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Maintenance low-dose capecitabine versus observation in early-stage triple-negative breast cancer: a randomized controlled trial assessing safety with exploratory survival outcomes

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Abstract

Background Triple-negative breast cancer (TNBC) carries a worse prognosis primarily because it does not have specific targeted therapies and is biologically aggressive, leading to a great probability of early relapse, especially involving visceral sites. At present, standard chemotherapy is the only available treatment in the adjuvant setting for early-stage triple-negative breast cancer, creating a critical need for effective maintenance strategies to reduce relapse and death rates. This study was intended to assess the impact of maintenance low-dose capecitabine for females diagnosed with early triple-negative breast cancer on safety, disease-free survival, and overall survival following completion of all standard adjuvant treatment.

Methods Eligible patients were randomly assigned in a 1:1 ratio to either receive maintenance low-dose capecitabine therapy or undergo observation within one month of completing standard adjuvant treatment. Patients allocated to the intervention arm received oral capecitabine at a dose of 650 mg/m^2 twice daily, administered continuously for 12 months in a metronomic schedule.

Results Seventy-five patients were randomized to maintenance capecitabine ($n=39$) or observation ($n=36$), with comparable baseline characteristics. Regarding the primary endpoint, maintenance low-dose capecitabine was generally well tolerated. The most frequent adverse event was hand–foot syndrome, occurring in 28.2% of patients, with one grade 3 case (2.6%). Other toxicities, including gastrointestinal upset, neutropenia, and thrombocytopenia, were infrequent.

After a median follow-up of 32 months, 24 disease-free survival (DFS) events were recorded: six in the capecitabine group (two local recurrences and four distant metastases) and 18 in the observation group (three local recurrences and 15 distant metastases). Kaplan–Meier analysis demonstrated a significantly lower event rate in the capecitabine arm ($p=0.003$). Survival analysis demonstrated a hazard ratio of 5.3 (95% CI: 1.04–26.8). The cumulative metastasis rate was 15.4% in the capecitabine group compared with 50% in the control group ($p=0.003$). Estimated 32-month overall survival (OS) rates were 94.9% and 77.8%, respectively ($p=0.04$).

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Conclusions One year of maintenance low-dose capecitabine after standard adjuvant treatment was well tolerated, with hand–foot syndrome identified as the most frequent adverse event. While the trial was powered for safety, exploratory analyses also showed significant improvements in disease-free and overall survival along with reduced metastasis rates, in early-stage triple-negative breast cancer, warranting confirmation in larger, dedicated efficacy trials.

Trial registration: ClinicalTrials.gov, NCT07143097. Registered 19 August 2025—Retrospectively registered, https://clinicaltrials.gov/study/NCT07143097?tab=history.

Keywords Triple-negative breast cancer, Maintenance capecitabine, Early-stage breast cancer, Disease-free survival, Overall survival

Background

Breast cancer is the most commonly diagnosed worldwide among females, coming before lung cancer with about two million three thousand new cases per year [1, 2]. About fifteen–twenty percent of breast cancer cases are diagnosed with triple-negative subtype, more prevalent among young premenopausal women < forty years, African American and Latino as well as low socioeconomic standards [3–6].

The aggressive biological behavior as well as lack of available targeted therapies will explain the poor prognosis of TNBC subtype, which is characterized by high incidence of early relapse mostly visceral metastasis [7, 8]. TNBC has high tendency for visceral metastases practically hepatic, pulmonary, and to brain, with a median survival of about 18 months [3, 9].

Although TNBC is very sensitive to chemotherapy, it is come with early relapse and rapid resistance [10]. In all newly diagnosed cases, chemotherapy with taxane and anthracycline-based protocols are the standard treatment in both adjuvant and neoadjuvant settings [11]. So, it's crucial to do balance between effectiveness of treatment and possible toxicity, early-stage TNBC to avoid either overtreatment or undertreatment which may cause poor outcomes [12].

TNBC with disease residual after neoadjuvant treatment was gained the benefit of adjuvant capecitabine as established by CREATE-X, while the idea of one year of low-dose metronomic capecitabine in early-stage TNBC and its' benefit on improving DFS was suggested in SYSUCC-001 trial [13]. Angiogenesis and immune evasion are two main mechanisms of developing metastasis which can be targeted by Low-dose, high-frequency chemotherapy called metronomic therapy so may help in preventing metastatic progression in TNBC [14].

Capecitabine, an oral chemotherapy agent widely used in metastatic setting, represents a promising option for low-dose maintenance therapy to prevent relapse [15–17], while high-dose capecitabine added to standard adjuvant treatment was studied in previous several clinical trials that reported conflicting data [18–22]; however, TNBC was not included in many of them.

