ENLIGHTN I

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

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EnligHTN I: Background / Study Objectives

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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 occuring 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*

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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

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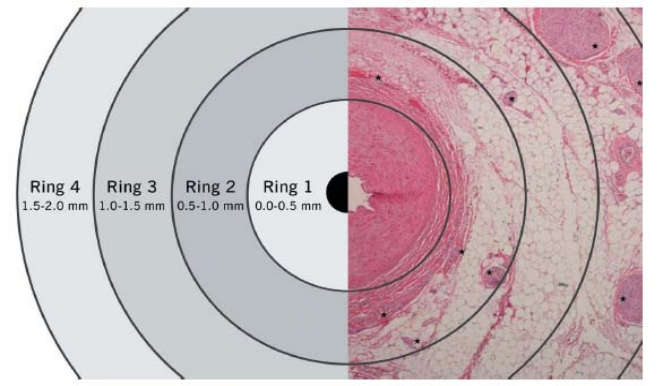
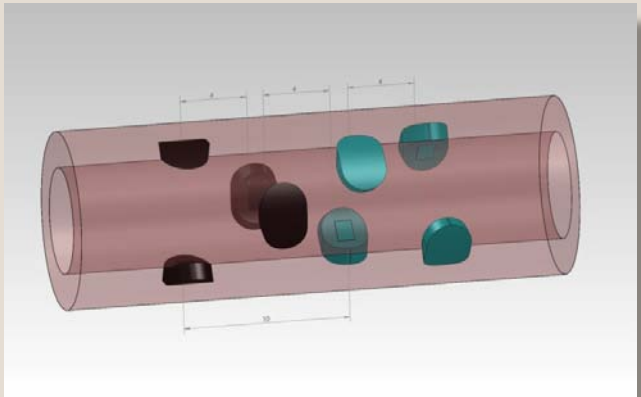
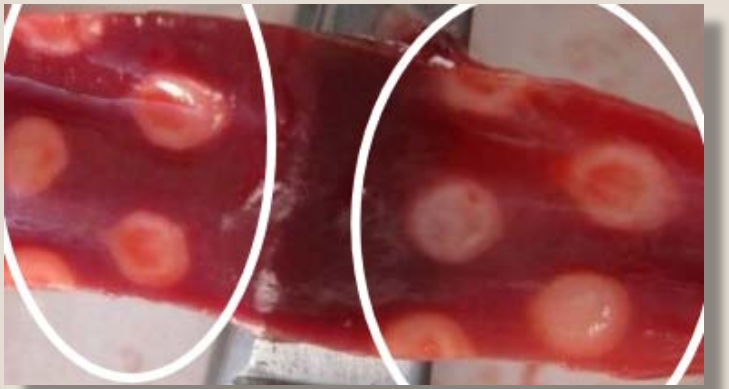
Transmurality*



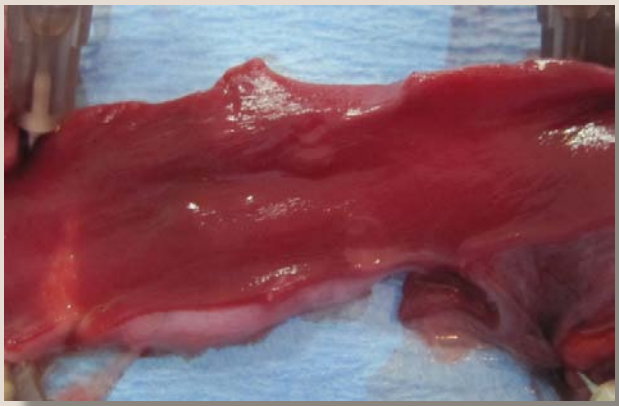
Predictable Pattern



Acute lesion formation**



After one month**



* Atherton DS, Deep NL, Mendelsohn FO, Micro-Anatomy of the Renal Sympathetic Nervous System: A Human Postmortem Histological Study, Clinical Anatomy 2011.

