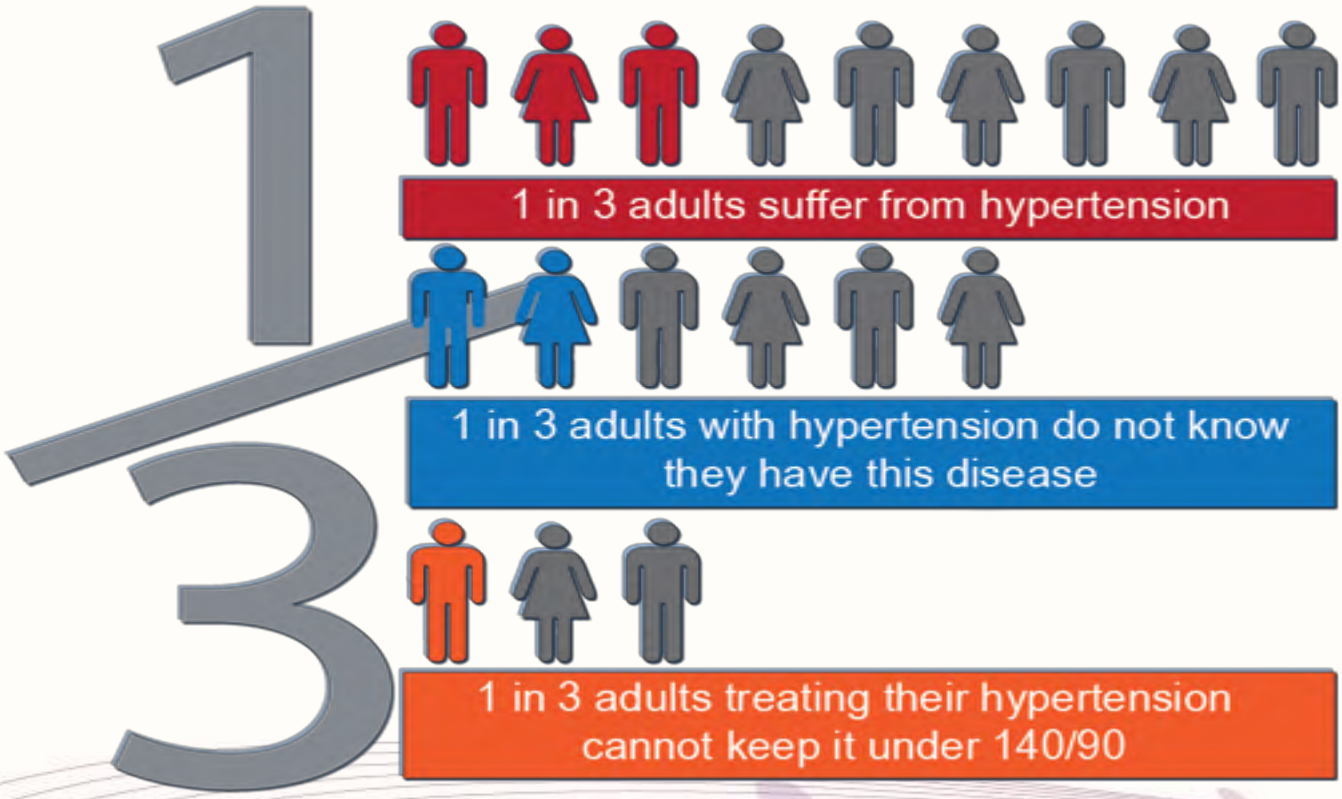
BƯỚC ĐỘT PHÁ TRONG ĐIỀU TRỊ TĂNG HUYẾT ÁP 2018

PGS TS Trương Quang Bình

ĐHYD TP HCM

Hypertension: the facts



http://www.paho.org/hipertension

Prevalence, awareness, treatment and control rates of hypertension in Asia (1)

	Number of subjects	Prevalence	Awareness	Treated	Controlled
Bangladesh 2011	7876	24.4%	50.1%	41.2%	31.4%
Cambodia 2010 (25-64 y)[2]	5433	12.3%	45.4%	19.2%	13.0%
China 2002	141,892	18.8%	30.2%	24.7%	6.1%
India 1950-2013 (>18 y)[4]	326,644	29.9%	25.3% 42.0%	25.1% 37.6%	10.7% 20.2%
Indonesia 2002	3080	58.9%	-%	62.7%	25.0%
Iran 2012 (18-65 y)[6]	3497	21.2%	58.7%	51.0%	21.9%

1. J Hypertens 2015, 33:465. 2. Otgontuya et al. BMC Public Health 2012;12:254. 3. Li L, et al. ChinJ E pidemiol 2005; 26: 478. 4. J Hypertens 2014, 32:1170. 5. Setiati S et al. Indones J Intern Med 2005;37:20-25. 6. J CV Thorac Res 2012; 4, 37.

Prevalence, awareness, treatment and control rates of hypertension in Asia (2)

	Number of patients	Prevalence	Awareness	Treated	Controlled
Japan NIPPON data 2010[7]	-	43 million	-%	-50%	-35%
Korea 2007-2008 (>30 y)[8]	9146	24.9%	60.6%	52.2%	36.7%
Malaysia 2006	16,440	27.8%	34.6%	32.4%	26.8%
Mongolia 2009 (25-64 y)[10]	4539	36.5%	65.8%	34.8%	15.9%
Nepal 2010 (>20 y)[11]	14,009	33.9%	37.0%	25.1%	-%
Pakistan 1990-1994	8972	19.6%	-%	-%	-%

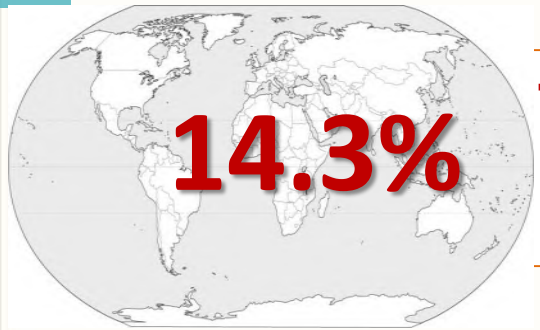
7. NIPPON data 2010. 8. Lee HS, et al. J Hum Hypertens. 2013 Jun;27(6):381. 9. Public Health 2008;122:11. 10. Otgontuya et al. BMC Public Health 2012;12:254. 11. Int J Hypertens 2011;82197112. 12. CMAJ 2006 ;175:1071.

Prevalence, awareness, treatment and control rates of hypertension in Asia (3)

	Number of patients	Prevalence	Awareness	Treated	Controlled
Saudi 2005 (15-64 y)[13]	4,758	25.5%	44.7%	32.1%	16.5%
Singapore 2004-2007 (≥24 y)[14]	5,022	41.5%	51.8%	43.7%	11.8%
Thailand 2004	39,290	22.0%	69.8%	54.6%	20.0%
Viet Nam 2012	9,832	25.1%	48.4%	29.6%	10.7%
SAARC 2000-2013 (meta)[17]	220,539	27.1%	-%	-%	-%

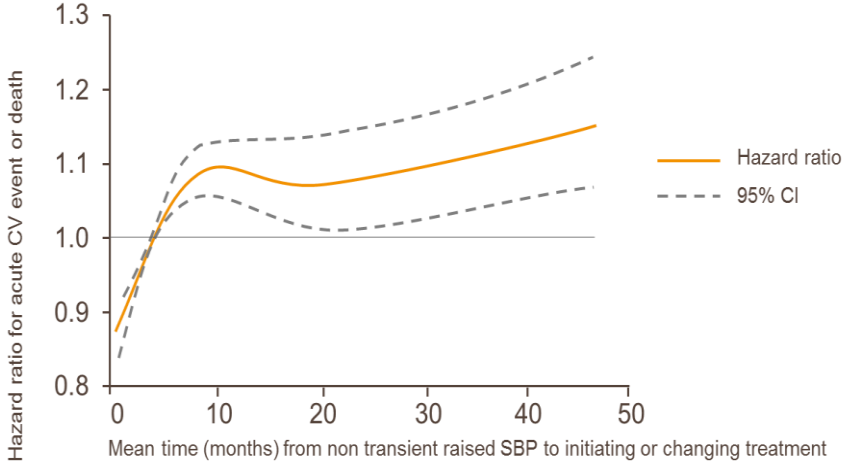
13. Int J Hypertens 2011;174135. 14. J Hypertens 2009;27:190. 15. J Hypertens 2008;26:191. 16. Son PT, et al. J Hum Hypertens. 2012;26:268. 17. Neupane D, et al. Medicine 2014;93:e74.

