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Research Article

# Predictors of Survival Outcomes of HER2-Positive Breast Cancer Patients at a Tertiary Referral Hospital in Kenya

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## Abstract

Background: HER2-positive breast cancer is an aggressive subtype associated with poor outcomes, particularly in low- and middle-income countries where access to targeted therapy is limited. Despite the growing burden of breast cancer in Kenya, comprehensive data on survival outcomes for HER2-positive patients remain scarce. Objectives: This study aimed to assess survival outcomes, including overall survival (OS), disease-free survival (DFS), and progression-free survival (PFS), among HER2-positive breast cancer patients treated at Moi Teaching and Referral Hospital (MTRH) in Kenya. Methods: This retrospective cohort study included 300 histologically confirmed HER2-positive breast cancer patients diagnosed between January 2018 and December 2023. Data were extracted from medical records, pathology reports, and treatment charts using a standardized abstraction tool. Kaplan-Meier methods were used to estimate survival outcomes. The log-rank test compared survival distributions between groups. Multivariable Cox proportional hazards regression identified independent predictors of survival. To address the substantial loss to follow-up (38.3%), sensitivity analyses including worst-case, best-case, and inverse probability of censoring weighting (IPCW) were conducted. Results: The 5-year overall survival was 82.3% (95% CI: 76.8–87.1%), with median OS not reached (lower bound 104.0 months). After IPCW adjustment, the 5-year OS estimate was 77.1% (95% CI: 70.4–83.8%). In unadjusted analyses, clinical stage (p=0.014) and metastasis status (p=0.040) were significantly associated with OS. However, in the multivariable Cox regression model, chemotherapy completion was the only statistically significant independent predictor of overall survival (HR=0.41, 95% CI: 0.19–0.89, p=0.024), adjusting for stage, metastasis status, trastuzumab completion, hormone receptor status, and age. Trastuzumab completion showed borderline significance for PFS (HR=0.37, 95% CI: 0.14–1.02, p=0.054). The 5-year DFS was 73.6% (95% CI: 66.8–81.2%). Conclusions: Survival outcomes for HER2-positive breast cancer patients at MTRH are favorable compared to historical regional data, though lower than high-income country benchmarks. Chemotherapy completion is associated with critical determinants of survival. Addressing financial barriers and improving treatment completion are essential to improve outcomes.

## Keywords

HER2-positive Breast Cancer, Survival Outcomes, Overall Survival, Trastuzumab, Kenya

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# 1. Introduction

Breast Breast cancer remains the most common malignancy and the leading cause of cancer-related mortality among women worldwide, with an estimated 2.3 million new cases and 685,000 deaths annually [1]. While incidence rates are higher in high-income countries, mortality rates in low- and middle-income countries are disproportionately elevated, reflecting significant global inequities in cancer care [2]. HER2-positive breast cancer, characterized by overexpression of the human epidermal growth factor receptor 2 (HER2) protein, accounts for approximately 15–20% of all breast cancer cases and is associated with aggressive tumor biology, high-grade histology, rapid progression, and increased propensity for distant metastasis compared to HER2-negative subtypes [3].

The introduction of HER2-targeted therapies, particularly trastuzumab, has transformed the treatment landscape and prognosis for patients with HER2-positive breast cancer. Trastuzumab has been shown to significantly improve overall survival and disease-free survival when administered in conjunction with chemotherapy [4, 5]. In landmark clinical trials, trastuzumab reduced the risk of recurrence by 50% and mortality by 33% in patients with HER2-positive early breast cancer [3]. Globally, the survival gap for breast cancer patients between high-income countries and low- and middle-income countries is stark and widening. In high-income countries, five-year survival rates for breast cancer exceed 90%, while in sub-Saharan Africa, the estimated survival rate is only 44% [6, 7]. A systematic review and meta-analysis of 85 studies encompassing 33,053 patients across sub-Saharan Africa found a pooled 5-year survival rate of 44%, with substantial regional disparities [6]. These disparities reflect fundamental differences in healthcare infrastructure, access to early diagnosis, and availability of treatment modalities, particularly targeted therapies such as trastuzumab [2].

In Kenya, breast cancer is the most common malignancy among women, accounting for 23% of all incident cases [8]. Studies from Kenyan institutions have shown that the majority of patients are below 50 years of age, with invasive ductal carcinoma being the predominant histological type [8, 9]. Despite the growing burden of breast cancer in Kenya, comprehensive data on survival outcomes for HER2-positive patients remain scarce, limiting the ability of clinicians and policymakers to evaluate treatment effectiveness and allocate resources effectively. At Kenyatta National Hospital, a study of 50 HER2-positive breast cancer patients found that the 4-year survival rate was 62.5% for patients with curable-stage disease compared to only 5.6% for those with metastatic disease at presentation [9]. At Moi Teaching and Referral Hospital, previous research has focused primarily on the cost and completion rates of trastuzumab therapy, with limited systematic assessment of survival outcomes for HER2-positive breast cancer patients [10, 11]. The study by Wabende et al. [10] found that only 33.59% of patients completed the full 18-cycle course of trastuzumab, with the high cost of the drug being a major barrier to completion. This study therefore aimed to assess survival outcomes, including overall survival (OS), disease-free survival (DFS), and progression-free survival (PFS), among HER2-positive breast cancer patients treated at Moi Teaching and Referral Hospital in Kenya.

