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biomarkers

135P ACE and CXCL10 as predictive biomarkers in the LEA study

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Background: LEA Study (GEICAM/2006-11/GBG51), is a randomized clinical trial comparing bevacizumab in combination with endocrine therapy (ET + B) with endocrine therapy (ET) in postmenopausal women with advanced or metastatic HR-positive/HER2-negative breast cancer (BC) with indication of hormonotherapy as first-line treatment. Patients with secondary hypertension had better progression-free survival (PFS) and overall survival (OS). We have evaluated the role of two hypertension-related biomarkers, Angiotensin-Converting Enzyme (ACE) and Small-Inducible Cytokine B10 (CXCL10) as prognostic and/or predictive biomarkers of benefit to bevacizumab in the first line metastatic disease.

Methods: From 380 patients, 266 were included in 33 Spanish sites. Median age was 64 years, 63.5% had measurable disease, 97.4% were metastatic at randomization, 51.5% had visceral disease and 52.6% received previous chemotherapy. PFS was 14.3 months (range 0.8-61.1), OS was 34 months (range 0.8-71.6) and 93 patients had Objective Response (OR). We analyzed 124 plasma samples collected before treatment (52 from ET and 72 from ET + B arms). Circulating levels of ACE and CXCL10 were determined by ELISA. ACE levels of 115ng/ml and 135ng/ml were pre-defined as cutoff values. CXCL10 was explored as a quantitative variable.

Results: PFS was 15.1 months (range 1.4-61.1), OS was 31.1 months (range 2.8-61.1) and 40.3% had OR. OR was significantly different between treatment arms ($p < 0.001$) but not PFS or OS. Median ACE concentration was 130.9ng/ml (range 35.3-315.4). Low ACE (<135ng/ml) had better PFS in the whole population ($p = 0.048$) and in the ET + B arm ($p = 0.041$). ACE cutoff of 115 ng/ml was not able to identify any subgroup with better prognosis. Median CXCL10 concentration was 230.3pg/ml (range 15.1-4129.6). A higher expression of CXCL10 was significantly associated with worse OS in the whole population ($p < 0.0001$) and each treatment arm ($p = 0.002$ and $p = 0.001$ in ET and ET + B, respectively). No association with OR were identified neither for ACE nor for CXCL10.

Conclusions: ACE levels could be considered a prognostic and a bevacizumab predictive biomarker of PFS. CXCL10 could be prognostic of OS. Confirmatory studies are warranted.

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