



مركز دبي للإعلام

# RAAS Inhibition After Acute MI

*Dr. Amr Zaki, MD*

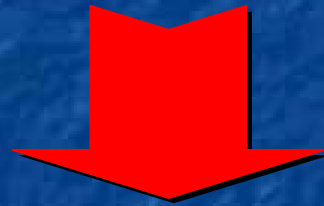
**Alex University**

**Our understanding of RAAS has advanced considerably in recent years**

- **Control of water balance**
- **Regulation of B.P.**
- **CVS homeostases**

**The hemodynamic changes in the period after MI stimulate intense activation of both circulating and local RAAS**

# Angiotensin II Aldosterone



- **Na<sup>+</sup> & H<sub>2</sub>O retention**
- **↑↑ Cardiac contractility**
- **↑↑ Syst. Vasc. tone**

**Long-term ... Harmful**

**The response of the RAAS after MI  
can be modified pharmacologically**

# ACE-I

**ACE-I** are already the mainstay of Rx in heart failure, and have been shown to have a crucial role in prevention of ventricular remodelling after MI.

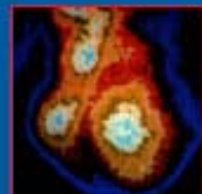
# ACE-I

- ↓↓ Risk of Death
  - ↓↓ MACE
- } After MI

## **The patient who have benefited the most**

- **LV dysfunction**
