

RESEARCH ARTICLE

Applying the EDAS Method for Prognostic Evaluation in Metastatic Breast Cancer

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ABSTRACT: Metastatic breast cancer, or stage IV breast cancer, occurs when breast cancer cells have spread beyond the breast and nearby lymph nodes to distant parts of the body, such as the bones, liver, lungs, or brain. This advanced stage can develop from any breast cancer type, including hormone receptor-positive, HER2-positive, or triple-negative. Symptoms vary based on where cancer has spread and may include bone pain, difficulty breathing, or neurological changes. Treatment for metastatic breast cancer typically involves a combination of systemic therapies like hormone therapy, targeted therapy, chemotherapy, and occasionally radiation therapy, all aimed at controlling disease progression and enhancing quality of life. Ongoing research is focused on finding more effective treatments and better understanding of the spread of the disease. Metastatic breast cancer, which involves cancer cells proliferating from the breast to other distant organs, is a major research focus due to its complex nature and significant impact on patient outcomes. Research in this area is vital for raising the rate of survival and raising the standard of living for patients. Key advancements include understanding the molecular mechanisms behind metastasis, identifying relevant biomarkers, and developing targeted therapies to create more effective treatment options. Additionally, research contributes to the development of early detection techniques, leading to earlier and more effective interventions. Studying resistance mechanisms to current treatments can also guide the creation of new therapeutic strategies. Overall, dedicated research into metastatic breast cancer is essential for improving treatment methods, personalizing patient care, and working towards a potential cure. By evaluating each option in relation to the average performance, the Evaluation Based on Distance from Average Solution (EDAS) method quantifies the deviations from this average, both positive and negative, providing a thorough assessment across multiple criteria. This balanced view of strengths and weaknesses aids decision-making, making it particularly useful in complex scenarios involving numerous factors, like choosing among different technological solutions. EDAS enhances objectivity, helping analysts, managers, and researchers make informed decisions aligned with desired outcomes and priorities. The results show that Combination therapy had the highest ranking from the results, while reduction in tumor size received the lowest ranking.

Keywords: Radiation Therapy, Combination Therapy, EDAS, Cancer.

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1. INTRODUCTION

Metastatic breast cancer, also known as stage IV breast cancer, represents the most advanced form of breast malignancy, characterized by the spread of cancer cells from the primary

tumor in the breast to distant organs and tissues throughout the body. This progression fundamentally alters the clinical picture, as cancer cells disseminate through the bloodstream or lymphatic system to establish secondary tumors in locations such as the bones, liver, lungs, and brain. Notably, the cancer cells in metastatic breast cancer maintain the molecular and genetic characteristics of the original breast tumor, meaning that when breast cancer spreads to the bones, it is breast cancer cells that are present, not bone cancer cells. This distinction is crucial for treatment decisions, as therapies must target the breast cancer biology rather than the organ of

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metastasis. The clinical significance of metastatic breast cancer cannot be overstated, as it accounts for the vast majority of breast cancer-related deaths, making it a paramount concern in oncology research and clinical practice [1].

Over the past quarter-century, substantial progress has been made in understanding and treating breast cancer, with numerous therapeutic advancements emerging that have transformed the management of this disease. The 1990s witnessed the introduction of taxanes and dose-dense anthracycline regimens, while aromatase inhibitors became available for metastatic breast cancer in 1997. The approval of fulvestrant in 2005 and trastuzumab in 2000, the first immunotherapy specifically targeting HER2-positive breast cancer, represented significant milestones in the evolution of breast cancer treatment. These developments have collectively contributed to improved outcomes, though the impact on metastatic disease has been more modest than for early-stage breast cancer. It was reported that survival rates for patients with metastatic breast cancer have improved over time, though the extent of this improvement varies across patient populations and disease subtypes [2].

The heterogeneity of metastatic breast cancer presents a substantial challenge to effective treatment. This heterogeneity manifests in multiple dimensions, including variations in disease patterns, severity, and the patient's overall health status. The first type of heterogeneity pertains to the differing patterns or severity of disease that influence initial treatment decisions. In this context, there is ongoing debate regarding the role of surgical intervention—whether removing either the primary tumor or metastatic sites can influence outcomes, particularly in cases with limited metastatic involvement. A retrospective analysis revealed that some patients who achieve "no evidence of disease" (NED) through a combination of systemic therapy, surgery, and radiation can maintain this status for prolonged periods, suggesting that treatment strategies should be customized according to disease extent, even in metastatic cases. The second type of heterogeneity concerns individual patient health status, encompassing age, performance status, comorbidities, and organ function. Research has demonstrated that Eastern Cooperative Oncology Group (ECOG) performance status serves as an independent predictive factor, while older age has been associated with poorer survival outcomes [3].