Previously, patients with TNBC whom did not reach a complete pathological response after the standard neoadjuvant chemotherapy were observed only, until recent studies which allow treatment adjustment based on the presence or absence of residual tumor, demonstrated a survival benefit when added to adjuvant treatment [23].

This study aimed to assess the impact of maintenance low-dose capecitabine for females diagnosed with early triple-negative breast cancer on safety, disease-free survival and overall survival following completion of all standard adjuvant treatment.

Patients and methods

Study design and patient eligibility

The trial was randomly evaluated in a 1:1 ratio comparing the efficacy and adverse events of maintenance low-dose capecitabine with observation after standard adjuvant treatment early-stage TNBC.

The study was approved by the Research Ethics Committee and according to the ethical values of the Declaration of Helsinki. A written informed consent was gained from all participants after a well explanation of the study objectives and events.

Eligible participants were female patients with early-stage invasive BC; no supraclavicular or internal mammary LN positivity (T1b–T3N0–N3cM0) according to the (AJCC) 2010, seventh edition staging criteria, confirmed pathologically and have Estrogen Receptor (ER)–progesterone receptors (PR) Human Epidermal Receptor (Her2) negative. All Participants had received standard treatments, including surgery, neoadjuvant or adjuvant chemotherapy, and radiotherapy.

History of invasive breast cancer or other cancers, inflammatory or bilateral breast cancer, pregnancy or lactation, previous treatment with biologic or immunotherapeutic agents, or the presence of severe comorbid illnesses were excluded from the study.

Intervention

We randomly assigned patients to either the maintenance low-dose capecitabine (LDC) group or the observation group within one month of their completing standard adjuvant treatment. Patients in the intervention group received oral capecitabine at a dose of 650 mg/m^2 twice daily, taken continuously for one year. The control group underwent observation only. To ensure safety and treatment adherence, we evaluated patients every month to record the total dose received and monitor for any treatment-related adverse events (AEs). Every three months, we performed a comprehensive clinical assessment, including physical examinations, menopausal status checks, and ultrasound (U/S) imaging of the breast, abdomen, and pelvis. At the time of our final analysis, patients who had not experienced disease recurrence or death were censored as event-free and alive.

Randomization, allocation, and blinding

We randomly assigned 75 patients to either the maintenance capecitabine group or the observation group at a 1:1 ratio. A computer-generated program was used to ensure the groups remained balanced throughout the enrollment period with a block size of four. We maintained strict allocation concealment by using sequentially numbered, opaque, sealed envelopes; these were handled by a third party, and only opened once a patient was confirmed eligible and officially enrolled. Because this was an open-label trial comparing active medication to observation, neither the participants nor the clinical team were blinded to the treatment. However, to maintain the integrity of our results, the statistician responsible for the final analysis remained blinded to the group assignments.

Outcome measures

The primary endpoint of this study was to assess the adverse events (AEs) of capecitabine after 6 months of treatment initiation. These AEs were evaluated and classified according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Hand–foot syndrome (HFS), a common effect of fluoropyrimidine agents like capecitabine, was specifically monitored and graded from 1 to 3 based on severity. Disease-free survival (DFS) and overall survival (OS) were included as pre-specified secondary endpoints. DFS was defined as the time from diagnosis to the first event of local relapse, distant metastasis, or contralateral breast cancer. OS was defined as the time from diagnosis to death from any cause. Given that the study was primarily powered for toxicity, survival outcomes are interpreted as exploratory.

Sample size

Based on previously reported incidences of hand–foot syndrome (HFS) associated with capecitabine (approximately 45%) and the negligible incidence observed in control (observation) groups, we calculated the required sample size to identify a statistically significant difference in adverse event (AE) rates between groups using a two-sided chi-square test. Assuming a power of 80% and $\alpha = 0.05$, the minimum required sample size was estimated to be 38 patients (19 per group). To account for an anticipated attrition rate of approximately 20%, we aimed to enroll approximately 40 patients per group. Ultimately, 75 patients were enrolled (39 in the capecitabine arm and 36 in the observation arm), exceeding the minimum required sample size of 38 patients and providing > 99% statistical power to detect clinically meaningful differences in treatment-emergent adverse events.

