Who are the most appropriate hypertension patients for BAROSTIM THERAPY?

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Agenda

- Who is the suitable patient?
- Exclusion of pseudoresistance and secondary causes
- Special conditions

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Who is the suitable patient?

According to the current ESC/ESH guidelines interventional treatment should be considered in patients with truly resistant hypertension:

- Office cuff blood pressure >160/110 mmHg
- after lifestyle modification and
- under at least 3 antihypertensive drugs (incl. diuretics)

Mineralocorticoid receptor antagonists, amiloride, and the alpha-1-blocker doxazosin should be considered, if no contraindication exists.	IIa	B

Mancia G et al, Eur Heart J. 2013;34(28):2159-219

Who is the suitable patient?

According to the current ESC/ESH guidelines interventional treatment should be considered in patients with truly resistant hypertension:

- ✓ Exclusion of pseudoresistance and/or secondary causes.

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 ambulatory BP monitoring.	I	C

Mancia G et al, Eur Heart J. 2013;34(28):2159-219

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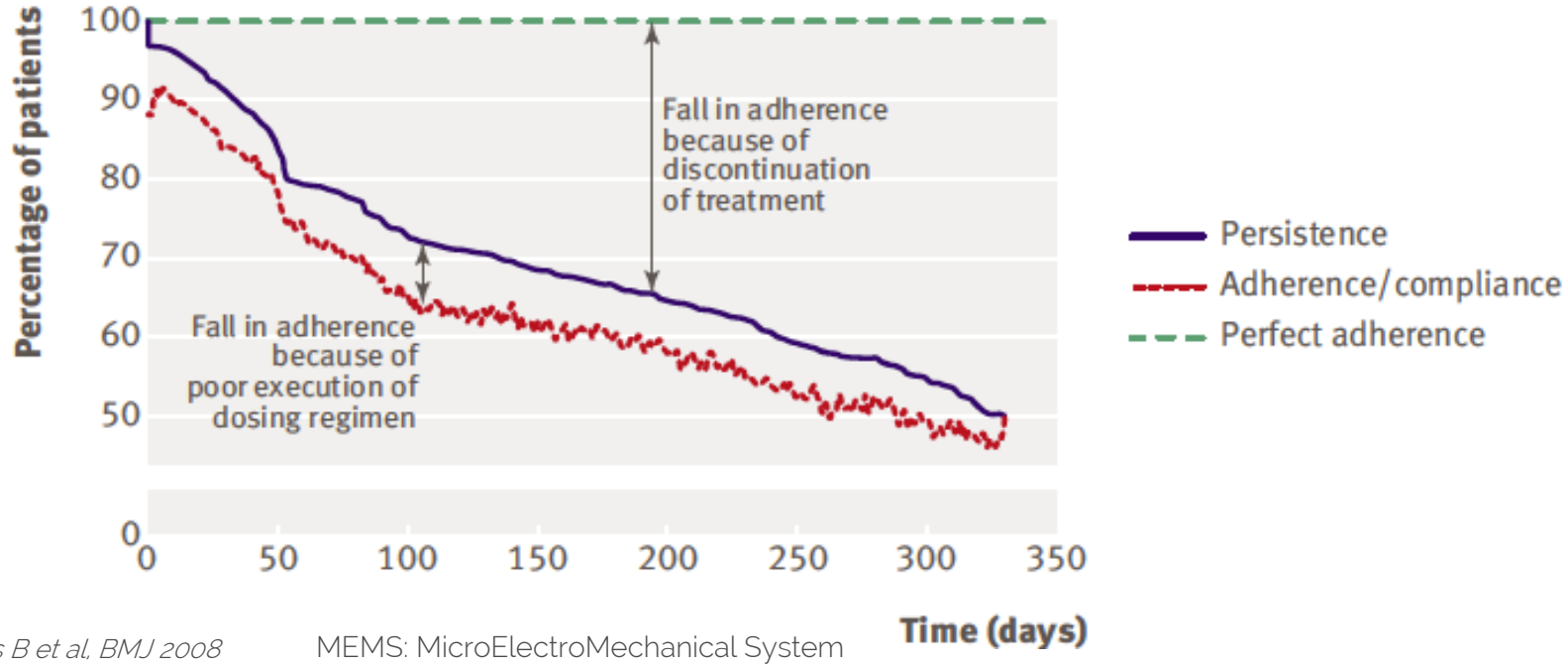
High prevalence of non-adherence in hypertensive patients

