

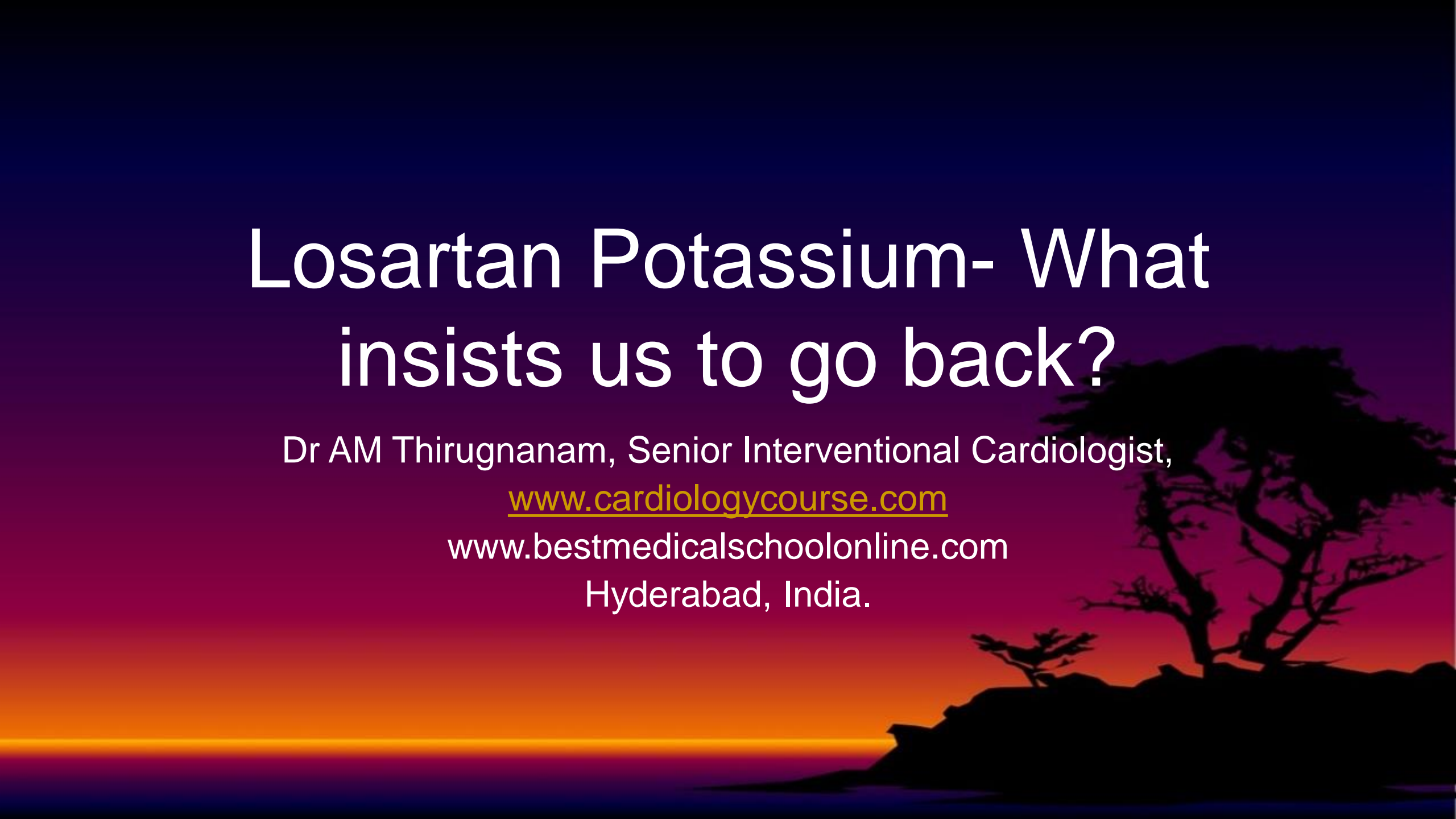
Losartan Potassium- What insists us to go back?

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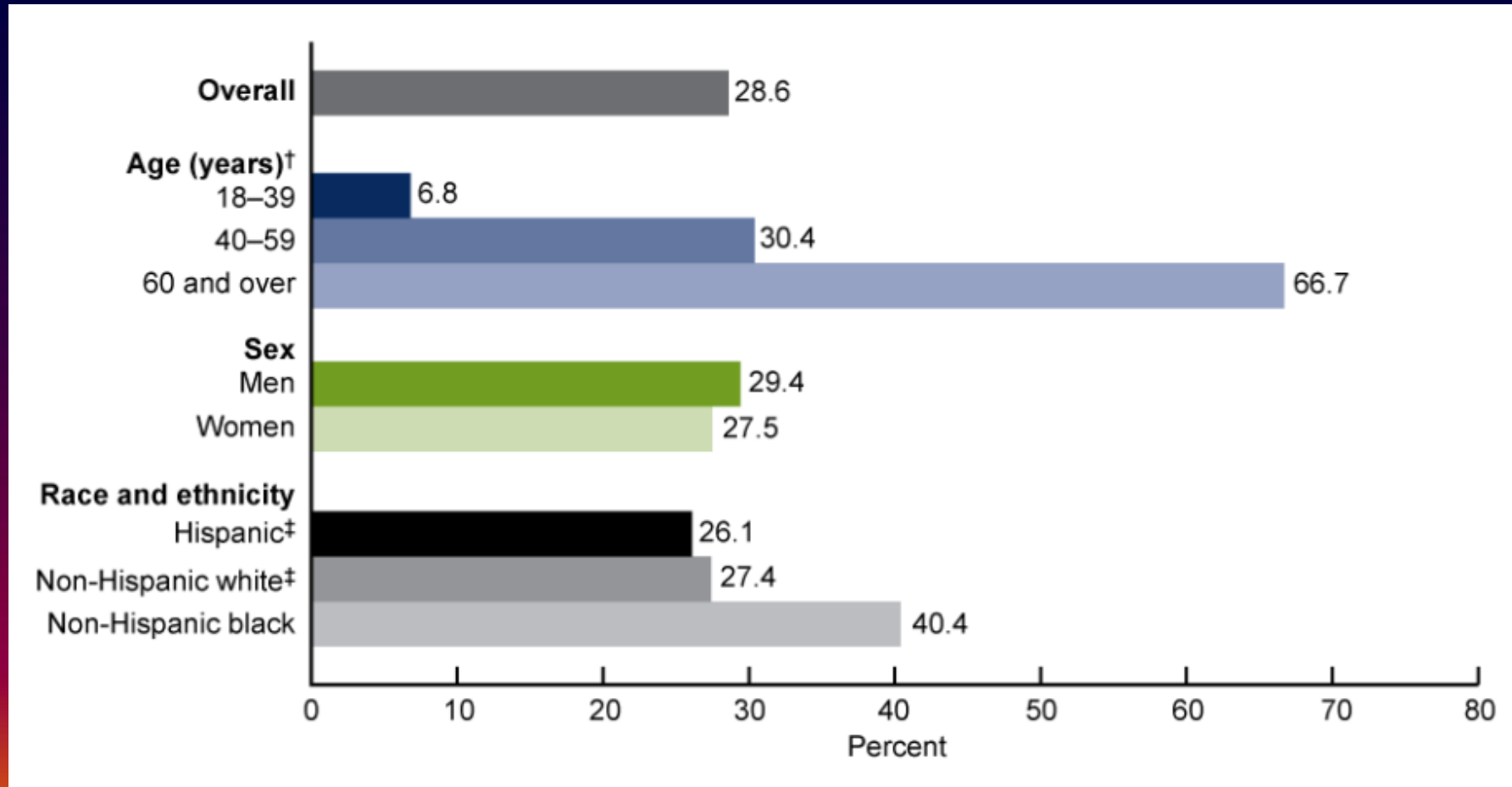


Non pharmacological Treatment of hypertension



High Blood Pressure*: Prevalence in Different Patient Groups

National Health and Nutrition Examination Survey (NHANES)

