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Efficacy and safety profile of capecitabine-based regimens in women with metastatic breast cancer

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Abstract
Background: Breast cancer is the most frequent cancer in women and the leading cause of cancer deaths. The major treatment for metastatic hormone receptor–negative breast cancer is chemotherapy. It is also suggested in hormone receptor–positive breast cancer with fast advancing or symptomatic illness, visceral crises, and endocrine resistance despite targeted therapies. A rationally designed oral, tumor-activated fluoropyrimidine carbamate, capecitabine is effective in metastatic breast cancer. This study was designed to evaluate the efficacy and safety profile of capecitabine based regimens in female patients with metastatic breast cancer.
Method: The 52 female metastatic breast cancer patients in this retrospective cross-sectional analysis got capecitabine alone or in combination with other agents. From January 2020 to December 2020, Oncology Teaching Hospital outpatient consultation clinic patients were covered. History, physical, radiological, laboratory, pathology, and molecular (ER, PR, HER2) reports were recorded. From the commencement of capecitabine until the end of treatment owing to illness progression or toxicity, months were calculated.
Results: In a study of 52 patients (mean age 52.9 ± 11.4 years), disease control was achieved in 59.6%, with a mean PFS of 11.8 months. Significant PFS difference was noted between triple-negative and non-triple-negative patients (p=0.024). Common side effects included nausea (57.7%), hand-foot syndrome (55.8%), and diarrhea (32.7%). Grade III/IV side effects led to dose reductions in 9.6% and treatment withholding in 19.2% of patients.
Conclusion: The current study's findings indicate that capecitabine is a well-tolerated and efficacious treatment for metastatic breast carcinoma. Furthermore, it is an appealing agent for outpatient treatment due to its orally administered, convenient nature.

Keywords: Efficacy, safety, capecitabine-based, women, metastatic, breast cancer

Introduction
Breast cancer is the most common malignancy among women worldwide, with about 1.7 million new cases in 2012, accounting for 25% of all new cancer cases [1]. Incidence rates are higher in economically developed regions such as North America, Western Europe, and Australia/New Zealand, and lower in economically developing areas like sub-Saharan Africa and Asia. Between 1980 and 1990, breast cancer incidence in developed countries increased due to heightened screening and changes in reproductive factors. However, since 2000, postmenopausal breast cancer incidence has declined in these regions due to reduced use of menopausal hormone therapy [2]. In Iraq, breast cancer remains the most common malignancy, with approximately 6,206 new cases diagnosed in 2018, representing 19.70% of all malignancies [3]. Globally, breast cancer was the leading cause of cancer death in women, causing 521,817 of the estimated 8.2 million cancer-related deaths in 2012 [4]. Since 1990, countries like the United States, the United Kingdom, and France have seen reductions in breast cancer-related deaths due to more effective systemic therapies and early detection. Conversely, changes in reproductive patterns, increased obesity, and decreased physical activity have contributed to a 2- to 3-fold increase in breast cancer incidence in African and Asian countries, with a corresponding rise in breast cancer deaths [5]. The incidence of metastatic disease diagnosed at presentation has remained stable at 6% annually [6]. Mortality from breast cancer decreased by 36% from 1989 to 2012 and remained stable among women younger than 50 [7]. Hormone receptors, such as estrogen (ER) and progesterone (PR) receptors, are weak prognostic indicators but highly predictive of response to endocrine

therapy. Most hormone receptor-positive breast cancers have functional ER and PR. ER-negative/PR-positive cancers are less frequent but still respond to endocrine therapy, while ER-negative/PR-positive cancers, occurring in 1-5% of cases, may not derive significant benefit from endocrine therapy [8]. Among all breast cancers, 55% are ER-positive/PR-positive, 16% are ER-positive/PR-negative, and 4% are ER-negative/PR-positive [9]. The recurrence risk for hormone receptor-negative breast cancer is highest within the first five years' post-diagnosis and then declines sharply [10]. Conversely, hormone receptor-positive breast cancer shows a more gradual decline, with a significant risk of late distant recurrences occurring more than ten years after diagnosis [11]. HER2, a member of the epidermal growth factor receptor (EGFR) tyrosine kinase family, is overexpressed due to gene amplification in approximately 20% of breast cancers. HER2 status is determined according to ASCO/CAP guidelines [12]. HER2 overexpression is a strong predictive factor for response to HER2-directed therapies, including trastuzumab, pertuzumab, ado-trastuzumab emtansine, and lapatinib [13]. HER2-positive disease, if untreated with anti-HER2 therapy, is associated with shorter disease-free survival (DFS) and breast cancer-specific survival, independent of other prognostic indicators [14]. Breast cancer staging employs the AJCC system based on the TNM classification: T (tumor size), N (lymph node involvement), and M (metastasis). Stage 0 represents carcinoma in situ, while Stage IV signifies any breast cancer with distant metastasis [15]. Metastatic breast cancer treatment aims to slow disease progression, improve quality of life, and prolong survival while minimizing toxicity. Sequential single-agent chemotherapy is preferred over combination regimens, except in cases of visceral crisis or rapidly progressive disease requiring prompt cytoreduction [16]. Capecitabine, an oral fluoropyrimidine, has demonstrated efficacy in multiple phase II trials for metastatic breast cancer, with response rates around 28% and median overall survival (OS) of 15.2 months [17]. In another study, capecitabine showed a higher ORR compared with cyclophosphamide, methotrexate, and fluorouracil (CMF) [18]. Combination therapies with agents like vinorelbine have also shown benefits [19]. Capecitabine's design allows for selective 5-FU activation in tumor tissue, making it an effective treatment option with a favorable toxicity profile [20]. This study was designed to evaluate the efficacy and safety profile of capecitabine based regimens in female patients with metastatic breast cancer.

