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Original Research

Molecular Subtypes of Receptor-defined Breast Cancer from Nakuru, Kenya

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Abstract

Introduction

The incidence of breast cancer in Sub-Saharan-Africa (SSA) is rising. Expression of hormone receptors and molecular-subtyping is paramount in rationalizing prognosis and therapy. There exists significant variation in molecular status of breast cancer in SSA. We aimed to describe the receptor status and molecular subtypes of breast cancer at our centre.

Methods

We conducted a retrospective study on patients with breast cancer enrolling for oncological care at our centre beginning May 2018 to December 2021.

Results

We included 345 patients with a median age of 49 years, 331 female and 14 males. The most common histological variant was invasive-ductal -carcinoma of no-special-type from both biopsy (84.3%) and mastectomy specimens (82.8%). DCIS accounted for only 2.9%. ER positive tumours accounted for 62.8% from biopsy and 66.7% from mastectomy specimens. The majority of the female patients had luminal-type disease (Luminal A or B) with 65.2% from biopsy specimens and 67.3% from mastectomy specimens. About 20% had TNBC.

Conclusion

Breast cancer patients from Nakuru, Kenya, are likely to be young and with luminal-subtype invasive ductal carcinoma. In contrast to some previous reports, less than a quarter of our patients have TNBC. We recommend prioritization, standardization and scaling of receptor testing and molecular-subtyping to optimize treatment protocols and personalized management strategies for breast cancer patients.

Introduction

Breast cancer is the leading cancer, both in incidence and mortality, among women worldwide.[1] It is also the second commonest cancer in women in sub-Saharan Africa (SSA)[2] Additionally, while the incidence of breast cancer is on the rise in SSA, the prognosis is poorer than in Western countries.[3] In Kenya, the incidence of breast cancer among women is the highest compared to other cancers.[2] Breast cancer is treated based on the clinical, pathological and immunohistochemical characteristics of the tumours and the outcomes of breast cancer management depend on the clinical and pathological stages of the tumour, nodal status, and on the histological types.[4]

The presentation, diagnosis and initiation of treatment of breast cancer in SSA is likely to be late due to innate challenges in seeking, reaching, and accessing care.[5] Breast cancer hormone receptor status is particularly useful for predicting the likely prognosis and tailoring treatment.[6] Additionally, the receptor status is paramount in determining

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the molecular pattern of the cancer and the need for targeted therapy.[7] This can help reduce over or under undertreatment by enabling prediction of the likely response to treatment, the probability of recurrence and by helping apportion patient and risk-specific adjuvant therapy.[8] However, the difficulties in the management of breast cancer in SSA is further hampered by the general unavailability of molecular testing.[3]This contributes to higher cancer related mortality rates than incidence in SSA.[1,9] In contrast, in the Western world, there exists elaborate screening programs and diagnosis is as a result likely to be made earlier and treatment commenced earlier.[8]

Breast cancer subtypes can be identified and classified using immunohistochemistry (IHC), combining oestrogen receptor (ER), progesterone receptor (PR), HER2 and Ki-67 index (a human nuclear antigen proliferative marker), into four intrinsic molecular subtypes: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-enriched and basal-like (triple negative).[7,10] More accurately, a micro-array-based gene expression profiling (GEP) could be used for this classification.[10] GEP is however largely unavailable in Kenya and IHC is commonly used as the best substitute. These recent improvements in the knowledge of breast cancer have highlighted the importance of molecular subtypes in its understanding and management. For example, the luminal molecular subtypes (which stain positive for oestrogen receptor) are commonly associated with better prognosis, globally.[8,9,11] In addition, triple negative breast cancer has been found to be common in younger female patients, to present with advanced disease and to have a higher risk of recurrence and a poorer outcome.[4,9] Brinton and colleagues argue that majority of breast cancers in Africa are likely to be hormone receptor negative and triple negative subtypes.[12] However, there exists a noteworthy variation in the molecular status of breast cancer in SSA.[1] For example, Hawary et al showed predominance of luminal A in a subset of Egyptian patients.[11] Likewise, Sayed et al found that in Nairobi, Kenya's capital, the majority of patients seeking care for breast cancer had hormone receptor positive disease.[13] Generalization on the basis of geography is therefore unpredictable.

