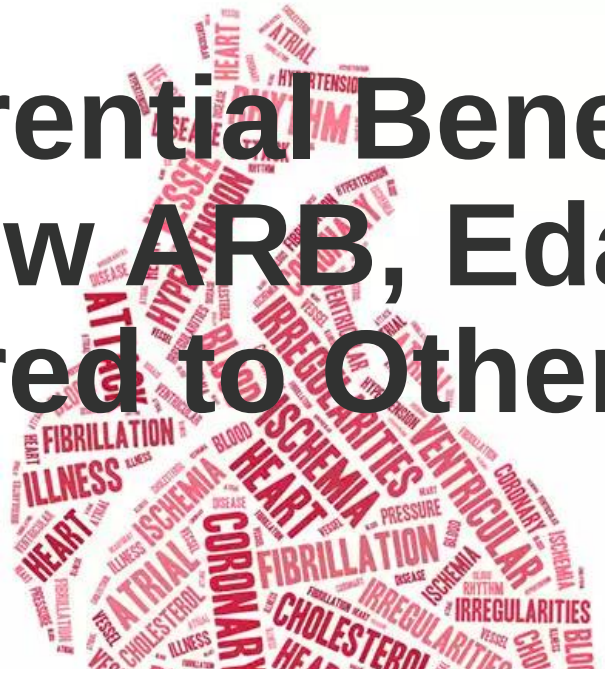
Differential Benefits of New ARB, Edarbi Compared to Other Sartans



Jung Ho Heo MD, PhD

Division of Cardiology

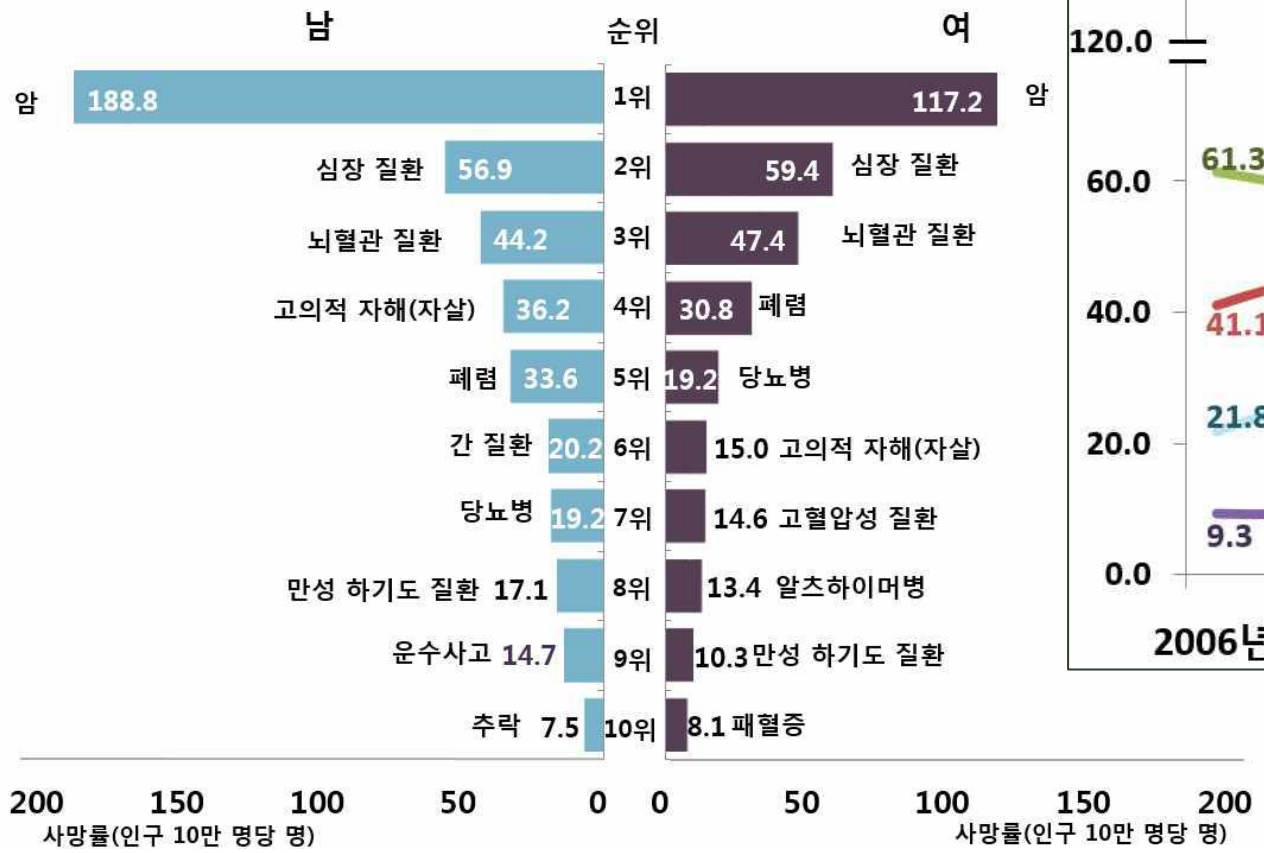
Kosin University Hospital

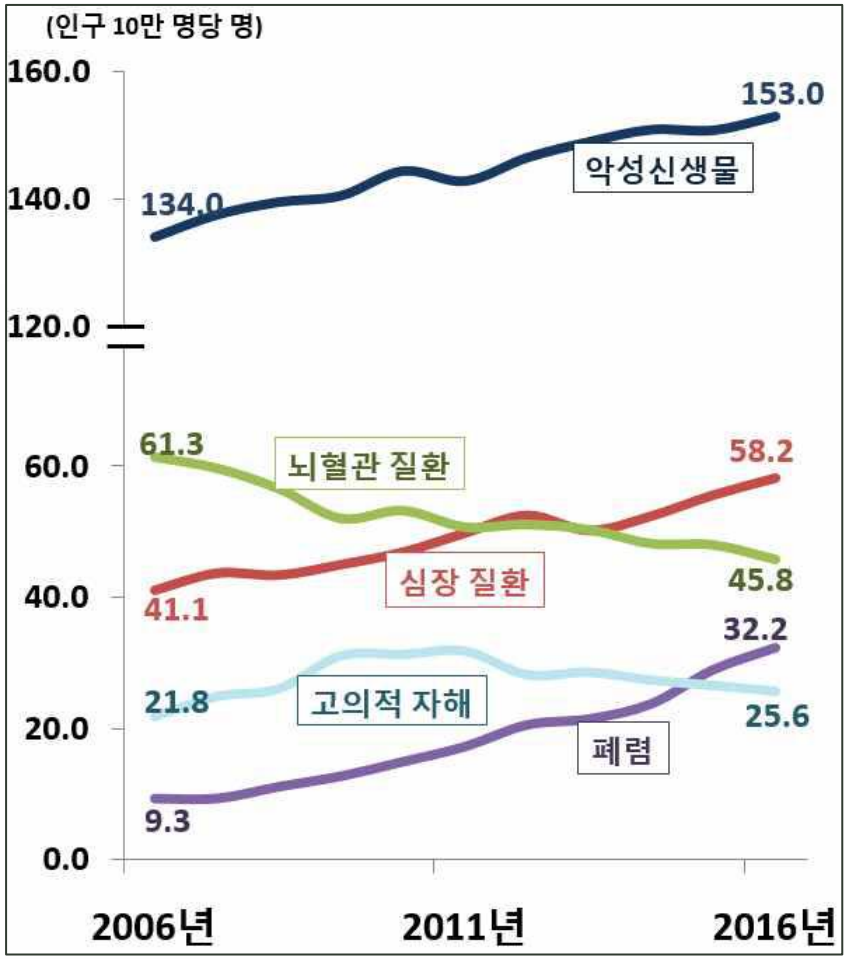
Busan, Korea South.

Hypertension the BAD !!

The Lower BP, The Better Outcomes

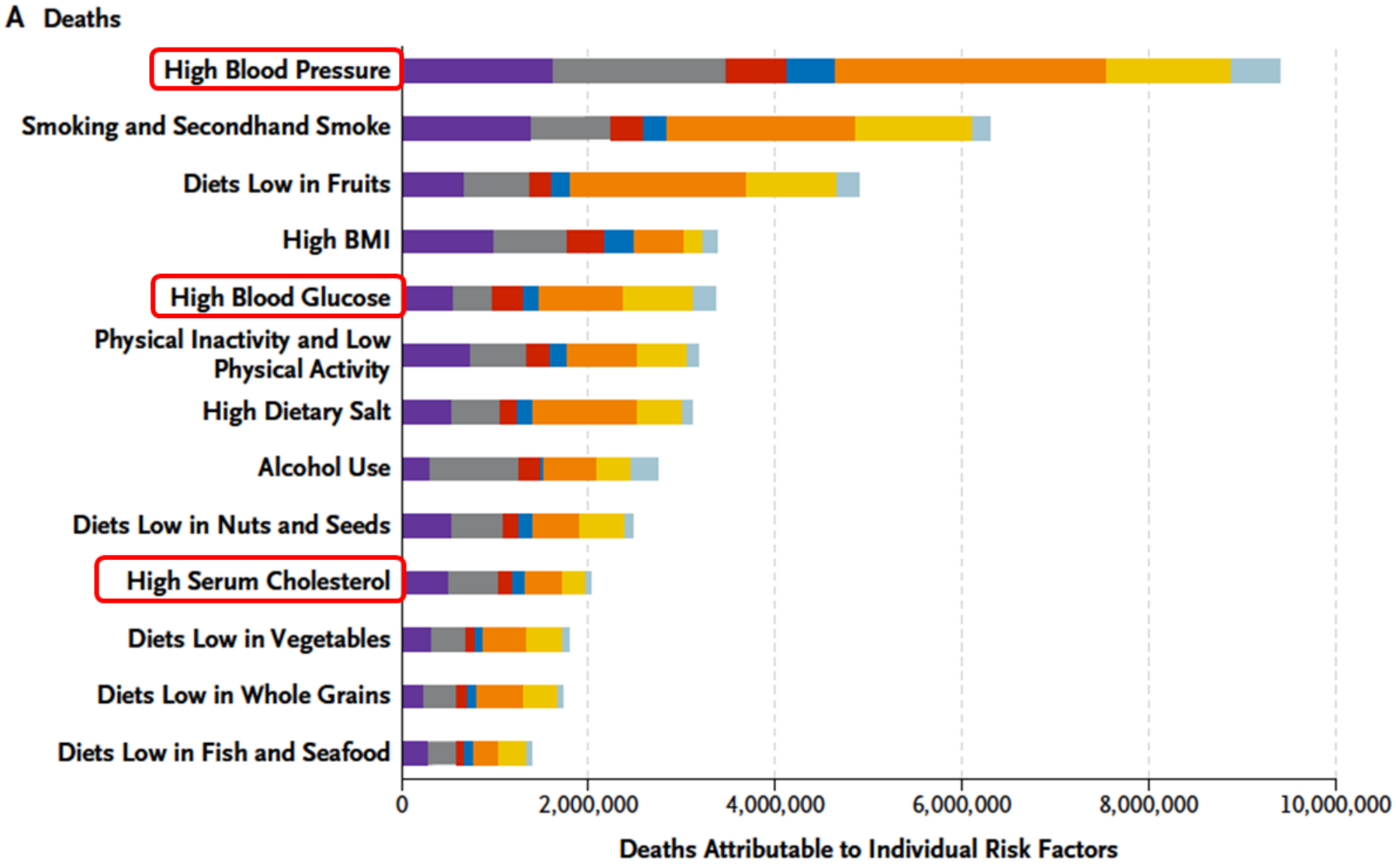
성별 사망원인 순위





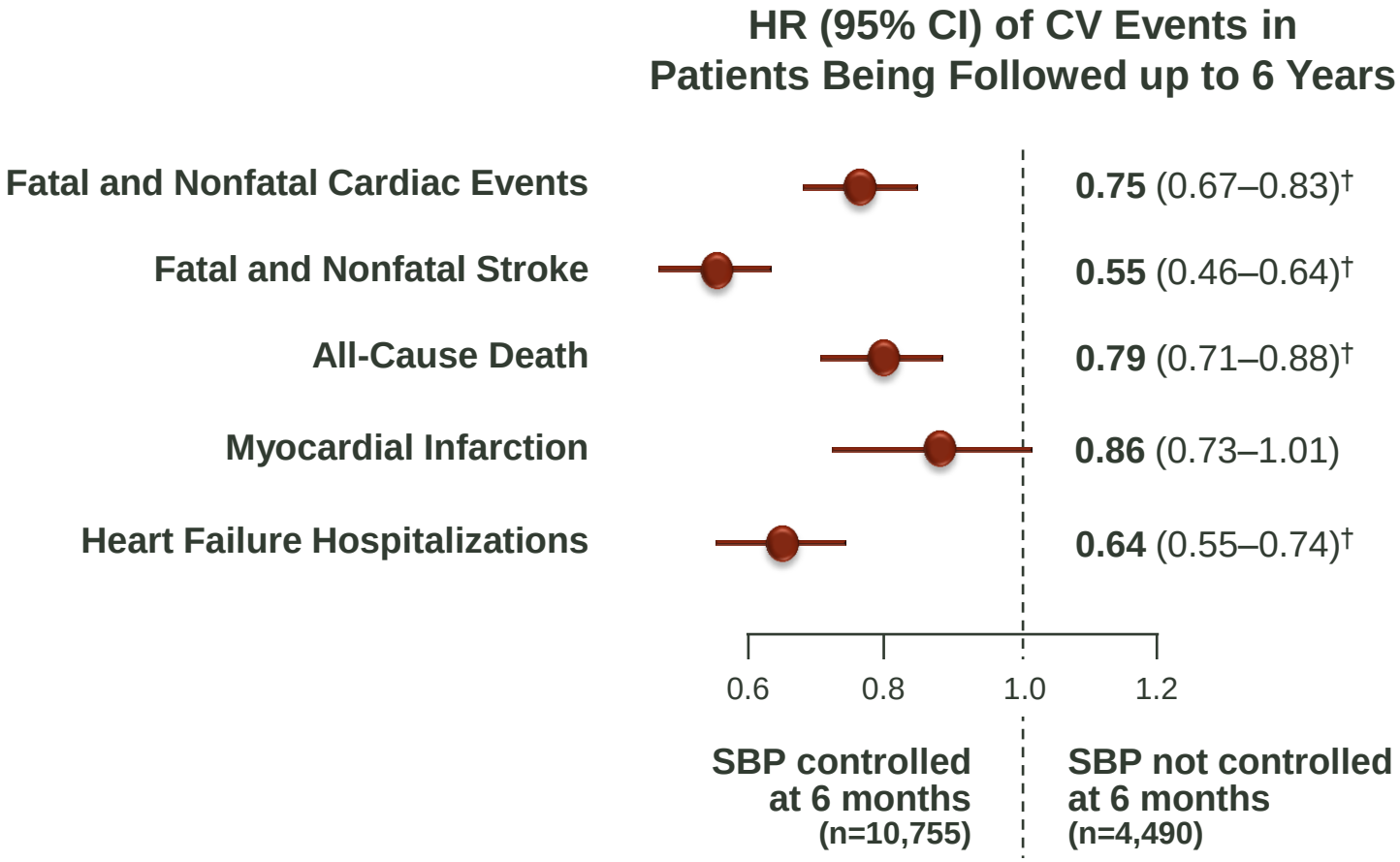
2017. 9.22. 통계청. 2016년 사망원인 통계

Mortality due to Leading Global Risk Factors



Lim et al. Lancet 2012;380:2224-2260.

