Real-World Treatment Patterns for Breast Cancer in an HIV-prevalent Malawian Cohort

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Background

In Sub-Saharan Africa (SSA), treatments for breast cancer in concordance with National Comprehensive Cancer Network (NCCN) Harmonized Guidelines for SSA are increasingly available however their application under SSA conditions are infrequently described. Our aim is to determine the type of breast cancer treatment received including neoadjuvant (NAC),adjuvant (AC) or palliative chemotherapy (PC) and surgery (S), based on breast cancer stage and HIV status, and their associated outcomes. We also aimed to determine patient factors associated with completion of curative-intent treatment.

Methods

We utilized a prospective cohort of newly diagnosed breast cancer patients at Kamuzu Central Hospital in Malawi enrolled between December 2016 and October 2018. Descriptive statistics were computed to determine patient demographics and type of treatment received. Chi square and one way ANOVA tests were used to determine differences between groups. Unadjusted odds ratios (OR) with 95% confidence limit (CI) were calculated to determine factors associated with completion of curative-intent treatment. A logistic regression model was constructed including variables with p<0.1 in unadjusted analysis to compute adjusted odds ratio with 95% CI. Survival analysis was performed using Kaplan Meier methods and log-rank test.

Results

Of 100 patients, 91 had available staging and 19 were HIV+.13 (14%) patients presented as Stage II, 54 (59%) as Stage III, 24 (26%) as Stage IV. Patient demographics and type of treatment received, by stage, are listed. For curative-intent patients, inability to complete recommended S and ≥4 cycles of NAC or AC was associated with Stage III disease (OR 0.10 CI (0.01-0.89;p=0.040)), HIV+ (OR 0.25 CI(0.06-0.99); p=0.049) and ER/PR-/HER2+ disease (OR 0.07 CI (0.01-0.49);p=0.007)) on unadjusted analyses with persistence of ER/PR-/HER2+ disease on adjusted analysis. Median OS for patients varied based on first chemotherapy received (AC 37.1, NAC 28.5, PC 10.2 and never received chemotherapy 3.2 months; p=0.00).

Types of Breast Cancer Treatment Received, by Stage

	Stage 2A/B (n=13)	Stage 3A/B/C (n=54)	Stage IV (n=24)
Confirmed Surgery	11 (92)	n=42 26 (62)	0 (0)
Curative-Intent Chemotherapy			
Received neoadjuvant chemotherapy alone **Median number of cycles n (IQR)**	1 6 (-)	14 3 (2-4)	--
Received adjuvant chemotherapy alone **Median number of cycles n (IQR)**	5 6 (5-9)	7 6 (4-6)	--
Received neoadjuvant and adjuvant chemotherapy, n (%) **Median number of cycles n (IQR)**	6 8 (7-9)	16 11 (10-13)	--
Palliative Chemotherapy **Received palliative treatment after curative chemotherapy** **Median number of cycles n (IQR)**	0 0	9 12 (9-14) 2 11 (9-12)	-- 23 3 (1-9)
Received only palliative chemotherapy **Median number of cycles n (IQR)**	1	6	1
No chemotherapy			
Endocrine Therapy if Hormone Receptor Positive n (%)	n=10 3 (30)	n=20 8 (40)	n=13 4 (31)[#]

[#]Endocrine therapy may not be indicated for all hormone receptor positive stage IV patients

Results

Demographics, Clinical and Pathologic Characteristics of Newly Diagnosed Breast Cancer Patients in Malawi, by Stage