The treatment paradigm for metastatic breast cancer has evolved from a curative to a palliative focus, with the primary objectives being symptom management, disease progression control, and preservation of quality of life while extending overall survival. Historically, taxanes and anthracyclines represented the most effective therapeutic options for metastatic breast cancer. Although numerous randomized clinical trials have demonstrated improved response rates, only a few have shown definitive survival advantages. However, recent years have witnessed an increasing number of studies reporting modest but significant survival improvements, particularly with taxanes used in combination with antimetabolites. The development of biologic medicines

with specific molecular targets, such as bevacizumab and trastuzumab, has demonstrated promise in enhancing chemotherapy efficiency and generating significant survival gains [4].

Breast cancer remains the most frequent malignancy in women worldwide, excluding skin cancers, with over 232,670 new cases reported in 2014 alone. It also ranks as the second leading cause of cancer-related mortality among women, with approximately 40,000 deaths in the United States attributed to the disease that year. While breast cancer can often be successfully treated when confined to the breast and regional lymph nodes, once the disease has metastasized to distant organs, it is generally considered incurable. Several molecular subtypes of breast cancer exist, typically classified according to receptor status, including hormone receptors such as estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). These receptors play a critical role in determining prognosis and predicting responses to targeted therapy. When metastasis is suspected, biopsy is essential not only to confirm disease recurrence but also to determine receptor status, as this information is vital for selecting appropriate targeted therapies and facilitating patient participation in clinical trials [5].

The management of taxane therapy in metastatic breast cancer has advanced considerably, particularly with the introduction of albumin-bound paclitaxel formulations that enhance drug delivery to tumors. Since the introduction of Cremophor EL-paclitaxel in the mid-1990s, research has progressed in areas including drug formulations, dosing regimens, scheduling, and overcoming taxane resistance, providing physicians with more flexible treatment options. However, the increasing use of taxanes in neoadjuvant and adjuvant settings has led to a declining number of taxane-naïve patients, which affects their response to taxane retreatment for metastatic disease. Despite these challenges, taxane-based treatments remain essential components of metastatic breast cancer management [6].

Pain management represents another critical aspect of metastatic breast cancer care, as many patients experience significant pain that adversely affects quality of life. Pain can be conceptualized as a combination of physical incapacity and psychological distress, influenced by factors including the personal significance of the pain, expectations regarding illness, emotional state, family support, and treatment effectiveness. The diagnosis of cancer brings distressing consequences such as physical decline, pain, and the prospect of death, all of which contribute to the overall suffering experienced by patients [7].

The metastatic process itself remains incompletely understood, presenting a major challenge in developing effective therapeutic interventions. While there are similarities in the metastatic process across various cancers, notable differences exist in the likelihood, extent, and specific sites of metastasis, as well as the mechanisms and timing involved. Breast cancer presents unique characteristics compared to other cancers, and progress in preclinical models, coupled with the discovery of important

signaling pathways and genetic regulators specific to breast cancer metastases, is advancing the development of new targeted therapies aimed at combating metastasis [8].

Drug resistance continues to be a significant challenge in treating metastatic breast cancer, contributing to patient mortality. Targeting specific molecular defects in breast cancer cells offers potential for improved outcomes. For instance, trastuzumab and lapatinib have demonstrated effectiveness against HER2-overexpressing breast cancer, while the combination of everolimus and endocrine therapy has benefited hormone receptor-positive metastatic breast cancer. However, significant genetic and epigenetic changes have been identified in breast cancer, revealing complex patterns of genetic variation within tumors known as intratumoral heterogeneity. This heterogeneity, driven by a branched rather than linear model of tumor evolution, can lead to resistance to targeted therapies as pre-existing cancer cell subpopulations with genetic flaws may persist and repopulate the tumor despite treatment [9].

Chemotherapy continues to play a critical role in treating metastatic breast cancer, with anthracyclines and taxanes being among the most effective agents for advanced disease. Typically, 5-fluorouracil and cyclophosphamide are used in combination with anthracyclines, although taxanes have demonstrated comparable efficacy when used alone. Other options for patients who do not respond to conventional medicines include capecitabine, vinorelbine, and gemcitabine. High-dose chemotherapy remains experimental, while novel cytotoxic strategies continue to be explored [10]. Recent advances in understanding breast cancer biology are paving the way for innovative treatments targeting oncogenes and tumor-suppressor genes, with trastuzumab demonstrating increased survival rates in patients with metastatic breast cancer [11].