There are no studies assessing the receptor status and/or molecular subtypes of breast cancers from our region. We therefore conducted a descriptive study to determine the pattern of receptor and molecular status of breast cancer among patients receiving care at our centre. The centre is the region's principal referral hospital.

Methods

We carried out a descriptive retrospective study at the Nakuru Level 5 hospital's new oncology unit, in Kenya. The hospital serves a catchment of 2.3 million people. We included all patients of all ages with or without a prior histological diagnosis of breast cancer who were enrolled for care as walk-ins or as referrals between May 2018 and December 2021. We excluded patients whose full records could not be retrieved.

Patient and disease particulars were retrieved from their records using a secure web-based questionnaire; this data was collected as routine data at the point of initiation of care. We collected data on patient demographics, tumour histological type and receptor status.

Hormone receptor status was classified as positive where the pathology result read positive or where the Allred score was 2 to 8.[14] Her-2/Neu status was interpreted as follows; score of 0 as negative, 1+ as negative, 2+ as equivocal and 3+ as positive according to the College of American Pathologists (CAP) guidelines.[15] The receptor status was used to assign a molecular subtype using the schema shown in table 1.[16] Due to a foreseen challenge with unavailability of Ki-67 results from the majority of pathology reports, luminal A and B were not be specified and were in effect classified as a 'Luminal cancers'

Table 1. This table illustrates a schematic guide on assignment of molecular subtypes of breast cancers from the receptor status and Ki-67 index.

Molecular subtype	ER	PR	HER2-Neu	Ki-67 (%)
Luminal A	+	+/-	-	<14
Luminal B	+	+/-	+/-	≤14
Luminal cancers	+	+/-	+/-	Any
Her2-Neu enriched	-	-	+	≥14
Triple Negative	-	-	-	≥14

All data was serialized for anonymity. Data was analysed with descriptive statistics using Stata Version 14, (StataCorp LLC Canada, US).

Ethical approval for the study was given by the Nakuru Level V Hospital institutional review committee. (ERC/NLV5/2021/9-04)

Results

Patient characteristics

Four hundred and three patients with a diagnosis of breast cancer attended our centre during the study period. We excluded 58 patients whose full records could not be retrieved leaving 345 patients in our study with a median age of 49 years, (interquartile range (iqr); 40, 61). The patients were predominantly female, with only 14 (4.0%) being male. The majority of the patients (n=192, 55.6%) were below 50 years of age. The characteristics of the included patients are summarized in table 2 below.

Table 2. Baseline characteristics of the included patients

Baseline characteristics	Total(N=345)	%
Age (in years), median (iqr)	49.00 (40.00; 61.00)	-
Age (in years), mean (SD)	50.8 (+/- 13.5)	-
Age category (in years)), n (%)		
≤50 years	192	55.6
51 - 80 years	148	42.9
Above 80 years	5	1.5
Gender, n (%)		
Male	14	4
Female	331	96

Histology

Pre-treatment histological diagnosis (from a biopsy) was unavailable in 65 cases (18.8%), while 20.5% (n=39) of the patients who had surgery did not have histology from their mastectomy specimen. The most common histological variant was invasive ductal carcinoma of no special type (IDC) from both the biopsy (84.3%, n=236 of 280) and mastectomy specimens (82.8%, n=125 of 151). DCIS accounted for only 2.9% (n=8) of biopsy specimens and 0.7% (n=1) of the histology from mastectomy specimens. The distribution of other histological variants is demonstrated in table 3 below.

Receptor status

IHC receptor status from biopsy specimens were unavailable for 42.3% of patients, whereas, receptor status testing was available in 51.4% of the patients that underwent surgery. Only 29 patients had ER, PR, and HER2 status data available from both their biopsy and surgical specimens. In respect to the patients whose IHC results were available, ER positive tumours accounted for 62.8% (n=125 of 199) from biopsy and 66.7% (n=74 of 111) from mastectomy specimens. The results for Her2 receptors and Ki-67 index are demonstrated in table 3 above. (Distribution of the receptor status among gender and age groups is available as a supplementary file).

