</td>
</tr>
<tr>
<td>Total ablation time (min)</td>
<td>4.33 ± 0.62 (39)</td>
</tr>
</tbody>
</table>
EnligHTN III – Safety Results: Adverse Events, Renal Function

Adverse Events

- Serious Device or Procedure Related Adverse Events: NONE
- Non-Serious Device or Procedure Related Adverse Events
  - Examples: vascular access site hematoma, vascular access site bruise, vascular access site drainage, hypotensive episodes, non-flow limiting vasospasm, back pain, pain, vascular access site pain

Renal Function

- No clinically significant change in renal function through 6-months

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean ±SD (n)</th>
<th>Month 1 Mean ±SD (n)</th>
<th>Month 3 Mean ±SD (n)</th>
<th>Month 6 Mean ±SD (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>74.0 ± 16.8 (38)</td>
<td>75.9 ± 15.7 (39)</td>
<td>73.7 ± 16.4 (38)</td>
<td>73.8 ± 17.4 (37)</td>
</tr>
<tr>
<td>Serum Creatinine (umol/L)</td>
<td>88.9 ± 19.4 (39)</td>
<td>86.7 ± 21.2 (39)</td>
<td>88.2 ± 24.4 (38)</td>
<td>88.3 ± 26.2 (37)</td>
</tr>
<tr>
<td>Cystatin-C (mg/L)</td>
<td>1.03 ± 0.30 (37)</td>
<td>1.01 ± 0.28 (39)</td>
<td>1.04 ± 0.28 (35)</td>
<td>1.09 ± 0.30 (37)</td>
</tr>
<tr>
<td>Urine Albumin-to-Creatinine Ratio (mg/g)</td>
<td>306.5 ± 841.9 (36)</td>
<td>230.2 ± 659.0 (36)</td>
<td>106.0 ± 234.2 (33)</td>
<td>274.6 ± 613.2 (31)</td>
</tr>
</tbody>
</table>
EnligHTN III – Office Blood Pressure Reduction From Baseline

Month 1 (n=39)  Month 3 (n=38)  Month 6 (n=37)

Change in Blood Pressure (mmHg)

Systolic  Diastolic

-19  -7  -19  -9  -7  -25

95% CI

<0.0001  0.0005  <0.0001  <0.0001  <0.0001  <0.0001  p-values

St. Jude Medical
EnligHTN III – 24 Hour Ambulatory Blood Pressure Reduction From Baseline

Month 1 (n=39)  
Systolic: -7  
Diastolic: -4  
95% CI: 0.0030

Month 3 (n=37)  
Systolic: -10  
Diastolic: -4  
95% CI: 0.0002

Month 6 (n=37)  
Systolic: -8  
Diastolic: -2  
95% CI: 0.0008

p-values: 0.0030, 0.0006, 0.0002, 0.0046, 0.0008, 0.1401
**EnligHTN III – Office Systolic Blood Pressure Reduction By Group**

- **Responder Rate:** Defined as $\geq 10$ mmHg reduction from baseline value
  - 67% at One-Month ($n=26/39$)
  - 82% at Three-Months ($n=31/38$)
  - 81% at Six-Months ($n=30/37$)

![Bar chart showing blood pressure distribution across different time points](chart.png)
## Summary

| Safety                        | No serious device related adverse events  
|                              | No serious procedure related adverse events  
|                              | No change in renal function  
| Efficiency                   | 15.85 ablations per patient  
|                              | 4.3 minutes total ablation time  
| Efficacy                     | Sustained office and ambulatory blood pressure reduction observed through six months  