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

Procedure Overview

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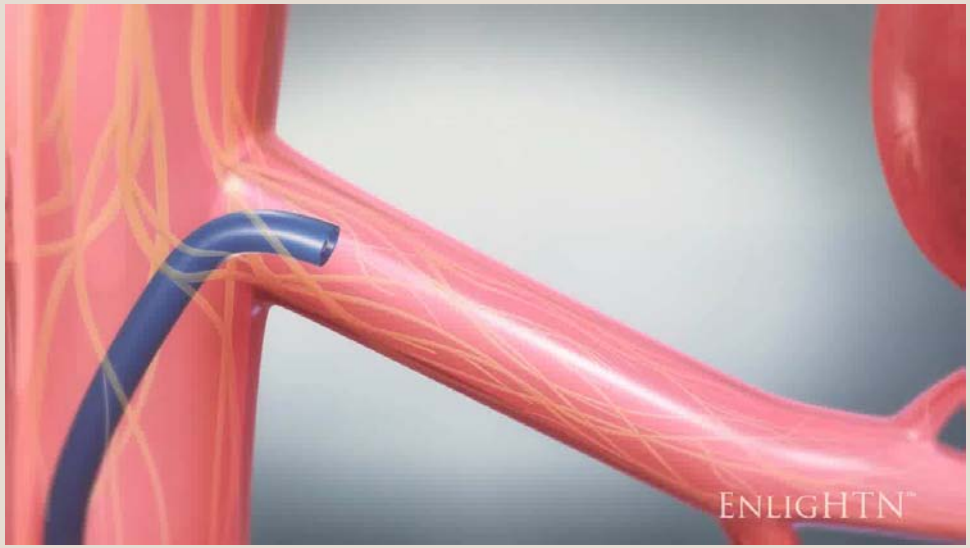
- Initial basket positioning proximal to the bifurcation
- Expand basket and perform generator diagnostic check for electrode contact
- Ablate – 90 seconds per electrode
- For a second set of ablations the basket is collapsed, pulled back 1 cm, rotated and expanded, contact is checked and ablation sequence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



EnligHTN I: First-in-Human Clinical Trial Inclusion / Exclusion Criteria

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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/1.73m^2 (MDRD formula)
- Type 1 Diabetes Mellitus or identified secondary cause of hypertension
- Hemodynamically significant valvular heart disease

Study Design

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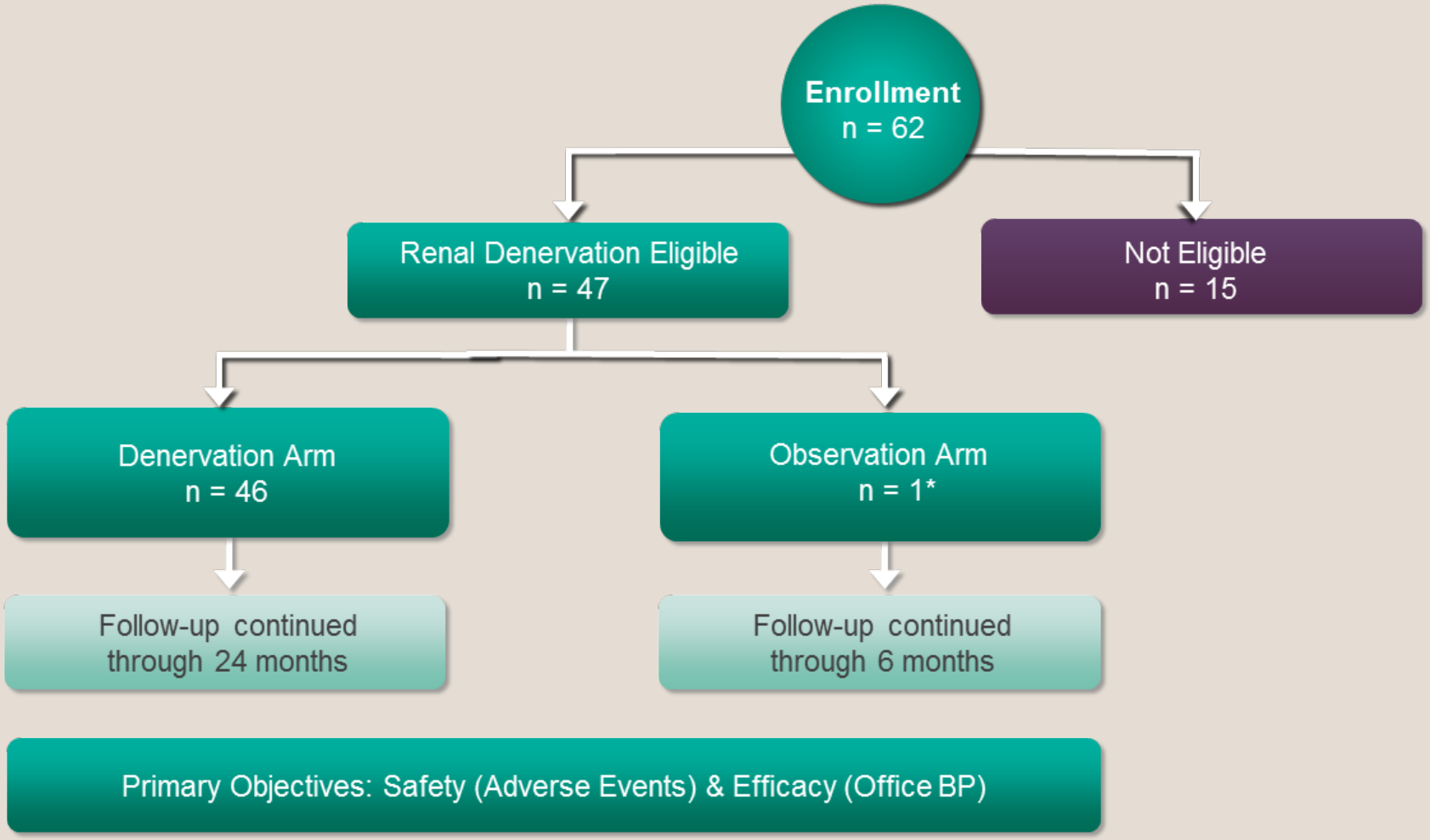