Statistical analysis

Data collected and coded to facilitate data manipulation and double entered into Microsoft Access and data analysis performed using the Statistical Package of Social Science (SPSS) software version 22 in windows 11 (SPSS Inc., Chicago, IL, USA): simple descriptive analysis in the form of numbers and percentages of qualitative data, and arithmetic means as central tendency measurement, standard deviations as a measure of dispersion of quantitative parametric data. Quantitative data included in the study first tested for normality by One-Sample Kolmogorov–Smirnov test in each study group then inferential statistic tests selected. Independent samples t-test was used to compare quantitative measures between two independent groups. One-way ANOVA test used to compare quantitative measures between more than two independent groups of quantitative data. Chi square test used to compare between two of more than two qualitative groups. Survival outcomes, including disease-free survival (DFS) and overall survival (OS), were estimated using the Kaplan–Meier method, with group comparisons performed via the log-rank test. For patients who remained recurrence-free or were alive at the time of data cutoff, data were right-censored at the date of the last clinical follow-up. The Kaplan–Meier formula accounted for this censoring by adjusting the number at risk at each time interval without assuming the subject had experienced an event. All analyses were conducted on an intention-to-treat (ITT) basis. A P-value < 0.05 was considered statistically significant.

Results

From November 2021 to May 2024, 85 patients from the University Hospital Oncology Department were assessed for eligibility, and 75 patients were collected and assigned randomly for the capecitabine group ($n=39$) or for observation group ($n=36$). All patients were under regular follow-up throughout the study. Participant flow is illustrated in Fig. 1.

Participant baseline demographic and clinical features are summarized in Table 1. The mean age was 50.1 ± 10.1 years in the intervention group and 47.3 ± 10.3 years in the control group ($p=0.24$). High Ki-67 (>20%) expression was observed in 64% of the intervention group and 75% of the control group ($p=0.44$). Clinical parameters included relevant laboratory values and tumor characteristics. Overall, no significant differences were observed between the groups across these baseline variables, indicating well-balanced cohorts that support the integrity and comparability of subsequent analyses.

Primary end point

The primary outcome was the assessment of treatment-related adverse effects in the capecitabine group; the

