## OS 30 Hot topics: experimental and clinical studies

### OS30/THU/07 - Effect of different antihypertensive treatments on Ras/ MAPKinases/ Akt activation in hypertension and diabetes

*Fernández-Campo L.[1], Grande M.T.[2], Fuentes-Calvo I.[2], Macías-Núñez J.F.[3], Sánchez-Rodríguez A.[3], Grande J.[4], García-Ortiz L.[5], López-Novoa J.M.[2], Martínez-Salgado C.[6]*

[1]Centro de Salud de Matilla de los Caños, Salamanca, Spain, [2]Unidad de Fisiopatología Renal y Cardiovascular, Instituto Reina Sofía de Investigación Nefrológica, Departamento de Fisiología y Farmacología, Universidad de Salamanca, Salamanca, Spain, [3]Unidad de Hipertensión, Hospital Universitario de Salamanca, Salamanca, Spain, [4]Servicio de Nefrología, Hospital Virgen de la Concha, Zamora, Spain, [5]Unidad de Investigación, Centro de Salud de La Alamedilla, Salamanca, Spain, [6]Hospital Universitario de Salamanca, Unidad de Investigacion, Salamanca, Spain

**Objectives:** We have evaluated whether the antihypertensive treatment with angiotensin II receptor blockers (ARB), angiotensin converting enzyme inhibitors (ACEi), and diuretics induce changes on Ras GTPase activation and in some of its effectors (Erk and Akt) in lymphocytes from hypertensive and diabetic patients.
**Methods:** peripheral blood samples were obtained from patients with newly diagnosed essential arterial hypertension, with or without diabetes, before and after 1 week and 1, 2 and 3 months of treatment. Lymphocytes were isolated in a ficoll gradient. Ras activation was evaluated by a Raf pull-down assay. Phospho-Erk and phospho-Akt activation was evaluated by western blot.
**Results:** ACEi treatment transiently reduced Ras activation in the first month of treatment, but diuretics induced a sustained increase in Ras activation throughout the 3 months of the study. In diabetic-hypertensive patients, ARB, ACEi and diuretics increased Ras activation only during the first week. ACEi treatment increased phospho-Erk expression during the first week and also in the last 2 months of the study; however, diuretic treatment reduced phospho-Erk expression during the last 2 months of the study. In diabetic-hypertensive patients, antihypertensive treatments did not induce changes on phospho-Erk expression in lymphocytes. ACEi treatment reduced phospho-Akt expression in diabetic patients only in the first month of treatment.
**Conclusion:** These data show that antihypertensive therapy with ACEi, and diuretics in a lesser extent modify Ras activation and some of its signalling pathways, even though in different directions; ARB do not seem to have any influence on Ras signalling pathways.