

HTA 2023

Professor Atul PATHAK, MD, PhD.

Cardiovascular Medicine
Hopital Princesse Grace,
MONACO



GRACE-PENN
MEDICINE



European
Hypertension
Excellence
Center
Princess Grace
Hospital
Monaco

16 Chiffres clés

Hypertension

PRÉVALENCE



1 adulte sur **3**
est hypertendu^{1,16}

FARDEAU



17 millions
de personnes de plus de 18
ans atteintes d'HTA en
France²⁰

TRAITEMENT



1 hypertendu sur **2**
est traité
pharmacologiquement^{1,16}

PRESSION ARTÉRIELLE MOYENNE

126/77 mm Hg

Pression artérielle moyenne de la
population française¹



CONTRÔLE



1 hypertendu sur **4**
a une pression artérielle
contrôlée^{1,16}

SPÉCIALISTES

11%

des hypertendus
sont suivis par un
cardiologue³⁴



PRISE EN CHARGE

22% des hypertensions non traitées sont de grade 2 ou 3^{1,16}

TRAITEMENT

1,6 million de Français initient un traitement anti HTA chaque année¹⁸

DÉPISTAGE

84% De la population a eu une mesure de la pression artérielle dans l'année¹

CONNAISSANCE



1 hypertendu sur **2** ne sait pas qu'il est hypertendu^{1,16}

TRAITEMENT

60%



des hypertendus traités pharmacologiquement avaient une monothérapie^{1,16}

TRAITEMENT

93%



des patients émettent des réserves lors de la prescription d'un traitement antihypertenseur¹⁴

AUTOMESURE

59%



des hypertendus traités possèdent un appareil d'automesure tensionnelle¹

RECOURS AUX SOINS

10



consultations par an chez le généraliste pour les hypertendus³⁴

OBSERVANCE

40%

des hypertendus traités sont observants³⁴

TRAITEMENT

57%

Des patients hypertendus déclarent ne pas avoir reçu de conseils hygiéno-dététiques dans l'année¹⁹

La classification de l'hypertension artérielle n'a pas changée

à moins de 120/80 mm Hg, la pression est dite "optimale »




à 120-129/80-85 la pression est "normale",

à 130-140/85-90, la pression est dite "normale haute",

au-delà, c'est "hypertension artérielle" grade 1, grade 2, grade 3.

Grade , Stage et Risque CV

Hypertension disease staging	Other risk factors, HMOD, CVD or CKD	BP (mmHg) grading			
		High-normal SBP 130–139 DBP 85–89	Grade 1 SBP 140–159 DBP 90–99	Grade 2 SBP 160–179 DBP 100–109	Grade 3 SBP ≥ 180 DBP ≥ 110
Stage 1	No other risk factors ^a	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to moderate risk	Moderate to high risk	High risk	High risk
Stage 2	HMOD, CKD grade 3, or diabetes mellitus	Moderate to high risk	High risk	High risk	Very high risk
Stage 3	Established CVD or CKD grade ≥4	Very high risk	Very high risk	Very high risk	Very high risk

	<50 years	60–69 years	≥70 years
	<2.5%	<5%	<7.5%
	2.5 to <7.5%	5 to <10%	7.5 to <15%
	≥7.5%	≥10%	≥15%

Complementary risk estimation in Stage 1 with SCORE2/SCORE2-OP

- *Stage 1*, le patient va bien à part son hypertension artérielle – pas d'atteinte d'organes, pas de risque cardiovasculaire.
- *Stage 2*, il a des atteintes d'organes cibles, un diabète ou une maladie rénale chronique jusqu'à stade 3.
- *Stage 3*, il a des complications cardiovasculaires, il est en prévention secondaire, ou il a une maladie rénale chronique avancée.

Mesure de PA

Toujours en dehors du cabinet

PA de Consultation dans le cas contraire

Et les autres

Devices for BP measurement

Recommendations and statements	CoR	LoR
Automatic electronic, upper-arm cuff devices are recommended for office and out-of-office BP measurement (home and ambulatory).	I	B
Hybrid manual auscultatory devices with LCD or LED display, or digital countdown, or shock-resistant aneroid devices can be used for office BP measurement if automated devices are not available.	I	B
Only properly validated devices should be used. www.stridebp.org	I	B
Cuffless BP devices should not be used for the evaluation or management of hypertension in clinical practice.	III	C

Drug-classes for BP lowering

Prescribing patterns:

- Start with dual combination therapy in most patients
- Uptitrate to maximum well tolerated doses and to triple therapy if needed
- **Once daily (preferred in the morning)**
- **Add further drugs if needed**
- Preferred use of SPCs at any step



T/TL **Diuretic^a**

Additional drug classes

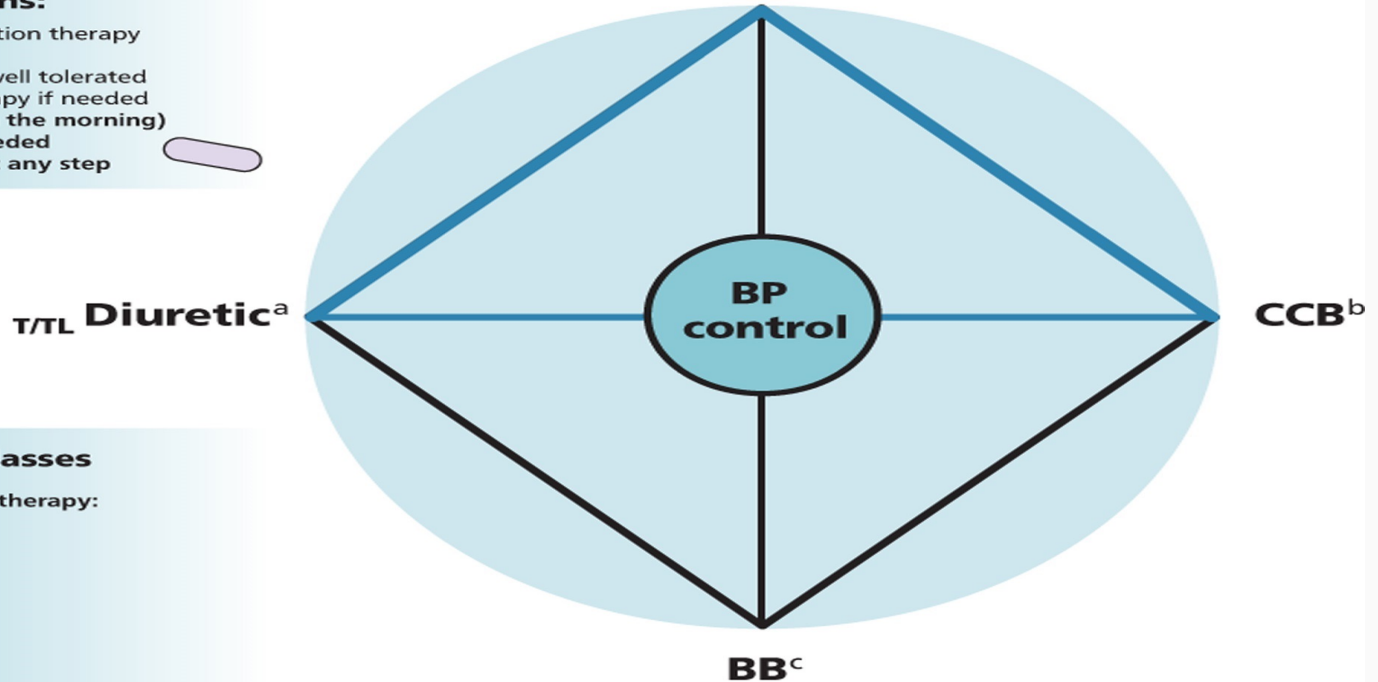
General antihypertensive therapy:

- Steroidal MRA
- Loop Diuretic
- Alpha-1 Blocker
- Centrally acting agent
- Vasodilator

Special comorbidities:

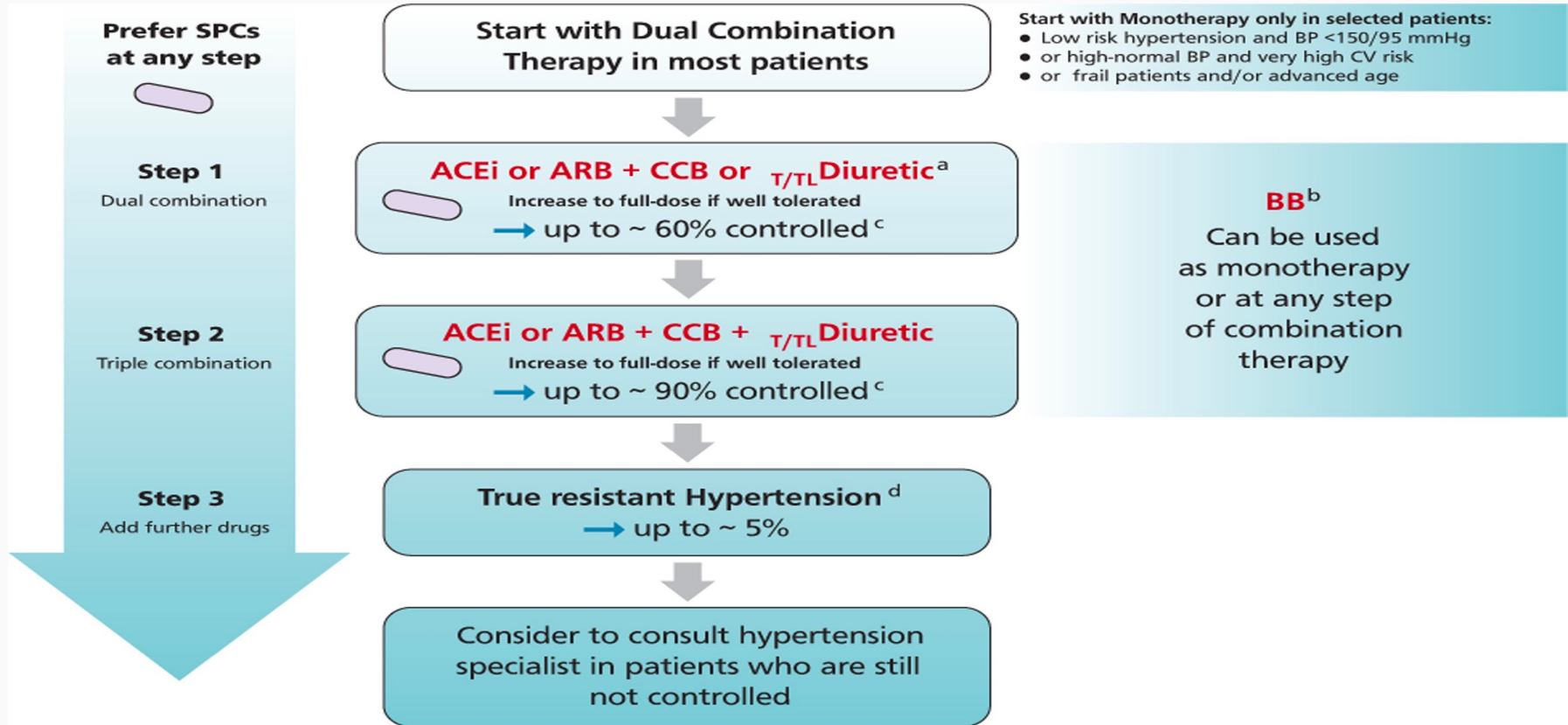
- ARNi
- SGLT2i
- Non-Steroidal MRA

ACEi or ARB



JOURNAL OF HYPERTENSION

Pharmacotherapy Hypertension



Beta Blockers in ESH Guidelines 2023

General recommendations for antihypertensive drug treatment

Five major drug classes including, ACEis, ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics have effectively reduced BP and CV events in RCTs. These drugs and their combinations are recommended as the basis of antihypertensive treatment strategies.

I

A

BBs should be used at initiation of therapy or at any treatment step as GDMT, examples:

- Heart failure with reduced ejection fraction HFrEF
- Anti-ischemic therapy in chronic coronary syndromes
- Heart rate control in atrial fibrillation

I

A

BBs can be considered in the presence of several other conditions in which their use can be favorable as summarized in Table xx.