Despite advances, conventional treatments frequently fail to cure breast cancer when the disease spreads to distant organs [12]. Cytotoxic and hormonal agents offer significant relief for individuals with advanced breast cancer, with objective response rates ranging from 20% to 80%. However, complete responses remain rare, with fewer than 20% of patients maintaining complete response for more than five years [13]. Bone metastases affect 30% to 85% of patients throughout their illness and represent the first site of metastasis in 26% to 50% of cases, with complications including bone pain, pathological fractures, and spinal cord compression [14].

The global burden of metastatic breast cancer is substantial, with approximately 500,000 individuals succumbing to the disease annually. Despite slight improvements over the past decade, patients often lack adequate information about their condition, and preserving quality of life remains challenging [15]. Approximately 12% of women worldwide suffer from breast cancer, accounting for 14% of cancer-related fatalities, with up to 5% of patients presenting with incurable metastases at diagnosis [16]. MicroRNAs have emerged as potential biomarkers for metastatic breast cancer, offering possibilities for early detection and disease monitoring [17].

In this paper, the Evaluation Based on Distance from Average Solution (EDAS) method is applied to conduct a prognostic evaluation of various treatment modalities for metastatic breast cancer. The EDAS approach provides a comprehensive multi-criteria decision-making framework that quantifies deviations from average performance across multiple evaluation criteria. By assessing both positive and negative deviations, this method offers a balanced view of treatment strengths and weaknesses, facilitating objective decision-making in complex clinical scenarios. The analysis encompasses eight treatment alternatives, including chemotherapy, hormone therapy, targeted therapy, immunotherapy, bone-directed therapy, radiation therapy, combination therapy, and clinical trials. These are evaluated against five criteria: progression-free survival, quality of life improvement, reduction in tumor size, side effects, and patient compliance. The findings aim to inform clinical decision-making and guide treatment selection for metastatic breast cancer patients.

2. MATERIAL AND METHODS

2.1. Alternative

2.1.1. Chemotherapy

Chemotherapy is a cornerstone for treating a variety of malignancies, such as breast cancer that has spread. It includes applying medication to eradicate cancer cells or stopping their proliferation, targeting cells that are rapidly dividing. Chemotherapy can be administered orally or intravenously and works by interfering with the cell cycle, thereby stopping the proliferation of cancer cells. While effective, chemotherapy also affects rapidly dividing healthy cells, such as those in the bone marrow and digestive tract, leading to side effects like nausea, hair loss, and fatigue. The choice of chemotherapy regimen depends on the features of the disease and the general state of health of the patient.

2.1.2. Hormone Therapy

Breast cancer that is hormone receptor-positive, is treated with hormone treatment, commonly referred to as endocrine therapy. Hormones such as progesterone and estrogen stimulate the growth of this particular type of cancer. The mechanism of hormone treatment is to either prevent or reduce the effects of the body's endogenous hormones on cancer cells. Aromatase inhibitors like anastrozole, selective estrogen receptor degraders (SERDs) like fulvestrant, and selective estrogen receptor modulators (SERMs) like tamoxifen are examples of common hormone therapy. For postmenopausal women, aromatase inhibitors are often used, while premenopausal women may receive treatments that suppress ovarian function. Hormone therapy can be effective in reducing the risk of cancer recurrence and extending survival.

2.1.3. Targeted Therapy

Drugs that target cancer cells specifically are used in targeted therapy, based on their genetic, molecular, or cellular characteristics. Unlike chemotherapy, which affects all rapidly dividing cells, targeted therapies aim to disrupt specific pathways or molecules involved in cancer growth and survival. Examples include HER2-targeted therapies, such as Herceptin (trastuzumab) and Perjeta (pertuzumab), which are used for HER2-positive breast cancer. These therapies can inhibit the HER2 receptor, a protein that promotes cancer cell growth. Targeted therapies can be more precise, reducing compared to conventional chemotherapy, it frequently causes less side effects and does less damage to healthy cells.

2.1.4. Immunotherapy

Using immunotherapy, cancer is combated by the body's immune system. It uses a variety of strategies, like checkpoint inhibitors, which prevent cancer cells from using certain proteins to elude immune recognition. In metastatic breast cancer, immunotherapy is less commonly used compared to other cancers but is an area of active research. Drugs like pembrolizumab (Keytruda) and atezolizumab (Tecentriq) target immune checkpoints and have demonstrated potential in some cases of breast cancer. Furthermore, new approaches that try to strengthen the immune system's capacity to identify and eliminate cancer cells include cancer vaccines and adoptive cell therapy.

