



ОСОБЕННОСТИ ПРИМЕНЕНИЯ САРТАНОВ ПРИ СОЧЕТАНИИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ И ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

Долженко М.Н.
Кафедра кардиологии и
функциональной диагностики
НМАПО им.П.Л.Шупика



OSCAR
The Comparison of High-dose Angiotensin II Receptor Blocker (ARB) Monotherapy Versus Combination Therapy of ARB with Calcium Channel Blocker on Cardiovascular Events in Japanese Elderly High-Risk Hypertensive Patients: Olmesartan and Calcium Antagonists Randomized
Hisao Ogawa, MD, PhD, Fukuoka University, Fukuoka, Japan



NAGOYA HEART Study
Comparison between Valsartan and Amlodipine Regarding Cardiovascular Morbidity and Mortality in Hypertensive Patients with Glucose Intolerance
Toyoaki Murohara, MD, PhD, on behalf of Nagoya Heart Study Investigators, Department of Cardiology, Nagoya University School of Medicine, Nagoya, Japan



Rheos Trial
Baroreflex Activation Therapy Sustainably Lowers Blood Pressure in Patients with Resistant Hypertension: Results from the Rheos Pivotal Trial
John D. Bisognano, MD, PhD, University of Rochester Medical Center, Rochester, NY, University of Chicago, Chicago, IL

ПРОВОДИТЬ АНТИГИПЕРТЕНЗИВНОЕ ЛЕЧЕНИЕ И ВТОРИЧНУЮ ПРОФИЛАКТИКУ ЛИЦАМ БЕЗ АГ?



**VBWG US Chapter Meeting
at ACC 2011**

**Saturday, April 2, 2011
New Orleans, Louisiana**



Antihypertensive Treatment and Secondary Prevention of Cardiovascular Disease Events Among Persons Without Hypertension

A Meta-analysis

Angela M. Thompson, MSPH; Tian Hu, MS, BM; Carrie L. Eshelbrenner, MD;
Kristi Reynolds, PhD; Jiang He, MD, PhD; Lydia A. Bazzano, MD, PhD

Conclusions Among patients with clinical history of CVD but without hypertension, antihypertensive treatment was associated with decreased risk of stroke, CHF, composite CVD events, and all-cause mortality. Additional randomized trial data are necessary to assess these outcomes in patients without CVD clinical recommendations.

ЗАКЛЮЧЕНИЕ

Outcome	Relative Risk Reduction	Absolute Risk Reduction (per 1000 persons)
Stroke	-23% (RR, 0.77 [95% CI, 0.61-0.98])	-7.7 (95%CI, -15.2 to -0.3)
MI	-20% (RR, 0.80 [95% CI, 0.69-0.93])	-13.3 (95% CI, -28.4 to 1.7)
CHF events	-29% (RR, 0.71 [95% CI, 0.65-0.77])	-43.6 (95% CI, -65.2 to -22.0)
CVD events	-15% (RR, 0.85 [95% CI, 0.80-0.90])	-27.1 (95% CI, -40.3 to -13.9)
CVD Mortality	-17% (RR, 0.83 [95% CI, 0.69-0.99])	-15.4 (95% CI, -32.5 to 1.7)
All-cause Mortality	-13% (RR, 0.87 [95% CI, 0.80-0.95])	-13.7 (95% CI, -24.6 to -2.8)

Лечение АГ у пожилых 2011

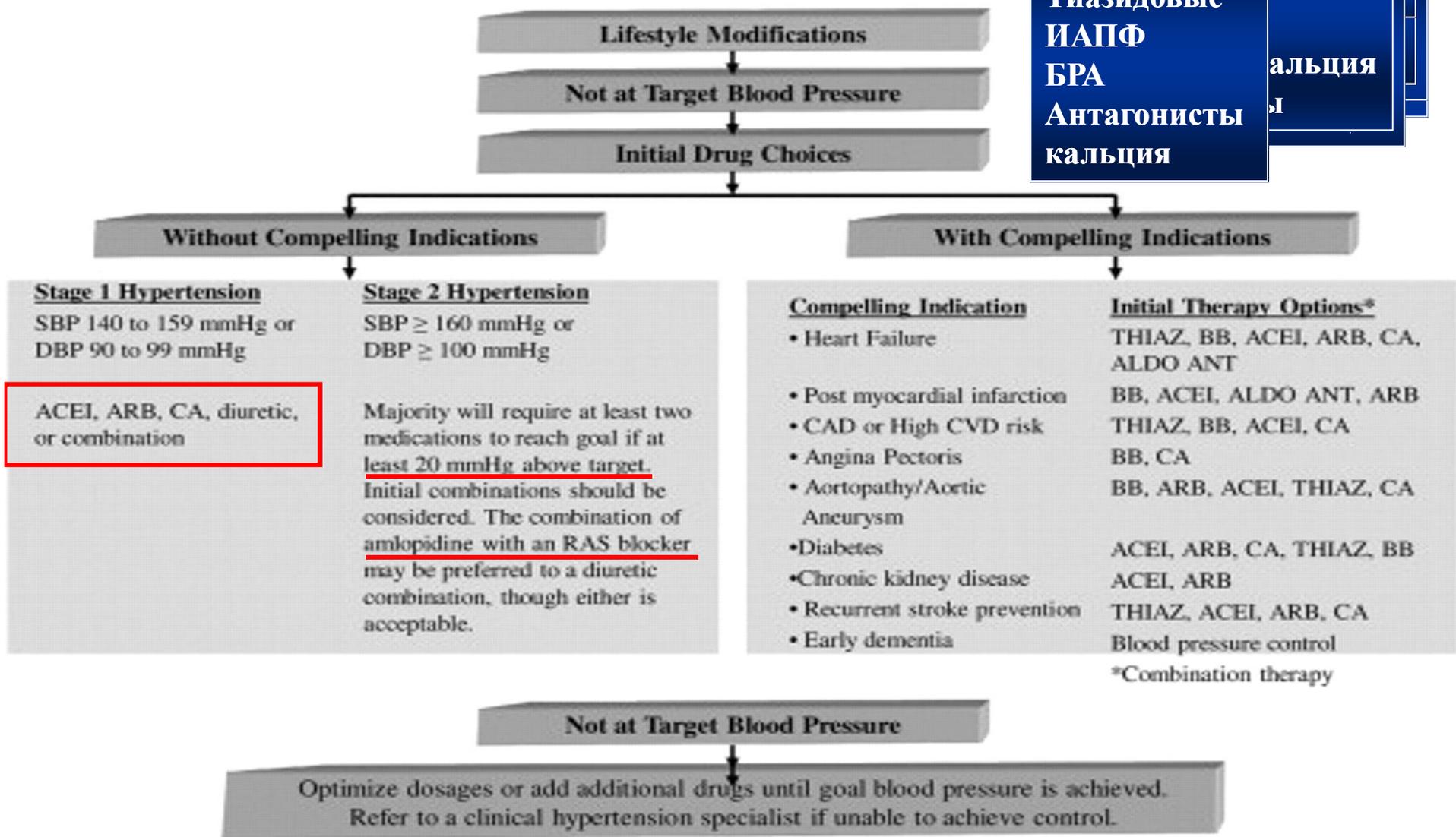


Principles of Hypertension Treatment

Target systolic blood pressure is ≤ 140 mmHg in patients aged 55 to 79
 Target systolic blood pressure is ≤ 140 mmHg in patients \geq age 80
 Achieved values < 140 mmHg for those aged ≤ 79 are appropriate, but for those aged ≥ 80 , 140 to 145 mmHg, if tolerated, can be