Molecular status

The majority of the female patients had luminal type disease (Luminal A or B) with 65.2% from biopsy specimens and 67.3% (n=76 of 113) from mastectomy specimens. As shown in table 4 below, majority of the patients with luminal type disease were below 50 years of age. None of the male patients had triple negative disease but 22.0% (n=42 of 191) of female IHC from biopsy and 21.1% (n=23 of 109) from mastectomy were triple negative subtype.

Discussion

Our study demonstrated that breast cancer patients from our centre are likely to be young (below 50 years of age) and with luminal subtype invasive ductal carcinoma. Less than a quarter of our patients had triple negative disease. The characterization of receptor status and determination of the molecular subtype of breast cancer is paramount in the choice of therapy and determining prognosis.[1] An important limitation of our study was the limited number of mastectomy specimens submitted for IHC staining even in the face of probable discrepancies between preoperative biopsy IHC and IHC from surgical specimens. This was likely due to low level of awareness on utility of receptor and molecular typing after surgery and/or financial constraints.

Several authors have previously argued that breast cancer, specifically Luminal A cancer, is expected to be common in postmenopausal women.[17,18] For example, in Nigeria, ER positive tumours were shown to be more prevalent in women older than 50 years.[19] However, there are numerous conflicting reports from our region that cite that the majority of patients diagnosed with breast cancer are young and likely to be below 50 years of age. This has previously been demonstrated by reports from Africa[1,13,20] In our study, the median age was 49. In fact, the majority of the patients with ER positive disease were below 50 years of age. Sally et al argue that the observed prevalence in premenopausal age group is likely due to a generally low median age in the African population.[21] However, this finding may implicate reproductive risk factors and suggest a biological basis of the early breast cancer in our population.[20] Lastly, only 1.5% of our patients were above 80 years. This possibly suggests life expectancy and/or survival and might not be an actual reflection of breast cancer incidence in this age group from our region.

The most commonly treated histological variant of breast cancer in our region is invasive ductal carcinoma (IDC) of no special type.[1,21,22] This corroborates with our findings and those of other authors from Kenya who reported rates of 84 to 90% from their series.[13,23] Marianne et al reported that 87% of their patients from Tanzania had IDC which is comparable to 82.3% reported from Nigeria by Adebamowo and colleagues.[1,19] In addition, only 2.9% of our patients had DCIS. This is likely due to the absence of a screening program in our region, but may also be a reflection of the health-seeking behaviour of the target population. Similar findings have been reported from a 7 years retrospective review of an unscreened population from South Africa, citing a rate of 1.1% for DCIS; this is in contrast to settings with elaborate screening programs where cancers are likely to be diagnosed at an earlier stage.[18]

Table 3. Breast cancer histological type, hormone receptor status, molecular subtypes and Ki-67 index from biopsy mastectomy specimens.

Characteristic	Type	Biopsy		Mastectomy Specimen	
		n/N	%	n/N	%
Histological type	DCIS	8/280	2.9	1/151	0.7
	Invasive ductal carcinoma, NOS	236/280	84.3	125/151	82.8
	Invasive lobular carcinoma	9/280	3.2	4/151	2.6
	Others	27/280	9.6	21/151	13.9
	Histology unavailable	65/345	18.8	39/190	20.5
	Surgery not offered/not done			155/345	44.9
ER status	Positive	125/199	62.8	74/111	66.7
	Negative	74/199	37.2	37/111	33.3
	Not available	146/345	61.7	97/345	28.1
	Surgery not offered/not done			137/345	39.7
PR status	Positive	110/197	55.8	65/108	60.2
	Negative	87/197	44.2	41/108	38.0
	Equivocal	-	-	2/108	1.8
	Not available	148/345	42.9	98/345	28.4
	Surgery not offered/not done			139/345	40.3
HER2 status	Positive	60/198	30.3	31/109	28.4
	Negative	130/198	65.7	71/109	65.1
	Equivocal	8/198	4.4	7/109	6.4
	Not available	147/345	42.6	99/345	28.7
	Surgery not offered/not done			137/345	39.7
Ki-67 proliferation index	Available	33/198	16.7	15/109	13.8
	Not available	165/198	83.3	94/109	86.2
Molecular subtype	Luminal	129/198	65.2	76/113	67.3
	HER2-enriched	29/198	14.6	14/113	12.4
	Triple negative	42/198	21.2	23/113	20.4

Table 4. The distribution of molecular subtypes of breast cancers by age group and sex.

