Hypertension Update 2008

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Definition of Hypertension

- Continuous variable
- At some point the risk becomes high enough to justify treatment
- Treatment decisions based on overall risk
- The higher the risk the lower the threshold for treatment
- Office BP taken in sitting position with arm at the level of the heart is long standing standard

Is Systolic or Diastolic BP more important

- Younger patients – diastolic BP is more important
- After the age of 50 diastolic BP gradually falls and systolic BP becomes more important

24 hour Ambulatory BP

- Better correlation with end organ damage
- Better correlation with cardiovascular events
- Impractical to do in everyone

Blood pressure Treatment thresholds and Targets

- Depends on risk profile of the patient
- 140/90 recommended by most guideline groups
- The lower the better down to 110/70
- Lower has been proven to be better for high risk groups, cardiovascular disease, renal disease

24hr BP measurement

	24 h	Daytime	Nighttime
Optimal BP	<115/75	<120/80	<100/65
Normal BP	<125/75	<130/85	<110/70
Ambulatory BP	>130/80	>140/85	<120/70

Main uses of 24 Hr BP are, suspected white coat hypertension, resistant hypertension, end organ damage with “normal BP”

Other uses ? Borderline BP, labile hypertension

Role of home BP measurements?

- Increasing use in most western countries
- Devices cheaper and more reliable (avoid in AF and frequent ectopics)
- 2 BP’s at 5 min intervals morning and night for 7 days
- Often show BP is better than office BP
- May stop additional medication and over-treatment

Masked hypertension

- abnormal 24hr or home BP with normal office pressure
- suspect in patients with evidence of end organ damage and normal office BP
- Said to occur in 10% of patients in large population studies using 24Hr BP monitoring

Significance of intermittent BP elevations

- White coat hypertension
- sporadic spikes in BP – labile hypertension
- Prognosis not quite normal
- Higher risk of more sustained BP later in life
- Lifetime risk of cardiovascular complications increased

Obesity and Hypertension

- Bogalusa heart study tracked children over many years into adulthood and showed a strong correlation between BMI and hypertension in middle age
- Weight loss often difficult to achieve and effects on BP are variable

Salt and Hypertension

- Reduced salt intake over many years reduces cardiovascular risk independent of initial BP
- Salt restriction in hypertensive patients with normal renal function has very modest effect on BP.
- Very low salt diets relatively ineffective at reducing BP in most patients

Obstructive Sleep Apnea

- Sleep apnea a common cause of HT
- CPAP reduces BP
- Reductions may be dramatic
- Common cause of resistant hypertension

Non Steroidal Anti-inflammatory drugs

- In some patients make BP much more difficult to control
- Also applies to Cox2 inhibitors
- Careful evaluation of the need for these drugs in hypertensive patients with difficult control

Alcohol and BP

- Intake of up to 2 drinks per day has no effect on BP
- Increased BP at greater levels especially in men

Etiology of Hypertension

- “Primary” in vast majority of cases
- Genetic basis has proved elusive
- Even in animal models of hypertension candidate genes not easily identified
- Human genome study found no significant gene association for hypertension

Secondary Hypertension

- Suspect in young patients with severe hypertension, older patient with resistant hypertension
- Renal Artery stenosis, FMD versus atherosclerosis
- Coarctation of Aorta
- Pheochromocytoma
- Conn's syndrome

Drug Therapy of Hypertension Diuretics

- Differences between thiazides (longer acting chorthalidone more effective in some studies than hydrochlorthiazide
- May cause gout and abnormal glucose metabolism
- Spironolactone – impressive BP drop when added to 3 drugs in ASCOT study – average 22/11
- Often good effect at 25mg
- Need to monitor K
- Gynecomastia a problem in some (dose related)

B Blockers

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Conditions	Weak to none	Some evidence	Strong evidence
Hypertension (uncomplicated)	✓		
Heart failure			✓
Acute coronary syndrome		✓	
Post MI			✓
Stable angina without MI		✓	
Perioperative (noncardiac surgery)		✓	
HOCM		✓	

HOCM = hypertrophic obstructive cardiomyopathy; MI = myocardial infarction.

