Early Eplerenone Treatment in Patients with Acute ST-elevation Myocardial Infarction without Heart Failure

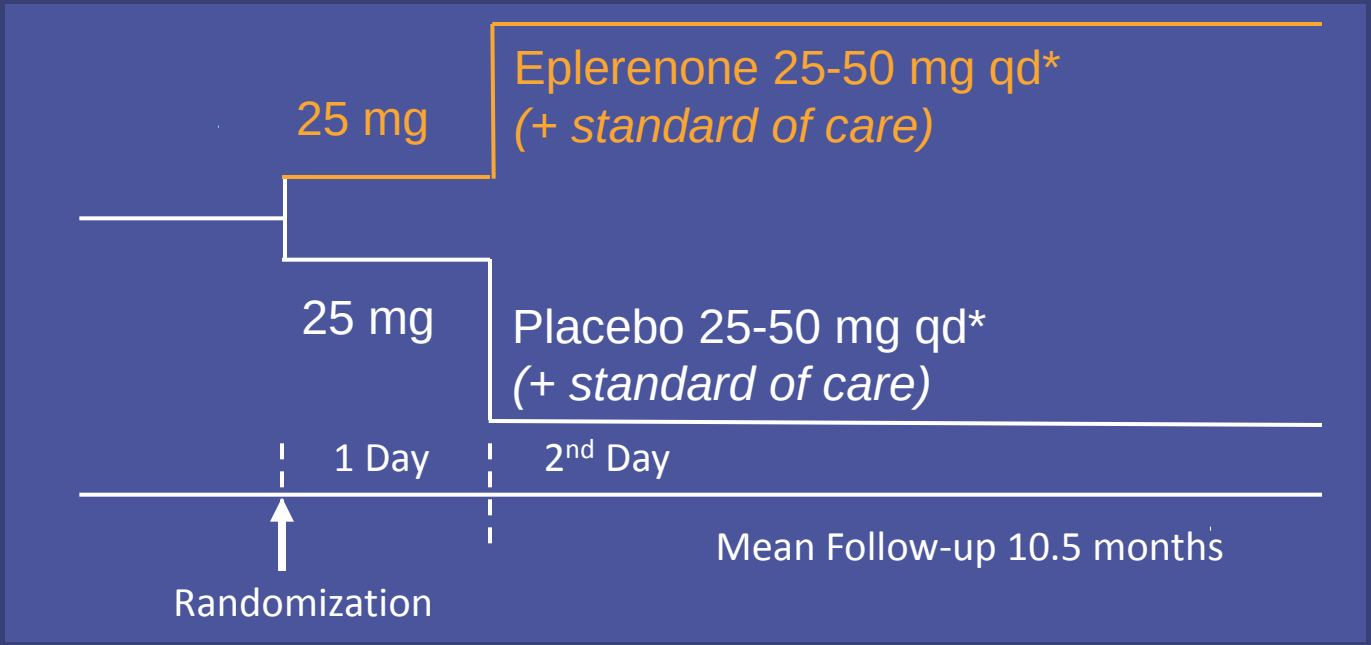
REMINDER*

Gilles Montalescot, Bertram Pitt, Esteban Lopez de Sa, Christian W. Hamm, Marcus Flather, Freek Verheugt, Harry Shi, Eva Turgonyi, Miguel Orri, John Vincent and Faiez Zannad for the REMINDER Investigators

ClinicalTrials.gov, NCT01176968

*A Double-Blind, Randomized, Placebo-Controlled Trial Evaluating The Safety And Efficacy Of Early Treatment With Eplerenone In Patients With Acute Myocardial Infarction

Study Design



* Dosing based on serum potassium levels and eGFR levels; 88.6% finally received 50 mg in the eplerenone group

REMINDER

Study Patients

INCLUSION

- Eligible subjects were identified for inclusion following emergency room or ambulance evaluation and diagnosis of acute STEMI in the absence of a diagnosis of HF
- Randomization had to take place as early as possible following diagnosis and the first dose of study drug administered as early as possible within 24 hours of the onset of symptoms of acute MI and preferably within 12 hours.

KEY EXCLUSION CRITERIA

- Known ejection fraction < 40%, any previous history of heart failure
- Implanted cardioverter defibrillator
- Known renal insufficiency or eGFR ≤ 30 ml/min/1.73m^2
- Uncontrolled hypotension (systolic blood pressure < 90 mmHg)
- Any other clinically significant coexisting condition