* Exclusion due to renal artery anatomy therefore renal denervation was not attempted.

Baseline Characteristics

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	n = 46*
Gender (female)	15 (33%)
Ethnic origin (white)	45 (98%)
Body Mass Index (kg/m^2)	32 (±5)
Coronary Artery Disease	9 (20%)
Hyperlipidemia	27 (59%)
Type II Diabetes Mellitus	15 (33%)
Sleep Apnea	14 (30%)
eGFR (mL/min/1.73m^2)	87 (±19)
Serum Creatinine (μmol/L)	78 (±17)
Cystatin C (mg/L)	1.14 (±0.29)
Number of Anti-Hypertensive Medications	4.1 (±0.6)
Office Systolic Blood Pressure (mmHg)	176 (±16)
Office Diastolic Blood Pressure (mmHg)	96 (±14)
Heart Rate (bpm)	71 (±12)

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

Results: Safety Data

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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

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- 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:

	Baseline (n=46)	Month 1 (n=46)	Month 3 (n=46)	Month 6 (n=45)
eGFR (mL/min/1.73m^2)	87 (±19)	85 (±20)	84 (±22)	82 (±20)
Serum Creatinine (mmol/L)	78 (±17)	79 (±19)	81 (±20)	83 ± (20)
Cystatin C (mg/L)	1.14 (±0.29)	1.00 (±0.25)	0.97 (±0.20)	1.00 (±0.23)