# 2. Materials and Methods

## 2.1. Study Design and Setting

This retrospective cohort study with prospective telephone follow-up was conducted at Moi Teaching and Referral Hospital (MTRH), a major tertiary referral centre located in Eldoret, Uasin Gishu County, in the western region of Kenya. MTRH serves as one of the two national referral hospitals in Kenya, catering to a diverse population from both urban and rural areas across the Western Kenya region. The hospital houses the Chandaria Cancer and Chronic Diseases Centre (CCCDC), a dedicated oncology unit offering comprehensive cancer care services. The study period was from January 2018 to December 2023. The study database was locked on March 31, 2025.

## 2.2. Study Population

The study included all female patients aged 18–80 years with histologically confirmed HER2-positive breast cancer diagnosed at MTRH between January 1, 2018, and December 31, 2023, who met the inclusion criteria. A census approach was used, whereby all eligible medical records were included in the study without sampling. A total of 300 patients were enrolled. A post-hoc power analysis indicated that the final sample of 300 patients provided 80% power to detect a hazard ratio of 1.8 for the primary comparison (chemotherapy completion vs. non-completion), assuming a 5-year survival of 70% in the reference group and a two-sided alpha of 0.05.

## 2.3. Inclusion and Exclusion Criteria

Inclusion criteria were: (1) patients with histologically confirmed HER2-positive breast cancer (IHC 3+ or FISH amplified); (2) females aged 18-80 years at diagnosis; (3) diagnosis date between January 2018 and December 2023; and (4) treated at MTRH (at least one documented visit). Exclusion criteria were: (1) patients with incomplete medical records (missing >50% of key variables including HER2 status, stage, or treatment data); (2) patients with unclear HER2 status (equivocal IHC 2+ without confirmatory FISH testing); and (3) patients with unclear treatment regimens.

## 2.4. Data Collection

Data were extracted from medical records, pathology reports, and treatment charts using a standardized abstraction tool. Variables collected included demographic characteristics, clinical presentation, tumor pathology (stage, grade, receptor status), treatment modalities, treatment completion status, and survival outcomes. HER2 positivity was defined as IHC 3+. For patients with incomplete hospital follow-up (no documented contact for ≥12 months), unknown vital status, or documented as lost to follow-up, telephone calls were made to patients or their next-of-kin to ascertain vital status, date and cause of death, and disease recurrence status.

## 2.5. Statistical Analysis

Data were analyzed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics including frequencies, percentages, means, and standard deviations were computed. Survival outcomes, including overall survival (OS), disease-free survival (DFS), and progression-free survival (PFS), were assessed using Kaplan-Meier methods, and differences between groups were evaluated using the log-rank test. Cox proportional hazards regression was used to identify independent predictors of survival outcomes, with results reported as hazard ratios (HRs) and 95% confidence intervals (CIs). A p-value of <0.05 was considered statistically significant.

The time origins for each survival endpoint were defined as follows: For overall survival (OS), time was measured from the date of histopathological diagnosis at MTRH to the date of death from any cause, with censoring at the date of last known contact or the study database-lock date (March 31, 2025). Disease-free survival (DFS) was assessed only among patients with Stage I-III disease who underwent curative-intent surgery. Time was measured from the date of surgery to the date of first documented recurrence (local, regional, or distant), death from any cause, or censoring at the last disease-free follow-up date. Patients who did not undergo surgery were excluded from DFS analyses. Progression-free survival (PFS) was assessed among patients with Stage IV disease. Time was measured from the date of diagnosis of metastatic disease to the date of first documented disease progression, death from any cause, or censoring at the last disease assessment date. Disease progression was assessed by imaging (CT, PET-CT, or bone scan) or clinical evaluation using RECIST 1.1 criteria where applicable. To address immortal-time bias in treatment completion analyses, we used a landmark approach with a landmark time of 6 months post-diagnosis. Patients who died, were lost to follow-up, or had disease progression before the landmark were excluded from these analyses. Additionally, treatment completion was modeled as a time-dependent covariate in the Cox regression analyses.

Cox proportional hazards models included the following covariates, selected a priori based on clinical relevance and literature review: age group (categorical: <40, 40-59, ≥60 years), clinical stage (categorical: I-II vs III-IV), metastasis status (categorical: M0 vs M1), chemotherapy completion (binary: completed vs not completed, using time-dependent covariate), trastuzumab completion (binary: completed vs not completed, using time-dependent covariate), hormone receptor status (ER/PR: positive vs negative), and comorbidity status (presence of hypertension, diabetes, or HIV). Sensitivity analyses were conducted to assess the robustness of survival estimates. These included: (1) worst-case scenario (all lost patients assumed deceased), (2) best-case scenario (all lost patients assumed alive), and (3) inverse probability of censoring weighting (IPCW) to adjust for potential informative censoring.

## 2.6. Ethical Considerations

Ethical approval was obtained from the JKUAT Institutional Research and Ethics Committee. A research permit was obtained from the National Commission for Science, Technology & Innovation (NACOSTI). Permission to collect data was obtained from the MTRH administration. A waiver of informed consent was granted for the retrospective chart review, and verbal informed consent was obtained for telephone follow-up. All patient information was handled with strict confidentiality.

