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Clinical Outcome of Combinations of Endocrine Therapy with Targeted Therapy in Women with HR +/ HER2 - Postmenopausal Advanced Breast Cancer: A Systematic Review and Meta-analysis

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ABSTRACT

Background and aim: Breast cancer is one of the most common and worrying health problems of women in the world. The efficacy and safety of first-line and second-line/next-line treatments in women with HR + / HER2 − postmenopausal advanced breast cancer is unclear. Therefore, the present study aimed to determine progression-free survival and overall survival of endocrine therapy combinations with targeted therapy in this population.

Material and methods: To obtain documentation and scientific evidence related to the first and second line/further line in the treatment of postmenopausal women with HR +/ HER2 - advanced breast cancer, articles published in international databases such as PubMed, Web of Science, Scopus, Sites Direct, Elsevier, Wiley, and Google Scholar search engine were used. Data were analyzed using STATA software, Version 17. the odds ratio, hazard ratio, and risk ratio with 95% confidence interval (CI), fixed effect model, and inverse–variance method were used.

Results: Twenty-four studies were reviewed. Abemaciclib/Letrozole showed the best PFS in first-line therapies (HR:0.51 95% CI -2.26, 3.28). Dalpiciclib/Fulvestrant showed the best PFS in second/further-line therapies(HR:0.43 95% CI 0.09, 0.77). Ribociclib/Fulvestrant improved overall survival by 0.67 (HR:0.67 95% CI -0.31, 1.65) for first-line treatments, and Abemaciclib/Fulvestrant improved overall survival for second/further-line treatments65 (HR:0.65 95% CI 0.10, 1.20).

Conclusions: Based on the findings of the present study, superior efficiency can be seen in first-line treatment with combinations of endocrine therapy with targeted therapy.

1. Introduction

Breast cancer is the most common cancer among women.[1] According to the Global statistics for 2020 to 2040 of the World Health Organization, one out of every 8 to 10 women will get breast cancer.[2] Breast cancer is the second most common cause of death from cancer.[3] Breast cancer growth in humans is often regulated by steroid hormones such as estrogen and peptide growth factors that interact with epidermal growth factor receptors one and two. The level of hormone receptors in normal breast tissue is low, but in two-thirds of cases of breast cancer, the level of these receptors is higher.[4] According to clinical findings, hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) are breast cancer subgroups. Based on the findings, the two subgroups of HR-positive/HER2-negative are almost the most common indicators.[5] Evidence shows that the growth and survival of cancer cells in these tumors are related to the estrogen receptor signalling pathway, and endocrine glands were used for treatment.[6] The reported limitations of the effectiveness of endocrine therapy and drug resistance have made this therapy seem insufficient. Therefore, targeted treatments such as Cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) were introduced.[7] However, the efficacy and relative safety of most of these first- and second-line/next-line treatments have not been determined.

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Clinical studies have shown that treatments have effectively treated patients with HR+/HER2.[8-10] However, no findings compare treatments' effectiveness on survival rates. Previous meta-analysis studies have also investigated the effectiveness and safety of some treatments, as shown in the present study.[11-13] It has been tried to eliminate the limitations of previous studies, and the effectiveness and safety of first and second-line/next-line treatments in the treatment of postmenopausal women with HR +/ HER2 - advanced breast cancer should be investigated.

2. Material and methods

Search strategy and data sources

To obtain documentation and scientific evidence related to the first and second line/further line in the treatment of postmenopausal women with HR +/ HER2 - advanced breast cancer, articles published in international databases such as PubMed, Web of Science, Scopus, Sites Direct, Elsevier, Wiley, and the Google Scholar search engine were used. The search process in these databases was carried out using the keywords.

Breast cancer, Breast Neoplasms, Breast Tumors, Mammary Cancer, Breast Malignant Neoplasms, Cancer of the Breast, Mammary Carcinoma, Breast Carcinoma, metastasis, ERBB2 protein, human, v-erb-b2 erythroblastic leukaemia viral oncogene homolog two protein, human, human epidermal growth factor receptor 2, hormone receptor, estrogen receptor, Progesterone receptor, and possible combinations, and medical subject headings (MeSH) terms were also used, which included (((((("Breast Cancer Lymphedema"[Mesh] OR "Breast Neoplasms"[Mesh]) OR ("Breast Neoplasms/classification"[Mesh] OR "Breast Neoplasms/mortality"[Mesh] OR "Breast Neoplasms/prevention and control"[Mesh] OR "Breast Neoplasms/surgery"[Mesh] OR "Breast Neoplasms/therapy"[Mesh])) OR "Neoplasm Metastasis"[Mesh]) AND "ERBB2 protein, human" [Supplementary Concept]) AND "Hormones"[Mesh]) OR "Receptors, Estrogen"[Mesh]) OR "Receptors, Progesterone"[Mesh]) AND ("Postmenopause"[Mesh] OR "Estrogen Replacement Therapy"[Mesh]).

In addition, the reference list of articles not obtained using the above methods was checked to identify those articles. All articles were selected based on inclusion criteria and the PICOS strategy.

Inclusion and exclusion criteria

Inclusion criteria included women with advanced postmenopausal HR+/HER2 breast cancer (P: Population), Cancer patients who were under targeted therapy, and a combination of endocrine therapy with targeted therapy (I: Interventions). Studies that had a control group that could be single-agent chemotherapy or endocrine therapy monotherapy (C: Comparison); Studies that reported findings such as overall survival, progression-free survival (PFS), and safety outcomes (O: Outcome); All randomized clinical trials studies (S: Studies). Studies published in different languages except English, review studies and books, qualitative studies, studies without complete findings, non-randomized controlled trials, and scientific sources without full text were excluded from the study.

Selection and data collection process

A form designed based on the purpose of the research was used to extract data. This form included the first author's name, year, research population, sample size, average age of patients, follow-up time, and clinical outcomes. Two independent authors and Koror checked the data separately, and then the third independent author evaluated the completed form. All articles were entered into End. Note X.8 software and the full text of the articles were reviewed by two independent authors. All disagreements between the two authors were resolved through discussion, and a third reviewer was consulted when needed. Studies that reported survival data were prioritized for review.