Hậu quả



Thời gian kiểm soát huyết áp bị TRÌ HOÃN

Tỉ lệ kiểm soát huyết áp còn THẤP



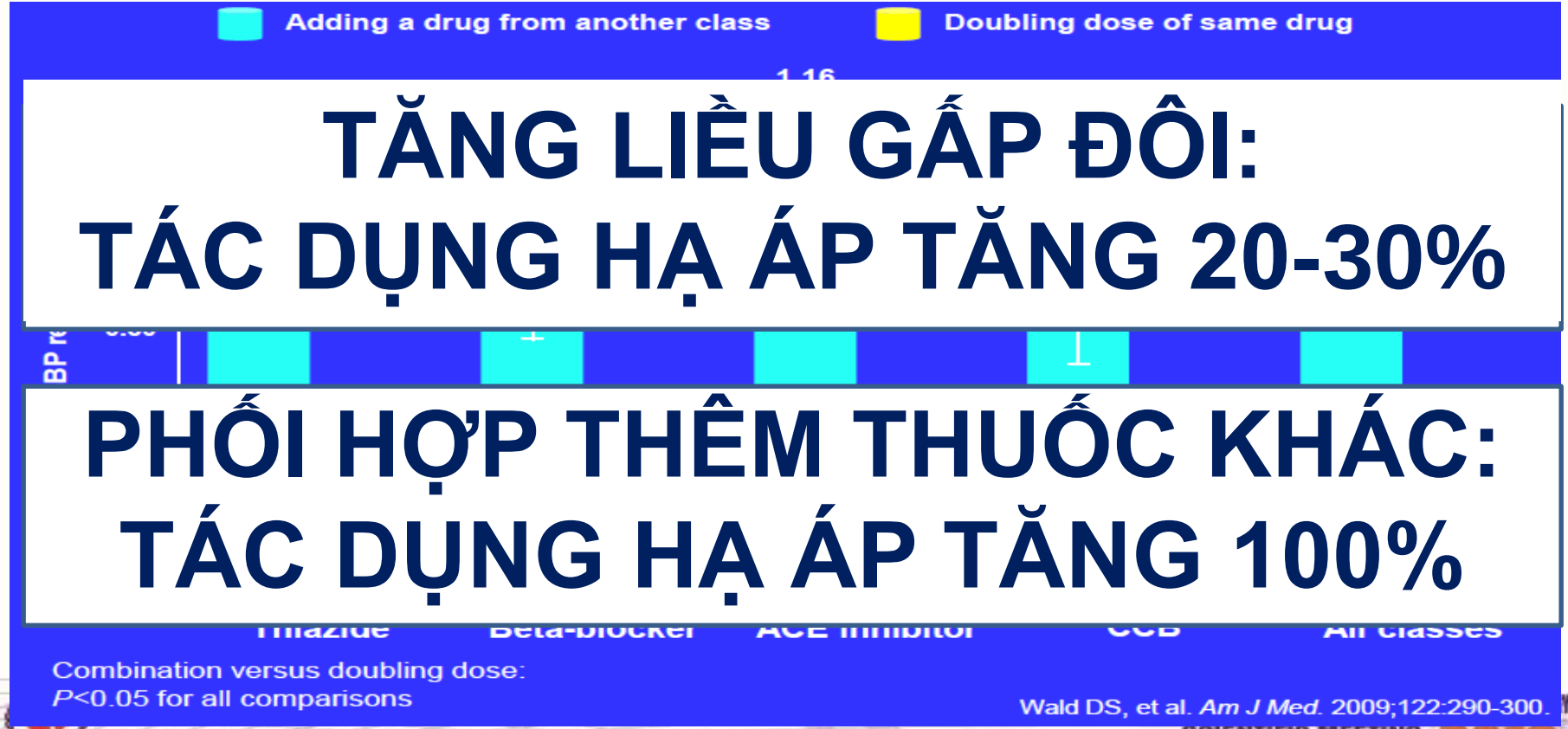
Delays of greater than 6 weeks, after SBP elevation, before initiating or increasing treatment **significantly increase risk** of an acute CV event or death.

Retrospective cohort study, UK primary care practices, 1986-2010; n=88 756 adults with hypertension, >10 years follow-up

1. Xu W et al. *BMJ*. 2015;350:h158

Chow CK, et al. JAMA 2013

Combination therapy is more effective than increasing the dose of one drug



TĂNG LIỀU GẤP ĐÔI:
TÁC DỤNG HẠ ÁP TĂNG 20-30%

PHỐI HỢP THÊM THUỐC KHÁC:
TÁC DỤNG HẠ ÁP TĂNG 100%

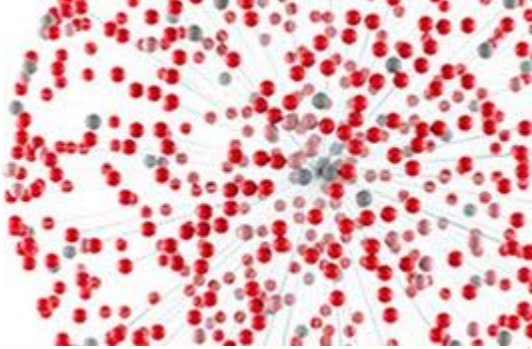
NEW!

ESC Congress
Munich 2018

25-29 August

Where the world of cardiology comes together

ESC European Society of Cardiology



EUROPEAN SOCIETY OF CARDIOLOGY®

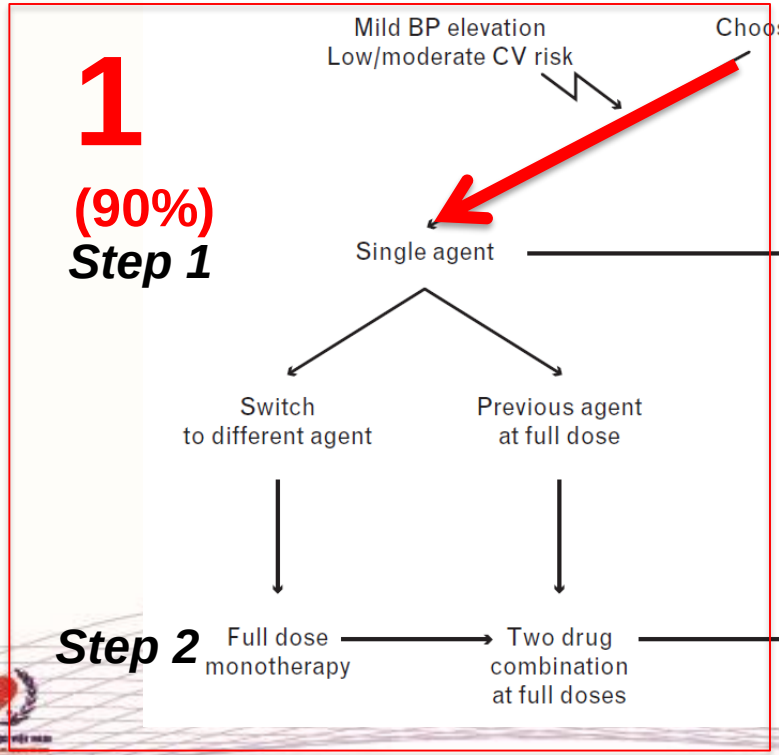
European Heart Journal
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

2018 ESH/ESC Guidelines for the management of arterial hypertension

2013 ESH-ESC Guidelines for the management of Hypertension

Initiation with monotherapy or combination therapy?



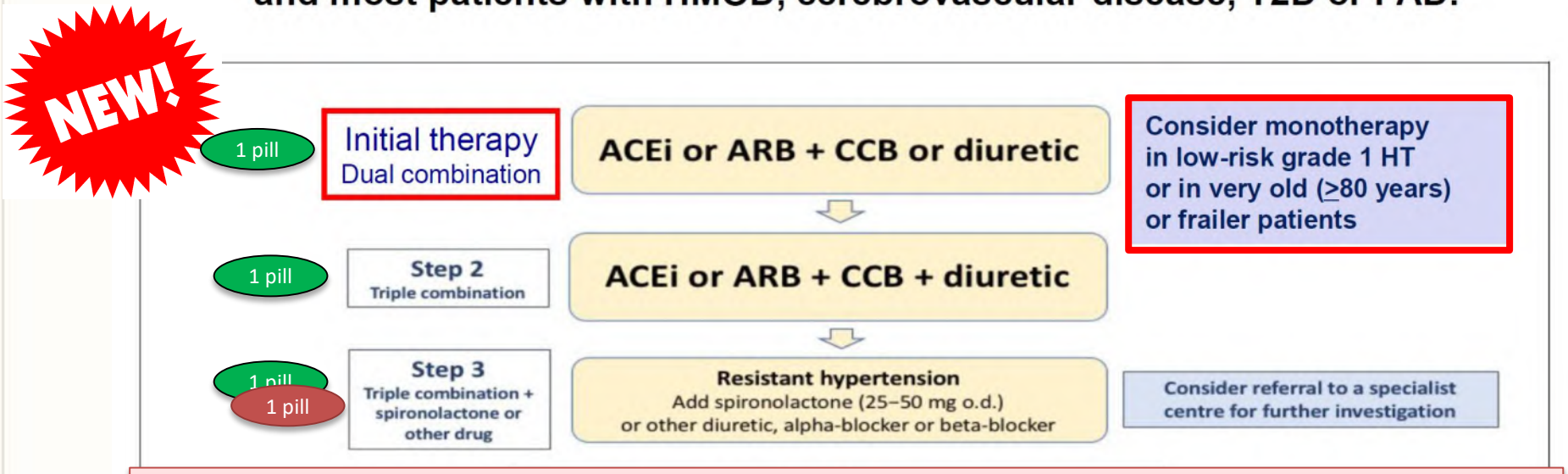
Recommendations	Class[a]	Level[b]
Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C

2018

2018 ESH-ESC Guidelines

Initial therapy with dual combination for uncomplicated HT,

and most patients with HMOD, cerebrovascular disease, T2D or PAD.