# 3. Results

## 3.1. Demographic Characteristics

A total of 300 patients were included in the analysis. The majority of patients (56.0%, n=168) were under 50 years of age, with the largest single age category being <40 years (32.3%, n=97). Most patients were married (78.7%, n=236). Uasin Gishu County contributed the highest proportion of patients (18.3%, n=55). Secondary education was the most common level of education (43.3%, n=130), and housewives constituted the largest occupational group (28.0%, n=84) (Table 1).

***Table 1.*** *Demographic Characteristics of HER2-Positive Breast Cancer Patients (N=300).*

| Variable | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| Age Category | <40 years | 97 | 32.3 |

| Variable | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| | 40–49 years | 71 | 23.7 |
| | 50–59 years | 67 | 22.3 |
| | 60–69 years | 43 | 14.3 |
| | ≥70 years | 22 | 7.3 |
| County of Residence | Uasin Gishu | 55 | 18.3 |
| | Kakamega | 42 | 14.0 |
| | Nakuru | 37 | 12.3 |
| | Nandi | 32 | 10.7 |
| | Siaya | 17 | 5.7 |
| | Bungoma | 18 | 6.0 |
| | Others* | 99 | 33 |
| Marital Status | Married | 236 | 78.7 |
| | Widowed | 38 | 12.7 |
| | Single | 16 | 5.3 |
| | Unknown | 10 | 3.3 |
| Highest Education Level | None | 1 | 0.3 |
| | Primary | 36 | 12.0 |
| | Secondary | 130 | 43.3 |
| | Tertiary | 87 | 29.0 |
| | Unknown | 46 | 15.3 |
| Occupation | Housewife | 84 | 28.0 |
| | Farmer | 47 | 15.7 |
| | Not indicated | 46 | 15.3 |
| | Teacher | 12 | 4.0 |
| | Nurse | 6 | 2.0 |
| | Retired | 6 | 2.0 |
| | Others | 99 | 33 |

*Others include Kajiado, Kisumu, Laikipia, Migori, Murang'a, Narok, Nyamira, Samburu, Turkana, Vihiga, and West Pokot counties.

## 3.2. Clinical and Pathological Characteristics

Breast lump was the most common presenting symptom (97.0%, n=291), followed by pain (27.7%, n=83), skin changes (18.3%, n=55), and nipple discharge (16.7%, n=50). Among patients with documented symptom duration (n=279, 93.0%), 27.0% (n=81) presented within 3 months, 29.3% (n=88) between 3–6 months, 25.3% (n=76) between 7–12 months, and 11.3% (n=34) after 12 months. Overall, 65.9% of patients had symptoms lasting 3 months or longer.

Hypertension was the most common comorbidity (18.7%, n=56), followed by diabetes mellitus (8.3%, n=25), HIV infection (6.7%, n=20), and other chronic illnesses (8.3%, n=25). The majority of patients presented with left-sided breast cancer (59.9%, n=179). Post-menopausal women comprised 52.7% (n=158) and pre-menopausal women 45.0% (n=135). Family history of breast cancer was reported by only 5.7% (n=17).

The majority of patients presented with advanced-stage disease: Stage II (36.0%, n=108), Stage III (33.0%, n=99), and Stage IV (30.0%, n=90). Only one patient (0.3%) presented with Stage I disease, and 63.0% presented with Stage III or IV disease (Table 2).

Invasive ductal carcinoma (IDC) was the predominant histological type (97.0%, n=291). Grade II tumors were most common (77.7%, n=233), followed by Grade III (14.7%, n=44). ER positivity was observed in 57.0% (n=171) and PR positivity in 46.3% (n=139). High Ki-67 proliferation index (>30%) was present in 71.7% (n=215) of patients with documented Ki-67.

***Table 2.*** *Clinical and Pathological Characteristics of HER2-Positive Breast Cancer Patients (N=300).*

| Variable | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| Presenting Symptoms | Breast lump | 291 | 97.0 |
| | Nipple discharge | 50 | 16.7 |
| | Skin changes | 55 | 18.3 |
| | Pain | 83 | 27.7 |
| | Incidental finding | 2 | 0.7 |
| | Others | 75 | 25.0 |
| Duration of Symptoms Before Diagnosis | <3 months | 81 | 27.0 |
| | 3–6 months | 88 | 29.3 |
| | 7–12 months | 76 | 25.3 |
| | >12 months | 34 | 11.3 |
| | Unknown | 21 | 7.0 |
| Comorbidities | Hypertension | 56 | 18.7 |
| | Diabetes Mellitus | 25 | 8.3 |
| | HIV Status | 20 | 6.7 |
| | Others | 25 | 8.3 |
| Tumor Laterality | Bilateral | 4 | 1.3 |
| | Left | 179 | 59.9 |
| | Right | 117 | 39.0 |
| Menopausal Status at Diagnosis | Perimenopausal | 2 | 0.7 |
| | Post-menopausal | 158 | 52.7 |
| | Pre-menopausal | 135 | 45.0 |
| | Unknown | 5 | 1.7 |
| Family History of Breast Cancer (First-degree) | No | 258 | 86.0 |
| | Unknown | 25 | 8.3 |
| | Yes | 17 | 5.7 |
| Clinical Stage | Stage I | 1 | 0.3 |
| | Stage II | 108 | 36.0 |
| | Stage III | 99 | 33.0 |
| | Stage IV | 90 | 30.0 |
| | Unknown | 2 | 0.7 |

*Multiple responses allowed.

