CLINICAL AND MOLECULAR PREDICTORS OF LONG-TERM RESPONDER IN HER2 POSITIVE METASTATIC BREAST CANCER PATIENTS

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Background: Several multigene tests have been developed in Metastatic Breast Cancer (MBC), in order to identify predictive factors correlated to clinical outcomes. The purpose of this study is to investigate the characteristics that could differentiate long-term responders from patients experiencing early progression during anti-HER2 treatment.

Methods: 34 HER2 positive MBC patients were included: 20 patients in Long Responders group (LR) with a time to progression longer than 3 years and 14 patients in Poor Responders group (PR) with a progression disease within one year of anti-HER2 therapy. The expression of 770 genes and 13 pathways were evaluated using Nanostring PanCancer pathway panel performed on BC tissues.

Results: Baseline characteristics were similar between the two groups. Gene expression analysis identified 30 genes with significantly different expression in the two cohorts, five were driver genes (BRCA1, PDGFRA, AR, PHF6 and MSH2). The majority of these genes were over-expressed, mainly in LR patients, and encoded growth factors, inflammatory interleukins and DNA repair factors. Only four genes were down-regulated, all in PR group. Most of these genes were involved in MAPK and PI3K pathways. MAPK pathway was differently expressed between LR and PR (p=0.05). Even if not statistically but clinically relevant, PI3K was the only pathway overexpressed in PR patients (median expression LR: 1441 ± 485 vs 1759 ± 762 in PR group; p= 0.1).

Conclusions: Genome expression analysis identified a group of genes that may predict more favourable outcomes. Up-regulation of MAPK and down-regulation of PI3K pathways could be a positive predictive factors.

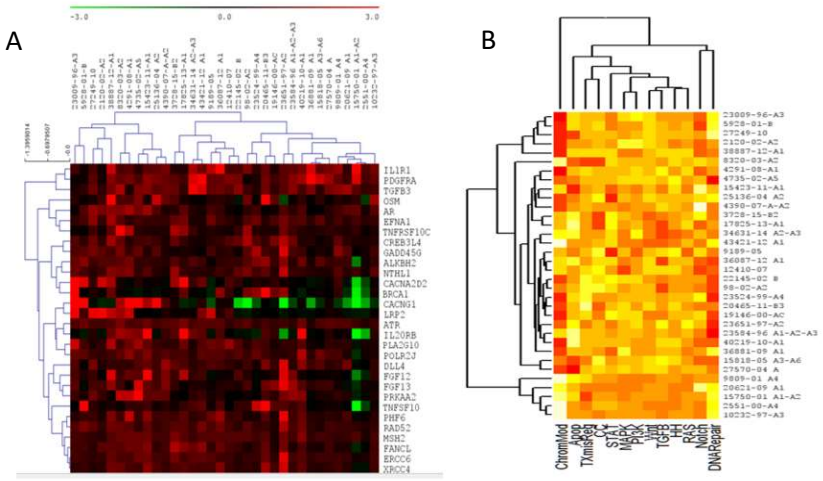

Figure 1. (A) Hierarchical clustering based on RNA expression levels of 30 genes out of 770 genes analysed by PanCancer panel. Rows: genes, columns: samples. Expression level of each gene in a single sample was related to its median level across all samples and is depicted according to a colour scale show at the top. Red and green, expression levels above and below the median, respectively. (B) Pathways deregulation score for each tumor sample on the basis of gene expression data. Each row corresponds to a pathway and each column to a sample. Pathways and samples are clustered according to pathways deregulation score. Red color represents low score, yellow color high score.