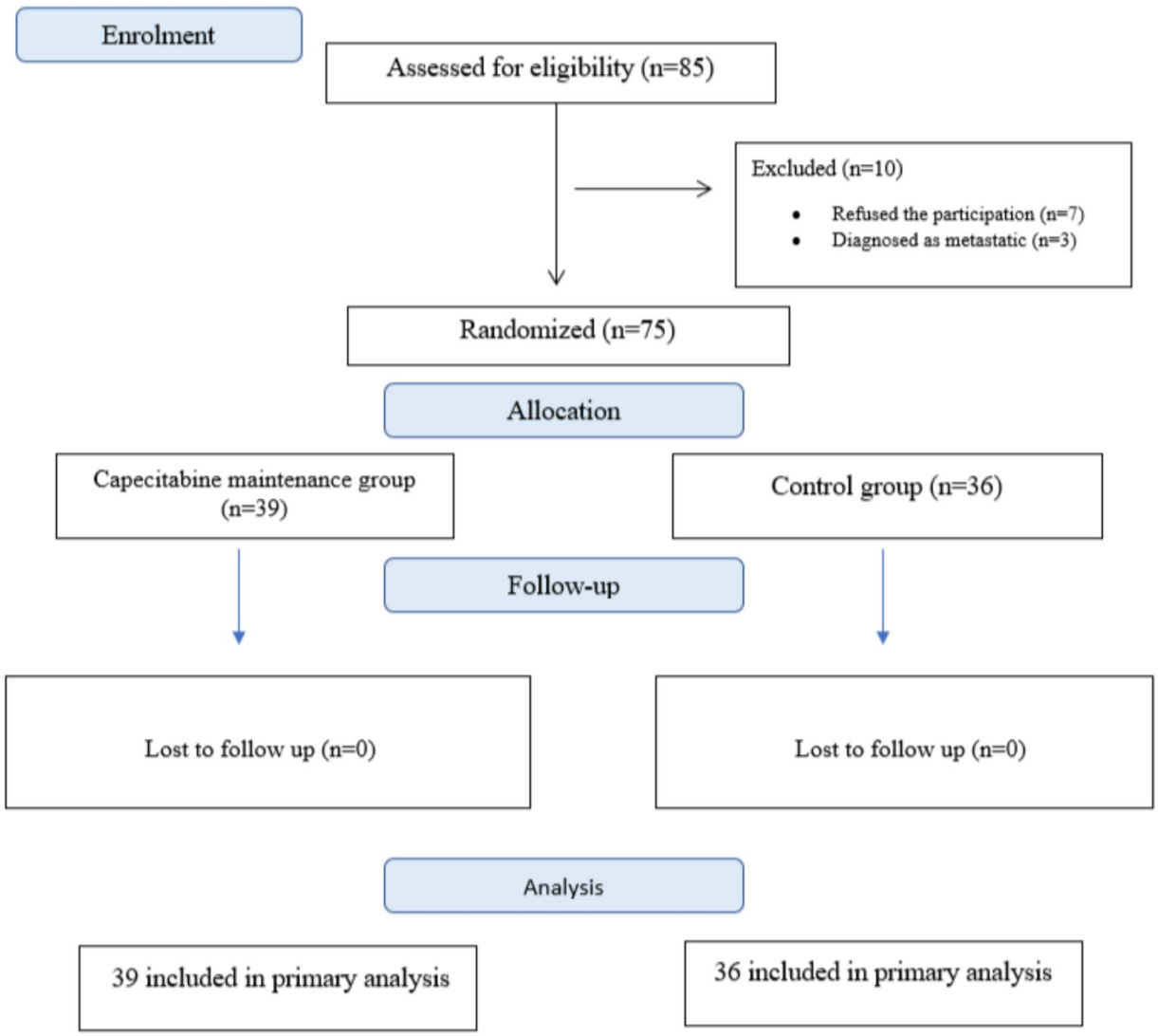


Fig. 1 Consort flowchart of study participants

Table 1 Baseline patient demographics and tumor characteristics

Variables		Intervention group ($n=39$)	Control ($n=36$)	*p*-value
Age (year)	Mean ± SD	50.1 ± 10.1	47.3 ± 10.3	0.24
Menopausal status, *n* (%)	Premenopausal Postmenopausal	21(53.8%) 18(46.2%)	26(72.2%) 10(27.8%)	0.15
Surgery, *n* (%)	CBS MRM	17 (43.6%) 22 (56.4%)	21 (58.3%) 15 (41.7%)	0.25
Tumor staging, n (%)	T0 T1 T2 T3 T4	3 (7.7%) 8 (20.5%) 24 (61.5%) 3 (7.7%) 1 (2.6%)	2 (5.6%) 4 (11.1%) 24 (66.7%) 6 (16.7%) 0 (0%)	0.49
Lymph node, *n* (%)	N0 N1 N2 N3	24 (61.5%) 6 (15.4%) 6 (15.4%) 3 (7.7%)	18 (50%) 13 (36.1%) 1 (2.8%) 4 (11.1%)	0.07
Pathological staging, *n* (%)	Stage 0 Stage 1a Stage 2a Stage 2b Stage 3a Stage 3c	3 (7.7%) 3 (7.7%) 19 (48.7%) 5 (12.8%) 6 (15.4%) 3 (7.7%)	2 (5.6%) 1 (2.8%) 17 (47.2%) 9 (25%) 3 (8.3%) 4 (11.1%)	0.62
Pathological subtype, *n* (%)	IDC Papillary	38 (97.4%) 1 (2.6%)	36 (100%) 0 (0%)	0.99
Ki67	< 20% > 20% Not done	4 (10.3%) 25 (64.1%) 10 (25.6)	4 (11.1%) 27 (75%) 5 (13.9%)	0.44

Table 2 Adverse events in the capecitabine group ($n=39$)

Adverse event	Grade 1, *n* (%)	Grade 2, *n* (%)	Grade 3, *n* (%)	Total, *n* (%)
Hand–foot syndrome	7 (17.9%)	3 (7.7%)	1 (2.6%)	11 (28.2%)
Gastrointestinal upset	5 (12.8%)	1 (2.6%)	0 (0%)	6 (15.4%)
Neutropenia	1 (2.6%)	0 (0%)	0 (0%)	1 (2.6%)
Thrombocytopenia	1 (2.6%)	0 (0%)	0 (0%)	1 (2.6%)

most frequent toxicity was hand–foot syndrome, as shown in Table 2 happening in 11 patients (28.2%), one (2.6%) with grade three. Other adverse effects included neutropenia (2.6%), thrombocytopenia (2.6%), and gastrointestinal upset (15.4%), all of grade 1 or 2 severity (Table 2). In general, maintenance low-dose capecitabine was well tolerated, and most patients ended one year of the therapy without interruption.

Among the intervention group, eight patients (20.5%) required temporary treatment interruption; 94.9% of this resumed therapy. Two patients (5.1%) discontinued permanently due to intolerance. Five patients (12.8%) required a 25% dose reduction, which was sufficient to resume treatment.

The maximum interruption duration was 4 weeks. Of the 39 patients assigned to the capecitabine arm, 21 (53.8%) completed the full 12-month course. Eight (20.5%) discontinued early: one by choice after 6 months, two due to grade 3 hand–foot syndrome, and five (12.8%) due to disease recurrence. The remaining ten patients (25.6%) were still on treatment at data cutoff (Table 3).

Table 3 Treatment compliance and modifications ($n=39$)

Variable	*n* (%)	Clinical context
Full completion (12 months)	21 (53.8%)	Completed the full protocol
Dose reduction (25%)	5 (12.8%)	Required due to toxicity
Temporary interruption	8 (20.5%)	Resumed after 1–4 weeks
Permanent discontinuation	8 (20.5%)	Total early withdrawals
Due to Disease Recurrence	5 (12.8%)	Discontinued to start new therapy
Due to Intolerance/HFS	2 (5.1%)	Permanent stop due to Grade 3 HFS
Due to Patient Choice	1 (2.6%)	Stopped at 6 months
Ongoing treatment	10 (25.6%)	Active at time of data cutoff

Secondary end points

At a median follow-up of 32 months, maintenance capecitabine was associated with significant improvements in survival outcomes compared with observation alone.