4783 hypertensive patients from 21 phase IV trials with MEMS-based supervision

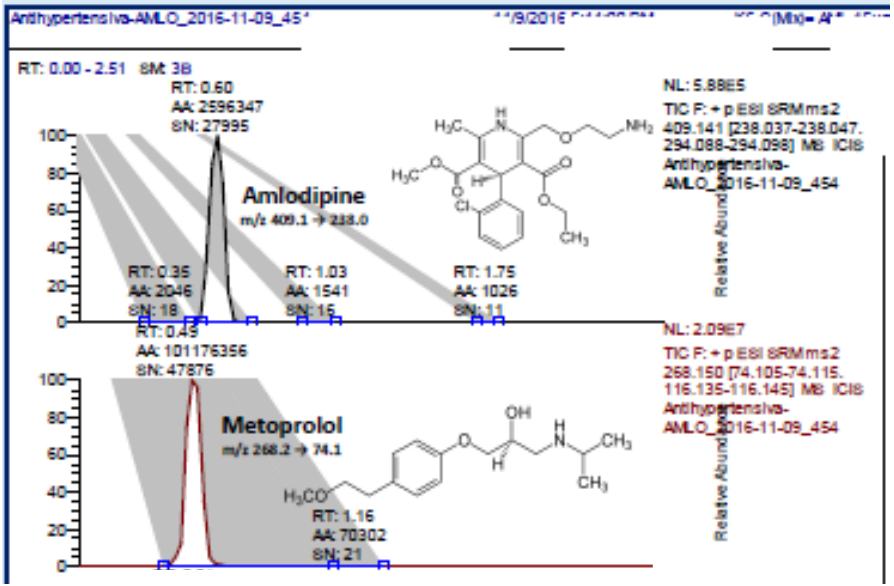


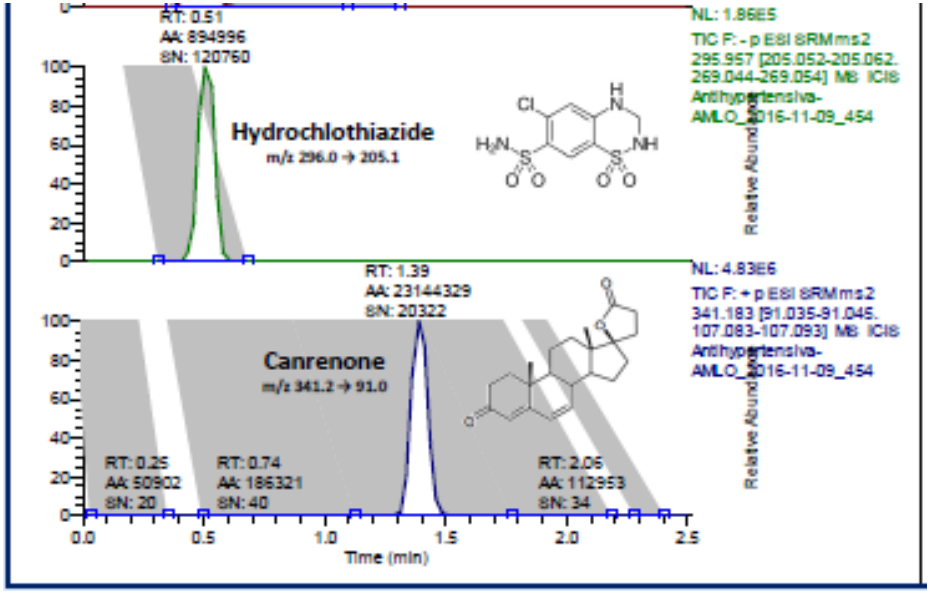
Vrijens B et al, BMJ 2008

MEMS: MicroElectroMechanical System

Therapeutic drug monitoring

Simultaneous determination of Metoprolol, Amlodipine, Canrenone and HCT via liquid chromatography – mass spectrometry in serum