Тиазидовые
 ИАПФ
 БРА
 Антагонисты
 кальция

кальция



применения антигипертензивных препаратов

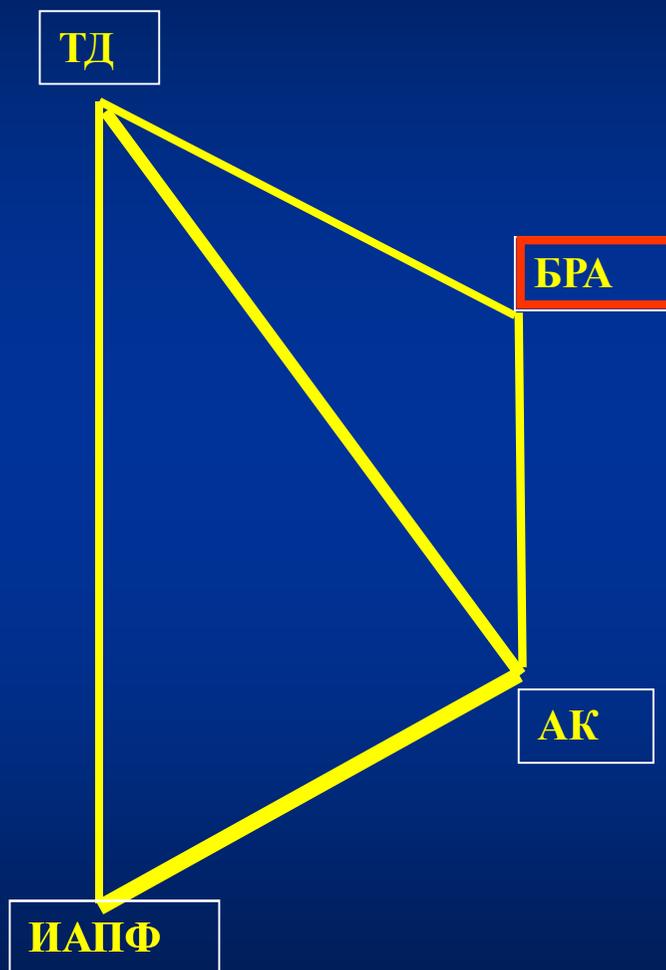
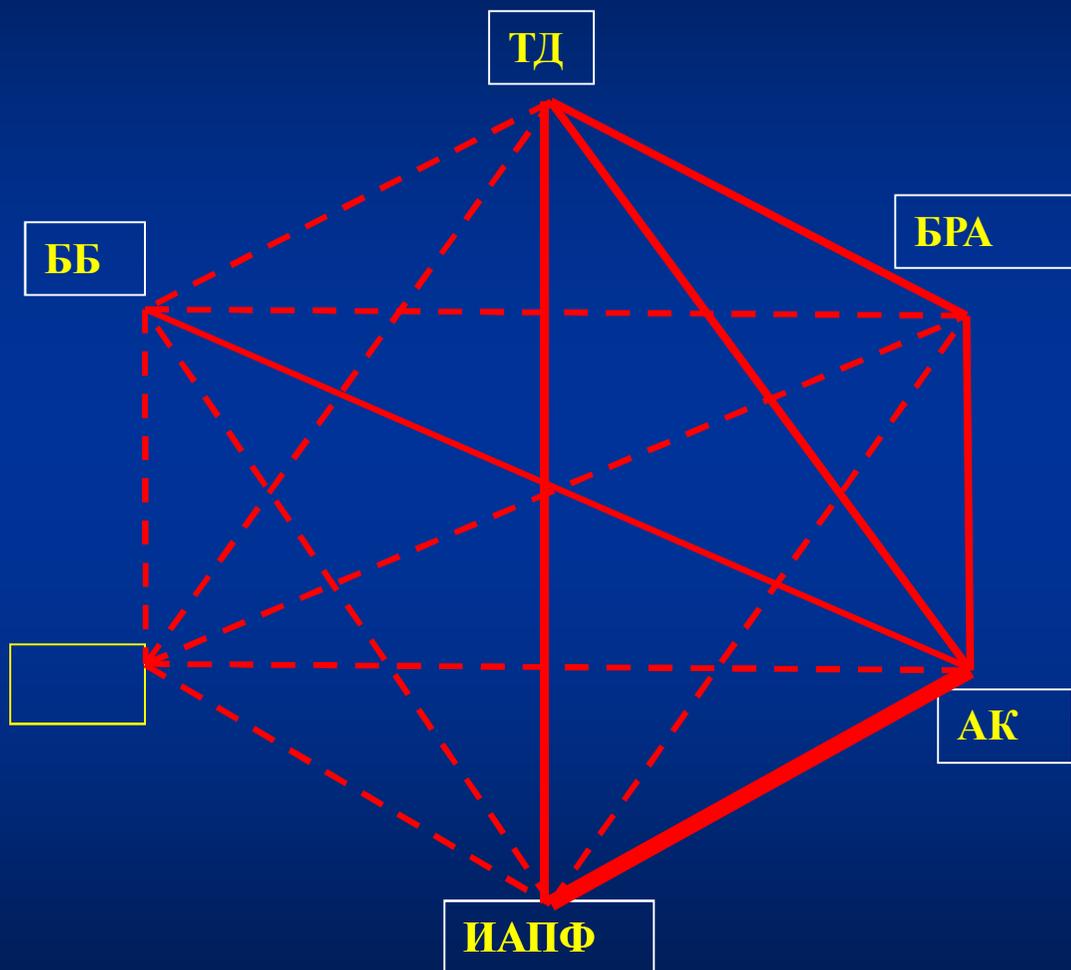


Guidelines 2007:

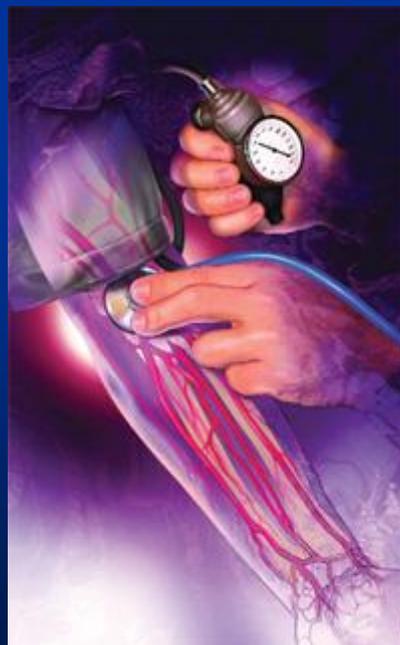
Комбинированная терапия

ESH/ESC Guidelines 2009:

Комбинированная терапия



БРА для лечения АГ



ИАПФ: Снижение АД ?

CENTRAL (The Cochrane Library 2007, Issue 1), MEDLINE (1966 to February 2007), EMBASE (1988 to February 2007) and reference lists of articles.

Анализ 44 исследований

**Анализ эффективности БРА в 9 двойных плацебо контролируемых рандомизированных исследованиях
13 451 пациентов АД 156/101 mm Hg**

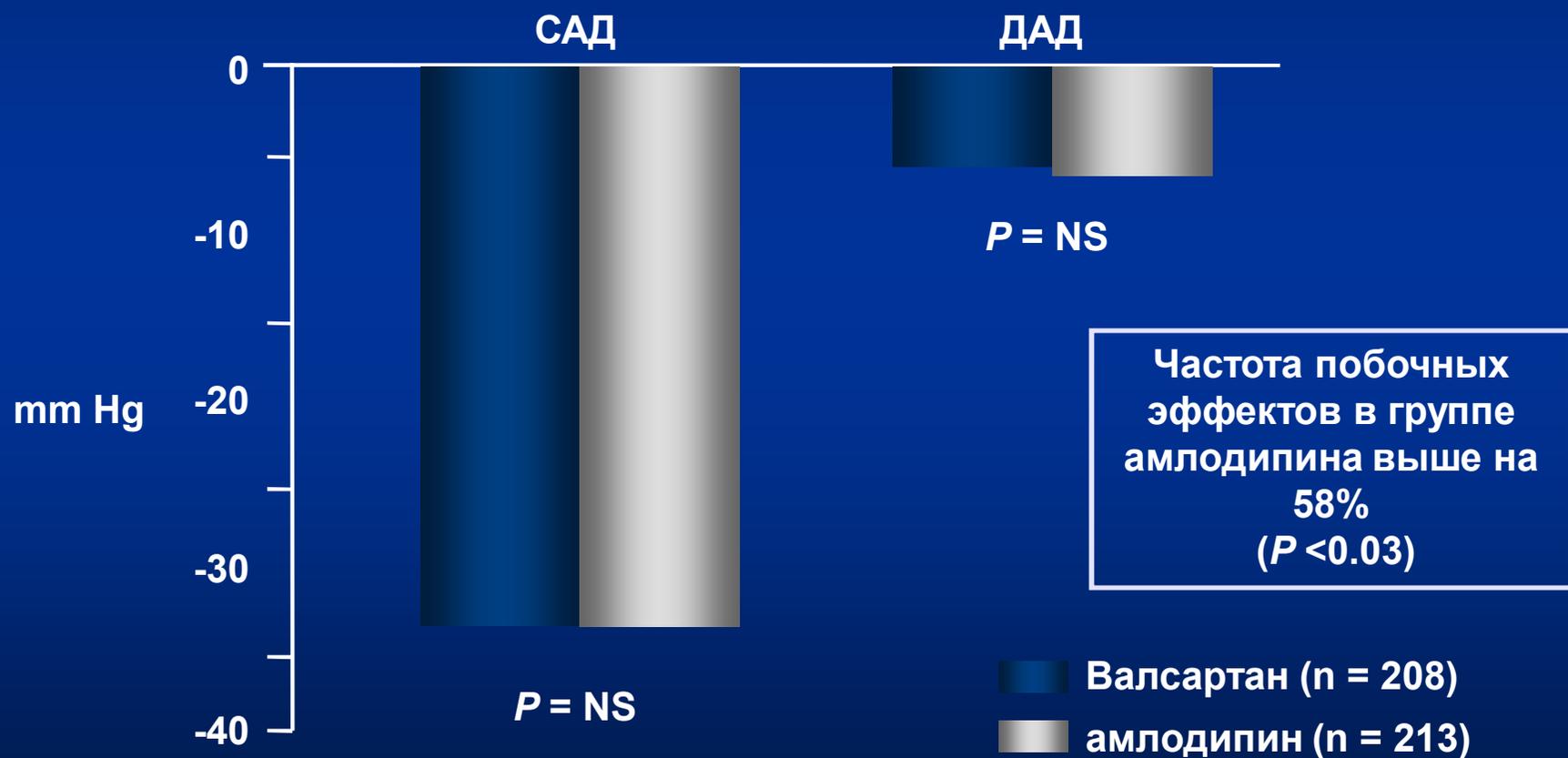
-8 mm Hg for SBP and -5 mm Hg for DBP.

ARBs reduced BP measured 1 to 12 hours after the dose by about 12/7 mm Hg.

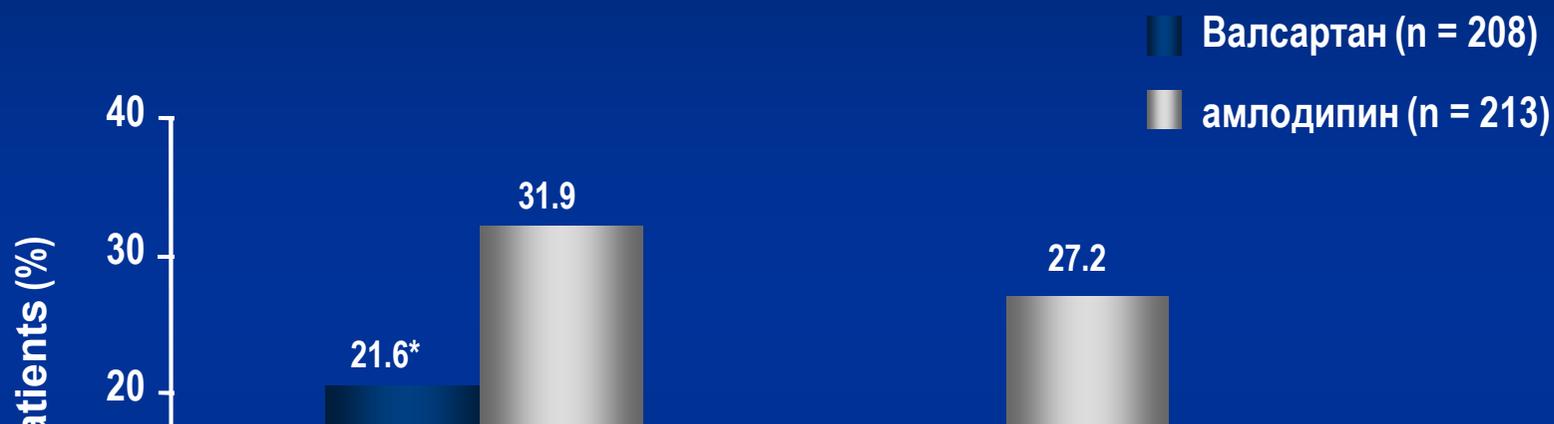
**БРА против ИАПФ: снижение АД -
одинаковое**

The Val-Syst Study

Снижение АД через 24 недели



(Val-Syst)



При одинаковом контроле САД у одинакового количества пациентов (75% и 73% соответственно) Валсартан лучше переносился, чем амлодипин

С побочными эффектами

Отеки

*P = 0.0026; †P < 0.0001.