Method

A cross-sectional study was conducted at The Oncology Teaching Hospital from January to December 2020, involving 52 Iraqi female patients with metastatic breast cancer. All patients were treated with capecitabine, either alone (35 patients) or in combination with vinorelbine (17 patients). Participants included those who had received chemotherapy, hormonal therapy, or targeted therapy as adjuvant treatment or for metastatic disease.

Data Collection: Sociodemographic data and medications were recorded, including age, weight, height, body surface area, and previous treatments. ER, PR, and Her2 statuses were obtained from molecular study reports using immunohistochemistry (IHC) or in situ hybridization for equivocal results. The duration of capecitabine treatment was calculated from the start date to the last follow-up or the date of treatment cessation due to disease progression or unacceptable toxicity.

Capecitabine Dose: Patients received different doses of capecitabine: 37 patients received 1000 mg/m², 9 received 850 mg/m², and 5 received 1250 mg/m².

Laboratory Measurements: Blood investigations included hemoglobin, white blood cells (total and differential count), platelets, blood urea, and serum creatinine.

Response to Treatment: Treatment response was assessed using RECIST 1.1 criteria:

- **Complete Response:** Complete disappearance of all disease.
- **Partial Response:** ≥30% reduction in the sum of the longest diameter of target lesions.
- **Stable Disease:** Changes not meeting criteria for response or progression.
- **Progression:** ≥20% increase in the smallest sum of the longest diameters of target lesions.

Adverse Effects: Adverse effects were classified using the Common Terminology Criteria for Adverse Events (CTCAE) created by the US National Cancer Institute (NCI).

Statistical Analysis: Data analysis was performed using SPSS version 23. Descriptive statistics were presented as frequency tables. Continuous variables were expressed as mean ± standard deviation, and categorical variables as numbers and percentages. Associations between categorical variables were analyzed using the Chi-square test or Fisher exact test when sample sizes were small. Survival analysis was conducted using log-rank and Kaplan-Meier tests, with a p-value ≤ 0.05 considered statistically significant.

Results

A total of 52 patients with metastatic breast cancer were enrolled in this study. The mean ± SD age of patients was 52.9±11.4 years, ranging between 30-84 years, table 1.

Table 1: Age Distribution of studied sample.

Age	Number	Percentage
< 40 years	5	9.6%
40-59 years	31	69.2%
≥60 years	16	30.8%
Total	52	100%

The Estrogen receptor(ER), Progesterone receptor (PR) and HER2 status of breast cancer at diagnosis was triple negative in 15.4% (8) of patients only, figure 1.

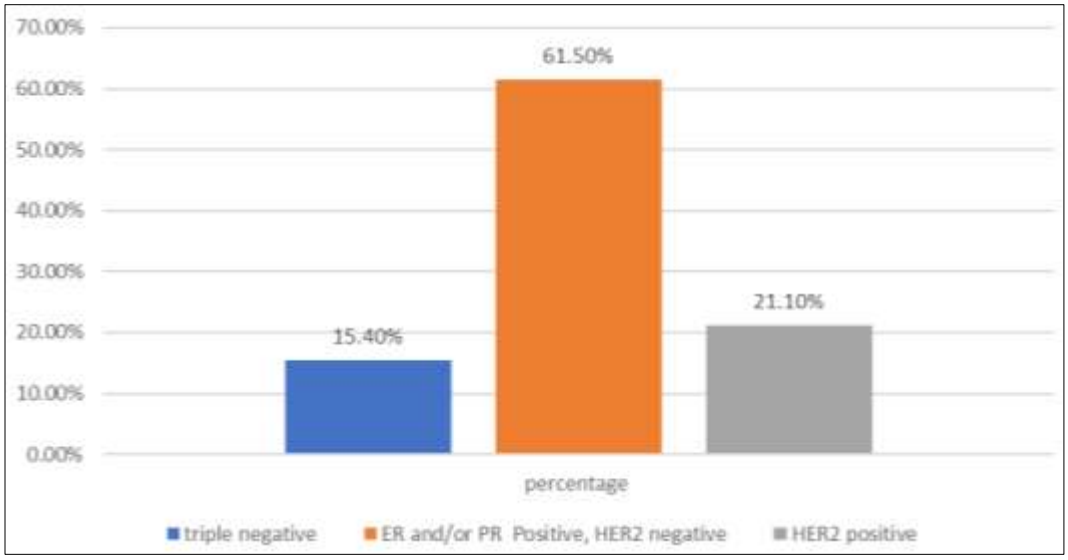

Fig 1: ER, PR and HER2 status of breast cancer.

The stage of breast cancer at diagnosis was stage II at 23.1% of patients, stage III at 55.8% of patients and stage IV at 21.2% of patients, table 2.