- **Signs or symptoms of CHF**
- **Both**

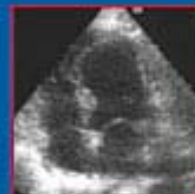
# RAAS Inhibition After Acute MI



**SAVE**  
Radionuclide  
EF  $\leq$  40%

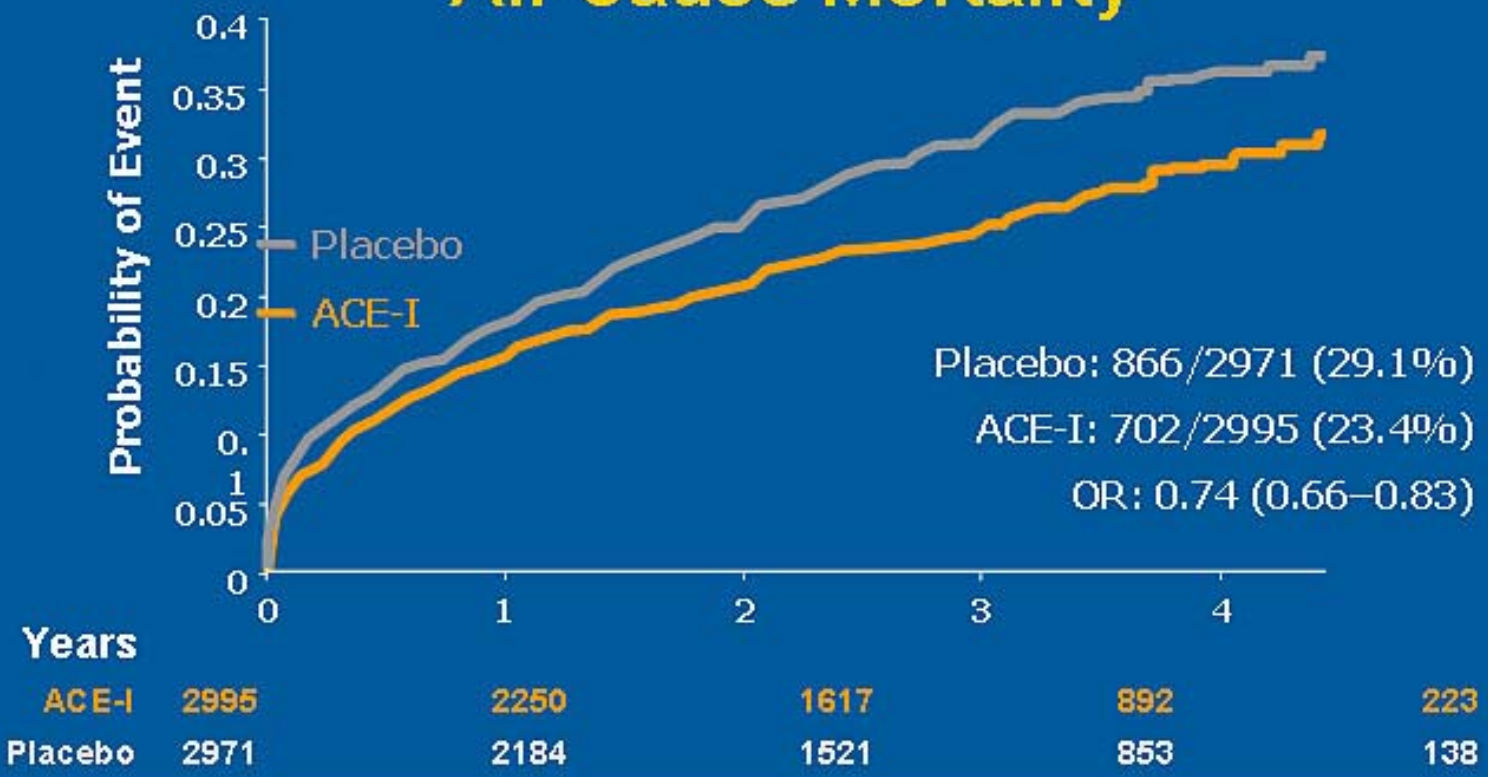


**AIRE**  
Clinical and/or  
radiographic  
signs of HF



**TRACE**  
Echocardiographic  
EF  $\leq$  35%

## All-Cause Mortality



Flather MD, et al. *Lancet*. 2000;355:1575–1581

# ARBs

**ARBs block the activity of  
Angiotensin II more completely  
than ACE-I**

**OPTIMAL**  
**(5,477)**

**Losartan**  
**(50 mgm.)**

**Captopril**  
**(50 mgm t.d.s.)**

• **10 days → 6 months**

# Results

**No Significant difference**

- **All cause Mortality**
- **SCD**
- **Fatal or Non fatal MI**

# *RAAS Inhibition After Acute MI*

**Captopril**

**Losartan**

**CV Death**

**13.3%**

**vs**

**15.3%**

**P=0.03**

**VALIANT**

# VALIANT 14,703

Time: 0.5-10 days

- **Captopril**  
50 mgm. t.d.s.

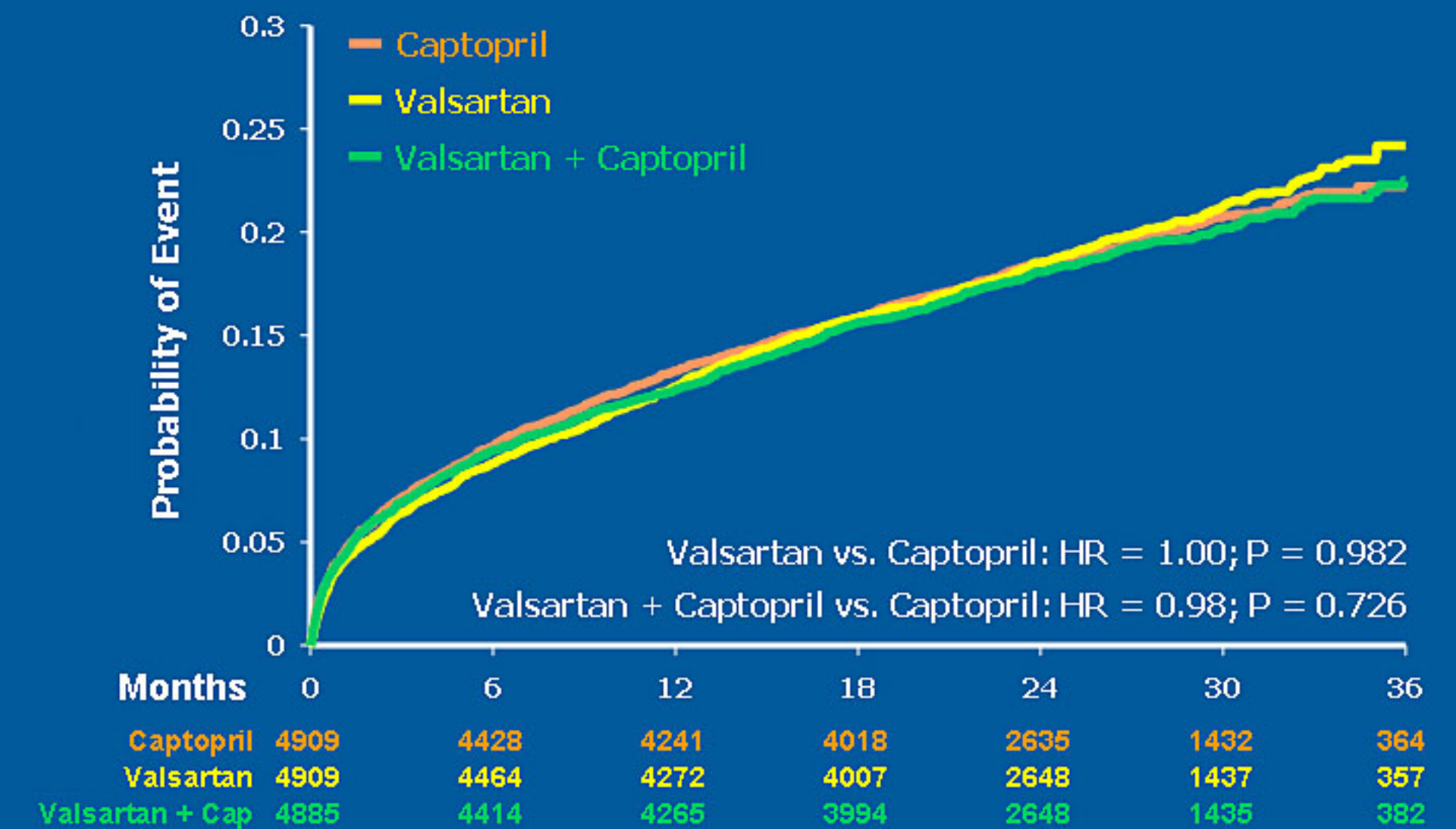
- **Valsartan**  
160 mgm. Bid.