Mean Office Blood Pressure

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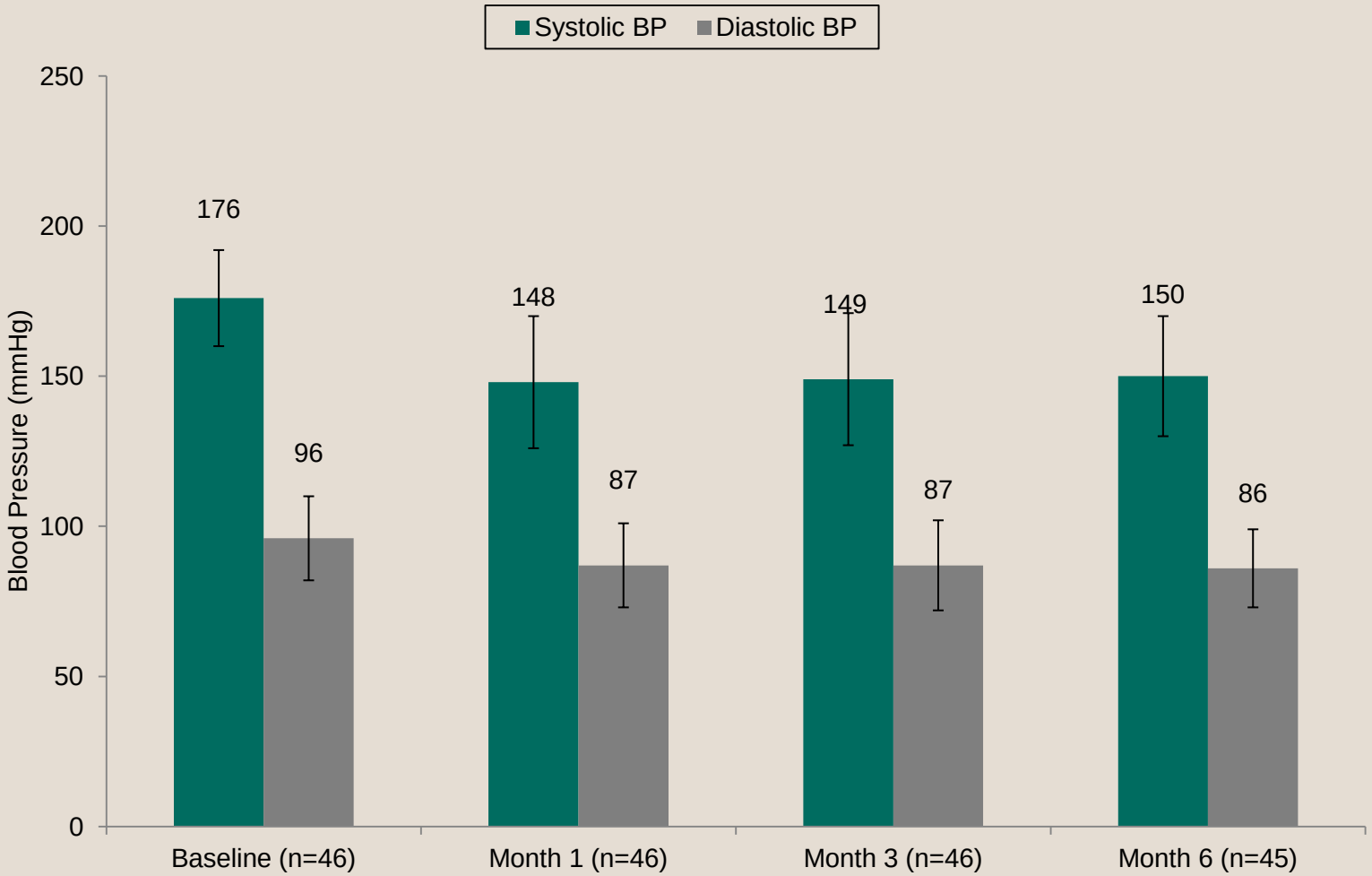

