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| Title               | Trastuzumab Resistance in HER2 +ve Metastatic Breast Carcinoma Patients  |
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| Aim                 | Currently, no biomarkers of trastuzumab (T) clinical resistance have been validated. The aim of this pilot study was to evaluate the impact of PIK3CA mutations and p95HER2 (pHER2 truncated form) expression on the efficacy of a T based-therapy in a HER2-positive metastatic breast cancer (MBC) patients (pts).   |
| Materials & Methods | 107 HER2-positive MBC pts, treated in the last 10 years, were evaluated. Median age was 54 years (25-79); ECOG performance status was 0 in 56% of pts; all pts received several lines of treatment including T; biomarkers molecular analysis was performed in 70 tumor specimens. The IHC expression of p95HER2 was evaluated by a monoclonal antibody that specifically recognizes only the HER2 external domain; the HER2 integrity was defined by the presence of a homogeneous membrane staining (moderate or intense) in at least 30% of the cells, otherwise the HER2 was defined as p95HER2 positive. PIK3CA mutations in exons 9 and 20 were detected by automated sequencing. The molecular data were correlated to Time to progression (TTP) of the first line treatment including T and the Overall Survival (OS) by using the Kaplan-Meir method and the log-rank-test.   |
| Result              | p95HER2 positive pts and PIK3CA mutations in exon 9 or 20 were detected in 42% and 22% of tumor specimens, respectively. p95HER2 positive tumors showed a shorter TTP and OS that did not reach statistical significance; PIK3CA mutations correlated with a worse TTP (median 7,6 vs 11,3 months) and OS (median 20,1 vs 41,0 months, p= 0,046).  |
| Conclusion          | These preliminary results suggest a possible role of PIK3CA mutational status in predicting the outcome of MBC pts treated with T.   |