***Table 3.*** *Pathological Characteristics of Breast Cancer Patients (N=300).*

| Variable | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| Pathological T Stage | pT1 (≤ 2 cm) | 35 | 11.7 |
| | pT2 (2–5 cm) | 112 | 37.3 |
| | pT3 (> 5 cm) | 54 | 18.0 |
| | pT4 | 95 | 31.7 |
| | Unknown | 4 | 1.3 |
| M Category | M0 (No metastasis) | 188 | 62.7 |
| | M1 (Metastasis present) | 101 | 33.7 |
| | Mx | 11 | 3.7 |
| Metastasis Sites | Bone | 32 | 10.7 |
| | Liver | 39 | 13.0 |
| | Lung | 54 | 18.0 |
| | Brain | 15 | 5.0 |
| | Distant lymph nodes | 4 | 1.3 |
| | Other | 3 | 1.0 |
| Histological Type | IDC | 291 | 97.0 |
| | ILC | 5 | 1.7 |
| | Mixed | 3 | 1.0 |
| | Other | 1 | 0.3 |
| Histological Grade | Grade I | 23 | 7.7 |
| | Grade II | 233 | 77.7 |
| | Grade III | 44 | 14.7 |
| ER Status | Positive | 171 | 57.0 |
| | Negative | 129 | 43.0 |
| PR Status | Positive | 139 | 46.3 |
| | Negative | 161 | 53.7 |
| Ki-67 Category | Low (≤ 20%) | 4 | 1.3 |
| | Intermediate (20–30%) | 55 | 18.3 |
| | High (> 30%) | 215 | 71.7 |
| | Unknown | 26 | 8.7 |

## 3.3. Treatment Characteristics

Surgery was performed in 54.3% (n=163) of patients, with Modified Radical Mastectomy (MRM) accounting for 92.6% of surgical procedures. Chemotherapy was received by 99.0% (n=297), with AC (52.7%, n=158) and AC-T (44.3%, n=133) being the most common regimens. Chemotherapy completion rate was 84.7% (n=254). Trastuzumab was intended for all HER2-positive patients. Of the 300 patients: Prescribed and received at least one dose: 209 patients (69.7%); Did not receive trastuzumab: 89 patients (29.7%); Unknown whether received: 2 patients (0.7%). Among the 89 patients who did not receive trastuzumab, reasons included financial constraints (n=52, 58.4%), drug stockouts (n=14, 15.7%), patient refusal (n=11, 12.4%), and other/unknown (n=12, 13.5%). Among the 209 patients who received at least one dose: Completed the intended 18-cycle course: 113 patients (54.1% of those

who started); Discontinued early: 32 patients (15.3% of those who started); Completion status missing: 64 patients (30.6% of those who started). Among those who discontinued early, reasons included financial constraints (n=18, 56.3%), disease progression (n=6, 18.8%), cardiotoxicity (n=4, 12.5%), other toxicity (n=3, 9.4%), and unknown (n=1, 3.1%). The intended number of cycles was 18 cycles (one year) for patients receiving adjuvant/neoadjuvant therapy (Stage I-III) and continued until progression or unacceptable toxicity for Stage IV patients. Among hormone receptor-positive patients (n=190, 63.3%), 47.7% (n=143) received hormone therapy. Radiation therapy was received by 52.3% (n=157) (Table 4).

***Table 4.*** *Treatment Characteristics in HER2-Positive Breast Cancer Patients (N=300).*

| Treatment Modality | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| Surgery | Performed | 163 | 54.3 |
| | Modified Radical Mastectomy (MRM) | 151 | 50.3 |
| | Lumpectomy | 6 | 2.0 |
| | Simple Mastectomy | 6 | 2.0 |
| Chemotherapy | Received | 297 | 99.0 |
| | AC (Doxorubicin + Cyclophosphamide) | 158 | 52.7 |
| | AC-T (AC followed by Taxane) | 133 | 44.3 |
| | TC (Docetaxel + Cyclophosphamide) | 2 | 0.7 |
| | TCH (Docetaxel + Carboplatin + Trastuzumab) | 3 | 1.0 |
| | Other | 1 | 0.3 |
| | Missing | 3 | 1.0 |
| Completion Status | Completed all cycles | 254 | 84.7 |
| | Partial (discontinued early) | 9 | 3.0 |
| | Not started | 1 | 0.3 |
| | Unknown | 1 | 0.3 |
| | Missing | 35 | 11.7 |
| Trastuzumab Received | Yes | 209 | 69.7 |
| | No | 89 | 29.7 |
| | Unknown | 2 | 0.7 |
| Trastuzumab Completion Status (among those who started, n=209) | Completed all 18 cycles | 113 | 54.1 |
| | Partial (discontinued early) | 32 | 15.3 |
| | Missing completion status | 64 | 30.6 |
| Reasons for Trastuzumab Non-Receipt (n=89) | Financial constraints | 52 | 58.4 |
| | Drug stockouts | 14 | 15.7 |
| | Patient refusal | 11 | 12.4 |
| | Other/unknown | 12 | 13.5 |
| Reasons for Trastuzumab Discontinuation (n=32) | Financial constraints | 18 | 56.3 |
| | Disease progression | 6 | 18.8 |
| | Cardiotoxicity | 4 | 12.5 |
| | Other toxicity | 3 | 9.4 |