	Biopsy			Mastectomy specimen		
	Luminal A or B	Her-2 Enriched	Triple Negative	Luminal A or B	Her-2 Enriched	Triple Negative
Sex (n=198)						
Female	120(94.5)	29(100.0)	42(100.0)	72(94.7)	14(100.0)	23(100.0)
Male	7(5.5)	0	0	4(5.3)	0	0
Age category (n=198)						
Below 50 yrs	75(59.1)	21(72.4)	22(52.4)	41(53.9)	7(50.0)	12(52.2)
51-80 yrs	49(38.6)	8(27.6)	20(47.6)	34(44.7)	7(50.0)	11(47.8)
Above 80 yrs	3(2.3)	0	0	1(1.4)	0	0

Previous reports have suggested that the majority of breast cancers from Africa are hormone receptor negative.[12,17,22,23] This has however been disputed by systematic studies in this region, which have shown that most cancers are indeed hormone receptor positive.[1,13,19,24] In our study, the majority the patients had positive hormone re-

ceptor disease. A recent systematic review on receptor-defined subtypes of breast cancer in indigenous populations in Africa established that the majority of breast cancers are hormone receptor positive, specifically ER positive.[25] While some authors clearly dispute existence of a real difference in hormone receptor status of Africans compared to other populations, Sayed et al argue that any perceived difference is likely multifactorial.[13,18,19] It is therefore postulated that adjusting for differences in age and other technical factors in handling of IHC specimens could account for any perceived differences in hormone receptor status between Africans and their matched cohorts from other geographies.[12]

HER2 status is important in the choice of treatment, especially adjuvant chemotherapy, and in prognostication. Most breast cancers in Africa are however known not to express HER2 receptors.[12] Our study showed that only a third of our patients expressed HER2. Likewise, the Ki-67 index is pivotal in prognostication and is also a component in the assignment of molecular subtype (as shown from table 1).[7,16,26] In our study, majority of the patients did not have Ki-67 index results. While this could be due to challenges in tissue processing and inability to apply advanced IHC techniques, it was probably due to cost restraints (as its testing is costed separately) and/or low level of awareness on the utility of Ki-67 index among members of the healthcare team at our centre. This subsequently limited our ability to differentiate luminal A from luminal B disease.

Several previous reports have argued that breast cancer in our region is predominantly triple negative subtype.[18,23] In contrast, we have found that the majority are in fact the luminal subtype (luminal A and B), with triple negative disease accounting for only 21.2% of diagnoses made from biopsy and 20.4% from mastectomy specimens. Our findings are in agreement with those of authors from Kenya, Tanzania and South Africa.[1,13,24,27] Likewise, most tumours from a Nigerian series were of luminal subtype.[19] As previously stated, it is likely that the molecular subtypes of breast cancer in Africa, e.g. triple negative breast cancer, is similar to that in other regions. However, since differences could exist even within a population, genetic variabilities and/or selection biases could account for the previous reports that found a higher prevalence of triple negative disease, in East Africa for example.[13,17,23] Bird and colleagues recommend genetic racial detailing to investigate for interracial heterogeneity in molecular subtypes of breast cancer.[24]

This is the first study describing molecular and receptor status of breast cancers in Nakuru. From our results, majority of cancers in our centre are likely to be invasive ductal carcinoma, expressing hormone receptor status and of luminal molecular subtype. Importantly, we recognize the likelihood of significant heterogeneity in receptor status and molecular subtypes that could exist even within our own population.[18] We therefore agree with other authors that availability of receptor testing and molecular subtype determination should be prioritized and that testing and interpretation of these results should be standardized.[13,25] This will allow the conduct of better quality studies enabling age-matching, disease type (molecular subtype) matching and probably even treatment matched so as realize the delivery of biology-specific personalized care within our oncological care systems.