Adapted with permission from Malacco E et al. *Am J Hypertens.* 2003;16:126A.

Valsartan Anti-hypertensive Long-term Use Evaluation

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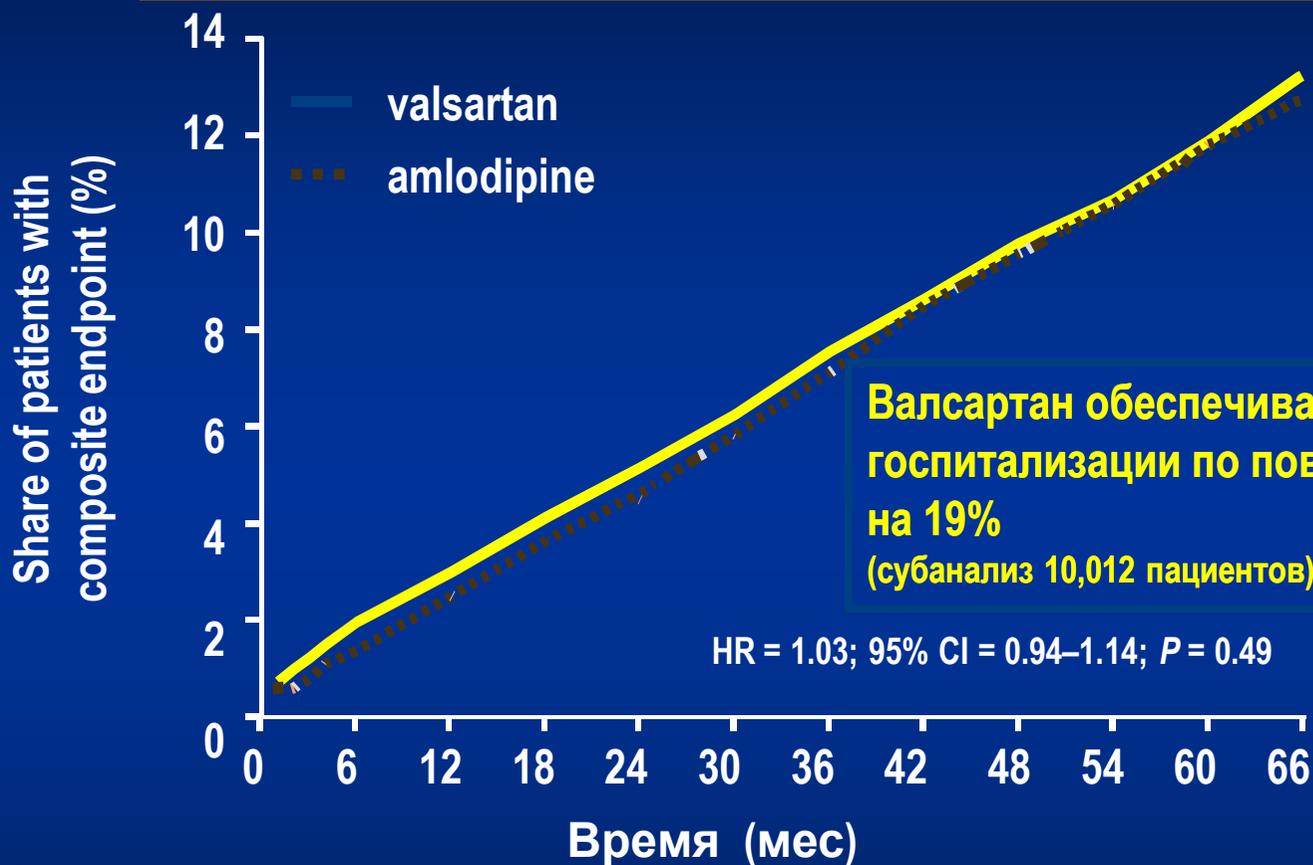
“ : 15,313 (50 , ,)

“ : (, ,)

“ (follow-up): 4.2



Риск госпитализации в первичной точке было достигнуто



Number of patients at risk

valsartan	7649	7459	7407	7250	7085	6906	6732	6536	6349	5911	3765	1474
amlodipine	7596	7469	7424	7267	7117	6955	6772	6576	6391	5959	3725	1474

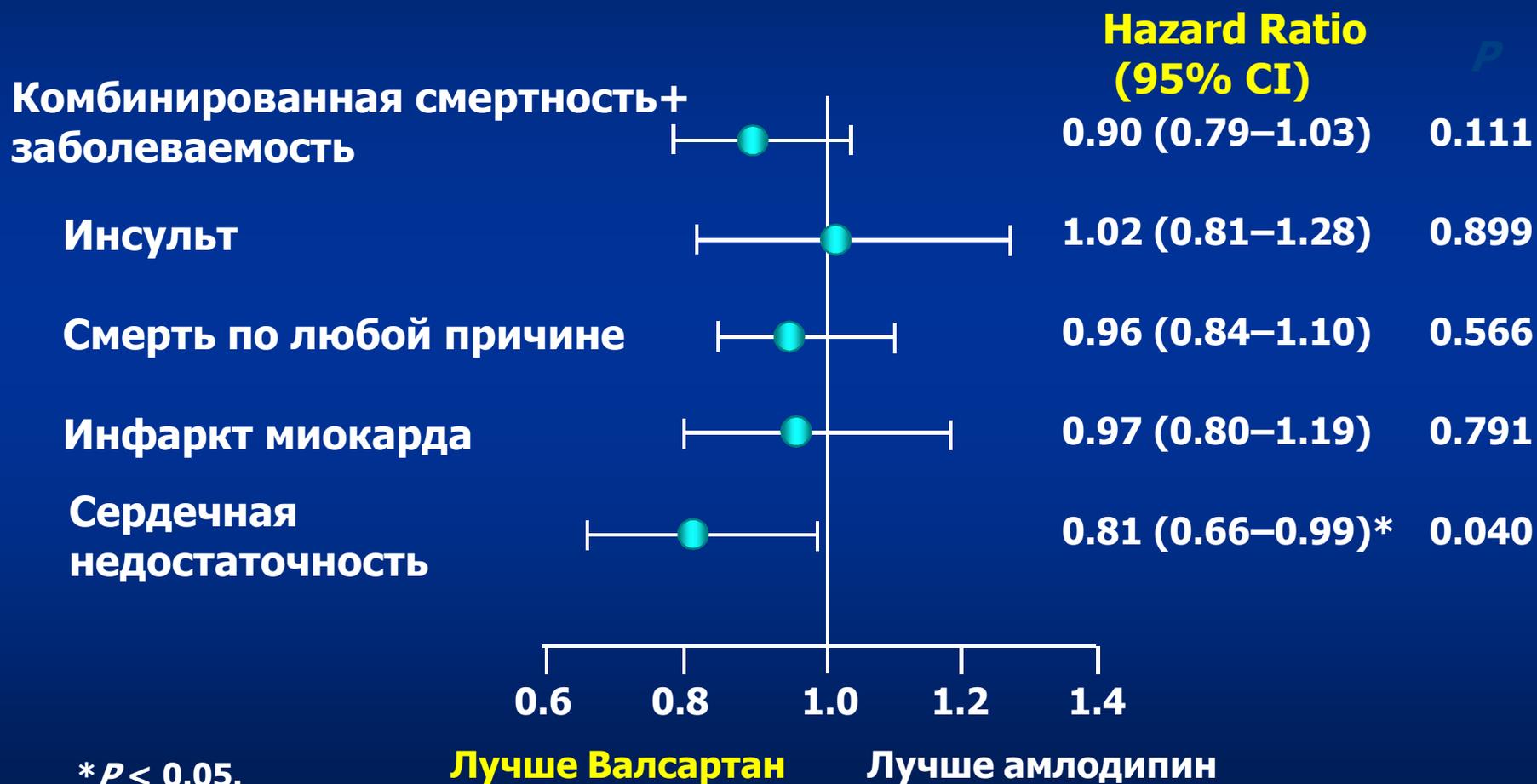


И снижал риск возникновения

новых случаев сахарного диабета на 23%



Результаты у 5006 пар больных с одинаковым контролем АД





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КАРДИОВАСКУЛЯРНЫЙ РИСК

АПФ: кардиоваскулярный риск?