Risk assessment

The Cochrane risk-of-bias tool for randomized trials (RoB 2) is recommended to assess the risk of bias in randomized trials.[14] Bias is assessed as a judgment (high, low, or unclear) for individual elements from five domains (selection, performance, attrition, reporting, and others).

Statistical analysis

Data were analyzed using STATA software, Version 17. The I^2 index and P-value <0.1 were used for the Q test; I^2 values of 25%, 50%, and 75% correspond to small, moderate, and large amounts of heterogeneity to evaluate the heterogeneity of the studies. The odds ratio, hazard ratio, and risk ratio with 95% confidence interval (CI), fixed effect model, and inverse–variance method were used. Egger's test checked publication bias.

3. Results

Study selection

One hundred thirty-four articles were found in the initial search. First, by reading the titles of the articles, 241 articles were removed due to duplication. In the second step, by studying the abstracts of the 564 articles, 398 articles unrelated to the objectives of the present study were excluded from the study based on the inclusion and exclusion criteria. In the third stage, they were removed after a detailed study of the full text of the remaining 166 articles, 142, due to incomplete data, irrelevant data, and inconsistent objectives. Finally, 24 articles were used in this research.

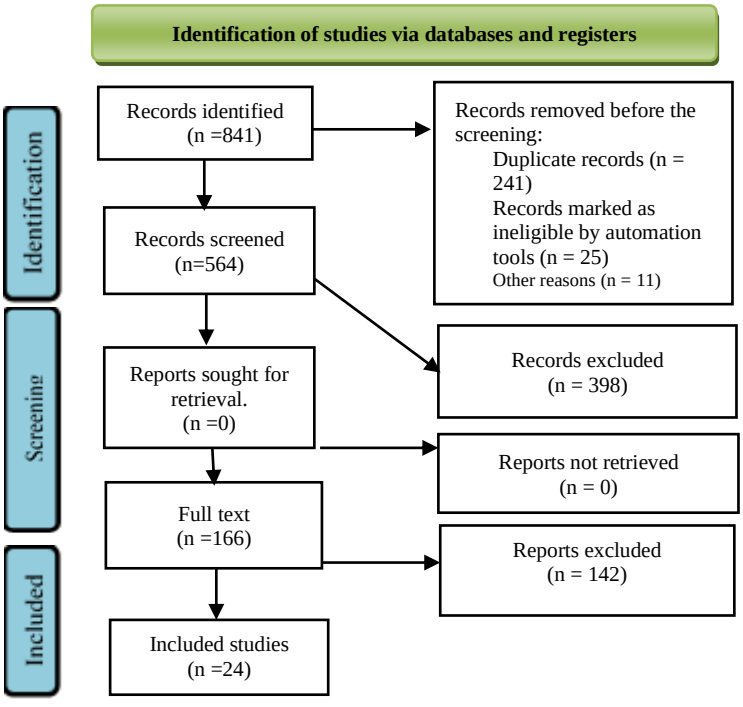

Fig. 1. PRISMA 2020 Checklist.

Study characteristics

Four thousand two hundred seventy-eight individuals in the control group and 6616 individuals in the intervention group underwent examinations. In twelve studies, therapy was the second line; in twelve other studies, it was the first. Table 1 summarizes the chosen studies' features.

Risk of bias

The risk of bias in the RCT study was low (Table 2).

Table 1. Characteristics of included studies.

Study. Years	Number of Patients		Therapy Line	Median Age	Intervention Group	Control Group	Mean of Follow-up (Month)
	Intervention Group	Control Group					
Mayer et al.,2024[15]	111	55	2nd line	57	Palbociclib/Fulvestrant	Fulvestran	NR
Mayer et al., 2023[16]	111	55	2nd line	57	Palbociclib/Fulvestrant	Fulvestran	NR
Howell et al., 2022[17]	69	71	2nd line	60	Capivasertib+Fulvestrant	Fulvestrant	20
Xu et al., 2022[18]	303	153	1st line	51	Dalpiciclib/Letrozole	Letrozole	25.2
Zhang et al., 2022[19]	241	120	2nd line	52	Dalpiciclib/Fulvestrant	Fulvestrant	16
Goetz et al., 2022[20]	328	165	1st line	63	Abemaciclib+Letrozole	Letrozole	47.7
Hortobagyi et al., 2022[21]	334	334	1st line	61	Ribociclib/Letrozole	Letrozole	80
Xu et al., 2022[22]	169	171	1st line	53	Palbociclib plus letrozole	Placebo plus letrozole	52.8
Finn et al., 2022[23]	444	222	1st line	61	Palbociclib plus letrozole	Placebo plus letrozole	38
Cristofanilli et al., 2022[24]	347	174	2nd line	57	Palbociclib–fulvestrant	Placebo–fulvestrant	73
Xu et al., 2021[25]	241	120	2nd line	52	Dalpiciclib/Fulvestrant	Fulvestrant	16
Slamon et al., 2021[26]	237	128	1st line	63	Ribociclib/Fulvestrant	Fulvestrant	70.8
Neven et al., 2021[27]	446	223	2nd line	59	Abemaciclib/Fulvestrant	Fulvestrant	53.5
Llombart-Cussac et al., 2021[28]	243	243	1st line	64	Palbociclib/Fulvestrant	Palbociclib/Letrozole	70.2
André et al., 2021[29]	284	288	2nd line	62	Alpelisib/Fulvestrant	Fulvestrant	16.3
Sledge et al., 2020[30]	446	223	2nd line	59	Abemaciclib/Fulvestrant	Fulvestrant	53.5
Finn et al., 2020[31]	84	81	1st line	63	Palbociclib/Letrozole	Letrozole	64.7
Rugo et al., 2019[32]	444	222	1st line	61	Palbociclib-letrozole	Placebo-letrozo	38
André et al., 2019[33]	284	288	2nd line	62	Alpelisib/Fulvestrant	Fulvestrant	16.3
Turner et al., 2018[34]	347	174	2nd line	57	Palbociclib–fulvestrant	Placebo–fulvestrant	73
Hortobagyi et al., 2018[35]	334	334	1st line	61	Ribociclib/Letrozole	Letrozole	80
Goetz et al., 2017[36]	328	165	1st line	63	Abemaciclib+Letrozole	Letrozole	47.7
Turner et al.,2015[37]	347	174	2nd line	57	Palbociclib–fulvestrant	Placebo–fulvestrant	73

Table 2: Bias assessment of Cochrane Risk of Bias Tool.