Office BP Reduction from Baseline

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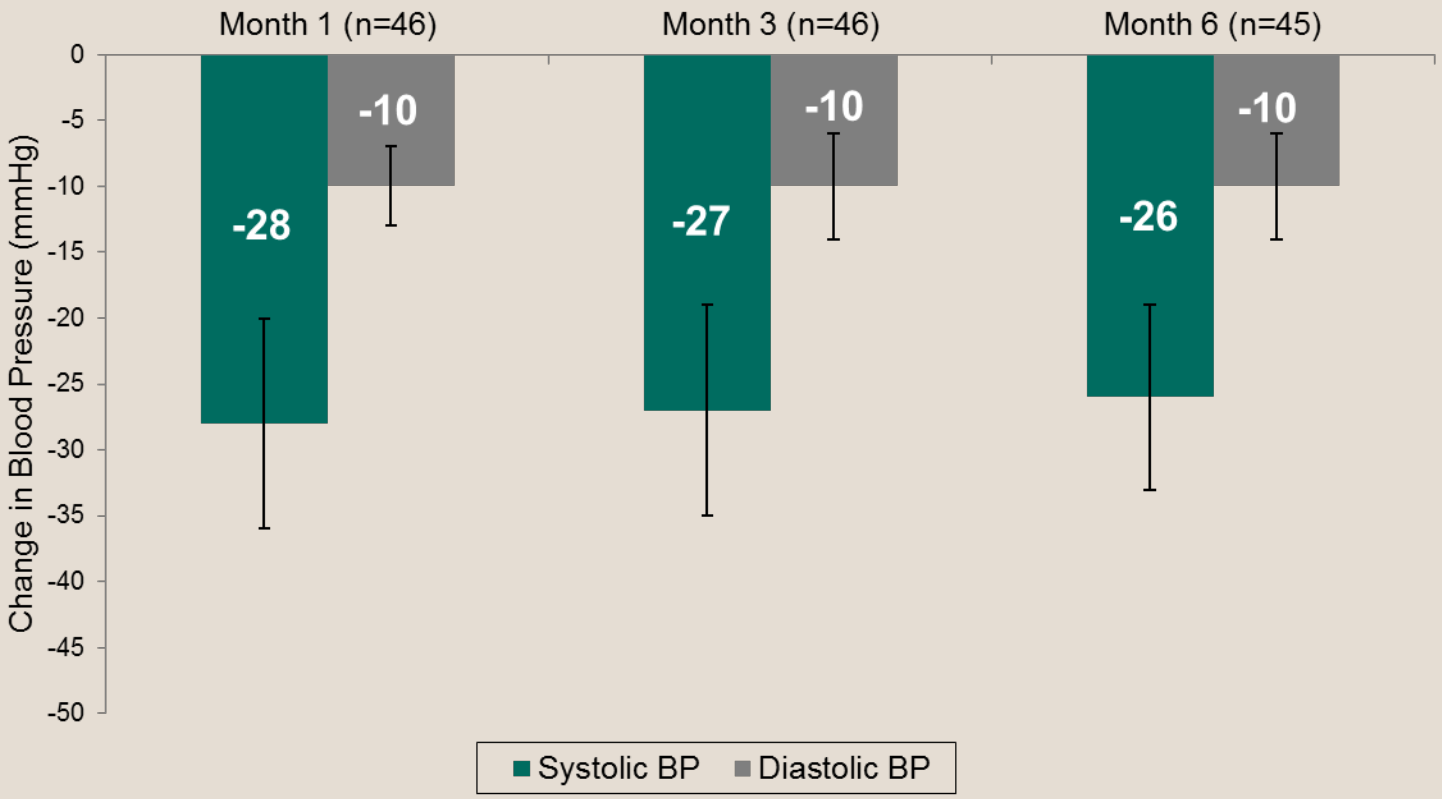

p <0.0001

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

24 hr Ambulatory BP Reduction from Baseline

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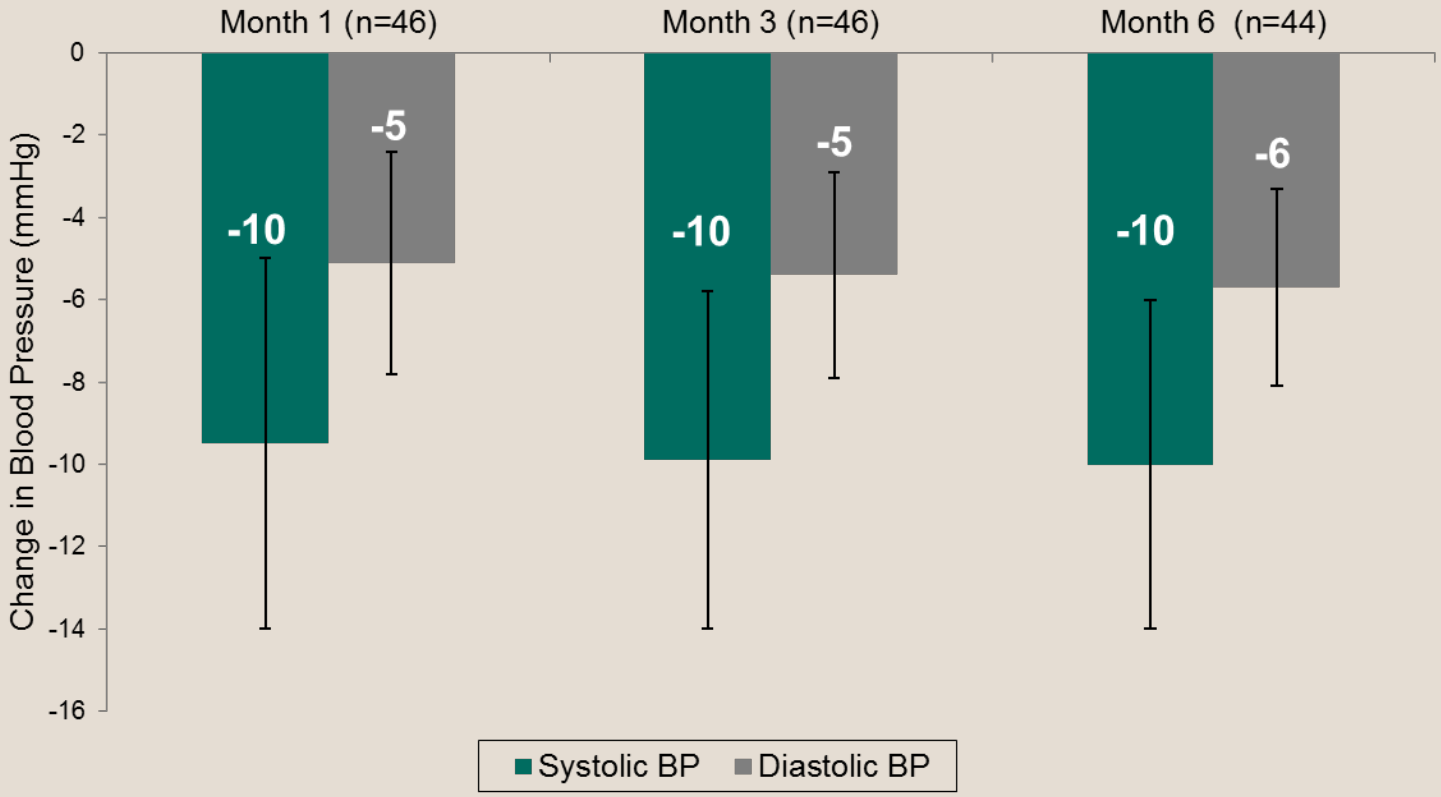