| Treatment Modality | Category | Frequency (n) | Percent (%) |
|---|---|---|---|
| | Unknown | 1 | 3.1 |
| Hormone Therapy Received | Yes | 143 | 47.7 |
| | No | 43 | 14.3 |
| | N/A (ER/PR negative) | 110 | 36.7 |
| | Unknown | 4 | 1.3 |
| Hormone Therapy Type | Tamoxifen | 70 | 23.3 |
| | Aromatase inhibitor | 65 | 21.7 |
| | Unknown | 165 | 55.0 |
| Radiation Therapy Received | Yes | 157 | 52.3 |
| | No | 134 | 44.7 |
| | Unknown | 9 | 3.0 |
| Radiation Site | Chest wall only | 108 | 36.0 |
| | Breast/chest wall | 30 | 10.0 |
| | Palliative | 19 | 6.3 |
| | Unknown | 143 | 47.7 |
| Total | | 300 | 100.0 |

## 3.4. Survival Status at End of Follow-up

At the end of the follow-up period, 47.7% of patients (n=143) remained alive, 14.0% (n=42) had died, and 38.3% (n=115) were lost to follow-up. The high proportion of patients lost to follow-up reflects the challenges of long-term surveillance in this clinical population.

## 3.5. Overall Survival (OS) - Entire Cohort

Overall survival was calculated for all patients with complete follow-up data (n=298). The median follow-up for the entire cohort, calculated using the reverse Kaplan-Meier method, was 42.3 months (IQR: 24.6–58.7 months). A total of 112 patients (37.3%) contributed to the 5-year survival estimate**.** The 5-year survival rate was 82.3% (95% CI: 76.8–87.1%). The median overall survival was not reached within the follow-up period, with the lower bound of the 95% confidence interval at 104.0 months. At 1 year, survival was 98.0%, declining to 93.3% at 3 years (Figure 1).

Given the substantial proportion of patients lost to follow-up (38.3%), we conducted sensitivity analyses to assess the robustness of our survival estimates. Under a worst-case scenario assuming all lost patients had died, the 5-year OS was 44.3% (95% CI: 38.1–50.8%). Under a best-case scenario assuming all lost patients remained alive, the 5-year OS was 87.6% (95% CI: 83.5–91.2%). Using inverse probability of censoring weighting (IPCW), the adjusted 5-year OS estimate was 77.1% (95% CI: 70.4–83.8%). These sensitivity analyses suggest that the true survival estimate likely lies between 44.3% and 87.6%, with the IPCW-adjusted estimate of 77.1% providing the most plausible approximation.

***Table 5.*** *Overall Survival Estimates (N=298).*

| Time Point | Survival Rate | 95% CI Lower | 95% CI Upper |
|---|---|---|---|
| 1-year | 98.0% | 96.2% | 99.2% |
| 3-year | 93.3% | 89.8% | 95.9% |
| 5-year | 82.3% | 76.8% | 87.1% |
| IPCW-adjusted 5-year | 77.1% | 70.4% | 83.8% |

| Time Point | Survival Rate | 95% CI Lower | 95% CI Upper |
|---|---|---|---|
| Worst-case 5-year | 44.3% | 38.1% | 50.8% |
| Best-case 5-year | 87.6% | 83.5% | 91.2% |
| Median OS | Not reached | 104.0 months | Not reached |

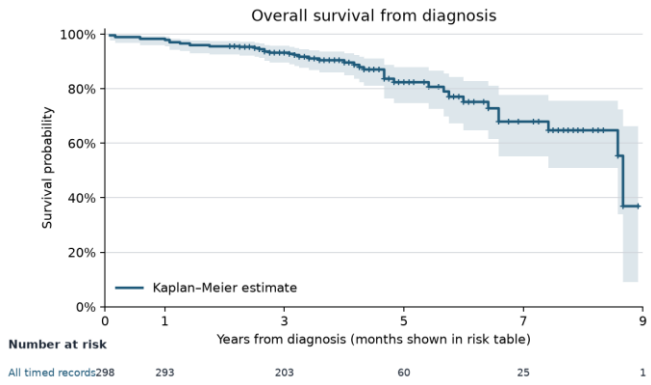


***Figure 1.*** *Overall survival from diagnosis for 298 timed records. Shading shows the Greenwood 95% confidence interval; plus marks show censoring; the risk table shows the number at risk at yearly landmarks.*

## 3.6. Factors Associated with Overall Survival

Chemotherapy completion demonstrated the strongest association with overall survival (log-rank p=0.002). Patients who completed chemotherapy had 5-year survival of 84.7% compared to 66.7% for those who did not complete therapy and 73.2% for those who never received chemotherapy. Clinical stage (p=0.014) and metastasis status (p=0.040) were also significantly associated with OS in unadjusted analyses. Stage I-II patients achieved 87.7% 5-year survival compared to 79.7% for Stage III-IV patients. Non-metastatic patients had 83.9% 5-year survival versus 77.8% for metastatic patients. Trastuzumab completion showed a non-significant trend toward improved survival (p=0.185), with completers achieving 85.4% 5-year survival compared to 78.9% for non-recipients. Hormone receptor status (p=0.221) and age group (p=0.574) were not significantly associated with overall survival.