- **Valsartan**  
80 mg Bid.

- **Captopril**  
50 mgm. t.d.s.

[1/2 → Thrombolysis or PCI]

# Mortality by Treatment



## **VALIANT outcomes**

**Combined therapy**

**Monotherapy**

**Adverse effect**

**35%**

**28-29%**

## **The 2 Valsartan gps =**

- **The most hypotension**
- **The most renal impairment**

## **VALIANT outcomes**

- **Valsartan equivalent to captopril.**
- **Combined therapy = No additional benefit**
- **Combined therapy = Significant higher adverse effect.**

# **Aldosterone Blockade [AB] in MI**

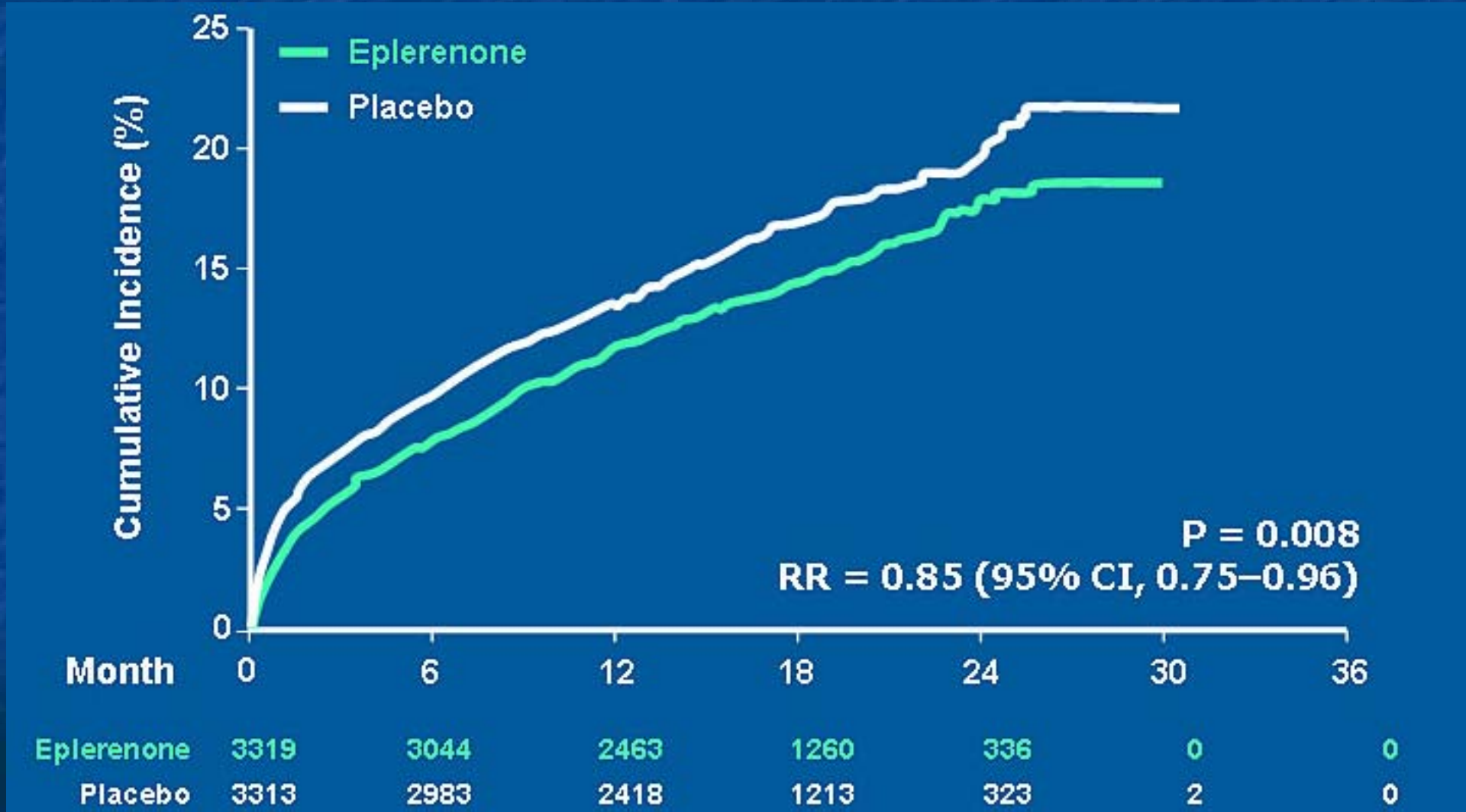
**AB has found increasing use in  
patients with severe CHF  
(RALES)**