Table 2: Stage of breast cancer at diagnosis among studied patients.

Stage at diagnosis	Number	Percentage
Stage II	12	23.1%
Stage III	29	55.8%
Stage IV	11	21.2%
Total	52	100%

Site of metastasis was the bone in 57.8% (30) of patients, liver in 38.5% (20) of patients, lung in 26.9% (14) of patients, LN in 7.7% (4) of patients and 7.7% (4) of patients had other site metastasis like pleura, peritoneum, other breast and ovary, figure 2.

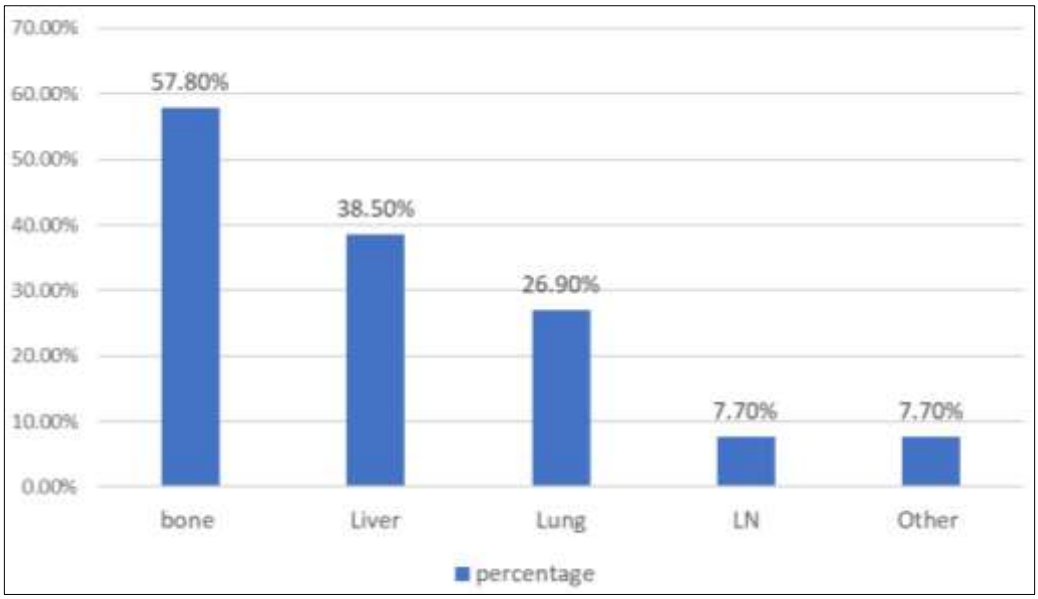

Fig 2: Site of metastasis among studied patients.

All patients received capecitabine based regimen; the dose was varied between 850 mg/m^2 to 1250 mg/m^2 based on BSA of patients. And the regimen was accompanied with vinorelbine in 32.7% (17) of patients, table 3.

Table 3: Treatment regimens among studied patients.

Treatment regimen	Number	Percentage
Capecitabine only	35	67.3%
Capecitabine +vinorelbine	17	32.7%
Total	52	100%

The outcome of capecitabine based regimens was either; disease controlled in 59.6% (31) of patients or disease progression in 40.4% (21) of patients, figure 3. The partial response after 3 months of receiving capecitabine was achieved in 25% of patients.

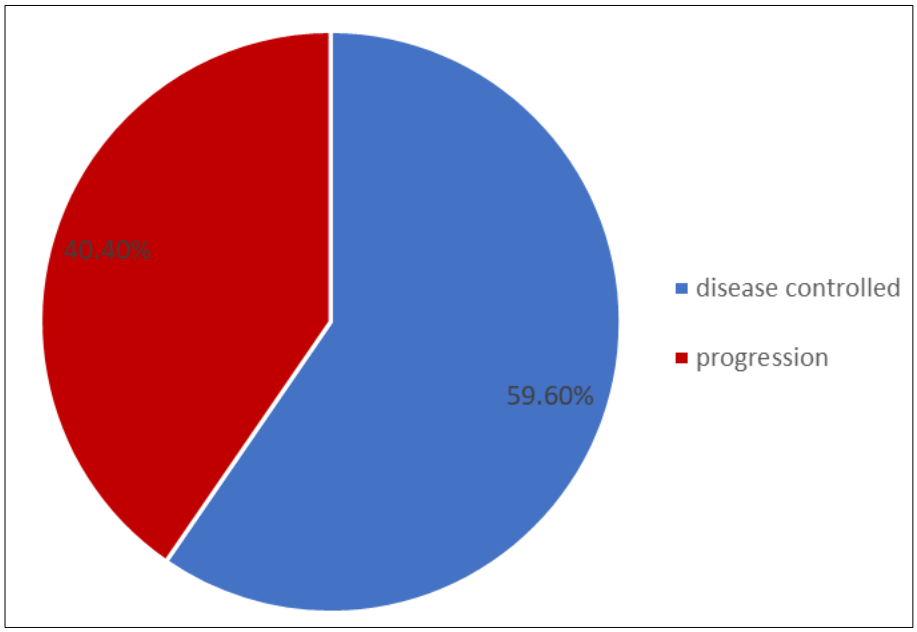

Fig 3: Disease outcome after receiving capecitabine based regimen.