Effect of Early Blood Pressure Control on Cardiovascular Risk*



*Pooled analysis of patients enrolled in the VALUE trial; blood pressure control defined as SBP <140 mmHg
†Statistically significant difference (P<0.05) vs SBP not controlled at 6 months
BP=blood pressure; CI=confidence interval; CV=cardiovascular; HR=hazard ratio; SBP=systolic blood pressure; VALUE=Valsartan Antihypertensive Long-term Use Evaluation

Weber MA, et al. *Lancet*. 2004;363:2049-2051.

SPRINT study

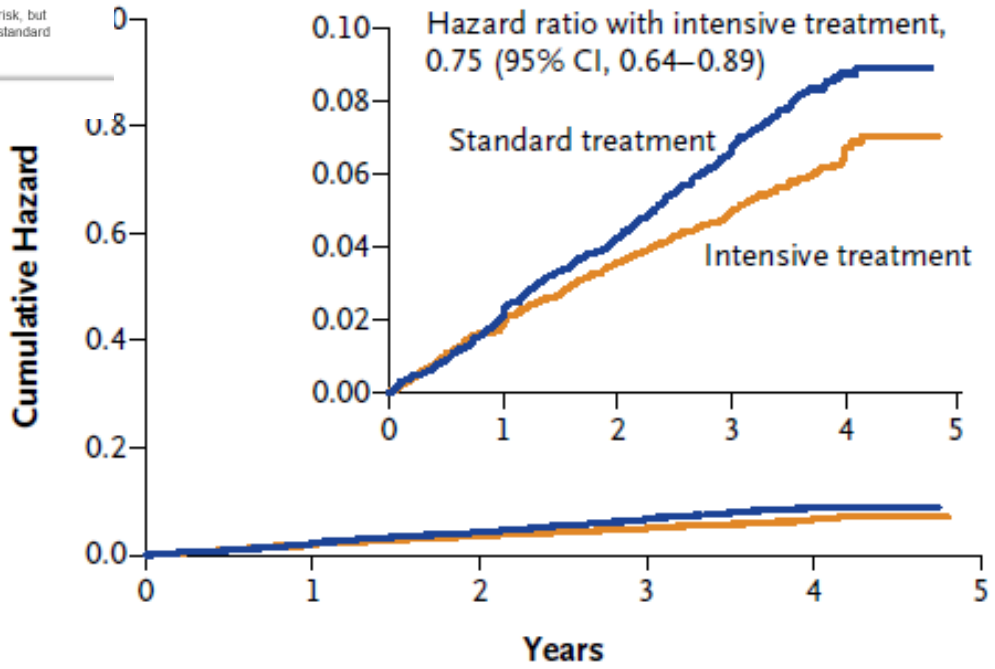
Examine effect of more intensive high blood pressure treatment than is currently recommended

Randomized Controlled Trial Target Systolic BP

Intensive Treatment Goal SBP < 120 mm Hg	***Standard Treatment Goal SBP < 140 mm Hg***
N=4,678	N=4,683

SPRINT study randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg intensive treatment) or a target of less than 140 mm Hg (standard treatment)
SPRINT Research Group, NEJM 2015;373(22):2103-2116

Primary Outcome



The primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes. The intervention was stopped early after a median follow-up of 3.26 years owing to a signifi-cantly lower rate of the primary composite outcome in the intensive-treatment group than in the standard-treatment group (1.65% per year vs. 2.19% per year; hazard ratio with intensive treatment, 0.75; 95% confidence interval [CI], 0.64 to 0.89; P<0.001). SPRINT Research Group, NEJM 2015;373(22):2103-2116

Hypertension Paradox

More Uncontrolled Disease despite Improved Therapy

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

SHATTUCK LECTURE

The Hypertension Paradox — More Uncontrolled Disease despite Improved Therapy

Aram V. Chobanian, M.D.

THE TREATMENT OF HYPERTENSION HAS BEEN ONE OF MEDICINE'S MAJOR successes of the past half-century. The remarkable advances in therapy have provided the newfound capability for lowering blood pressure in almost every person with hypertension. Nevertheless, hypertension continues to be a major public health problem whose prevalence is increasing worldwide.[1] Moreover, the number of people with uncontrolled blood pressure is also increasing, despite the therapeutic advances. Here, I discuss the factors responsible for this paradox and the strategies required for addressing the growing problem.

The treatment of hypertension has been one of medicine's major successes of the past half-century. The remarkable advances in therapy have provided the newfound capability for lowering blood pressure in almost every person with hypertension.

Nevertheless, hypertension continues to be a major public health problem whose prevalence is increasing worldwide.

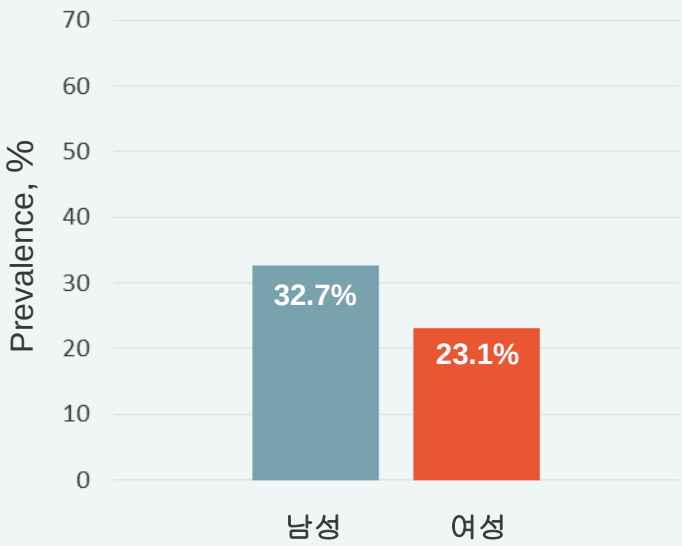
Moreover, the number of people with uncontrolled blood pressure is also increasing, despite the therapeutic advances.

NEJM 2009:361:878-887

혈압분류기준에 따른 국내 고혈압 유병률의 변화

국내 가이드라인 기준 유병률

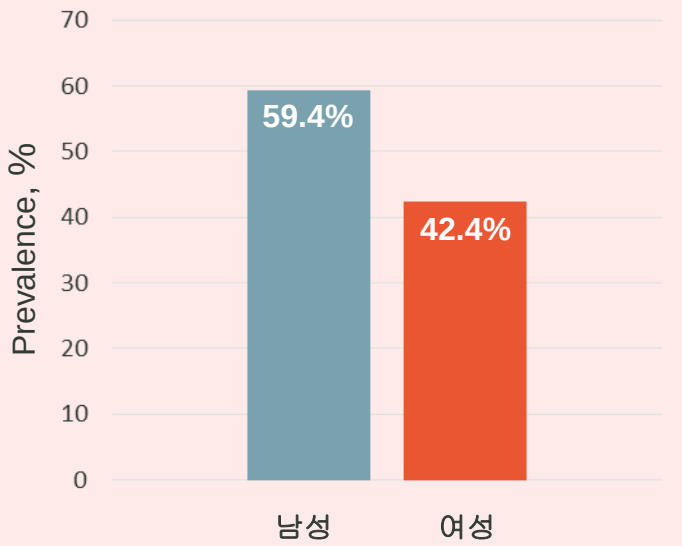
한국 성인 대략 **3-4명 중 1명**이 **고혈압**
(1,180만명 추정, 전체 인구의 32%)



변경후

2017 ACC/AHA 가이드라인 기준 유병률

한국 성인 **2명 중 1명**이 **고혈압**
(1,652만 7천명, 전체 인구의 50.5%)



1. 2015 건강행태 및 만성질환 통계. 2. http://www.dailypharm.com/Users/News/NewsView.html?ID=233465

Population Effect of Blood Pressure Reduction on Mortality

Analysis of 5 major observational studies demonstrated that small differences in SBP resulted in significant risk difference in developing complications:[1]

SBP by 5 mmHg →

- Stroke mortality by 14%
- CHD mortality by 9%
- All-cause mortality by 7%

A meta-analysis of 61 prospective randomized studies involving 12.7 million person-years demonstrated that modest SBP reduction was associated with significant risk reduction in developing complications:[2]

SBP by 2 mmHg →

- Stroke mortality by 10%
- IHD mortality by 7%

CHD=coronary heart disease; IHD=ischemic heart disease; SBP=systolic blood pressure

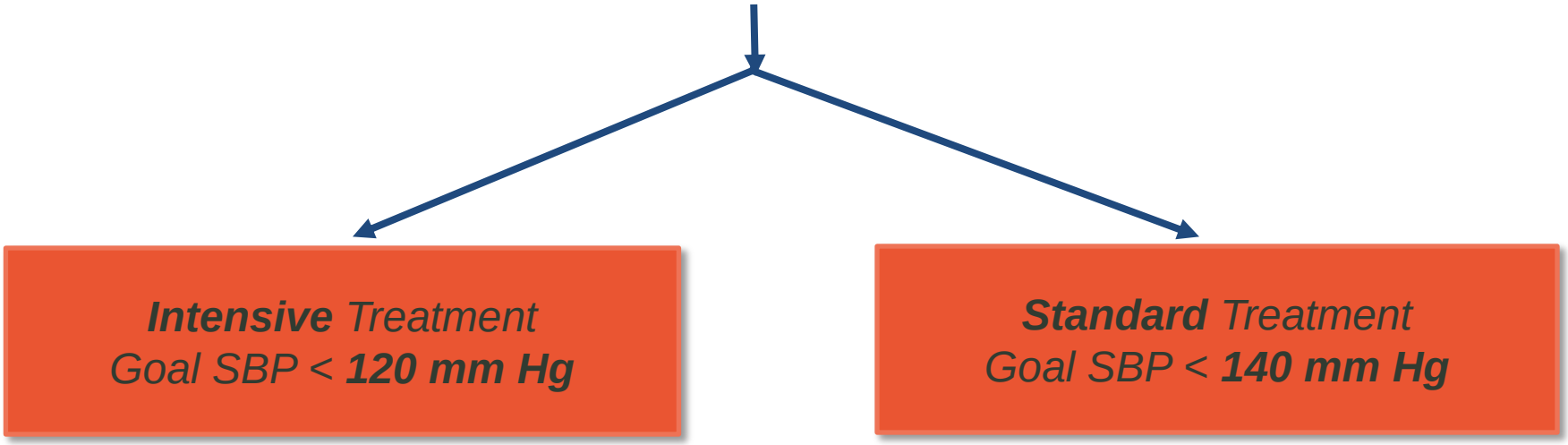
1. Stalmer R. *Hypertension*. 1991;17(Suppl1):I16-I20.
2. Lewington S, et al. *Lancet*. 2002;360:1903-1913.

SPRINT Research Question

Intensive versus standard blood-pressure control

Examine effect of more intensive high blood pressure treatment than is currently recommended

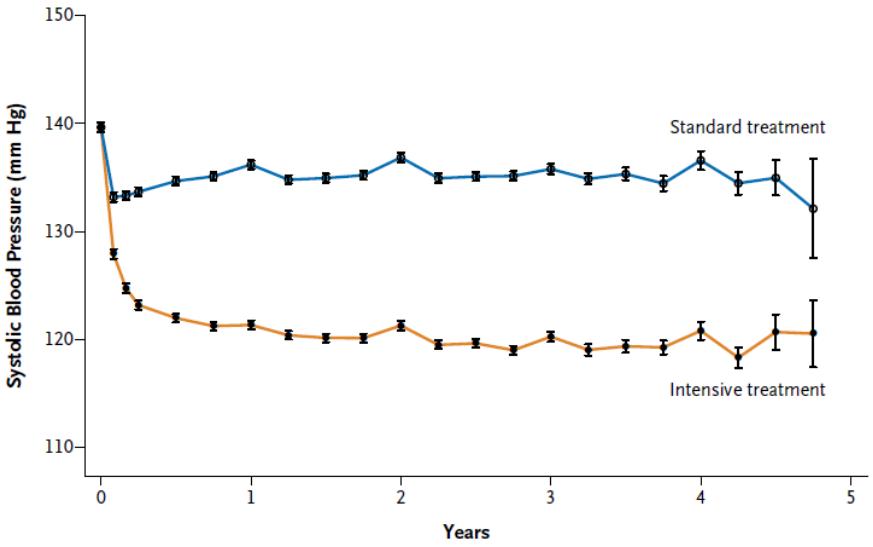
Randomized Controlled Trial
Target Systolic BP

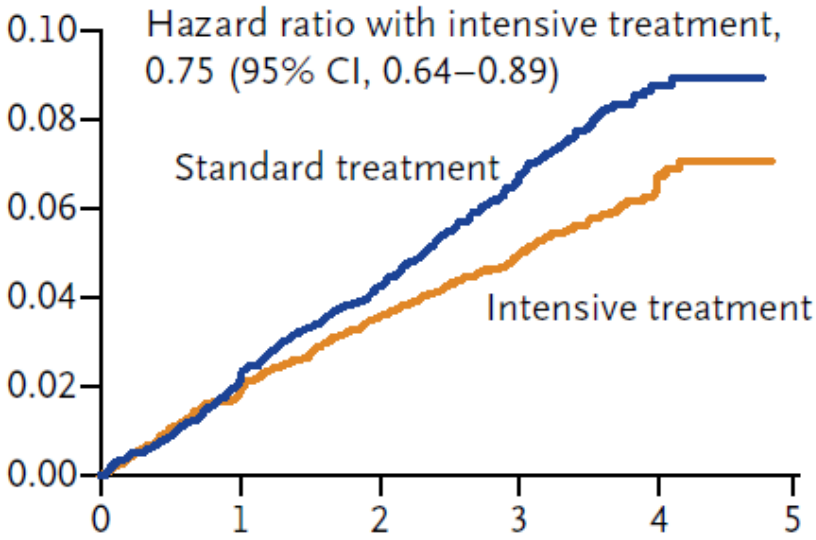


NEJM 2015; 373(22): 2103-2116

SPRINT Study

The Lower BP, The Better Outcomes





NEJM 2015; 373(22): 2103-2116

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 26, 2015 VOL. 373 NO. 22

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

ABSTRACT

BACKGROUND

The most appropriate targets for systolic blood pressure to reduce cardiovascular morbidity and mortality among persons without diabetes remain uncertain.