61 плацебо-оконтролируемое рандомизированное исследование

MEDLINE (1966 to 2007), the Cochrane Central Register of Controlled Trials (Issue 2, 2006), and selected reference lists were searched for relevant English-language trials

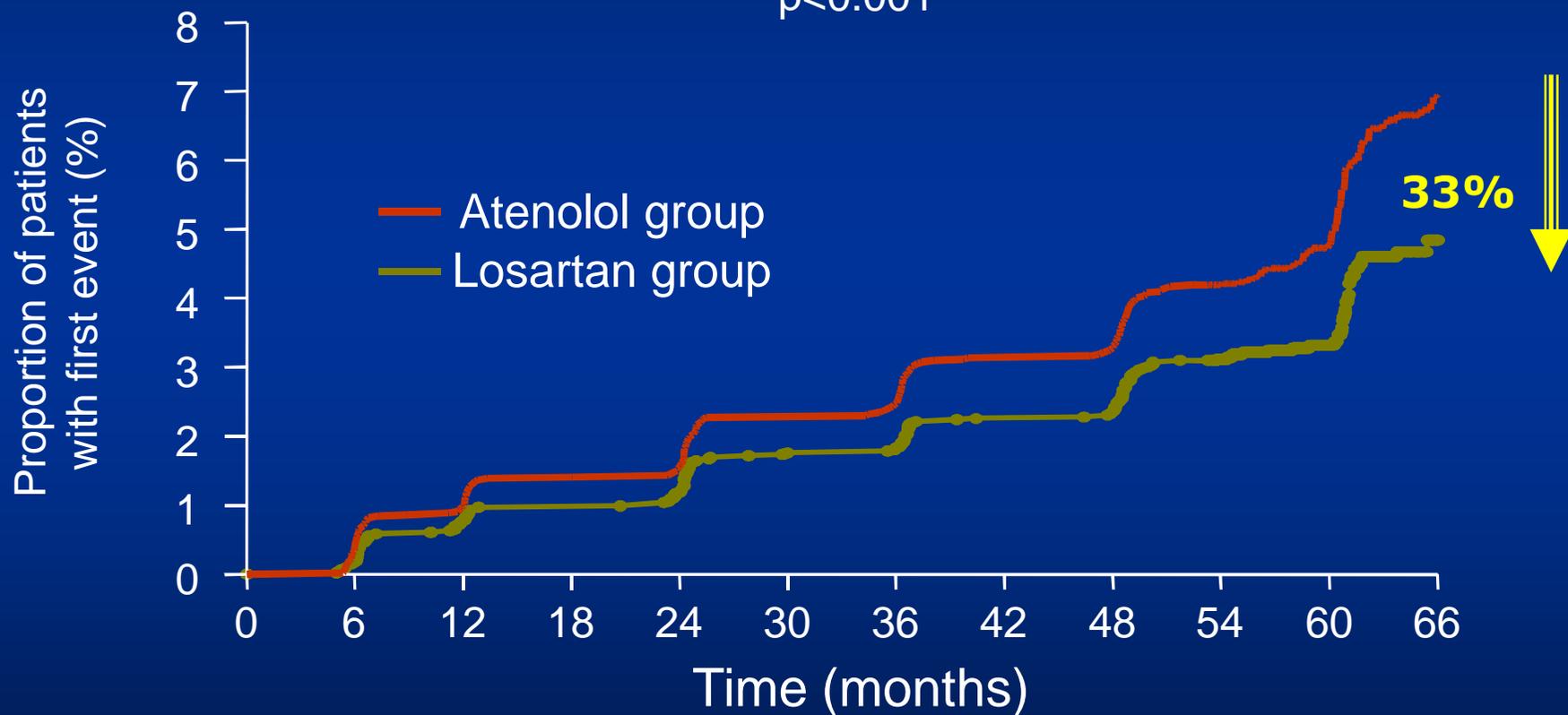
ACE inhibitors and ARBs had similar long-term effects on blood pressure (50 studies; strength of evidence, high).

**ОТСУТСТВУЕТ РАЗНИЦА В НАБЛЮДАЕМЫХ
ИСХОДАХ ВКЛЮЧАЯ СМЕРТЬ, КАРДИОВАСКУЛЯРНЫЕ
СОБЫТИЯ, КАЧЕСТВО ЖИЗНИ, УРОВЕНЬ ЛИПИДОВ,
ПРОГРЕСИРОВАНИЯ ДИАБЕТА, ГИПЕРТРОФИИ ЛЖ,
ЗАБОЛЕВАНИЯ ПОЧЕК**

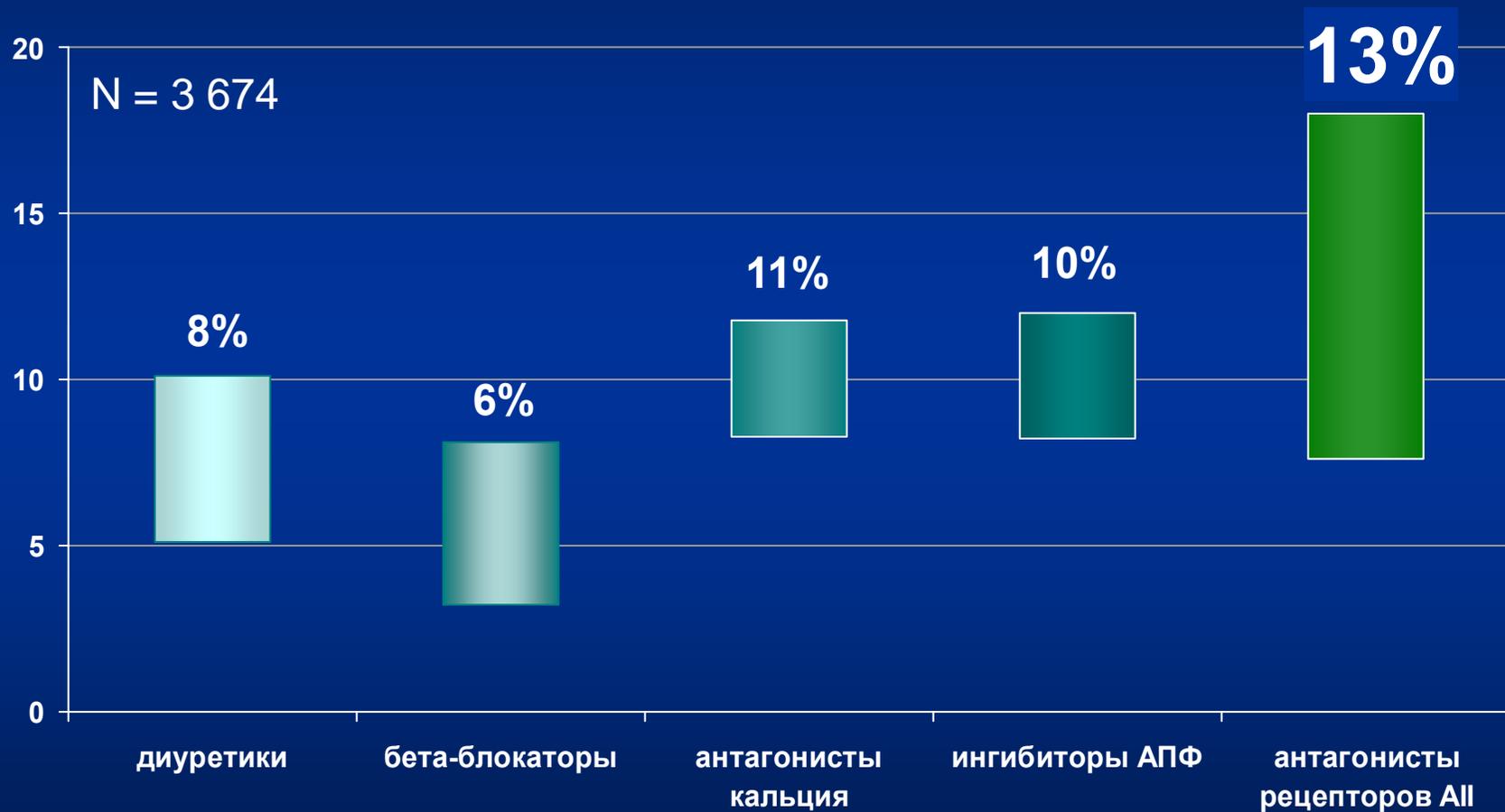
ACE inhibitors have higher rates of cough than ARB

ARBs reduce risk of AF in humans (LIFE Study)

Adjusted hazard ratio: 0.67 [95% CI: 0.55, 0.83]
p<0.001



CI = confidence interval

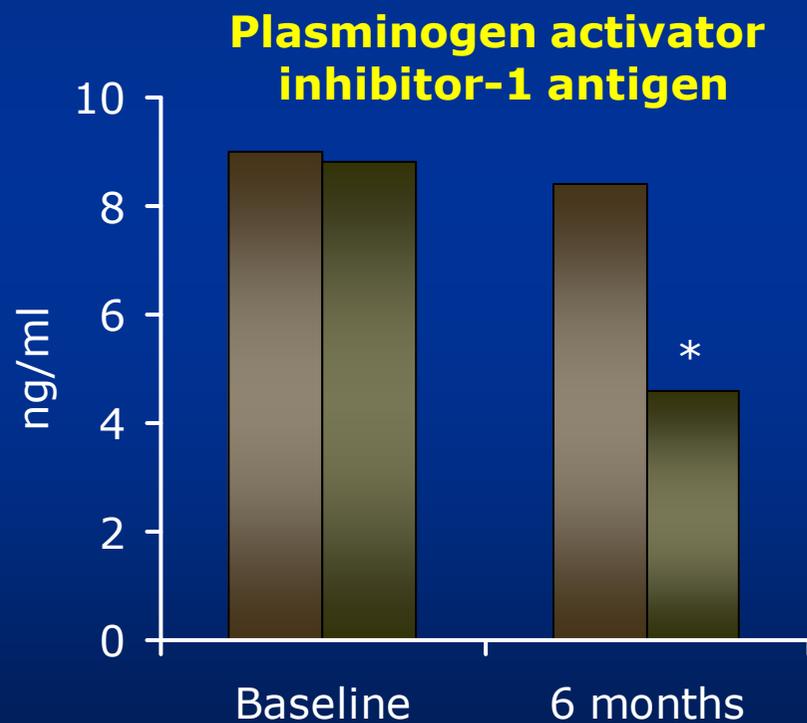
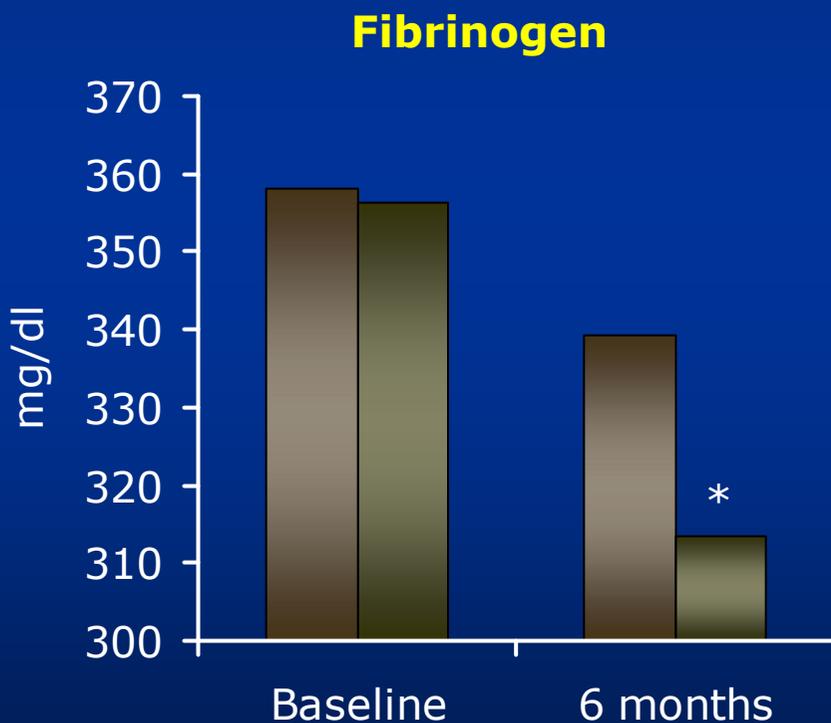