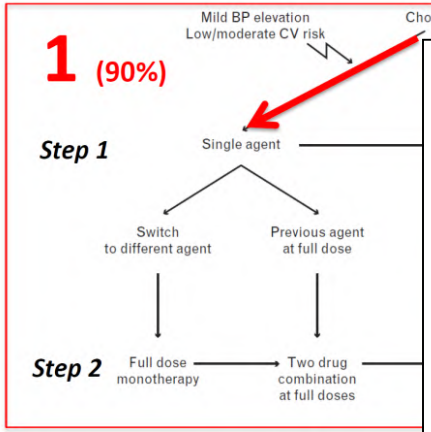
Initial therapy: Dual combination → Next step: Triple combination

Mono-therapy just for low risk grade 1 – very old – frailer patients

BIG change in HTN treatment from NOW

2013 ESH-ESC Guidelines for the management of Hypertension

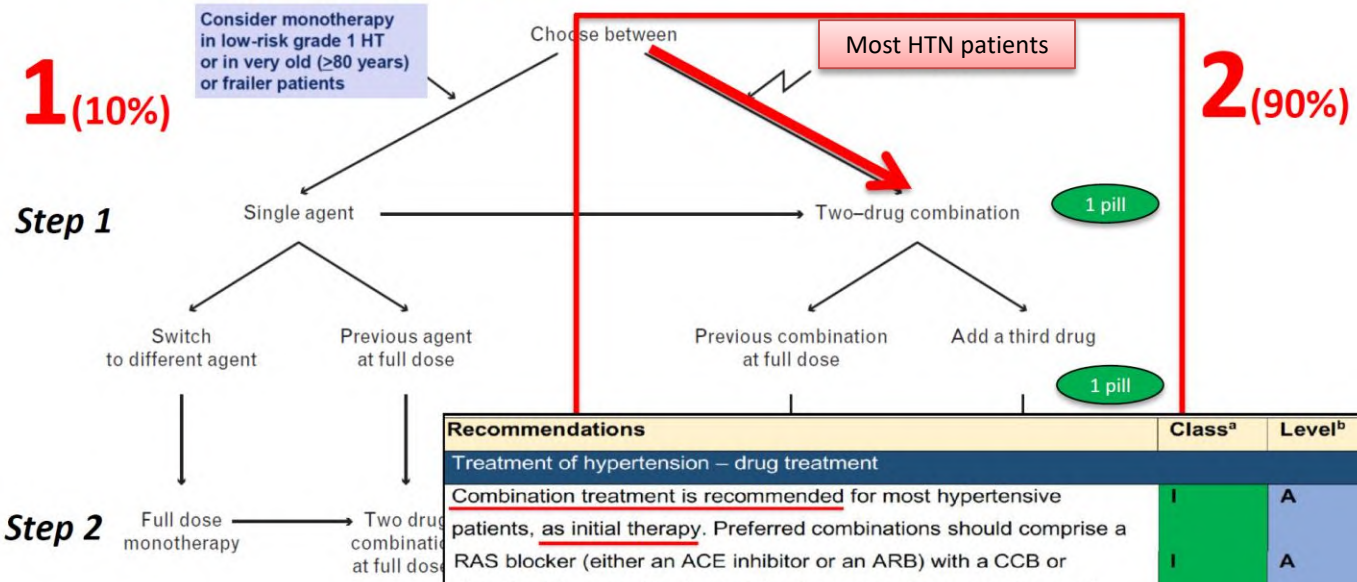
Initiation with monotherapy or combination therapy?



European Heart Journal
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

2018 ESH/ESC Guidelines for the management of arterial hypertension



Recommendations	Class[a]	Level[b]
Treatment of hypertension – drug treatment		
Combination treatment is recommended for most hypertensive patients, as initial therapy. Preferred combinations should comprise a RAS blocker (either an ACE inhibitor or an ARB) with a CCB or diuretic. Other combinations of the five major classes can be used.	I I	A A

4 lý do nên phối hợp thuốc ngay từ đầu đối với BN THA

1. Phối hợp thuốc giúp giảm HA mạnh hơn và nhanh hơn về mức mong muốn
2. Khi BN có nguy cơ cao, các biến cố có thể xảy ra trong thời gian ngắn → hạ HA phải được thực hiện nhanh chóng
3. Trong một số NC, hiệu quả bảo vệ cơ quan đích của điều trị THA có thể xuất hiện nhanh sau khi đạt mức HA mục tiêu
4. Việc phối hợp thuốc từ đầu làm tăng độ tuân trị

Mancia G, et al. *J Hypertens.* 2009;27:2121-2158.

2013 ESH-ESC Guidelines

Single pill fixed dose combination – SPC

Recommendat

Combinations of
antihypertensive
fixed doses in a s
may be recomme
favoured, becaus
the number of da
improves adhere
low in patients w
hypertension.

2018 ESH-ESC Guidelines: SPC first-line

Recommendations	Class[a]	Level[b]
Treatment of hypertension – drug treatment		
It is recommended to initiate an antihypertensive treatment with a two-drug combination, preferably in a SPC. Exceptions are frail older patients and those at low risk and with grade 1 hypertension (particularly if SBP is < 150 mmHg).	I	B[342, 346, 351342, 346, 351]

NEW!

European Heart Journal
doi:10.1093/eurheartj/eht151

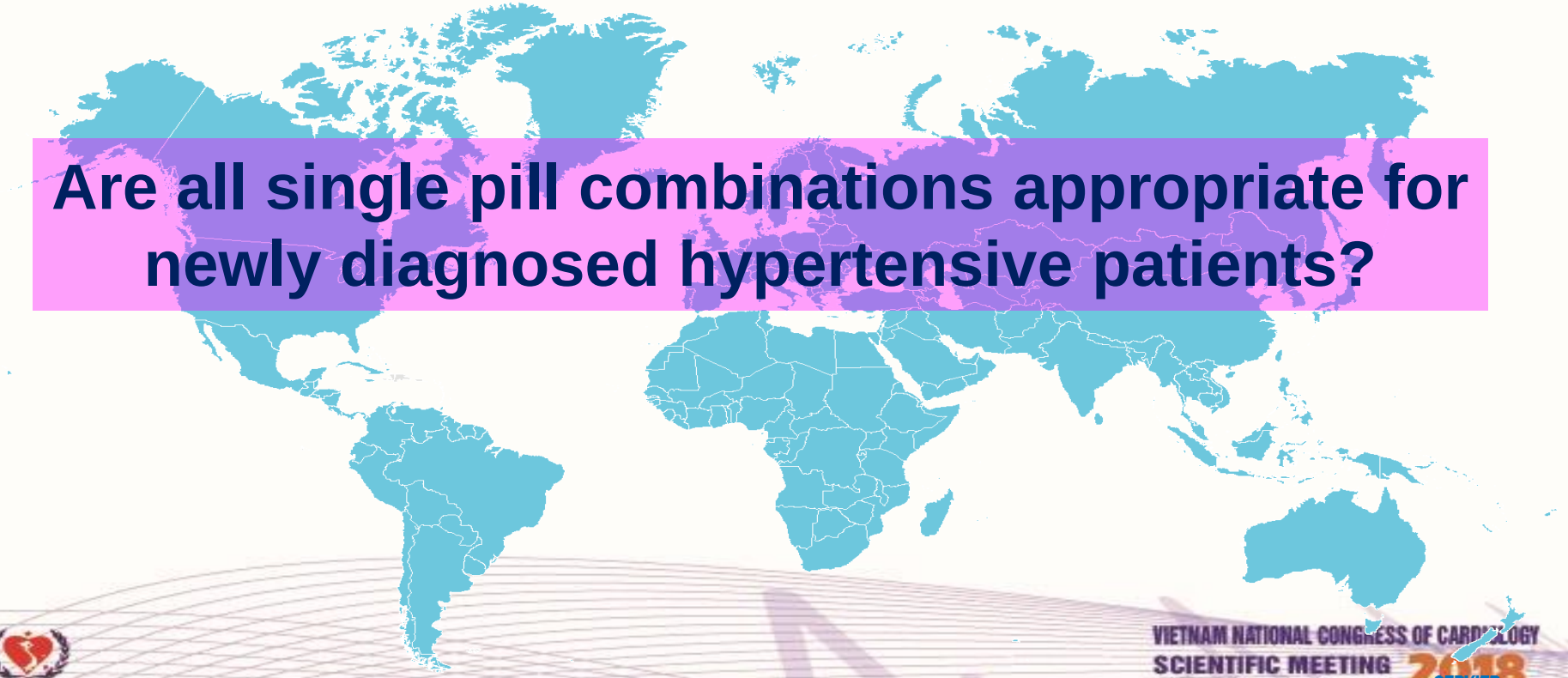
ESH AND ESC GUIDELINES

2018 ESH/ESC Guidelines for the management of arterial hypertension

COMBINATION RIGHT FROM THE START

Initial therapy: Dual combination → Next step: Triple combination

ROLE OF SINGLE PILL COMBINATION



Are all single pill combinations appropriate for newly diagnosed hypertensive patients?

