Hypertension consensuses: The Netherlands & Germany

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BAROSTIM THERAPY SUMMIT
September 30th, 2017 • Radisson Blu, Berlin, Germany
BAROSTIM THERAPY™

Agenda

- The Dutch Hypertension Experience
- The German Hypertension Consensus

BAROSTIM™ THERAPY™

Agenda

- The Dutch Hypertension Experience
  - Long-term efficacy
  - Evolution of BAROSTIM THERAPY
  - Dutch Consensus
- The German Hypertension Consensus

BAROSTIM THERAPY™

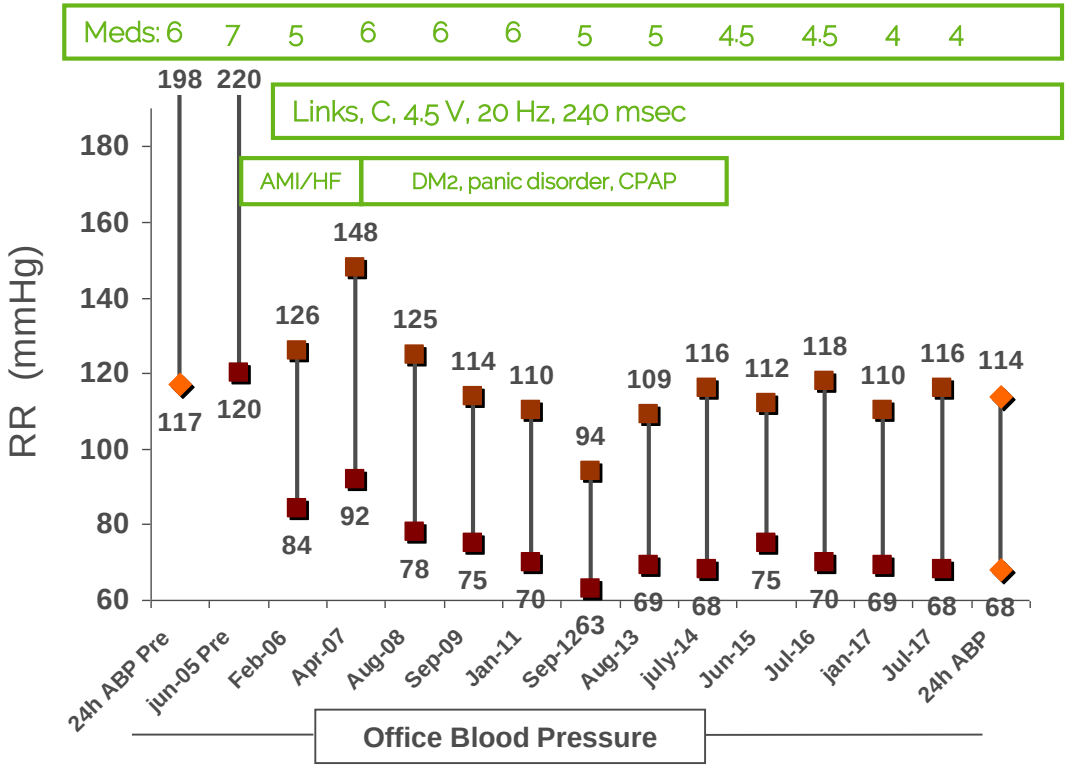
Male, born 1962

- Medical History:
  - 2000: hypertension, obesity (BMI 32), OSAS
  - 2003: depression (R/ SSRI)
  - 2004: atherosclerotic renal artery stenosis R [PTRA(S)]
  - 2005: jun/ BAT (implantation), 6 antihypertensives
    - sep/ AMI, PCI(BMS)
    - nov/ heart failure (EF 39%)
  - 2007: mar/ diabetes mellitus t.2
    - apr/ panic disorder, agoraphobia
    - sep/ C-PAP started

Male, born 1962

- Medication:
  - 2005: metoprolol succ.r. 1 x 200 mg, nifedipine GITS 1 x 60 mg, HCTZ 1 x 25 mg, lisinopril 2 x 20 mg, doxazosine XL 1 x 8 mg, moxonidine 3 x 0.4 mg.
  - + carbasalate calcium 1 x 100 mg, atorvastatine 1 x 40 mg

