ORAL SESSION

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THERAPEUTIC ASPECTS

3A.01 INADEQUATE MANAGEMENT OF UNCONTROLLED HYPERTENSIVES UNDER BITHERAPY: THE SEVICAP STUDY

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Objective: To describe practitioners' management, according to patient individual risk and characteristics, for uncontrolled blood pressure in patients currently treated with bitherapy including calcium channel blocker in France.

Design and Method: Observational retrospective study by French GP (n = 353) and cardiologists (n = 271), to assess the management of uncontrolled hypertensives currently treated with bitherapy including calcium channel blocker in homogeneous subtypes of patients resulting from non supervised classification procedure.(Fastclus procedure in SAS 9.2). Strategies were classified as follows: i)similar treatment (SimTT) : inertia, changing of one and/or two drugs in the same pharmacological family; ii)modification without increase (ModTT): changing of one and /or two drugs by other compound from other class; iii) enhancement (EnhTT): increasing dosage of one and/or two drugs, addition of a third drug. Strategies were described according to patients subtypes.

Results: 1851 hypertensives were included (men: 62%, 64 ± 11 years, BMI 27.9 ± 4.5 kg/m^2, SBP 159 ± 11 mmHg, DBP 92 ± 8 mmHg). Five subtypes of patients were observed (Calinski's criteria): C1: 22% (uncomplicated young males with risk factors), C2: 20% (metabolic: diabetes, hyperlipidemia), C3: 16% (vascular disease: elderly, hyperlipidemia, cardiac, coronary artery, cerebro-vascular diseases), C4: 9% (severe BP), C5: 33% (low risk, no target organ damage (TOD)). The observed strategy was C1, C2, C3, C4, C5, Total; SimTT: 32%, 30%, 36%, 31%, 31%, 35%; EnhTT: 22%, 24%, 30%, 43%, 19%, 24%; ModTT: 46%, 39%, 36%, 26%, 47%, 41%; Cardiologists enhanced treatment twice to thrice as much than GP.

Conclusion: 5 subtypes of uncontrolled hypertensives treated with bitherapy are observed according to age, levels of BP, TOD, metabolic disease. The practitioners' strategy to control BP is clearly inadequate in 35%, and delayed in 41%. The enhancement of pharmacological power is observed in only 24%, and large differences are observed according to types of patients, but also between GP and cardiologists. More directive recommendations for treatment strategy are needed particularly for these second/third lines management of hypertensives.

3A.02 ALISKIREN PENETRATES ADIPOSE AND SKELETAL MUSCLE TISSUE, AND REDUCES RENIN–ANGIOTENSIN SYSTEM ACTIVITY IN OBESE HYPERTENSIVE PATIENTS

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Objective: Tissue Renin-Angiotensin System (RAS) activity is increased in obesity and may contribute to obesity-related hypertension and metabolic abnormalities. This open-label pilot study investigated the local effects of Aliskiren in adipose tissue and skeletal muscle.

Design and Method: After a 1-2 week washout, 10 patients with hypertension and abdominal obesity received placebo for 2 weeks, then Aliskiren 300 mg once daily for 4 weeks, followed by a 4-week washout period and then another 4 weeks treatment period with Amlodipine 5 mg once daily. Drug concentrations and RAS biomarkers were measured in interstitial fluid employing the microdialysis zero-flow method, and in biopsies from subcutaneous abdominal adipose tissue and skeletal muscle.

Results: After 4 weeks treatment, microdialysate concentrations (mean ± SD, ng/mL) of Aliskiren were 2.4 ± 2.1 (adipose) and 7.1 ± 4.2 (skeletal muscle), similar to plasma levels (8.4 ± 4.4). Tissue concentrations (ng/g) of Aliskiren were 29.0 ± 16.7 (adipose) and 107.3 ± 68.6 (skeletal muscle) after 4 weeks treatment. Angiotensin II (ANG II) concentrations in microdialysates were below the lower limit of quantification in most patients, but pooled data from two patients suggested that Angiotensin II was reduced by Aliskiren and unchanged by Amlodipine. Aliskiren 300 mg significantly reduced mean Plasma Renin Activity (PRA) by 68% and Angiotensin II by 61% ($p<0.05$ vs. baseline). Amlodipine 5 mg increased PRA by 48% ($p<0.05$ vs. baseline), and non-significantly increased Ang II by 60%. Both treatments increased Plasma Renin Concentration (PRC).

Conclusion: Aliskiren 300 mg once daily penetrates adipose and skeletal muscle tissue at levels sufficient to reduce tissue Renin- Angiotensin system activity in obese patients with hypertension.

3A.03 EFFECT OF ACE INHIBITORS AND ANGIOTENSIN II RECEPTOR BLOCKERS ON ALL-CAUSE MORTALITY IN HYPERTENSION TRIALS

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Objective: Although both angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are well established for the reduction of cardiovascular morbidity, their role in all-cause mortality reduction among hypertensive patients remains unclear.

Design and Method: We conducted a pooled analysis of morbidity-mortality trials with a renin-angiotensin-aldosterone system inhibitor and published since year 2000, in which at least 2/3 of patients had hypertension.

Results: 19 trials in 165 971 patients, of whom 92% were hypertensive, met the inclusion criteria. The pooled results of 7 trials investigating ACE inhibitors in 88 860 patients demonstrated a significant reduction in all-cause death of 6% (HR, 0.94 (0.90–0.98), P = 0.007; Figure). No significant reduction in all-cause mortality could be demonstrated with ARBs in 12 trials featuring 77 111 patients (HR, 0.99 (0.95–1.04), P = 0.75; Figure). No heterogeneity was found in treatment effect between ACE inhibitors and ARBs (P for interaction 0.11). Interestingly, significant heterogeneity was found with respect to mortality reduction with different ACE inhibitors (P for heterogeneity <0.001, I^2 99%). Perindopril-based regimens were associated with a statistically significant reduction in all-cause mortality (HR, 0.87; 95% CI, 0.81 to 0.94, P<0.0001), whereas the remaining ACE inhibitors were not. No heterogeneity was observed with respect to the effects of the different ARBs.

Conclusion: ACE inhibition leads to a robust reduction in mortality in hypertensive patients. Because of the high prevalence of hypertension this treatment may result in a considerable number of lives saved.

3A.04 ACE-INHIBITOR PHARMACOGENOMICS: CANDIDATE GENES AND GENOME-WIDE SCAN APPROACH

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Hypertension is a health problem that affects about 15 million people in Italy. Less than 25% (about 1 million) of patients currently under antihypertensive agents has correct blood pressure control despite numerous antihypertensive drugs available. Aim of our study was to identify environmental, hormonal and genetic factors that influence antihypertensive response after one month of ACE-