I

C

Hypertension

REVIEW

Individualized Beta-Blocker Treatment for High Blood Pressure Dictated by Medical Comorbidities: Indications Beyond the 2018 European Society of Cardiology/European Society of Hypertension Guidelines

Giuseppe Mancia¹, Sverre E. Kjeldsen², Reinhold Kreutz³, Atul Pathak⁴, Guido Grassi⁵, Murray Esler⁶

Other cardiac indications for BB

Acute coronary syndrome
Chest pain
LQTS
HOCM, subaortic stenosis, septal thickness
Uncontrolled rapid atrial fibrillation combined with diltiazem or verapamil to avoid toxic amiodarone
Paroxysmal supraventricular arrhythmias, ventricular arrhythmias, other arrhythmias
Post ICD implantation
Attacks of tachycardia after PM implantation for tachy-brady syndrome
After CABG, valve and other major cardiac surgery, consider in HF with medium range (HFmrEF) and HFpEF
Unpleasant palpitations

Indications for BB related to peripheral circulation

Emergency, urgency, and parenteral administration of labetalol
Perioperative hypertension
Major noncardiac surgery
Excessive pressor response to exercise and stress
Hyperkinetic heart syndrome
POTS
Orthostatic hypertension
Obstructive sleep apnea syndrome
Peripheral arterial disease with claudication
Portal hypertension, cirrhosis-related oesophageal varices and recurrent variceal bleeding
Pregnancy related disorders (eclampsia, preeclampsia)

Other indications for BB

COPD
Diabetes
Thyrotoxicosis, hyperthyroidism, thyroiditis, and Graves' disease
Hyperparathyroidism in uremia
Migraine headache
Essential tremor
Glaucoma
Performance anxiety and anxiety disorders
Olympic sports (negative) as doping and sabotage
Psychiatric disorders (posttraumatic stress)

Denervation rénale installée

Use of renal denervation

Recommendations and statements	CoR	LoE
RDN can be considered as a treatment option in patients an eGFR >40 ml/min/1.73m ² who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	II	B
RDN can be considered as an additional treatment option in patients with resistant hypertension if eGFR is >40 ml/min/1.73m ² .	II	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
Renal denervation should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

Pharmacotherapy Resistant Hypertension

If eGFR ≥ 30 ml/min/1.73 m²



Patients not controlled with
ACEi or ARB + CCB + T/TL Diuretic^b



Add

- I) **Spironolactone^d** (preferred)
or other **MRA^d**
- or
- II) **BB^e** or **Alpha1-blocker**
- or
- III) **Centrally acting agent**
or consider
Renal Denervation

If eGFR > 40 ml/min/1.73 m²

If eGFR < 30 ml/min/1.73 m²
(not on dialysis)



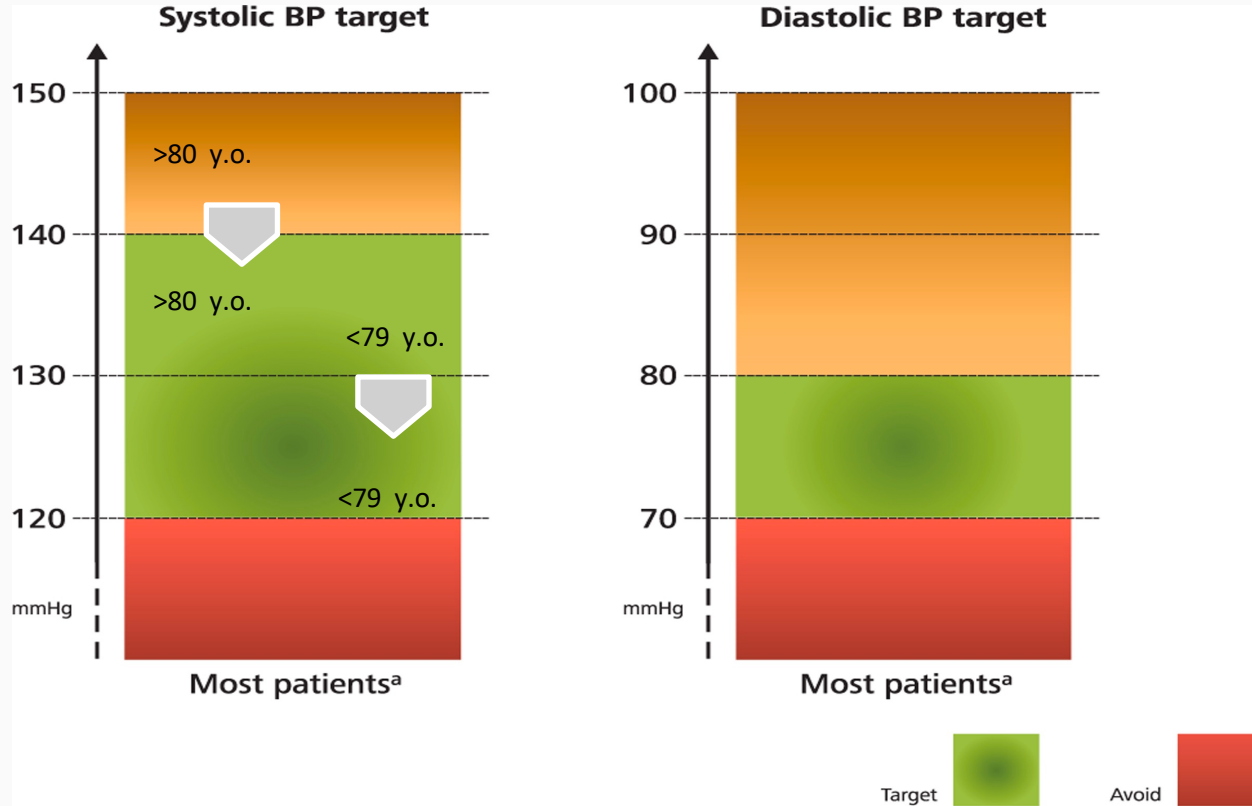
Patients not controlled with
ACEi or ARB + CCB + Loop Diuretic^b