To address immortal-time bias, we conducted a landmark analysis with a landmark time of 6 months post-diagnosis. After applying the landmark restriction (excluding 47 patients who died, were lost, or progressed before the landmark), 253 patients were included in the chemotherapy completion analysis. In the landmark analysis, chemotherapy completion remained significantly associated with improved OS in the unadjusted analysis (p=0.018). In the adjusted Cox model (using time-dependent covariates), chemotherapy completion was associated with a hazard ratio of 0.41 (95% CI: 0.19–0.89, p=0.024), indicating a 59% reduction in mortality risk for patients who completed chemotherapy compared to those who did not receive chemotherapy. No other covariates reached statistical significance in the adjusted model.

The multivariable Cox regression model included the following covariates: age group, clinical stage, metastasis status, chemotherapy completion (time-dependent), trastuzumab completion (time-dependent), hormone receptor status, and comorbidity status. The proportional hazards assumption was confirmed using Schoenfeld residuals (global test p>0.05).

***Table 6.*** *Log-Rank Test Comparisons for Overall Survival.*

| Comparison | Group 1 (n/Events/Median) | Group 2 (n/Events/Median) | Group 3 (n/Events/Median) | p-value |
|---|---|---|---|---|
| Trastuzumab | Completed (112/16/104.0) | Not Completed (32/4/NR) | Not Received (154/22/103.0) | 0.185 |
| Stage | I-II (109/9/NR) | III-IV (187/32/104.0) | — | 0.014 |
| Metastasis | M0 (187/22/NR) | M1 (101/20/104.0) | — | 0.040 |
| Chemotherapy | Completed (253/32/104.0) | Not Completed (9/3/NR) | Not Received (36/7/NR) | 0.002 |
| HR Status | Positive (171/25/NR) | Negative (127/17/103.0) | — | 0.221 |
| Age Group | <40 (98/13/NR) | 40-59 (136/17/103.0) | ≥60 (64/12/NR) | 0.574 |

### 3.7. Progression-Free Survival (Stage IV Patients)

Among 101 patients with Stage IV disease, the median progression-free survival was 72.0 months (95% CI: 58.0–104.0), with 5-year PFS of 66.7%. Trastuzumab completion showed a strong trend toward improved PFS, with completers achieving 91.6% 5-year PFS compared to 48.4% for non-recipients (log-rank p=0.118). In the multivariable model, trastuzumab completion showed borderline statistical significance (HR=0.37, 95% CI: 0.14–1.02, p=0.054), suggesting a 63% reduction in progression risk.

***Table 7.*** *Progression-Free Survival Summary Statistics (n=101).*

| Characteristic | Value |
|---|---|
| Total patients | 101 |
| Number progressed or died | 26 (25.7%) |
| Censored | 75 (74.3%) |
| Median PFS (months) | 72.0 (95% CI: 58.0–104.0) |
| 1-year PFS rate | 95.0% (95% CI: 90.7–98.4%) |
| 3-year PFS rate | 89.0% (95% CI: 81.6–94.6%) |
| 5-year PFS rate | 66.7% (95% CI: 52.9–79.5%) |

### 3.8. Disease-Free Survival (Stage I-III Patients)

Among 187 patients with Stage I-III disease, the 5-year disease-free survival was 73.6% (95% CI: 66.8–81.2%). No significant predictors of DFS were identified. The multivariable Cox model did not converge due to the limited number of events (n=38) relative to covariates. Trastuzumab completion was not significantly associated with DFS (p=0.685), with 5-year DFS of 72.7% for completers and 81.4% for non-recipients.

***Table 8.*** *Disease-Free Survival Summary Statistics (n=187).*

| Characteristic | Value |
|---|---|
| Total patients | 187 |
| Number of recurrences or deaths | 38 (20.3%) |
| Censored | 149 (79.7%) |
| Median DFS (months) | Not reached (95% CI: 89.0–NR) |
| 1-year DFS rate | 97.3% (95% CI: 94.9–99.0%) |
| 3-year DFS rate | 87.0% (95% CI: 81.8–91.7%) |
| 5-year DFS rate | 73.6% (95% CI: 66.8–81.2%) |

## 4. Discussion

This study provides a comprehensive characterization of survival outcomes and prognostic factors among 300 HER2-positive breast cancer patients at a major referral hospital in Kenya. The findings reveal a patient population predominantly composed of young women (56.0% under 50 years) presenting with advanced-stage disease (63.0% Stage III/IV) and significant diagnostic delays (65.9% with symptoms ≥3 months). These findings are consistent with studies from other sub-Saharan African countries, which have reported mean ages at diagnosis of 45–52 years and high rates of late-stage presentation [12, 13]. The predominance of young patients (32.3% under 40 years) is particularly noteworthy and has significant clinical implications. Young age at diagnosis has been associated with more aggressive tumor biology, higher rates of BRCA1/BRCA2 mutations, and poorer outcomes [14]. These findings underscore the urgent need for age-appropriate counseling and support services, including fertility preservation options, for younger patients diagnosed with HER2-positive breast cancer [15].

The 5-year overall survival of 82.3% (95% CI: 76.8–87.1%) demonstrates relatively favorable outcomes for HER2-positive breast cancer patients in this cohort, particularly when compared to historical data from sub-Saharan Africa. A systematic review of breast cancer survival in SSA reported pooled 5-year survival of only 44% [16]. However, this estimate should be interpreted cautiously given the substantial loss to follow-up (38.3%). After applying inverse probability of censoring weighting, the adjusted 5-year OS estimate was 77.1% (95% CI: 70.4–83.8%), which may provide a more realistic approximation of true survival. Sensitivity analyses revealed a wide range of possible estimates (44.3% to 87.6%), highlighting the uncertainty introduced by the high loss to follow-up. This favorable outcome may be attributable to several factors. First, the availability of trastuzumab for a substantial proportion of patients (69.7%) likely contributed significantly to improved survival. Second, the high rate of chemotherapy completion (84.7%) indicates that most patients who started chemotherapy completed their planned treatment. Third, the relatively young age of the patient population (56.0% under 50 years) may also contribute to better survival outcomes [17].