The estimated mean disease-free survival (DFS) was 44.46 months (95% CI: 42.38–46.53) in the capecitabine group versus 34.67 months (95% CI: 30.16–39.19) in the control group ($p=0.019$) (Table 4, Fig. 2). Survival analysis demonstrated a hazard ratio (HR) of 5.3 (95% CI: 1.04–26.8), indicating a markedly higher risk in the control arm relative to the capecitabine arm.

Similarly, the estimated mean overall survival (OS) was significantly longer in the capecitabine group (43.96 months; 95% CI: 41.30–46.62) compared with the control group (37.05 months; 95% CI: 33.92–40.17) ($p=0.019$) (Table 4, Fig. 3). The survival rate at 32 months was significantly higher in the interventional group (94.9%) compared with the control group (77.8%) ($p=0.04$).

Table 4 Summary of survival outcomes at 32-month follow-up (DFS and OS)

Outcome measure	Group	Mean				*p*-value
		Estimate	Std. error	95% Confidence interval		
				Lower bound	Upper bound	
Disease-free survival (DFS)	Interventional	44.46	1.06	42.38	46.53	0.019*
	Control	34.67	2.30	30.16	39.19	
Overall survival (OS)	Interventional	43.96	1.36	41.30	46.62	0.019*
	Control	37.05	1.59	33.92	40.17	