B Blockers in Hypertension

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Meta-Analysis	Parameter	No. of Trials	Mortality	Myocardial Infarction	Stroke
Cochrane (2007)	Overall	4	0.99 (0.88-1.11)	0.93 (0.81-1.07)	0.80 (0.66-0.96)
Bradley et al. (2006)	Overall	4	0.99 (0.88-1.11)	0.93 (0.81-1.07)	0.80 (0.66-0.96)
Khan et al. (2006)	Younger	2	0.94 (0.79-1.10)	0.85 (0.71-1.03)	0.84 (0.65-1.10)
Khan et al. (2006)	Elderly	5	0.91 (0.74-1.12)	0.98 (0.83-1.16)	0.78 (0.63-0.98)
Lindholm et al. (2005)	Overall	7	0.95 (0.86-1.04)	0.93 (0.83-1.05)	0.81 (0.71-0.93)
Carlberg et al. (2004)	Overall	4	1.01 (0.89-1.15)	0.99 (0.83-1.19)	0.85 (0.72-1.01)

Numbers represent hazard ratio (95% confidence interval).

B Blockers - summary

- Reduce stroke but about half as well as other drugs
- Do not reduce cardiac or total mortality – especially atenolol
- Less effective at reducing central BP than other drugs
- Higher discontinuance rate in drug trials and associated with a small weight gain
- Increase insulin resistance , may not apply to newer vasodilating B Blockers

Renin Angiotensin system

- Renin released by kidney, converts the peptide angiotensinogen to angiotensin1.
- Angiotensin 1 is converted by angiotensin converting enzyme to angiotensin 2
- Angiotensin 2 is bioactive and acts on receptors to cause a number of different actions
- vasoconstriction increasing BP
- Releases aldosterone from the adrenal gland and vasopressin from pituitary (water and salt retention increasing BP)
- Has specific tissue effects that promote release of many mediations involved in metabolic processes

Blocking the renin angiotensin system RAS

- Angiotensin converting inhibitors ACE
- Angiotensin receptor blockers ARB
- Direct renin inhibitors DRI

- May be a benefit of using more than 1 agent to more completely block the RAS
- Particularly important in high risk patients