Marketed SPC developped as first-line therapy

VIACORAM ®

Perindopril arginine 3.5 mg + Amlodipine besilate 2.5 mg

PRETERAX®

Perindopril 2.5 mg + Indapamide 0.625 mg

ZIAC ®, WYTENS ®, LODOZ ®

Bisoprolol 2.5 mg + Hydrochlorothiazide 6.25 mg

Low dose of ACEi (perindopril) + CCB (Amlodipine)

Low dose of ACEi (perindopril) + CCB (Amlodipine) a new antihypertensive strategy

The largest-scale development in hypertension of the past decade

A total of 3 studies

More than 6600 patients included.[1-3]

Involving 21 countries.[1-3]

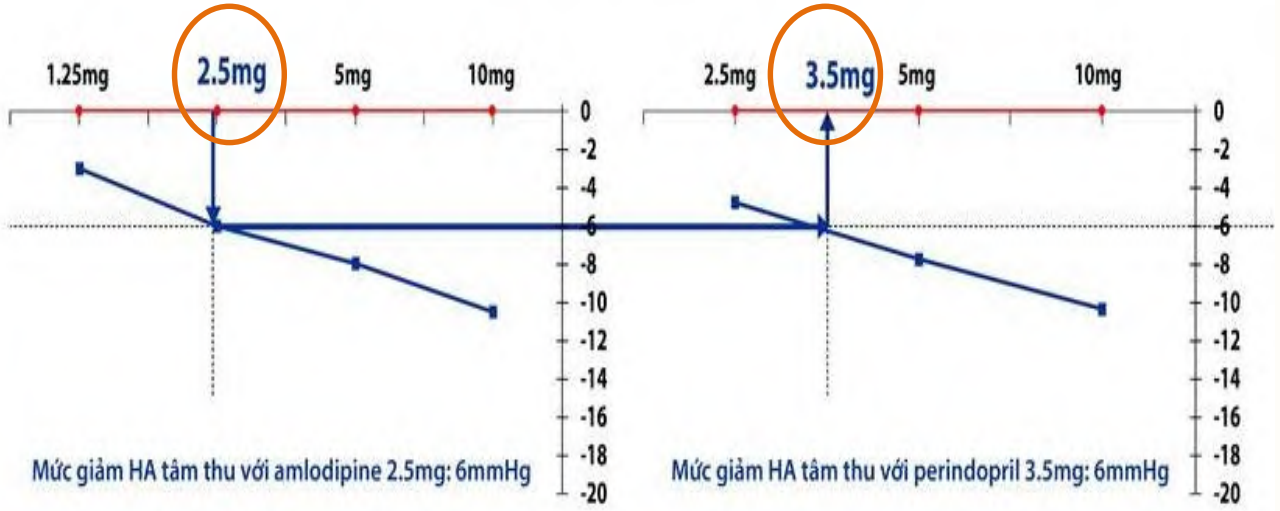
** In comparison with drugs developed for an indication in hypertension that have obtained their marketing authorization since 2004, by comparing the number of patients included in Phase 1, 2, and 3 studies.* 1. Laurent S, Parati G, Chazova I, et al. Randomized evaluation of a novel, fixed-dose combination of perindopril 3.5 mg/amlodipine 2.5 mg as a first-step treatment in hypertension. J Hypertens. 2015;33(3):653-661. 2. Mancia G, Asmar R, Amodeo C, et al. Comparison of single-pill strategies first line in hypertension: perindopril/amlodipine versus valsartan/amlodipine. J Hypertens. 2015;33(2):401-411. 3. Poulter N. A randomized, double-blind study of the efficacy and safety of new first-line perindopril/amlodipine combinations. Submitted for presentation at: 25th European Meeting on Hypertension and Cardiovascular Protection; June 12-15, 2015; Milan, Italy.

Specially designed for treatment initiation instead of monotherapy

3.5 / 2.5 (mg)

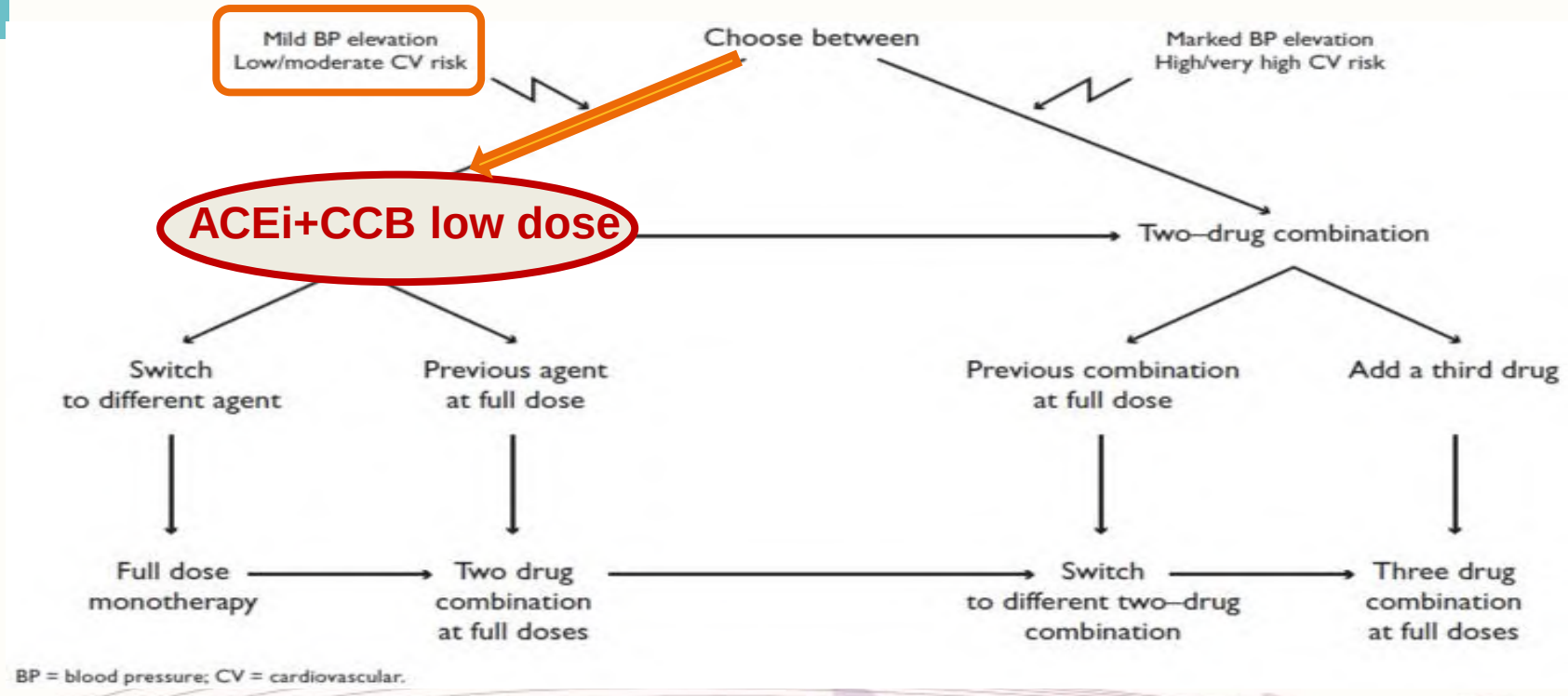
perindopril amlodipine

FIRST LINE



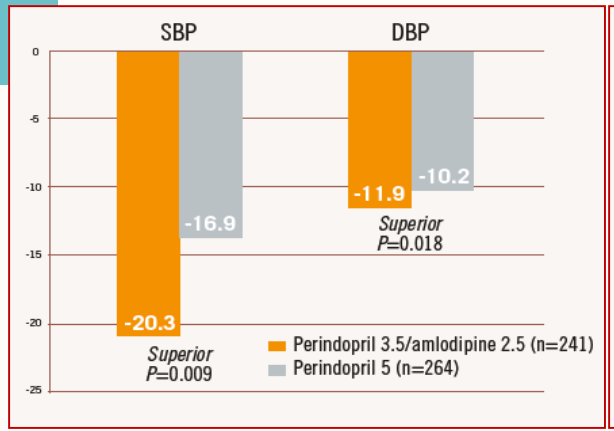
A dual mode of action right from the start

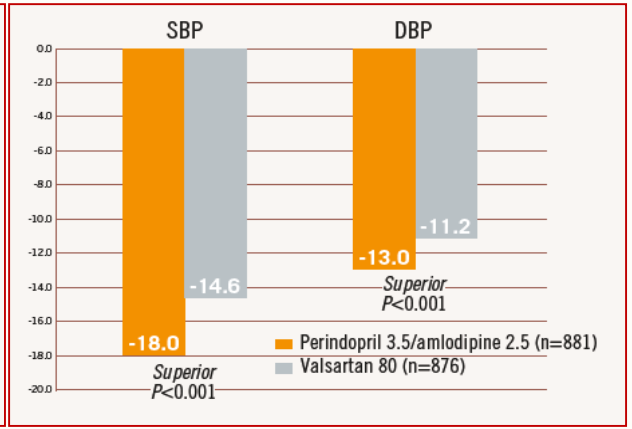
ACEi+CCB (low dose), instead of monotherapy

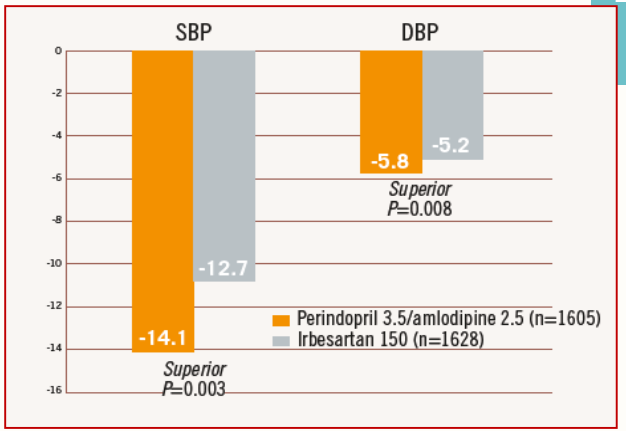


BP = blood pressure; CV = cardiovascular.