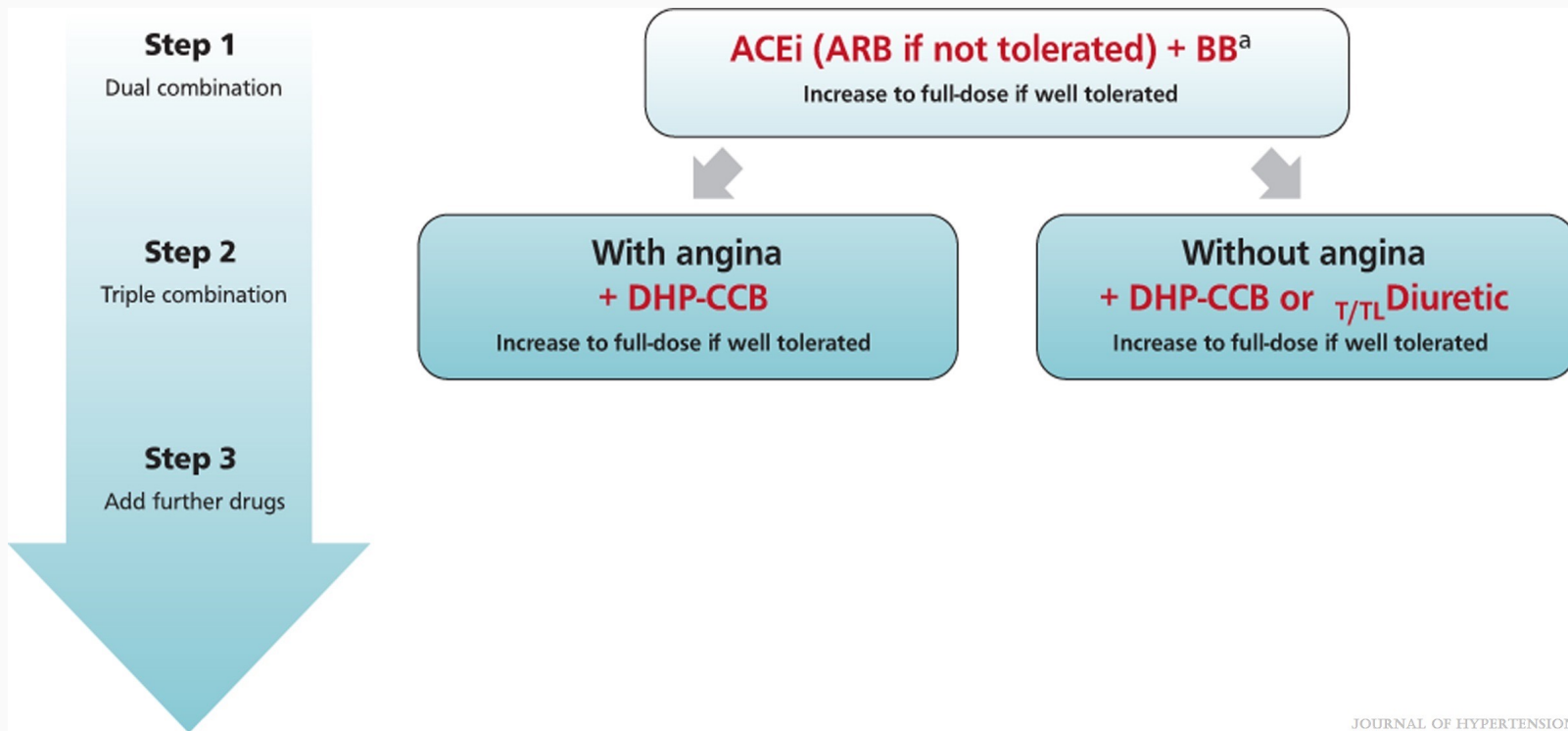
Add^c

- I) **Chlorthalidone** (preferred)
or other **T/TL Diuretic**
- or
- II) **BB^e** or **Alpha-1 Blocker**
- or
- III) **Centrally acting agent**