Male, born 1962: Baroreflex Activation Therapy (Rheos©)



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  - + carbasalate calcium 1 x 100 mg, atorvastatine 1 x 40 mg

  - July 2014: nebivolol 1 x 5 mg, amlodipine 1 x 10 mg, HCTZ 1 x 12.5 mg, irbesartan 1 x 300 mg, eplerenone 1 x 50 mg.
  - + carbasalate calcium 1 x 100 mg, rosuvastatine 1 x 40 mg, ezetimibe 1 x 10 mg, metformine 3 x 1000 mg, insuline glargine (1x) en insuline aspart (3dd)

Male, born 1962

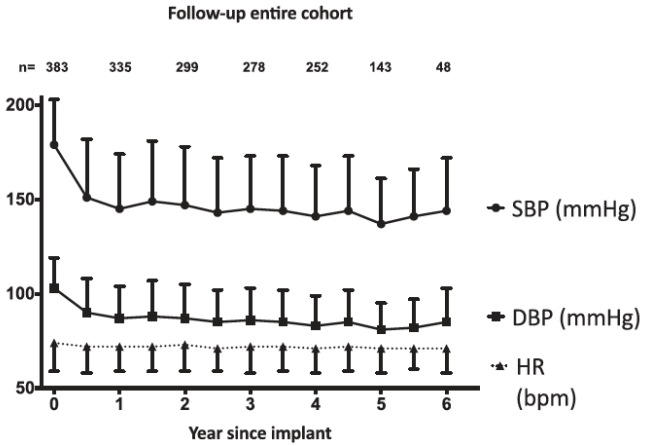
- Co-morbidities
  - Heart failure, diabetes mellitus t.2, panic disorder
- Battery replacements
  - 2007, 2009, 2011, 2013, 2015, 2017
- Lab-results (2005→2017)
  - kreatinine 113 → 121 uM
  - proteinurie 1.3 g/24u → 120 mg/24u
  - LVEF 39 → 51%

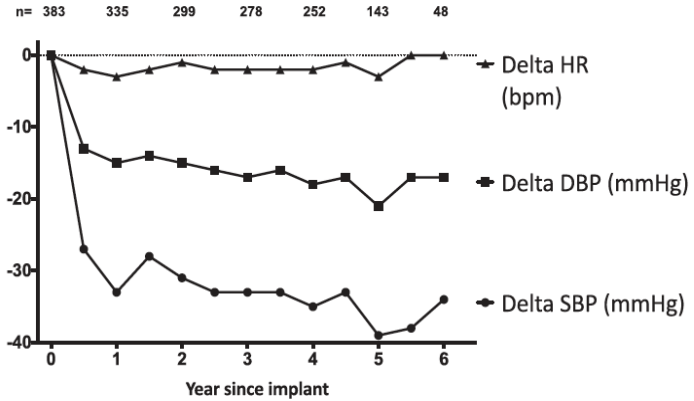
Sustained Reduction of Blood Pressure With Baroreceptor Activation Therapy

Results of the 6-Year Open Follow-Up

Peter W. de Leeuw, John D. Bisognano, George L. Bakris, Mitra K. Nadim, Hermann Haller, Abraham A. Kroon; on behalf of the DEBuT-HT and Rheos Trial Investigators

Rheos system: US-Rheos (n=16), DEBuT-HT(n=45), Pivotal (n=322)





