The beneficial effect of beta-blockers on the treatment of patients with essential hypertension (EH) has been demonstrated, but there is evidence of differential effects among them. We assess the effects of Talliton (Carvedilol) on coronary flow reserve (CFR) in patients with EH.

**Methods:** 54 II WHO hypertensive patients (28 m, 26f, mean age 47.6 years) without coronary artery disease underwent standard Doppler echocardiography. The exam was performed at baseline and after 6-week monotherapy by Talliton in a daily dose of 12.5 mg.

**Results:** At baseline the prevalence of left ventricular (LV) hypertrophy (LV mass index > 50 g/m powered to 2.8) was 64.6% after 6-week Talliton therapy. Blood pressure (BP) decreased in 82.4% of the patients (p < 0.01). Heart rate also significantly reduced (p < 0.01). No change could be detected in LV mass index, relative wall thickness, fractional shortening and Doppler-derived diastolic inflow indexes. LV end-diastolic internal diameter and stroke volume tended to increase (p = 0.06 and p = 0.08 respectively). After 6-week therapy, CFR increased in 86.6% of the patients (p < 0.0001).

**Conclusion:** In patients with essential hypertension Talliton improves coronary flow reserve after 6-week therapy. This improvement occurs despite decrease in blood pressure and independently of changes in left ventricular mass.

Key Words: Beta-Blocker, Coronary Flow Reserve, Hypertension

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**P-117**

2-ARACHIDONYLGlycerol and its Metabolite, Glycerated epoxyeicosatrienoic Acid Mediate Ca2+-induced Relaxation of Isolated Mesenteric Art

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We have previously showed that Ca2+-induced relaxation of pre-contraction mesenteric arteries is blocked by the KCa channel blockers, iberiotoxin and charybdotoxin as well as the cannabinoid receptor antagonists, SR141716 and O-1918, suggesting a role for a hyperpolarizing vasodilator with activity at an endocannabinoid receptor. In the present study we demonstrate that Ca2+-induced relaxation of isolated arteries, pre-contraction with phentolamine, was reversibly blocked by the diacylglycerol (DAG) lipase (DAGL) inhibitor, RCH 80267 (IC50 = 2.8 ± 0.4 vs 1.4 ± 0.3 mM, control; n = 4) and by cytochrome P450 epoxigenase inhibitors, miconazole (complete) and quinacrine (partially; IC50 = 4.9 ± 0.4 vs 2.0 ± 0.3 mM, control; n = 3) indicating involvement of metabolites of this pathway (Figure 1). The data suggest that DAG was metabolized to 2-arachidonyl glycerol (2-AG), an endocannabinoid, and subsequently to glycated epoxyeicosatrienoic acid (GEET). We next determined whether either or both of these metabolites cause relaxation of mesenteric arteries.

Synthetic 2-AG and 14,15-GEET induced dose-dependent relaxation of isolated arteries, which, in the latter case was blocked by iberiotoxin. The findings indicate that 2-AG and GEET play a role in Ca2+-induced relaxation of resistance arteries. Therefore this pathway is potential target for development of new anti-hypertensive therapy.

Key Words: 2-Arachidonoylglycerol, Calcium-Induced Relaxation, Glycated epoxyeicosatrienoic Acid

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**P-118**

Diuretic-AIIRA combination: Persistence of differences in AIIRA efficacy. Cosima study

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The purpose of the study was to compare the antihypertensive efficacy of irbesartan 150 mg vs. valsartan 80 mg, when combined with hydrochlorothiazide (HCTZ) 12.5 mg.

Untreated or uncontrolled treated hypertensive adults (n=800) were enrolled (V1) in a 5-week open-label lead-in phase in which they received 12.5 mg HCTZ. Those whose blood pressure remained uncontrolled (office SBP > 140 mm Hg after 4 weeks (V2) and SBP > 135 mm Hg by home blood pressure monitoring [HBPM] at week 5 - at least 12 valid measurements over 5 days) were randomised (n=464) at V3 to either irbesartan/HCTZ (150/12.5 mg) or valsartan/HCTZ (80/12.5 mg) for 8 weeks.

HBPM was performed at week 5 (before V3) and 13 (before V4) using a validated device (Tensioday®): after 5 minutes rest, 3 measurements were made at 1 minute intervals, in a sitting position in the morning (9-10 am) before treatment intake and in the evening (6-10 pm), for at least 3 days. Data were transferred automatically via teletransmission to an independent core laboratory blinded to treatment allocation.

The intent-to-treat dataset included 449 patients (irbesartan/HCTZ: 222 and valsartan/HCTZ: 227). Baseline characteristics were well matched: mean age 59.3, 56.1 m; men; initial home SBP/HBT 148/99.5 mm Hg and office SBP/DBP 153.0/90.6 mm Hg. The differences in BP (mm Hg) measured by HBPM (W5-W13) in the morning and in the evening are presented in the table below.

<table>
<thead>
<tr>
<th></th>
<th>Δ Home SBP (mm Hg)</th>
<th>Δ Home DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>morning</td>
<td>evening</td>
</tr>
<tr>
<td>irbesartan/HCTZ</td>
<td>12.4 ± 10.7</td>
<td>9.0 ± 6.7</td>
</tr>
<tr>
<td>valsartan/HCTZ</td>
<td>9.6 ± 10.7</td>
<td>6.7 ± 6.7</td>
</tr>
<tr>
<td>Δ mean [95CI]</td>
<td>2.9 [0.8;5.0]</td>
<td>2.3 [1.0;3.5]</td>
</tr>
<tr>
<td>p</td>
<td>0.0067</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± sd / CI: confidence interval.