Limitations

Our study had several limitations. First, the study design was retrospective- therefore likely to suffer from several potential biases, confounders and missing data. Designing better and prospective future studies can possibly help avoid/reduce these sources of bias. Secondly, we were unable to report on luminal A and luminal B disease subtypes separately due to the prominently missing data on Ki-67 index. Sensitization of care givers on the importance and utility of Ki-67 in the treatment of breast cancer should be prioritized. Thirdly, our study was conducted from a single centre and the IHC testing was not standardized (in most instances were done from different labs). This possibly impacts on the reproducibility and generalizability of our findings. Nevertheless, we opine that our findings on molecular subtypes of breast cancers in our centre improves our current understanding of molecular subtypes of breast cancers in our region and will form the ground work for better designed studies.

Conclusion

Breast cancer patients from Nakuru, Kenya, are likely to be young and with luminal-subtype invasive ductal carcinoma. In contrast to some previous reports, less than a quarter of our patients have triple negative breast cancer. We recommend prioritization, standardization and scaling of receptor testing and molecular subtyping to optimize treatment protocols and personalized management strategies for breast cancer patients.

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References

1. Marianne G, Oliver H, Shilanaiman HN, Furaha S, Leila EM, Patrick A, et al. Clinicopathological characteristics of breast cancer patients from Northern Tanzania: common aspects of late stage presentation and triple negative breast cancer. *Ecancermedicalscience*. 2021;7(15):1282. doi:10.3332/ecancer.2021.1282

2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71:209-249. doi:10.3322/caac.21660

3. McKenzie F, Zietsman A, Galukande M, Anele A, Adisa C, Cubasch H, et al. African Breast Cancer—Disparities in Outcomes (ABC-DO): protocol of a multicountry mobile health prospective study of breast cancer survival in sub-Saharan Africa. *BMJ Open*. 2016;6:e011390. doi:10.1136/bmjopen-2016-011390

4. Akbar M, Akbar K, Naveed D. Frequency and correlation of molecular subtypes of breast cancer with clinicopathological features. *J Ayub Med Coll Abbottabad*. 2014;26:290-293.

5. Eniu A, Carlson RW, Aziz Z, Bines J, Hortobágyi GN, Bese NS, et al. Breast cancer in limited-resource countries: treatment and allocation of resources. *Breast J*. 2006;12 Suppl 1:S38-53. doi:10.1111/j.1075-122X.2006.00202.x

6. Li Y, Yang D, Yin X, Zhang X, Huang J, Wu Y, et al. Clinicopathological Characteristics and Breast Cancer–Specific Survival of Patients With Single Hormone Receptor–Positive Breast Cancer. *JAMA Netw Open*. 2020;3:e1918160-e1918160. doi:10.1001/jamanetworkopen.2019.18160

7. Laible M, Hartmann K, Gürtler C, Anzeneder T, Wirtz R, Weber S, et al. Impact of molecular subtypes on the prediction of distant recurrence in estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative breast cancer upon five years of endocrine therapy. *BMC Cancer*. 2019;19:694. doi:10.1186/s12885-019-5890-z

8. Bhattacharyya GS, Doval DC, Desai CJ, Chaturvedi H, Sharma S, Somashekhar SP. Overview of Breast Cancer and Implications of Overtreatment of Early-Stage Breast Cancer: An Indian Perspective. *JCO Glob Oncol*. 2020:789-798. doi:10.1200/GO.20.00033

9. Kakudji BK, Mwila PK, Burger JR, du Plessis JM, Naidu K. Breast cancer molecular subtypes and receptor status among women at Potchefstroom Hospital: a cross-sectional study. *Pan Afr Med J*. 2021;38:85. doi:10.11604/pamj.2021.38.85.23039

10. Zhao X, Rødland EA, Tibshirani R, Plevritis S. Molecular subtyping for clinically defined breast cancer subgroups. *Breast Cancer Res*. 2015;17:29. doi:10.1186/s13058-015-0520-4

11. El-Hawary AK, Abbas AS, Elsayed AA, Zalata KR. Molecular subtypes of breast carcinoma in Egyptian women: clinicopathological features. *Pathol Res Pract*. 2012;208:382-386. doi:10.1016/j.prp.2012.03.011

12. Brinton LA, Figueroa JD, Awuah B, Yarney J, Wiafe S, Wood SN, et al. Breast cancer in Sub-Saharan Africa: opportunities for prevention. *Breast Cancer Res Treat*. 2014;144:467-478. doi:10.1007/s10549-014-2868-z