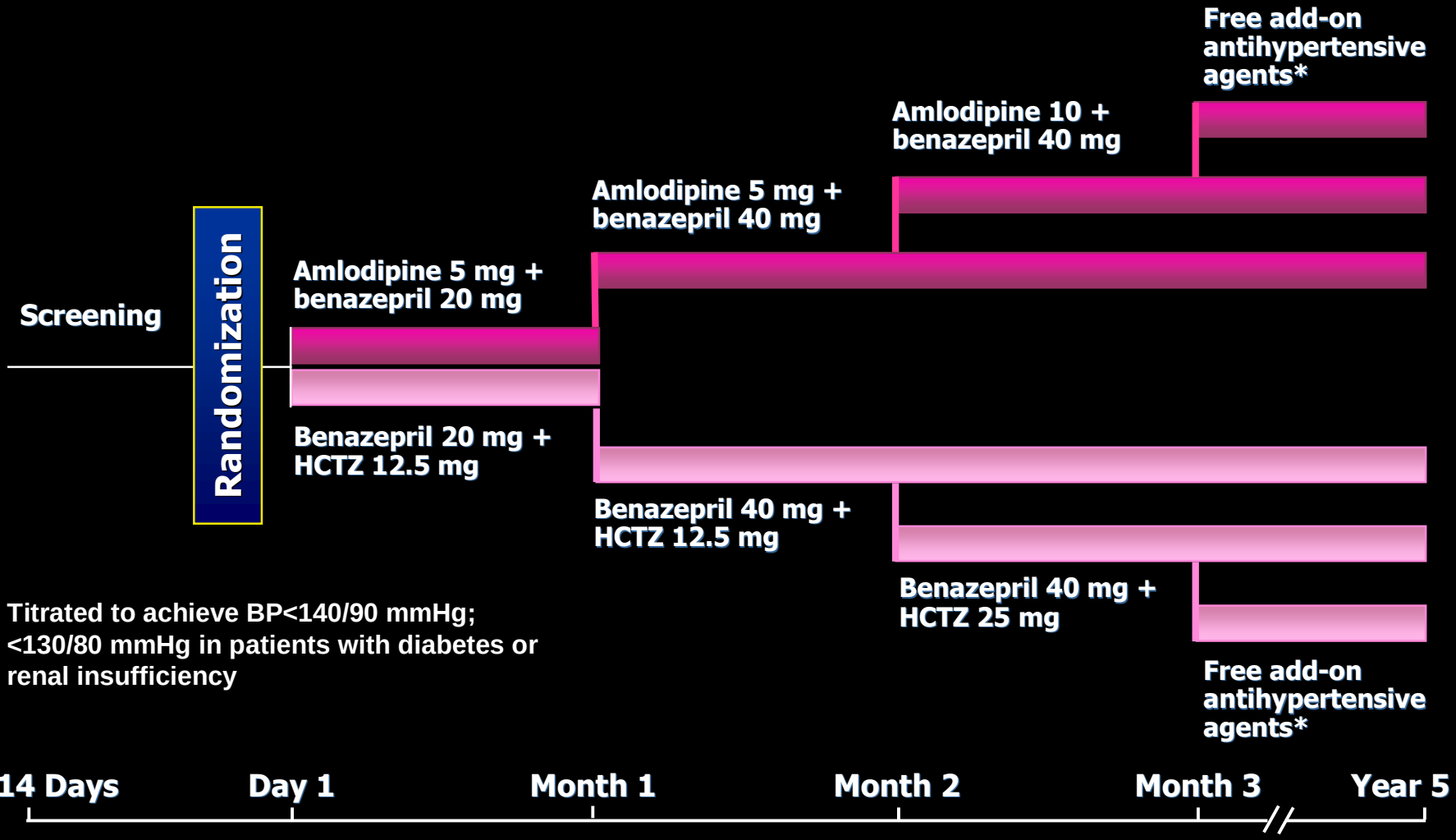
Angiotensin Receptor Blockers

- In NZ used primarily in patients with side effects from ACE inhibitors
- Overseas, primary treatment for the majority of patients because they have less side effects and are as, or more effective
- Relaxation for Losartan – cough on 1 ACE. Can be added to ACE for BP and CHF

ACCOMPLISH: A Novel Hypertension Trial

- **Traditional approach to hypertension management:**
  - **Initiate monotherapy then sequentially add medications to achieve target BP**
- **ACCOMPLISH:**
  - **Initiate single tablet combination therapy in high-risk hypertension**
  - **Specific combinations may confer target organ protection in addition to their BP-lowering effects**