Schmidt and Schmieder; Hypertension and LVH: How much attention should we pay to the RAAS; Dialogues on Cardiovascular Medicine- Vol. 10. No1.2005; page 36

Фибриногенез и фибринолиз

БРА улучшают фибринолитические /гемолитические ВОЗМОЖНОСТИ

“ 54 hypertensive patients given irbesartan or atenolol for 6 months
 ■ Atenolol ■ Irbesartan



* p < 0.05 vs atenolol

Есть ли эффективно и безопасно применять пациентов, перенесших ИМ с подъемом сегмента ST на фоне СН и/или систолической дисфункции ЛЖ: результаты исследования VALIANT?

The effect of valsartan, captopril, or both on atherosclerotic events after acute myocardial infarction: an analysis of the Valsartan in Acute Myocardial Infarction Trial (VALIANT).

[McMurray J](#), [Solomon S](#), [Pieper K](#), [Reed S](#), [Rouleau J](#), [Velazquez E](#), [White H](#), [Howlett J](#), [Swedberg K](#), [Maggioni A](#), [Køber L](#), [Van de Werf F](#), [Califf R](#), [Pfeffer M](#).

Department of Cardiology, Western Infirmary, Glasgow, Scotland, United Kingdom. j.mcmurray@bio.gla.ac.uk

Comment in:

[J Am Coll Cardiol. 2006 Oct 3;48\(7\):1471; author reply 1471.](#)

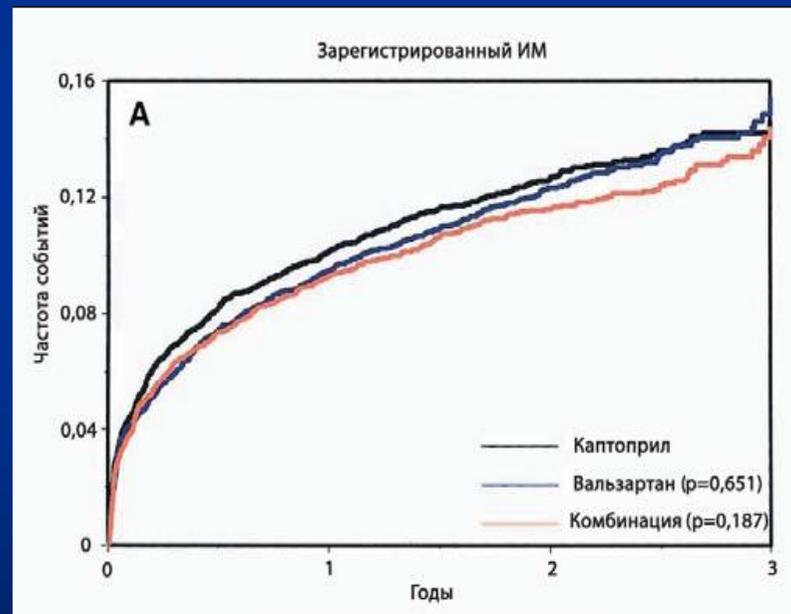
RESULTS: The number of individuals adjudicated as having a fatal or non-fatal MI in the captopril group was 559 (total investigator reported events 798), 587 (796) in the valsartan group, and 554 (756) in the combination group; valsartan versus captopril, $p = 0.651$ (0.965); combination versus captopril, $p = 0.187$ (0.350). Overall, all atherosclerotic events examined occurred at a similar frequency in the captopril and valsartan groups.

CONCLUSIONS: Angiotensin receptor blockers appear to be as effective as ACE inhibitors in reducing atherosclerotic events, even when used in addition to other secondary preventive treatments. These data, although not conclusive, also support the hypothesis that adding an ARB to an ACE inhibitor may have a small additional anti-infarction effect, a possibility that needs to be prospectively tested.

VALSARTAN (Valsartan in Acute Myocardial Infarction Trial)

12 10
(50 3
(160 2 /)
(50 3 /
80 2 /)
24,7

1,11; =0,98),
1,0 (97,5% 0,9-
- 0,98
(97,5% 0,89 1,09; =0,73).



Терапия валсартаном позволяет снизить риск смерти от любой причины на 25%

Japanese population with hypertension and cardiovascular disease (Jikei Heart Study): a randomised, open-label, blinded endpoint morbidity-mortality study

Seibu Mochizuki, Björn Dahlöf, Mitsuyuki Shimizu, Katsunori Ikewaki, Makoto Yoshikawa, Ikuo Taniguchi, Makoto Ohta, Taku Yamada, Kazuhiko Ogawa, Kiyoshi Kanae, Makoto Kawai, Shingo Seki, Fumiko Okazaki, Masayuki Taniguchi, Satoru Yoshida, Naoko Tajima, for the Jikei Heart Study group*

Lancet 2007; 369: 1431-39



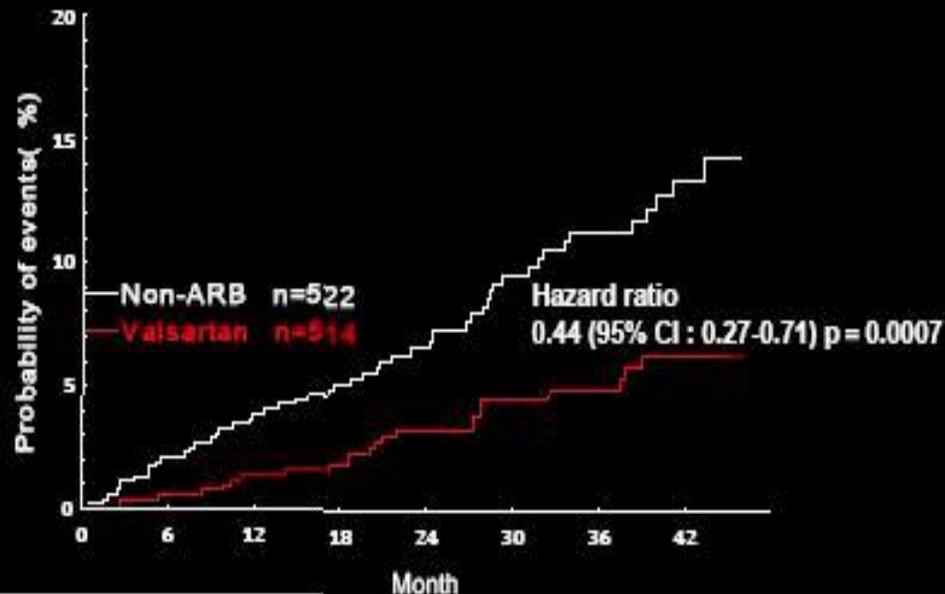
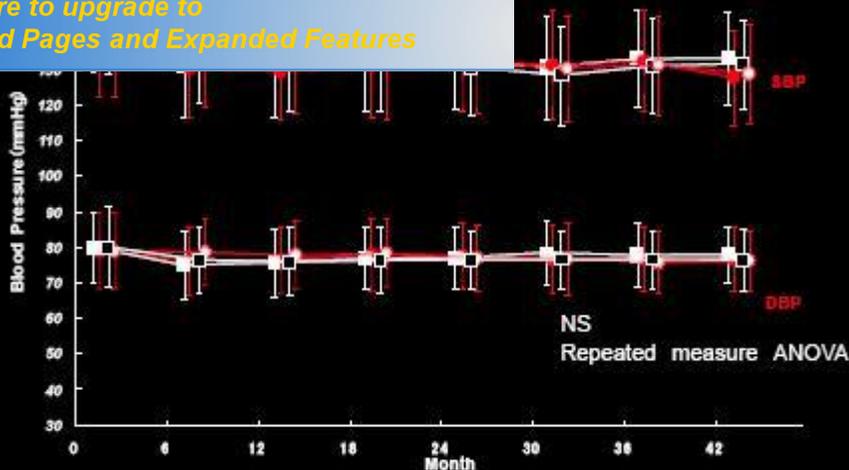
Effect of valsartan in Japanese hypertensive patients with coronary artery disease

AIM

The risk of cardiac events in hypertensive patients with coronary artery disease (CAD) was higher than in those without CAD. We here report the result of a sub-analysis of a large-scale trial [JIKEI HEART Study (JHS)] which demonstrated that the addition of the angiotensin II receptor blocker (ARB) valsartan to standard cardiovascular treatments significantly reduced the primary composite endpoint of cardiovascular complications as compared with conventional treatments without ARB in Japanese patients.

Interpretation The addition of valsartan to conventional treatment prevented more cardiovascular events than supplementary conventional treatment. These benefits cannot be entirely explained by a difference in blood pressure control.

