Results: In sodium-depleted marmosets, aliskiren (0.3–10 mg/kg p.o.) dose-dependently inhibited renin and lowered MAP. After a single oral dose of 3 mg/kg aliskiren, MAP was lowered maximally by 31±7 mmHg (n=6), and significant reductions in MAP persisted for up to 24 h. At equivalent doses, aliskiren lowered MAP as effectively as the ACE inhibitor benazepril and the AT1 receptor blocker valsartan, and more effectively than the previous generation RIs, remikiren and zanipril. In SHR, aliskiren (10–100 mg/kg/day via s.c. constant-infusion pumps for 2 weeks) dose-dependently lowered MAP. Administration of submaximal effectively doses of aliskiren in combination with either benazepril or valsartan strongly potentiated reductions in MAP. In human hypertensive patients, aliskiren (37.5, 75, 150 or 300 mg once daily for 4 weeks) also dose-dependently lowered BP and inhibited renin. Aliskiren treatment was well tolerated at all doses, with BP reductions not being accompanied by changes in heart rate, in marmosets, rats and humans. Conclusions: Aliskiren provides 24 h blood pressure lowering with good tolerability in sodium-depleted marmosets and human hypertensive patients after once-daily oral dosing. Blockade of the renin-angiotensin-aldosterone system with aliskiren may therefore represent an effective, novel approach to antihypertensive treatment both as monotherapy and in combination with other RAS inhibitors.

DOSAGE-RESPONSE STUDY OF THE EFFICACY AND SAFETY OF FOSINOPRIL IN CHILDREN AND ADOLESCENTS WITH HYPERTENSION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER CLINICAL TRIAL

Jennifer S. Li, Katherine Y. Berezny, Rashbi Kiany, Lydia Hazen, Ronald Portman, Ronald Hogg, Randall Kennis, Prapti Kanani, Carol M. Cottril, Tej K. Mattoo, Ludmila Zhrakova, Ludmilla Fyhrquist, Jonathan Edelman, Richard B. Devereux, Stevo Julius, Peter Aurup, Jonathan Edelman, Gareth Beever, Ulf de Faire, Frij Fyhrquist, Hans Isber, Krista Kivisto, Ole Lederballe-Pedersen, Lars H. Lindholm, Markku S. Nieminen, Per Omvik, Suzanne Oppli, Steven-M. Snapin, Hans-Henriksen A. Lycke, The LIFE study group, Umeå University Hospital, Oslo, Norway, University of Michigan, Ann Arbor, Stroke is now more common than myocardial infarction in hypertension. In a subset of the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study we tested the hypothesis that a losartan-based regimen beyond blood pressure control in reducing cardiovascular (CV) morbidity and mortality (composite CV death, stroke or myocardial infarction) in patients with ISH and left ventricular hypertrophy (LVH) on electrocardiogram (ECG). Men and women (60% aged 55-80 (average 70) years with ISH (sitting blood pressure 160-200/90 mmHg, average 174/83 mmHg) and ECG-LVH were followed for a mean of 4.7 years. Blood pressure was similarly reduced by 28.4/8.5 and 28.2/8.8 mmHg in the losartan (n=660) and atenolol (n=666) arms, respectively. The primary composite endpoint was reduced by 26% in the losartan group (35.8 per 1000 patient years; relative risk (RR) adjusted for Framingham risk score and degree of ECG-LVH 0.74 [95% CI 0.55 – 1.00], p=0.051, unadjusted RR 0.70 [95% CI 0.52 – 0.94], p=0.019). Stroke data in this ISH group follow. (Three atenolol patients had multiple strokes of different types. These patients are counted only once in the patients with any stroke category.)

THE EFFECT OF LIfe VS ATENOLOL ON HEMOSTASIS AND FIBRINOGEN IN HYPERTENSIVE PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY: A LIFE SUBSTUDY

Kurt A. Roesman, Sr., Michael Hecht Olsenn, Kristin Wachtell, Mona Olofsson, Hans Isben, Sr., Harriet Dige-Petersen, Torbjorn K. Nilsson, Sr., Umea University, Skelleftea, Sweden

Background: In some studies with angiotensin converting enzyme (ACE) inhibitors, an improvement to fibrinolysis. Our aim was to investigate the long-term effects of an angiotensin II receptor blocker, losartan, on mass-concentrations of tissue plasminogen activator (tPA), its inhibitor, PAI-1, and fibrinogen in hypertensive patients with left ventricular hypertrophy (LVH). Methods: In 44 participants recruited for the LIFE Study with stage II hypertension and ECG left ventricular hypertrophy we measured tPA, PAI-1, and fibrinogen level, and fibrinolytic balance with tPA and plasminogen and with fibrinogen and left ventricular hypertrophy. Results: Plasma levels of tPA (10.5 vs. 8.8 µg/l, p=0.01), PAI-1 (31.3 vs. 26.5 µg/l, p=0.015) and fibrinogen (10.6 vs. 8.4 µg/l, p=0.01) were reduced during five years of losartan-based antihypertensive treatment, whereas PAI-1 (24.4 vs. 11.4 µg/l, p=0.03) and fibrinogen (17.5 vs. 17.4%, p=0.05) were reduced in patients treated with atenolol-based antihypertensive treatment. Comparing the two treatments, there were no significant differences in plasma tPA, PAI-1, and fibrinogen at baseline, after one and five years of antihypertensive treatment. However, after at five years of treatment, plasma levels of PAI-1 and fibrinogen were not significantly lower in patients treated with losartan-based antihypertensive treatment compared to patients treated with atenolol-based antihypertensive treatment.

Eplerenone Improves Coronary Hemodynamics and Reduces Cardiac Fibrosis in Aging Spontaneously Hypertensive Rats

Dinko Susic, Jasmina Varagic, Iwari Arhn, Louis Matalle, Edward D. Fichtloth, Ochsner Clinic Foundation, New Orleans, LA

Background: Aldosterone is considered to be involved in development of age- and hypertension-related cardiac fibrosis and its consequences such as impaired coronary hemodynamics. Thus, the effects of aldosterone antagonist eplerenone (E) on systemic blood pressure, cardiac mass, myocardial collagen, and coronary circulation were examined in spontaneously hypertensive rats.

Methods: Male, 22-week old rats were randomly divided into two groups (30 rats in each). The control group did not receive any treatment, the second group was given E (meas in