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Titel des Beitrags: Role of TP53 mutations in triple negative and HER2-positive breast cancer treated with neoadjuvant anthracycline/taxane-based chemotherapy.

Abstract: TP53 mutations are frequent in breast cancer, however their clinical relevance in terms of response to chemotherapy is controversial. Pre-therapeutic, formalin-fixed, paraffin-embedded core biopsies from the phase II neoadjuvant GeparSixto trial that included HER2-positive and triple negative breast cancer (TNBC) were subjected to Sanger sequencing of exons 5-8 of the TP53 gene. TP53 status was correlated to response to neoadjuvant anthracycline/taxane-based chemotherapy with or without carboplatin and trastuzumab/lapatinib in HER2-positive and bevacizumab in TNBC. p53 protein expression was evaluated by immunohistochemistry in the TNBC subgroup. Of 450 breast cancer samples 297 (66.0%) were TP53 mutant. Mutations were significantly more frequent in TNBC (74.8%) compared to HER2-positive cancers (55.4%, P 0.05 each). Missense mutations tended to be associated with a better survival compared to all other types of mutations in TNBC (P = 0.093) and in
HER2-positive cancers (P = 0.071). In TNBC, missense mutations were also linked to higher numbers of tumor-infiltrating lymphocytes (TILs, P = 0.028). p53 protein overexpression was also linked with improved survival (P = 0.019). Our study confirms high TP53 mutation rates in TNBC and HER2-positive breast cancer. Mutations did not predict the response to an intense neoadjuvant chemotherapy in these two molecular breast cancer subtypes.