Baroreceptor activation therapy (BAT/Barostim®): Clinical evidence in resistant hypertension and heart failure

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Disclosure

Speaker name: Jochen Müller-Ehmsen, M.D.

I have the following potential conflicts of interest to report:

✔ Consulting

☐ Employment in industry

☐ Stockholder of a healthcare company

☐ Owner of a healthcare company

☐ Other(s)

☐ I do not have any potential conflict of interest
Clinical evidence in resistant hypertension: Controlled procedural success and titratable effect

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>1 Volt</th>
<th>2 Volts</th>
<th>3 Volts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bpm</td>
<td>71</td>
<td>56</td>
<td>58</td>
<td>50</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>210 / 96</td>
<td>168 / 73</td>
<td>156 / 72</td>
<td>144 / 66</td>
</tr>
</tbody>
</table>

Approx. 4 Min.
DeBuT-HT study: Long term results

Change in BP (mmHg)

Systolic
(Baseline = 193 ± 36 mmHg)

Diastolic
(Baseline = 111 ± 20 mmHg)

Heart Rate
(Baseline = 74 ± 12.8 mmHg)

Anti-hypertensive Medications Changes

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>4 years</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.0 ± 1.3</td>
<td>-0.2 ± 0.3</td>
<td>-0.7 ± 0.4</td>
<td>-0.8 ± 0.3</td>
<td>-1.6 ± 0.3</td>
<td>-1.6 ± 0.4</td>
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<tr>
<td>1 year</td>
<td></td>
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<td>2 years</td>
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<td>3 years</td>
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<td>4 years</td>
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<tr>
<td>5 years</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

193/111 mmHg \Rightarrow 140/82 mmHg at 5 Years

Scheffers et al., J. Am. Coll. Cardiol. 2010;56;1254-1258 Kroon et al, ESH 2010
Barostim Controls BP Several Years After Implant (Rheos Pivotal): Long term results

Bakris et al., J Am Soc Hypertens 2012.
New 5 Year Long Term SBP Data in Resistant HTN

SBP using BpTRU (mmHg)

Baseline

1 Year

2 Year

3 Year

4 Year

5 Year

N=216

N=209

N=205

N=207

N=182

N=40

Goal - 140

Change in SBP using BpTRU (mmHg, +/- SE)

-37.5 §

-34.2 §

-35.3 §

-31.3 §

-32.9 §

§ p<.001

de Leeuw et al., ESH/ISH 2014
On-Off Testing of BAT >1 yr. after implantation

n=17

Mean Change in BP (mmHg) / HR (bpm)

- On deactivation
- On reactivation

+/- 2 SEM
BAT: Change in blood pressure and heart rate in patients after RDN (n=9, median 11 months)

Baseline (office cuff)
- Systolic BP: 187 ± 20 mmHg
- Diastolic BP: 104 ± 15 mmHg

Change from baseline

- Systolic BP: -18 *
- Diastolic BP: -2 *
- Heart rate: -11 *
Milan Barostim for HFrEF Feasibility Study

- Single-center, open label study conducted in Milan, Italy
- NYHA Class III HF
- Optimal, Stable Medical Therapy Prior to Enrollment:
  - β-blocker, diuretic and ACE-Inhibitor/ARB unless contraindicated
  - Not treated with CRT
- 11 Patients
- 67 +/- 9 years
- EF = 31 +/- 7 %

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Gronda, EJHF 2014
NYHA Functional Class

Baseline | Month 3 | Month 6 | Month 9 | Month 12
---|---|---|---|---
I | 5 | 8 | 9 | 9
II | 6 | 2 | 2 | 1
III | 11 | 1 | | |
IV | | | | |

p < 0.001

Gronda EJHF 2014
XR1-HF Study: Preliminary clinical single-center observations

**Fig. 3.** Decrease of NTproBNP on BAT. NTproBNP was 2797±971 ng/l prior to BAT and fell to 1352±322 ng/l during an average follow-up of 7.1 months (p<0.05). NTproBNP was quantified as the average of all available values within 3 month before implantation and after activation of the device.

**Fig. 4.** Increase of walking distance in the 6-Minute-Walk-Test. During an average follow-up of 5.4 month, 6-Minute-Walk-Test improved from 314±42 m to 367±25 m (p<0.05). The individual increase was 24±14 %. Data from one patient are missing, since he died before the follow-up visit due to a sepsis (not related to the procedure or device).
Global Barostim HFReEF Study

- Randomized Controlled Study
- US, Canada, and Europe
- 140 Pts
- NYHA Class III HF
- EF ≤ 35%

Measures
- Device Safety
- 6 min Hall Walk
- QOL (MLHF)
- Biomarkers
- NYHA Class
- Echo

Data will be presented at ACC 2015 (accepted) and DCK 2015 (submitted)
Summary and Conclusions:

• First randomized studies indicate long term efficacy of baroreceptor stimulation in resistant hypertension.

• The procedural success can be controlled, the effect can be titrated, the long-term effect can be tested (on/off).

• BAT is also effective in patients after RDN.

• Larger studies are needed and underway.

• First clinical results in heart failure are promising.

• The randomized HF- study will be presented at ACC 2015.

• BAT must be considered as an important treatment option for resistant hypertension (heart failure?).
Thank you!
Barostim has entered the ESH/ESC guidelines as an option to treat resistant hypertension

## 2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redon (Section co-ordinator) (Spain), Alberto Zanchetti (Section co-ordinator) (Italy), Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Sirnes (Norway), Peter Sleight (UK), Margus Vlignaa (Estonia), Bernard Waeyer (Switzerland), Faiez Zannad (France)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>In resistant hypertensive patients it is recommended that physicians check whether the drugs included in the existing multiple drug regimen have any BP lowering effect, and withdraw them if their effect is absent or minimal.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>Mineralocorticoid receptor antagonists, amiloride, and the alpha-1-blocker doxazosin should be considered, if no contraindication exists.</td>
<td>IIa</td>
<td>B</td>
<td>604, 606, 607, 608</td>
</tr>
<tr>
<td>In case of ineffectiveness of drug treatment invasive procedures such as renal denervation and baroreceptor stimulation may be considered.</td>
<td>IIb</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>Until more evidence is available on the long-term efficacy and safety of renal denervation and baroreceptor stimulation, it is recommended that these procedures remain in the hands of experienced operators and diagnosis and follow-up restricted to hypertension centers.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values ≥160 mmHg SBP or ≥110 mmHg DBP and with BP elevation confirmed by ABPM.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
</tbody>
</table>

*Class of recommendation.

*Level of evidence.

*Reference(s) supporting levels of evidence.

ABPM = ambulatory blood pressure monitoring; BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.
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