Treat to Target

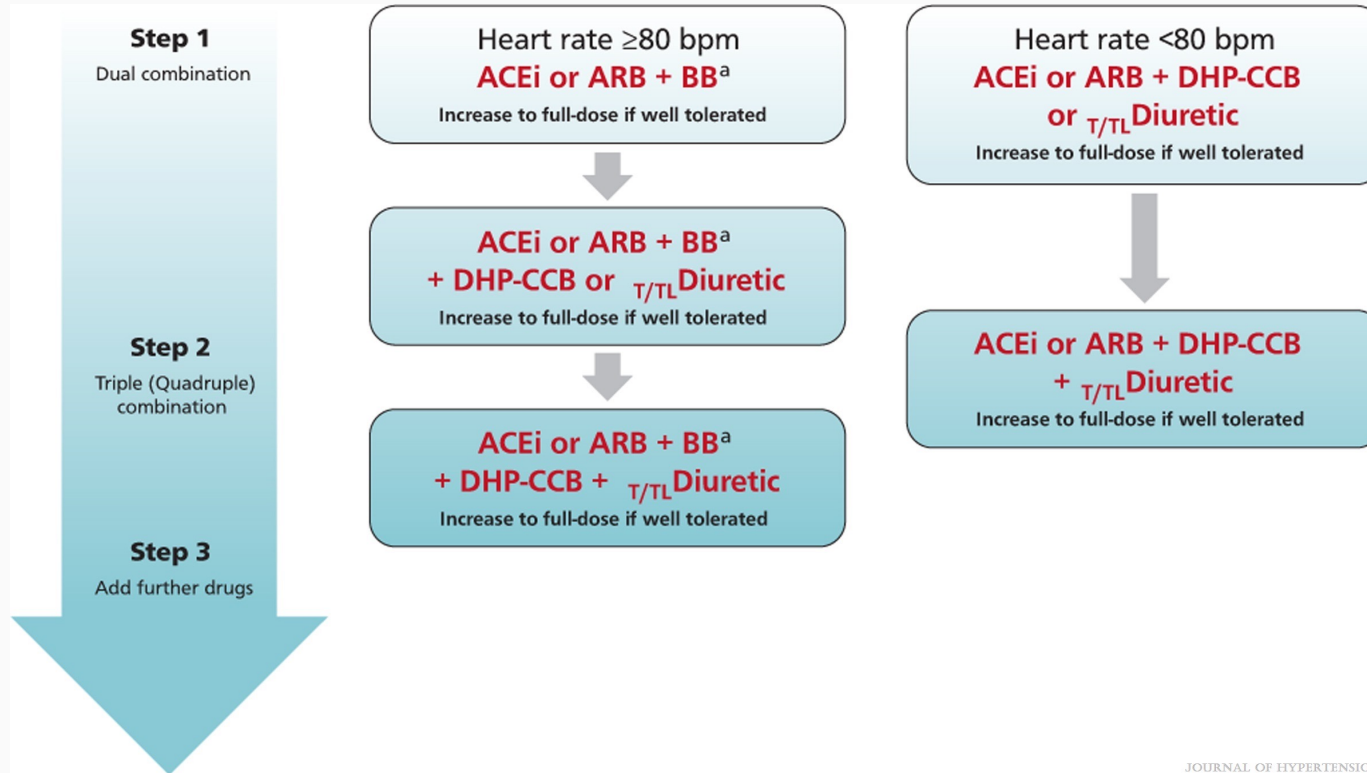


HTN and CAD

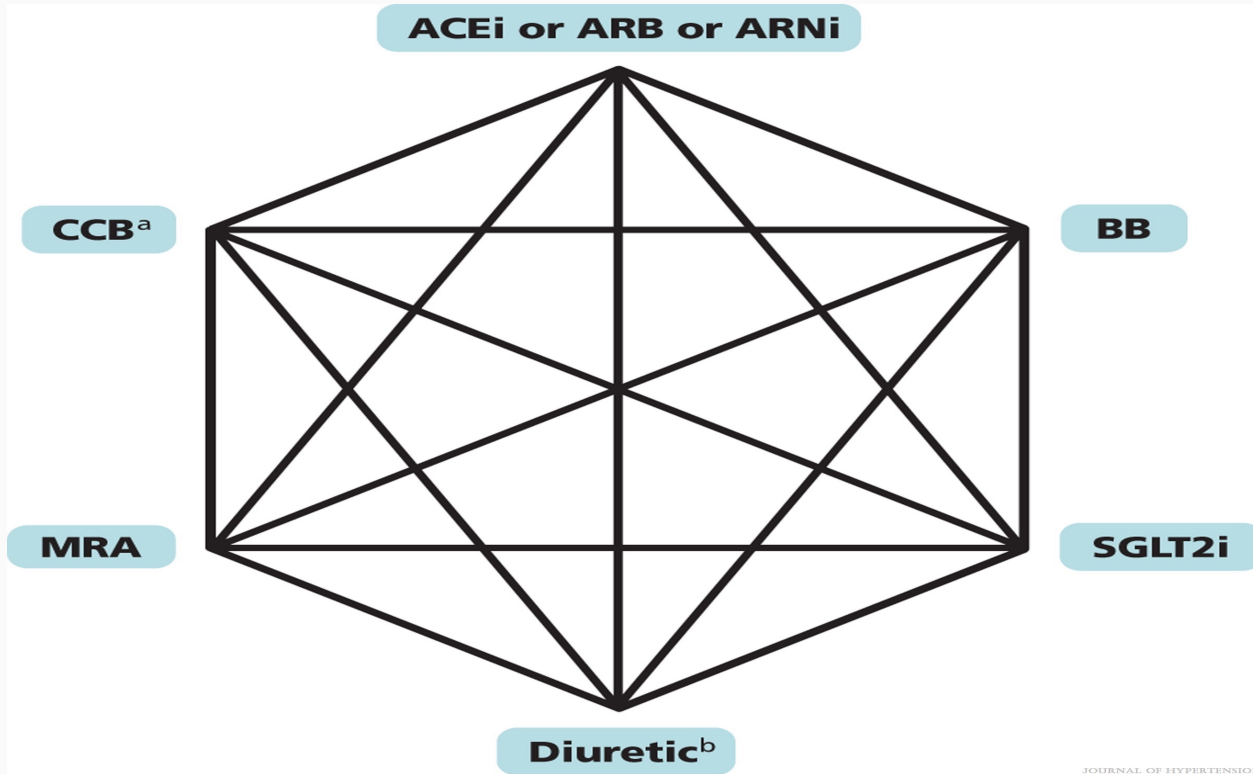


JOURNAL OF HYPERTENSION

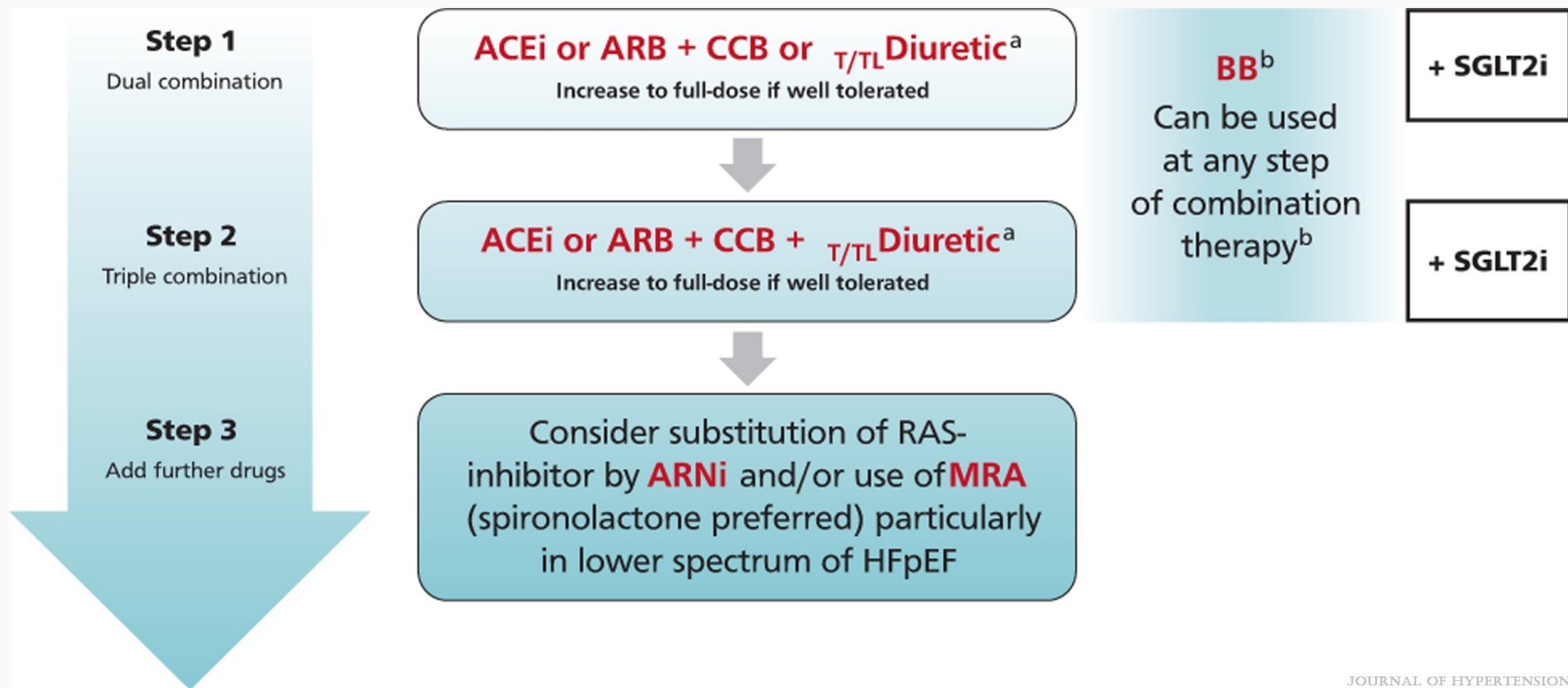
HTN and A Fib



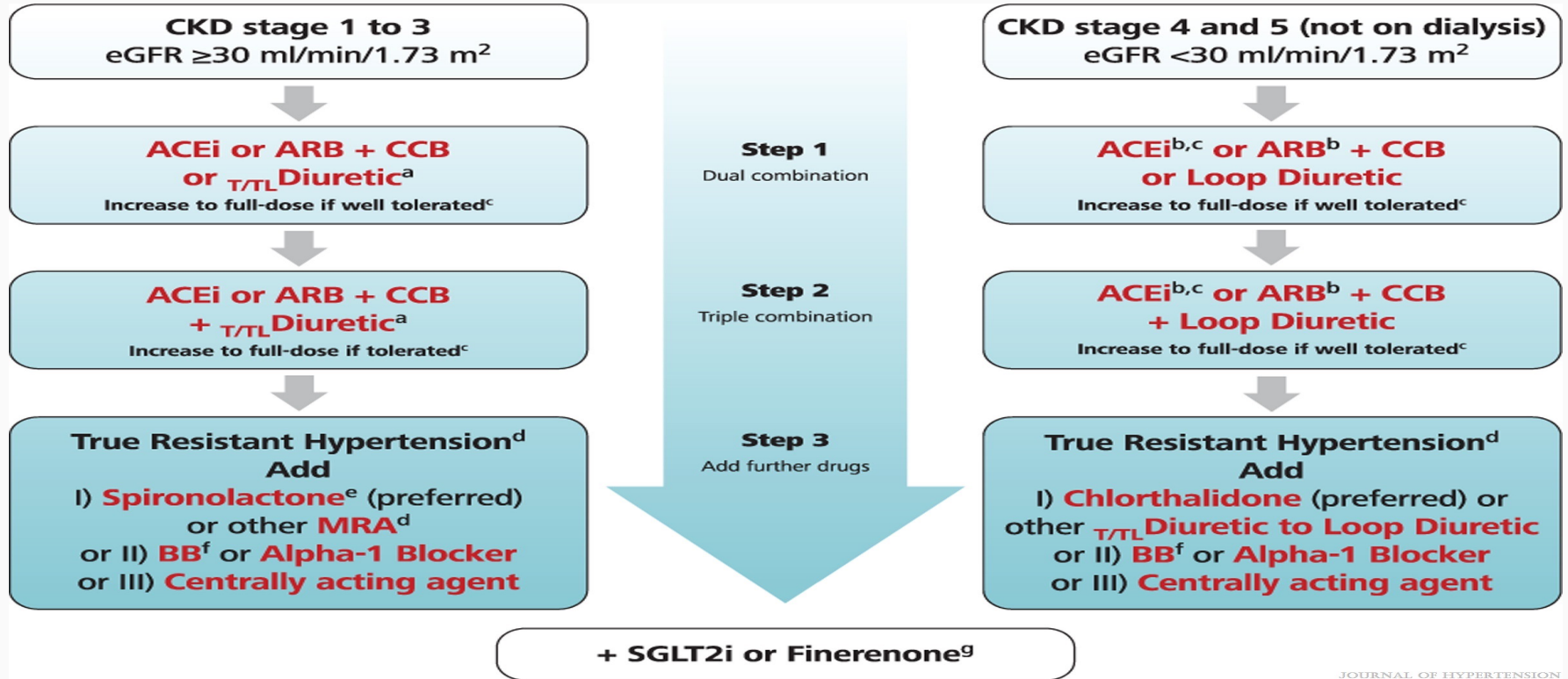
HF rEF



HF p EF



HT and CKD



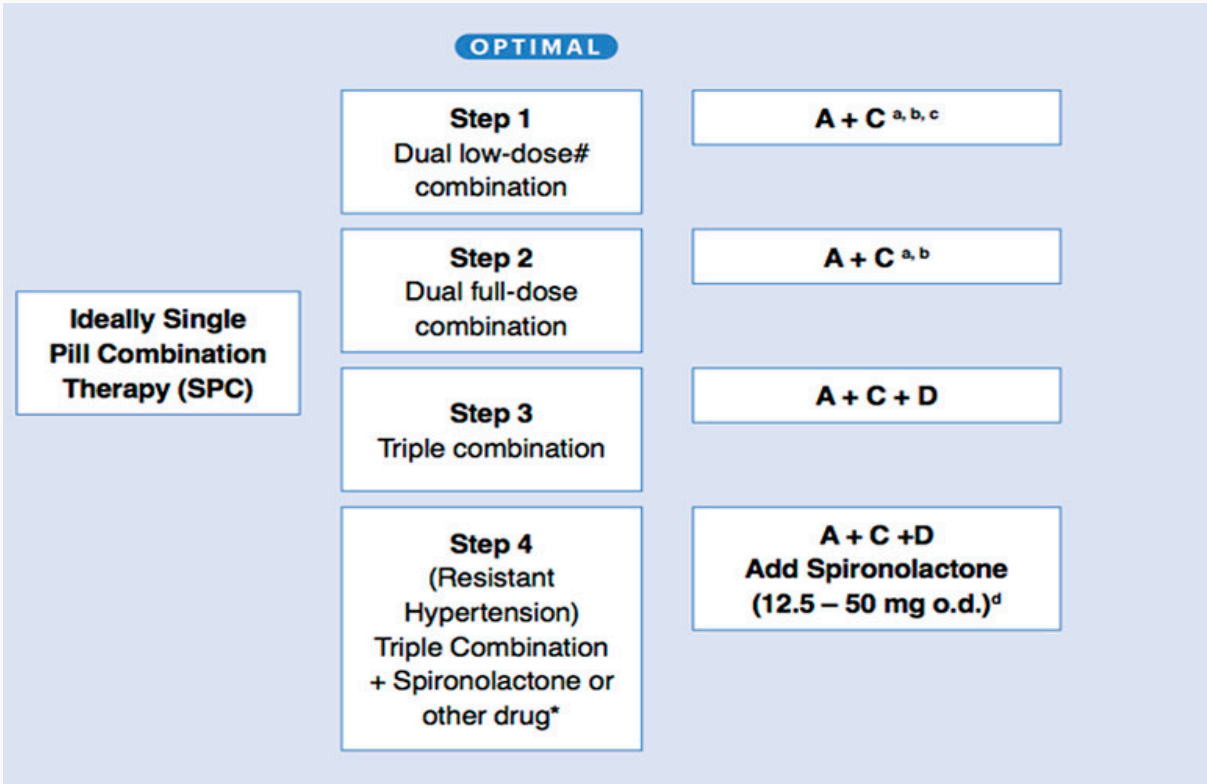
SGLT2 i and BP

BP	BP reduction
24h-SBP	-3.76 mm Hg [-4.23; -3.30]
24h-DBP	-1.83 mm Hg [-2.35; -1.31]
Daytime-SBP	-4.34 mm Hg [-5.09; -3.58]
Daytime-DBP	-2.09 mm Hg [-2.63; -1.54]
Nighttime-SBP	--2.61 mm Hg [-3.08; -2.14]
Nighttime-DBP	-1.49 mm Hg [-2.20; -0.78]

Specific Populations

- **Cancer**
- **Pregnancy**
- **Children**

Beyond Europe : ISH



**Beta blocker at any step
(specific indication)**

Use TL Diuretics otherwise T

**A+D : stroke, elderly, HF,
CCB intolerance**

A+C or C+D : Black patients

Beyond Europe : AHA / ACC

American College of Cardiology/American Heart Association

Treatment strategy

If there is no compelling clinical indication for selection of a BP-lowering medication, treat with ≥ 1 drugs from the following classes: diuretics, CCBs, ACE inhibitors, or ARBs. Combination therapy is required