Secondary hypertension
CRITERIA FOR SCREENING

- Poor response to therapy
- Stage 3 hypertension (systolic blood pressure >180 mmHg or diastolic blood pressure >110 mmHg)
- Worsening of control in previously stable hypertensive patient
- Onset of hypertension in persons younger than age 20 or older than age 50
- Significant hypertensive target organ damage
- Lack of family history of hypertension
- Findings on history, physical examination, or laboratory testing that suggest a secondary cause

Agenda

- Who is the suitable patient?
- Exclusion of pseudoresistance and secondary causes
- Special conditions
  - prior renal denervation
  - isolated systolic hypertension
  - patients with end organ damage

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Therapy resistant hypertension after RDN

Patient Characteristics:

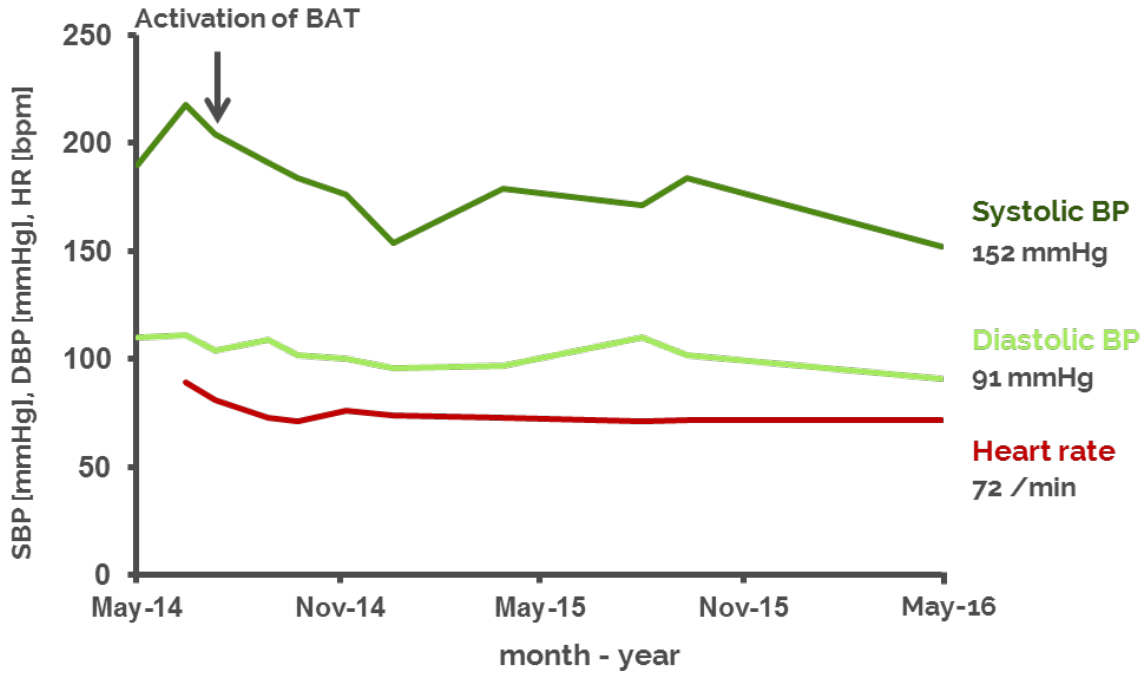
- 52 years old female patient
- Arterial hypertension, stage 3 (Dx 1990)
- History of renal denervation 2013
- Secondary causes repeatedly excluded
- Home BP (avg.): 190/110 mmHg

Medication at first presentation:

- Valsartan 320 mg/d
- Carvedilol 50 mg/d
- Amlodipine 10 mg/d
- HCT 25 mg/d

BAT Implantation

COURSE OF BP AND HR OVER 24 MONTHS



Baroreflex activation therapy in patients with prior renal denervation

Inclusion:

- 28 patients
- Uncontrolled resistant hypertension (182 ± 28 mmHg)
- Prior renal denervation (> 5 months before BAT implant)

TABLE 1. Patients' characteristics at baseline

n	*n*	
Sex		
Male *n* (%)	28	14 (50%)
Female *n* (%)	28	14 (50%)
Period between prior RD and BAT (months)	22	9.5 (5–25)
Age (years)	28	57 ± 12
BMI (kg/m^2)	28	32 ± 6
Weight (kg)	28	93 ± 20
Number of antihypertensive patients	28	6.2 ± 1.5
eGFR (MDRD) (ml/min)	26	78 ± 29
Relevant concomitant diseases		
Congestive heart failure	28	3 (11%)
Coronary heart disease	28	4 (14%)
Diabetes mellitus	28	12 (43%)
History of smoking	19	11 (58%)
Chronic kidney disease ≥ CKD stage 1	28	22 (79%)

Values are mean ± SD, *n* (%), or median (range). CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease.

Wallbach M, J Hypertens 2016; 34

Baroreflex activation therapy in patients with prior renal denervation

CHANGE IN OFFICE BP

Baseline: 182 ± 28 mmHg 96 ± 22 mmHg

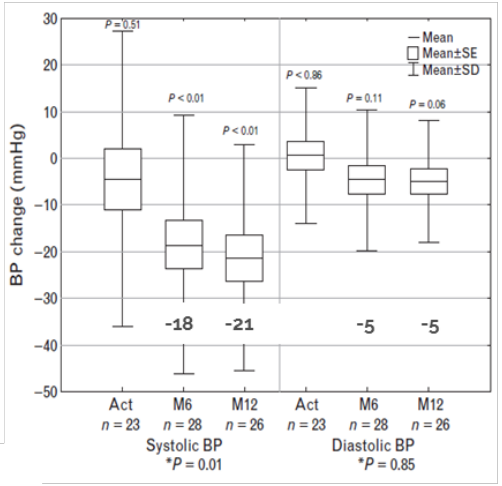
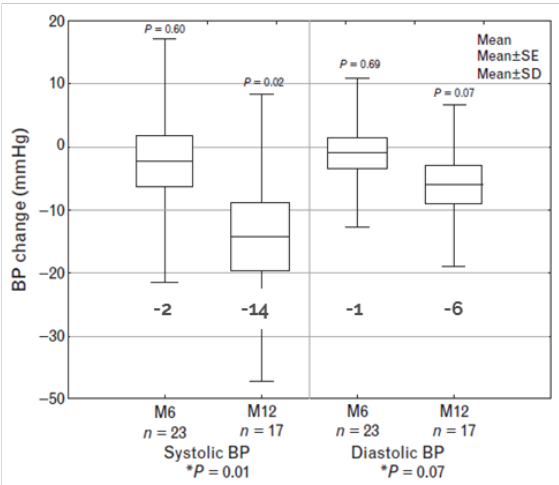


TABLE 3. Responder in office and ABPM at month 6 and 12

	Responder at M6	Responder at M12
Office SBP ≥10 mmHg	19/28 (68%)	20/26 (77%)