METHODS

We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment). The primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes.

RESULTS

At 1 year, the mean systolic blood pressure was 121.4 mm Hg in the intensive-treatment group and 136.2 mm Hg in the standard-treatment group. The intervention was stopped early after a median follow-up of 3.26 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group than in the standard-treatment group (1.65% per year vs. 2.19% per year; hazard ratio with intensive treatment, 0.75; 95% confidence interval [CI], 0.64 to 0.89; P<0.001). All-cause mortality was also significantly lower in the intensive-treatment group (hazard ratio, 0.73; 95% CI, 0.60 to 0.90; P=0.003). Rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls, were higher in the intensive-treatment group than in the standard-treatment group.

CONCLUSIONS

Among patients at high risk for cardiovascular events but without diabetes, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events were observed in the intensive-treatment group. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT01206062.)

The members of the writing committee (Jackson T. Wright, Jr., M.D., Ph.D., Jeff D. Williamson, M.D., M.H.S., Paul K. Whelton, M.D., Joni K. Snyder, R.N., B.S.N., M.A., Kaycee M. Sink, M.D., M.A.S., Michael V. Rocco, M.D., M.S.C.E., David M. Reboussin, Ph.D., Mahboob Rahman, M.D., Suzanne Oparil, M.D., Cora E. Lewis, M.D., M.S.P.H., Paul L. Kimmel, M.D., Karen C. Johnson, M.D., M.P.H., David C. Goff, Jr., M.D., Ph.D., Lawrence J. Fine, M.D., Dr.P.H., Jeffrey A. Cutler, M.D., M.P.H., William C. Cushman, M.D., Alfred K. Cheung, M.D., and Walter T. Ambrosius, Ph.D.) assume responsibility for the overall content and integrity of the article. The affiliations of the members of the writing group are listed in the Appendix. Address reprint requests to Dr. Wright at the Division of Nephrology and Hypertension, University Hospitals Case Medical Center, Case Western Reserve University, 1100 Euclid Ave., Cleveland, OH 44106-6053, or at jackson.wright@case.edu.

*A complete list of the members of the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 9, 2015, at NEJM.org.

N Engl J Med 2015;373:2103-16.
DOI: 10.1056/NEJMoa1511939

of cardiovascular events. Increased cardiovascular risk was defined by one or more of the following: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease, excluding polycystic kidney disease, with an estimated glomerular filtration rate (eGFR) of 20 to less than 60 ml per minute per 1.73 m² of body-surface area, calculated with the use of the four-variable Modification of Diet in Renal Disease equation; a 10-year risk of cardiovascular disease

mentary Appendix). All major classes of antihypertensive agents were included in the formulary and were provided at no cost to the participants. SPRINT investigators could also prescribe other antihypertensive medications (not provided by the study). The protocol encouraged, but did not mandate, the use of drug classes with the strongest evidence for reduction in cardiovascular outcomes, including thiazide-type diuretics (encouraged as the first-line agent), loop diuretics (for participants with advanced chronic kidney disease), and beta-adrenergic blockers (for those with coronary artery disease).[9,27] Chlorthalidone was encouraged as the primary thiazide-type diuretic, and amlodipine as the preferred calcium-channel blocker.[28,29] Azilsartan and azilsartan combined with chlorthalidone were donated by Takeda Pharmaceuticals International and Arbor Pharmaceuticals; neither company had any other role in the study.

Participants were seen monthly for the first 3 months and every 3 months thereafter. Medications for participants in the intensive-treatment group were adjusted on a monthly basis to target a systolic blood pressure of less than 120 mm Hg. For participants in the standard-

groups to minimize ascertainment bias. Medical records and electrocardiograms were obtained for documentation of events. Whenever clinical-site staff became aware of a death, a standard protocol was used to obtain information on the event.

Serious adverse events were defined as events that were fatal or life-threatening, that resulted in clinically significant or persistent disability, that required or prolonged a hospitalization, or that were judged by the investigator to represent a clinically significant hazard or harm to the participant that might require medical or surgical intervention to prevent one of the other events listed above.[30,31] A short list of monitored conditions were reported as adverse events if they were evaluated in an emergency department

Azilsartan and azilsartan combined with chlorthalidone were donated by Takeda Pharmaceuticals International and Arbor Pharmaceuticals; neither company had any other role in the study.

NEJM 2015; 373(22): 2103-2116

Table S1. SPRINT Formulary

Class	Drug	Available Strengths	Usual Dose Range / day	Usual Daily Frequency
Diuretic	Chlorthalidone	25mg	12.5-25 mg	1
	Furosemide	20mg, 40mg, 80mg	20-80 mg	2
	Spironolactone	25mg	25-50 mg	1
	Triamterene/HCTZ	75/50mg	37.5/25 mg – 75/50 mg	1
	Amiloride	5mg	5-10 mg	1-2
Ace Inhibitor	Lisinopril	5mg, 10mg 20mg, 40mg	5-40 mg	1
Angiotensin Receptor Blocker	Losartan	25mg, 50mg, 100mg	25 – 100 mg	1-2
	Azilsartan	40mg, 80mg	40-80 mg	1
	Azilsartan/ chlorthalidone	40/12.5mg, 40/25mg	40/12.5 – 40/25 mg	1
Calcium Channel Blockers	Diltiazem	120mg, 180mg, 240mg, 300mg	120-540 mg	1
	Amlodipine	2.5mg, 5mg, 10mg	2.5-10 mg	1
Beta Blockers	Metoprolol Tartate	25mg, 50mg, 100mg	50-200 mg	1-2
	Atenolol	25mg, 50mg, 100mg	25-100 mg	1
	Atenolol/ Chlorthalidone	50/25mg	50/25 mg	1
Vasodilators	Hydralazine	25mg, 50mg, 100mg	50-200 mg	2
	Minoxidil	2.5mg, 10mg	2.5-80 mg	1-2
Alpha 2 Agonist	Guanfacine	1mg, 2mg	0.5-2 mg	1
Alpha Blockers	Doxazosin	1mg, 2mg, 4mg, 8mg	1-16 mg	1
Potassium Supplements	KCL tablets	20mEq	20-80 mEq	1-2
	KCL oral solution (10%)	20mEq/15ml	20-80 mEq	1-2

Hypertension the BAD !!

Azilsartan Medoxomil

Advances in the Treatment of Hypertension

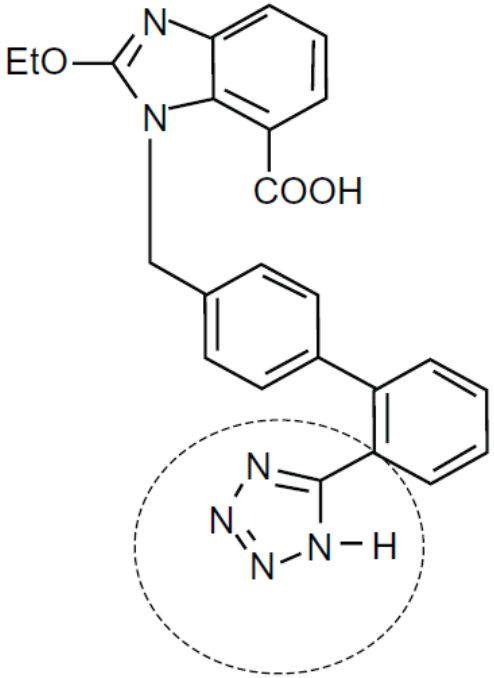
Decade	Therapy
1940s	Potassium thiocyanate Kempner diet Lumbodorsal sympathectomy
1950s	*Rauwolfia serpentina* Ganglionic blockers Veratrum alkaloids Hydralazine Guanethidine Thiazide diuretics
1960s	α2-Adrenergic–receptor agonists Spironolactone β-Adrenergic–receptor antagonists
1970s	α1-Adrenergic–receptor antagonists Angiotensin-converting–enzyme inhibitors
1980s	Calcium antagonists
1990s	Angiotensin-receptor blockers Endothelin-receptor antagonists*
2000s	Renin inhibitors

* This class of drugs has not been approved for clinical use in patients with hypertension

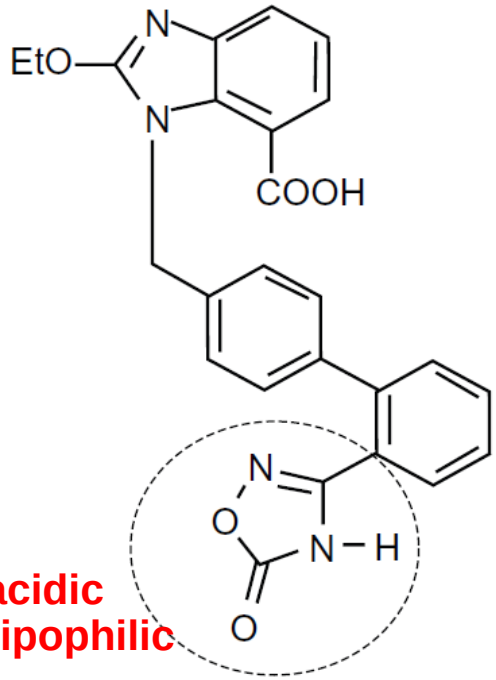
NEJM 2009:361:878-887

Development History of Azilsartan

Candesartan

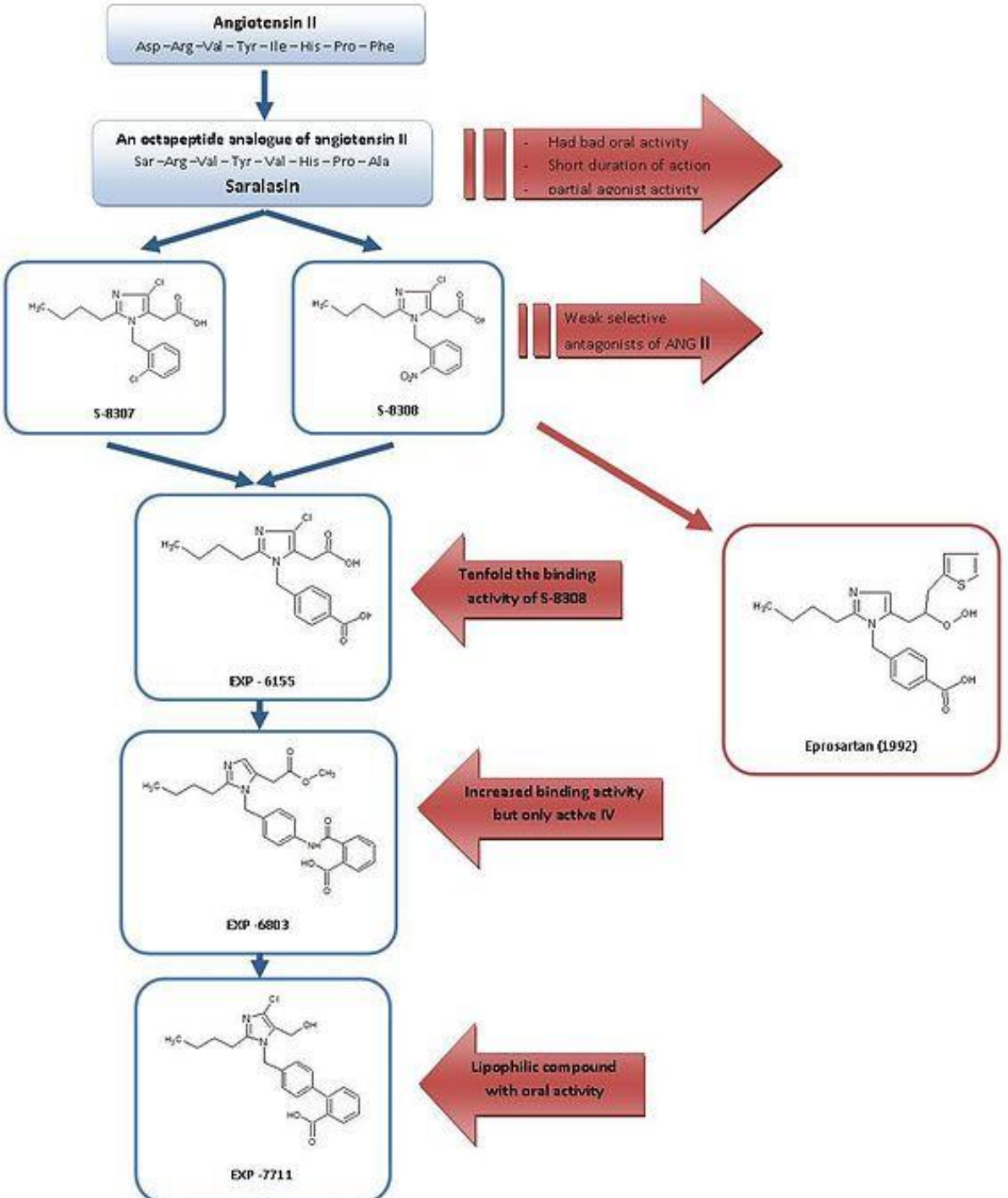


Azilsartan



Less acidic
More lipophilic

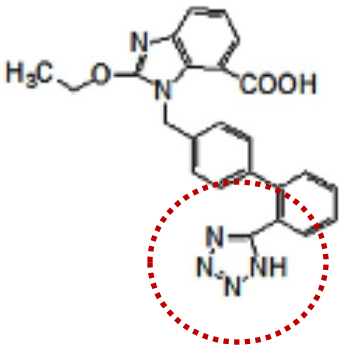
Kurts TW et al. Vasc Health Risk Manag 2012;8:133-143