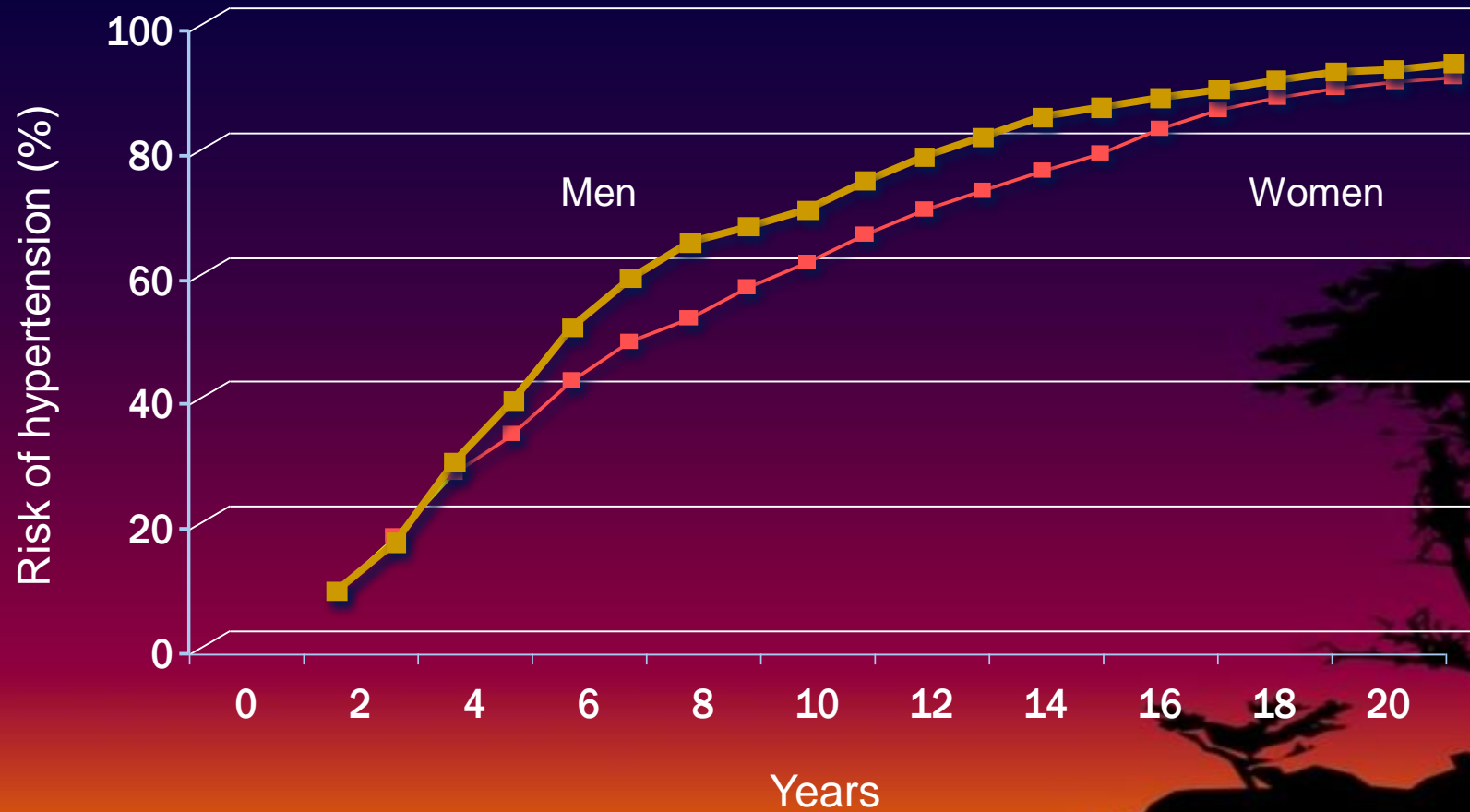


*High blood pressure defined as blood pressure $\geq 140/90$ mmHg or treatment

Source: Yoon SS et al. NCHS Data Brief 2012;107:1-7

High Blood Pressure: Lifetime Risk*

Framingham Heart Study



*Residual lifetime risk of developing hypertension among people with blood pressure <140/90 mmHg starting at age 55-65 years

Source: Vasani RS et al. *JAMA* 2002; 287:1003-1010

JNC VII Guidelines: Measurement of Blood Pressure

Method

Brief Description

In-office

Two readings, 5 minutes apart, sitting in chair
Confirm elevated reading in contralateral arm

Ambulatory BP
monitoring

Indicated for evaluation of “white-coat” HTN.
Absence of 10–20% BP decrease during sleep
indicates increased CVD risk

Self-measurement

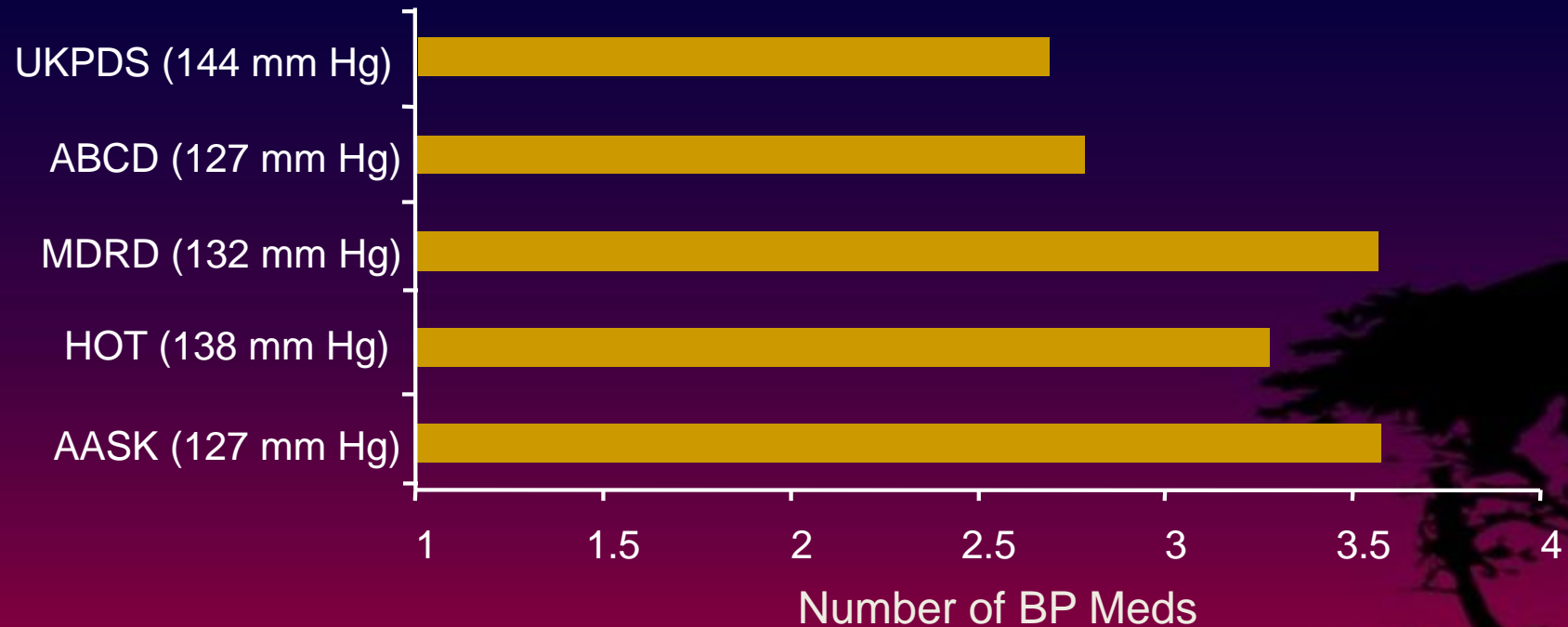
Provides information on response to treatment.
May help improve adherence to treatment and
evaluate “white-coat” HTN

BP=Blood pressure, CVD=Cardiovascular
disease, HTN=Hypertension

Source: Chobanian AV et al. *JAMA* 2003;289:2560-2572

High Blood Pressure Evidence: Number of Medications Needed

Trial (SBP Achieved)



AASK=African American Study of Kidney Disease and Hypertension,
ABCD=Appropriate Blood Pressure Control in Diabetes, BP=Blood pressure,
HOT=Hypertension Optimal Treatment, MDRD=Modification of Dietary Protein in Renal
Disease, SBP=Systolic blood pressure, UKPDS=UK Prospective Diabetes Study