The development of progression was not association with age, ER, PR and HER2 status or stage of breast cancer at diagnosis (p>0.05), table 4.

Table 4: Relation of the outcome of capecitabine based regimen with certain variables.

Variables		Outcome		P value
		Disease controlled	Progression	
Age	<60 years	24(66.7%)	12(33.3%)	0.12*
	≥60 years	7(43.8%)	9(56.3%)	
ER, PR and HER2 status	Non triple negative	26(59.1%)	18(40.9%)	0.59**
	Triple negative	5(62.5%)	3(37.5%)	
Stage at first diagnosis	IV	7(63.6%)	4(36.4%)	0.52**
	II, III	24(58.5%)	17(41.5%)	

*chi-square test, ** fisher-exact test, significant ≤0.05.

The estimation of the mean progression free survival after receiving capecitabine based regimen was 11.8 months and median was 12 months and 65% of patients was had progression free survival at 9 months, figure 4.

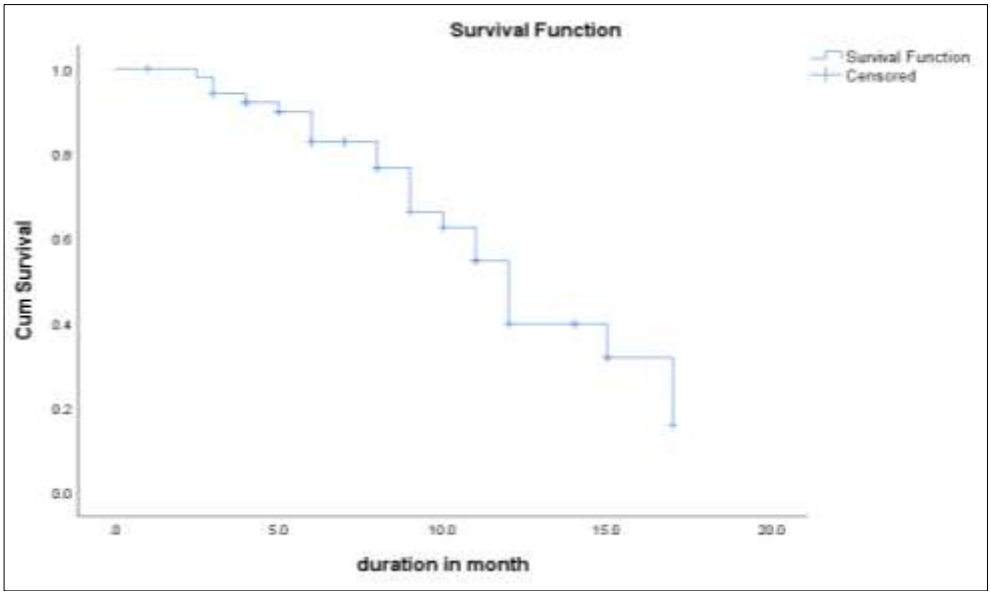

Fig 4: Kaplan Meier survival analysis for progression free survival after capecitabine based regimen.

The test of equality shown no significant difference in PFS according to treatment regimen (p= 0.32), table 5. And fig 5.

Table 5: Difference in PFS according to treatment regimen.

Treatment regimen	Mean PFS in months	P value
Capecitabine only	12.1	0.32*
Capecitabine +vinorelbine	10.5	

*Log rank test, significant≤0,05.