* statistically significant difference at $p<0.05$

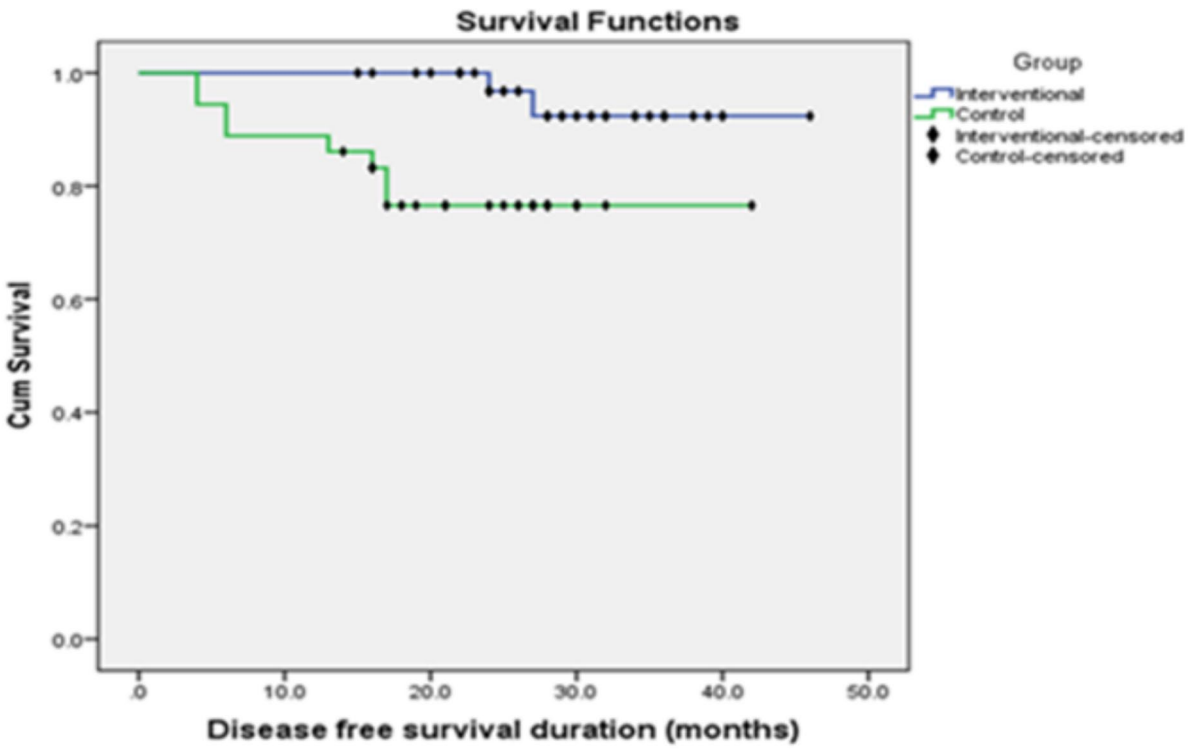
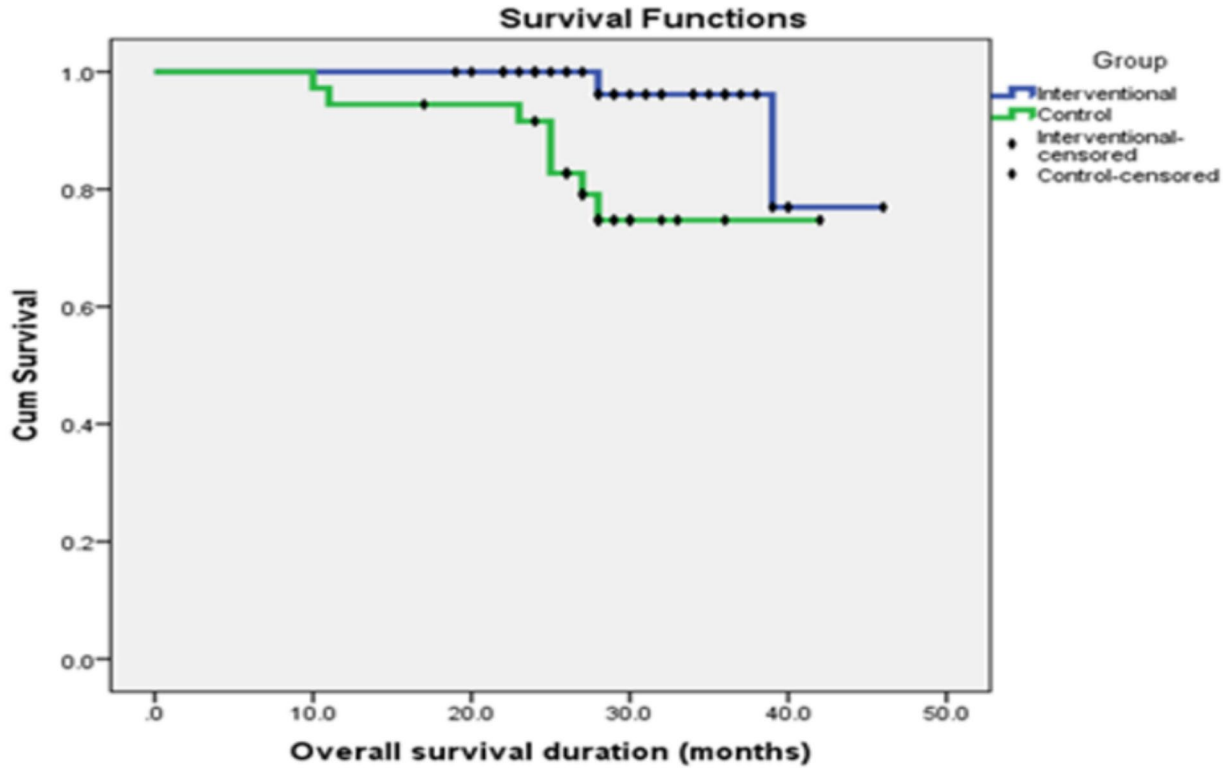


Fig. 2 Disease-free survival duration in study groups



No. at risk

Capecitabine	39	39	38	19	3
Observation	36	36	33	7	1

Fig. 3 Overall survival duration in study groups

Disease progression patterns further supported the benefit of capecitabine. The metastasis rate was significantly lower in the intervention group (15.4%) than in the control group (50%) ($p=0.003$). A total of 24 recurrence events occurred during follow-up: six events in the capecitabine group (two local recurrences and four distant metastases) versus 18 events in the control group (three local recurrences and 15 distant metastases) (Table 5).

Within the intervention group, survival outcomes were further analyzed according to treatment duration (6, 9, and 12 months) (Table 6).

A statistically significant difference in disease-free survival (DFS) was observed across treatment durations ($p<0.001$). The mean DFS was 24.7 ± 4.7 months in the 6-month group, 23.2 ± 5.8 months in the 9-month group, and 32.5 ± 6.4 months in the 12-month group. Patients treated for 12 months demonstrated the longest DFS.

Similarly, overall survival (OS) differed significantly according to treatment duration ($p=0.01$). The mean OS was 26.5 ± 5.1 months in the 6-month group, 30.0 ± 7.1 months in the 9-month group, and 32.8 ± 6.1 months in the 12-month group, with the most favorable outcomes observed in patients receiving 12 months of therapy.

No significant differences were observed between neoadjuvant ($n=18$) and adjuvant ($n=21$) subgroups in metastasis rates (16.7% vs 14.3%, $p=0.99$). Two deaths occurred during follow-up, both in the adjuvant subgroup. The mean DFS was 26.6 months in the neoadjuvant subgroup compared with 30.6 months in the adjuvant subgroup, without statistical significance. In contrast, the mean OS was significantly longer in the adjuvant subgroup (32.3 months vs 28 months; $p=0.03$). Given the small sample sizes and limited number of events, these subgroup analyses should be interpreted cautiously.