**Eplerenone Post acute myocardial  
infarction Hear failure Efficacy  
and Survival Study  
**(EPHESUS)****

## The EPHEBUS

- 6600 patients (MI)
- EF  $\leq$  40%
- Signs of CHF
- Eplerenone 50 mgm/day 3-14 day
- Standard therapy

# EPHESUS : All-Cause Mortality



# EPHESUS

## Results:

- 15%      ↓↓ total Mortality
- 21%      ↓↓ SCD
- 13%      Primary End points  
CV Mortality/hosp.

## EPHESUS

- **1.6%** incidence of serious hyperkalemia  
(K  $\geq$  6.0 mEq/L)
- **4.9%** ↓↓ incidence of hypokalemia  
(K < 3.5 mEq/L)

*Hayashi et al,*

**IV canrenoate [200 mg]**

**Spiroinolactone 25 mg/day**

**→ Signif. improvement**

- LV remodelling**
- LV EF**

## **AB in Acute MI**

### **Assumed mechanisms**

- i.** ↓↓ myocardial collagen formation
- ii.** ↓↓ myocardial stretch
  - less neurohormones
    - Endothelin
    - Angiot. II
  - Imp. homogeneity of vent. conduction  
= ↓↓ Vent. arrhythmias
- iii.** Favorable effect on intracellular K<sup>+</sup>
- iv.** ↓↓ circulating catecholamine levels  
→ Shortening QT dispersion

## ACE/ARB : Within 24 Hours



An ACE inhibitor should be administered orally within the first 24 hours of STEMI to the following patients without hypotension or known class of contraindications :

- Anterior infarction
- Pulmonary congestion
- LVEF < 0.40.



An ARB should be given to ACE-intolerant patients with either clinical or radiological signs of HF or LVEF < 0.40

## **Long Term Management**

**ACC/AHA Guidelines for the  
Management of patients with  
ST-Elevation Myocardial Infarction**

## Secondary prevention and Long Term Management

Goals	Recommendation
Renin-Angiotensin-Aldosterone System Blockers	ACE inhibitors in all patients indefinitely start early in stable, high-risk patients (ant. MI, previous MI, Killip class >2 (S3 gallop, rales, radiographic CHF), LVEF <0.40.
	Angiotensin receptor blockers in patients who are intolerant of ACE inhibitors and with either clinical or radiological signs of heart failure <0.40.
	Aldosterone blockade in patients without significant renal dysfunction or hyperkalemia who are already receiving therapeutic doses of an ACE inhibitor, have LVEF $\leq$ 0.40, and have either diabetes or heart failure.

## Summary of Pharmacologic treatment: LVD, Sec. Prev.,

	First 24 h	During Hosp	Hosp DC + Long Term
<b>ACEI</b>	Anterior MI, Pulmonary Congestion, EF < 40	Oral Daily	Oral Daily Indefinitely
<b>ARB</b>	ACEI intol., HF, EF < 40		
<b>Aldo. Blocker</b>		No renal dysfunction, K <sup>+</sup> ≤ 5.0 mEq/L on ACEI, HF or DM	Same as during Hosp
<b>Statin</b>		Start W/O lipid profile	Indefinitely, LDL << 100

A photograph of a modern architectural walkway at dusk. The walkway is illuminated by warm, recessed lights in the floor, creating a series of glowing rectangles. The walkway is flanked by white, cylindrical columns and a glass railing. In the background, a modern building with a glass facade is visible against a dark blue sky. The text 'Thank You' is overlaid in large, bold, red letters across the top half of the image.

# Thank You

Data show design & preparation by : **Dr. El-Sayed Amr - (012) 3106023**