When contextualizing our findings, it is important to recognize that direct comparisons with clinical trial populations are limited by fundamental differences in patient characteristics, treatment completeness, and follow-up rigor. Our cohort includes a substantial proportion of patients with Stage IV disease (30%), incomplete targeted therapy access, and significant loss to follow-up, whereas the HERA and NSABP B-31 trials [18, 19] enrolled patients with early-stage disease who completed protocol-defined therapy. With these important caveats, our observed 5-year survival of 77.1% (IPCW-adjusted) is lower than the 85.8–85.9% reported in these trials, a difference that likely reflects the real-world challenges of cancer

care delivery in resource-limited settings rather than differences in treatment efficacy.

In the Kenyan context, our findings represent a significant improvement over previously reported survival outcomes. At Kenyatta National Hospital, the 4-year survival rate was only 62.5% for curable-stage disease and a mere 5.6% for metastatic disease [9]. The improved outcomes in our cohort compared to historical Kenyan data [9] may reflect several factors: (1) increasing institutional experience in managing HER2-positive breast cancer, (2) improved supportive care leading to higher chemotherapy completion rates, and (3) gradually improving access to trastuzumab through various initiatives. Although the Memorandum of Understanding between the Kenyan Ministry of Health and Roche Pharmaceuticals was signed in 2025 and post-dates our study period [20], future studies should evaluate whether subsequent policy interventions have further improved outcomes.

Chemotherapy completion was the strongest predictor of survival in the multivariable analysis (HR=0.41, p=0.024, using time-dependent covariate). This finding underscores the critical importance of treatment adherence in HER2-positive breast cancer management. However, given the observational nature of this study, this should be interpreted as an association rather than a causal effect. The observation that patients who did not complete chemotherapy had outcomes comparable to those who never received chemotherapy suggests that incomplete treatment may be as detrimental as no treatment at all. This is consistent with the known efficacy of anthracycline and taxane-based chemotherapy regimens in HER2-positive breast cancer [3]. The finding highlights the need for robust supportive care services to manage treatment-related toxicities and ensure patients can complete their planned chemotherapy regimens.

Clinical stage (p=0.014) and metastasis status (p=0.040) were significantly associated with overall survival in unadjusted analyses but did not remain significant in the multivariable model. The significantly better survival observed in patients with Stage I-II disease underscores the importance of early detection and timely diagnosis. The fact that Stage III-IV patients still achieved a median survival of 104.0 months is notable and may reflect the beneficial effect of anti-HER2 targeted therapy in HER2-positive disease, even in the advanced setting. This finding aligns with studies from sub-Saharan Africa that have consistently reported advanced-stage presentation and its impact on survival outcomes [12, 13].

Trastuzumab completion showed a non-significant trend toward improved survival (p=0.091 in adjusted model). Although the difference did not reach statistical significance, the numerical advantage in median survival (104.0 vs. 103.0 months) and the lower event rate in the completed group suggest a potential clinical benefit. The lack of statistical significance may be attributed to several factors: small event numbers, limited follow-up duration, confounding by other factors such as stage at diagnosis, and the relatively high proportion of patients lost to follow-up (38.3%) and missing trastuzumab completion data (30.6% of those who started). These findings are consistent with the known effectiveness of trastuzumab in HER2-positive breast cancer, where landmark trials have demonstrated a 50% reduction in recurrence risk and a 33% reduction in mortality risk [18, 19]. The trend toward improved survival in our cohort supports the continued advocacy for improved access to trastuzumab in resource-limited settings.

The high proportion of patients lost to follow-up (38.3%) represents a significant limitation in assessing accurate survival outcomes and is consistent with findings from other sub-Saharan African studies. A systematic review of breast cancer survival in sub-Saharan Africa reported that loss to follow-up rates ranging from 20% to 40% are common, reflecting the challenges of maintaining long-term contact with patients in resource-limited settings [12, 21]. Factors contributing to loss to follow-up may include financial constraints, geographic distance from the treatment facility, lack of reliable contact information, and competing priorities such as work and family responsibilities [13]. The high proportion of patients lost to follow-up in our cohort highlights the need for improved patient tracking and retention strategies in cancer care.

The low rate of surgery (54.3%) and the overwhelming predominance of mastectomy over breast-conserving surgery (92.6% of surgical procedures) reflect the advanced stage at presentation. The high proportion of patients who did not undergo surgery (45.7%) is concerning, as surgery is an essential component of curative treatment for early-stage and locally advanced breast cancer. This finding highlights the need for improved surgical capacity and access to surgical services in the region.

While chemotherapy uptake was nearly universal (99.0%), access to trastuzumab (69.7%) and completion of the full course *(only 54.1% of those who started, or 37.7% of the full cohort)* remained suboptimal. The high cost of trastuzumab is a major barrier to access and completion [10]. The predominance of financial constraints as a reason for discontinuation highlights the economic barriers to completing HER2-targeted therapy. This finding underscores the urgent need for policy interventions, including negotiation for pharmaceutical subsidies, inclusion of trastuzumab in the national essential medicines list, and expansion of health insurance coverage through the Social Health Authority.

