Longer Term Safety and Efficacy of Sympathetic Renal Artery Denervation using a Multi-Electrode Renal Artery Denervation Catheter in Patients with Drug-Resistant Hypertension: Twenty-four Month Results of a First-in-Human, Multicenter Study

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St. Jude Medical
EnligHTN™ 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
- Sequential
- Diagnostic mode designed to assess electrode apposition

This FIH study is being conducted in Australia and Greece. Caution: Investigational device. Limited by Federal law to investigational use. Not for sale in the U.S.
Renal Procedure Goal: Effective Denervation

**Predictable Pattern**

**Acute lesion formation***

* Animal study. Results on file at St. Jude Medical
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.
Key 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
Exclusion due to renal artery anatomy therefore renal denervation was not attempted.

Primary Objectives: Safety (Adverse Events) & Efficacy (Office BP)
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>n = 46*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>15 (33%)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>59.9 ± 10.2</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>Urine Albumin-to-Creatinine Ratio (mg/g)</td>
<td>167.6 ±493</td>
</tr>
<tr>
<td>Number of Anti-Hypertensive Medications</td>
<td>4.7 ±1.0</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 (%)
## Procedure Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>n = 46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablations performed: Left renal artery (mean)</td>
<td>7.4 (±1.4)</td>
</tr>
<tr>
<td>Ablations performed: Right renal artery (mean)</td>
<td>7.7 (±0.8)</td>
</tr>
<tr>
<td>Total ablations performed per patient</td>
<td>15.0 (±2.4)</td>
</tr>
<tr>
<td>Median procedure time, min (initiation to completion of RF energy delivery)</td>
<td>34.0</td>
</tr>
</tbody>
</table>
Safety Results

Objective
The primary safety outcome was assessment of all adverse events.

- No Serious Peri-Procedural Events
- No new serious device/procedure related events between 18 and 24 months of follow-up
- Serious device/procedure related events through 24 months:
  - Worsening of pre-existing proteinuria (n=1)
  - Symptomatic hypotension (n=1)
  - Worsening of pre-existing renal artery stenosis and new stenotic lesion (n=2 events in 1 patient)

The EnligHTN System delivers renal denervation with no serious peri-procedural events and an acceptable safety profile through 24 months
## Renal Function Results

<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>
<th>Month 12 (n=45)</th>
<th>Month 18 (n=44)</th>
<th>Month 24 (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>eGFR (mL/min/1.73m²)</strong></td>
<td>87 (±19)</td>
<td>85 (±20)</td>
<td>84 (±22)</td>
<td>82 (±20)</td>
<td>86 (±21)</td>
<td>77 (±16)</td>
<td>77 (±22)</td>
</tr>
<tr>
<td><strong>Serum Creatinine (mmol/L)</strong></td>
<td>78 (±17)</td>
<td>79 (±19)</td>
<td>81 (±20)</td>
<td>83 (±20)</td>
<td>80 (±28)</td>
<td>86 (±21)</td>
<td>91 (±42)</td>
</tr>
<tr>
<td><strong>Cystatin C (mg/L)</strong></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>
<td>0.91 (±0.19)</td>
<td>1.1 (±0.3)</td>
<td>1.3 (±0.4)</td>
</tr>
<tr>
<td><strong>Urine Albumin-to-Creatinine Ratio (mg/g)</strong></td>
<td>167.6 (±493)</td>
<td>142.9 (±477)</td>
<td>141.3 (±449)</td>
<td>139.3 (±449)</td>
<td>116.9 (±421)</td>
<td>131.0 (±358)</td>
<td>157.5 (±609)</td>
</tr>
</tbody>
</table>

Renal function remains within expected range for this patient population.
EnligHTN therapy delivers a rapid and significant reduction in Office BP that is sustained through 24 months.
EnligHTN therapy delivers a rapid and significant reduction in Ambulatory BP that is sustained through 24 months.
Responder & Goal Blood Pressure Parameters

- 77% of patients are considered responders at 24 months (>10 mmHg OSBP Reduction from baseline)
- 39% of patients have OSBP <140 mmHg at 24 months

3/4 of patients demonstrated >10 mmHg OSBP reduction from baseline at 24 months
# Summary

## Safety
- No serious peri-procedural events
- Acceptable safety profile through 24 months

## Effectiveness
- Office BP was reduced by 28/10 mmHg at 1 month
- 15.0 ($\pm 2.4$) ablations performed; 7.4 ($\pm 1.4$) left and 7.7 ($\pm .8$) on the right

## Sustained Results
- A significant reduction in office of Systolic and Diastolic BP (29/13) was sustained through 24 months
- A significant reduction in ambulatory BP at 24 months (13/7)
- 77% of patients are responders at 24 months