Source: Abbott K et al. *J Clin Pharmacology* 2004;44:431-438

JNC VII Guidelines: Causes of Secondary Hypertension

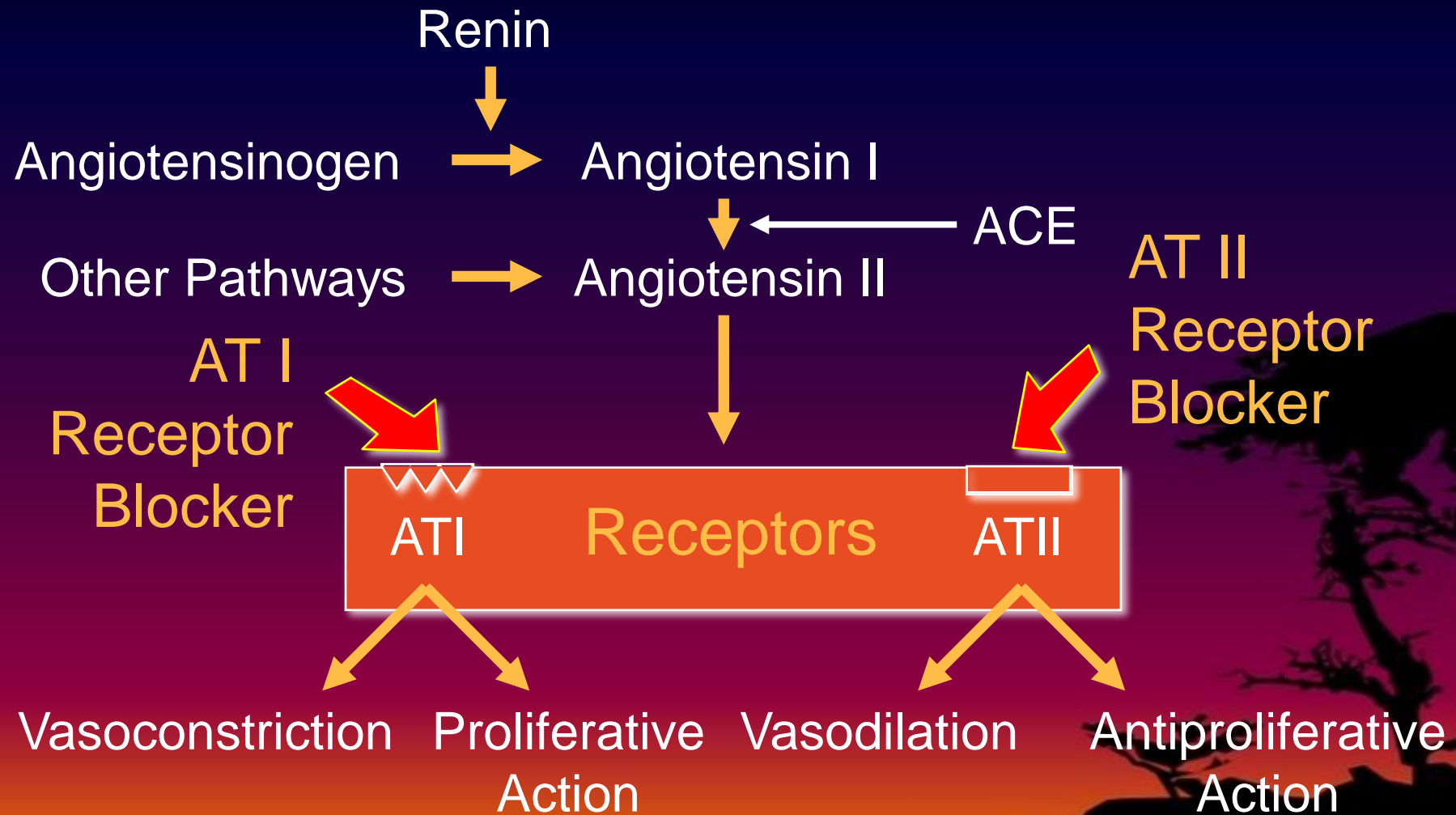
Medical Conditions
Chronic kidney disease
Primary hyperaldosteronism
Reno vascular disease
Chronic steroid therapy
Cushing's syndrome
Pheochromocytoma
Aortic Coarctation
Thyroid or parathyroid disease
Sleep apnea

Drugs
NSAIDs
Oral contraceptives
Adrenal steroids
Sympathomimetic
Cyclosporine or tacrolimus
Erythropoietin
Ephedra, mu huang, bitter orange
Cocaine or amphetamines
Alcohol

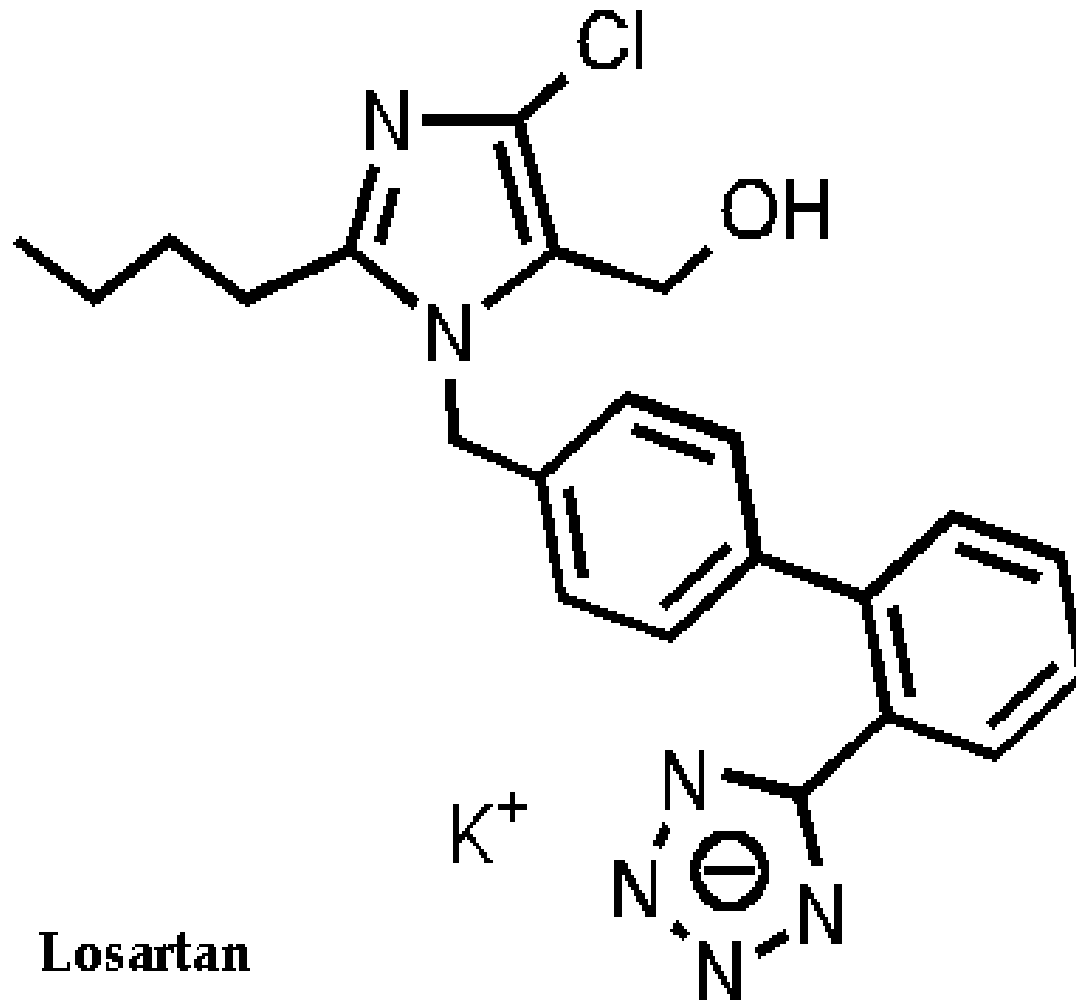
NSAIDs=Non-steroidal anti-inflammatory drugs

