LINC 2018

Update on renal denervation: Latest data

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Potential Conflicts of Interest

I have the following potential conflicts of interest to report:

Research grants:
• Deutsche Hochdruckliga
• Deutsche Gesellschaft für Kardiologie
• Saarländisches Ministerium für Wissenschaft und Forschung
• Medtronic, Recor

Consultant/Lecture fee:
• Medtronic, Recor
A Controlled Trial of Renal Denervation for Resistant Hypertension

Bhatt DL, NEJM 2014

Primary safety endpoint was met
Primary efficacy endpoint was not met

Optimum and stepped care standardised antihypertensive treatment with or without renal denervation for resistant hypertension (DENERHTN): a multicentre, open-label, randomised controlled trial

Azizi M, Lancet 2015

Primary efficacy endpoint was met
I. Medication

- Obtain data in off medication patients
- Standardize medication
- Measure adherence
  - Toxicological analyses

Mahfoud F, Eur Heart J 2017
II. Patient selection

- Exclude isolated systolic hypertensive patients
- Moderate hypertension, no severe resistant hypertension

Mahfoud F, Eur Heart J 2017
III. Procedural aspects

- Active (!) treatment
- Distally focused ablation
- Standardize procedural instructions

Mahfoud F, Eur Heart J 2017
REDUCE-HTN: REINFORCE Study

SPYRAL HTN
Global Clinical Trial Program

ON – n=100
OFF – n=100

THE RADIANCE-HTN STUDY
A Study of the ReCor Medical Paradise® System in Clinical Hypertension

SOLO – n=146
ON – n=146
REQUIRE – n=150

REDUCE-HTN: REINFORCE Study

OFF – n=100

ABLA TIVE SOLUTIONS
Target BP I

OFF – n=100
Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial


Townsend et al, Lancet. Published online ahead of print August 28, 2017
SPYRAL HTN – OFF MED

Study Design

Randomized, sham-controlled, blinded trial

Screening visit 1
- Office BP
- Drug naïve or medications D/C

Screening visit 2
- Office BP
- 24-hr ABPM
- Drug testing

2-wek safety check
- OSBP ≥180

Screen failure
- ABPM SBP ≥140 to <170
- Office SBP ≥150 to <180
- Office DBP ≥90

Follow-up every 2 weeks

Randomized, sham-controlled, blinded trial

Townsend RR, Lancet 2017
SPYRAL HTN – OFF MED

Study Design

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- Office SBP ≥150 to <180
- Office DBP ≥90

2-wk safety check

Screen failure

Office BP ≥150 to <180

Drug naïve or medications D/C

Randomization / Procedure

Sham control

Renal denervation

Follow-up every 2 weeks

ABPM Office BP
Drug testing

Drug titration until OSBP <140

Follow-up every 2 weeks

3M 6M 12-36M

Townsend RR, Lancet 2017
### SPYRAL HTN – OFF MED

#### Procedural Details

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>RDN (N = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of main renal arteries treated per patient</td>
<td>2.2 ± 0.5</td>
</tr>
<tr>
<td>Number of branches treated per patient</td>
<td>5.2 ± 2.5</td>
</tr>
<tr>
<td><strong>Total number of ablations per patient</strong></td>
<td><strong>43.8 ± 13.1</strong></td>
</tr>
<tr>
<td>Main artery ablations</td>
<td>17.9 ± 10.5</td>
</tr>
<tr>
<td>Branch ablations</td>
<td>25.9 ± 12.8</td>
</tr>
<tr>
<td>Treatment time (min)</td>
<td>57.1 ± 19.7</td>
</tr>
</tbody>
</table>
Blood pressure results

Townsend RR, Lancet 2017

Change in blood pressure from baseline to 3 months (mm Hg)

-5.0 (-9.9 to -0.2)

p = 0.0414

-4.4 (-7.2 to -1.6)

p = 0.0024

n = 36

n = 35

-5.5 (-9.1 to -2.0)

p = 0.0031

-4.8 (-7.0 to -2.6)

p < 0.0001

Baseline blood pressure (mm Hg)

153.4

151.6

99.1

98.7

24-h SBP

24-h DBP

Renal denervation

Sham control
Blood pressure results

Townsend RR, Lancet 2017
Relative risk reduction for a 10 mmHg fall in office blood pressure

123 studies with 613,815 participants

- CAD: 17%
- Stroke: 27%
- HF: 28%
- Mortality: 13%

Ettehad D, Lancet 2016
# SPYRAL HTN – OFF MED

## Safety Results at 3 Months

<table>
<thead>
<tr>
<th>%</th>
<th>RDN (n = 38)</th>
<th>Sham Control (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>New myocardial infarction</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Major bleeding (TIMI(^1))</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>New onset end stage renal disease</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Serum creatinine elevation &gt;50%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Significant embolic event resulting in end-organ damage</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hospitalization for hypertensive crisis/emergency</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>New stroke</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Townsend RR, Lancet 2017*
SPYRAL HTN–ON MED Study

Office SBP >150 and <180 mm Hg on 1,2 or 3 meds for 6 weeks

1st screening
- Office SBP

2nd screening
- Urinalysis
- Observed drug intake
- Office SBP

Drug testing
- Thiazide-type diuretic
- Calcium channel blocker
- ACE/ARB
- Beta Blocker
- Stable meds

Confirmed on meds

1 Mo
- N<50
- Renal denervation + meds

6 Mo
- 1 Mo
- 6 Mo
- 3 Mo

12 Mo
- Unblinding

≥140 to <170
Office ≥150 and <180
DBP ≥ 90

ABPM

2–4 weeks

N<50

1 Mo
3 Mo
6 Mo
12 Mo

12–36 Mo

Office BP

ABPM

Results expected mid-2018
Potential Outcomes

#1
ON ✔
OFF ✔

#2
ON ✗
OFF ✗

#3 and 4
ON ✔
OFF ✔

#5
ON ✔
OFF ✗

Distinct technologies are associated with distinct outcomes.
Potential Outcomes

#1
ON ✓
OFF ✓

#2
ON ✗
OFF ✓

#3 and 4
ON ✓
OFF ✓
ON ✓
OFF ✗

#5
Distinct technologies are associated with distinct outcomes
Device-based hypertension therapy

- Carotid Bulb Expansion
- Carotid Body Modulation
- Renal Denervation
- AV Fistula
- Baroreceptor Stimulation
- Aortic Arch Stimulation
- Pacemaker-mediated
- Median Nerve stimulation

© F. Mahfoud, 2017
More to come stay tuned!
Thank you!

Felix Mahfoud, MD FESC

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Baseline Office Systolic Blood Pressure and Decrease in Blood Pressure at 6 Month

Baseline Study Mean Systolic Office Blood Pressure (mmHg)

Change in Systolic Office Blood Pressure (mmHg)

SPYRAL HTN OFF MED

40 Device Trials
N=4,618 Patients

Mahfoud F, J Hypertens 2017
LINC 2018

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