P values are <0.0001, except
Diastolic 1 mo p-value 0.0003
Diastolic 3 mo p-value 0.0002

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

Responder & Goal Blood Pressure Parameters

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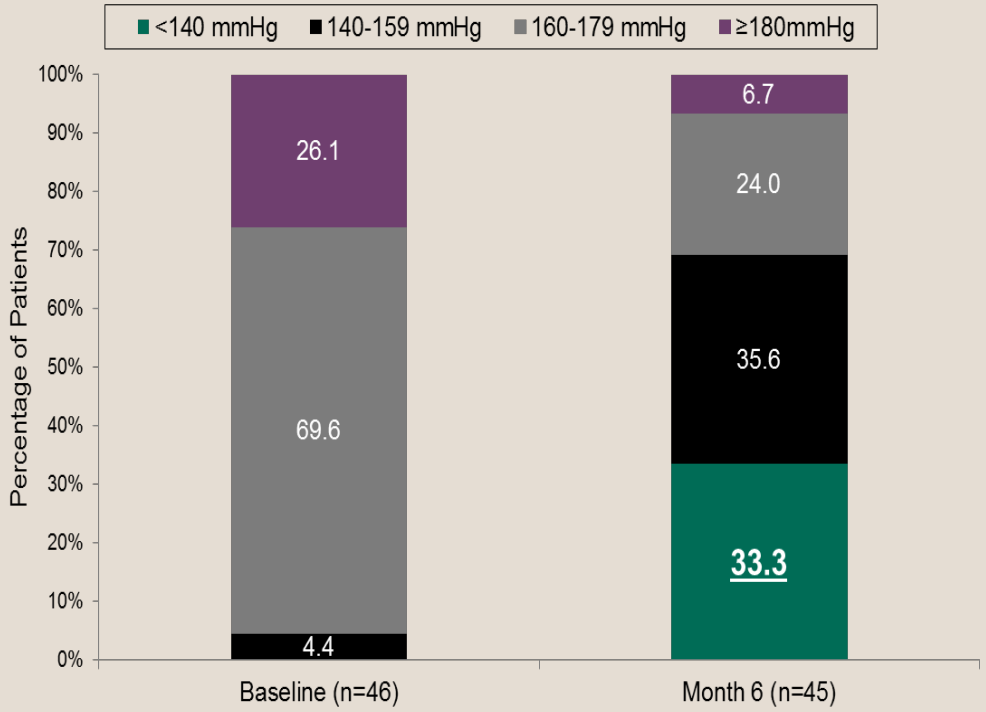
- % Responders (>10 mmHg Reduction from baseline) = 76% (n=34)
- At Goal SBP:



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

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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