Study	Risk of Bias due to the Randomization Process	Effect of Assignment of Innervation	Effect of Adhering to Intervention	Missing Outcome Data	Measuring of Outcome	Selection of the Report Result	Overall
Mayer et al.,2024[15]							
Mayer et al., 2023[16]							
Howell et al., 2022[17]							
Xu et al., 2022[18]							
Zhang et al., 2022[19]							
Goetz et al., 2022[20]							
Hortobagyi et al., 2022[21]							
Xu et al., 2022[22]							
Finn et al., 2022[23]							
Cristofanilli et al., 2022[24]							
Xu et al., 2021[25]							
Slamon et al., 2021[26]							
Neven et al., 2021[27]							
Llombart-Cussac et al., 2021[28]							
André et al., 2021[29]							
Sledge et al., 2020[30]							
Finn et al., 2020[31]							
Rugo et al., 2019[32]							
André et al., 2019[33]							
Turner et al., 2018[34]							
Hortobagyi et al., 2018[35]							
Goetz et al., 2017[36]							
Turner et al.,2015[37]							

High Unclear Low

Progression-free survival for first-line treatments

The hazard ratio for PFS in first-line therapies was 0.59 (HR:0.59 95% CI -0.52, 1.69) (Fig. 2). Based on subgroup meta-analysis, Abemaciclib/Letrozole showed the best PFS benefit 0.51 (HR:0.51 95% CI -2.26, 3.28) because its hazard ratio was lower compared to other treatments, followed by Dalpiciclib/Letrozole (HR:0.51 95% CI -3.41, 4.43) and Palbociclib/Letrozole (HR:0.54 95% CI -1.85, 2.93), which showed a lower hazard ratio compared to other treatments (Fig. 2). The results of heterogeneity of the studies for first-line treatments show that the heterogeneity between the studies is low (I^2=0; p=1.00. Q=0.08).

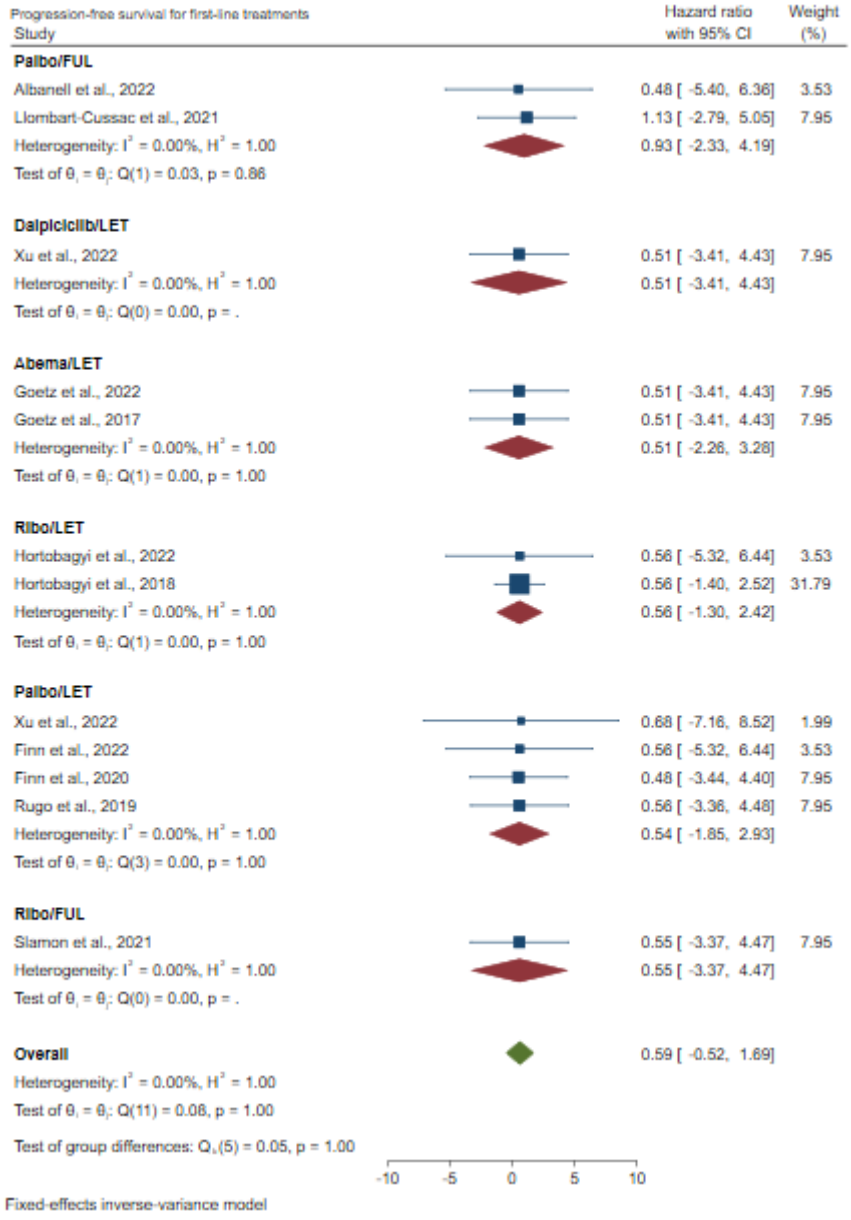

Fig. 2. Forest plots showed progression-free survival for first-line treatments.