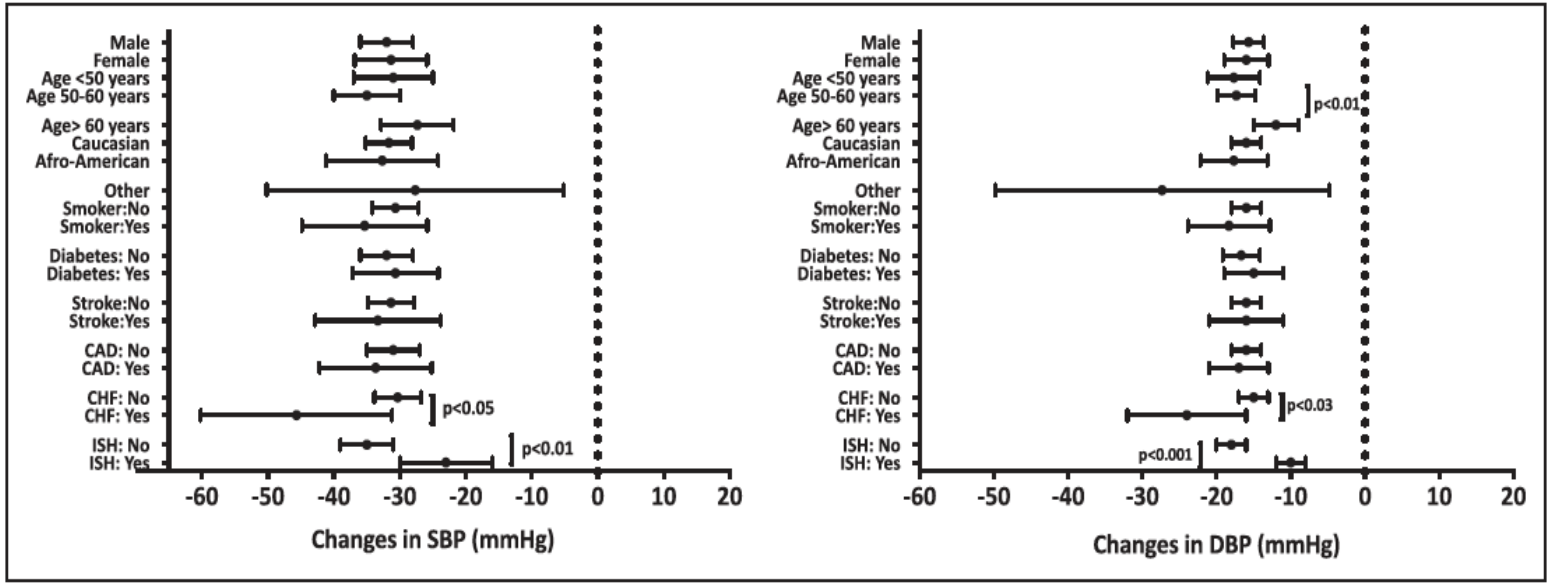
Baseline BP: 179/103 mmHg, HR 74 bpm
6-yrs f.u. BP: 144/ 85 mmHg, HR 71 bpm

Pts with BP < 140/90 mmHg: 161 (42%)
Non-responders (Δ<10 mmHg): 26 (7%)

Hypertension. 2017;69:836-843.

Long-term follow-up of Rheos system

SUBGROUP ANALYSIS



Overall mean ΔBP 32/16 mmHg

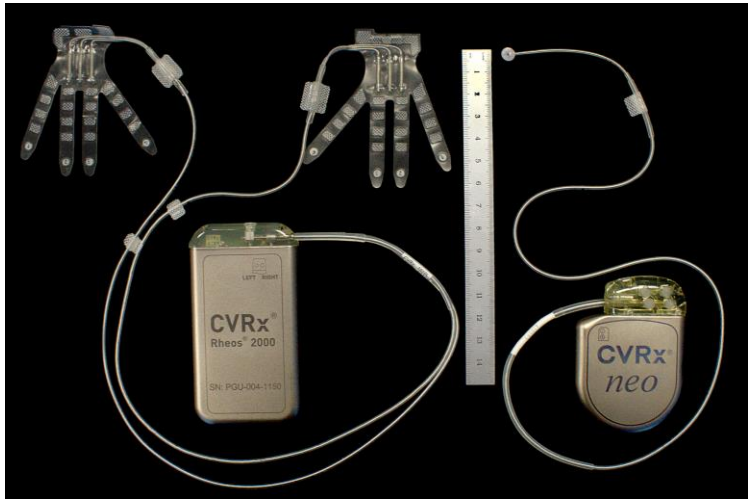
+ HF(pEF): ΔBP 46/24 mmHg
- ISH: ΔBP 23/8 mmHg