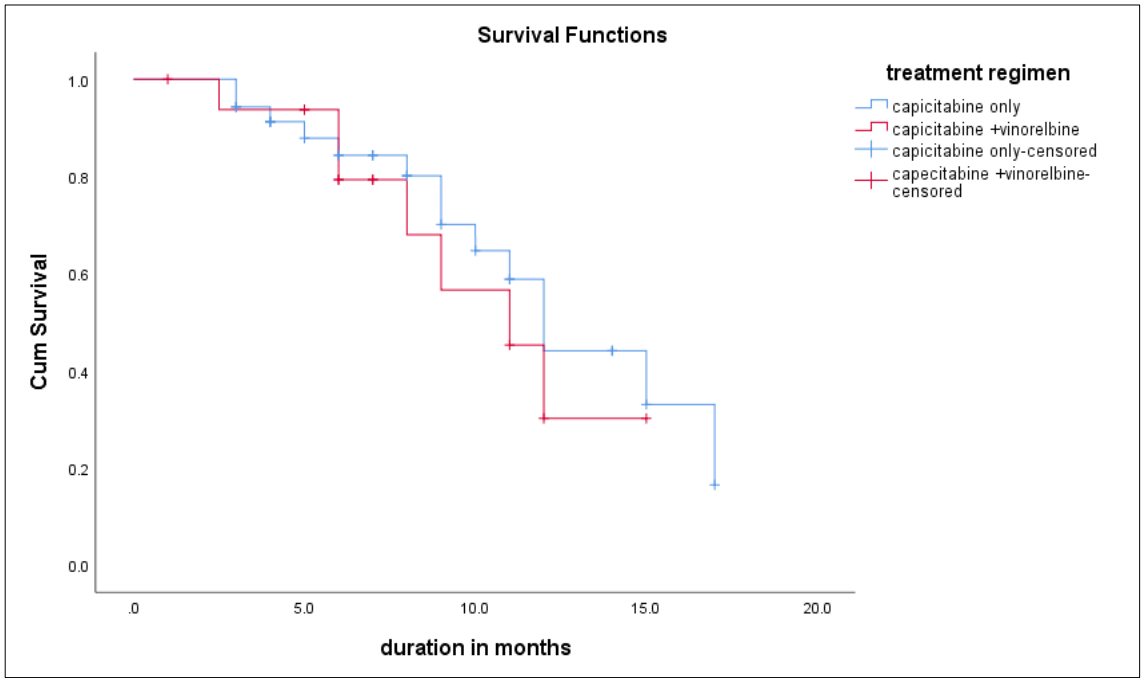

Fig 5: Kaplan Meier survival analysis for progression free survival according to treatment regimen.

The test of equality shown a significant difference in PFS between triple negative vs non triple negative (p=0.024), table 6, figure 6.

Table 6: Difference in PFS according to hormonal receptor status.

ER, PR and HER2 status	Mean PFS in months	P value
Triple negative	11.9	0.024*
Non triple negative	10.5	

*Log rank test, significant≤0,05.

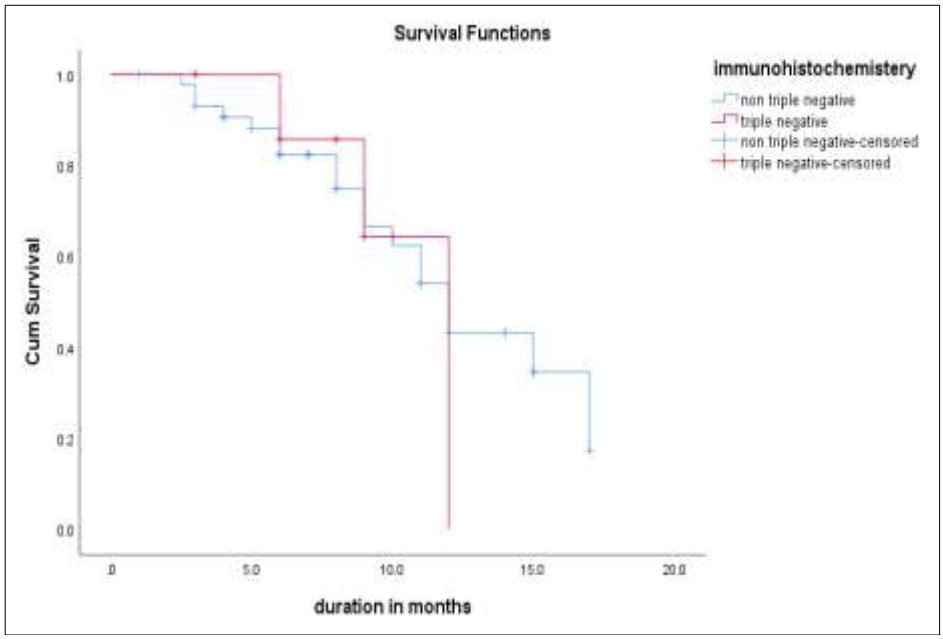

Fig 6: Kaplan Meier survival analysis for progression free survival according to ER, PR and HER2 status.

The side effect of capecitabine based regimen was shown in tables 7-9.

Table 7: Type of myelosuppression developed due to capecitabine based regimen.

Type of myelosuppression		Number	Percentage
Anemia	Negative	33	63.5%
	Grade I	9	17.3%
	Grade II	7	13.5%
	Grade III	3	5.8%
Neutropenia	Negative	35	67.3%
	Grade I	8	15.4%
	Grade II	6	11.5%
	Grade III	3	5.8%
Thrombocytopenia	Negative	44	84.6%
	Grade I	3	5.8%
	Grade II	2	3.8%
	Grade III	2	3.8%
	Grade IV	1	1.9%

Table 8: GIT side effect of capecitabine based regimen.

GIT side effect		Number	Percentage
Diarrhea	Negative	35	67.3%
	Grade I	15	28.8%
	Grade II	2	3.8%
Vomiting	Negative	36	69.2%
	Grade I	12	23.1%
	Grade II	3	5.8%
	Grade III	1	1.9%
Nausea	Negative	24	46.2%
	Grade I	22	42.3%
	Grade II	6	11.5%

Table 9: Other side effect of capecitabine based regimen.

Side effect		Number	Percentage
Hand & foot syndrome	Negative	23	44.2%
	Grade I	16	30.8%
	Grade II	7	13.5%
	Grade III	6	11.5%
Mucositis	Negative	37	71.2%
	Grade I	11	21.2%
	Grade II	4	7.7%

The capecitabine based regimen side effects caused decreases the dose in 9.6%(5) of patients and withholding the treatment in 19.2% (10) of patients, figure 7.