Progression-free survival for second/further-line treatments

The hazard ratio for PFS in second/further-line therapies was 0.50 (HR:0.50 95% CI 0.30, 0.70) (Fig. 3). Based on subgroup meta-analysis, Dalpiciclib/Fulvestrant showed the best PFS benefit 0.43 (HR:0.43 95% CI 0.09, 0.77) because its hazard ratio was lower compared to other treatments, followed by Abemaciclib/Fulvestrant (HR:0.47 95% CI 0.05, 0.89) showed a lower hazard ratio compared to other treatments (Fig. 3). The results of heterogeneity of the studies for second/further-line treatments show that the heterogeneity between the studies is low (I^2=0; p=0.99. Q=2.36).

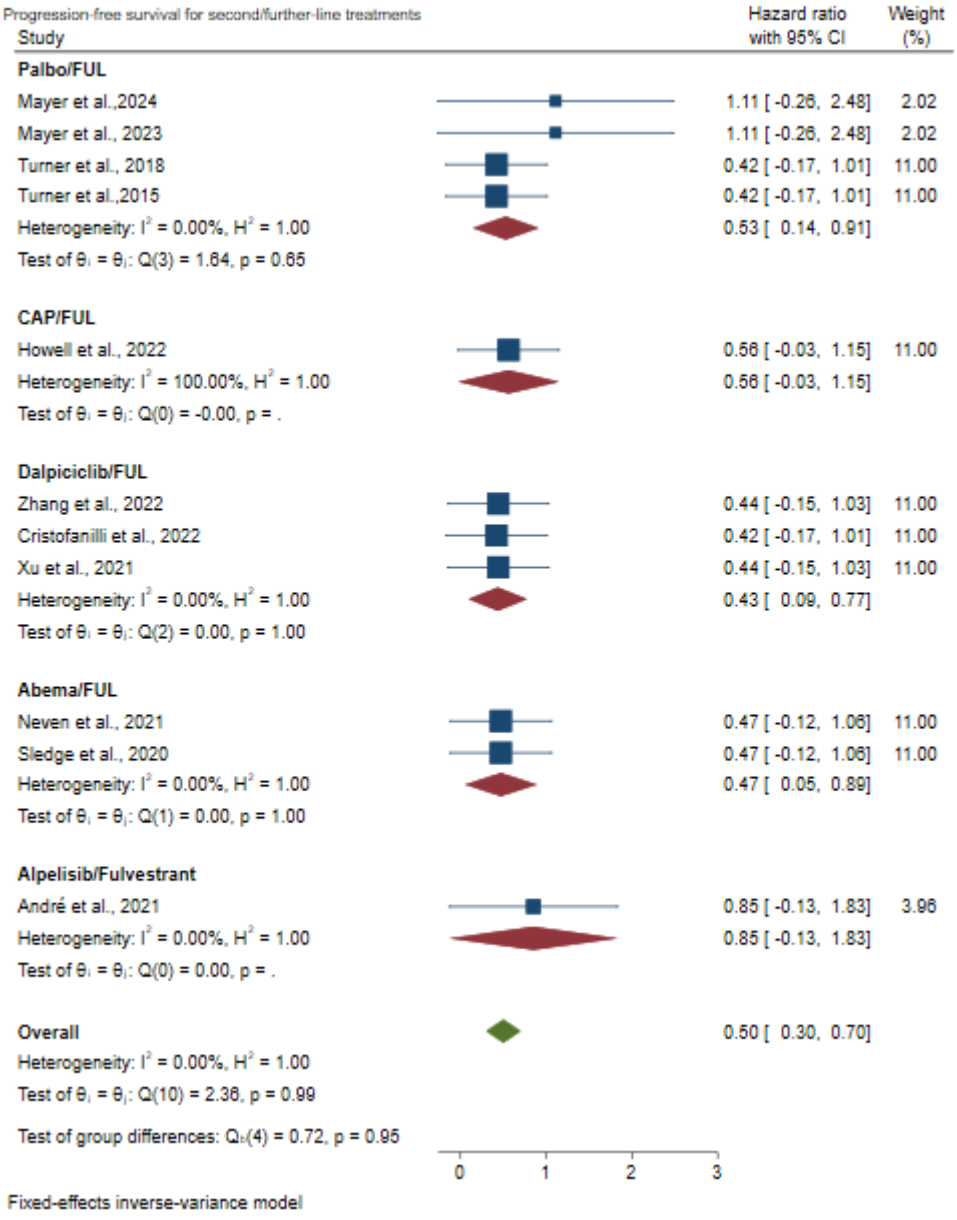

Fig. 3. Forest plots showed progression-free survival for second/further-line treatments.

Overall survival for first-line treatments

Hazard ratio of overall survival for first-line treatments was 0.81 (HR:0.81 95% CI 0.40, 1.21) (Fig. 4). Based on subgroup meta-analysis, Ribociclib/Fulvestrant improved overall survival 0.67 (HR:0.67 95% CI -0.31, 1.65) because its hazard ratio was lower compared to other treatments, followed by Abemaciclib/Fulvestrant (HR:0.75 95% CI -0.05, 1.55) and Ribociclib/Letrozole (HR:0.76 95% CI -0.11, 1.63), which showed a lower hazard ratio compared to other treatments (Fig. 4). The results of heterogeneity of the studies for first-line treatments show that the heterogeneity between the studies is low (I^2=0; p=1.00. Q=0.27).