Source: Chobanian AV et al. *JAMA* 2003;289:2560-2572

Angiotensin Receptor Blocker: Mechanism of Action



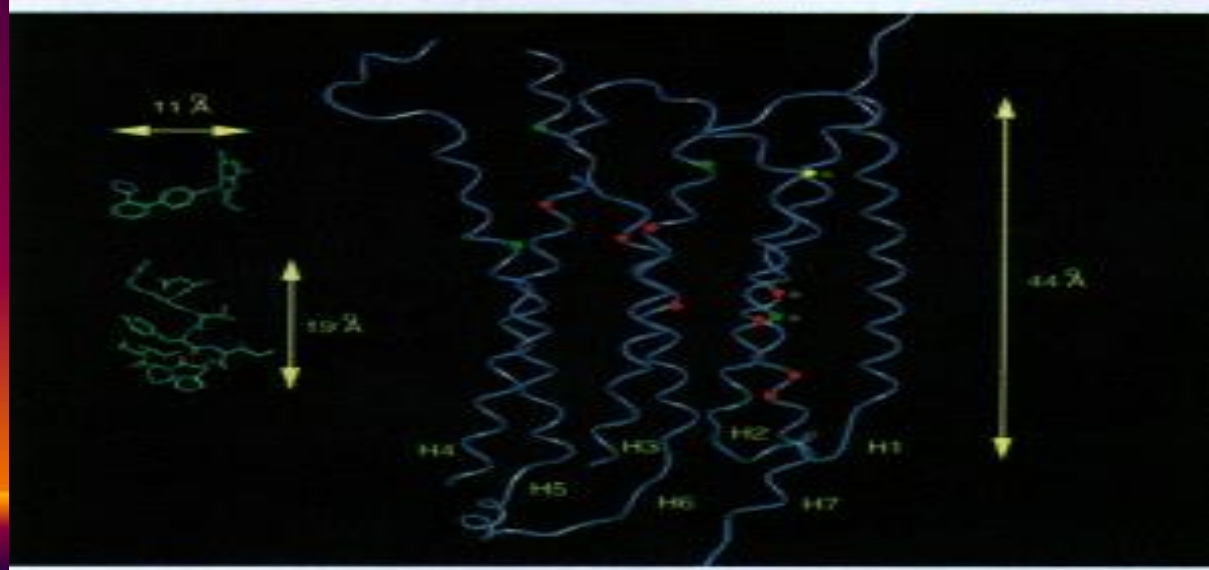
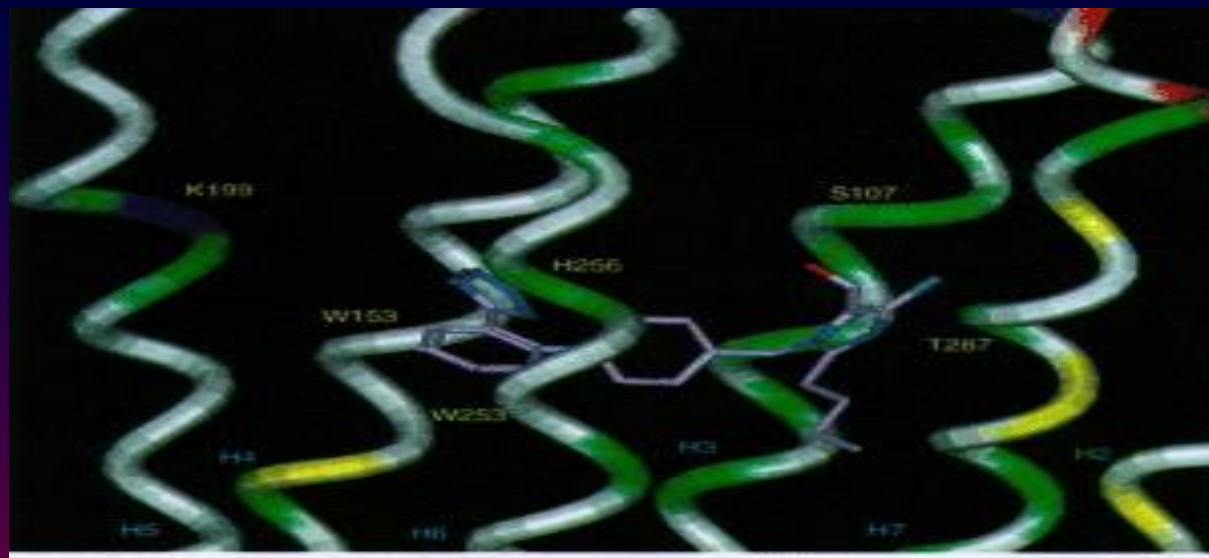
Molecular Structure of Losartan Potassium



Losartan

Taken from www.pharmazie.uni-marburg.de/Neue.Arzneimittel/Losartan.html

3D Structure Picture of Losartan Potassium



Previous Trials on Losartan Potassium

Losartan ELITE (1997)²³;

ELITE II (2000)²⁴;

LIFE (2000)^{25,26};

RENAAL (2001)²⁷;

OPTIMAAL (2002)²⁸;

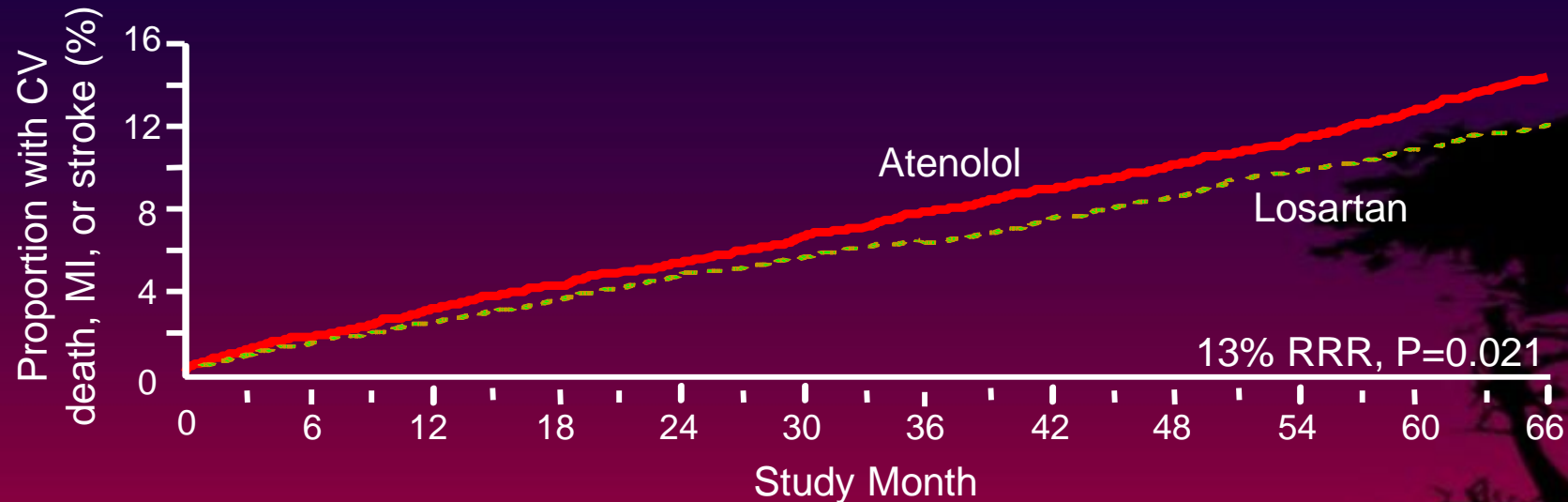
HEALL (2009)²⁹



Blood Pressure Lowering Therapy Evidence: Primary Prevention

Losartan Intervention for Endpoint (LIFE) Reduction in Hypertension Study

9,193 high-risk hypertensive* patients with LVH randomized to losartan (100 mg) or atenolol (100 mg) for 5 years