2.1.5. Bone-directed Therapy

Bone-directed therapy is particularly important for patients Having breast cancer that has metastasized and reached the bones. These therapies aim to strengthen bones, reduce pain, and prevent fractures. Bisphosphonates, such as zoledronic acid, and RANK ligand inhibitors, like denosumab, are commonly used. These medications help manage bone complications by reducing bone resorption and inhibiting bone loss, which can be a significant issue in metastatic disease.

2.1.6. Radiation Therapy

High-energy radiation is used in radiation therapy to eradicate cancer cells and reduce tumor size. It is often employed to target specific areas where cancer has metastasized, such as the bones, brain, or lungs. Radiation can help relieve symptoms like pain or bleeding and is typically used in combination with other therapies. Techniques like external beam radiation deliver focused radiation to the tumor, while internal radiation (brachytherapy) places radioactive material close to or inside the tumor.

2.1.7. Combination Therapy

Combination therapy refers to using multiple treatment modalities together to increase effectiveness. For instance, combining chemotherapy with targeted therapy or hormone therapy can be more effective than using any single treatment alone. This approach aims to address cancer from multiple angles, improve outcomes, and manage resistance. The specific combinations depend on the cancer's characteristics, the patient's condition, and treatment goals.

2.1.8. Clinical Trials

Research investigations called clinical trials are intended to test novel medicines or combinations of treatments, or approaches to cancer care. They are essential for advancing medical knowledge and improving patient outcomes. Trials can involve testing new drugs, exploring different treatment combinations, or evaluating novel strategies like personalized medicine or new technologies. Enrolling in clinical trials can provide access to state-of-the-art medications and aid in the creation of new ones. Patients considering clinical trials should discuss potential risks and benefits with their healthcare team.

2.2. Evaluation preference

2.2.1. Progression-Free Survival (PFS)

Progression-Free Survival is a critical metric used to evaluate the effectiveness of cancer treatments. It refers to the amount of time a patient can live with their illness during and after therapy without it getting worse. PFS provides an indication of how well a treatment is controlling the disease and can be a predictor of overall survival. A longer PFS generally indicates that the treatment is effective in delaying disease progression and is often used in clinical trials to measure the efficacy of new therapies. Improving PFS can be a significant goal in metastatic breast cancer, where controlling disease progression is crucial for extending survival and maintaining a patient's quality of life.

2.2.2. Quality of Life Improvement

Quality of Life (QoL) improvement is a fundamental consideration in cancer treatment evaluation. It encompasses various elements of a patient's welfare, such as their medical condition, mental state, social relationships, and daily functioning. Treatments for metastatic breast cancer often have the goal of not just prolonging life but also enhancing the life quality of the patient. The quality of life can be greatly enhanced by effective management of symptoms like pain, exhaustion, and cognitive impairment. Tools such as patient-reported outcome measures and quality of life questionnaires are used to assess these improvements. Therapies that offer

significant benefits in terms of QoL are highly valued, as they can lead to better overall patient satisfaction and adherence to treatment.

2.2.3. Reduction in Tumor Size

Reduction in tumor size is a direct measure of how well a treatment works in controlling cancer. It is often assessed through imaging investigations including PET, MRI, and CT scans. A decrease in tumor size can indicate that the treatment is effectively targeting and killing cancer cells. While tumor shrinkage is an important indicator of treatment efficacy, it is often considered alongside other factors such as PFS and QoL. In some cases, treatments that result in stable disease (where tumors do not grow) may also be considered effective, particularly if they lead to improvements in symptoms and overall well-being.

2.2.4. Side Effects

Side effects are a crucial factor in evaluating the overall success of a treatment regimen. Effective therapies should ideally offer benefits without causing undue harm. Side effects might vary from minor problems like weariness or nausea to more serious consequences like organ damage or significant changes in blood counts. Evaluating side effects involves assessing their frequency, severity, and impact on a patient's daily life. Treatments that have manageable side effects and allow patients to maintain a good quality of life are preferred. Balancing efficacy with tolerability is essential for long-term treatment success and patient satisfaction.

2.2.5. Patient Compliance

Patient compliance refers to how well patients adhere to their prescribed treatment regimens. High levels of compliance are often crucial for achieving the best possible outcomes. Factors influencing compliance include the complexity of the treatment regimen, side effects, and the patient's understanding of the treatment's benefits. Effective communication between healthcare providers and patients, along with support systems such as patient education and adherence aids, can enhance compliance. Treatments that are easier to adhere to, whether due to fewer side effects or simpler administration schedules, are generally preferred.