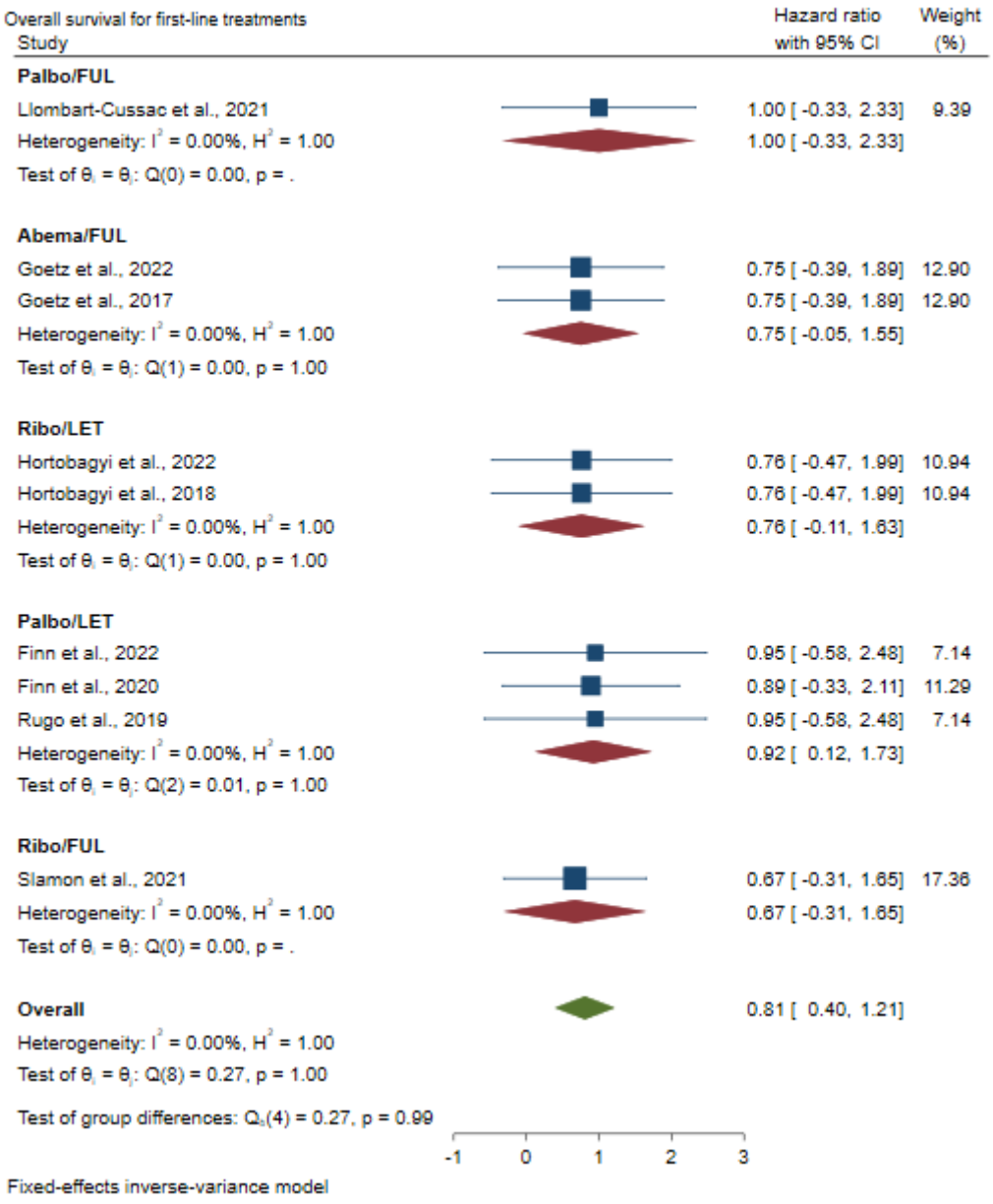

Fig. 4. Forest plot showed overall survival for first-line treatments.

Overall survival for second/further-line treatments

Hazard ratio of overall survival for second/further-line treatments was 0.76 (HR:0.76 95% CI 0.43, 1.09) (Fig. 5). Based on subgroup meta-analysis, Abemaciclib/Fulvestrant improved overall survival by 0.65 (HR:0.65 95% CI 0.10, 1.20) because its hazard ratio was lower compared to other treatments, suggesting superior performance by Abemaciclib/Fulvestrant (Fig. 5). The results of heterogeneity of the studies for first-line treatments show that the heterogeneity between the studies is low (I^2=0; p=1.00. Q=0.63).