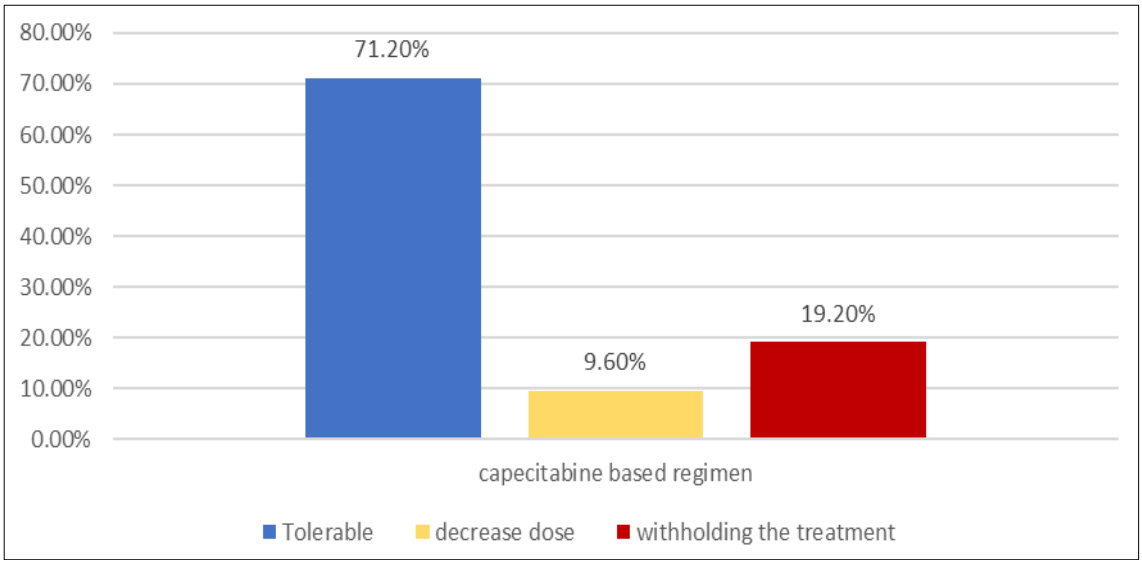

Fig 7: Outcome of capecitabine based regimens.

Discussion

A retrospective study involving 52 Iraqi female patients with metastatic breast cancer was conducted. The mean age of patients was 52.9 ± 11.4 years, comparable to the studies by Blum JL *et al*. [21] and Ghosn, Marwan, *et al*. [22], where the mean ages were 52.5 ± 11.4 and 54 years, respectively. In this study, 15.4% of patients were triple-negative, 61.5% were ER and/or PR positive HER2 negative, and 21.1% were HER2 positive. These results align with Pin Zhang *et al*. [23] but differ from J Wang *et al*. [24]. The bone was the most common metastasis site in 57.8% of patients, followed by the liver (38.5%), lung (26.9%), lymph nodes (7.7%), and other sites (7.7%). This is similar to findings by Iizumi S, Shimomura A *et al*. [25], but contrasts with Wist *et al*. [26] who found the liver to be the most common metastasis site. Disease control was achieved in 59.6% of patients, comparable to Blum JL *et al*. [21] and Reichardt P *et al*. [27], with control rates of 57% and 62%, respectively. Progression occurred in 40.4% of patients, not significantly associated with age, ER, PR, HER2 status, or cancer stage at diagnosis ($P > 0.05$), consistent with Prado CM *et al*. [28] but differing from Azuma Y *et al*. [29]. After three months of capecitabine treatment, 25% of patients achieved partial response, aligning with M. Kaufmann *et al*. (30) and Pin Zhang *et al*. [23] but differing from Iizumi S, Shimomura A *et al*. [25]. The mean progression-free survival (PFS) was 11.8 months, with 65% of patients having PFS at nine months, comparable to Ghosn, Marwan, *et al*. [22], Vaid AK *et al*. (31), and H Lv, M Yan *et al*. [32], but lower than other studies (Iizumi S, Shimomura A *et al*. [25], Pin Zhang *et al*. [23], M. Kaufmann *et al*.) [30]. No significant difference in PFS was found between capecitabine alone or in combination with vinorelbine ($p=0.32$), similar to Vernieri C *et al*. [33] but contrasting with Simon P. Gampenrieder *et al*. [34]. PFS was significantly different between triple-negative and non-triple-negative patients ($p=0.024$), consistent with O'Shaughnessy JA *et al*. [35] but not with H Lv, M Yan *et al*. [32]. Most patients experienced at least one treatment-related adverse event, with the most common being nausea (57.7%), hand-foot syndrome (55.8%), anemia (36.5%), diarrhea (32.7%), neutropenia (32.7%), vomiting (30.8%), mucositis (28.8%), and thrombocytopenia (15.4%). Grade III and IV side effects occurred in 28.8% of patients, comparable to Iizumi S, Shimomura A *et al*. [25], Pierga *et al*. [36], and Pin Zhang *et al*. [23], but higher than Taner Babacan *et al*. [37]. These side effects led to treatment withholding in 19.2% of patients, similar to J. A. O'Shaughnessy, J. Blum *et al*. [18], but higher than Pin Zhang *et al*. [23] and Iizumi S, Shimomura A *et al*. [25]. Dose reduction was required in 9.6% of patients, comparable to Taner Babacan *et al*. [37], but lower than B. T. Hennessy *et al*. [38] and Erik A. Wist *et al*. [27].

