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Poster Abstracts

Biomarkers

P1
Circulating adiponectin levels as a predictive factor of breast cancer in a double-blind 2×2 phase II trial of low-dose tamoxifen and fenretinide for breast cancer prevention

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Background: The assessment of breast cancer risk is a key step for an effective preventive treatment. Besides the established risk assessment models, independent predictive factors like circulating biomarkers may also be important to better select high risk subjects and to determine efficacy of chemopreventive treatment.
Adiponectin is a peptide hormone secreted from the adipose tissue that has been inversely related to breast cancer risk. In the present study, we measured plasma adiponectin levels in premenopausal women participating in a phase II trial of low-dose tamoxifen and fenretinide for breast cancer prevention.
Methods: Premenopausal women (n = 235) were randomly assigned in a double-blind 2×2 trial to receive tamoxifen 5 mg/d, fenretinide, a vitamin A derivative, 200 mg/d, both agents, or placebo for 2 years. A total of 181 premenopausal women with ductal intraepithelial neoplasia (DIN) and 54 unaffected women at higher risk according to the Gail model were enrolled.
Mammographic percent density was centrally measured using the computer-assisted method described by Boyd. Plasma adiponectin was measured by use of a commercial enzyme-linked immunosorbent assay kit.
Preliminary results: According to disease status (DIN vs Gail) at baseline, median plasma adiponectin levels were lower in women with a DIN (10 ug/ml; interquartile [IQ] range: 7.1–14) compared to unaffected women with a Gail risk (12 ug/ml; IQ range: 8.7–14.7) (p = 0.05).
Importantly, after a median follow-up of 5.5 years, plasma adiponectin levels were lower in women who had a breast cancer event (7.7 ug/mL; IQ range: 6.46–12.78) compared to women without event (11.02 ug/mL; IQ range: 7.8–14.4) (p = 0.015). This difference is also maintained after adjusting for BMI and treatment allocation (p = 0.011).
Considering the distribution of adiponectin levels at baseline, we observed a 9% reduction in the hazard ratio of breast cancer events by each unit increase of adiponectin levels (95% CI: 0.83–0.96; p = 0.02, cox model adjusted for BMI, treatment allocation, mammographic density and disease status at baseline).
Conclusion: We found that subjects with lower plasma adiponectin levels had a significantly higher risk of breast cancer event. The association appeared independent of known risk factors such as BMI and mammographic breast density. Further studies to better understand and confirm the role of adiponectin as independent predictive risk factor are warranted.

P1a
Promoter methylation of the BRCA1 gene in young breast cancer patients with no significant family history

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Background: Premenopausal breast cancer represents < 25% of all breast cancers, and only 5–10% of all breast cancer can be attributed to mutations in BRCA1/2 genes. Therefore, 90–95% of premenopausal patients may have a sporadic form of breast cancer. Although these women do not have germline mutations in the BRCA genes, it is possible that epigenetic modifications which lead to BRCA gene silencing may play a role and be a risk factor in these sporadic cases. Previous research has identified epigenetic changes in the BRCA1 gene in as many as 10–20% of sporadic cases. More recently, other investigators used peripheral blood cells (PBC) to evaluate the presence of somatic methylation of the BRCA1 promoter and suggested that promoter methylation in normal PBC can be identified and correlated with development of triple negative breast cancer. However, currently the presence and rate of BRCA1 promoter methylation is not well described in women with early onset breast cancer and high risk women. Therefore, in this current study our aim was to examine the rate of BRCA1 promoter methylation in breast cancer patients diagnosed at or under 40 who had no detectable BRCA1 mutations and in an effort to correlate BRCA1 promoter methylation with premenopausal breast cancer development.
Methods: 52 U.T. MD Anderson patients were identified from a prospective study database. 35 patients had a history of breast cancer or ducal carcinoma in situ (DCIS) who tested negative for a deleterious mutation in the BRCA1gene were enrolled in the study. As a control, 6 BRCA1 positive patients with breast cancer and 11 BRCA negative unaffected high risk patients were also examined. Median age was 35 (range 24–40). Twenty-eight (75.7%) of the patients had a positive family history of breast cancer, however only 12 (34.3%) had a first degree relative with breast cancer, other patients were tested for BRCA mutations based on their young age. Three (8.1%) had stage 0, 3 (8.1%) had stage I, 22 (59.5%) had stage II, 6 (16.2%) stage III, and 3 (8.1%) stage IV breast cancer. The estrogen receptor (ER) was positive in 27 (72.9%) of the samples, progesterone receptor (PR) in 20 (54.1%)