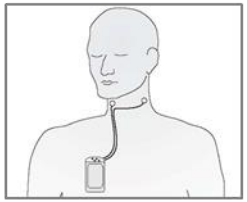
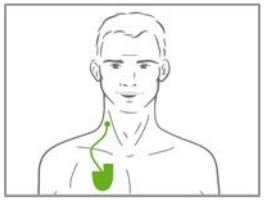
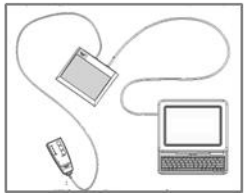
Medication use

- mean n of meds 5
- 109 (27%) reduction, 139 (34%) no change, 149 (39%) increase

Hypertension. 2017;69:836-843.

Evolution of BAROSTIM THERAPY System

	First Generation Rheos (obsolete)	Second Generation BAROSTIM NEO™
Device System		

	First Generation	Second Generation
Device Placement		
Programming System		

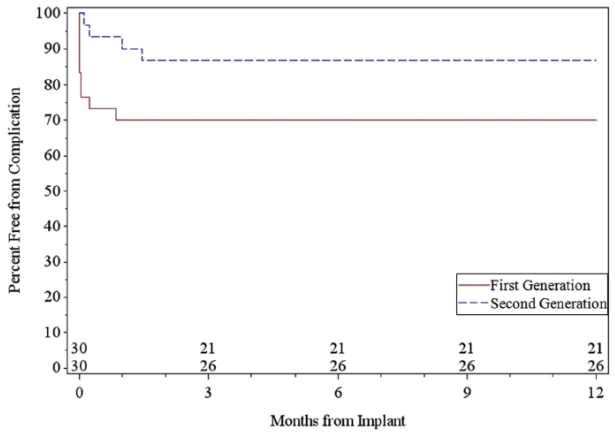
Safety & Efficacy
SECOND GENERATION DEVICE

Journal of the American Society of Hypertension ■(■) (2016) 1–11

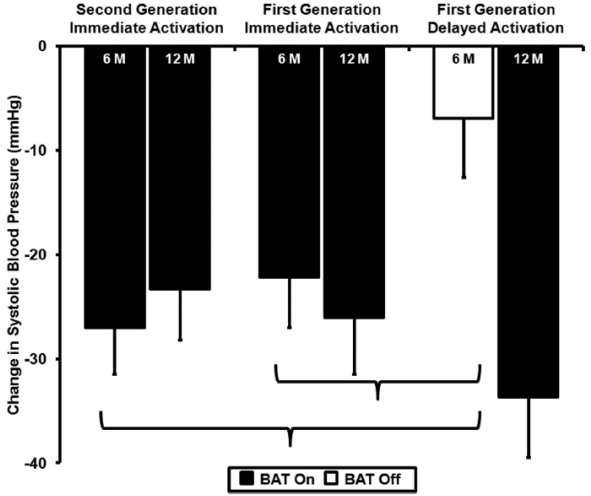
Research Article

An exploratory propensity score matched comparison of second-generation and first-generation baroreflex activation therapy systems

Safety



Efficacy



Wachter, et al., J Am Soc Hypertens 2016

Summary

- BAT–sustained effect for 5-6 yrs
- Largest drop in BP is in the first year
- ± 50% of resistant hypertension patients reach SBP threshold <140 mmHg
- Efficacy of 2nd generation device is likely to be identical to 1st generation
- BAROSTIM NEO: significant ambulatory ΔBP ± 10/5 mmHg
- Long-term treatment: may induce structural changes
- Ongoing RCT on BAROSTIM NEO

Consensus Document

BAROSTIM THERAPY for Treatment of Resistant Hypertension

Consensus Statement of the Dutch Hypertension Society

- Scientific evidence
  - Safety & Efficacy
  - Economic aspects
- Referral & treatment
- Registry

BAROSTIM THERAPY is a cost-effective therapeutic option over the long-term compared to optimal medical therapy

Original Article

OPEN

Cost-effectiveness of Barostim therapy for the treatment of resistant hypertension in European settings