2.3. Evaluation Based on Distance from Average Solution (EDAS)

Utilizing the average settlement evaluation based on distance, the Evaluation Based on Distance from Average Solution (EDAS) method creates an efficient Multi-Criteria Decision-Making (MCDM) framework. This method calculates the average of alternative options by assessing their distances

from a solution. EDAS offers a multi-criteria framework that fills gaps in existing literature by overcoming the limitations of current methodologies. Initially applied to address sorting issues in bank branches, EDAS was adapted for interval data following the transformative "cashovers" concept proposed by Gorabai et al. (2015). Ren et al. Toniolo (2018) further enhanced EDAS by introducing an interval version, effectively addressing its previous shortcomings. This section presents a new technique for problem-solving within the EDAS framework, detailing both the classical EDAS method and the novel interval data approach, thereby addressing a newly identified gap [18].

A major research goal focuses on the formation of speleothems and the importance of the various factors that influence this process, as well as investigating the dynamics of seepage in karst landscapes. The EDAS device was created to meet the needs of physicists within the European Geo and Earth science community for monitoring environmental parameters, and it was developed in a physics laboratory [19].

The Average Settlement Rating (EDAS) is a newly developed decision-making technique that assesses various criteria through distance measurements. Like the EDAS approach, it also relies on measurements, but the EDAS methodology, with its focus on both positive and negative aspects, surpasses methods that depend solely on average solutions. By taking into account the distances to the optimal solution and streamlining calculations, EDAS provides faster results [20].

The term "encephalo-dura-arterio-synangiosis" (EDAS) refers to an indirect surgical technique that replaces the scalp artery with vessels on the surface of the brain. Though it is relatively simple and comes with some potential complications, EDAS has proven advantages and does not disrupt blood flow. Recently, it has become a standard procedure for treating children with moyamoya syndrome (MMS), showing positive results. The procedure is also beneficial for adult patients with MMS. Long-term outcomes of EDAS, as shown by Park et al., are better compared to direct blood flow reconstruction. However, some studies suggest that additional surgeries may be necessary after EDAS due to insufficient collateral vessel formation [21].

The EDAS method utilizes limits based on both positive and negative distances, accommodating different risk preferences of decision-makers. As a result, a new four-branch EDAS model is introduced for fuzzy context Multi-Criteria Decision Making (MCDM). This model evaluates interval packages inside a fixed weight vector, utilizing programming to determine single-objective linear control, and integrates deviation stability analysis with the entropy weighting technique [22].

The EDAS method, developed by Keshavers Korapai and colleagues, originally emerged from the concept of estimating average settlements based on distance. This method has proven to be a multi-criteria decision-making (MCDM) technique that is incredibly successful. It was first created for inventory classification, but it has since been modified to handle a variety of problems, such as various engineering problems [23].

Originally presented by Ghorabae et al., the EDAS (Evaluation based on Distance from Average Solution) approach uses distance-based evaluations in Multi-Criteria Decision-Making (MCDM) to answer inherent imperfections. Peng and Chong adapted EDAS to handle neutrosophic-based soft decision-making. Kalina et al. enhanced the EDAS system by incorporating L1 measurements for multi-criteria decision-making. Liang et al. combined EDAS with the ELECTRE method to evaluate gold mine elimination and choice productivity. Li et al. proposed an integrated EDAS approach under linguistic neutrosophic conditions, focusing on group decision-making problems through distance evaluation and power aggregation operators [24].

The EDAS method evaluates how beneficial each option is by measuring its distance from the average solution while also considering the distance from less favorable outcomes. It is especially valuable for handling conflicting criteria. According to the authors, the EDAS method is reliable when used with other methods and integrates well with them. Furthermore, its straightforward approach and computational efficiency do not affect its accuracy, as these computational benefits do not compromise precision [25].

The Efficient Data for IoT Integration Program (EDAS) uses a bilinear coupling-like framework that simplifies complex mathematical operations through elliptic curve cryptography. This method supports flexible updates to identification and location privileges in IoT devices, enabling the issuance of pseudo-identities and private keys. It also tackles issues related to compromises and privilege escalation by coordinating with a central authority to prevent data breaches. Additionally, EDAS incorporates a 0/1-code technique to handle partial secret keys and dummy nodes, and it includes token expiration dates to enhance security [26]. The decision matrix X , which displays how various options perform with certain criteria, is created.

$$D = \begin{bmatrix} x_{11} & x_{12} & \cdots & x_{1n} \\ x_{21} & x_{22} & \cdots & x_{2n} \\ x_{31} & x_{32} & \cdots & x_{3n} \end{bmatrix} \quad (1)$$

Weights for the criteria are expressed in equation 2.

$$w_j = [w_1 \quad \cdots \quad w_n], \text{ where } \sum_{j=1}^n (w_1 \quad \cdots \quad w_n) = 1 \quad (2)$$