Discussion

Driven by biologically aggressiveness of TNBC, its management is still one of greatest challenges due to lack of targeted therapies. TNBC also characterized by early

Table 5 Incidence and patterns of disease recurrence and site of metastasis in different study groups

Variable	Intervention ($n=39$)	Control ($n=36$)	*p*-value
Total recurrence events, *n* (%)	6 (15.4%)	18 (50.0%)	0.003*
Site of first recurrence			
Local recurrence	2 (33.3%)	3 (16.7%)	0.18
Distant metastasis (only)	4 (66.7%)	15 (83.3%)	
Distant metastasis sites			
Visceral (lung, liver, brain)	2 (33.3%)	13 (72.2%)	
Bone only	1 (16.7%)	0 (0.0%)	
Combined bone and visceral	1 (16.7%)	2 (11.1%)	
Specific visceral sites			
Lung	2 (66.7%)	5 (33.3%)	0.78
Brain	1 (33.3%)	5 (33.3%)	
Liver	0 (0.0%)	3 (20.0%)	
Lung and brain	0 (0.0%)	1(6.7%)	
Lung and liver	0 (0.0%)	1(6.7%)	

* statistically significant difference at $p<0.05$

Table 6 Survival outcomes by duration of capecitabine therapy (intervention group)

Treatment Duration	DFS, Mean (SD)	*p*-value	OS, Mean (SD)	*p*-value
6 Months ($n=13$)	24.7 (4.7)	< 0.001*	26.5 (5.1)	0.01*
9 Months ($n=5$)	23.2 (5.8)		30.0 (7.1)	
12 Months ($n=21$)	32.5 (6.4)		32.8 (6.1)	

* statistically significant difference at $p<0.05$

relapse and high incidence of distant metastases. Our randomized controlled trial addressed this clinical gap by investigating the safety and efficacy of one year of maintenance low-dose capecitabine versus observation in women with early-stage TNBC, demonstrating a significant and clinically meaningful improvement in both disease-free survival (DFS) and overall survival (OS).

The CREATE-X was the first study to highlight the benefit of this approach, this study used capecitabine (1250 mg/m^2 orally BID, from day one to fourteen, for 6–8 cycles) in patients with TNBC and had residual disease after standard neoadjuvant therapy significantly improved overall survival versus observation (HR, 0.52; 95% CI, 0.39–0.90) [24].

Low-dose metronomic maintenance capecitabine was investigated in the SYSUCC-001 trial with promising results, where 424 patients diagnosed with TNBC were randomized to receive maintenance capecitabine ($n=222$, 650 mg/m^2 twice daily continuously for 1 year) versus observation ($n=221$); 5-year disease-free survival was significantly improved in the capecitabine arm (82.8% vs. 73.0%; HR, 0.64; 95% CI, 0.42–0.95; $P=0.03$) while 5-year overall survival was not statistically significant improved (85.5% vs. 81.3%; HR, 0.75; 95% CI, 0.47–1.19; $P=0.22$) [25].

The 10-year update of the Chinese phase III SYSUCC-001 trial, reported in The Lancet Oncology, showed that disease-free survival was 78.1% vs 66.6% with HR 0.61, $P=0.007$, distant DFS: 78.1% vs 66.5% with HR 0.61, $P=0.0075$, Locoregional RFS: 81.6% vs 69.9% with HR 0.60, $P=0.011$ and Overall survival: numerically better (82.4% vs 73.7%), trend toward significance [26].

Our principal finding was the demonstration of a significantly prolonged estimated 32-month DFS (44.46 months vs. 34.67 months; $p=0.019$) and OS (43.96 months vs. 37.05 months; $p=0.019$) in the capecitabine group compared to observation. This substantial survival benefit is further supported by a threefold reduction in the 32-month metastasis rate (15.4% vs. 50% in the control group; $p=0.003$).

While these survival findings are exploratory and derived from a trial primarily powered for safety outcomes, the magnitude and direction of benefit are broadly consistent with findings from larger randomized studies evaluating capecitabine in triple-negative breast cancer. In the CREATE-X trial, the hazard ratio for disease-free survival in the TNBC subgroup was approximately 0.58, reflecting a clinically meaningful reduction in recurrence risk with adjuvant capecitabine. Similarly, the SYSUCC-001 study reported a disease-free survival hazard ratio of 0.64 at 5 years, and 0.61 in the 10-year update, confirming sustained long-term benefit [24–26].

Metronomic efficacy, using (650 mg/m^2 twice daily, continuous), has different anti-tumor mechanism through anti-angiogenic and immune-modulatory

mechanisms rather than maximum-tolerated dose (MTD) chemotherapy which is direct cytotoxic [27].