	Stage II (n=13)^	Stage III (n=54)^	Stage IV (n=24)^	p value
Demographics				
Mean Age (years)	45	51	49	p=0.231[a]
Education status: n (%) **Did not complete primary school** **Completed at least primary school**	4 (31) 9 (69)	34 (63) 20 (37)	13 (54) 11(46)	p=0.108[b]
Socioeconomic Status **Occupation: n (%)** **Employed full time** **Employed part time** **Housewife** **Unemployed** **Other**	 6 (46) 2 (15) 3 (23) 1 (8) 1 (8)	 14 (26) 2 (4) 17 (31) 7 (13) 14 (26)	 2 (8) 1 (4) 9 (38) 9 (38) 3 (12)	p=0.026[b]*
House Flooring **Dirt/Dung/Sand#** **Cement/tiles$**	 10 (77) 3 (23)	 27 (50) 27 (50)	 11 (46) 13 (54)	p=0.215[b]
Residence: n (%) **Lilongwe** **Outside of Lilongwe**	 6 (46) 7 (54)	 8 (15) 46 (85)	 2 (8) 22 (92)	p=0.011[b]*
Family history of cancer **Family history of breast cancer n(%)**	n=53 5 (38) 3 (23)	 9 (17) 2 (4)	 3 (13) 2 (8)	 p=0.134[b] p=0.070[b]
HIV positive n (%)	1 (8)	11 (20)	5 (22;n=23)	p=0.532[b]
Clinical Findings n (%)				
Palpable breast mass >5cm	5 (38)	40 (74)	22 (92)	p=0.002[b]
Breast ulceration present	0 (0)	14 (26)	12 (50)	p=0.005[b]
ECOG **0-1** ≥ 2	 13 (100) 0 (0)	 52 (96) 2 (4)	 15 (63) 9 (37)	p=0.000[b]*
Tumor characteristics n (%)				
Histology **Invasive Ductal Carcinoma** **Invasive Lobular Carcinoma** **Other**	n=11 10 (91) 0 (0) 1 (9)	n=44 38 (86) 1 (2) 5 (11)	n=20 20 (100) 0 (0) 0 (0)	p=0.795[b]
Grade **1** **2** **3** **Unable to grade**	n=11 4 (36) 3 (27) 4 (36) 0 (0)	n=50 15 (30) 16 (32) 15 (30) 4 (8)	n=23 4 (17) 9 (39) 10 (43) 0 (0)	p=0.515[b]
Hormone Receptor Status **ER/PR+/HER2-** **ER/PR+/HER2+** **ER/PR-/HER2+** **ER/PR-/HER2-** **Undetermined^**	n=11 9 (82) 1 (9) 0 (0) 1 (9)	n=50 16(32) 2 (4) 9 (18) 19 (38) 4 (8)	n=23 9 (39) 4 (17) 5 (22) 3 (13) 2 (9)	p=0.0028[b]*

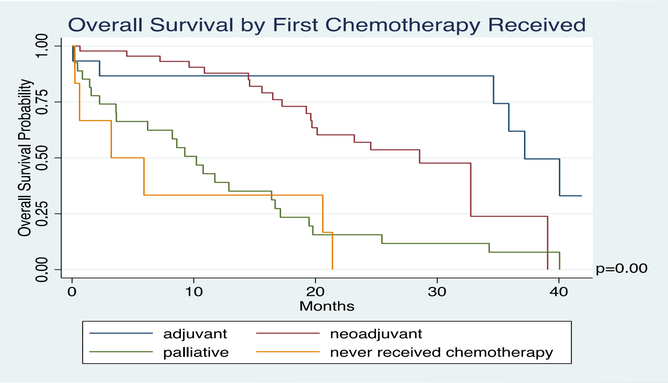
[a]one way ANOVA [b]Chi square test ^n unless otherwise noted *p values <0.05
#surrogate for low socioeconomic status $surrogate for higher socioeconomic status

Results

Unadjusted and Adjusted Odds Ratio for Completion of Curative Breast Cancer Treatment (S and≥ 4 cycles of CT)

Total (n=65)	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)[a]	p value
Age	0.99 (0.95-1.02)	0.53		
Residence **Lilongwe** **Outside Lilongwe**	 1 (Ref) 0.85 (0.22-3.18)	 0.80		
Occupation **Employed full time** **Employed part time** **Housewife** **Unemployed** **Other**	 1 (Ref) 0.66 (0.92-4.81) 0.45 (0.11-1.78) 0.33 (0.05-1.85) 0.53 (0.11-2.41)	 0.68 0.26 0.21 0.41		
HIV Status **Negative** **Positive**	 1 (Ref) 0.25 (0.06-0.99)	 0.049*	 0.17 (0.03-1.02)	 0.053**
Stage **II** **III**	 1 (Ref) 0.10 (0.01-0.89)*	 0.040*	 1 (Ref) 0.26 (0.02-2.76)	 0.26
Tumor >5cm **Yes** **No**	 0.73 (0.25-2.0) 1 (Ref)	 0.56		
ER/PR+/HER2- **ER/PR+/HER2+** **ER/PR-/HER2+** **ER/PR-/HER2-** **Unable to assess**	1 (Ref) 0.45 (0.03-6.05) 0.07 (0.01-0.49)* 0.49 (0.12-1.93) 0.11 (0.01-1.51)**	 0.5 0.007* 0.31 0.10**	1 (Ref) 0.36 (0.02-5.65) 0.12 (0.01-0.97)* 0.60 (0.12-2.90) 0.37 (0.02-6.87)	 0.46 0.047* 0.53 0.51

*p<0.05
**p≤0.1



Conclusions

This study demonstrates the challenges of administering breast cancer treatment in a resource constrained setting. Patients who did not receive chemotherapy or were treated with PC or NAC had a significantly shorter OS than patients who received upfront surgery and AC, reflecting the prognostic value of achieving surgical resectability in this setting. Stage III and HIV+ patients were less likely to complete curative-intent treatment than Stage II and HIV- counterparts. Further study is needed to identify barriers to treatment completion and inform targeted interventions to improve treatment outcomes in Malawi and SSA.