Next criteria vice average solutions are calculated

$$AV_j = \frac{\sum_{i=1}^n k_{ij}}{n} \quad (3)$$

PDA is expressed in equation 4 as:

$$PDA_{ij} = \begin{cases} \frac{\max(0, (x_{ij} - AV_{ij}))}{AV_{ij}} & | j \in B \\ \frac{\max(0, (AV_{ij} - x_{ij}))}{AV_{ij}} & | j \in C \end{cases} \quad (4)$$

The NDA is expressed in equation 5

$$NDA_{ij} = \begin{cases} \frac{\max(0, (AV_{ij} - x_{ij}))}{AV_{ij}} & | j \in B \\ \frac{\max(0, (x_{ij} - AV_{ij}))}{AV_{ij}} & | j \in C \end{cases} \quad (5)$$

Using equation 2, multiplied by factors 4 and 5, respectively, the weighted sum of the positive and negative distances from the average solution for all options is normalised. Weighted sums of the positive and the negative distance are calculated by the equation.

$$SP_i = \sum_{j=1}^n w_j \times PDA_{ij} \quad (6)$$

$$SN_i = \sum_{j=1}^n w_j \times NDA_{ij} \quad (7)$$

Equations 8 and 9 are used to normalize the weighted sum of the positive and negative distances from the average solution for all alternatives.

$$NSP_i = \frac{SP_i}{\max_i(SP_i)} \quad (8)$$

$$NSN_i = 1 - \frac{SN_i}{\max_i(SN_i)} \quad (9)$$

The final appraisal score (AS_i) for each alternative is calculated as the normalised weighted average of the positive and negative distances from the average solution for all alternatives.

$$AS_i = \frac{(NSP_i + NSN_i)}{2} \quad (10)$$

Where, $0 \leq AS_i \leq 1$.

3. RESULTS AND DISCUSSION

Table 1 presents various treatment modalities for metastatic breast cancer, highlighting their effectiveness across several criteria Progression-Free Survival (PFS): Targeted Therapy shows the highest PFS at 75%, indicating effective disease control, followed by Hormone Therapy at 70%. Quality of Life Improvement: Immunotherapy leads with 90%, reflecting significant enhancement in patient well-being, while Radiation Therapy shows the lowest at 40%. Reduction in Tumor Size: Combination Therapy achieves the highest reduction at 75%, suggesting strong efficacy in shrinking tumors. Side Effects: Immunotherapy has the fewest side effects (20%), whereas Radiation Therapy has the most (60%). Patient Compliance: Hormone Therapy and Bone-directed Therapy have high compliance rates (85% each), indicating better patient adherence.

Figure 1 compares different treatments for metastatic breast cancer across five metrics: Progression-Free Survival, Quality of Life Improvement, Reduction in Tumor Size, Side Effects, and Patient Compliance. Chemotherapy: High side effects (80) but moderate scores in other areas. Hormone

Therapy: Balanced across metrics with fewer side effects (40). Targeted Therapy: High in quality of life (70) and patient compliance (65). Immunotherapy: High quality of life (70) but higher side effects (45). Bone-Directed Therapy: Lowest patient compliance (20) but moderate scores in others. Radiation Therapy: Lower progression-free survival (40) but balanced otherwise. Combination Therapy: Highest side effects (72) but high in other metrics. Clinical Trial: Balanced but slightly lower in-patient compliance (50).

Table 2 shows the Positive Distance from Average (PDA) for different metastatic breast cancer treatments across various criteria. PDA measures how much each treatment exceeds the

average performance. Hormone Therapy stands out with the highest PDA for Quality-of-Life Improvement (0.153) and Patient Compliance (0.283), indicating it performs significantly better than average in these areas. Targeted Therapy excels in Progression-Free Survival (0.183) and Reduction in Tumor Size (0.155), showing strong efficacy. Radiation Therapy has the highest PDA for Side Effects (0.455), indicating the most significant negative impact. Combination Therapy shows notable PDAs in Reduction in Tumor Size (0.237) and Side Effects (0.333). PDA helps identify treatments with the most positive deviations from average performance.

Table 1. Performance metrics of various treatment modalities for metastatic breast cancer across five evaluation criteria.