in most patients and is specifically recommended in African Americans and in adults with a starting SBP/DBP $\geq 20/10$ mm Hg above the BP treatment target. Dual- and triple-drug therapy should include agents with complementary mechanisms of action. Single-pill combinations improve adherence but may contain lower -than-optimal doses of thiazide diuretic. Simultaneous use of an ACE inhibitors, ARB, and/or renin inhibitor is potentially harmful and not recommended.

Non adherence to antihypertensive therapy

Recommendations and statements	CoR	LoE
Screening for non-adherence to treatment is recommended in all patients with apparent resistant hypertension.	I	B
Consider screening for non-adherence patients who are on combination treatment (i.e. at least 2 drugs) and have an inadequate BP response to this treatment.	II	C
Check adherence prior to screening for secondary hypertension.	I	C
Physicians should collect information on adherence mindful that all methods have limitations.	I	C
Use of single pill combinations to improve adherence and persistence to antihypertensive treatment is generally recommended.	I	B
Several strategies can be considered to improve adherence and a multidimensional team-based care approach is recommended.	I	C

Challenges and Perspectives

- **Improve BP control**

(i.e. quadruple combination, endothelin antagonist)

- **Reduce Side Effects**

(i.e. potassium binder, aldosteron synthase inhibitor)

- **Increase adherence**

(siRNA)



Dual endothelin antagonist



Multicenter – N. America, Europe, Asia, Australia



Systolic BP \geq 140/90 on 3 antihypertensives (including diuretic)



Primary end point: Least square mean change in office SBP from baseline to week 4 and from withdrawal to week 40

730

patients

Part 1: 4 weeks



Double blind



Placebo

-11.5
mm Hg



Aprocitantan
12.5mg OD

-15.3
mm Hg

-3.8 mm Hg (-6.8 to -0.8, $p=0.0042$)



Aprocitantan
25mg OD

-15.2
mm Hg

-3.7 mm Hg (-6.7 to -0.8; $p=0.0046$)

704

patients

Part 2: 32 weeks

Single (patient) blind



All patients received
Aprocitantan 25mg OD

613

patients

Part 3: 12 weeks withdrawal



Double blind



Placebo

4.36
mm Hg



Aprocitantan
25mg OD

-1.47
mm Hg

↑ in SBP 4 weeks after withdrawal
in placebo arm vs Aprocitantan:
5.8 mm Hg (3.7 to 7.9, $p<0.0001$)