An ARB provides greater efficacy in patients with LVH

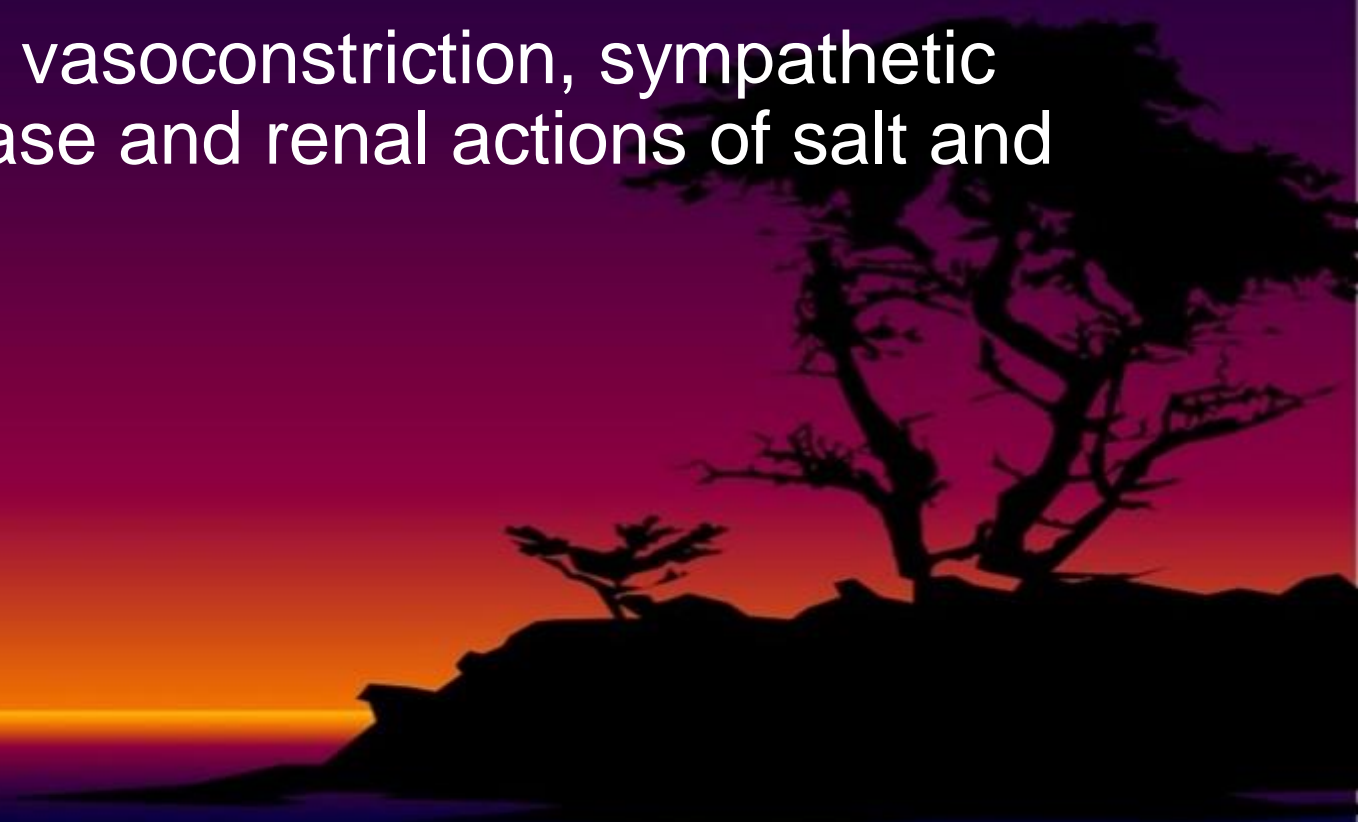
*Defined by SBP=160-200 mmHg or DBP=95-115 mmHg

ARB=Angiotensin receptor blocker, CV=Cardiovascular,
DBP=Diastolic blood pressure, LVH=Left ventricular hypertrophy,
MI=Myocardial infarction, SBP=Systolic blood pressure

Source: Dahlöf B et al. *Lancet* 2002;359:995-1003

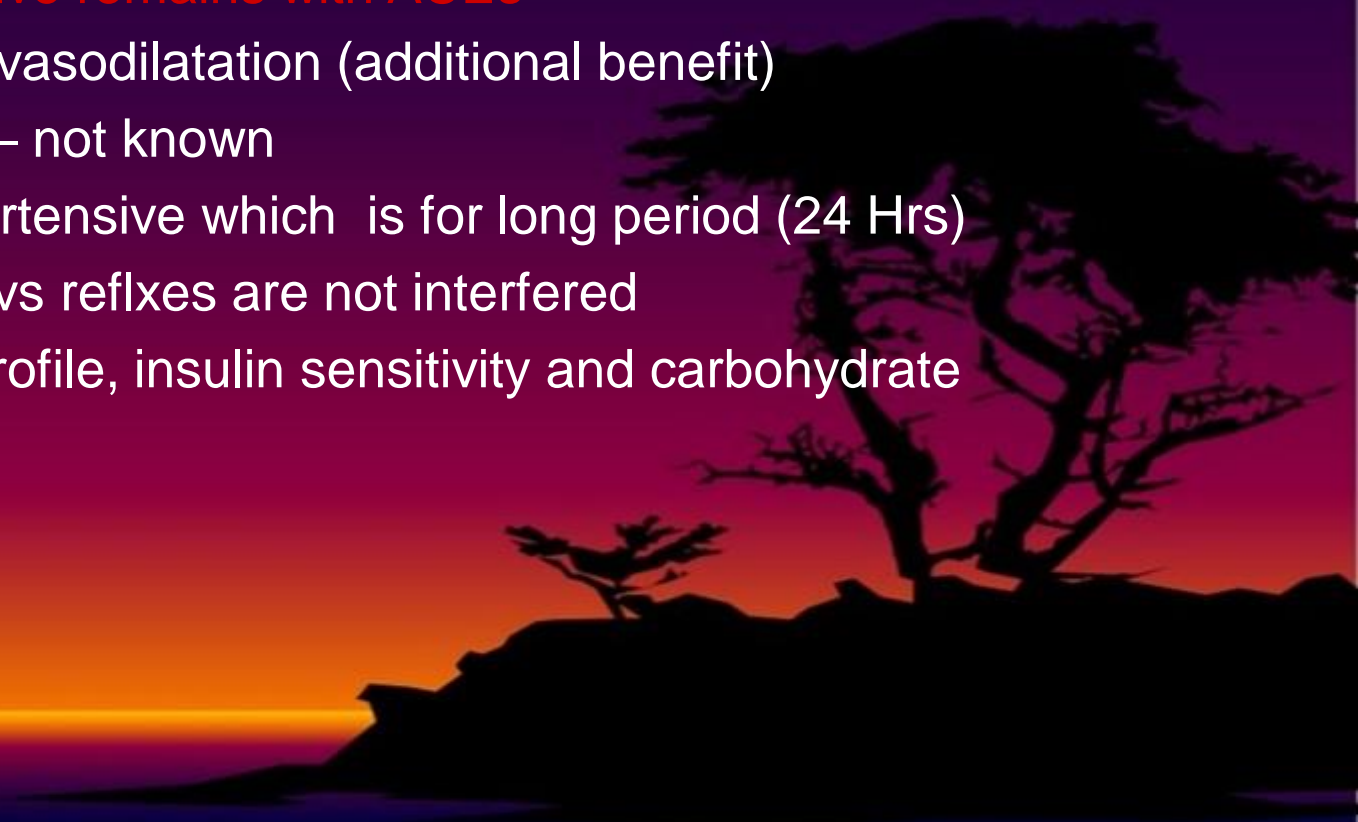
Angiotensin Receptor Blockers (ARBs) - Losartan

- Competitive antagonist and inverse agonist of AT1 receptor
- Does not interfere with other receptors except TXA2
- Blocks all the actions of A-II - vasoconstriction, sympathetic stimulation, aldosterone release and renal actions of salt and water reabsorption
- No inhibition of ACE



Losartan

- Theoretical superiority over ACEIs:
 - Cough is rare – no interference with bradykinin and other ACE substrates
 - Complete inhibition of AT1 – **alternative remains with ACEs**
 - Result in indirect activation of AT2 – vasodilatation (additional benefit)
 - Clinical benefit of ARBs over ACEIs – not known
- However, losartan decreases BP in hypertensive which is for long period (24 Hrs)
 - heart rate remains unchanged and cvs reflexes are not interfered
 - no significant effect in plasma lipid profile, insulin sensitivity and carbohydrate tolerance etc
 - Mild uricosuric effect