Better blood pressure-lowering efficacy and similar tolerability compared with RAAS monotherapies





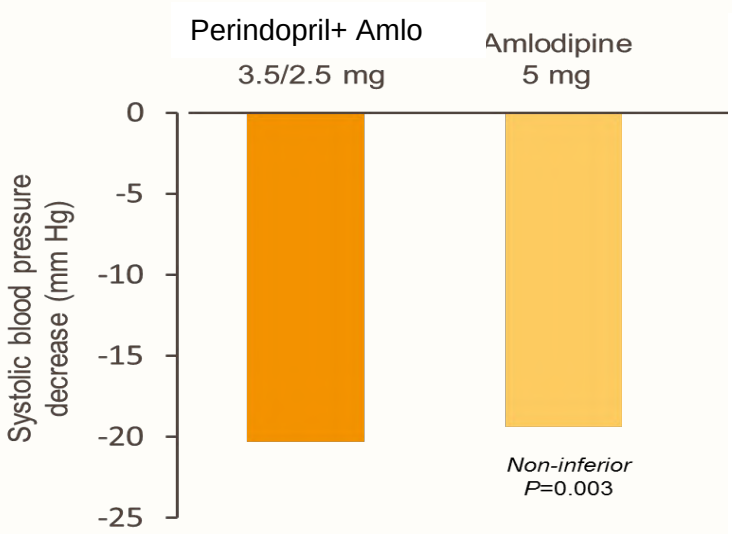


	Peri + Amlo 3.5 mg/2.5 mg n=2753	Comparator n=3072	*P*-value
EAE*	28.4%	27.2%	0.319
Severe EAE	0.8%	1.2%	0.112
Peripheral edema	2.1%	1.6%	0.165
Hypotension	-	0.1%	0.625
Headache	2.1%	3.0%	0.040
Cough	4.5%	1.0%	<0.001

1. Laurent S. *J Hypertens.* Vol 34, e-supplement 2, September 2016 – PP.26.16
Laurent S. Individual data meta-analysis in 5507 subjects of perindopril 3.5 mg/amlodipine 2.5 mg in comparison with RAS blocker monotherapies. Accepted at: 26th ESH; June 10-13, 2016; Paris, France.

Similar blood pressure-lowering efficacy with better tolerability compared to CCB

▪1. Laurent S et al. *J Hypertens*. 2015;33(3):653-662.

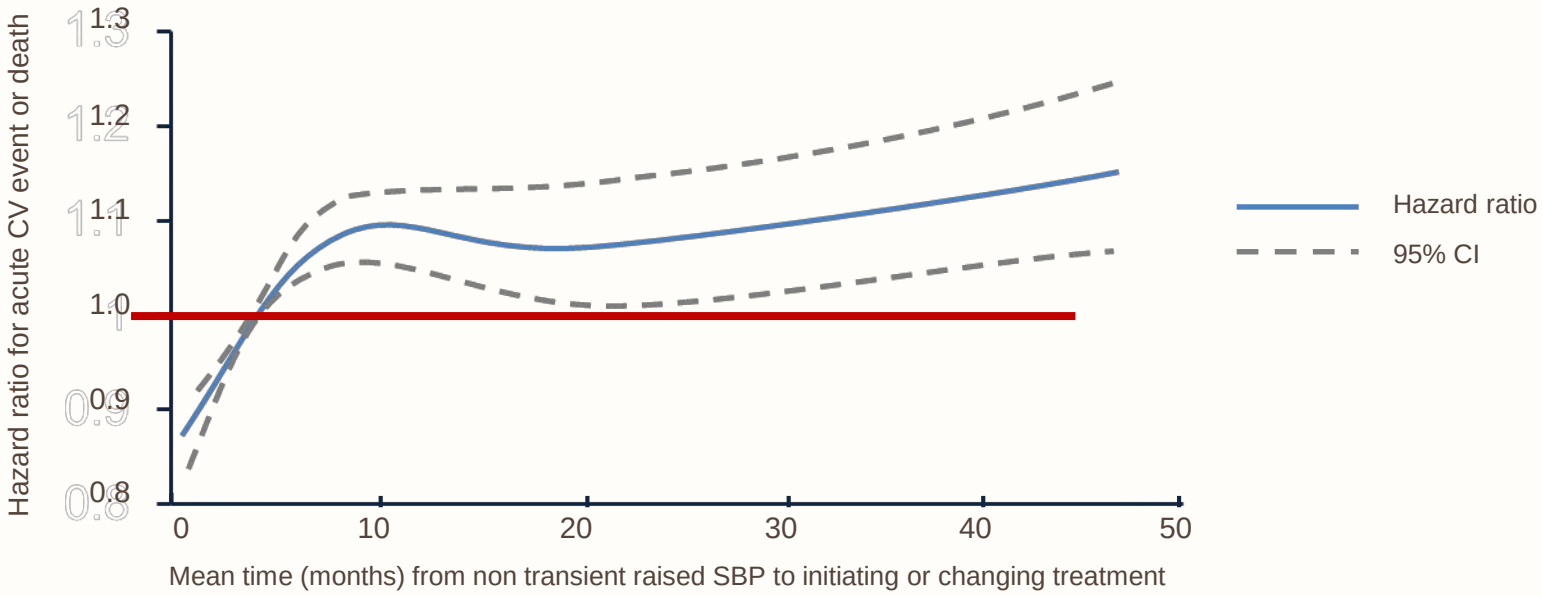


	Peri + Amlo 3.5 mg/2.5 mg n=249	Amlodipine 5 mg n=264
Any emergent adverse event n(%)	18.9%	21.6%
Edema n(%)	1.6%	4.9%*
Cough n(%)	0.8%	0.4%
Flushing n(%)	0.4%	1.9%
Hypotension n(%)	0	0

* Significant, $P<0.05$

Delaying BP control increases CV risk

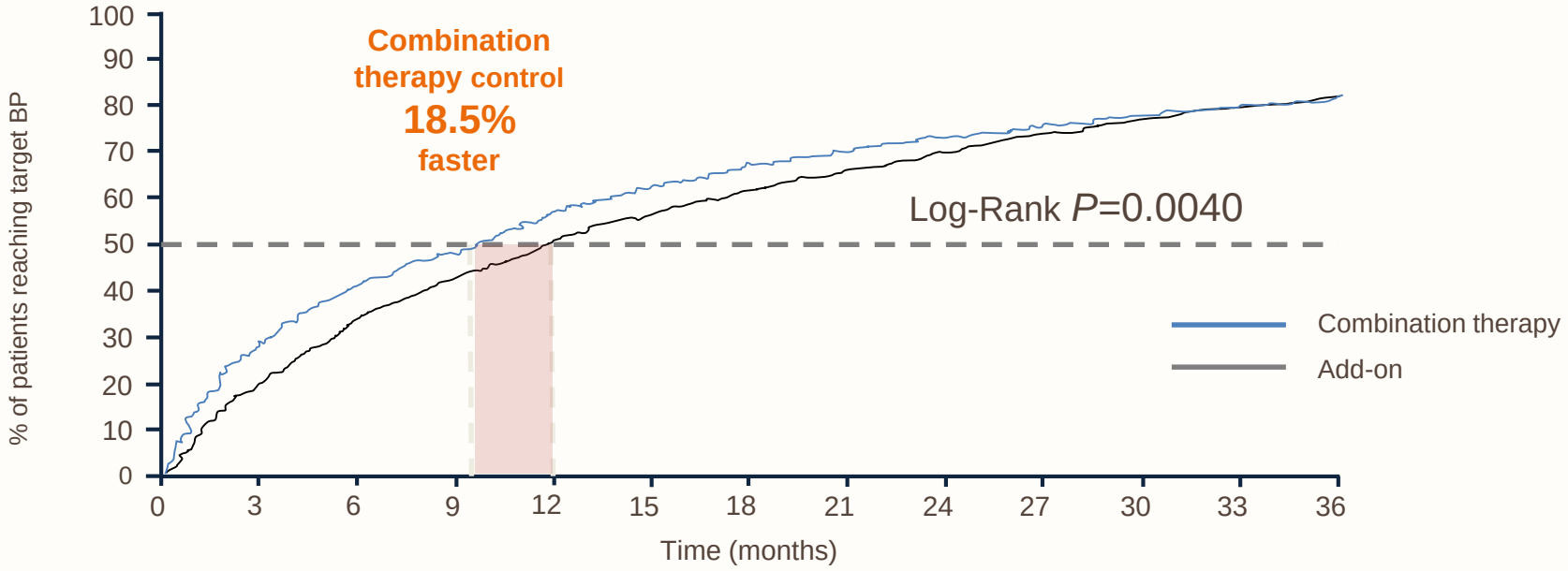
•**Delays of greater than 6 weeks,** after SBP elevation, before initiating or increasing treatment **significantly increase risk** of an acute CV event or death.



Retrospective cohort study, UK primary care practices, 1986-2010; n=88 756 adults with hypertension, >10 years follow-up