- Additional life-years gained:
  +1.66 vs. optimal medical therapy
- Additional Quality-Adjusted Life-years gained:
  +2.17 vs. optimal medical therapy
- Cost per QALY gained:
  EUR 7,797 vs. standard threshold of EUR 35,000 per QALY
- Deemed cost effective relative to optimal medical therapy

	BAT
QALY Gain	+2.17
Reduces rate of:	**by:**
Myocardial Infarction	19%
Stroke	35%
Heart Failure	12%
End Stage Renal Disease	23%

Borisenko et al, J Hypertension, 2014; 32(3):681-92

Referral & Treatment

- **Referral:** 5 centres
- **Implantation:** Maastrict, Utrecht & Amsterdam
- **Follow up:** Centre of referral
- **Insurance:** Agreement
- **Number of patients:** 10-20 per centre/year
- **Registry:** Dutch / European

Consensus Summary

"Based on the level of evidence with respect to safety and efficacy data, and taking into consideration the high cardiovacular risk and the economical data, **it is advocated to use BAROSTIM THERAPY in subjects with true resistant hypertension**."

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BAROSTIM THERAPY™

Agenda

- The Dutch Hypertension Experience
- The German Hypertension Consensus
  - Safety & Efficacy
  - Patient Selection
  - Unanswered Questions & Future Research

BAROSTIM THERAPY™

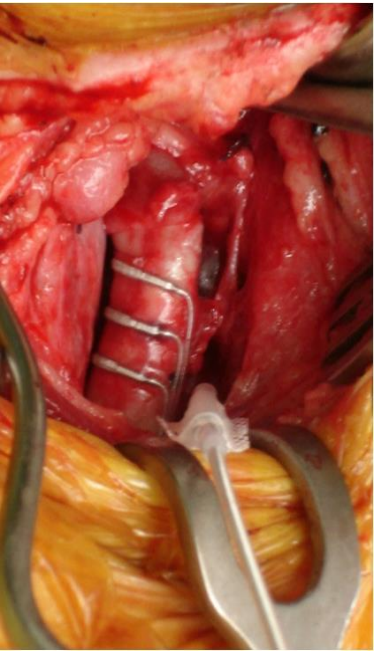
Recommendations of the BAT Consensus Group 2017

Baroreceptor activation therapy for therapy-resistant hypertension: indications and patient selection.

M. Koziolek[1] · J. Beige[2,3] · M. Wallbach[1] · D. Zenker[4] · G. Henning[5] · M. Halbach[6] · N. Mader[7] · F. Mahfoud[8,23] · G. Schlieper[9] · V. Schwenger[10] · M. Hausberg[11] · J. Börgel[12] · M. Lodde[12] · M. van der Giet[13] · J. Müller-Ehmsen[14] · J. Passauer[15] · S. Parmentier[15] · S. Lüders[16] · B. K. Krämer[17] · S. Büttner[18] · F. Limbourg[19] · J. Jordan[20] · O. Vonend[21] · H.-G. Predel[22] · H. Reuter[6]

Der Internist 2017; DOI 10.1007/s00108

First and second generation device



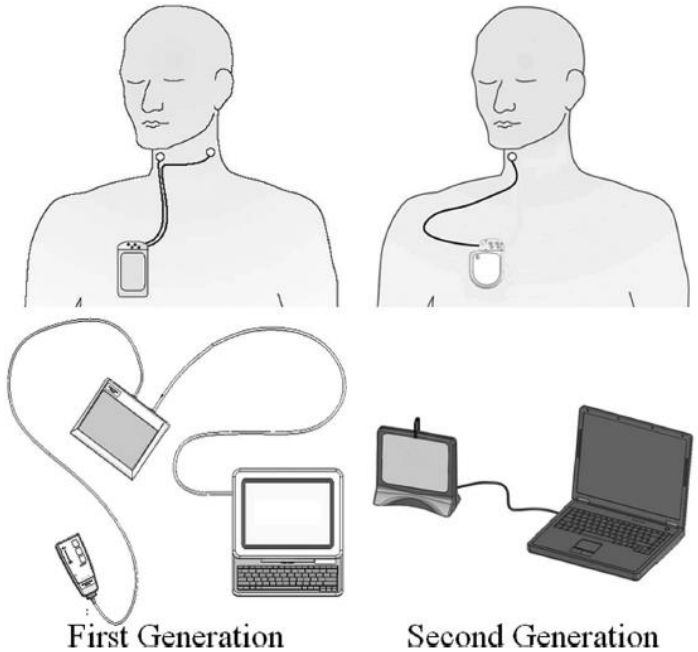


Figure 1. Schematic illustration of the first- (Rheos, left) and second-generation (Barostim *neo*) BAT systems. The second-generation system is smaller, less invasive, more efficient, and more easily programmable than the first. BAT, baroreflex activation therapy.

