Clinician and Patient Perspective on Potential of Renal Denervation

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Disclosures

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Outline

• What is the unmet clinical need?

• What is a clinically meaningful reduction in blood pressure?

• What is the benefit-risk of renal denervation vs adding another anti-hypertensive medication?

• Based on available data what would be a clinically appropriate indication to consider at this time?
Trends in Hypertension Control

Healthy People 2020 Goal = 61.2%
BP Treated But Not Controlled

NHANES Awareness, Treatment, Control 2013-14

Unaware
Aware-Untreated
Treated-Controlled
Treated but Uncontrolled

Uncontrolled Despite Active Treatment for Hypertension = 27%

Zhang Y, Hypertension 2017, online data supplement
Why Might Patients Be Treated But Not Controlled?

Multiple Reasons for Lack of Control:

- Medication non-adherence
- Medication intolerability (side effects)
- Therapeutic inertia
- Patient comorbidities & high pill burden
- Lack of access to health care

How Might RDN Potentially Address This?

- Procedure with durable effect
- Reduced dependence on medication adherence
- Reduced pill burden
- Reduced medication side effects

Only 39% of Patients are Controlled to New 2017 ACC/AHA BP Targets
What is a Meaningful Reduction in BP?

The European expert group determined:

- A 10mmHg reduction in office SBP to be a clinically meaningful outcome.
- This corresponds to 6-7mmHg reduction in ABP.

BP Reductions in RDN Arm of RADIANCE-HTN SOLO at 2M

Systolic

Diastolic

Office

Daytime ABP

-10.8

-5.5

-8.5

-5.1

0

-2

-4

-6

-8

-10

-12


What Is Clinically Meaningful Reduction in BP? 
Correlation Between BP Reduction and CV Events

Meta-analysis of 613,815 Patients from 123 Studies

Reduction of Systolic Office BP by 10 mmHg Leads to Reduction of Risk:

<table>
<thead>
<tr>
<th>CV Events</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>13%</td>
</tr>
<tr>
<td>Coronary Disease</td>
<td>17%</td>
</tr>
<tr>
<td>Stroke</td>
<td>27%</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>28%</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
<td>5%</td>
</tr>
</tbody>
</table>

Meta-regression plot shows the percentage risk reduction in major cardiovascular events regressed against the difference in achieved systolic blood pressure between study treatment groups.

Who Is A Potential Candidate for RDN?
My Clinical Perspective

### Treated But Uncontrolled Hypertension

<table>
<thead>
<tr>
<th>Unable to Tolerate Prescribed Medications (Perceived or Real)</th>
<th>Uncontrolled Despite 1-2 Meds</th>
<th>Apparent Treatment Resistant Hypertension 3+ Meds</th>
</tr>
</thead>
</table>

What is the potential relative benefit-risk of adding another antihypertensive medication vs RDN?

- Efficacy – roughly equivalent
- Tolerability – may favor RDN
- Safety – both appear safe
- Adherence – likely favors RDN
- Durability – unclear
- Cost – likely favors medication
- Patient Preference – vary based on individual
Patient Interest in RADIANCE-HTN Trial

- Short, targeted direct-to-patient campaigns: 5 days, 20-30 miles around trial sites
- 536 campaigns run in 6 countries at 41 RADIANCE-HTN sites

Strong Patient Interest Exhibited Across Genders, Ages, and All Geographies (from Charleston, SC to Los Angeles, CA to Reno, NV)

Clicks: expression of interest in other options for HTN
N=1,097,171

Answer 20 question survey on eligibility
N=47,403

Pass criteria & sent for secondary screening
N=10,839

Excluded for clinical reasons
N=33,918

Excluded out of lack of desire for a procedure
N=2,646

*ReCor Internal Data*
From a Clinical Perspective: Proposed Target Population for RDN

- Diagnosed with hypertension
- Have been prescribed antihypertensive medications
- Uncontrolled BP based on the following definition
  - Office BP $\geq 140$ mmHg systolic and $\geq 90$ diastolic, and
  - Confirmatory BP $\geq 135$ mmHg systolic using one of the following:
    - Mean daytime ABPM,
    - Documented mean home, or
    - Repeated office automated (i.e. SPRINT style BP)
- Patient preference for device therapy
Conclusions

• ReCor’s trial program will yield valuable data both in the absence and in the presence of medications
  – 3 independently powered RCTs: SOLO / TRIO / RADIANCE-II

• ReCor’s clinical program is designed to provide information on the safety & effectiveness of ultrasound based renal denervation
  – Blood pressure change over time
  – Blood pressure control
  – Medication burden reductions
  – Vascular and renal safety

• Plan to conduct post-market registry to capture real-world, long-term safety and durability

• Plan to conduct future studies to address additional patient populations