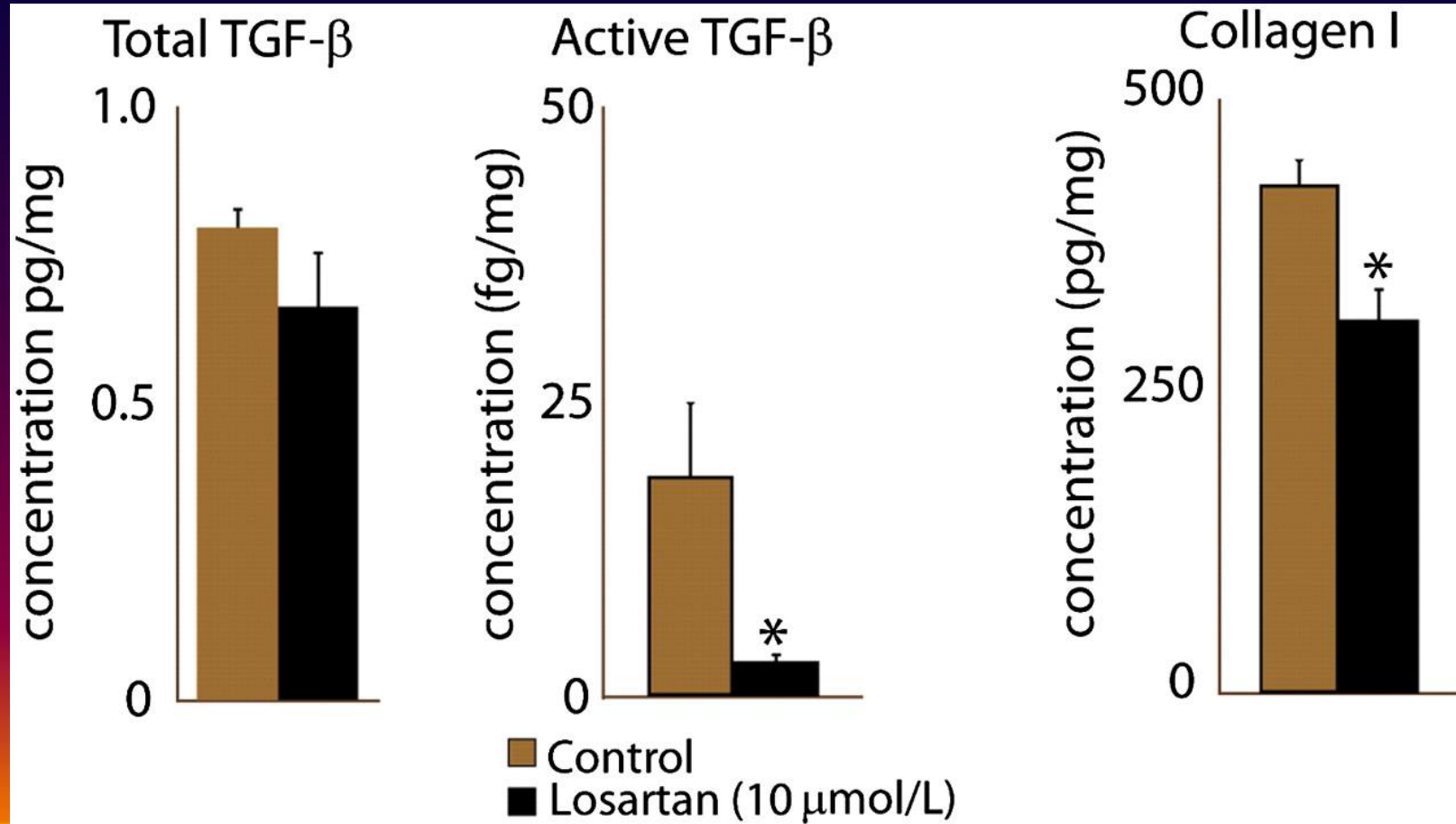


Losartan

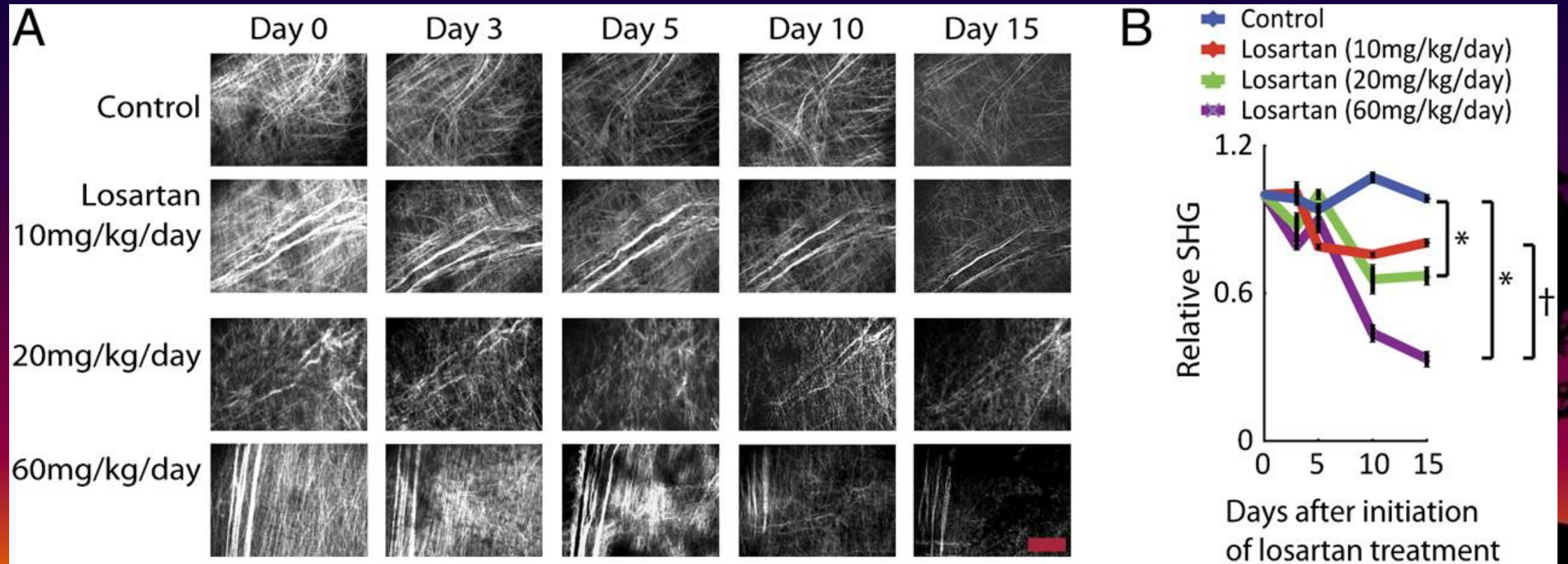
- Pharmacokinetic:
 - Absorption not affected by food but unlike ACEIs its bioavailability is low
 - High first pass metabolism
 - Carboxylated to active metabolite E3174
 - Highly bound to plasma protein
 - Do not enter brain
- Adverse effects:
 - Foetopathic like ACEIs – not to be administered in pregnancy
 - Rare 1st dose effect hypotension
 - Low dry cough
 - Lower incidence of angioedema
- Available as 25 and 50 mg tablets



Significantly reduces TGF-beta, Collagen I



Collagen level Reduction at high doses in Tumour



Losartan reduces inflammatory markers

- IL-6,
- TNF-alpha
- Endothelin level- (use in PAH)
- Thromboxane level- (use in CHD)



