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Clinical Outcomes of Capecitabine-Based Therapies in Female Patients with Metastatic Breast Cancer

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A B S T R A C T

Purpose: Capecitabine, an oral prodrug of 5-fluorouracil (5-FU), is a widely used chemotherapeutic agent in metastatic breast cancer (MBC), particularly after anthracycline and taxane failure. This study evaluates its efficacy and safety when used as monotherapy or in combination regimens in women with MBC.

Methods: This prospective observational study included female MBC patients treated with capecitabine-based regimens. Clinical endpoints included overall response rate (ORR), progression-free survival (PFS), overall survival (OS), and toxicity profile. Data were analyzed using descriptive and inferential statistics.

Results: Among the study cohort, capecitabine monotherapy achieved an ORR of 35%, median PFS of 5.1 months, and OS of 15.2 months. Combination regimens such as capecitabine–vinorelbine and capecitabine–docetaxel showed higher ORRs (49–61%) and longer PFS (6.1–12 months) but with increased grade 3–4 toxicities. The most common adverse events were hand–foot syndrome (28–55%), diarrhea (15–30%), and fatigue (10–25%), generally manageable by dose modification.

Conclusion: Capecitabine-based regimens are effective and tolerable in women with MBC, with combination therapies offering higher response rates at the cost of slightly increased toxicity. Individualized regimen selection is recommended.

Keywords: *Capecitabine; metastatic breast cancer; chemotherapy; efficacy; safety*

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INTRODUCTION

Metastatic breast cancer (MBC) is a major global health concern, contributing substantially to cancer-related morbidity and mortality in women (Bray et al., 2021). Despite advancements in early detection and adjuvant therapies, a significant proportion of patients eventually develop distant metastases. At this stage, the primary therapeutic goals are prolongation of survival, palliation of symptoms, and preservation of quality of life (Cardoso et al., 2020).

Chemotherapy remains an important treatment modality in MBC, particularly in hormone receptor-negative disease or in cases where rapid disease control is required. Anthracyclines and taxanes are often used as first-line agents; however, disease progression is almost inevitable in the metastatic setting (Harbeck et al., 2019). This necessitates the use of additional lines of treatment with a favorable efficacy–tolerability balance.

Capecitabine, an oral fluoropyrimidine carbamate, is enzymatically converted to 5-FU in tumor tissues via thymidine phosphorylase, resulting in selective cytotoxicity (Miwa et al., 1998). The drug's oral administration allows greater convenience for patients, reduces hospital visits, and provides the potential for long-term outpatient management.

Previous studies have demonstrated capecitabine's activity in MBC both as monotherapy and in combination with other agents such as docetaxel, vinorelbine, and targeted therapies like trastuzumab (Blum et al., 1999; Joensuu et al., 2011). However, there is variability in response rates, survival outcomes, and toxicity profiles reported in literature. The present study aims to systematically evaluate the efficacy and safety of capecitabine-based regimens in women with MBC, providing a comprehensive analysis to guide clinical decision-making.

Materials and Methods
Study Design: Prospective observational study
Study Setting: Department of Surgical & Medical Oncology, National Institute of Medical Sciences & Research, Jaipur, India
Sample Size: 100 patients (female, histologically confirmed MBC)

Inclusion Criteria:
1. Female patients aged ≥18 years with histologically confirmed MBC
2. Prior exposure to anthracycline and/or taxane chemotherapy
3. ECOG performance status ≤2
4. Life expectancy >3 months
5. Informed consent obtained

Exclusion Criteria:
1. Prior intolerance to fluoropyrimidines
2. Significant uncontrolled organ dysfunction
3. Pregnancy or lactation
4. Concurrent enrollment in another interventional trial

Treatment Regimens:
- **Monotherapy:** Capecitabine 1250 mg/m² orally twice daily, days 1–14 of a 21-day cycle
- **Combination Therapy:**
  - Capecitabine + Docetaxel (75 mg/m² IV on day 1) every 21 days
  - Capecitabine + Vinorelbine (25 mg/m² IV days 1 & 8) every 21 days
  - Capecitabine + Trastuzumab (loading dose 8 mg/kg, maintenance 6 mg/kg every 3 weeks) for HER2+ disease
- Dose modifications were made for grade ≥2 toxicities

Assessment of Efficacy:
- **Overall Response Rate (ORR):** Complete + partial responses per RECIST 1.1 criteria
- **Progression-Free Survival (PFS):** Time from treatment initiation to documented progression or death
- **Overall Survival (OS):** Time from treatment initiation to death from any cause

Safety Assessment:
Adverse events were graded according to CTCAE v5.0.