Wachter R et al, JASH 2017;11:81-91

Safety
COMPARING FIRST AND SECOND GENERATION

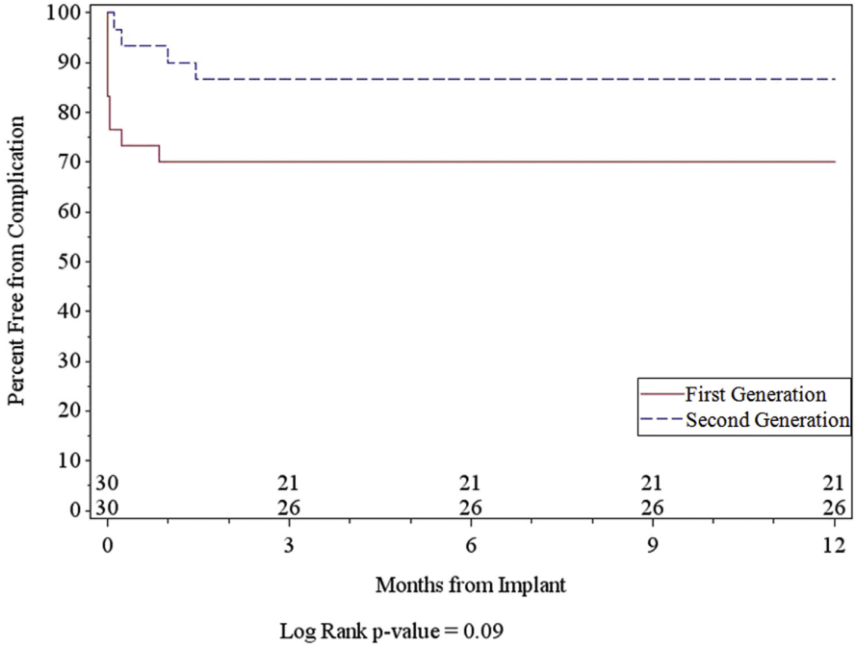
Summary of most common adverse events with baroreflex activation therapy.

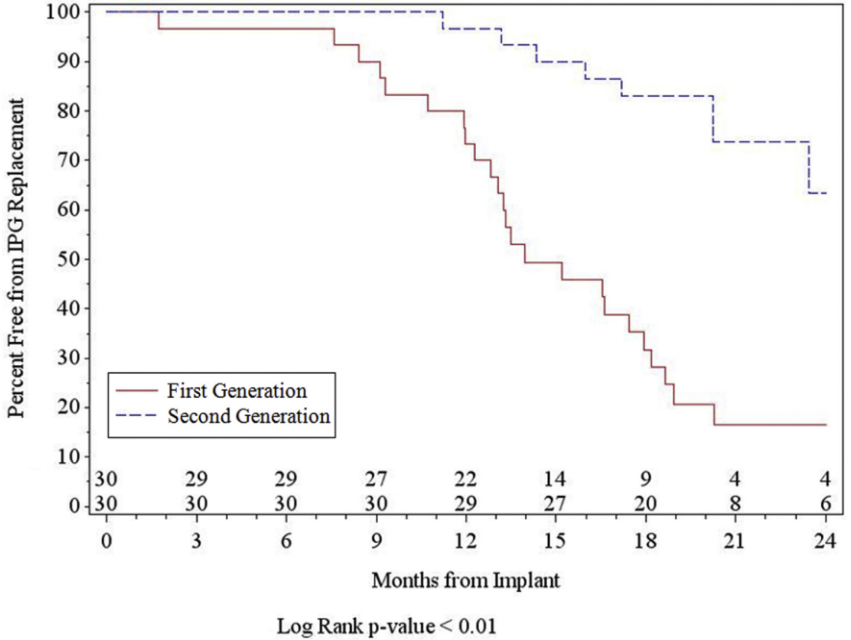
Adverse events	DEBuT-HT ($n=45$)	Rheos Pivotal Trial ($n=265$)	Barostim *neo* ($n=30$)
Procedure-related	**7 (15.6)**	**68 (25.5)**	**3 (10)**
Respiratory complication	2	7	0
Wound complication	3	7	1
Nerve injury	1	25	0
Surgical complication	1	13	2
Device-related	**1 (2.2)**	**34 (12.8)**	**1 (3.3)**
Device dislocation/pain	1	No information	1
Hypertension-related stroke	0	6	0