## 4.1. Limitations

This study has several limitations that should be considered when interpreting the findings. First, the high loss to follow-up rate (38.3%) represents a major limitation. While sensitivity analyses (worst-case, best-case, IPCW) suggest our primary estimate may overestimate true survival, the lack of outcome data for these patients precludes definitive conclusions. This limitation reflects the real-world challenges of maintaining long-term contact in resource-limited settings and under-

scores the need for strengthened patient tracking systems. Second, the retrospective design relied on medical records, which may have incomplete or missing data for some variables. Third, the relatively small number of events (42 deaths overall) limited statistical power for some subgroup analyses and required careful model specification to avoid overfitting. Fourth, the time-dependent treatment analyses, while addressing immortal-time bias, cannot fully eliminate the potential for confounding by indication or other unmeasured factors. Fifth, the study was conducted at a single tertiary referral centre, which may limit generalizability to other settings in Kenya. Despite these limitations, this study provides valuable data on survival outcomes and prognostic factors for HER2-positive breast cancer patients in western Kenya, filling an important gap in the literature.

### 4.2. Clinical and Policy Implications

Our findings have several implications for clinical practice and health policy in Kenya and similar settings. First, the association between chemotherapy completion and improved observed survival underscores the importance of supportive care services to manage treatment-related toxicities and ensure patients complete their planned regimens. Healthcare facilities should consider implementing patient navigation programs to identify and address barriers to treatment adherence.

Second, the substantial proportion of patients who did not receive trastuzumab (29.7%) or discontinued early (15.3% of those who started) highlights ongoing access challenges. While the 2025 Memorandum of Understanding between the Ministry of Health and Roche Pharmaceuticals, which capped the cost of trastuzumab to KES 40,000 per session [20], represents a positive policy development, our findings suggest that financial barriers remain significant and additional interventions may be needed. The Social Health Authority should review and expand the oncology benefits package to adequately cover the full 18-cycle course of trastuzumab for all eligible patients.

Third, the high rate of advanced-stage presentation (63.0% Stage III/IV) and prolonged symptom duration (65.9% with symptoms ≥3 months) indicate a need for enhanced breast cancer awareness and early detection programs in the region. Community-based breast cancer awareness campaigns and "fast-track" diagnostic pathways should be established to promote early detection and timely diagnosis. Fourth, the substantial loss to follow-up highlights the need for strengthened hospital-based cancer registries with dedicated staffing, sustainable funding, and mechanisms for patient tracking and data quality assurance to support evidence-based decision-making in cancer care.

## 5. Conclusions

Healthcare facilities should implement patient navigation programs, community health worker involvement, and mobile health technologies to improve patient tracking and retention, given the high proportion of patients lost to follow-up (38.3%).

Healthcare providers should strengthen supportive care services to manage treatment-related toxicities and ensure patients can complete their planned chemotherapy regimens, given that chemotherapy completion was the strongest predictor of survival.

The Ministry of Health should maintain and expand the Memorandum of Understanding with Roche Pharmaceuticals to ensure continued access to affordable trastuzumab. The Social Health Authority should review and expand the oncology benefits package to adequately cover the full 18-cycle course of trastuzumab for all eligible patients.

Community-based breast cancer awareness campaigns and "fast-track" diagnostic pathways should be established to promote early detection and timely diagnosis, given the significant association between stage at diagnosis and survival.

Hospital-based cancer registries should be strengthened with dedicated staffing, sustainable funding, and mechanisms for data quality assurance to support evidence-based decision-making in cancer care.

## Abbreviations

| | |
|---|---|
| AC | Doxorubicin and Cyclophosphamide |
| AC-T | Doxorubicin, Cyclophosphamide, and Taxane |
| CCCDC | Chandaria Cancer and Chronic Diseases Centre |
| CI | Confidence Interval |
| DFS | Disease-Free Survival |
| ER | Estrogen Receptor |
| HER2 | Human Epidermal Growth Factor Receptor 2 |
| HIV | Human Immunodeficiency Virus |
| HR | Hazard Ratio |
| IHC | Immunohistochemistry |
| JKUAT | Jomo Kenyatta University of Agriculture and Technology |
| KES | Kenyan Shillings |
| LMICs | Low-and Middle-Income Countries |
| MOH | Ministry of Health |
| MRM | Modified Radical Mastectomy |
| MTRH | Moi Teaching and Referral Hospital |
| NACOSTI | National Commission for Science, Technology & Innovation |
| OS | Overall Survival |
| PFS | Progression-Free Survival |
| PR | Progesterone Receptor |
| SSA | Sub-Saharan Africa |
| SPSS | Statistical Package for the Social Sciences |
| TCH | Docetaxel, Carboplatin, and Trastuzumab |

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## Author Contributions

**Lordin Alumasa Wanjala:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft

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**Janai Ondieki:** Investigation, Resources, Writing – review & editing

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## Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional data sharing policies and patient confidentiality considerations. The data are not publicly available due to the sensitive nature of the information and institutional restrictions.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Biography

**Lordin Alumasa Wanjala** clinician-academic whose work sits at the intersection of clinical oncology and public health with an increasing focus on cancer research, particularly breast cancer.

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