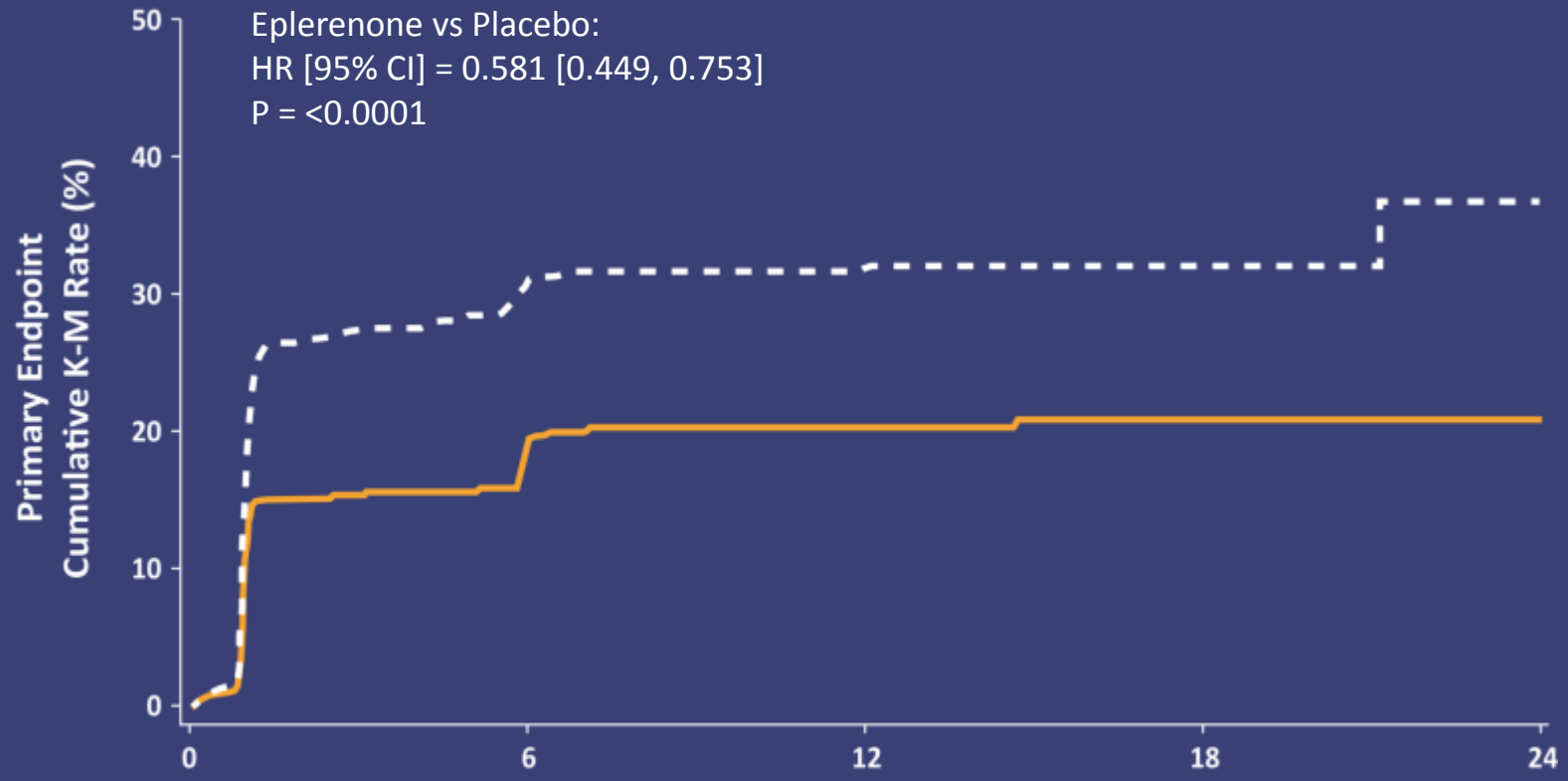
REMINDER

Baseline Characteristics

Characteristics	Eplerenone (N=506)	Placebo (N=506)
Age (years)	58.5±10.8	57.8±11.0
Female sex (%)	86 (17.0)	103 (20.4)
Heart rate (bpm)	73±13	74±13
Blood pressure (mmHg)	126±19 / 76±13	127±17 / 77±12
Body mass index (kg/m^2)	27.9±4.5	28.2±4.2
Serum creatinine (mg/dl)	0.91±0.20	0.91±0.21
eGFR (ml/min/1.73m^2)	86.5±28.2	86.4±24.9
Serum potassium (mmol/L)	4.07±0.46	4.05±0.45
Anterior MI (%)	180 (35.6)	205 (40.5)
Hypertension (%)	241 (47.6)	260 (51.4)
Diabetes (%)	65 (12.8)	78 (15.4)
Prior MI (%)	33 (6.5)	23 (4.5)

REMINDER

Primary Endpoint



No. at Risk					
Eplerenone	506	257	215	86	1
Placebo	506	211	175	67	0

PRIMARY ENDPOINT: Time to first occurrence of CV mortality, re-hospitalization or extended initial hospital stay due to diagnosis of HF or sustained ventricular tachycardia or ventricular fibrillation, as well as at 1 month post randomization: LVEF ≤ 40% or elevated BNP / NT-proBNP

REMINDER

Serum Potassium by Treatment Groups

Laboratory values	Eplerenone (N=506)	Placebo (N=506)	P-value
Potassium Δ from baseline to 1 month (mmol/L)	0.41 ± 0.56	0.32 ± 0.50	<0.0001
Hyperkalemia (>6.0 mmol/L)	8 / 498 (1.6)	2 / 496 (0.4)	0.11
Hyperkalemia (>5.5 mmol/L)	28 / 498 (5.6)	16 / 496 (3.2)	0.09
Hypokalemia (<4.0 mmol/L)	177 / 498 (35.5)	234 / 496 (47.2)	0.0002
Hypokalemia (<3.5 mmol/L)	7 / 498 (1.4)	28 / 496 (5.6)	0.0002

REMINDER

Conclusions

- This study shows that compared with placebo the addition of eplerenone to standard therapy within 24 hours of symptom onset improves the outcome of patients presenting with acute STEMI without evidence of HF or LVEF <40%.
- This is the first large study to demonstrate the safety profile of eplerenone during early administration (no prior potassium check, titrated from 25 to 50 mg on day 2).