▪1. Xu W et al. *BMJ*. 2015;350:h158

Initial combination therapy controls BP faster than monotherapy…



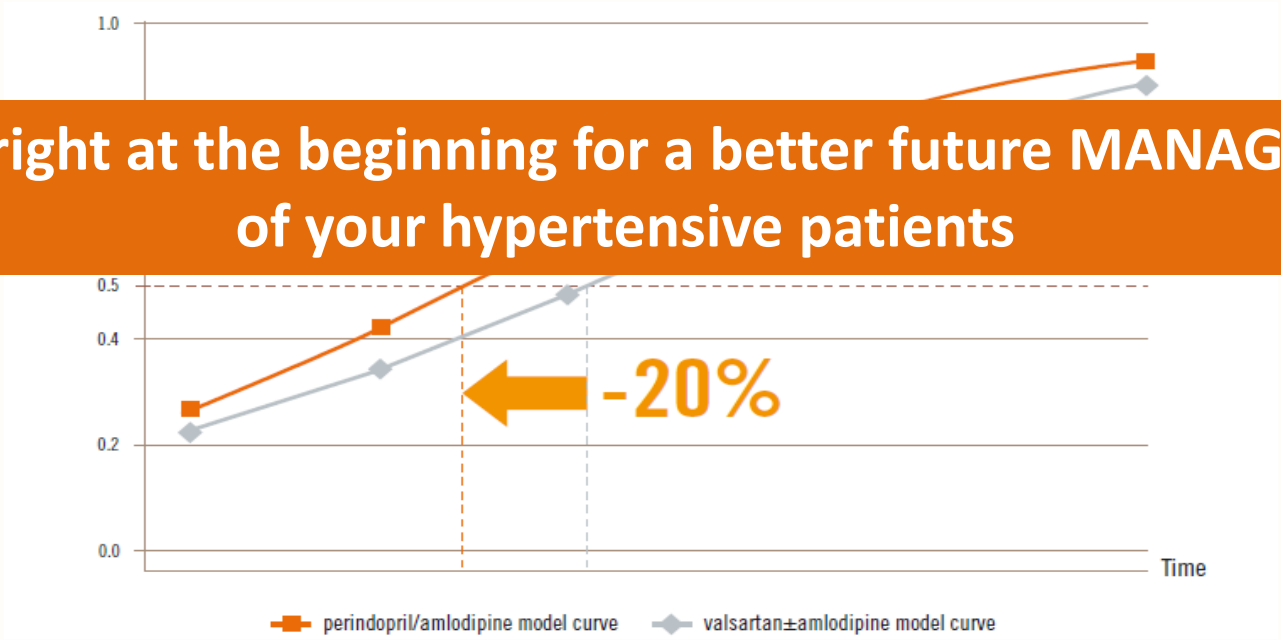
*Time to BP goal attainment was defined as the time from treatment initiation to the first of two consecutive target. BP readings (<140/90mm Hg, or <130/80 mm Hg for patients with diabetes mellitus or chronic kidney disease.

Retrospective matched cohort study; initial vs delayed treatment (median 13.5 months) with a combination n=3530; 67% grade 1, 33% grade 2, no CV events at baseline.

▪1. Gradman AH et al. *Hypertension*. 2013;61:309-318.

"Perindopril + Amlo" controls blood pressure more directly

To start right at the beginning for a better future MANAGEMENT of your hypertensive patients



Achieve blood pressure control more directly and quicker: 20% gain in time

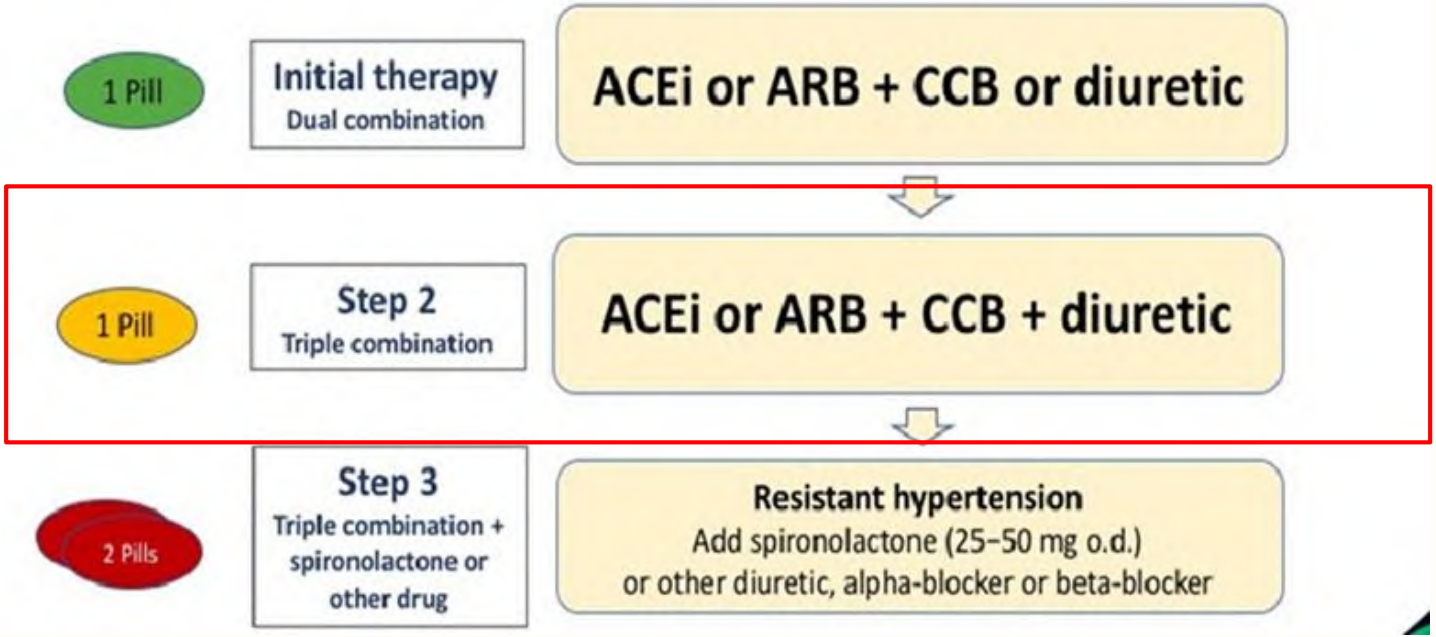
1 Mancia G et al. *J Hypertens*. 2017;35:225-233.

2018 ESH-ESC Guidelines

Initial therapy with dual combination for uncomplicated HT,

and most patients with HMOD, cerebrovascular disease, T2D or PAD.

NEW!



Initial therapy: Dual combination → Next step: Triple combination

Mono-therapy just for low risk grade 1 – very old – frailer patients

RIGHT COMPONENT

Perindopril - the BEST RAS

COVERSYL

ACEIs

ARBs

Số bệnh nhân

50.000
40.000
30.000
20.000
10.000
0
10.000
20.000
30.000

SAVE[1] post - MI
Total mortality -22%
p= 0.001
Captopril

TRACE[11] post - MI
Total mortality -22%
p= 0.001

ELITE-1
ELITE-2
OPTIMAAL
VALIANT

INVEST[12]
CAD patients
-2% CV Death + nonfatal MI + nonfatal stroke
P=_57

PEACE[13]
CAD patients
-4% CV Death + nonfatal MI + revascularization
P=_43
Trandolapril

SOLVD treatment[14]
PEP = -16% p= 0.0036

SOLVD prevention[15]
PEP = -20% p< 0.001

ANBP2[16]
Elderly hypertensives
PEP = -11% p=0.05

STOP 2[17]
Fatal stroke, fatal MI and other CV diseases
-1% P=0.89

CAMELOT[18]

CONSENSUS II[19]
Acute MI patients
+10% Death p=0.26
Enalapril

DETAIL

AIRE[20] 2006 acute MI
PEP = -27% Death p=0.002

HOPE[21]
9 541 High Risk patients
RRR In MI, stroke, CV death = -22% p<0.001

ASSK[22]

DIABHYCAR[23]
4 912 Type 2 diabetics p=0.06

DREAM[24]
5 269 patients
p=_15
Ramipril

ONTARGET

PREAMI[30] Post - MI patients
PEP (<.001)

EUROPA[6]
CAD patients
PEP (.0003)

PROGRESS[61]
PEP (<.0001)

ADVANCE[20]
Type 2 diabetic patients
PEP (.04)

ASCOT-BPLA[8]
Hypertensives
All mortality (.025)
CV mortality (.001)

COVERSYL

LIFE[62]
HT + HVG

RENAAL[63]
Add-on ACEi
Diabetic Nephropathy

OPTIMAAL[64]
Postin far clus vs cap topril

ELITE 2[65]
Heart failure vs cap topril
Losartan

Jikei Heart[66]