Angiotensin II
Asp –Arg –Val – Tyr – Ile – His – Pro – Phe
An octapeptide analogue of angiotensin II
Sar –Arg –Val – Tyr – Val – His – Pro – Ala
Saralasin
- Had bad oral activity
- Short duration of action
- partial agonist activity
S-8307
S-8308
Weak selective antagonists of ANG II
EXP - 6155
Tenfold the binding activity of S-8308
Eprosartan (1992)
EXP -6803
Increased binding activity but only active IV
EXP -7711
Lipophilic compound with oral activity

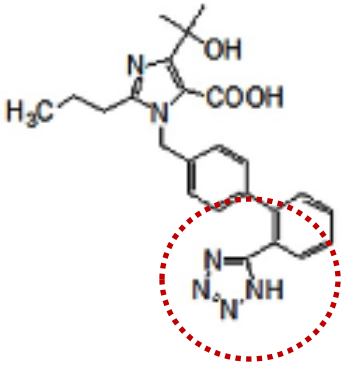
이달비, 옥시다졸 링

NDMA (테트라졸 링) 생성과 무관

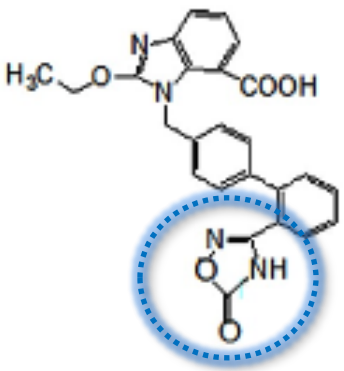
Candesartan



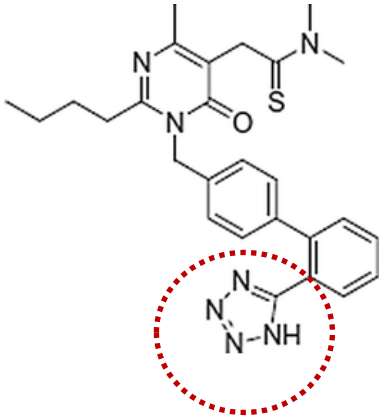
Olmesartan



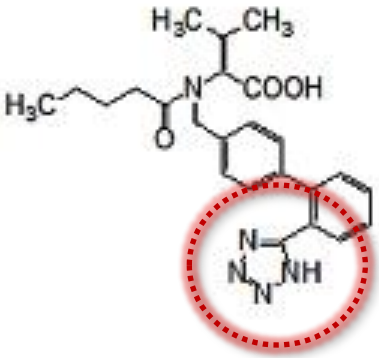
Azilsartan



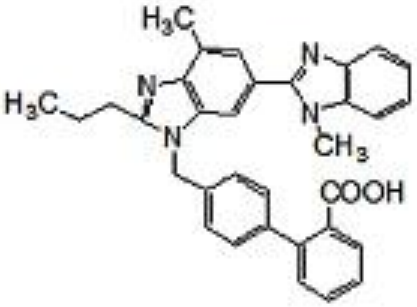
Fimasartan



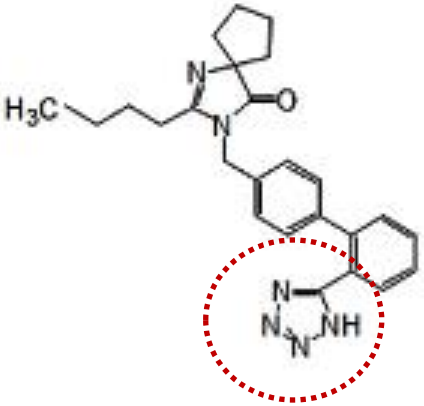
Valsartan



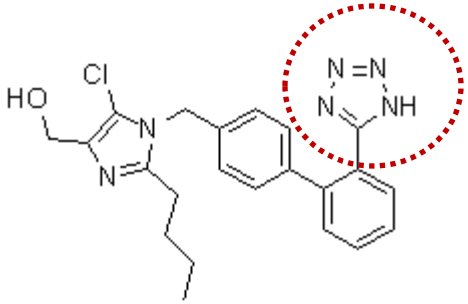
Telmisartan



Irbesartan



Losartan



Drug Safety and Availability
Drug Alerts and Statements
Medication Guides
Drug Safety Communications
Drug Shortages
Postmarket Drug Safety Information for Patients and Providers
Information by Drug Class
Medication Errors
Drug Safety Podcasts
Safe Use Initiative
Drug Recalls
Drug Supply Chain Integrity

FDA updates on angiotensin II receptor blocker (ARB) recalls including valsartan, losartan and irbesartan

Investigation ongoing – statement to be updated as more information is available

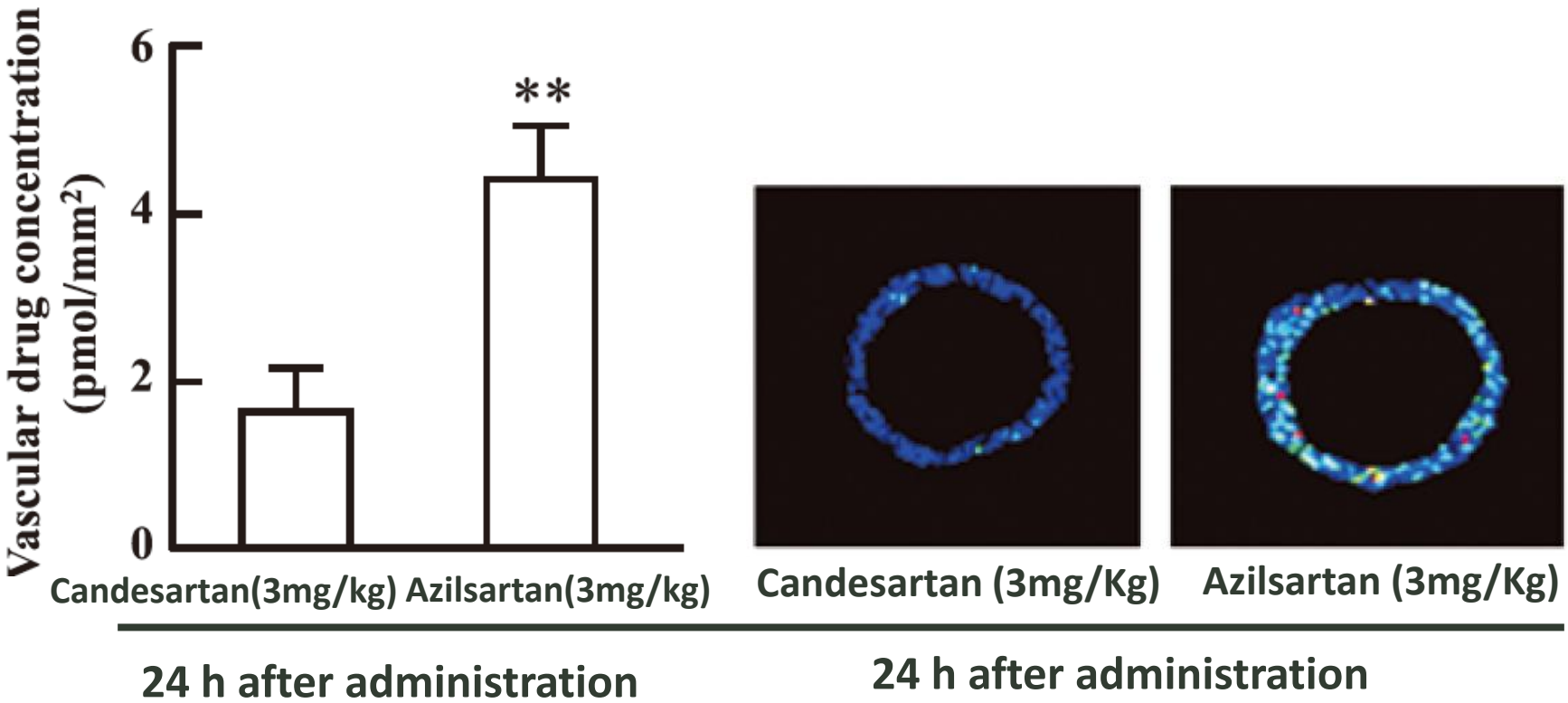
Mylan expands its voluntary recall of valsartan-containing products

Update [12/6/2018] Mylan Pharmaceuticals is expanding its voluntary recall to include all lots of non-expired valsartan-containing products due to trace amounts of N-Nitrosodiethylamine (NDEA) in the valsartan active pharmaceutical ingredient (API) manufactured by Mylan Laboratories Limited. The 104 additional lots include 26 lots of amlodipine and valsartan tablets, 51 lots of valsartan tablets and 27 lots of valsartan and hydrochlorothiazide tablets. These lots were distributed in the U.S. between March 2017 and November 2018.

The agency also updated the list of valsartan products under recall and the list of valsartan products not under recall.

FDA alerts patients and health care professionals to Teva's recall of valsartan products due to NDEA

Drug Concentrations at Vessels 24 Hours after Administration in SHR



Takai S et al. J Pharmacol Sci 2013;123:371 – 379

Pharmacokinetics of Azilsartan Medoxomil

	Active Metabolite	Bio-availability	Volume of Distribution	Dissociation Half-Life	Terminal Half-Life	Hepatic:Renal Elimination
Azilsartan medoxomil*	**Azilsartan***	**60%**	**16 L**	**NR**	**11 h**	**55:42**
Candesartan cilexetil	Candesartan	42%	0.13 L/kg	120 min	9–13 h	67:33
Eprosartan	No	13%	308 L	NR	5–7 h	90:10
Irbesartan	No	60%–80%	53–93 L	7 min	12–20 h	80:20
Losartan	EXP3174	33%	12 L	30 min	4–6 h	60:35
Olmesartan medoxomil	Olmesartan	26%	15–20 L	75 min	12–15 h	35%–49% renal
Telmisartan	No	43%	500 L	25 min	24 h	>98% hepatic
Valsartan	No	23%	17 L	17 min	7 h	83:13
Fimasartan	No	18%	42 L	63.7 min	5 h	

*Azilsartan medoxomil is available in all regions except for Japan, while Azilsartan is available in Japan
ARB=angiotensin receptor blocker; h=hour; min=minute; NR=not reported

Farsang C. *Vasc Health Risk Manag.* 2011;7:605-622.
Van Liefde I, et al. *Mol Cell Endocrinol.* 2009;302:237-243.
Kurtz TW, et al. *Vasc Health Risk Manag*. 2012;8:133-143. Biol Pharm Bull 2017;40(7):992-1001.

Human AT1 Receptors 에 대한 potency 비교

Inhibitory effects on the specific binding of ^{125}I-Sar^{1}-Ile$_{8}$-AII to human AT$_1$ receptors

Compound	IC_{50}		Ratio :Washout (+) /Washout (-)
	Washout (-)	Washout (+)	
	nM		
Azilsartan	2.6 (1.7-4.1)	7.4 (3.9-14.2)	3
Olmesartan	6.7 (3.8-10.8)	242.5 (91.0-1056.8)	36
Telmisartan	5.1 (3.0-8.1)	191.6 (124.1-303.2)	37
Valsartan	44.9 (30.5-64.7)	> 10,000	> 223
Irbesartan	15.8 (8.5-29.7)	> 10,000	> 635

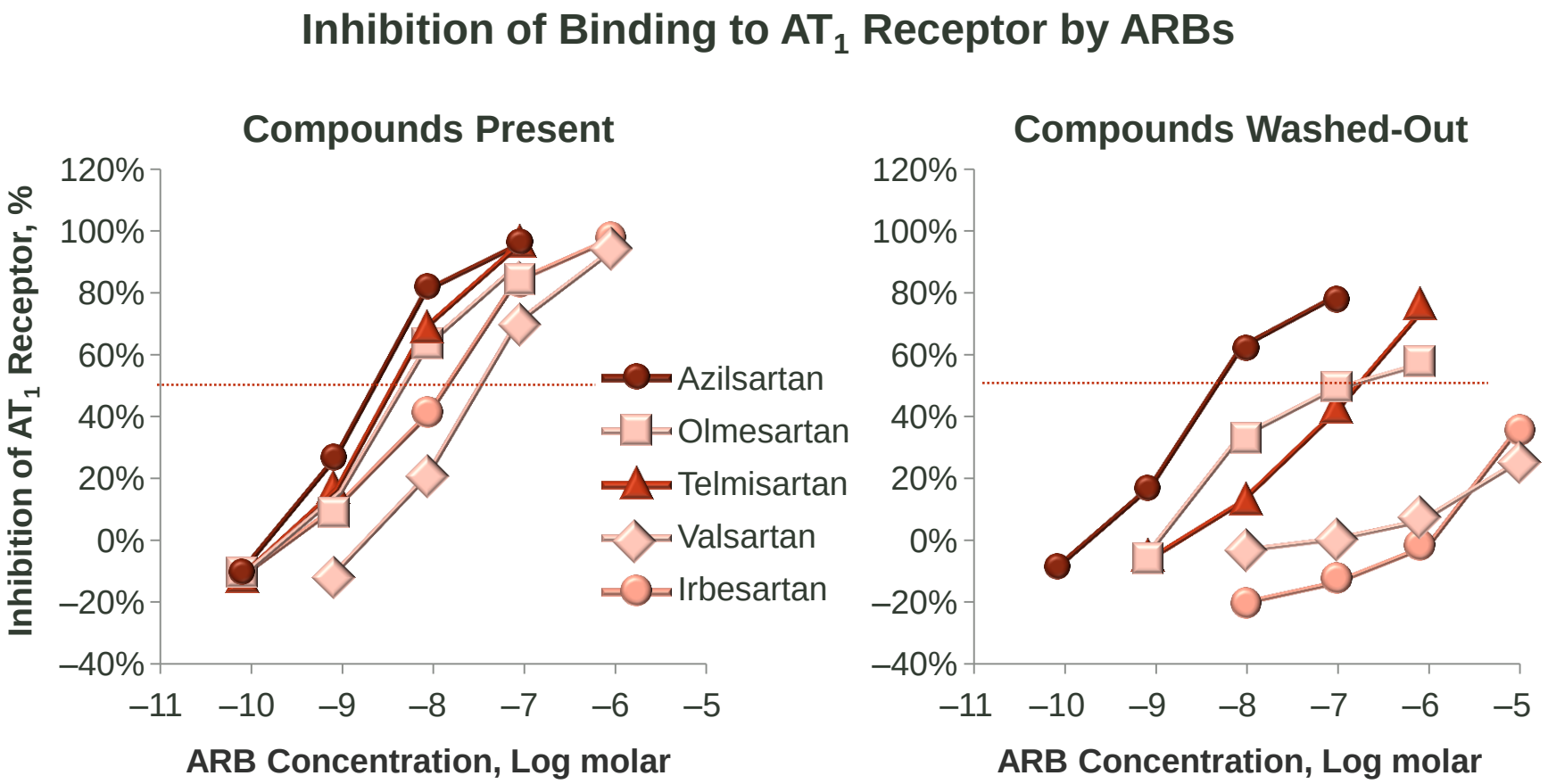
20배

AT$_1$=angiotensin II type 1 receptor AZL=Azilsartan

Ojima M, et al. *J Pharmacol Exp Ther*. 2011;336:801-808.

