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Editorial

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Significance of Estrogen Receptor Alpha Progesterone Receptor and Her-2 Testing in South East Nigeria. A Good Template for Sub-Saharan Africa Breast Cancer Management

Martin N[1*], Joseph U[2], Omotowo B[2], Onyekachi N[1], Sunday N[1], Vincent EC[3], Onyekachi A[1], Victor N[5], Okhen NC[5], Ogochukwu N[1], Anthony E[6], Vincent O[5], Isioma O[3], Isaiah N[6]

[1]*Department of Morbid Anatomy, University of Nigeria, Nsukka, Nigeria*

[2]*Department of Community Medicine, University of Nigeria, Nsukka, Nigeria*

[3]*Department of Surgery, University of Nigeria, Nsukka, Nigeria*

[4]*Department of Medicine, University of Otago, Dunedin, New Zealand*

[5]*Department of Anatomy, Grace Pathology Consults, Enugu, Nigeria*

[6]*Department of Surgery, Enugu State University of Science and Technology, Enugu, Nigeria*

DESCRIPTION

Estrogen receptor alpha, progesterone and Her-2 neu (ER/PgR/Her-2) testing are now routinely performed in breast cancer evaluations in South-eastern Nigeria, as well as in many centers in Sub-Saharan Africa. Its significance remains to be fully harnessed maximally. Estrogen receptor assessment is key in the management of breast cancer. Its relevance as a predictive and prognostic factor is well documented. Patients with ER positive breast cancers have a better prognosis compared to those with ER-negative breast cancers. Thisis in part due to the availability of anti-estrogen agents such as tamoxifen that binds and inhibits ERα, leading to inhibition of ER breast cancer growth. The relevance of progesterone receptor however is uncertain, though it is usually recommended. It is pertinent to note that the basis of estrogen receptor positivity in these cases was an algorithm of at least 1% nuclear positivity as recommended by the American society of clinical oncologists/ College of American pathologist guidelines recommendation for immuno-histochemically testing of estrogen and progesterone receptor of 2010.

Anti-estrogen treatments are typically combined with other treatments. For example, combined administration of Fluoro-pyrimidine plus tamoxifen or tamoxifen plus anthracyclines and/or taxanes has been used to treat both ERþ and ER-patients. However, anti-hormone treatments can also negatively impact the efficacy of chemotherapy.In particular, several clinical studies have reported antagonistic effects of tamoxifen on the efficacy of chemotherapeutic agents based on timing of administration. The exact mechanism leading to the synergistic or antagonistic effects of anti-hormone therapies with these chemotherapeutic agents has yet to be fully understood. Cockery et al had previously demonstrated that low PRP4K expression is associated with intrinsic and acquired taxane resistance in breast and ovarian cancer. Thus, changes in PRP4K protein levels mediated by estrogen signaling could conceivably alter the taxane response of ERþ breast cancer cells. Cockery specifically sort to determine if tamoxifen treatment could alter the taxane response of ER breast cancer cells. This data published indicates that inhibition of estrogen receptor signaling results in a reduction in PRP4K expression that correlates with reduced efficacy of paclitaxel.

Typically, patients with ER positive breast cancer will receive chemotherapy that includes DNA damaging agents (e.g. Doxorubicin and cyclophosphamide) and anti-mitotic drugs such as the taxanes (e.g. paclitaxel). Patients are then treated with anti-hormone therapies such as tamoxifen, an inhibitor of ERα, for 5 to 10 years. Unfortunately, a significant number of patients will relapse even with long-term anti-hormonal treatment and develop tumors that are refractory to treatment with tamoxifen and may need to be treated with other hormonal therapies and/or additional systemic chemotherapy, including treatment with taxanes. Previous clinical studies have shown that sequential use of tamoxifen and anthracycline/cyclophosphamide chemotherapy is more efficient than concurrent use of these drugs. These studies suggest that differential sequencing or timing of tamoxifen with chemotherapy isan important factor in improving treatment response.

Interestingly also Estrogen receptor alpha positivity signaling regulates the expression of taxane biomarker PRP4K thus reducing the sensitivity of these cells to taxanes as well as providing an important regulator of cancer sensitivity to paclitaxel in neo-adjuvant chemotherapy for breast cancer mediating resistance through.

On this basis we have advised non-use of paclitaxel as a first line drug in ER positive breast cancer opting rather for the use of anthracycline in a sequential manner and introducing tamoxifen after chemotherapy but not concurrently. It appears from preliminary observations this is the best approach with longer lasting effects. Relapses could be treated with taxanes after which aromatase inhibitors may be substituted for tamoxifen.