577

patients



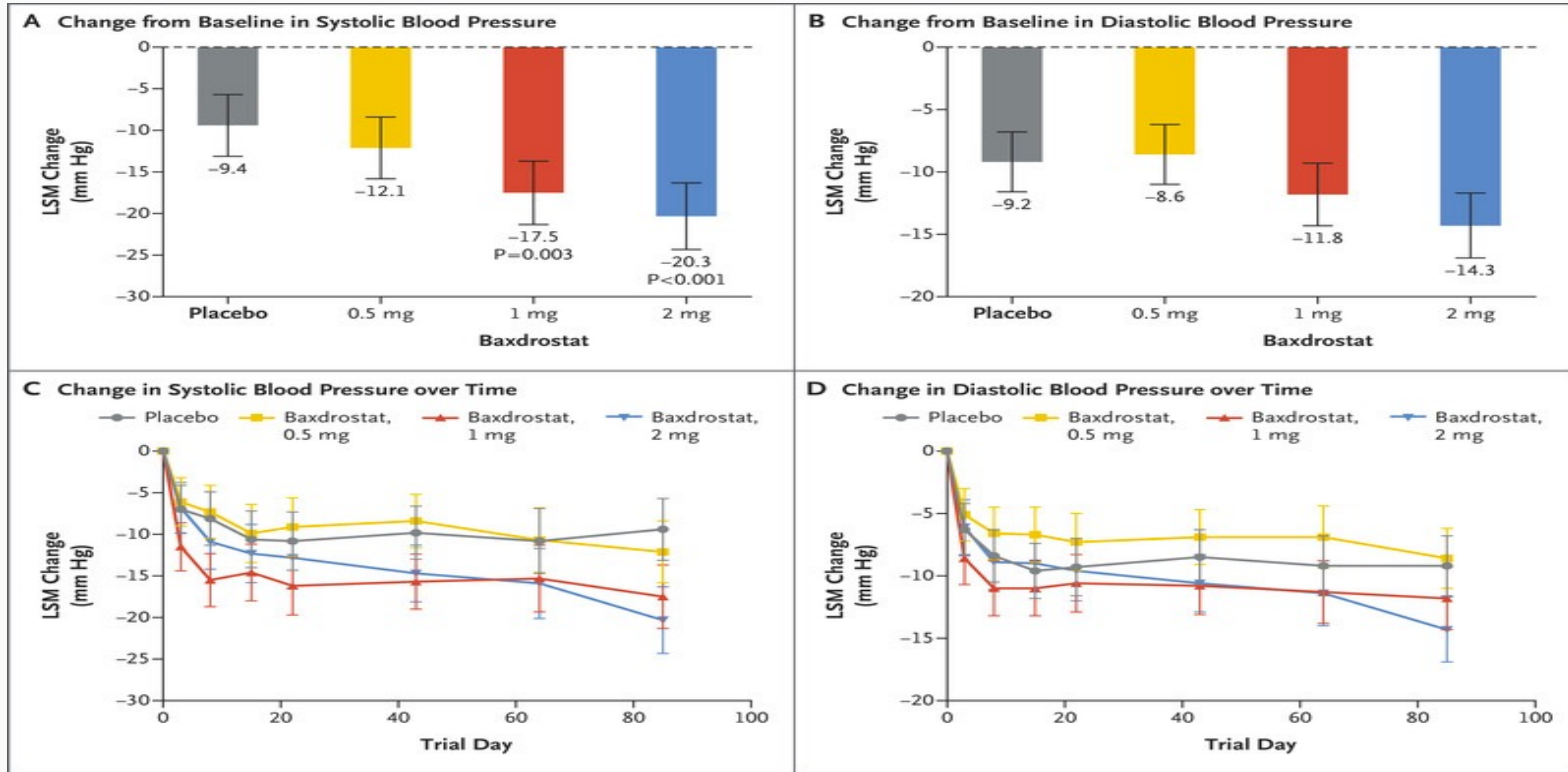
Adverse events:
Edema, fluid retention

2%

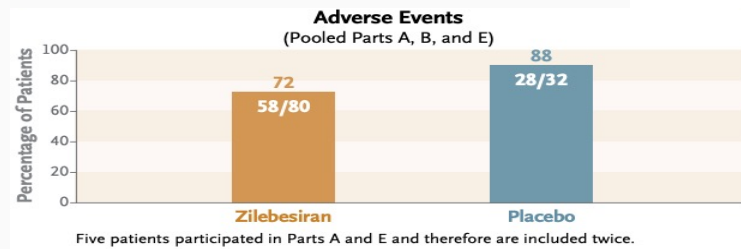
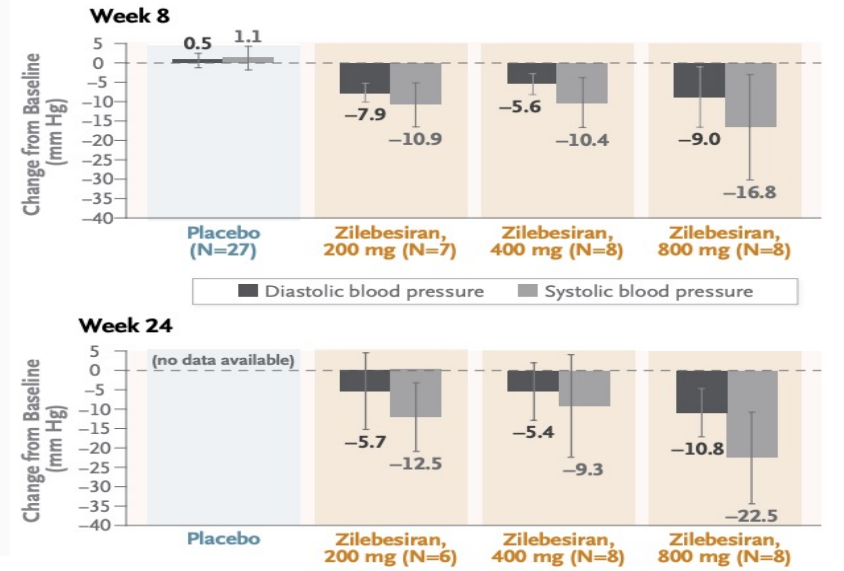
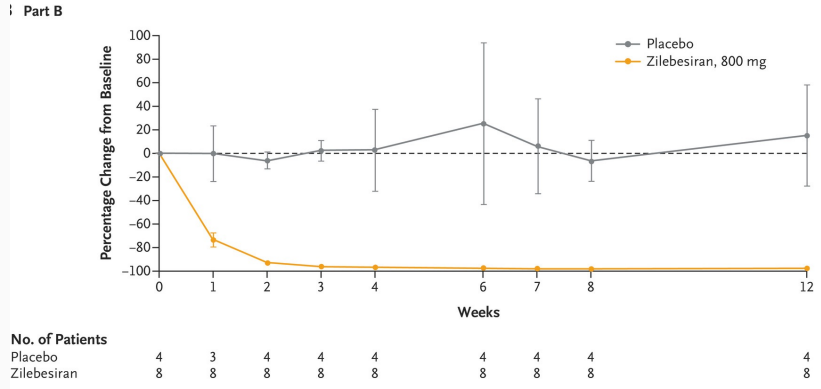
9%

18%

Aldosterone synthase inhibitor



Zilebesiran, an RNA Interference Therapeutic Agent for Hypertension



Conclusions

- ESH guidelines : few changes wait for ESC 2024
- ISH / AHA : few modulations
- Future : great expectations
- Perspectives beyond the pill:
 - *CV risk managements with lipid lowering therapy,*
 - *lifestyle with apps,*
 - *device with Renal Denervation*