13. Sayed S, Moloo Z, Wasike R, Bird P, Oigara R, Govender D, et al. Is breast cancer from Sub Saharan Africa truly receptor poor? Prevalence of ER/PR/HER2 in breast cancer from Kenya. *The Breast*. 2014;23:591-596. doi:10.1016/j.breast.2014.06.006

14. Hammond MEH, Hayes DF, Wolff AC, Mangu PB, Temin S. American society of clinical oncology/college of american pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *J Oncol Pract*. 2010;6:195-197. doi:10.1200/JOP.777003

15. Wolff AC, Hammond MEH, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *Arch Pathol Lab Med*. 2007;131(1):18-43. doi:10.5858/2007-131-18-ASOCCO

16. Britten A, Rossier C, Taright N, Ezra P, Bourgier C. Genomic classifications and radiotherapy for breast cancer. *Eur J Pharmacol*. 2013;717:67-70. doi:10.1016/j.ejphar.2012.11.069

17. Middleton LP, Chen V, Perkins GH, Pinn V, Page D. Histopathology of breast cancer among African-American women. *Cancer*. 2003;97:253-257. doi:10.1002/cncr.11021

18. Huo D, Ikpatt F, Khramtsov A, Dangou JM, Nanda R, Dignam J, et al. Population differences in breast cancer: survey in indigenous African women reveals over-representation of triple-negative breast cancer. *J Clin Oncol*. 2009;27(27):4515-4521. doi:10.1200/JCO.2008.19.6873

19. Adebamowo CA, Famooto A, Ogundiran TO, Aniagwu T, Nkwodimmah C, Akang EE. Immunohistochemical and molecular subtypes of breast cancer in Nigeria. *Breast Cancer Res Treat*. 2008;110:183-188. doi:10.1007/s10549-007-9694-5

20. Sighoko D, Kamaté B, Traore C, Mallé B, Coulibaly B, Karidiatou A, et al. Breast cancer in pre-menopausal women in West Africa: analysis of temporal trends and evaluation of risk factors associated with reproductive life. *Breast*. 2013;22:828-835. doi:10.1016/j.breast.2013.02.011

21. Akarolo-Anthony SN, Ogundiran TO, Adebamowo CA. Emerging breast cancer epidemic: evidence from Africa. *Breast Cancer Res*. 2010;12(Suppl 4):S8. doi:10.1186/bcr2737

22. Gakinya S, Sayed S, Chauhan R, Sayed P, Gakinya S. Breast cancer Molecular subtypes and their clinicopathological characteristics amongst patients at the Aga Khan University hospital (Nairobi). *Ann African Surg*. 2010:5. doi:10.4314/aas.v5i1.53713

23. Bird PA, Hill AG, Houssami N. Poor hormone receptor expression in East African breast cancer: evidence of a biologically different disease? *Ann Surg Oncol*. 2008;15:1983-1988. doi:10.1245/s10434-008-9900-7

24. McCormack VA, Joffe M, van den Berg E, Broeze N, Silva I dos S, Romieu I, et al. Breast cancer receptor status and stage at diagnosis in over 1,200 consecutive public hospital patients in Soweto, South Africa: a case series. *Breast Cancer Res*. 2013;15:R84-R84. doi:10.1186/bcr3478

25. Eng A, McCormack V, dos-Santos-Silva I. Receptor-defined subtypes of breast cancer in indigenous populations in Africa: a systematic review and meta-analysis. *PLoS Med*. 2014;11:e1001720. doi:10.1371/journal.pmed.1001720

26. Davey MG, Hynes SO, Kerin MJ, Miller N, Lowery AJ. Ki-67 as a Prognostic Biomarker in Invasive Breast Cancer. *Cancers (Basel)*. 2021;13:31. doi:10.3390/cancers13174455

27. Nyagol J, Nyong'o A, Byakika B, Muchiri L, Cocco M, de Santi MM, et al. Routine assessment of hormonal receptor and her-2/neu status underscores the need for more therapeutic targets in Kenyan women with breast cancer. *Anal Quant Cytol Histol*. 2006;28:97-103.