Potency of ARBs on Inhibition of AT_1 Receptor

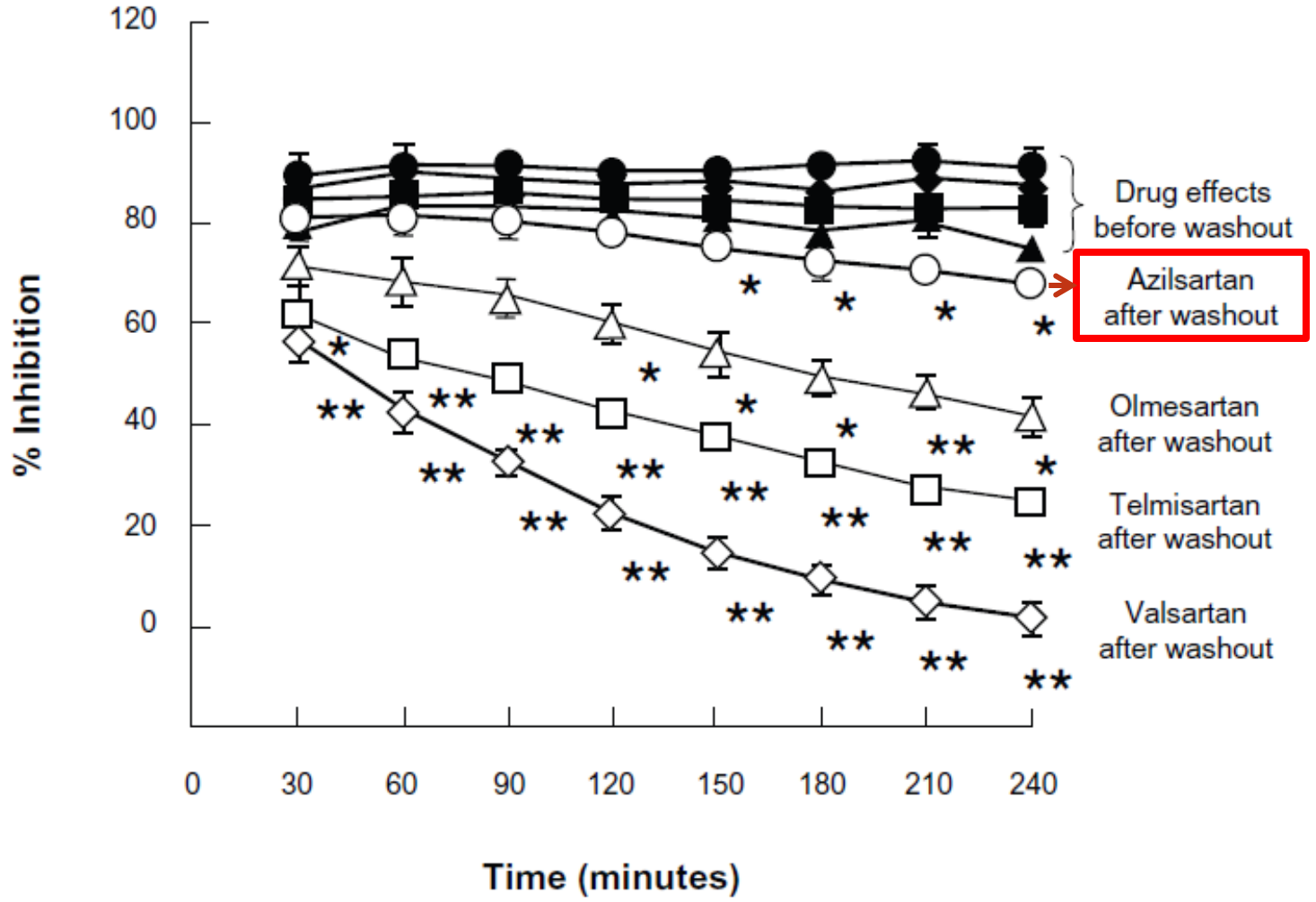
Azilsartan, tight binding



ARB=angiotensin receptor blocker; AT_1=angiotensin II type 1 receptor

Ojima M, et al. *J Pharmacol Exp Ther*. 2011;336:801-808.

Rate of Dissociation of ARBs from AT_1 Receptor



Statistically significant difference * *P*<0.05, **P<0.01 vs presence of the compound, Azilsartan Medoxomil is a prodrug of Azilsartan
ARB=angiotensin receptor blocker; AT_1=angiotensin II type 1 receptor

Ojima M, et al. *J Pharmacol Exp Ther*. 2011;336:801-808.

Edarbi® 의 특징

① 약물 구조 변형으로 **AT_1 Receptor 결합력**이 다른 ARB보다 강하다

② AT_1 Receptor에 결합하고 나서 **잘 분리되지 않는다**

Hypertension the BAD !!

Azilsartan Medoxomil

Clinical Evidence

Drug Approval Package

Edarbi (Azilsartan medoxomil)
Company: Takeda Pharmaceuticals America, Inc.
Application No.: 200796
Approval Date: 2/25/2011

Persons with disabilities having problems accessing the PDF files below may call (301) 796-3634 for assistance.

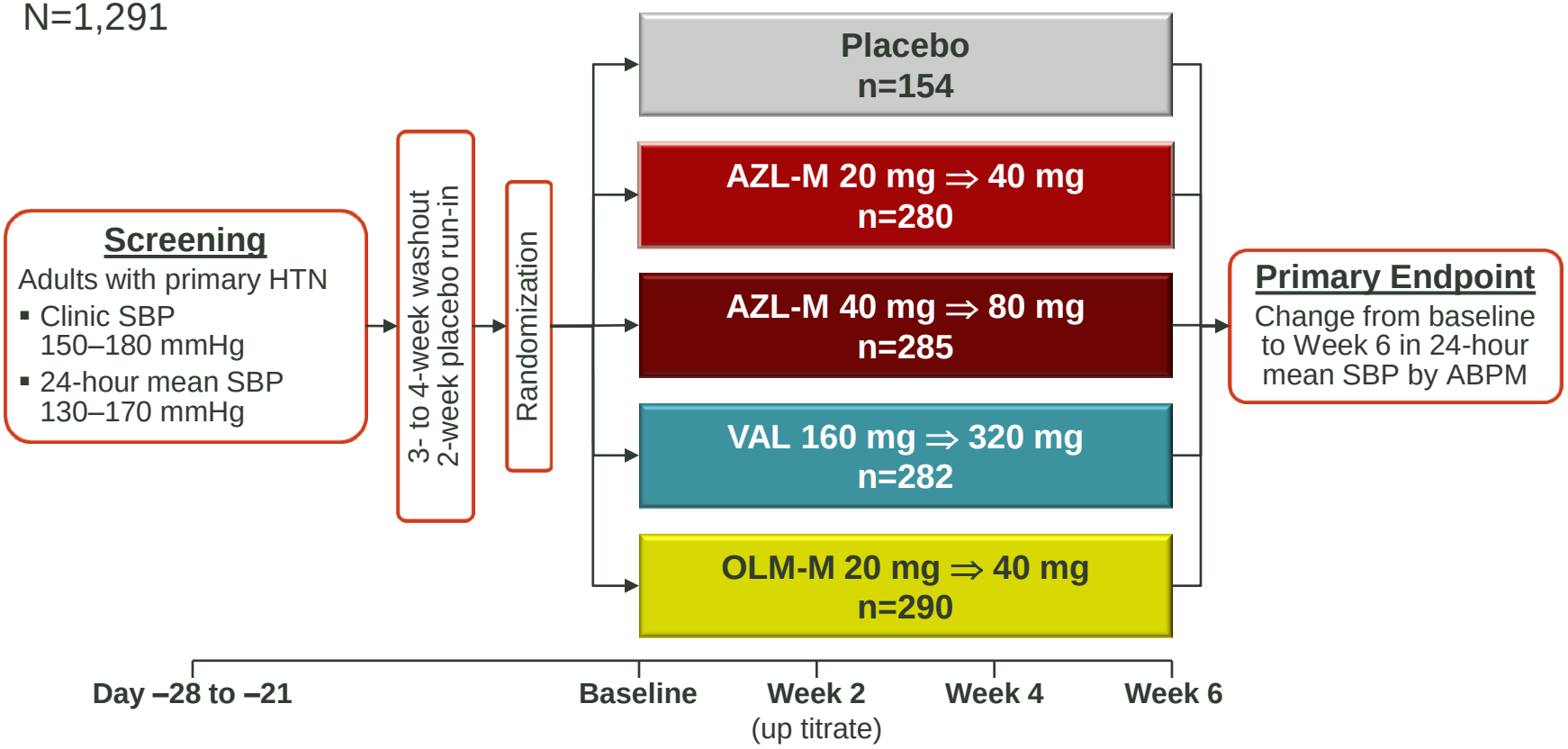
- Approval Letter(s) (PDF)
- Summary Review (PDF)
- Officer/Employee List (PDF)
- Office Director Memo (PDF)
- Printed Labeling (PDF)
- Medical Review(s) (PDF)
- Chemistry Review(s) (PDF)
- Pharmacology Review(s) (PDF)
- Statistical Review(s) (PDF)
- Clinical Pharmacology Biopharmaceutics Review(s) (PDF)
- Risk Assessment and Risk Mitigation Review(s) (PDF)
- Proprietary Name Review(s) (PDF)
- Other Review(s) (PDF)
- Administrative Document(s) & Correspondence (PDF)

Date created: April 4, 2011

Azilsartan Medoxomil vs. Valsartan and Olmesartan

Phase 3, multicenter, parallel-group, double-blind, randomized, placebo- and active-controlled 6-week trial

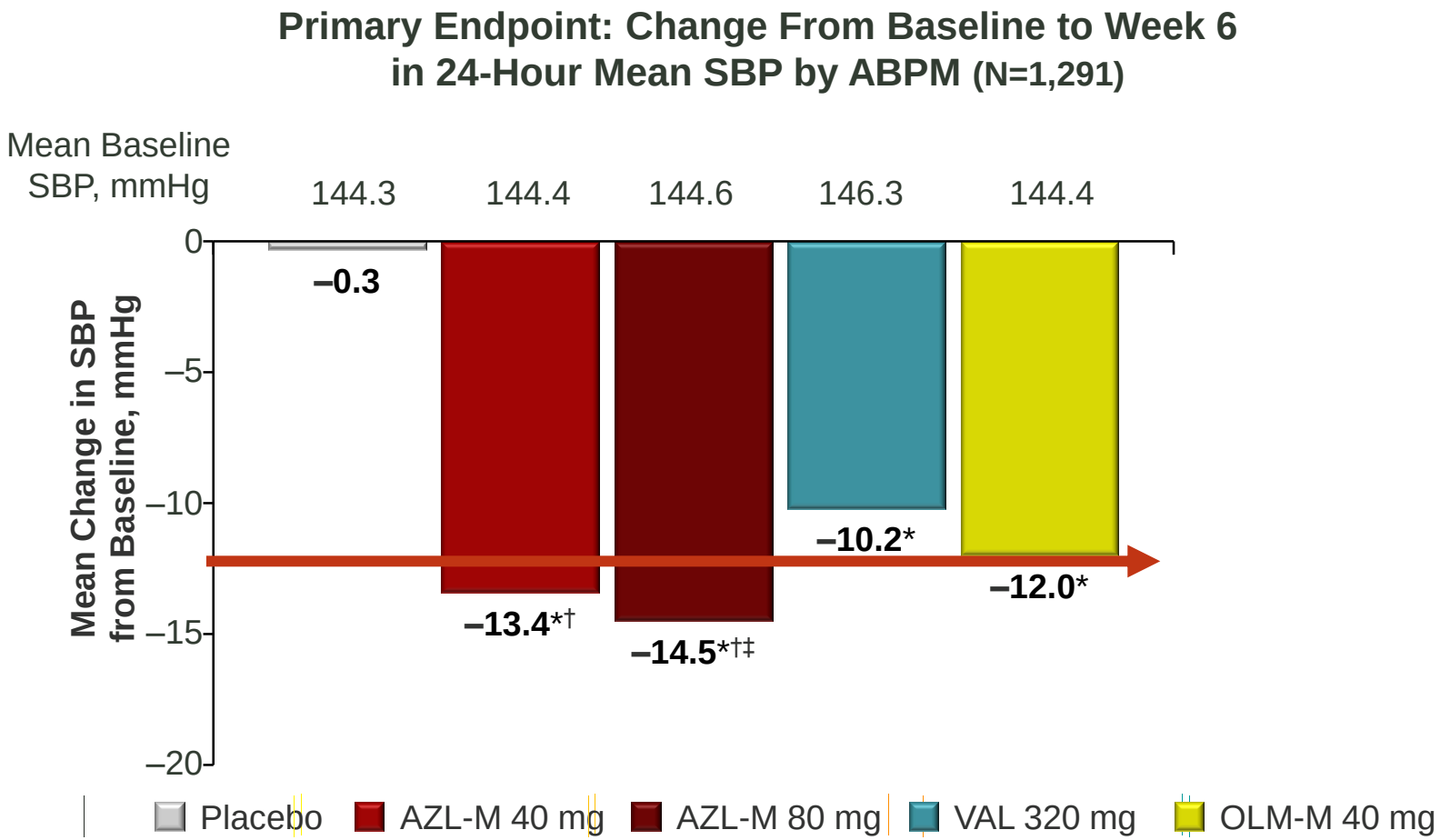
N=1,291



ABPM=ambulatory blood pressure monitoring; AZL-M=azilsartan medoxomil; HTN=hypertension; OLM-M=olmesartan medoxomil; SBP=systolic blood pressure; VAL=valsartan

White WB, et al. *Hypertension*. 2011;57:413-420.