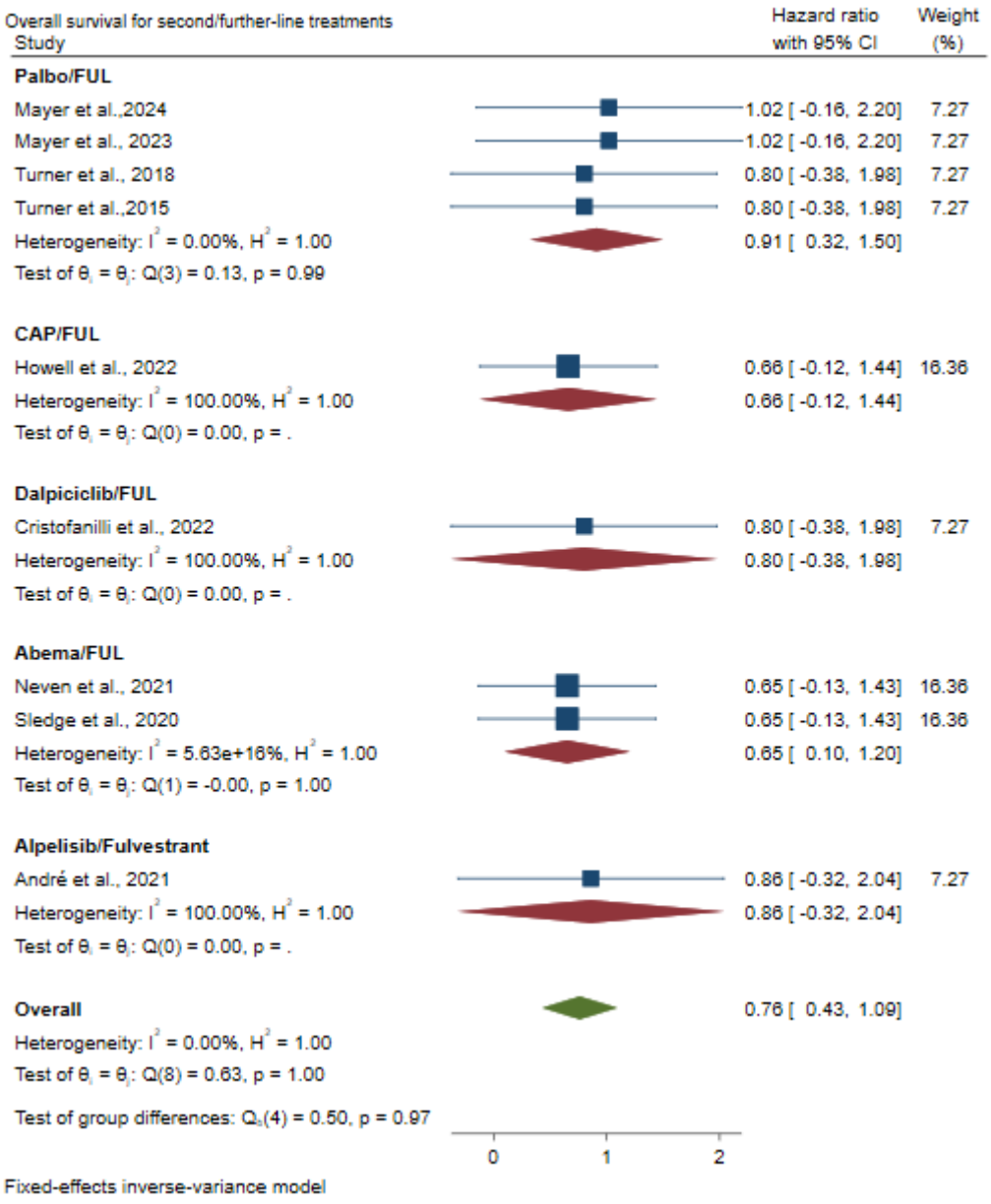

Figure 5. Forest plots showed overall survival for second/further-line treatments.

4. Discussion

In the present study, progression-free survival and overall survival of combinations of endocrine therapy with targeted therapy in women with HR + /HER2 − postmenopausal advanced breast cancer were investigated. Based on the present meta-analysis, Abemaciclib/Letrozole showed good PFS compared to other drugs in first-line therapies. In PFS in second/further-line therapies, Dalpiciclib/Fulvestrant showed good results in treatment. Also, the present meta-analysis showed that Ribociclib/Fulvestrant and Abemaciclib/Fulvestrant improved overall survival for first-line and second/further-line treatments, respectively. Previous studies have evaluated the safety and efficacy of advanced treatment regimens for HR+/HER2- breast cancer. Previous studies have shown that adding CDK4/6i to endocrine therapy has a positive effect on the patient's prognosis and is effective in its improvement.[38-40] Sacituzumab govitecan-hziy is FDA-approved for the treatment of HR + /HER2 − advanced breast cancer patients who have received at least two chemotherapy regimens and endocrine-based therapies.[41] Targeted therapies should be considered suitable for future breast cancer treatment strategies.[42] The present study had some limitations that it is hoped will be addressed in future studies; firstly, all the selected studies were clinical trials that had very little heterogeneity. However, the biases of different bases cannot be ignored; secondly, the therapeutic effects in different studies should be considered in future studies. Third, the sample size of the studies was not very high, and it was reported that menopausal patients need to be investigated in larger RCTs. Moreover, treatment regimens after progress in the first line can cause certain biases.

5. Conclusion

Based on the findings of the present study, superior efficiency can be seen in first-line treatment with combinations of endocrine therapy with targeted therapy. Also, this combination was observed in second/further-line treatments. It is suggested that the toxicity of drugs and their side effects should be investigated in future studies. More studies are needed to determine the most effective treatment strategies in HR+/HER2- advanced breast cancer so that promising results can occur in the treatment with day-by-day progress. Further studies are needed to confirm the evidence of the present study on new treatments.

Conflict of Interest

The authors declared that there is no conflict of interest.

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References

[1] Coughlin SS. Epidemiology of breast cancer in women. Breast Cancer Metastasis and Drug Resistance: Challenges and Progress. 2019:9-29. https://doi.org/10.1007/978-3-030-20301-6_2.

[2] Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast. 2022;66:15-23. https://doi.org/10.1016/j.breast.2022.08.010.

[3] Cuthrell KM, Tzenios N. Breast Cancer: Updated and Deep Insights. International Research Journal of Oncology. 2023;6(1):104-18.

[4] Dickson RB, Lippman ME. Growth factors in breast cancer. Endocrine reviews. 1995;16(5):559-89. https://doi.org/10.1210/edrv-16-5-559.

[5] Giaquinto AN, Sung H, Miller KD, Kramer JL, Newman LA, Minihan A, et al. Breast cancer statistics, 2022. CA: a cancer journal for clinicians. 2022;72(6):524-41. https://doi.org/10.3322/caac.21754.

[6] Mouabbi JA, Raghavendra AS, Bassett RL, Hassan A, Tripathy D, Layman RM. Survival Outcomes in Patients With Hormone Receptor–Positive Metastatic Breast Cancer With Low or No ERBB2 Expression Treated With Targeted Therapies Plus Endocrine Therapy. JAMA Network Open. 2023;6(5):e2313017. https://doi.org/10.1001/jamanetworkopen.2023.13017.

[7] Mouabbi JA, Osborne CK, Schiff R, Rimawi MF. Management of hormone receptor–positive, human epidermal growth factor 2–negative metastatic breast cancer. Breast Cancer Research and Treatment. 2021:189-201. https://doi.org/10.1007/s10549-021-06383-5.

[8] Bian L, Xu FR, Jiang ZF. Endocrine therapy combined with targeted therapy in hormone receptor-positive metastatic breast cancer. Chinese medical journal. 2020;133(19):2338-45.

[9] Cao LQ, Sun H, Xie Y, Patel H, Bo L, Lin H, et al. Therapeutic evolution in HR+/HER2-breast cancer: from targeted therapy to endocrine therapy. Frontiers in Pharmacology. 2024;15:1340764. https://doi.org/10.3389/fphar.2024.1340764.

[10] Montagna E, Colleoni M. Hormonal treatment combined with targeted therapies in endocrine-responsive and HER2-positive metastatic breast cancer. Therapeutic Advances in Medical Oncology. 2019;11:1758835919894105. https://doi.org/10.1177/1758835919894105.

[11] Rossi V, Berchialla P, Giannarelli D, Nisticò C, Ferretti G, Gasparro S, et al. Should all patients with HR-positive HER2-negative metastatic breast cancer receive CDK 4/6 inhibitor as first-line based therapy? A network meta-analysis of data from the PALOMA 2, MONALEESA 2, MONALEESA 7, MONARCH 3, FALCON, SWOG and FACT trials. Cancers. 2019;11(11):1661. https://doi.org/10.3390/cancers11111661.

