C50 Differential gene expression patterns in HER2 positive metastatic breast cancer patients according to hormone receptor status

C. Omarini[1], S. Kaleci[2], G. Guaitoli[1], S. Bettelli[3], C. Caprera[3], S. Manfredini[3], F. Caggia[1], M.C. Baschieri[1], L. Moscetti[1], A. Maiorana[3], S. Cascinu[1], F. Piacentini[1]

[1]Division of Oncology - University Hospital of Modena, Modena; [2]Division of Statistics - University Hospital of Modena, Modena; [3]Division of Pathology - University Hospital of Modena, Modena

Background: HER2 positive breast cancer (HER2+ BC) is a heterogeneous disease. Presenting features, patterns of recurrence and survival of HER2+ BC can differ according to hormone receptors (HR) status. The purpose of this study is to highlight different gene profile and molecular pathways between HR+ and HR- metastatic HER2+ BCs.

Materials and methods: 34 HER2+ metastatic BC patients were included: 18 patients with HR+/HER2+ and 14 with HR-/HER2+. Data regarding tumor characteristics, treatment information and clinical outcomes were collected. The expression of 770 genes and 13 molecular pathways were evaluated by means of *Nanostring PanCancer pathway panel* performed on BC formalin-fixed paraffin-embedded tissues from diagnostic core biopsy or surgical resection specimen.

Results: Gene expression analysis identified 118 genes with significantly different expression in the two cohorts. All but one of these genes were over-expressed; only the gene CACNG6 was down-regulated in HR+/HER2+ group. In particular, 93 genes were over-expressed in HR-/HER2+ while 24 were overexpressed in HR+/HER2+. Most of these genes encoded growth factors, pro- or anti-inflammatory interleukins and DNA repair factors. 62% of these genes were involved in PI3K, MAPK and RAS pathways (32, 22 and 18, respectively). PI3K, MAPK and NOTCH pathways were differently expressed between HR+/HER2+ and HR-/HER2 + ($p = 0.003$, $p = 0.0018$, $p = 0.02$, respectively). All these three pathways were overexpressed in HR-/HER2+ BC. In particular, all the significantly different expression genes in NOTCH pathways were overexpressed in HR-/HER2+ group.

Conclusions: This genome expression analysis identified a gene expression profile able to differentiate HR+ versus HR- HER2+ metastatic BC. The overexpression of PI3K, MAPK and NOTCH pathways in HR-/HER2+ BC could justify its more aggressive behaviour. The validation of this HER2+ BC profile needs further investigation.