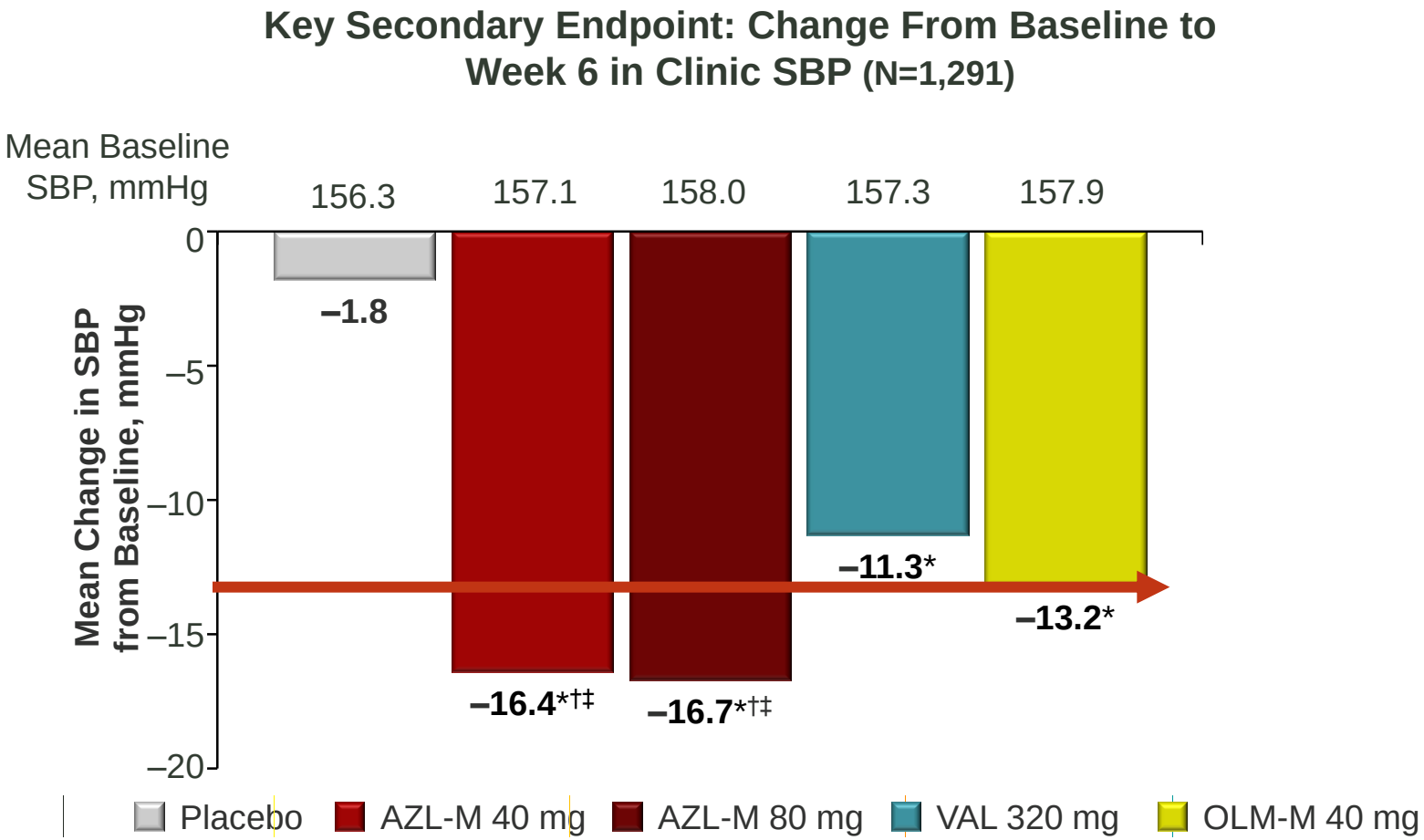
6주 후 활동 수축기 혈압 감소 비교



*Statistically significant difference ($P<0.05$) vs placebo; †Statistically significant difference ($P<0.05$) vs VAL;
‡Statistically significant difference ($P<0.05$) vs OLM-M
ABPM=ambulatory blood pressure monitoring; AZL-M=azilsartan medoxomil; OLM-M=olmesartan medoxomil; SBP=systolic blood pressure; VAL=valsartan

White WB, et al. *Hypertension*. 2011;57:413-420..

6주 후 진료실 수축기 혈압 감소 비교



*Statistically significant difference ($P<0.05$) vs placebo; †Statistically significant difference ($P<0.05$) vs VAL;
‡Statistically significant difference ($P<0.05$) vs OLM-M
AZL-M=azilsartan medoxomil; OLM-M=olmesartan medoxomil; SBP=systolic blood pressure; VAL=valsartan

White WB, et al. *Hypertension*. 2011;57:413-420.

Safety Profile

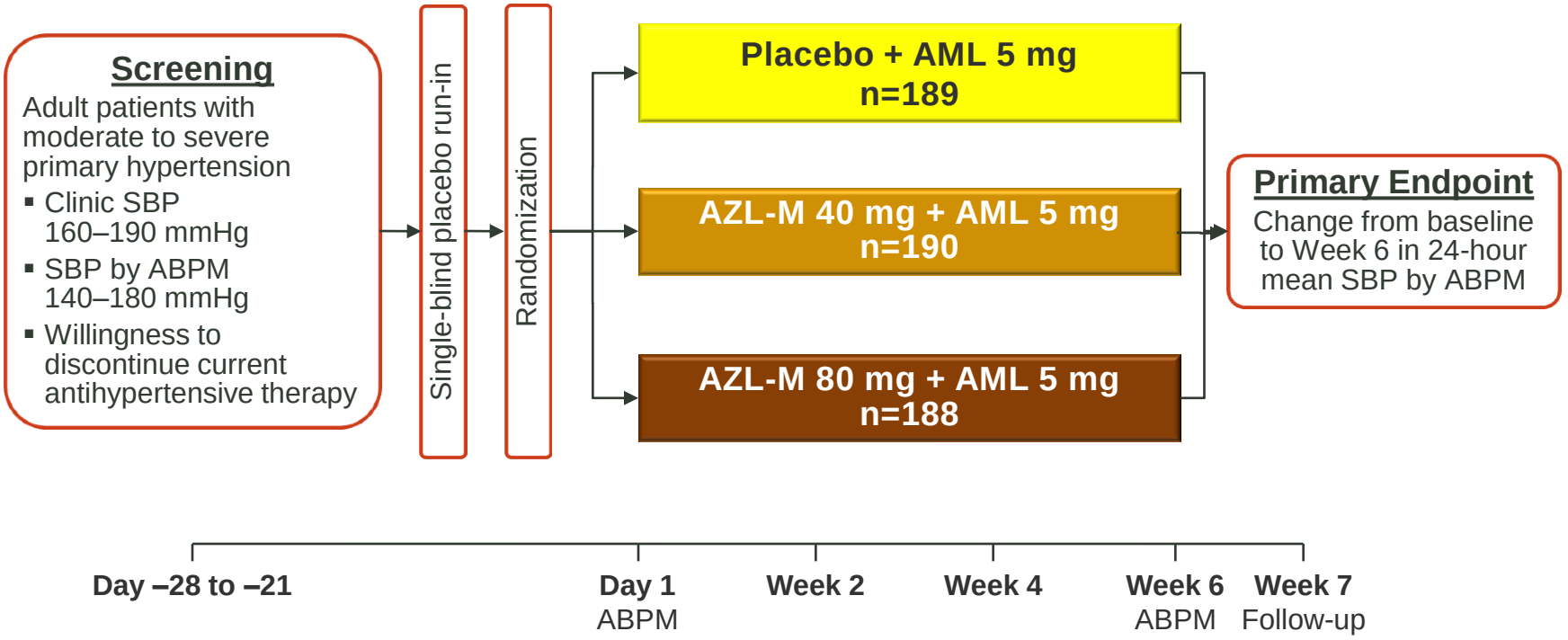
	Placebo (N=155)	AZL-M 40 mg (N=280)	AZL-M 80 mg (N=284)	VAL 320 mg (N=277)	OLM-M 80 mg (N=290)
Total AE, N (%)	**74** (47.7)	**134** (47.9)	**145** (51.1)	**131** (47.3)	**151** (52.1)
AE leading to discontinuation, N (%)	3 (1.9)	7 (2.5)	8 (2.8)	7 (2.5)	6 (2.1)
Serious AE, N (%)	2 (1.3)	2 (0.7)	3 (1.1)	3 (1.1)	4 (1.4)
Treatment emergent events in >3% of any treatment groups, N (%)					
Headache	14 (9.0)	18 (6.4)	12 (4.2)	21 (7.6)	23 (7.9)
Dizziness	4 (2.6)	10 (3.6)	10 (3.5)	5 (1.8)	9 (3.1)
Urinary tract infection	5 (3.2)	9 (3.2)	6 (2.1)	3 (1.1)	6 (2.1)
Fatigue	1 (0.6)	3 (1.1)	7 (2.5)	4 (1.4)	13 (4.5)
Edema, peripheral	1 (0.6)	5 (1.8)	4 (1.4)	9 (3.2)	8 (2.8)
Diarrhea	2 (1.3)	3 (1.1)	12 (4.2)	4 (1.4)	5 (1.7)
Laboratory abnormalities of interest					
Creatinine > 1.5 baseline	0 (0)	2 (0.7)	3 (1.1)	1 (0.4)	2 (0.7)
Increased liver enzymes	5 (3.3)	8 (2.9)	15 (5.5)	17 (6.1)	14 (4.9)
Potassium> 6.0 mmol/L	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

AE = Adverse Event *Data show aspartate aminotransferase, alanine aminotransferase, and gamma glutamyl transpeptidase 3 times upper limit of normal

White WB, et al. *Hypertension*. 2011;57:413-420

Azilsartan Medoxomil + Amlodipine

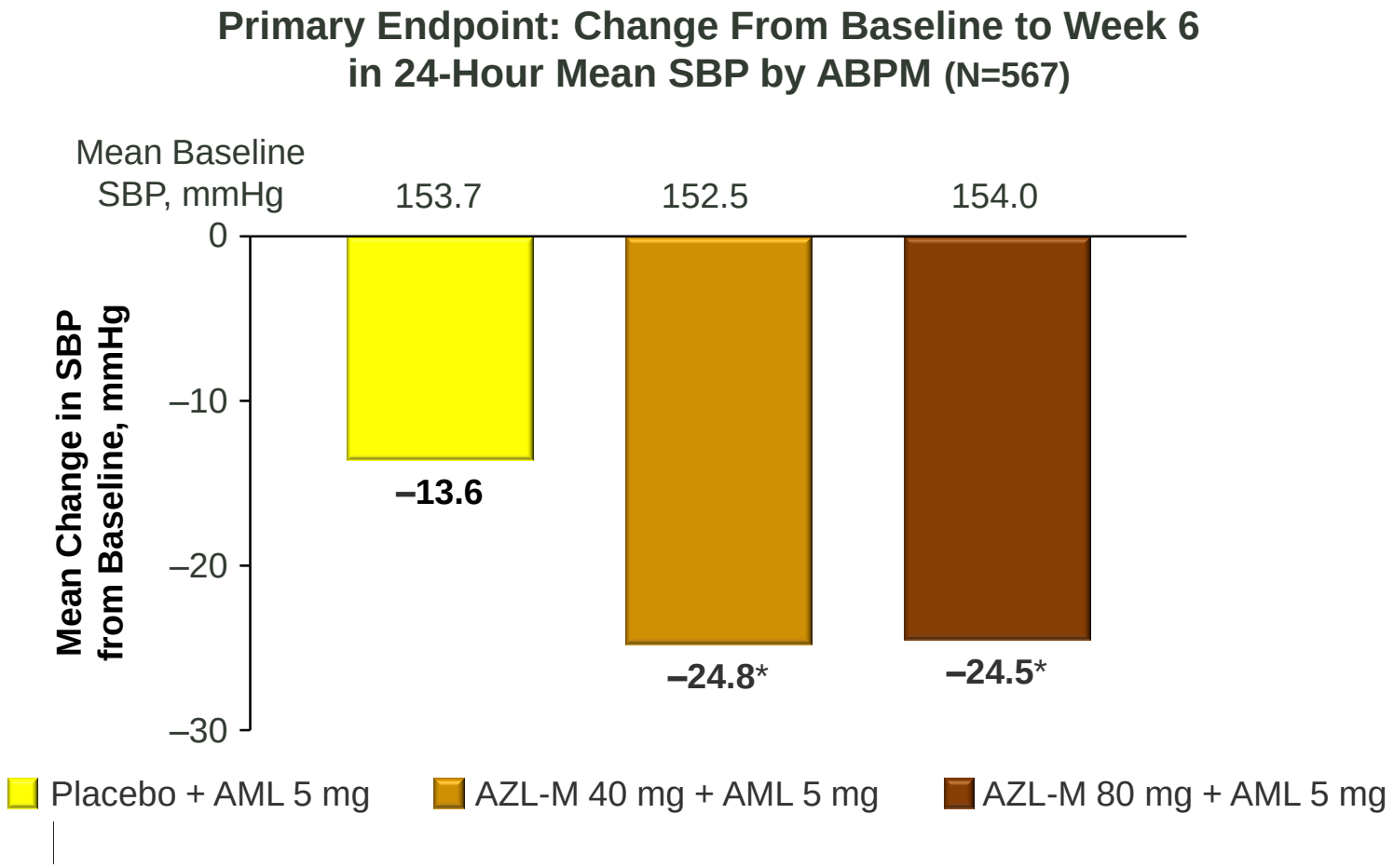
Phase 3, multicenter, double-blind, randomized placebo-controlled trial
N=567



ABPM=ambulatory blood pressure monitoring; AML=amlodipine; AZL-M=azilsartan medoxomil; SBP=systolic blood pressure

Weber MA, et al. Blood Press Monit. 2014;19(2):90-97.