[12] Ji D, Luo Y, Wang J, Chen S, Lan B, Ma F, et al. CDK4/6 inhibitors, PI3K/mTOR inhibitors, and HDAC inhibitors as second-line treatments for hormone receptor-positive, HER2-negative advanced breast cancer: a network meta-analysis. BMC cancer. 2023;23(1):805. https://doi.org/10.1186/s12885-023-11290-7.

[13] Giuliano M, Schettini F, Rognoni C, Milani M, Jerusalem G, Bachelot T, et al. Endocrine treatment versus chemotherapy in postmenopausal women with hormone receptor-positive, HER2-negative, metastatic breast cancer: a systematic review and network meta-analysis. The Lancet Oncology. 2019;20(10):1360-9. https://doi.org/10.1016/S1470-2045(19)30420-6.

[14] Minozzi S, Cinquini M, Gianola S, Gonzalez-Lorenzo M, Banzi R. The revised Cochrane risk of bias tool for randomized trials (RoB 2) showed low interrater reliability and challenges in its application. Journal of clinical epidemiology. 2020;126:37-44. https://doi.org/10.1016/j.jclinepi.2020.06.015.

[15] Mayer EL, Ren Y, Wagle N, Mahtani R, Ma C, DeMichele A, et al. PACE: A Randomized Phase II Study of Fulvestrant, Palbociclib, and Avelumab After Progression on Cyclin-Dependent Kinase 4/6 Inhibitor and Aromatase Inhibitor for Hormone Receptor–Positive/Human Epidermal Growth Factor Receptor–Negative Metastatic Breast Cancer. Journal of Clinical Oncology. 2024:JCO-23. https://doi.org/10.1200/JCO.23.01940.

[16] Mayer EL, Ren Y, Wagle N, Mahtani R, Ma C, DeMichele A, et al. Abstract Gs3-06: Gs3-06 Palbociclib after Cdk4/6I and endocrine therapy (PACE): A randomized phase II study of Fulvestrant, Palbociclib, and Avelumab for endocrine pre-treated ER+/Her2- metastatic breast cancer. Cancer Research. 2023;83(5_Supplement):GS3-06. https://doi.org/10.1158/1538-7445.SABCS22-GS3-06.

[17] Howell SJ, Casbard A, Carucci M, Ingarfield K, Butler R, Morgan S, et al. Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive, HER2-negative breast cancer (FAKTION): overall survival, updated progression-free survival, and expanded biomarker analysis from a randomised, phase 2 trial. The Lancet Oncology. 2022;23(7):851-64. https://doi.org/10.1016/S1470-2045(22)00284-4.

[18] Xu B, Zhang QY, Zhang P, Tong Z, Sun T, Li W, et al. LBA16 Dalpiciclib plus letrozole or anastrozole as first-line treatment for HR+/HER2-advanced breast cancer (DAWNA-2): A phase III trial. Annals of Oncology. 2022;33:S1384-5. https://doi.org/10.1016/j.annonc.2022.08.010.

[19] Zhang P, Zhang QY, Hu X, Li W, Tong Z, Sun T, et al. 229P Dalpiciclib plus fulvestrant in HR+/HER2− advanced breast cancer (ABC): Updated analysis from the phase III DAWNA-1 trial. Annals of Oncology. 2022;33:S642-3. https://doi.org/10.1016/j.annonc.2022.07.268.

[20] Goetz MP, Toi M, Huober J, Sohn J, Tredan O, Park IH, et al. LBA15 MONARCH 3: Interim overall survival (OS) results of abemaciclib plus a nonsteroidal aromatase inhibitor (NSAI) in patients (pts) with HR+, HER2-advanced breast cancer (ABC). Annals of oncology. 2022;33:S1384. https://doi.org/10.1016/j.annonc.2022.08.009.

[21] Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Hart L, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. New England Journal of Medicine. 2022;386(10):942-50. https://doi.org/10.1056/NEJMoa2114663.

[22] Xu B, Hu X, Li W, Sun T, Shen K, Wang S, et al. Palbociclib plus letrozole versus placebo plus letrozole in Asian postmenopausal women with oestrogen receptor–positive/human epidermal growth factor receptor 2–negative advanced breast cancer: Primary results from PALOMA-4. European Journal of Cancer. 2022;175:236-45. https://doi.org/10.1016/j.ejca.2022.08.012.

[23] Finn RS, Rugo HS, Dieras VC, Harbeck N, Im SA, Gelmon KA, et al. Overall survival (OS) with first-line palbociclib plus letrozole (PAL+ LET) versus placebo plus letrozole (PBO+ LET) in women with estrogen receptor–positive/human epidermal growth factor receptor 2–negative advanced breast cancer (ER+/HER2− ABC): Analyses from PALOMA-2. 2022;40(17). https://doi.org/10.1200/JCO.2022.40.17_suppl.LBA1003.

[24] Cristofanilli M, Rugo HS, Im SA, Slamon DJ, Harbeck N, Bondarenko I, et al. Overall survival with palbociclib and fulvestrant in women with HR+/HER2− ABC: updated exploratory analyses of PALOMA-3, a double-blind, phase III randomized study. Clinical Cancer Research. 2022;28(16):3433-42. https://doi.org/10.1158/1078-0432.CCR-22-0305.

[25] Xu B, Zhang Q, Zhang P, Hu X, Li W, Tong Z, et al. Dalpiciclib or placebo plus fulvestrant in hormone receptor-positive and HER2-negative advanced breast cancer: a randomized, phase 3 trial. Nature medicine. 2021;27(11):1904-9. https://doi.org/10.1038/s41591-021-01562-9.

[26] Slamon DJ, Neven P, Chia S, Jerusalem G, De Laurentiis M, Im S, et al. Ribociclib plus fulvestrant for postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer in the phase III randomized MONALEESA-3 trial: updated overall survival. Annals of oncology. 2021;32(8):1015-24. https://doi.org/10.1016/j.annonc.2021.05.353.