Values are presented in frequency (percentage).

Alnima T et al, Eur J Pharmacol 2015;763: 23-27

Safety
COMPARING FIRST AND SECOND GENERATION





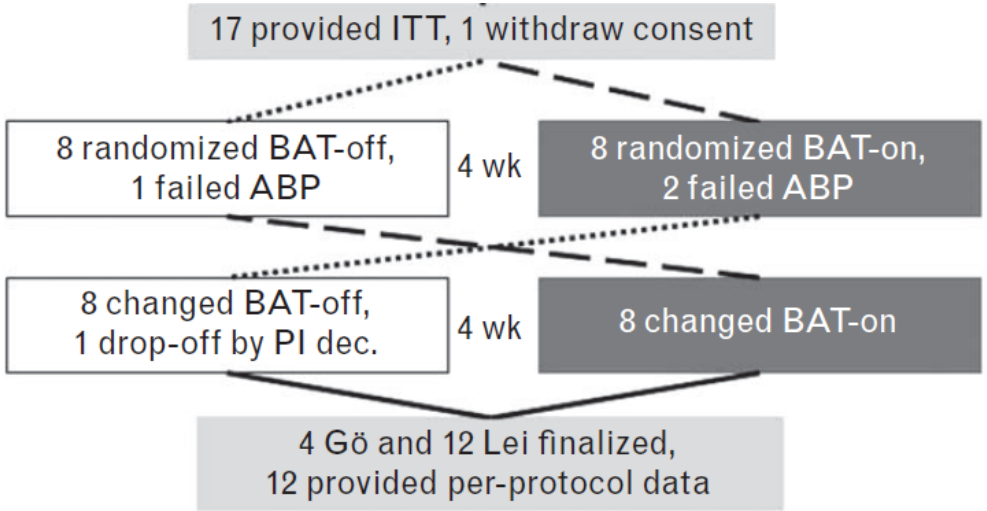
Wachter R et al, JASH 2017;11:81-91

Efficacy

SECOND GENERATION DEVICE, BAROSTIM NEO

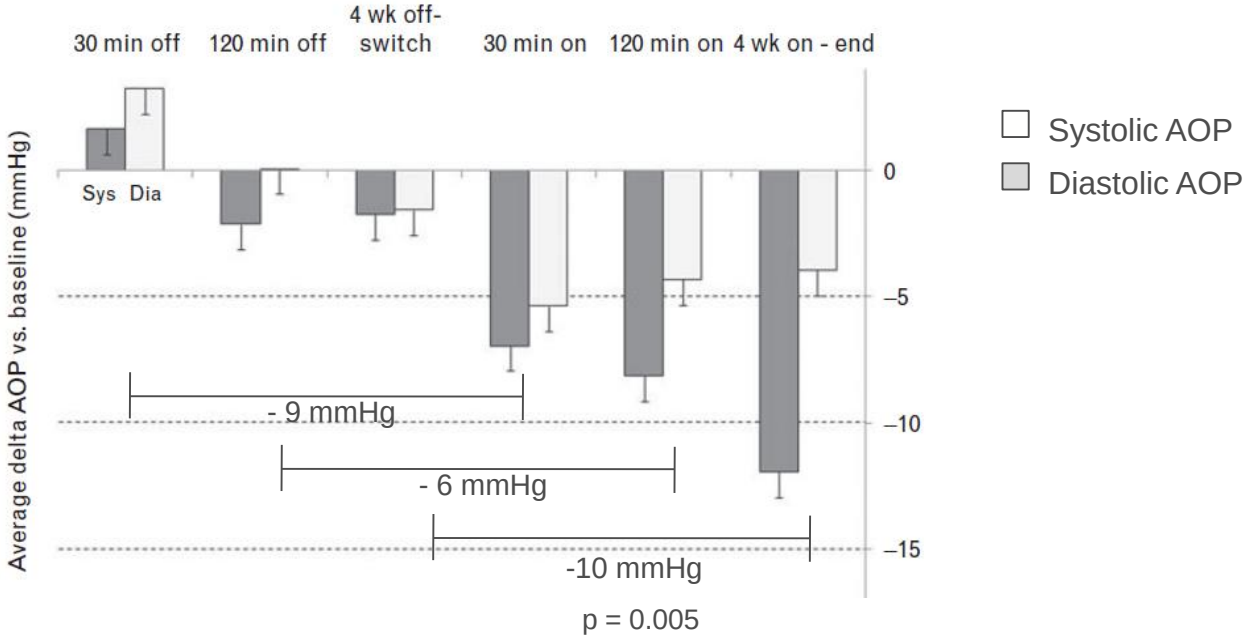
Blood pressure after blinded, randomized withdrawal, and resumption of baroreceptor-activating therapy

Joachim Beige[a,*], Theresa Jentzsch[a,*], Ralph Wendt[a], Gert Hennig[b], Michael Koziolek[c], and Manuel Wallbach[c]



Beige J et al, J Hypertens 2017

Efficacy
SECOND GENERATION DEVICE, BAROSTIM NEO



AOP: automated office blood pressure

Beige J et al, J Hypertens 2017

Patient Selection

According to the evidence from clinical trials, **BAT should be considered in patients with therapy resistant hypertension**:

- Office cuff blood pressure >160/90 mmHg
- after lifestyle modification and
- under at least 3 antihypertensive drugs (incl. diuretics)

Patient Selection

- ✓ Initiation of MRA treatment (i.e. Spironolactone) prior to BAT evaluation.
- ✓ Exclusion of pseudoresistance and/or secondary causes; (repeat in case of doubt or after longer intervals)
- ✓ End organ damage:
  - BAT in heart failure - symptomatic improvement [1]
  - BAT in renal failure - potentially nephroprotective
