EnligHTN™ I, First-in-Human Multicenter Study of a Multi-Electrode Renal Denervation Catheter in Patients with Drug-Resistant Hypertension

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### Background

- Renal denervation has emerged as a new treatment for patients with drug-resistant hypertension.
- Single-tip electrode radiofrequency ablation catheters have been used to achieve sympathetic fiber interruption through the renal artery wall.
- However, systems designed to create predetermined predictable ablation patterns have not been tested.
- Ideal lesions are transmural, causing fiber interruption, but no scar or charring.

### Study Objectives

- To investigate the safety and efficacy of a multi-electrode catheter ablation system (EnligHTN) in patients with drug-resistant hypertension.
- Safety Markers: Any adverse event occurring during the study.
- Primary Efficacy Marker: Change in office BP at 6 months.
- Additional Endpoints Assessment Over Time:
  - Renal artery evaluation
  - Renal function
  - Home based BP
  - 24 hr. ambulatory BP
  - Anti-hypertensive medication changes
EnligHTN™ Multi-Electrode Renal Denervation System*

**Ablation Catheter**

- Multi-electrode
- Radiopaque electrodes
- 8 F compatible
- Deflectable, atraumatic tip
- Femoral access

**Generator**

- Default settings:
  - Power output (6 Watts)
  - Impedance (400Ω)
  - Electrode temperature (75 degrees C)
  - Time (90 seconds per ablation)
  - Temperature controlled

*CE Mark — December 2011. Not for sale in the U.S.
Renal Procedure Goal: Effective Denervation

**Transmurality***


** Predictable Pattern

Acute lesion formation**

** Animal study. Results on file at St. Jude Medical

After one month**
Procedure Overview

- Initial basket positioning proximal to the bifurcation
- Expand basket and perform generator diagnostic check for electrode contact
- Ablate – 90 seconds per electrode
- For a second set of ablations the basket is collapsed, pulled back 1 cm, rotated and expanded, contact is checked and ablation sequence repeated
EnligHTN I: First-in-Human Clinical Trial

Inclusion / Exclusion Criteria

**Inclusion Criteria**
- Patient written informed consent
- Willing / able to comply with follow-up schedule
- Appropriate renal artery anatomy
- Office Systolic BP ≥ 160 mmHg
- 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
- ≥ 18 and ≤ 80 years old

**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 of <45 mL/min/1.73m² (MDRD formula)
- Type 1 Diabetes Mellitus or identified secondary cause of hypertension
- Hemodynamically significant valvular heart disease
The document discusses the study design and enrollment criteria for a renal denervation study. It states that due to renal artery anatomy, renal denervation was not attempted for some participants. The study included 62 enrollments, with 47 eligible for renal denervation and 15 not eligible. Of the eligible participants, 46 were assigned to the denervation arm and observed for 24 months, while 1 was assigned to the observation arm and observed for 6 months. The primary objectives were to assess safety (adverse events) and efficacy (office blood pressure).
Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n = 46*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>15 (33%)</td>
</tr>
<tr>
<td>Ethnic origin (white)</td>
<td>45 (98%)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>32 (±5)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>9 (20%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>27 (59%)</td>
</tr>
<tr>
<td>Type II Diabetes Mellitus</td>
<td>15 (33%)</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>14 (30%)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>87 (±19)</td>
</tr>
<tr>
<td>Serum Creatinine (µmol/L)</td>
<td>78 (±17)</td>
</tr>
<tr>
<td>Cystatin C (mg/L)</td>
<td>1.14 (±0.29)</td>
</tr>
<tr>
<td>Number of Anti-Hypertensive Medications</td>
<td>4.1 (±0.6)</td>
</tr>
<tr>
<td>Office Systolic Blood Pressure (mmHg)</td>
<td>176 (±16)</td>
</tr>
<tr>
<td>Office Diastolic Blood Pressure (mmHg)</td>
<td>96 (±14)</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>71 (±12)</td>
</tr>
</tbody>
</table>

- Two patients did not meet all inclusion criteria, but are included in the analyses
- Data are mean (±SD) or number (%)
Results: Safety Data

Safety outcomes up to 6 months:

- **Serious Peri-Procedural Events: NONE**
  - No renal artery dissections, aneurysms or new stenosis
  - No flow-limiting renal artery vasospasms
  - No major vascular access complications

- **Non-Serious Peri-Procedural Events:**
  - Non-flow limiting vasospasms, puncture site hematomas, vasovagal reactions, low back pain, hypotensive episodes, transient hematuria, nausea and bradycardia

- **Serious device/procedure events include:**
  - Worsening of pre-existing proteinuria (n=1)
  - Symptomatic hypotension (n=1)
  - Worsening of pre-existing renal artery stenosis (n=1)

*The EnligHTN System delivers renal denervation with an acceptable safety profile through 6 months*
Renal Function

- There was no clinically significant change in renal function
  - No patient experienced:
    - a reduction in eGFR >50%,
    - a two-fold increase in Serum Creatinine, or
    - progressed to end stage renal disease

- Laboratory Values:

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=46)</th>
<th>Month 1 (n=46)</th>
<th>Month 3 (n=46)</th>
<th>Month 6 (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>87 (±19)</td>
<td>85 (±20)</td>
<td>84 (±22)</td>
<td>82 (±20)</td>
</tr>
<tr>
<td>Serum Creatinine (mmol/L)</td>
<td>78 (±17)</td>
<td>79 (±19)</td>
<td>81 (±20)</td>
<td>83 ± (20)</td>
</tr>
<tr>
<td>Cystatin C (mg/L)</td>
<td>1.14 (±0.29)</td>
<td>1.00 (±0.25)</td>
<td>0.97 (±0.20)</td>
<td>1.00 (±0.23)</td>
</tr>
</tbody>
</table>
Mean Office Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=46)</th>
<th>Month 1 (n=46)</th>
<th>Month 3 (n=46)</th>
<th>Month 6 (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>176</td>
<td>148</td>
<td>149</td>
<td>150</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>96</td>
<td>87</td>
<td>87</td>
<td>86</td>
</tr>
</tbody>
</table>

Blood Pressure (mmHg)
Office BP Reduction from Baseline

EnligHTN therapy delivers a rapid and significant reduction in Office BP that is sustained through the 6M timeframe

Month 1 (n=46): Systolic BP change = -28 mmHg, Diastolic BP change = -10 mmHg
Month 3 (n=46): Systolic BP change = -27 mmHg, Diastolic BP change = -10 mmHg
Month 6 (n=45): Systolic BP change = -26 mmHg, Diastolic BP change = -10 mmHg

p <0.0001
24 hr Ambulatory BP Reduction from Baseline

EnligHTN therapy delivers a rapid and significant reduction in Ambulatory BP that is sustained through the 6M timeframe.
% Responders (>10 mmHg Reduction from baseline) = 76% (n=34)

At Goal SBP:

2/3 of patients will have a great enough reduction in their BP to move to a lower stage of HTN classification / treatment and approximately 1/3 of patients treated with EnligHTN no longer meet HTN classification.
Conclusions

- **Safe**
  - No renal artery dissections, aneurysms, or new stenoses
  - No flow-limiting renal artery vasospasms
  - No major vascular access complications

- **Rapid Treatment Effect**
  - Office BP was reduced by 28/10 mmHg at 1 month

- **Sustained Results**
  - Office and Ambulatory BP results were concordant and sustained at 6 months
  - 76% of patients were responders at 6 months

*The EnligHTN™ system delivers a promising therapy for the treatment of patients with drug-resistant hypertension*