[27] Neven P, Johnston SR, Toi M, Sohn J, Inoue K, Pivot X, et al. MONARCH 2: subgroup analysis of patients receiving abemaciclib plus fulvestrant as first-line and second-line therapy for HR+, HER2−-advanced breast cancer. Clinical Cancer Research. 2021;27(21):5801-9. https://doi.org/10.1158/1078-0432.CCR-20-4685.

[28] Llombart-Cussac A, Pérez-García JM, Bellet M, Dalenc F, Gil-Gil M, Ruíz-Borrego M, et al. Fulvestrant-palbociclib vs letrozole-palbociclib as initial therapy for endocrine-sensitive, hormone receptor–positive, ERBB2-negative advanced breast cancer: a randomized clinical trial. JAMA oncology. 2021;7(12):1791-9. https://doi.org/10.1001/jamaoncol.2021.4301.

[29] André F, Ciruelos EM, Juric D, Loibl S, Campone M, Mayer IA, et al. Alpelisib plus fulvestrant for PIK3CA-mutated, hormone receptor-positive, human epidermal growth factor receptor-2–negative advanced breast cancer: Final overall survival results from SOLAR-1. Annals of Oncology. 2021;32(2):208-17. https://doi.org/10.1016/j.annonc.2020.11.011.

[30] Sledge GW, Toi M, Neven P, Sohn J, Inoue K, Pivot X, Burdaeva O, Okera M, Masuda N, Kaufman PA, Koh H. The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor–positive, ERBB2-negative breast cancer that progressed on endocrine therapy

[41] Arora S, Narayan P, Osgood CL, Wedam S, Prowell TM, Gao JJ, Shah M, Krol D, Wahby S, Royce M, Ghosh S. US FDA drug approvals for

MONARCH 2: a randomized clinical trial. JAMA oncology. 2020;6(1):116-24. https://doi.org/10.1001/jamaoncol.2019.4782.

[31] Finn RS, Boer K, Bondarenko I, Patel R, Pinter T, Schmidt M, Shparyk YV, Thummala A, Voitko N, Bananis E, McRoy L. Overall survival results from the randomized phase 2 study of palbociclib in combination with letrozole versus letrozole alone for first-line treatment of ER+/HER2− advanced breast cancer (PALOMA-1, TRIO-18). Breast cancer research and treatment. 2020;183:419-28. https://doi.org/10.1007/s10549-020-05755-7.

[32] Rugo HS, Finn RS, Diéras V, Ettl J, Lipatov O, Joy AA, Harbeck N, Castrellon A, Iyer S, Lu DR, Mori A. Palbociclib plus letrozole as first-line therapy in estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer with extended follow-up. Breast cancer research and treatment. 2019;174:719-29. https://doi.org/10.1007/s10549-018-05125-4.

[33] André F, Ciruelos E, Rubovszky G, Campone M, Loibl S, Rugo HS, Iwata H, Conte P, Mayer IA, Kaufman B, Yamashita T. Alpelisib for PIK3CA-mutated, hormone receptor–positive advanced breast cancer. New England Journal of Medicine. 2019;380(20):1929-40. https://doi.org/10.1056/NEJMoa1813904.

[34] Turner NC, Slamon DJ, Ro J, Bondarenko I, Im SA, Masuda N, Colleoni M, DeMichele A, Loi S, Verma S, Iwata H. Overall survival with palbociclib and fulvestrant in advanced breast cancer. New England journal of medicine. 2018;379(20):1926-36. https://doi.org/10.1056/NEJMoa1810527.

[35] Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Paluch-Shimon S, Campone M, Petrakova K, Blackwell KL, Winer EP, Janni W. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. Annals of Oncology. 2018;29(7):1541-7. https://doi.org/10.1093/annonc/mdy155.

[36] Goetz MP, Toi M, Campone M, Sohn J, Paluch-Shimon S, Huober J, Park IH, Trédan O, Chen SC, Manso L, Freedman OC. MONARCH 3: abemaciclib as initial therapy for advanced breast cancer. Journal of Clinical Oncology. 2017;35(32):3638-46. https://doi.org/10.1200/JCO.2017.75.6155.

[37] Turner NC, Ro J, André F, Loi S, Verma S, Iwata H, Harbeck N, Loibl S, Huang Bartlett C, Zhang K, Giorgetti C. Palbociclib in hormone-receptor–positive advanced breast cancer. New England Journal of Medicine. 2015;373(3):209-19. https://doi.org/10.1056/NEJMoa1505270.

[38] Tian F, Zhang S, Liu C, Han Z, Liu Y, Deng J, Li Y, Wu X, Cai L, Qin L, Chen Q. Protein analysis of extracellular vesicles to monitor and predict therapeutic response in metastatic breast cancer. Nature communications. 2021;12(1):2536. https://doi.org/10.1038/s41467-021-22913-7.

[39] Fan L, Wang ZH, Ma LX, Wu SY, Wu J, Yu KD, Sui XY, Xu Y, Liu XY, Chen L, Zhang WJ. Optimising first-line subtyping-based therapy in triple-negative breast cancer (FUTURE-SUPER): a multi-cohort, randomised, phase 2 trial. The Lancet Oncology. 2024;25(2):184-97. https://doi.org/10.1016/S1470-2045(23)00579-X.

[40] Han Y, Wang J, Xu B. Clinicopathological characteristics and prognosis of breast cancer with special histological types: a surveillance, epidemiology, and end results database analysis. The Breast. 2020;54:114-20. https://doi.org/10.1016/j.breast.2020.09.006.
breast cancer: A decade in review. Clinical Cancer Research. 2022;28(6):1072-86. https://doi.org/10.1158/1078-0432.CCR-21-2600.

[42] Yang F, Xiao Y, Ding JH, Jin X, Ma D, Li DQ, Shi JX, Huang W, Wang YP, Jiang YZ, Shao ZM. Ferroptosis heterogeneity in triple-negative breast cancer reveals an innovative immunotherapy combination strategy. Cell metabolism. 2023;35(1):84-100. https://doi.org/10.1016/j.cmet.2022.09.021.

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