	Progression-Free Survival	Quality of Life Improvement	Reduction in Tumor Size	Side Effects	Patient Compliance
Chemotherapy	60	50	65	30	80
Hormone Therapy	70	80	60	50	85
Targeted Therapy	75	85	70	45	65
Immunotherapy	70	90	65	20	40
Bone-directed Therapy	55	55	50	25	85
Radiation Therapy	40	40	45	60	60
Combination Therapy	72	85	75	55	65
Clinical Trial	65	70	55	45	50
AVj	63	69	61	41	66

Metastatic Breast Cancer

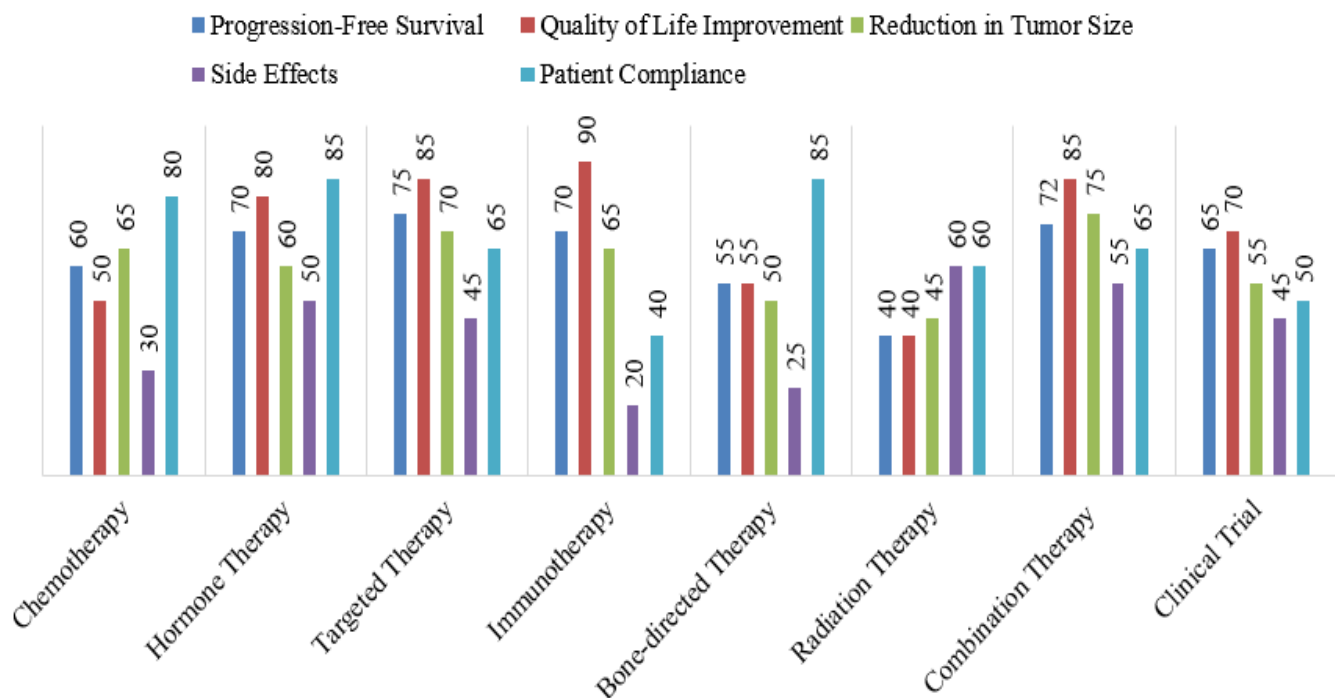


Fig. 1. Comparative bar chart illustrating the performance of different metastatic breast cancer treatments across five evaluation metrics: Progression-Free Survival, Quality of Life Improvement, Reduction in Tumor Size, Side Effects, and Patient Compliance.

Table 2. Positive Distance from Average (PDA) values for each treatment modality across all evaluation criteria.

	Positive Distance from Average (PDA)				
	Progression-Free Survival	Quality of Life Improvement	Reduction in Tumor Size	Side Effects	Patient Compliance
Chemotherapy	0.000	0.000	0.072	0.000	0.208
Hormone Therapy	0.105	0.153	0.000	0.212	0.283
Targeted Therapy	0.183	0.225	0.155	0.091	0.000
Immunotherapy	0.105	0.297	0.072	0.000	0.000
Bone-directed Therapy	0.000	0.000	0.000	0.000	0.283
Radiation Therapy	0.000	0.000	0.000	0.455	0.000
Combination Therapy	0.136	0.225	0.237	0.333	0.000
Clinical Trial	0.026	0.009	0.000	0.091	0.000