Val - HeFT[67]
Add-on ACEi (93%)
Heart failure

VALIANT[68]
Post-MI + HF
vs cap topril

VALUE[69]
HTA + 3RF or diabetes
vs amlodipine
Valsartan

IDNT[70]
vs amlodipine
Diabetic Nephropathy
Irbesartan

CHARM - Alternative[71]
Heart failure

CHARM - added[72]
Add-on ACEi (100%)HF

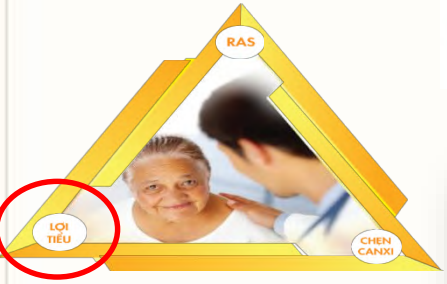
CHARM - preserved[73]
HF

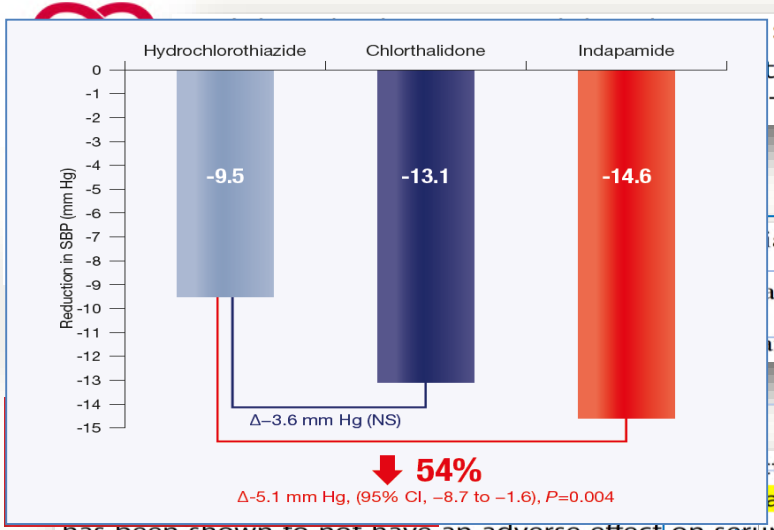
SCOPE[74]
Elderly HT vs placebo

CASE-J[75]
High-risk HT
Candesartan

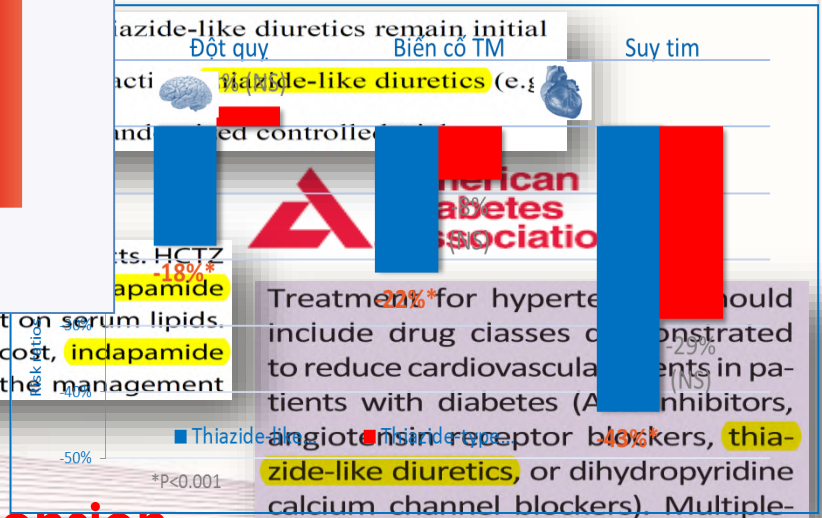
RIGHT COMPONENT

Indapamide - the BEST Diuretic





such as chlorthalidone or inda-
to conventional thiazide diure-
The statement that 'There is



iazide-like diuretics remain initial
ide-like diuretics (e.g
ed controlled
ts. HCTZ
apamide
has been shown to not have an adverse effect on serum lipids.
Due to its widespread availability, and low cost, indapamide
is considered to be the diuretic of choice in the management

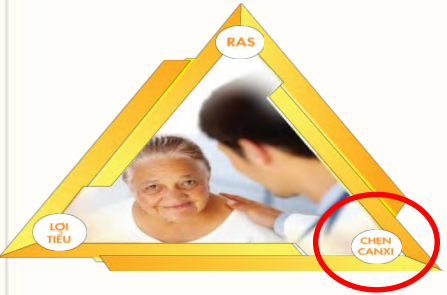
Treatment for hyperte ould
inciude drug classes c onstrated
to reduce cardiovascula ents in pa-
tients with diabetes (A nhibitors,
angiotensin receptor blockers, thia-
zide-like diuretics, or dihydropyridine
calcium channel blockers). Multiple-

INDAPAMIDE – The Diuretic for hypertension

(Superior in both BP control and CV Protection)

RIGHT COMPONENT

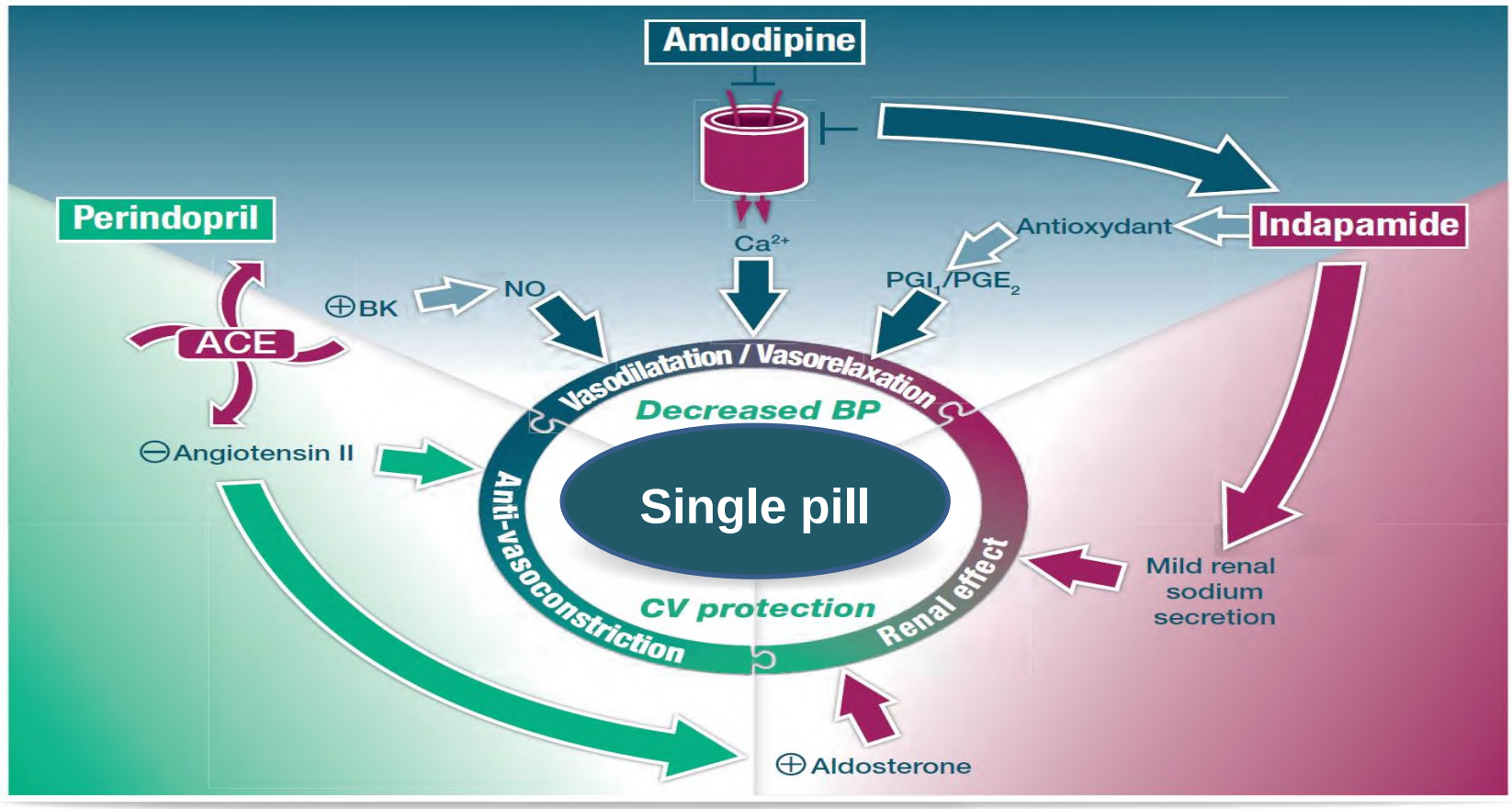
Amlodipine - the CCB has strongest evidence



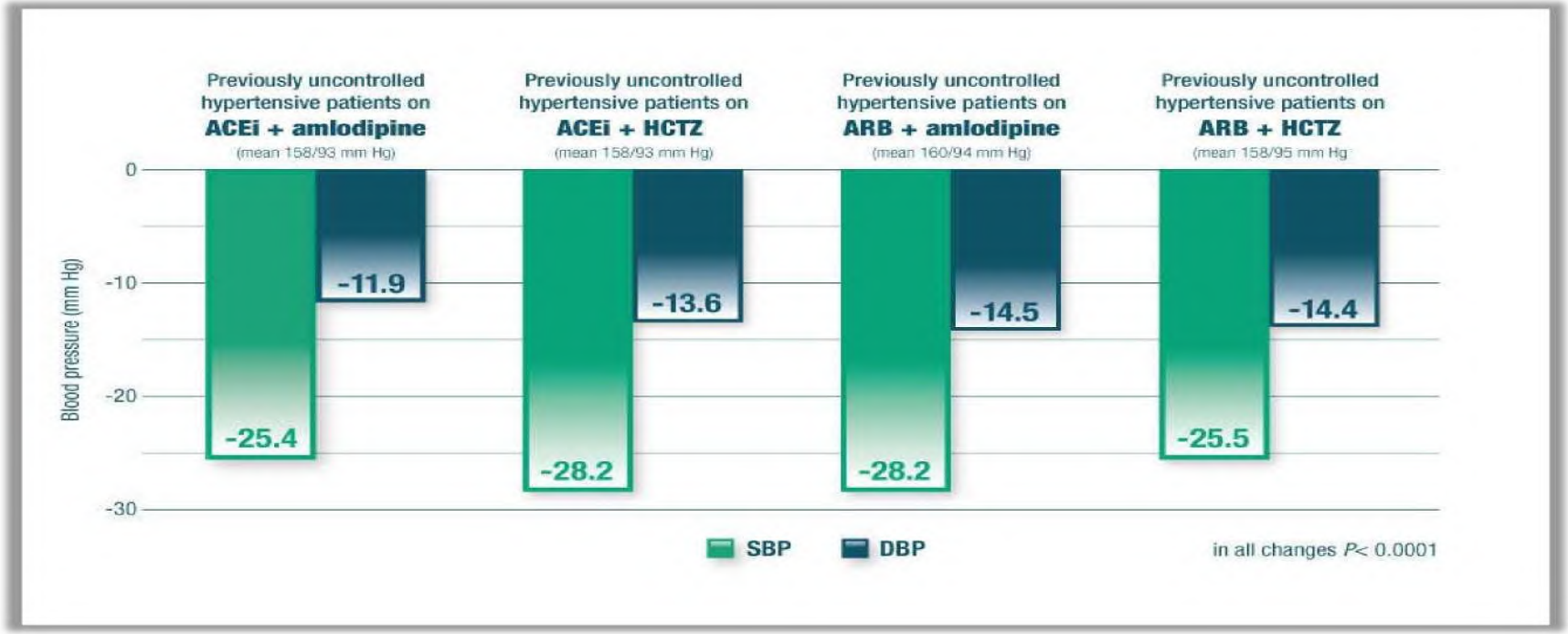
ACCOMPLISH[1] 11 506 hypertensive patients amlodipine/benazepril vs HCTZ/benazepril	Primary outcome: 20% ↓ in CV events vs. placebo 22% ↓ myocardial infarction (0.04)
ALLHAT[2] 18 102 hypertensive patients: amlodipine vs lisinopril vs chlorthalidone	Primary outcome: No difference in composite of fatal CHD + non-fatal MI vs. lisinopril 6% ↓ combined CVD 23% ↓ stroke
VALUE[3] 15 245 hypertensive patients: amlodipine +/- HCTZ vs valsartan +/- HCTZ	Primary outcome: No difference in composite of fatal CHD + non-fatal MI vs valsartan 19% ↓ myocardial infarction

1 ACCOMPLISH Investigators. *N Engl J Med.* 2008;359:2417-2428; 2 ALLHAT Research Group. *JAMA.* 2002;288:2981-2997. 3 Julius S, Kjeldsen SE, Weber M, et al. *Lancet.* 2004;363:2022-2031.