CHANGE IN AMBULATORY BP

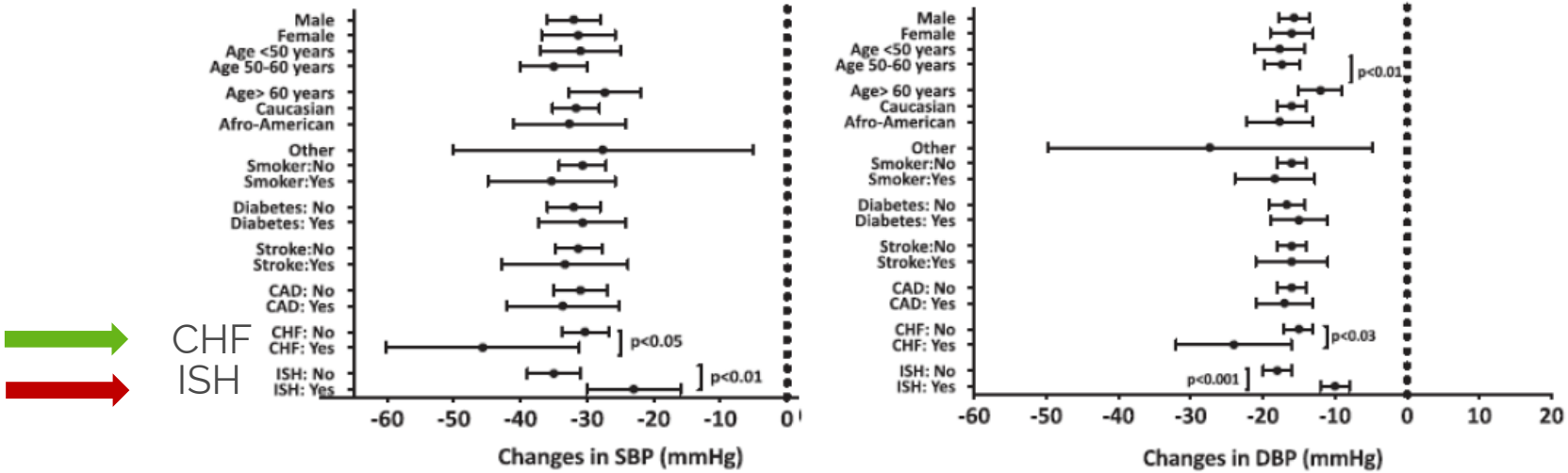
Baseline: 162 ± 21 mmHg 90 ± 17



Wallbach M, J Hypertens 2016; 34

Isolated systolic hypertension is a negative predictor for response

6 year long-term follow up of 383 patients
from the 3 controlled BAT trials that focused on treatment-resistant hypertensive patients



CHF: Chronic heart failure
ISH: Isolated systolic hypertension

de Leeuw et al, Hypertension 2017; *69*: 836-843.

Potential effects of BAT on end organ damage

[1] BAT may improve left atrial and ventricular structure and function.
BAT may reduce left ventricular mass.

[2] Potential nephroprotective effects of BAT in patients with chronic kidney disease (CKD) by stabilization of estimated GFR and mild reduction of proteinuria.

[3] Limited acute effect of BAT on muscle glucose metabolism (insulin sensitivity, glucose- or insulin-concentration).

[4] No effect of BAT on oral glucose tolerance, fasting insulin levels, C-peptide levels, hemoglobin A1c, HOMA-IR, HOMA-β.

[5] BAT reduces central blood pressure, augmentation index and pulse wave velocity, suggesting a strong potential to reduce cardiovascular risk.

HOMA-IR: Homeostasis model assessment – insulin resistance
HOMA-β: Homeostasis model assessment – beta-cell function

[1] Bisognano et al. JACC 2011;57:1787-91
[2] Walbach M et al. Am J Nephrol 2014;40:371-80
[3] May M et al. Diabetes 2014;63:2833-37
[4] Walbach M et al. Acta diabetol 2015;52:829-35
[5] Walbach M et al. J Hypertens 2015;33:181-86

Conclusions

- Efforts should be made to select patients with truly resistant hypertension for interventional treatment, including:
  - optimization of medical therapy
  - exclusion of pseudoresistance and
  - screening for secondary causes
- BAT is effective in patients with resistant hypertension and prior renal denervation.
- BAT has a stronger effect in patients with chronic heart failure.
- BAT is less effective in patients with isolated systolic hypertension.
- Potential nephroprotective effects of BAT in patients with chronic kidney disease.

Thank you.

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