  - BAT in carotid artery disease >50% - contraindication

[1] Abraham WT et al. JACC Heart Fail 2015;3:487-96

MRA: Mineralocorticoid receptor antagonist

Unanswered Questions & Future Research

- Randomized trial on efficacy of second generation BAROSTIM NEO™ System:

ONGOING TRIALS	CLIN TRIAL NUMBER	COUNTRY	SAMPLE SIZE
Nordic BAT Study	NCT02572024	Scandinavia	est. 100 patients
BAROSTIM THERAPY™ in Res. Hypertension	NCT02880631	Germany	est. 500 patients
ESTIM-rHTN	NCT02364310	France	est. 128 patients

- Effect of BAROSTIM THERAPY on clinical endoints in high risk patients (CKD, diabetes, a.o.)
- Definition of predictors for therapy response
- Effect of co-medication on efficacy of BAROSTIM THERAPY
- Systematic evaluation of device programming on efficacy and side effects

Many thanks to the committee members for the great collaboration!

M. Koziolek[1] · J. Beige[2,3] · M. Wallbach[1] · D. Zenker[4] · G. Henning[5] · M. Halbach[6] · N. Mader[7] · F. Mahfoud[8,23] · G. Schlieper[9] · V. Schwenger[10] · M. Hausberg[11] · J. Börgel[12] · M. Lodde[12] · M. van der Giet[13] · J. Müller-Ehmsen[14] · J. Passauer[15] · S. Parmentier[15] · S. Lüders[16] · B. K. Krämer[17] · S. Büttner[18] · F. Limbourg[19] · J. Jordan[20] · O. Vonend[21] · H.-G. Predel[22] · H. Reuter[6]

Thank you.