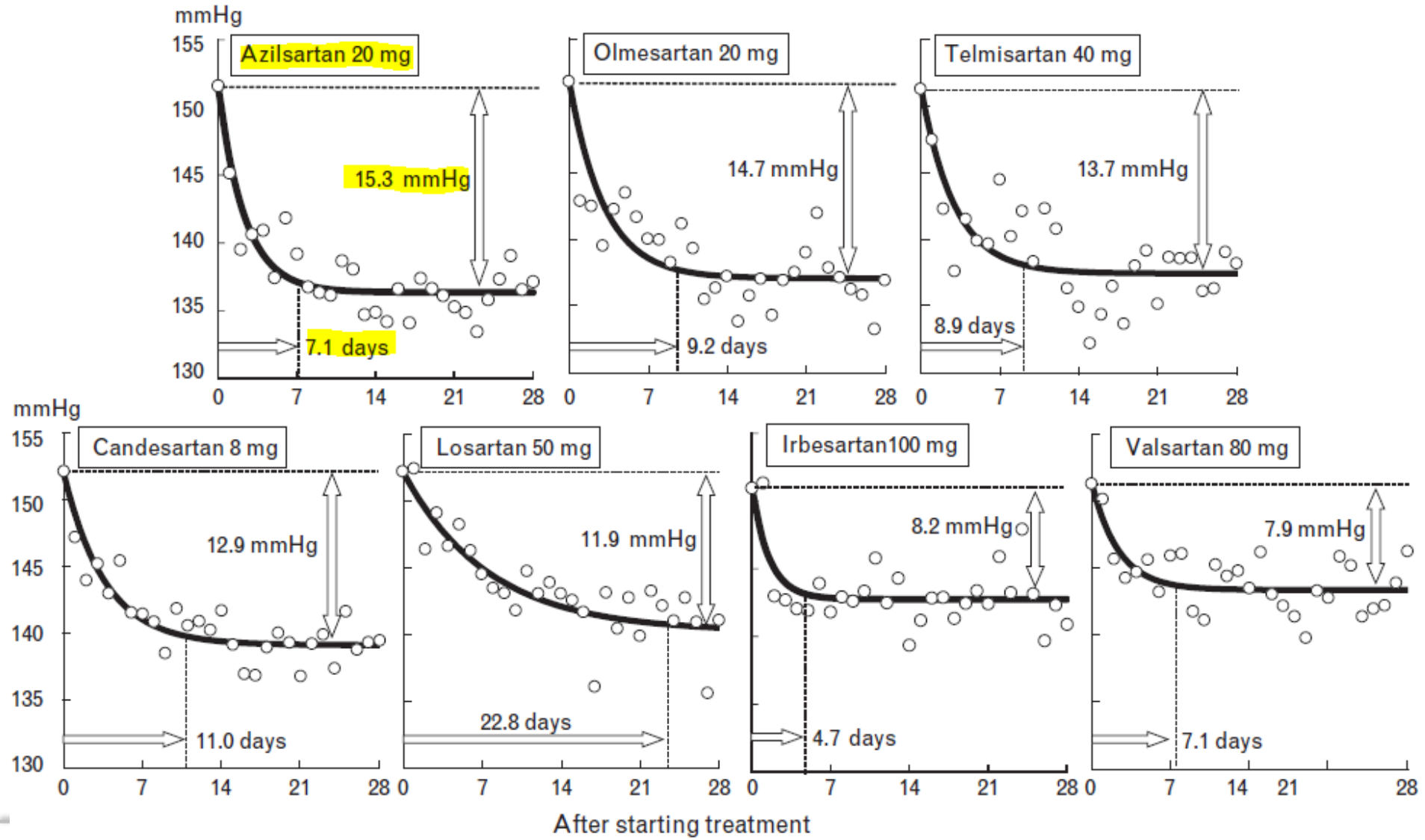
6주 후 활동 수축기 혈압 감소 비교



*Statistically significant difference (*P*<0.05) vs placebo + AML
ABPM=ambulatory blood pressure monitoring; AZL-M=azilsartan medoxomil; CLD=chlorthalidone; SBP=systolic blood pressure

Weber MA, et al. Blood Press Monit. 2014;19(2):90-97.

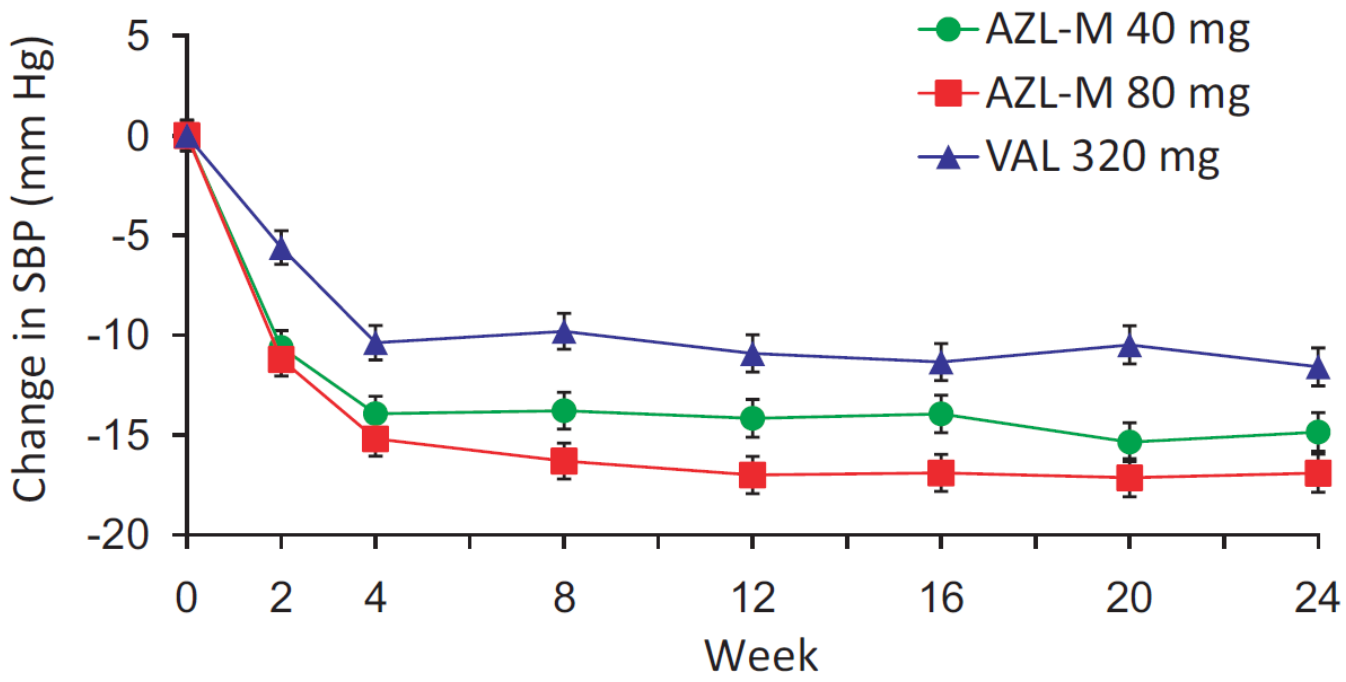
Blood pressure-lowering effect and stabilization time



J Hypertens 2016;34(6):1218-23

Rapid BP reduction vs. Valsartan

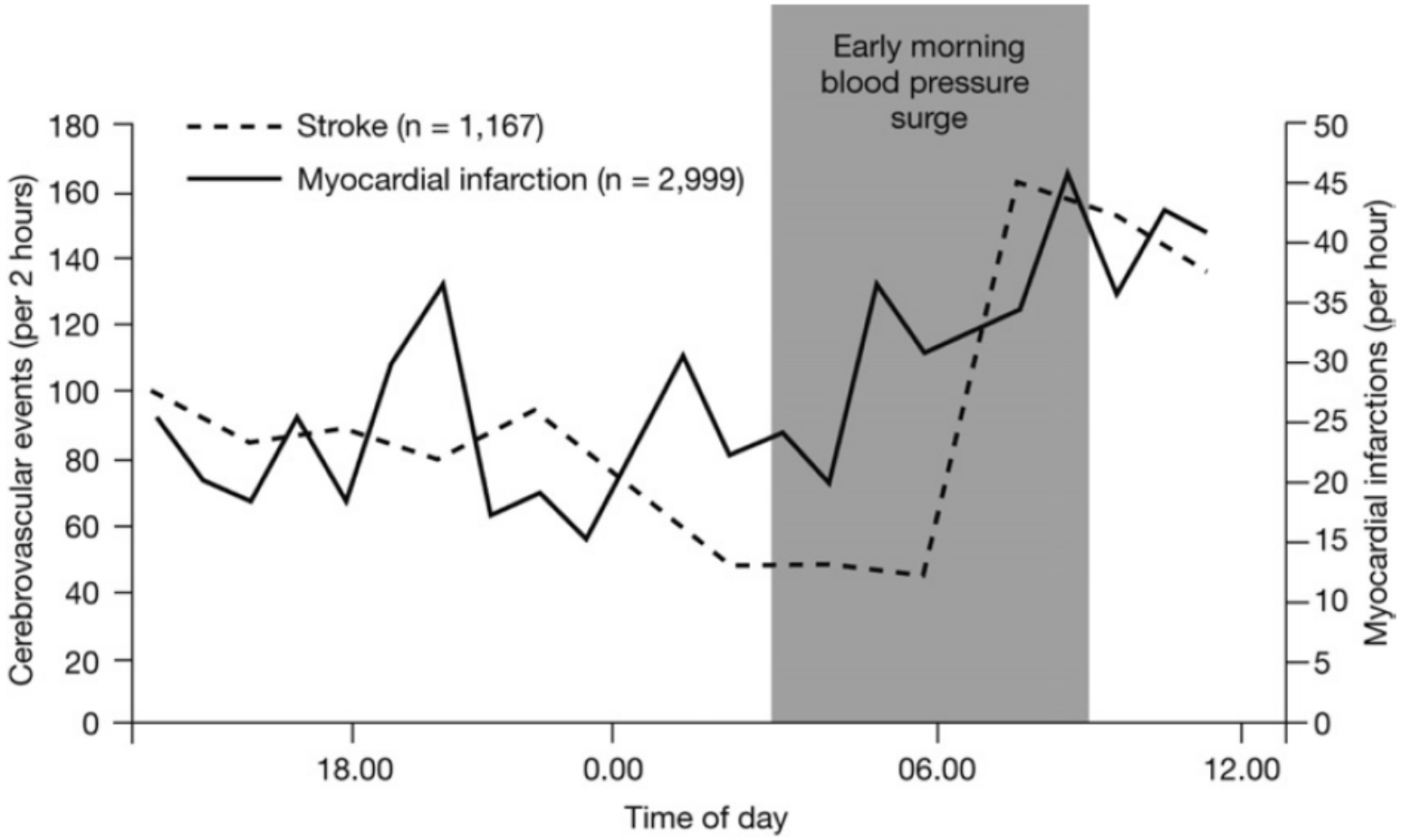
Change From Baseline
clinic systolic blood pressure by study visit (N=984)



AZL-M=azilsartan medoxomil; SBP=systolic blood pressure; VAL=valsartan; BP=blood pressure

Sica D, et al. *J Clin Hypertens (Greenwich).* 2011;13:467-472.

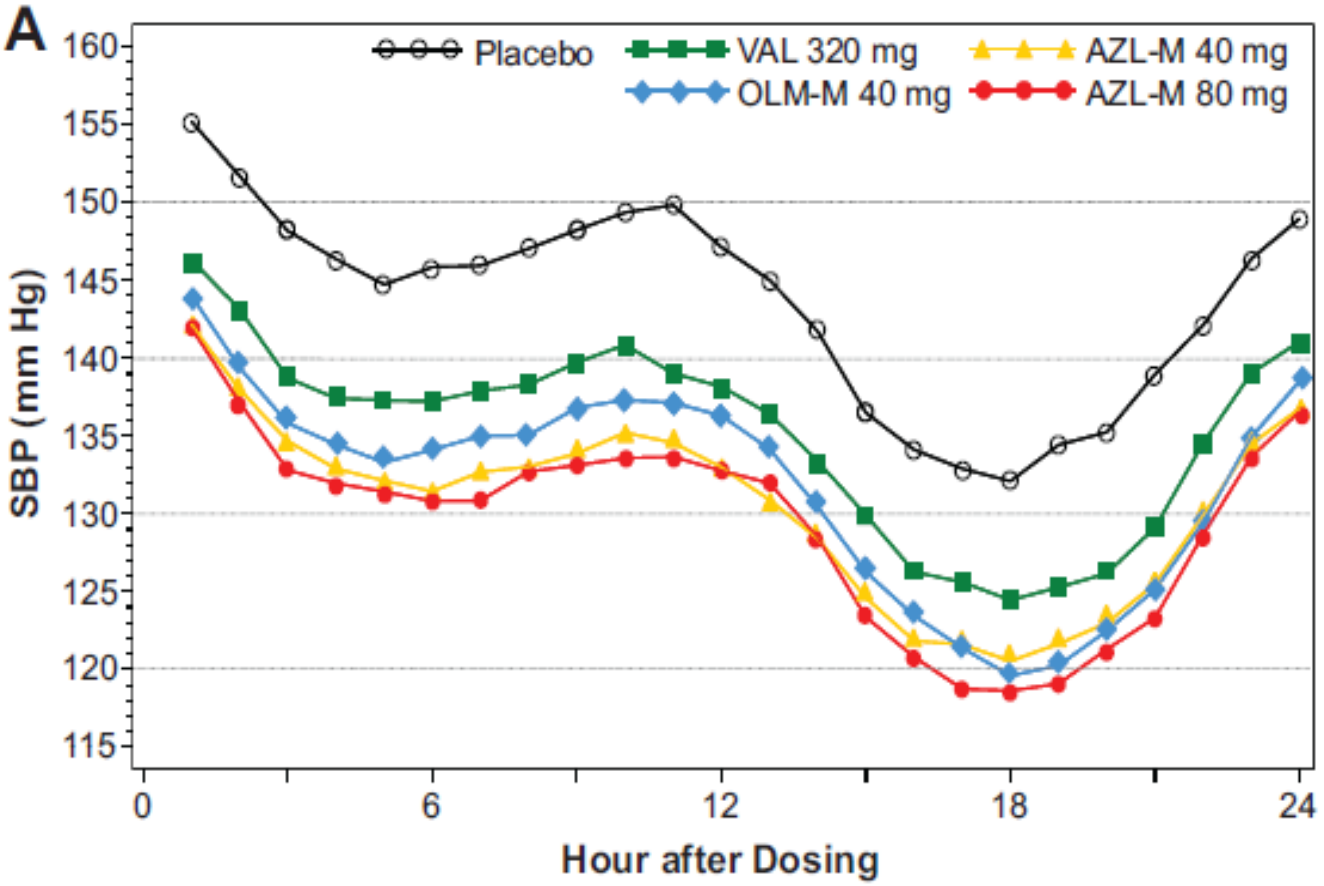
Morning BP surge correlates with CV risk