Blood pressures



EndPoint	Valsartan n=514	Non-ARB n=522	Hazard ratio (95% CI)	p
Cardiac events	28 5.5%	65 13%	0.44 (0.28 - 0.67)	0.0001
Fatal and nonfatal Coronary event	23 4.5%	53 10%	0.44 (0.27 - 0.71)	0.0007
Acute myocardial infarction	11 2.1%	10 1.9%	1.12 (0.48 - 2.61)	0.7878
Angina Pectoris	12 2.3%	43 8.2%	0.28 (0.16 - 0.63)	0.0001
Heart failure	6 1.0%	16 3.1%	0.32 (0.12 - 0.88)	0.0240
Cardio vascular death	3 0.6%	6 1.1%	0.78 (0.17 - 3.39)	0.7208
All cause mortality	12 2.3%	11 2.1%	1.11 (0.48 - 2.49)	0.8038

Cardiac events: Angina pectoris, Acute myocardial infarction, Heart failure
 Fatal and nonfatal Coronary event: Angina pectoris, Acute myocardial infarction

Conclusion

Представленное исследование доказывает, что БРА Валсартан значительно уменьшает случаи стенокардии и ХСН у пациентов высокого кардиоваскулярного риска

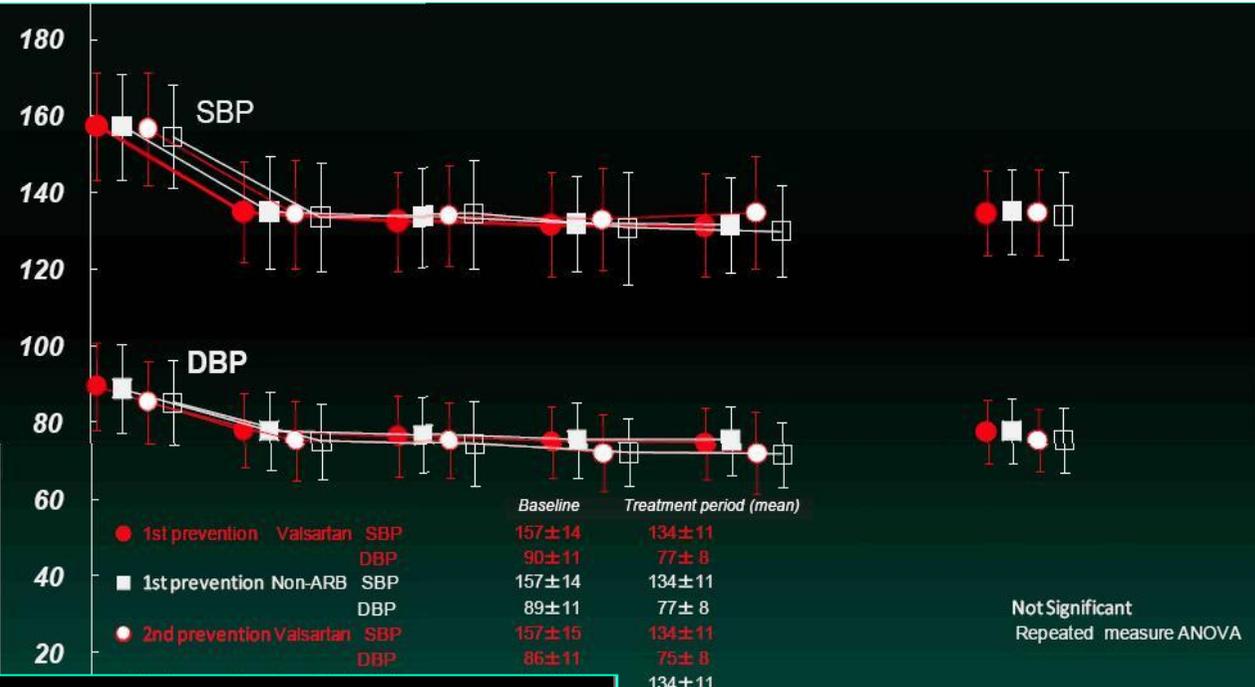


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rtan on
with high-
analyses

risk hypertension, updated primary analyses



Not Significant Repeated measure ANOVA

EndPoint	Prevention		Hazard ratio (95%CI)	p
	1st	2nd		
Primary endpoint	32 3.0%	52 11.5%	0.44 (0.29 - 0.68)	0.0002
Acute myocardial infarction	3 0.3%	4 0.4%	0.74 (0.17 - 3.30)	0.6931
Angina Pectoris	8 0.8%	14 3.1%	0.53 (0.22 - 1.25)	0.1483
Heart failure	2 0.2%	11 2.4%	0.39 (0.08 - 2.03)	0.2659
Stroke	14 1.3%	11 2.4%	0.45 (0.24 - 0.86)	0.0152
Dissecting aneurysm of aorta	2 0.2%	1 0.2%	0.49 (0.09 - 2.69)	0.4141
Lower limb arterial obstruction	1 0.1%	10 2.2%	0.25 (0.03 - 2.20)	0.2103
Transition to dialysis or doubling serum creatinine level	3 0.3%	3 0.7%	0.32 (0.09 - 1.20)	0.0912
All cause mortality	9 1.2%	13 0.7%	0.61 (0.15 - 2.56)	0.5033
Cardio vascular death	3 0.5%	5 1.1%	0.73 (0.31 - 1.73)	0.4730

48 month Mean of treatment period

Cardiovascular events: Angina pectoris, Acute myocardial infarction, Heart failure

11.0%

TIA SAH Bleeding Infarction* Total



● Valsartan was more effective for both primary prevention (3.0% vs 6.7%) and secondary prevention (11.5% vs

Валсартан более эффективен для первичной и вторичной профилактики инсульта

● Комбинация валсартана +БКК показывает более выраженное снижение первичной КТ, чем без валсартана

● Предупреждение инсульта с помощью валсартана более эффективно снижает частоту церебральных инфарктов без усиления кровотечения

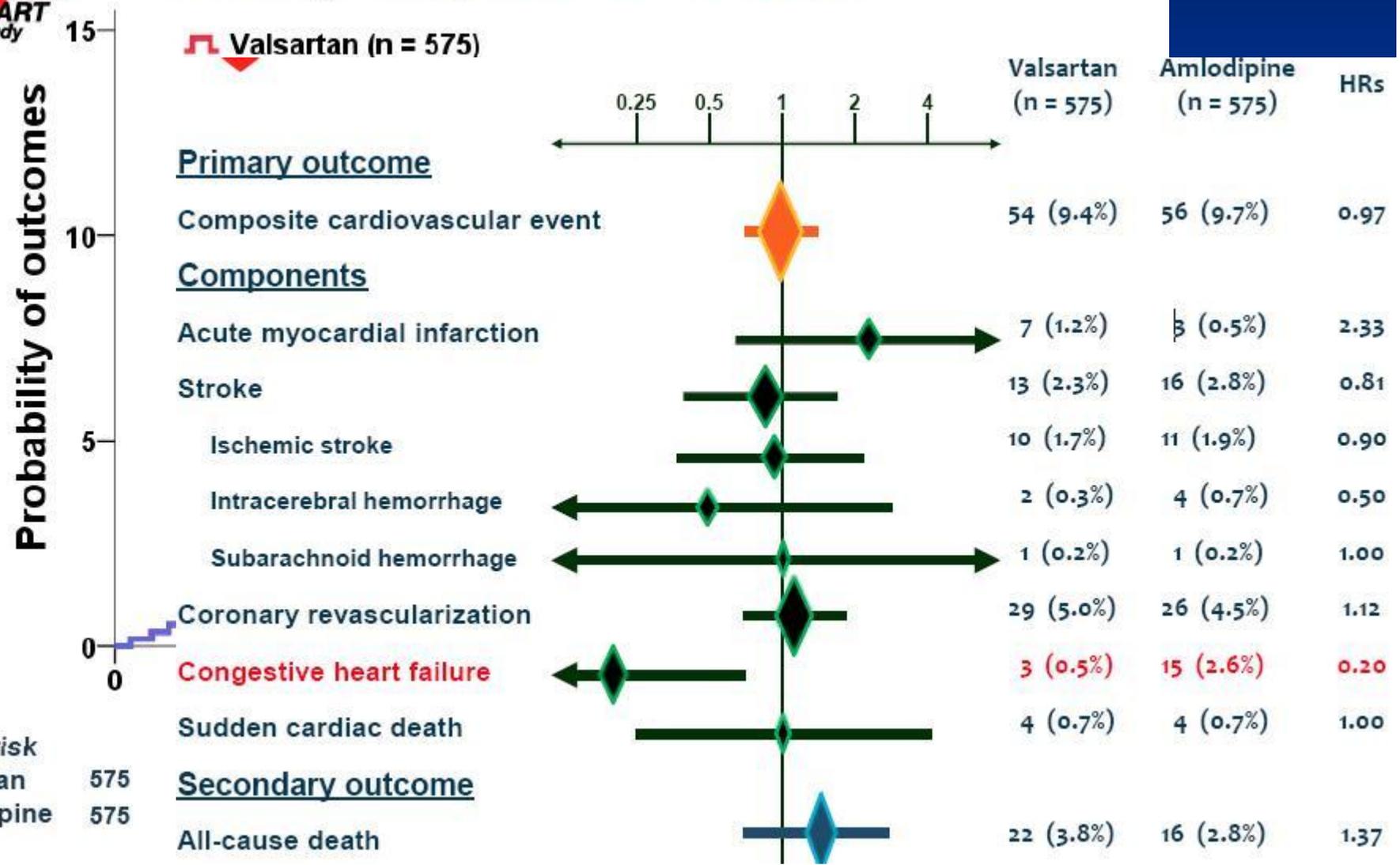
● Валсартан значительно эффективен для предупреждения стенокардии напряжения, но не для нестабильной стенокардии

ПОКАТЕЛОРОВ РАС У ПАЦИЕНТОВ С АГ+СД 2 ТИП

	NC7 2003	ADA 2004	ESC-ESH 2007	JSH 2009			
ACEIs	⊙	⊙	⊙	⊙			
ARBs	⊙	⊙	⊙	⊙			
CCBs	Trials	n	DM	Control	CV outcomes	HRs	(95% CIs)
β-blockers	LIFE DM-subgroup (2001)	1195	100%	BB	Composite	0.76	(0.6-0.98)
					CV death	0.63	(0.4-0.95)
					Acute MI	0.83	(0.6-1.3)
					Stroke	0.79	(0.6-1.1)
α-blockers	IDNT CV outcomes-analysis (2003)	1146	100%	CCB	Composite	0.90	(0.7-1.1)
					CV death	1.36	(0.9-2.1)
					Acute MI	1.54	(0.97-2.5)
					PCI/CABG	0.93	(0.6-1.6)
					Heart Failure	0.65	(0.5-0.9)
Diuretics					Stroke	1.55	(0.8-2.9)
	VALUE (2004)	15245	34%	CCB	Composite	1.04	(0.9-1.2)
					CV death	1.01	(0.9-1.2)
					Acute MI	1.20	(1.0-1.4)
					Heart Failure	0.89	(0.8-1.03)
	CASE-J (2008)	4728	43%	CCB	Composite	1.01	(0.8-1.3)
					Sudden death	0.73	(0.3-1.6)
					Acute MI	0.95	(0.5-1.8)
					Stroke	1.28	(0.9-1.9)
					Angina	0.57	(0.2-1.4)
				Heart Failure	1.25	(0.7-2.4)	



