Current Status Of Catheter Based Renal Radiofrequency Denervation For Hypertension: Where Is It Going?

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You know the story!

Renal denervation did not come out of the Blue
• Histology findings
• Pathophysiological background
• Animal data
• Surgical experience
• Proof of concept studies
• Results from prospective controlled clinical trials
• Clinical experience

SYMPLICITY HTN-1
Shows Long-Lasting Changes in Office Blood Pressure
Mean BP decrease in 88 patients seen until 30 months

SYMPLICITY HTN-2
Primary Endpoint: 6-Month Office BP
- 84% of RDN patients had ≥ 10 mmHg reduction in SBP
- Only 10% of RDN patients had no reduction in SBP

Krum H, ESC 2013
Krum EBC 2013

Disclosures

Physician name  Company  Relationship
Horst Sievert  Abbott, Access Closure, AGA, Angiomed, Aptus, Atrium, Avinger, Bard, Boston Scientific, Bridgpoint, Calecs, CardioKinetix, CardioMEMS, Coherex, Contego, Cordis, CSI, CVRx, EndoC无人, FlowCantia, Gieta, Gore, Guided Delivery Systems, InSeal Medical, Lumen Biomedical, HTL, Lifetech, Lutonix, Maya Medical, Medtronic, MLC, Occlutech, Oskey, Ostial, Pendrane, pfm Medical, Peric, RealMed, Rex Medical, SinterHeart, Spectranetics, SquareOne, Timere, Trivascular, Venus Medical, Visan, Vexx
CardioKinetix, Access Closure, Lumen Biomedical, Coherex, STK
Cook, St. Jude Medical

Consulting fees, Travel expenses, Study honoraria

Stock options, Stocks
Grant Research Support

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So there was no doubt that renal denervation as a concept is working… renal denervation was one of the most promising new treatment options in cardiovascular medicine.

Millions of people all over the world ….

… including myself …

… at that time had been very sad that they did not have Ardian stocks.

Even before these results became available, …

The deal involves possible milestone-based payments equal to annual revenue growth over the next four and half years, the statement said.

In Jan 2014

A surprising press release had caused a little earthquake:

Everybody involved in renal denervation will remember forever where he was when this message did come out.

In Jan 2014

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1.4 billion $
And everybody….

… including those who had been against renal denervation from the very beginning…

… asked: “How could this happen?”

So what is the current status?
• Guidelines and recommendations of scientific societies still see renal denervation as an option for patients with resistant hypertension
  - because per definition these patients do not have other options
• But there is almost no reimbursement anymore even in countries like Germany
• Very few referrals
• Renal denervation market went down by 98%
• Many companies have stopped their programs

Why HTN-3 may have failed
• Placebo effect?
• Technical issues
  - Operator experience
  - Device?
• Patient selection
• Medication
• Trial design

Great past!
Almost no today
What about the future?

Future plans
• Better understanding
  - Educate colleagues, patients and payers why HTN-3 failed
  - Difficult in times when most of us are just interested in headlines and primary endpoints
• Better trials
• Better technique
• Better devices

Better trials
• Almost everybody agrees that future trials should be sham controlled
  - although HTN-3 has shown that sham alone does not make a good clinical trial
• Objective parameters (ABPM)
• Patients without medication or optimized control or standardization of medication
• Not focusing on the worst of the worst
  - Avoiding patients who may be resistant against anything including renal denervation
**We already have a new positive trial**

**DENER-HTN Primary Endpoint:**
Ambulatory BP From Randomisation to 6 Months

<table>
<thead>
<tr>
<th></th>
<th>Denervation</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP Change</td>
<td>∆: –5.9 mm Hg (95% CI: –11.3 to –0.5)</td>
<td>∆: –6.3 mm Hg (95% CI: –12.0 to –0.6)</td>
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<tr>
<td>P</td>
<td>0.0329</td>
<td>0.0296</td>
</tr>
</tbody>
</table>


**Better technique**

- "More is better"
- Total number of ablations is important
- Circumferential ablation is important
- "Go distal"
  - In distal vessel segments the nerves are closer to the vessel wall

**Better devices**

- Devices easier to use
  - Making result less dependent on operator experience
  - Balloons, multiple electrodes, spiral electrodes, ...
- Other energy sources with deeper penetration
  - Ultrasound, cryo, microwave, radiation, ...
- Chemical ablation
- Non-invasive techniques

**Conclusions**

- HTN-3 was not the end of the story
- New trials and new devices are under way
- My personal lesson:
  - Even if there comes a very promising new technology with excellent initial results,
  - I will never invest 1.4 billion in just one project too early

**Thank you!**