J Am Soc Hypertens 2008;2(4suppl):S16-22

24시간 혈압조절 비교

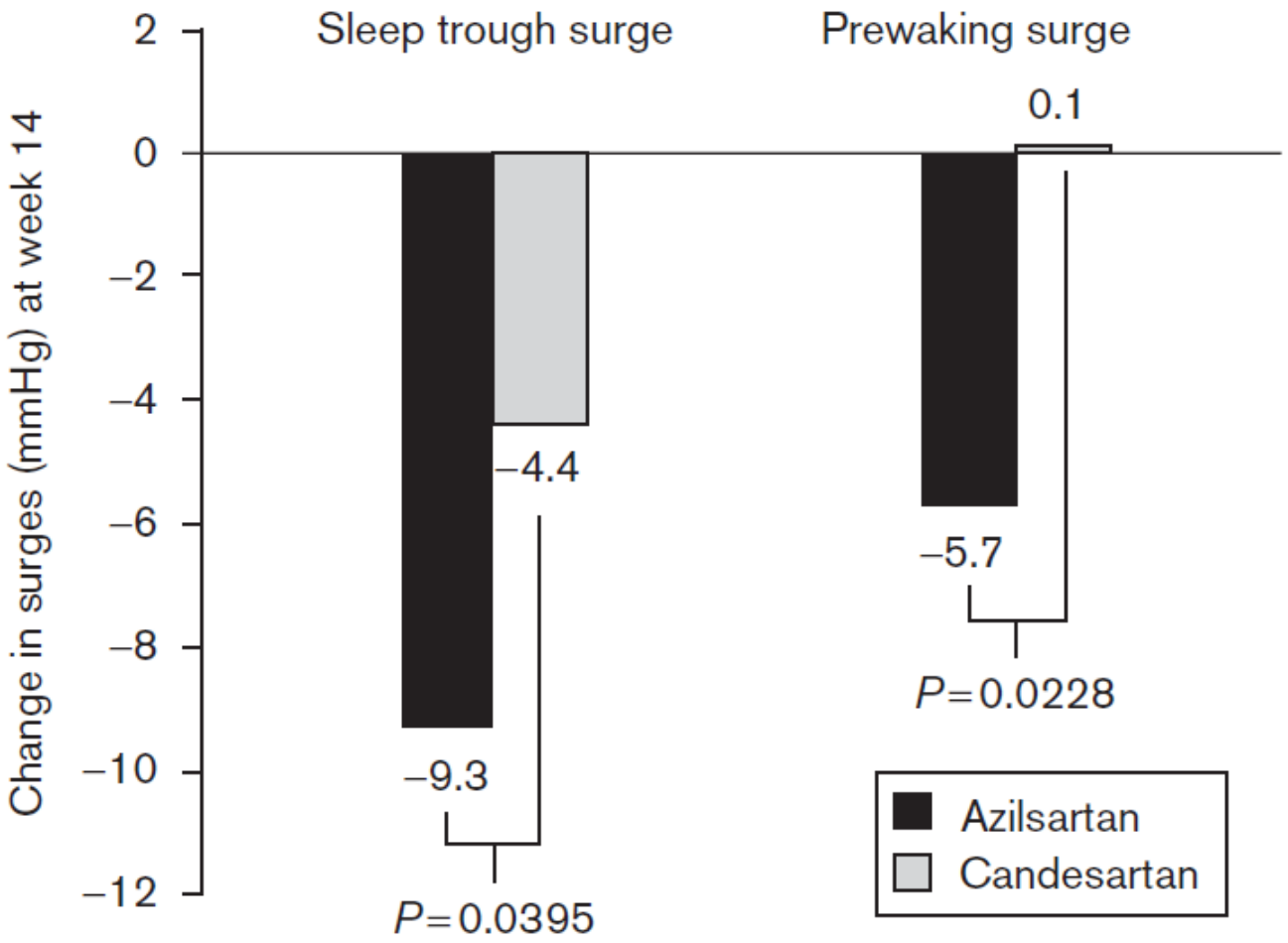
Azilsartan Medoxomil vs. Valsartan and Olmesartan



AZL-M=azilsartan medoxomil; OLM-M=olmesartan medoxomil; SBP=systolic blood pressure; VAL=valsartan

White WB, et al. *Hypertension*. 2011;57:413-420.

Morning blood pressure surge

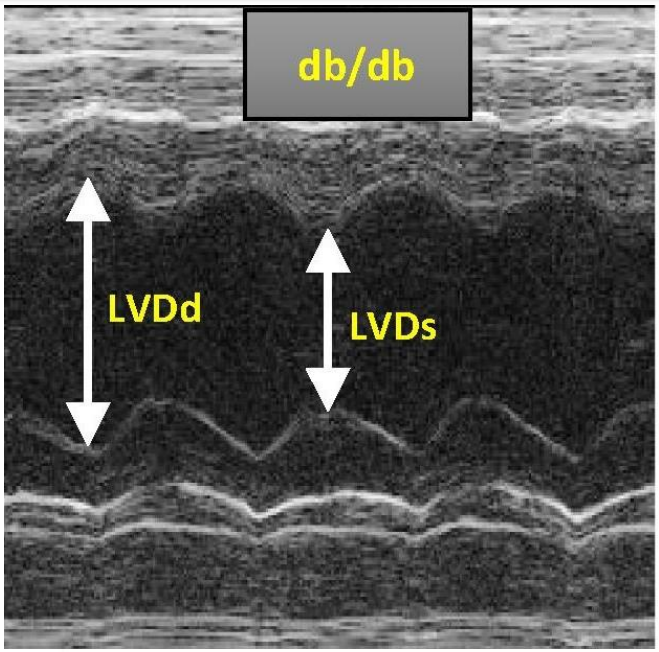


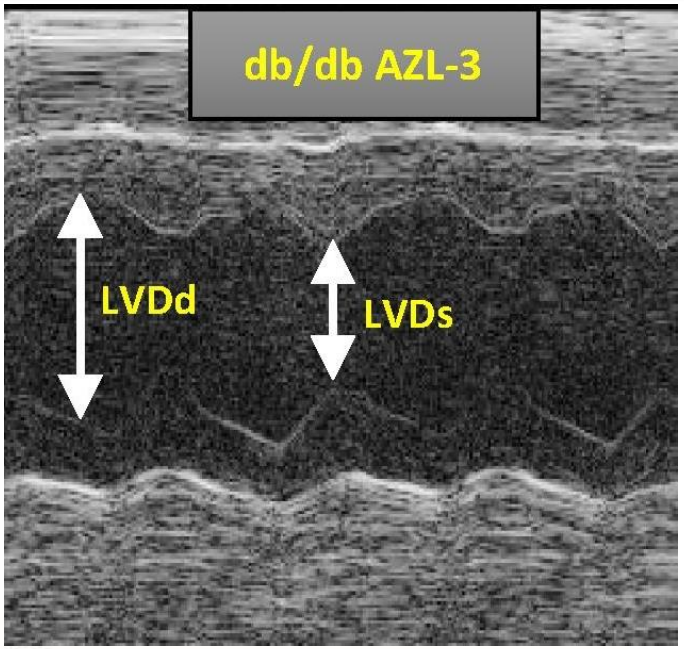
Blood Press Monit 2014;19(3):164-169.

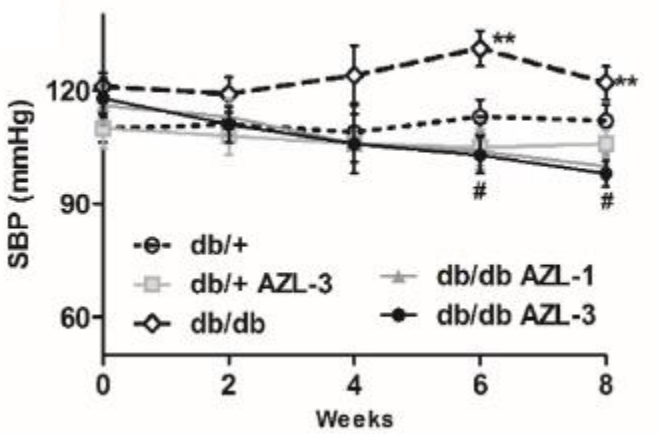
Preclinical Data

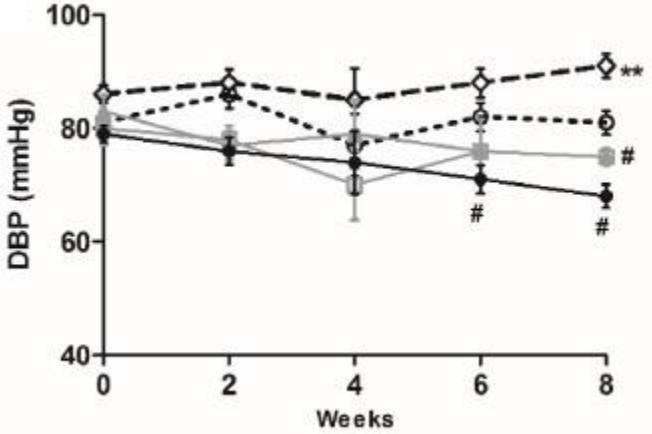
- Azilsartan ameliorates diabetic cardiomyopathy in db/db mice

Azilsartan improves cardiac function in db/db mice





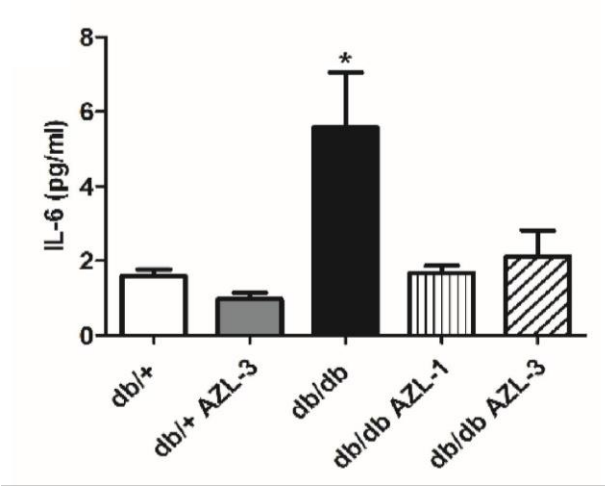


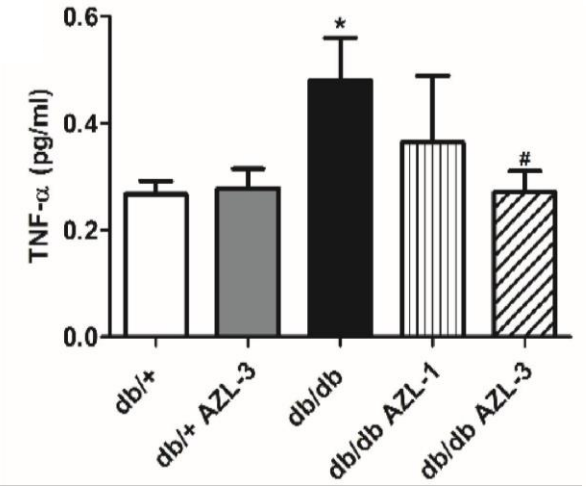


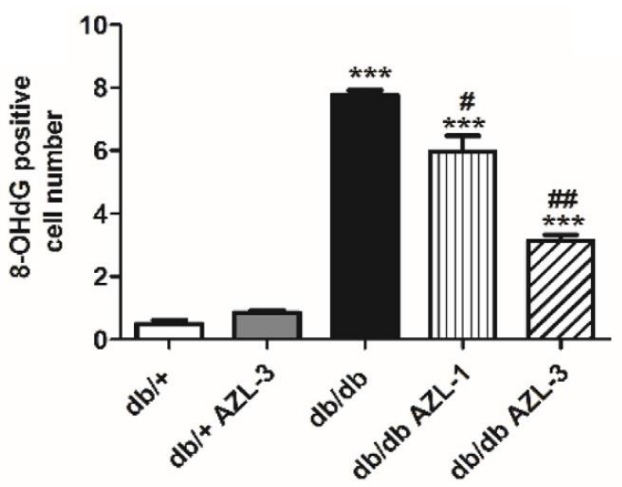
*P < 0.05, **P < 0.01, ***P < 0.001 vs vehicle-treated db/+; #P < 0.05, ##P < 0.01, ###P < 0.001 vs vehicle-treated db/db.

Sukumaran V, et al. Biochemical Pharmacology Available online 5 August 2017 In Press

Azilsartan **reduces inflammatory cytokines** and protects against oxidative stress







*P < 0.05 vs vehicle-treated db/+; #P < 0.05 vs vehicle-treated db/db.

Sukumaran V, et al. Biochemical Pharmacology Available online 5 August 2017 In Press

Satoh M et al.J Hypertens 2016;34(6):1218-23

내게 필요한 혈압약은...

- ❖ 빠르고 강력한 혈압 강하효과
- ❖ 안정적이고 지속적인 혈압 강하효과
- ❖ 장기 보호 효과와 같은 추가 효과
- ❖ 환자의 생명 연장효과

Thank You for Your Attention

이달비

스무날비, 삼복비, 추석비, 겨울비
복비, 약비, 떡비
이슬비, 가랑비, 소슬비, 보슬비, 소나기