96P ERBB2 and PI3KCA mutations in endocrine resistant breast cancer (BC)

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Background: An increasing number of molecularly targeted drugs are now available and, for some of these therapies, predictive biomarkers have already been identified. In particular, mutations in ERBB2 might represent an alternative mechanism for HER2 activation. They occur more frequently in HER2-negative (HER2-) tumors and seem to be good target for HER2 therapy. Furthermore, PI3KCA mutations showed to predict sensitivity to Fulvestrant, Buparlisib, Taselisib and resistance to Lapatinib. We evaluated the incidence of ERBB2 and PI3KCA mutations in 14 hormone receptor (HR)-positive BC and in their matched endocrine-resistant recurrences.

Methods: We evaluated a panel of genes including ERBB2 and PI3KCA, in FFPE tissues. We analysed 14 HR-positive BCs and their matched recurrences. All the relapses have been developed during an endocrine treatment.

Results: 4/14 pts were diagnosed with HER2+ BC, while 10/14 pts developed HER2- BC. Overall, we found 8 different mutations of ERBB2 in 9 samples: A356D, Q1206X, Q396X, Q393X, P523L, I654V, G1220C, 135 + 3G>T. We found 6 different mutations of PI3KCA in 10 samples: N345K, V344M, E542K, E545K, A1035V, H1047R. ERBB2 mutations were found in the 28.6% of primary tumors and in the 35.7% of relapsed sites. PI3KCA mutations were found in the 35.7% of primary tumors and in the 35.7% of relapsed sites. mOS in PI3KCA mutated pts was 112,8 months, while mOS in PI3KCA wild-type pts was 99. mOS in HER2+ and/or ERBB2 mutated pts was 115.6 months, while mOS in HER2-ERBB2 wild type pts was 97.5. mDFS in PI3KCA mutated pts was 41.2 months, while mDFS in PI3KCA wild-type pts was 28. mDFS in HER2+ and/or ERBB2 mutated pts was 46.4 months, while mDFS in HER2- wild-type pts was 28.5.

Conclusions: We found an overall detection rate of ERBB2 mutations higher than that described in literature, while PI3KCA mutations were in line with the literature. The identification of ERBB2 or PI3KCA mutation might justify a more targeted neo/adjuvant approach and might guide the subsequent treatment choices. According to the literature, pts with PI3KCA mutation showed better prognosis, while, contrary to the previous literature, in our study the majority of ERBB2 mutations occurred in HER2+ samples and HER2+ and/or ERBB2 mutated samples did not show worse outcomes.

Legal entity responsible for the study: Marta Venturelli.

Funding: Angela Serra Association.

Disclosure: All authors have declared no conflicts of interest.