Conclusion

Capecitabine is a highly effective chemotherapeutic agent that has a favourable DFS in females with metastatic breast cancer, particularly in the triple negative subtype of the disease. The combination of vinorelbine and capecitabine does not produce a substantial difference in DFS. Capecitabine is an appealing agent for outpatient use due to its efficacy and manageable toxicity profile, as well as its convenient oral administration style. Capecitabine enables patients to experience the advantages of a long-term treatment without the potential for cumulative toxicity. This will be especially significant when used in conjunction with other chemotherapeutic or novel targeted agents during long-term treatment.

References

1. World Health Organization. International Agency for Research on Cancer. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. Cancer Fact Sheets. Ravdin PM, Cronin KA, Howlader N, *et al*. The decrease in breast-cancer incidence in 2003 in the United States. New England Journal of Medicine. 2007;356:1670–1674. PMID: 17442911.
2. Ravdin PM, Cronin KA, Howlader N, Berg CD, Chlebowski RT, Feuer EJ, Edwards BK, Berry DA. The decrease in breast-cancer incidence in 2003 in the United States. New England Journal of Medicine. 2007 Apr 19;356(16):1670-1674.
3. Iraqi Cancer Board. Annual report, Iraqi cancer registry 2018. iqcaboard@moh.gov.iq
4. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA: A Cancer Journal for Clinicians. 2011 Mar;61(2):69-90.
5. Porter P. "Westernizing" women's risks? Breast cancer in lower-income countries. New England Journal of Medicine. 2008 Jan 17;358(3):213-216.
6. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA: A Cancer Journal for Clinicians. 2016 Jan;66(1):7-30.
7. Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A. SEER Cancer Statistics Review, 1975–2013. Bethesda, MD: National Cancer Institute; 2016 Apr 8;19.
8. Early Breast Cancer Trialists' Collaborative Group. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. The Lancet. 2011 Aug 27;378(9793):771-784.
9. Rakha EA, El-Sayed ME, Lee AH, Elston CW, Grainge MJ, Hodi Z, Blamey RW, Ellis IO. Prognostic significance of Nottingham histologic grade in invasive breast carcinoma. Journal of Clinical Oncology. 2008 Jul 1;26(19):3153-3158.
10. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, Lickley LA, Rawlinson E, Sun P, Narod SA. Triple-negative breast cancer: clinical features and patterns of recurrence. Clinical Cancer Research. 2007 Aug 1;13(15):4429-4434.
11. Hess KR, Pusztai L, Buzdar AU, Hortobagyi GN. Estrogen receptors and distinct patterns of breast cancer relapse. Breast Cancer Research and Treatment. 2003 Mar;78(1):105-118.
12. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, Allred DC, Bartlett JM, Bilous M, Fitzgibbons PL, Hanna W. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. Archives of Pathology & Laboratory Medicine. 2014 Feb;138(2):241-256.