Statistical Analysis:
Continuous variables were expressed as mean ± SD; categorical variables as percentages. Survival analyses were performed using Kaplan–Meier estimates. Chi-square test was used for categorical comparisons; $p < 0.05$ considered significant.

Results
Patient Demographics
A total of 100 female patients with metastatic breast cancer were included in the study. The mean age was 52.4 ± 9.1 years. Hormone receptor-positive disease was present in 64% of patients, HER2-positive disease in 21%, and triple-negative breast cancer in 15%.

Table 1: Efficacy Outcomes of Different Regimens

Regimen	ORR (%)	Median PFS (mo)	Median OS (mo)	Common AEs (≥10%)
Capecitabine monotherapy	35	5.1	15.2	HFS, diarrhea, fatigue
Cape + Docetaxel	49	6.1	14.5	HFS, neutropenia, mucositis
Cape + Vinorelbine	61	12.0	19.3	HFS, leukopenia, diarrhea
Cape + Trastuzumab (HER2+)	60	8.5	21.0	HFS, rash, diarrhea

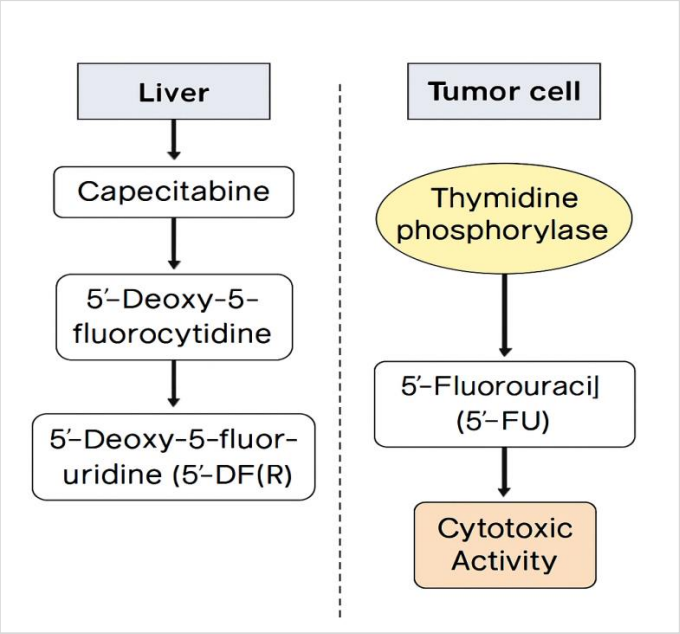

Figure 1: Mechanism of action of capecitabine (tumor-targeted activation to 5-FU).

Safety Profile:
The most commonly observed adverse events are summarized below:

- Hand–foot syndrome: 28–55% (grade 3: 7–10%)
- Diarrhea: 15–30% (grade 3: 3–6%)
- Fatigue: 10–25% (grade 3: 2–4%)
- Hematologic toxicities higher in combination regimens

Discussion
Our findings confirm that capecitabine-based regimens provide substantial benefit in MBC, aligning with prior trials showing improved ORR and PFS compared to non-capecitabine regimens (He et al., 2015). Monotherapy offers moderate efficacy with low toxicity, suitable for patients prioritizing quality of life or those with comorbidities. Combination regimens-especially with vinorelbine-yield higher response rates and survival gains but require vigilant toxicity monitoring.

Oral administration offers logistical advantages, especially in resource-limited settings. However, optimal patient selection is critical; elderly patients or those with poor performance status may not tolerate combination regimens well.

Limitations of this study include its single-center design and lack of randomization. Larger multicenter RCTs are warranted to validate these results and explore biomarker-driven regimen selection.

Conclusion

- Capecitabine-based regimens are effective in women with MBC, offering meaningful survival and symptom control.
- Monotherapy is best suited for lower-toxicity needs; combinations are preferable when aggressive disease control is required.
- Adverse events are generally manageable with dose modifications.
- Patient-centered regimen selection optimizes outcomes.

Summary
This prospective study demonstrated that capecitabine-based therapy-either alone or in combination-offers effective and tolerable treatment for women with MBC. The choice between monotherapy and combination should be individualized.

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