In trials included unselected populations including all molecular subtypes, failed to show overall benefit of adding capecitabine to standard adjuvant chemotherapy; however, subgroup analysis suggested benefit for TNBC in phase III trial GEICAM/CIBOMA trial [28]. Shorter duration therapy studied in GEICAM/CIBOMA 2003–10 trial using capecitabine (1250 mg/m^2 twice a day on days 1 to 14, ×four cycles) showed invasive disease-free survival, but not OS, and was significantly superior for patients with node-positive early BC TNBC [29].

Finally, the primary endpoint focused on safety, confirming that maintenance low-dose capecitabine was well tolerated. Hand–foot syndrome was the most common toxicity (28.2%), with only a low rate of grade 3 events (2.6%). Similarly, in SYSUCC-001 trail, hand–foot syndrome was the most frequent adverse event, occurring in 100 patients (45.2%), including 17 patients (7.7%) with a grade 3 event [13]. However, the incidence in our cohort was comparatively lower suggesting a favorable tolerability profile in our population. The high rate of therapy completion (53.8% completed the full 12-month course) and the low rate of permanent discontinuation (5.1%) affirm the clinical feasibility of this continuous oral regimen.

Despite the significant findings, our study has several limitations. First, the single-center design and relatively small sample size may limit generalizability to broader populations. Second, the trial was statistically powered to evaluate treatment-related adverse events as the primary endpoint; consequently, the disease-free and overall survival findings, though pre-specified as secondary endpoints, should be interpreted cautiously as exploratory results. Third, the median follow-up of 32 months remains relatively short for early-stage breast cancer, and longer observation is needed to confirm durability of benefit. Validation through multicenter studies with larger cohorts and extended follow-up will be essential to definitively establish the role of maintenance low-dose capecitabine in this setting.

Conclusions

This randomized trial demonstrates that one year of maintenance low-dose capecitabine (650 mg/m^2 twice daily) is a feasible and well-tolerated adjuvant strategy in patients with early-stage triple-negative breast cancer, successfully meeting its primary safety objective. Hand–foot syndrome was the most common adverse event (28.2%), predominantly grades 1–2 in severity. Pre-specified secondary analyses suggested improvements in disease-free survival, overall survival, and distant metastasis rates in the maintenance arm. However, as the study was powered for toxicity rather than survival outcomes, these efficacy findings should be considered exploratory and interpreted with caution. These findings support the safety and potential therapeutic role of maintenance low-dose capecitabine in early-stage TNBC.

Abbreviations

AE	Adverse Event
AJCC	American Joint Committee on Cancer
BC	Breast Cancer
CBS	Conservative Breast Surgery (Lumpectomy)
CI	Confidence interval
CTCAE	Common Terminology Criteria for Adverse Events
DFS	Disease-free survival
ER	Estrogen receptor
HFS	Hand-foot syndrome
HR	Hazard ratio
HER2	Human Epidermal Growth Factor Receptor 2
IDC	Invasive ductal carcinoma
LN	Lymph node
MRM	Modified Radical Mastectomy
MTD	Maximum-tolerated dose
NCI	National Cancer Institute
OS	Overall survival
PR	Progesterone receptor
RFS	Relapse-free survival
ROC	Receiver operating characteristic
SD	Standard deviation
TNBC	Triple-Negative Breast Cancer
U/S	Ultrasound

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Author contributions

Study conception and design were created by Sarah Hamdy Ali, Engy A. Wahsh, and Ahmed Hassan shaaban.

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Data availability

The authors confirm that the data supporting the findings of this study are available within the article. Raw data supporting the findings of this study are available from the first author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Faculty of Medicine, Beni-Suef University Research Ethics Committee with approval number FMBSUREC/10102021/Sayed and according to the ethical values of the Declaration of Helsinki. The study was registered online at ClinicalTrials.gov, with the identifier NCT07143097, Record Verification date: August 19, 2025 Retrospectively registered. https://clinicaltrials.gov/study/NCT07143097?tab=history. *Data analysis and interpretation were developed by* Sarah Hamdy Ali, Enas Mohsen El Nadi, Abeer Mokhles Gadallah, and Ahmad Mahrous Dewidar. *Drafting, revision of the paper and Final approval of the published version were done by* Sarah Hamdy Ali, Enas Mohsen El Nadi, Abeer Mokhles Gadallah, Ahmad Mahrous Dewidar, Engy A. Wahsh, and Ahmed Hassan shaaban.

Consent for publication

Not applicable.

Informed consent
A written informed consent was obtained from all subjects involved in the study.

Conflicts of interest
The authors declare that there was no conflict of interest in this study.

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