Three complementary modes of action

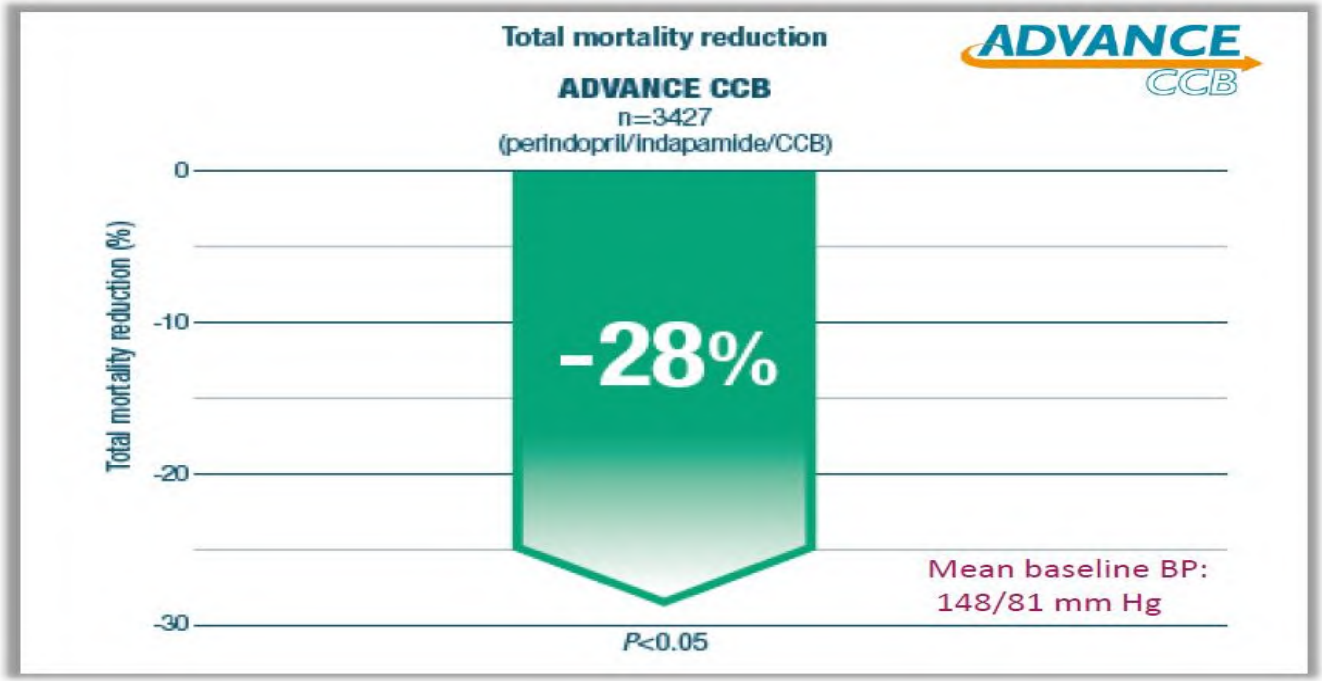


Effective regardless of the previous two-drug therapy



Toth K et al; PIANIST Investigators. *Am J CardiovascDrugs.* 2014;14:137-145.

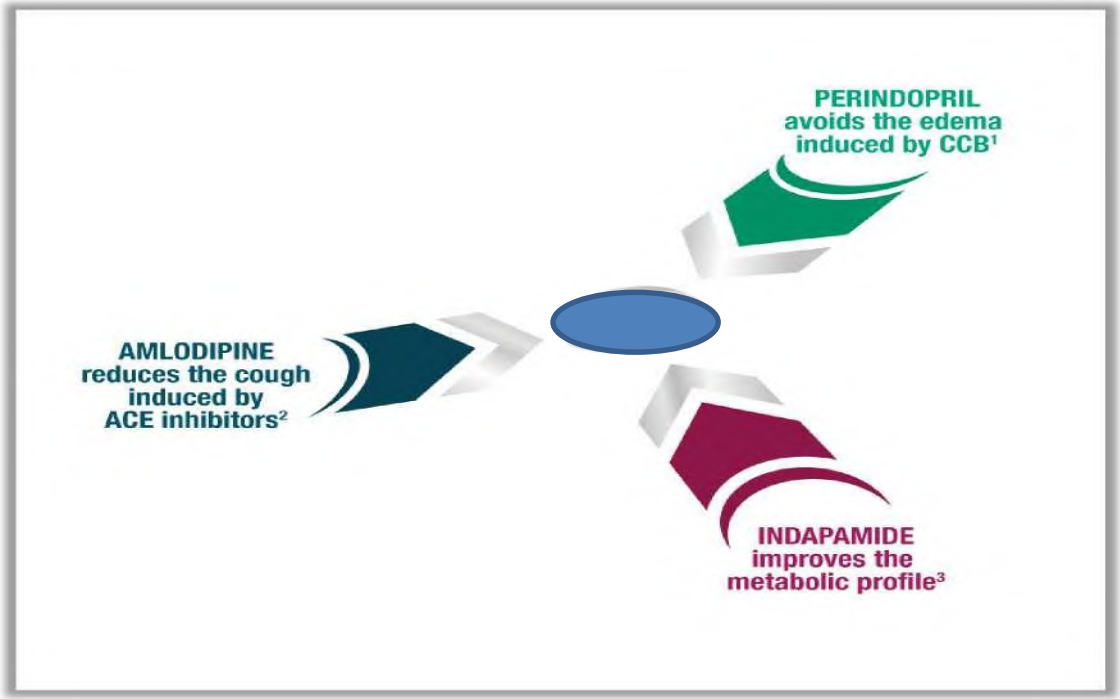
Significant lifesaving benefits with a perindopril-based triple combination



Hypertension 2014

Chalmers J et al. *Hypertension*. 2014;63:259-264.

Three complementary compounds for optimized tolerability



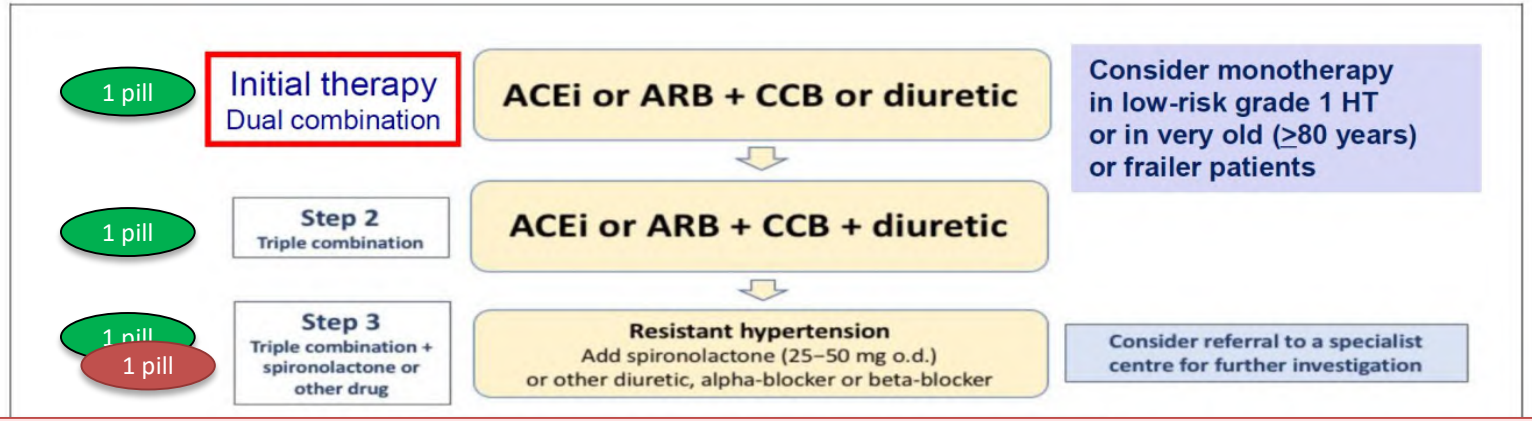
1. Makani H et al. *Am J Med.* 2011;124:128-135.
2. Fogari R et al. *Curr Ther Res Clin Exp.* 1999;60:121-128.

Kết luận

2018 ESH-ESC Guidelines

Initial therapy with dual combination for uncomplicated HT,

and most patients with HMOD, cerebrovascular disease, T2D or PAD.



Initial therapy: Dual combination → Next step: Triple combination

Mono-therapy just for low risk grade 1 – very old – frailer patients