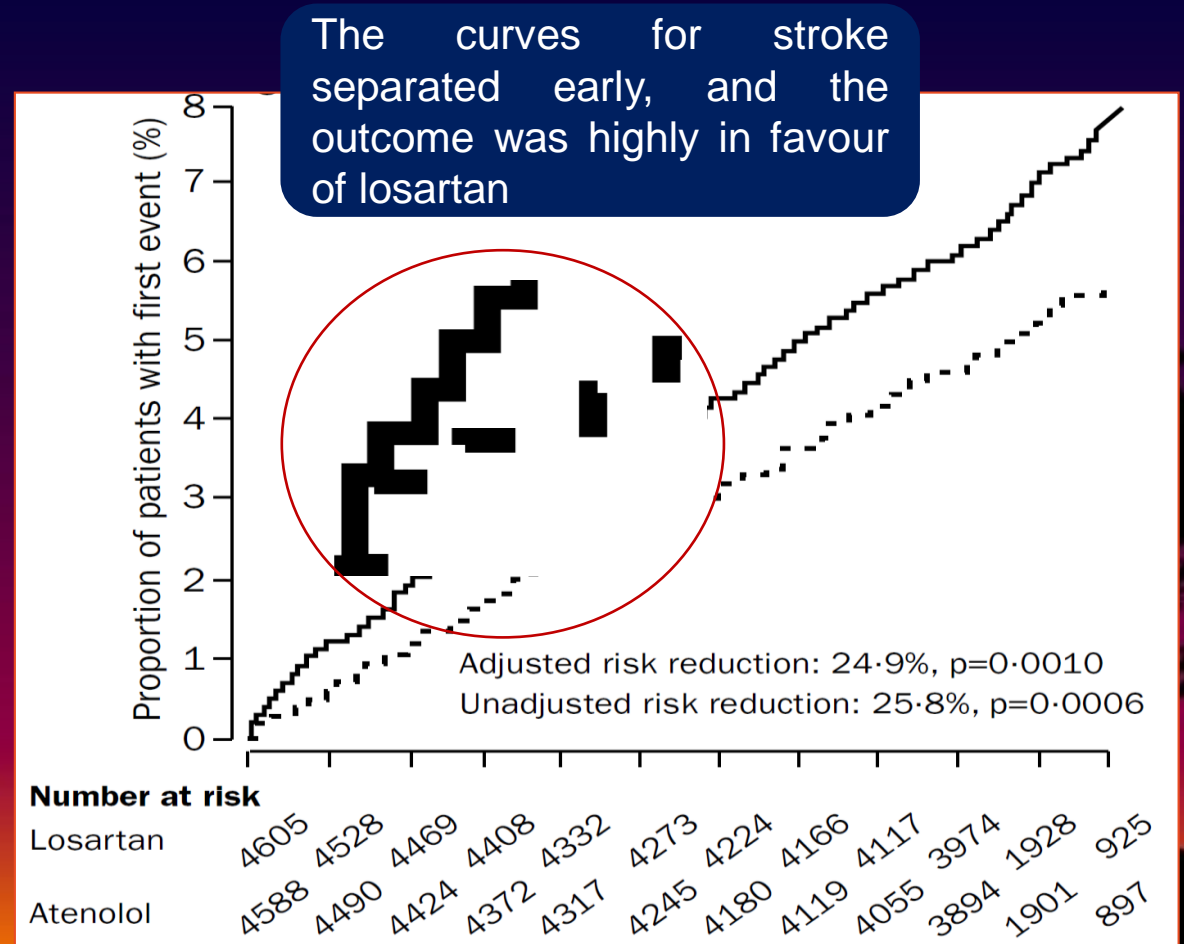
LOSARTAN on Atrial Fibrillation

- 33% risk reduction in new onset AF



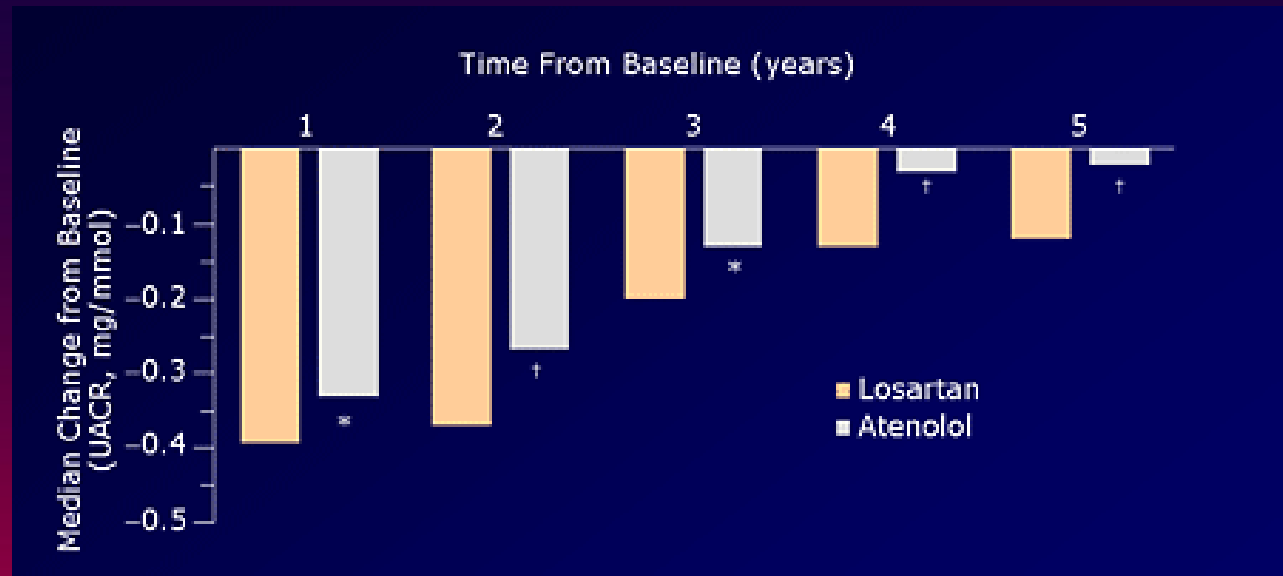
Effect of Losartan on stroke

- Significantly lowered the risk of fatal and nonfatal stroke vs. Atenolol-based therapy.



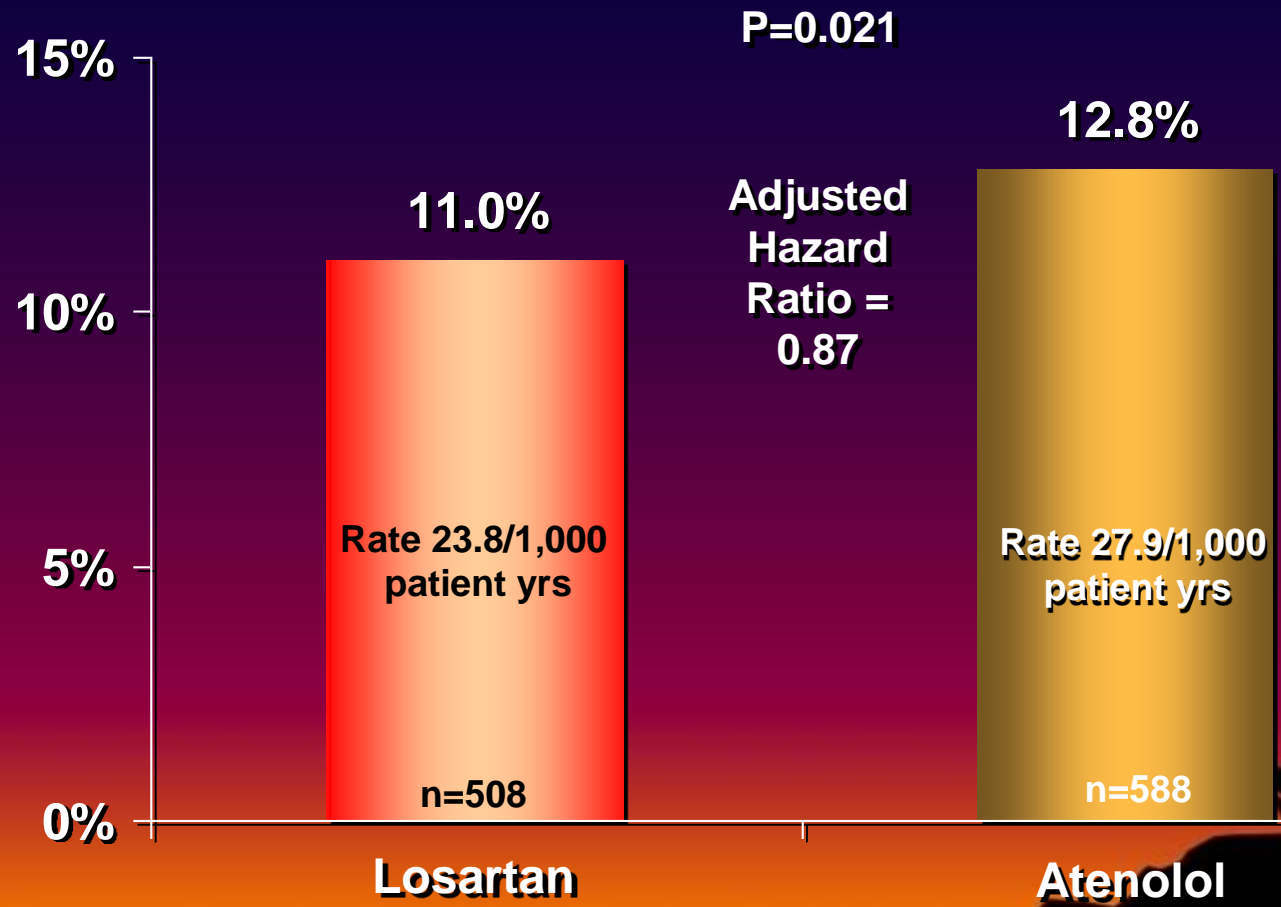
Effect of Losartan on albuminuria:-

- Greater reduction in albuminuria vs. Atenolol (33% vs. 25%)