Comparison between valsartan and amlodipine regarding cardiovascular morbidity and mortality in hypertensive patients with glucose intolerance: Primary composite CV outcome



No. at risk
 Valsartan 575
 Amlodipine 575

СЛУЖБА ВАЛСАРТАНОМ И АМЛОДИПИНОМ В УМЕНЬШЕНИИ РИСКА СЕРДЕЧНО-СОСУДИСТОЙ ЗАБОЛЕВАЕМОСТИ И СМЕРТНОСТИ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ

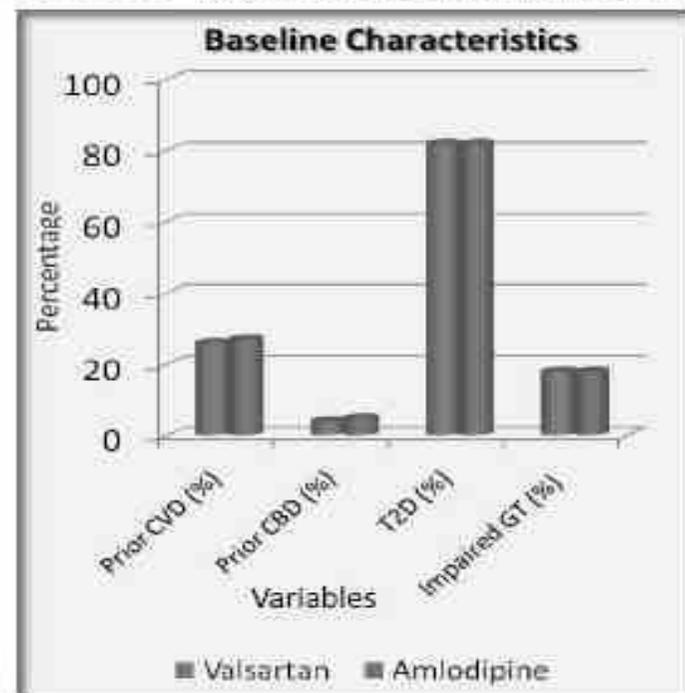


NAGOYA HEART

Comparison between Valsartan and Amlodipine regarding Cardiovascular Morbidity and Mortality in Hypertensive Patients with Glucose Intolerance

BACKGROUND: Various guidelines recommended angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor-1 blockers (ARBs) for hypertensive patients with diabetes on the basis of the cardiac- and reno-protective effects of these drugs. Despite these recommendations, these guidelines could not be extrapolated to Japanese patients, because Japan has been known as a country with a low incidence of coronary artery disease and a high incidence of cerebrovascular disease.

PURPOSE: To test whether ARBs or CCBs are superior in treating Japanese diabetic hypertensive patients.



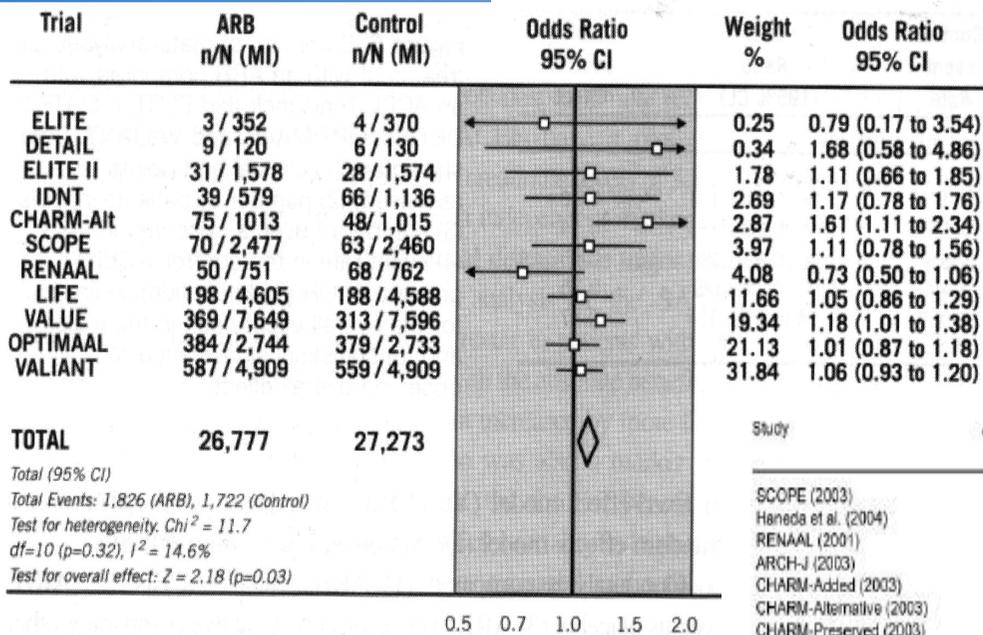
DESIGN: A prospective randomized open-label blinded-endpoint study to compare valsartan and amlodipine, and their effectiveness on cardiovascular morbidity and mortality in 1150 Japanese hypertensive patients with glucose intolerance.

PRIMARY ENDPOINT: Composite cardiovascular events - myocardial infarction, stroke, admission due to heart failure, coronary intervention and sudden cardiac death.

SECONDARY ENDPOINTS: Total death; cardiac function evaluated by ultrasonography; incidence of atrial fibrillation/flutter; control of blood glucose; and renal function.

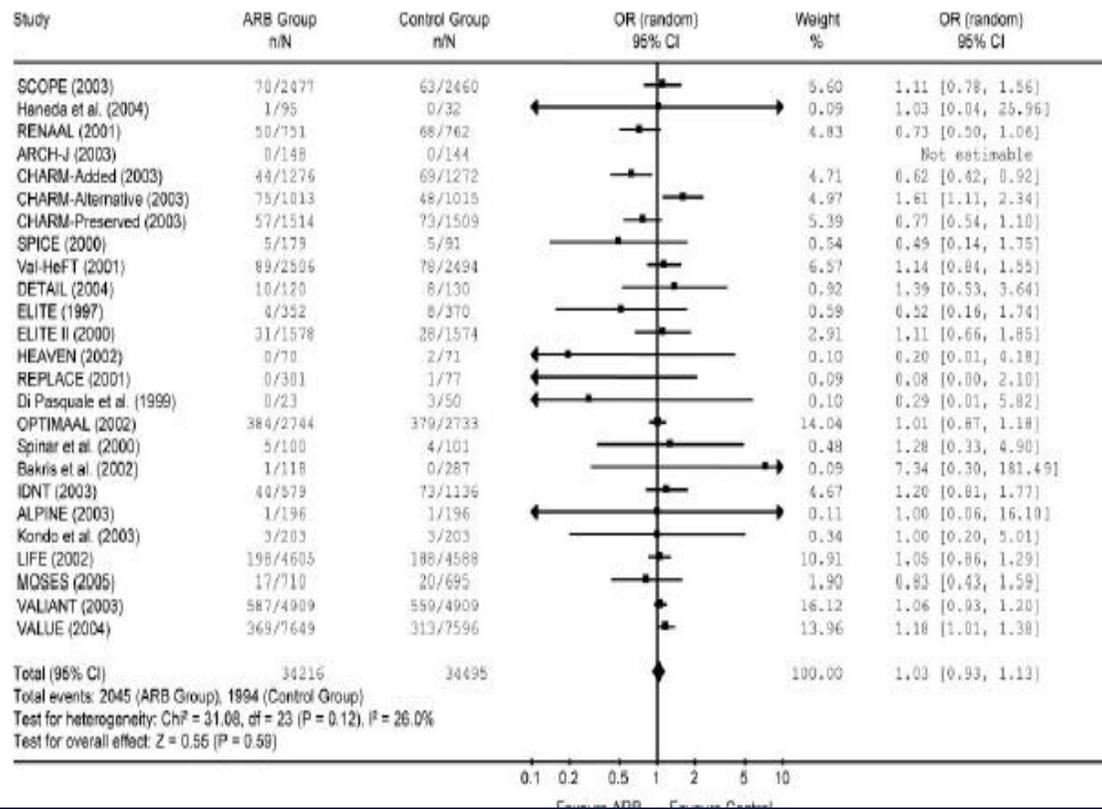
RESULTS: Study showed no difference between valsartan-based and amlodipine-based antihypertensive treatment in preventing composite cardiovascular outcomes. Valsartan-based treatment significantly reduced risk of CHF when compared to the amlodipine-based treatment.

CONCLUSION: Results highlight the safety and efficacy of an ARB valsartan in preventing HF and support current recommendations for hypertensive diabetic patients.

