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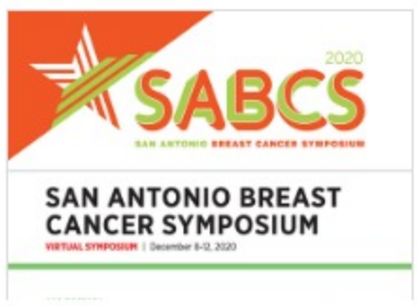

POSTER SESSION ABSTRACTS | FEBRUARY 15 2021

Abstract PS11-35: Mipra, a window of opportunity study evaluating mifepristone treatment for postmenopausal breast cancer patients with higher levels of progesterone receptor isoform a than b FREE

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Abstract

Background: Different antiprogestins have been clinically evaluated in gynecological andbreast cancers. Mifepristone (MFP), as well as onapristone and telapristone acetate, showedpartial responses in breast cancer clinical trials. Preclinical data indicates that antiprogestinsinhibit cell proliferation of luminal breast carcinomas expressing higher levels of progesteronereceptor isoform A (PRA) than those of isoform B (PRB) evaluated by western blots (WB). Thus,we designed a pre-surgical window trial to determine the therapeutic effects of oral MFP oncell proliferation and on differential gene expression in 20 breast cancer patients selected bytheir high PRA/PRB isoform ratio.**Methods**. MIPRA is an open-label, one-arm, prospective interventional study (NCT02651844).We interviewed 140 naive breast cancer patients and 133 accepted to participate. Four coreultrasound-guided biopsies were performed, two were formalin-fixed for diagnosis, ER, PR,HER2, and Ki67 evaluation and two were snap-frozen for WB and molecular studies. Patientsthat met the inclusion criteria, with ER+, PRA/PRB>1.5 and total PR ≥50% determined by WBand immunohistochemistry (IHC), respectively, were included for MFP treatment. Plasma wasobtained before and after treatment for future studies. Patients were treated with oral MFP(200 mg/day) for 14 days before surgery which was performed on day 15. Clinical examinationwas performed at days 7 and 14 to register possible adverse effects and to measure tumorsize. During surgery, samples were formalin-fixed for IHC studies, and others were snap-frozenfor further molecular studies. One patient had a bilateral breast cancer, and both tumorsmatched with the inclusion criteria and were included. The primary endpoint was Ki67labeling, comparing diagnostic core needle biopsy to post-therapy surgical specimens.Considering previous studies performed with tamoxifen, we pre-specified that 30% of relativereduction in Ki67 would be considered as a positive response. Differences in Ki67 expressionwere quantitated by an expert pathologist counting at least ten 40x fields per slide. Theseresults are currently being validated by a second pathologist. One patient, with a core biopsywith less than 500 total cells, was excluded. Ongoing experiments include secondary and otherendpoints: comparison of apoptotic, proliferative and hormone receptor markers by IHC,measurement of MFP plasma levels and, RNAseq analysis in samples pre- and post-treatment. Ki67 changes from baseline were tested with paired Wilcoxon matched-pairssigned-rank test.**Results:** The median (range) Ki67 value of biopsies was 11.87% (2.70- 34.56) and for surgicalspecimens was 6.45% (0.48-23.77). A 45.67% of decrease in the median % Ki67 (41.63%comparing the arithmetic mean values and 50.83% comparing the geometric mean values) wasregistered in all surgical specimens compared to baseline (p= 0.003). Using the pre-specifiedresponse parameter (30% relative reduction in Ki67), we identified 15/20 (75%) responders.Considering only responsive tumors, a 49.87% decrease in the median % Ki67 (50.83%,arithmetic mean; 62.34% geometric mean) was observed (p<0.0001) between baseline andsurgical specimens. In those cases with the highest response, the decrease in Ki-67 wasaccompanied by a decrease in tumor volume (ultrasound measurements).**Conclusion**: Our results show that MFP treatment may be effective in patients showing a highPRA/PRB ratio. The magnitude of the inhibition was similar or higher to that reported fortamoxifen in ER+ breast cancer patients in short-term treatment studies. Ongoing analysis willdetermine if there are changes in other markers that may help to further define MFP-responsive patients.

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