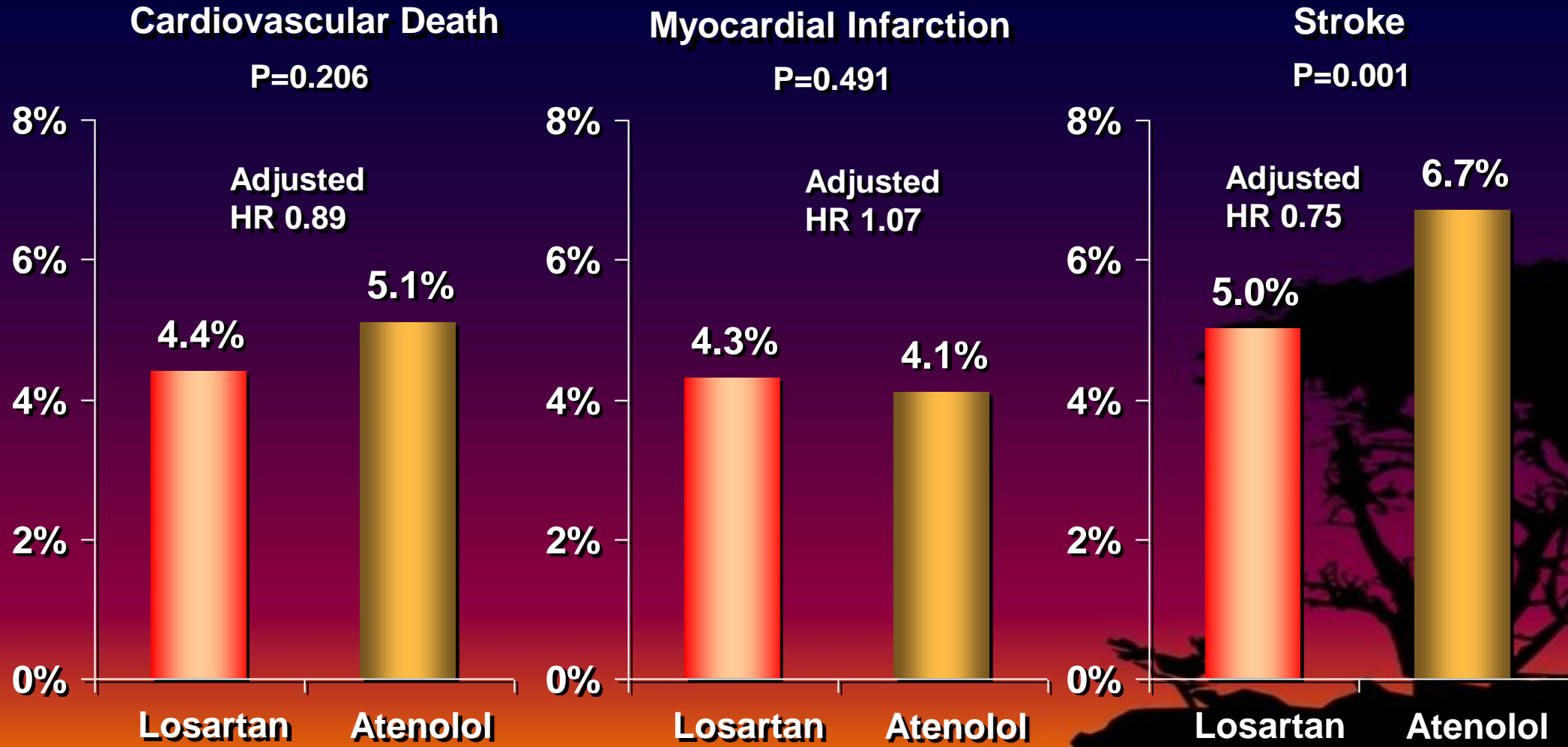


LIFE: Primary Composite Endpoint

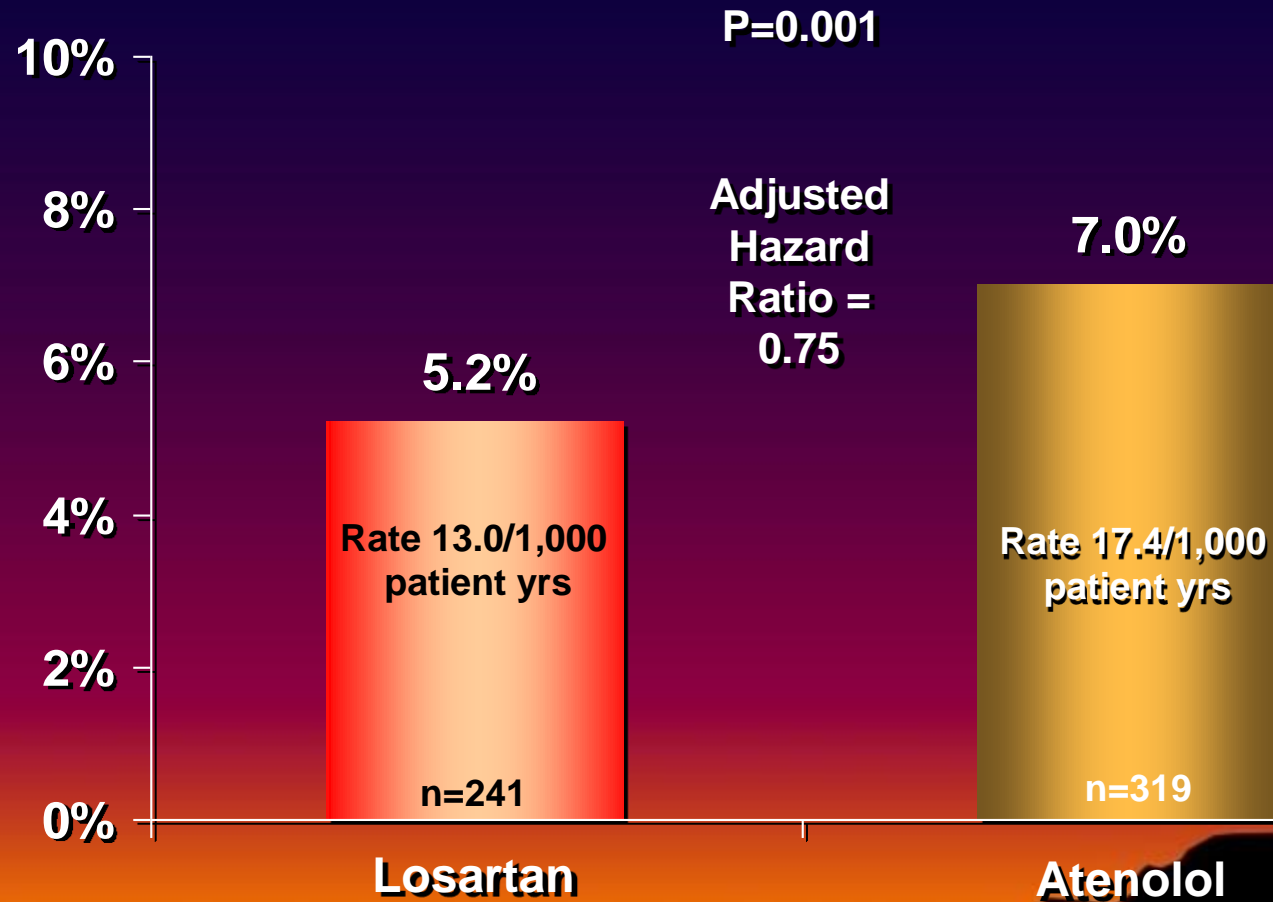
Composite of CV Death / MI / Stroke



LIFE: Individual Endpoint Results



LIFE: New-onset diabetes



Role in Prehypertension

- Losartan used in white coat HTN
- Prehypertension with LVH
- Normotension with LVH



Thank you for kind attention



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