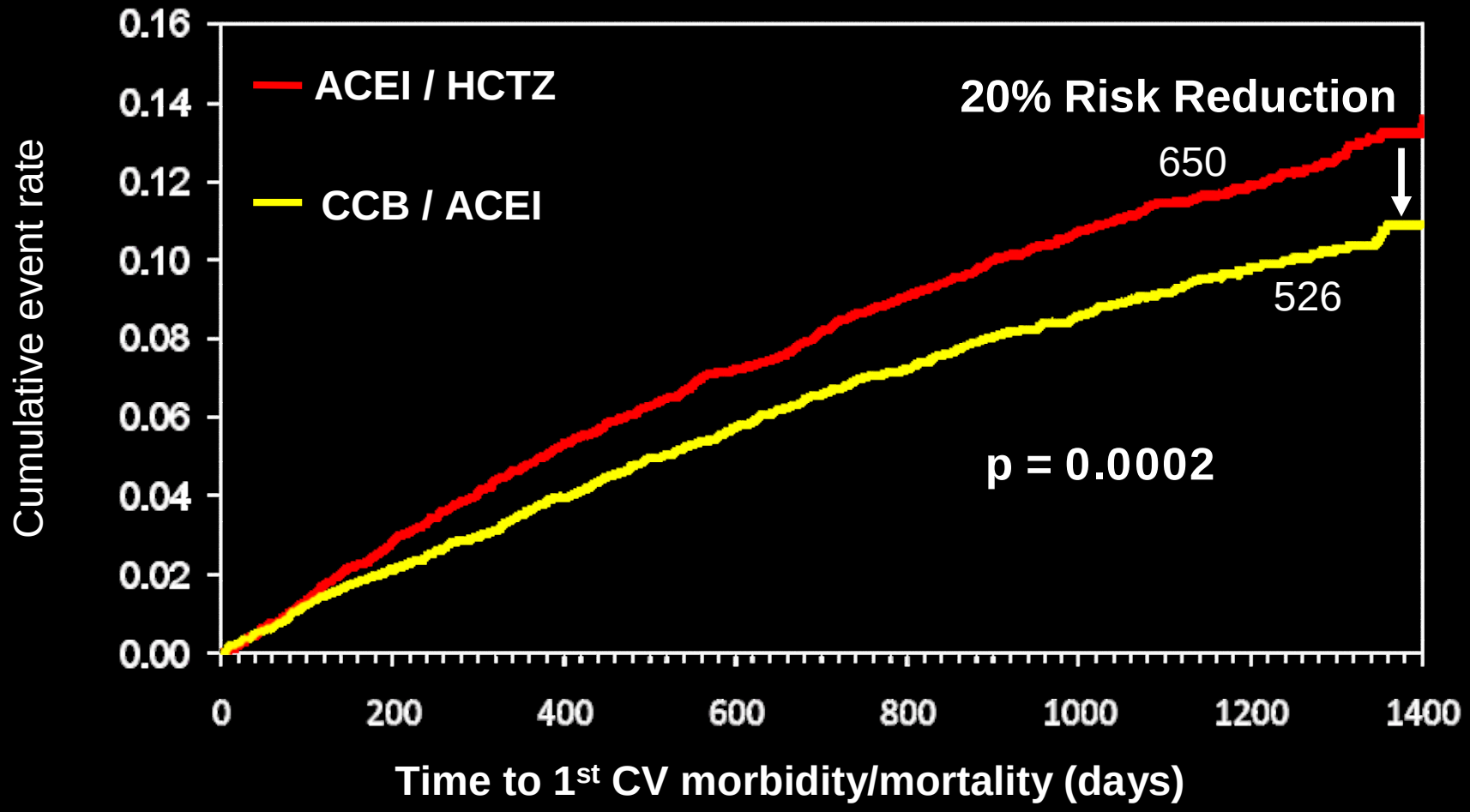
ACCOMPLISH: Design



***Beta blockers; alpha blockers; clonidine; (loop diuretics).**

Jamerson KA et al. *Am J Hypertens*. 2003;16(part2)193A

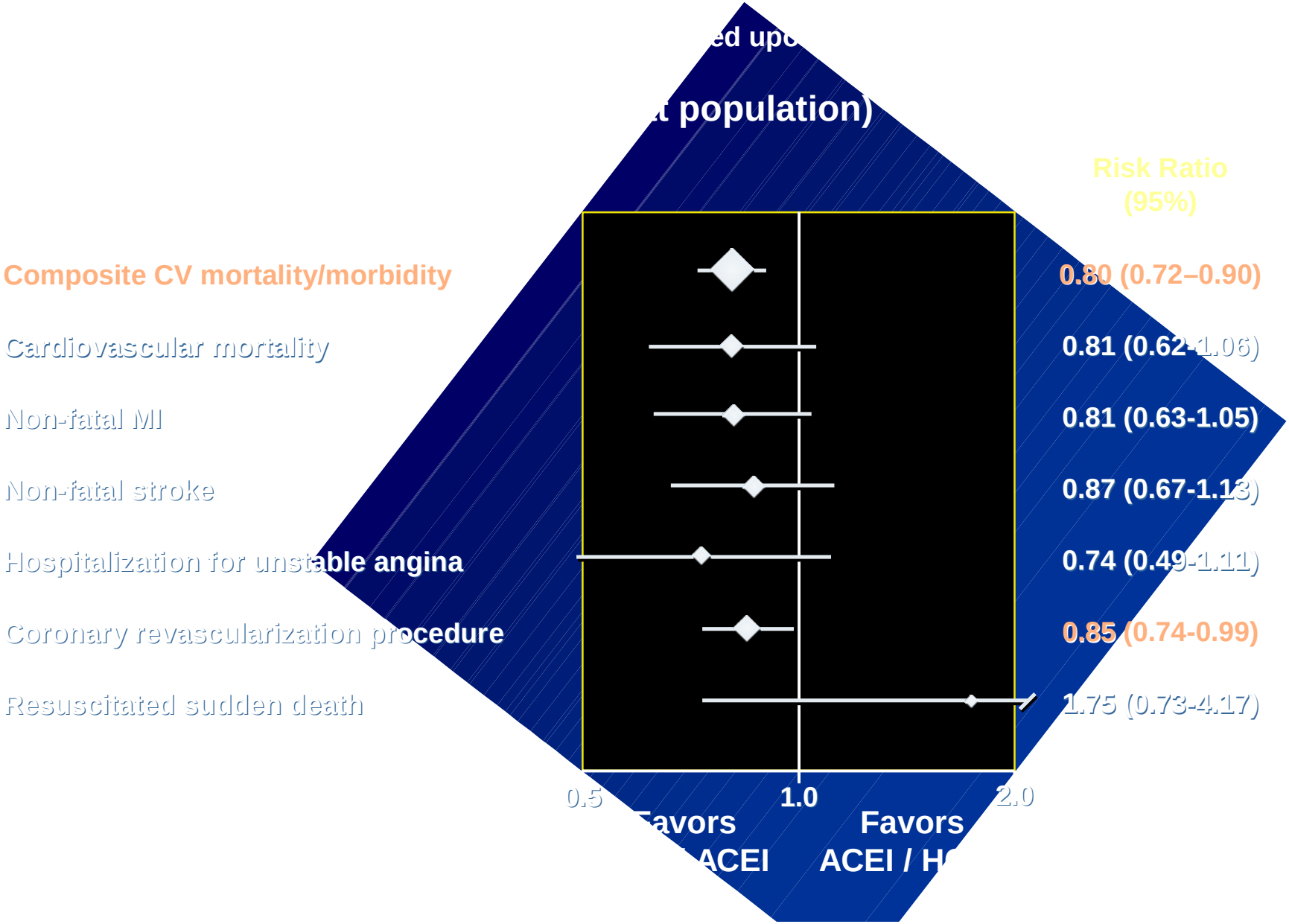
Kaplan Meier for Primary Endpoint



HR (95% CI): 0.80 (0.72, 0.90)

INTERIM RESULTS Mar 08

Primary Endpoint and Components



Summary

- Single tablet combination therapy was initiated in 11,462 high risk hypertensive patients
- After mean follow-up of 39 months,
  - The combination of ACEI / CCB was superior to ACEI / diuretic
  - CV morbidity / mortality was reduced by 20% (p=0.0002)
  - Hard CV Endpoint (CV death, stroke and MI) was reduced by 20% (p=0.007)

Approach to treatment

- Different national organizations have different recommendations
- Most controversial are NICE (UK) - excludes B Blockers
- Cost of drugs less of an issue with generics now available and much reduced prices for ACE inhibitors

Younger Patients

- Longer acting ACE inhibitor
- Followed by Calcium channel blocker
- Followed by diuretic/ACE combination
- Followed by B Blocker
- Followed by spironolactone

- Use ARB if intolerant of ACE
- Use B Blocker earlier if have IHD

Older patients

- Diuretic or CCB first
- Followed by ACE/diuretic combination
- Followed by spironolactone
- Followed by B Blocker

- Start with ACE in diabetics
- B Blockers earlier in IHD patients