13. Haddad TC, Loprinzi CL. Breast Cancer. In: Hensley ML, editor. ASCO-SEP, Medical Oncology Self-Evaluation Program. 6th ed. 2018. p. 339.
14. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science. 1987 Jan 9;235(4785):177-182.
15. Jagsi R, King TA, Lehman C, Morrow M, Harris JR, Burstein HJ. Malignant tumors of the breast. In: DeVita VT, Lawrence TS, Rosenberg SA, editors. Cancer: Principles & Practice of Oncology. 11th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; c2019. p. 2274.
16. Cardoso F, Bedard PL, Winer EP, Pagani O, Senkus-Konefka E, Fallowfield LJ, Kyriakides S, Costa A, Cufer T, Albain KS, ESO-MBC Task Force. International guidelines for management of metastatic breast cancer: combination vs sequential single-agent chemotherapy. Journal of the National Cancer Institute. 2009 Sep 2;101(17):1174-1181.
17. Fumoleau P, Largillier R, Clippe C, Dieras V, Orfeuvre H, Lesimple T, Culine S, Audhuy B, Serin D, Cure H, Vuillemin E. Multicentre, phase II study evaluating capecitabine monotherapy in patients with anthracycline-and taxane-pretreated metastatic breast cancer. European Journal of Cancer. 2004 Mar 1;40(4):536-542.
18. O'Shaughnessy JA, Blum J, Moiseyenko V, Jones SE, Miles D, Bell D, Rosso R, Mauriac L, Osterwalder B, Burger HU, Laws S. Randomized, open-label, phase II trial of oral capecitabine (Xeloda®) vs. a reference arm of intravenous CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) as first-line therapy for advanced/metastatic breast cancer. Annals of Oncology. 2001 Sep 1;12(9):1247-1254.
19. Pajk B, Cufer T, Canney P, Ellis P, Cameron D, Blot E, Vermorken J, Coleman R, *et al*. Anti-tumor activity of capecitabine and vinorelbine in patients with anthracycline-and taxane-pretreated metastatic breast cancer: findings from the EORTC 10001 randomized phase II trial. The Breast. 2008 Apr 1;17(2):180-185.
20. Walko CM, Lindley C. Capecitabine: a review. Clinical Therapeutics. 2005 Jan 1;27(1):23-44.
21. Blum JL, Dieras V, Lo Russo PM, Horton J, Rutman O, Buzdar A, Osterwalder B. Multicenter, phase II study of capecitabine in taxane-pretreated metastatic breast carcinoma patients. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2001 Oct 1;92(7):1759-1768.
22. Ghosn M, Kattan J, Farhat F, Younes F, Gasmi J. Phase II trial of capecitabine and vinorelbine as first-line chemotherapy for metastatic breast cancer patients. Anticancer Research. 2006 May 1;26(3B):2451-2456.
23. Zhang P, Sun T, Zhang Q, Yuan Z, Jiang Z, Wang XJ, *et al*. Utidelone plus capecitabine versus capecitabine alone for heavily pretreated metastatic breast cancer refractory to anthracyclines and taxanes: A multicentre, open-label, superiority, phase 3, randomised controlled trial. The Lancet Oncology. 2017 Mar 1;18(3):371-383.
24. Wang J, Xu B, Yuan P, Ma F, Li Q, Zhang P, *et al*. Capecitabine combined with docetaxel versus vinorelbine followed by capecitabine maintenance medication for first-line treatment of patients with advanced breast cancer: phase 3 randomized trial. Cancer. 2015 Oct 1;121(19):3412-3421.
25. Iizumi S, Shimomura A, Shimoi T, Sudo K, Noguchi E, Yonemori K, Shimizu C, Fujiwara Y, Tamura K. Efficacy of capecitabine in patients with locally advanced or metastatic breast cancer with or without prior treatment with fluoropyrimidine: a retrospective study. Cancer Chemotherapy and Pharmacology. 2018 Aug;82(2):275-283.
26. Wist EA, Sommer HH, Østenstad B, Risberg T, Bremnes Y, Mjaaland I. Oral capecitabine in anthracycline-and taxane-pretreated advanced/metastatic breast cancer. Acta Oncologica. 2004 Mar 1;43(2):186-189.
27. Reichardt P, Von Minckwitz G, Thuss-Patience PC, Jonat W, Kölbl H, Jänicke F, *et al*. Multicenter phase II study of oral capecitabine (Xeloda®) in patients with metastatic breast cancer relapsing after treatment with a taxane-containing therapy. Annals of Oncology. 2003 Aug 1;14(8):1227-33.
28. Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, *et al*. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clinical Cancer Research. 2009 Apr 15;15(8):2920-2926.
29. Azuma Y, Hata K, Sai K, Udagawa R, Hirakawa A, Tohkin M, *et al*. Significant association between hand-foot syndrome and efficacy of capecitabine in patients with metastatic breast cancer. Biological & Pharmaceutical Bulletin. 2012 May 1;35(5):717-724.
30. Kaufmann M, Maass N, Costa SD, Schneeweiss A, Loibl S, Sütterlin MW, *et al*. First-line therapy with moderate dose capecitabine in metastatic breast cancer is safe and active: results of the MONICA trial. European Journal of Cancer. 2010 Dec 1;46(18):3184-91.
31. Vaid AK, Gupta S, Doval D, Talwar V, Shrestha S, Pavithran K, *et al*. Capecitabine: Single institution experience from North India in metastatic breast cancer. Journal of Clinical Oncology. 2004 Jul 15;22(14_suppl):815.
32. Lv H, Yan M, Zhang M, Niu L, Zeng H, Cui S. Efficacy of capecitabine-based combination therapy and single-agent capecitabine maintenance therapy in patients with metastatic breast cancer. Chinese Journal of Cancer Research. 2014 Dec;26(6):692.
33. Vernieri C, Prisciandaro M, Nichetti F, Lobefaro R, Peverelli G, Ligorio F, *et al*. Oral Capecitabine-Vinorelbine Is Associated with Longer Overall Survival When Compared to Single-Agent Capecitabine in Patients with Hormone Receptor-Positive Advanced Breast Cancer. Cancers. 2020 Mar;12(3):617.
34. Gampenrieder SP, Bartsch R, Matzneller P, Pluschnig U, Dubsky P, Gnant MX, *et al*. Capecitabine and vinorelbine as an all-oral chemotherapy in HER2-negative locally advanced and metastatic breast cancer. Breast Care. 2010;5(3):158-62.
35. O'Shaughnessy JA, Kaufmann M, Siedentopf F, Dalivoust P, Debled M, Robert NJ, *et al*. Capecitabine monotherapy: review of studies in first-line HER-2-negative metastatic breast cancer. The Oncologist. 2012 Apr;17(4):476.

36. Pierga JY, Fumoleau P, Brewer Y, Zelek L, Martin D, Turpin FL, *et al*. Efficacy and safety of single agent capecitabine in pretreated metastatic breast cancer patients from the French compassionate use program. Breast Cancer Research and Treatment. 2004 Nov;88(2):117-129.
37. Babacan T, Efe O, Hasirci AS, Demirci F, Buyukhatipoglu H, Balakan O, *et al*. Efficacy of capecitabine monotherapy as the first-line treatment of metastatic HER2-negative breast cancer. Tumori Journal. 2015 Jul;101(4):418-23.
38. Hennessy BT, Gauthier AM, Michaud LB, Hortobagyi G, Valero V. Lower dose capecitabine has a more favorable therapeutic index in metastatic breast cancer: retrospective analysis of patients treated at MD Anderson Cancer Center and a review of capecitabine toxicity in the literature. Annals of Oncology. 2005 Aug 1;16(8):1289-1296.

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