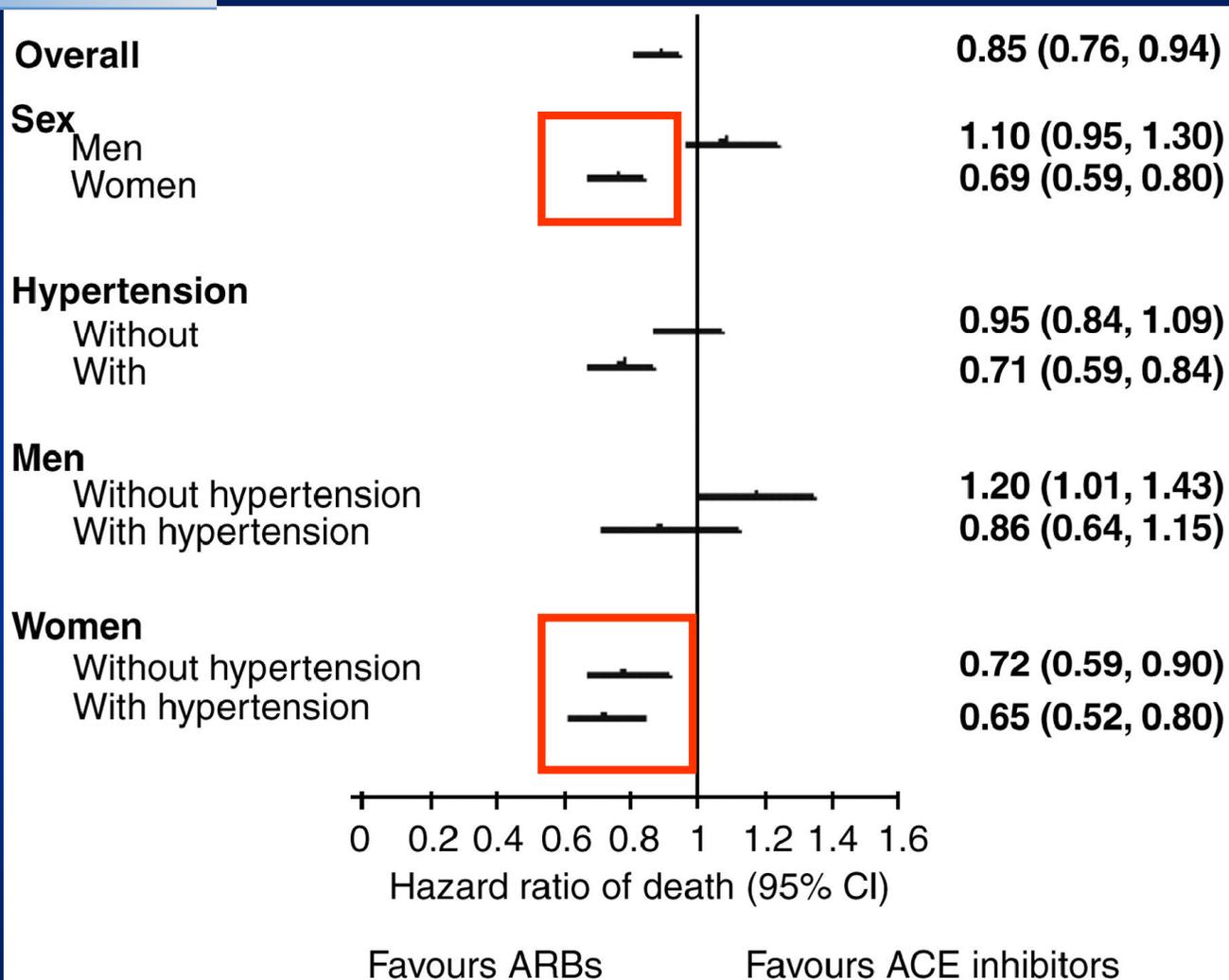


“Angiotensin Receptor Blockers Do Not Increase Risk of Myocardial Infarction”
Tsuyuki RT, McDonald MA-
Circulation-2006-114-855-860

Strauss M., Hall A. Angiotensin Receptor Blockers May Increase Risk of Myocardial Infarction: Unraveling the ARB-MI Paradox // Circulation. — 2006. — Vol. 114. — P. 838-854.

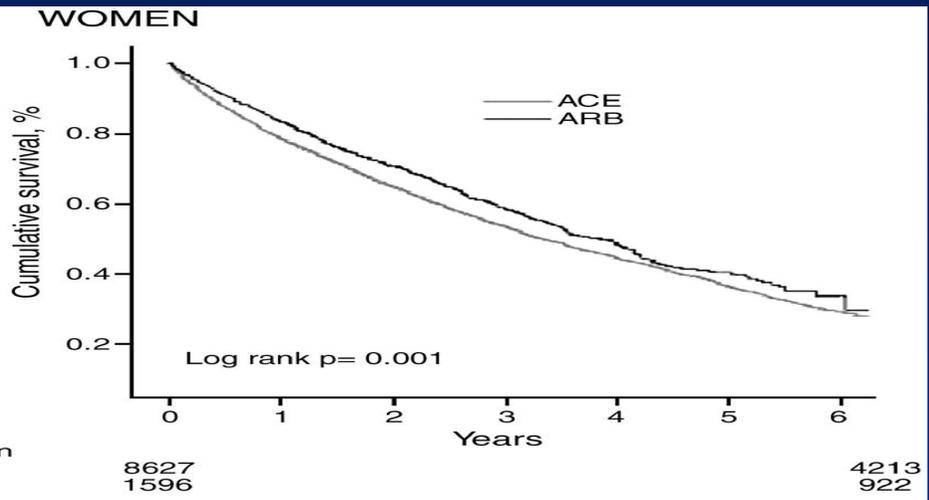


Results and 95% confidence intervals of survival in patients with CHF treated with ARBs compared to ACE inhibitors according to sex and the presence or absence of hypertension.

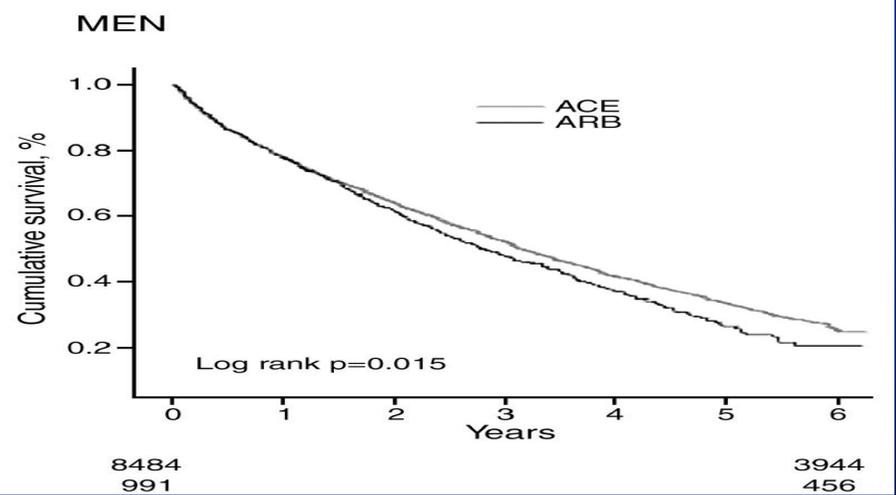


Hudson M et al. Eur J Heart Fail 2007;9:602-609

Survival curves for women and men prescribed an ARB or an ACE inhibitor of discharge from an admission for congestive heart failure.



Patients, n	8627	4213
ACE	1596	922
ARB		



Patients, n	8484	3944
ACE	991	456
ARB		

Hudson M et al. Eur J Heart Fail 2007;9:602-609



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**БЕЗОПАСНОСТЬ БРА:
где миф,
а где реальность**

Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials

Methods

We searched Medline, Scopus (including Embase), Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the US Food and Drug Administration website for studies published before November, 2009, that included any of the seven currently available ARBs. Randomised controlled trials with an ARB given in at least one group, with a follow-up of at least 1 year, and that enrolled at least 100 patients were included. New-cancer data were available for 61 590 patients from five trials. Data on common types of solid organ cancers were available for 68 402 patients from five trials, and data on cancer deaths were available for 93 515 patients from eight trials.

Interpretation

This meta-analysis of randomised controlled trials suggests that ARBs are associated with a modestly increased risk of new cancer diagnosis. Given the limited data, it is not possible to draw conclusions about the exact risk of cancer associated with each particular drug. These findings warrant further investigation.

FDA Drug Safety Communication: Ongoing safety review of the angiotensin receptor blockers and cancer

Additional Information for Healthcare Professionals

- Know that FDA's meta-analysis of 31 randomized controlled trials comparing ARBs to other treatment found no evidence of an increased risk of incident (new) cancer, cancer-related death, breast cancer, lung cancer, or prostate cancer in patients receiving ARBs.
- Report adverse events involving ARB medications to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Patients

- Do not stop taking your ARB medication without talking to your healthcare professional.
- Discuss any questions or concerns about ARB medications with your healthcare professional.
- Report any side effects you may experience to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

Применение валсартана у больных с ИБС, постинфарктным кардиосклерозом через 12 мес после операции АКШ +АЭ

Після операції АКШ + Аневризмектомія спостережувались в течение 12 мес

Клінічна характеристика	Показник
Вік, роки	56,38 ± 9,28
Чоловіки	133 (89,6%)
Жінки	15 (10.1%)
Курці	101 (68%)
Гіпертонічна хвороба	86 (58.1%)
Цукровий діабет тип 2	14 (9,4%)
Стенокардія напруги	112 (75,67%)

Локалізація ІМ:	
передньо-перетинково-верхівковий	69 (46,6%)
передньо-перетинково-верхівково-боковий	31 (20,9%)
циркулярне ураження	29 (19,6%)
ураження ЗСЛШ та верхівки ЛШ	19 (12,8%)

	До операції АКШ+АЕ n=148	Через 1 рік після операціїАКШ+АЕ n=137
β-блокатори	142 (95,9%)	101 (73,7%)
Інгібітори АПФ	145 (97,9%)	90 (66,5%)
БРА (ВАЛЬСАКОР)	0	18 (20%)
спіронолактон	67 (45,3%)	37 (27%)
діуретики	63 (45,9%)	56 (37,8%)
статини	148 (100%)	72 (52,5%)
нітрати	131 (88,5%)	38 (27%)
НМГ	148 (100%)	0 (0%)
аспірин	0 (0%)	98 (67,2%)
клопідогрель	0 (0%)	21 (15,3%)
непрямі антикоагулянти	0 (0%)	12 (8,8%)
аміодарон	6 (4,1%)	38 (27,7)

Лечение пациентов до и после операции АКШ+АЭ

Состояние больных, которые получали валсартан через 12 мес после операции АКШ+АЭ

Клінічна характеристика	ІАПФ n=90	БРА n=18
Стенокардія напруги I-II ф.к.	32%	30%

При непереносимости ИАПФ пациенты с ИБС, постинфарктным кардиосклерозом после операции АКШ+АЭ могут получать валсартан, что не ухудшает их клинического состояния

	ІАПФ n=90	БРА n=18
II	40%	39%
III	17%	19%
IV	0%	0%

P>0.05