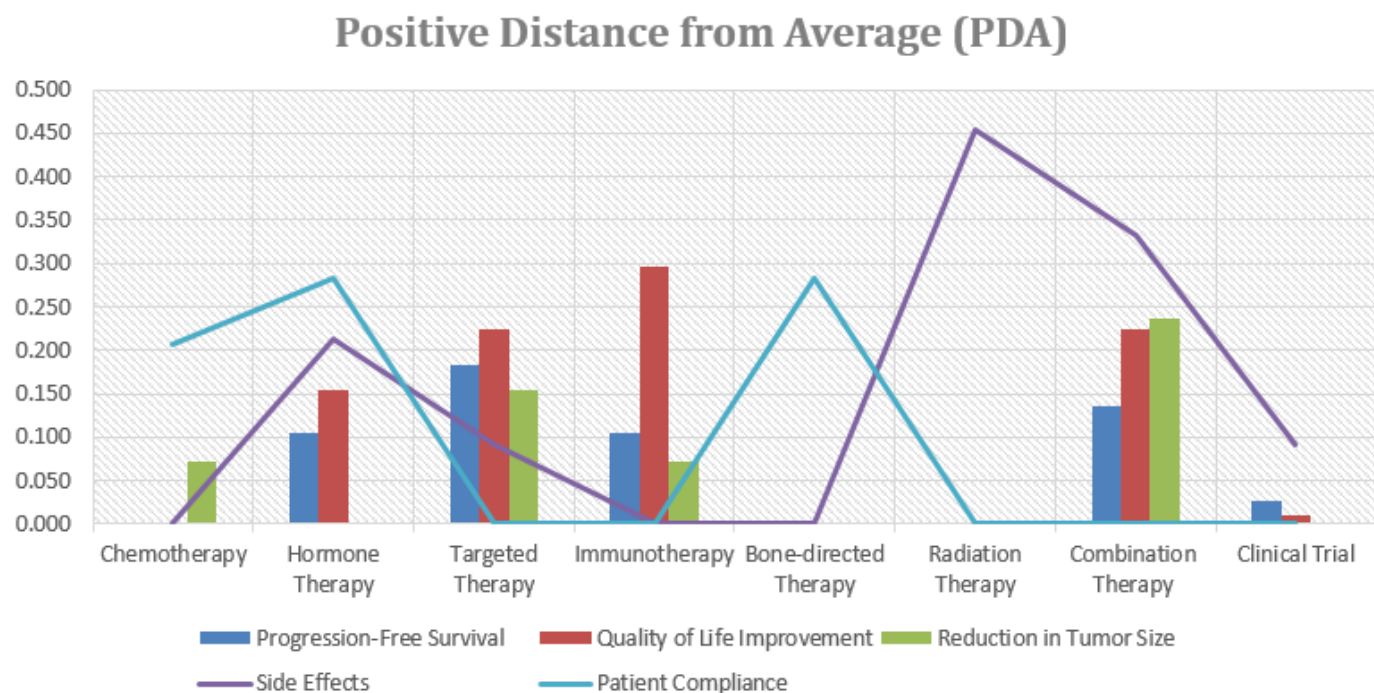
**Fig. 2.** Bar chart showing the Positive Distance from Average (PDA) for each treatment modality across five evaluation criteria, highlighting treatments that perform above the average.

Figure 2 positive Distance from Average (PDA) shows the Positive Distance from Average (PDA) for various metastatic breast cancer treatments across five metrics: Progression-Free Survival, Quality of Life Improvement, Reduction in Tumor Size, Side Effects, and Patient Compliance. Combination Therapy stands out with the highest PDA in Progression-Free Survival and overall high scores, except for Side Effects. Targeted Therapy and Immunotherapy show strong PDA in Quality-of-Life Improvement and Reduction in Tumor Size. Hormone Therapy and Radiation Therapy display balanced PDAs. Bone-Directed Therapy has lower PDAs across most metrics. Clinical Trials show a moderate

PDA for Side Effects but lower in other metrics.

Table 3 presents the Negative Distance from Average (NDA), indicating how much each treatment falls short of average performance. Radiation Therapy has the highest NDA for Progression-Free Survival (0.369) and Quality of Life Improvement (0.423), suggesting it performs significantly below average in these areas. Immunotherapy shows high NDA for Side Effects (0.515) and Patient Compliance (0.396), reflecting substantial negative impacts. Bone-directed Therapy has notable NDAs in Reduction in Tumor Size (0.175) and Side Effects (0.394). Hormone Therapy and Combination Therapy have minimal negative

deviations, indicating relatively consistent performance close to the average. NDA helps highlight areas where treatments are less effective compared to the average.

Figure 3 negative Distance from Average (NDA) shows the graph illustrates how different patient outcomes deviate from their average values over time. Positive NDA values indicate outcomes better than average, while negative values show outcomes worse than average. Progression-free survival generally improves initially but then declines. Quality of life shows early improvement before stabilizing. Tumor size reduction is initially effective but diminishes over time. Side effects increase initially but then decrease. Patient compliance fluctuates, with periods of better and worse adherence. Overall, the graph provides a visual representation of how various patient outcomes change relative to their expected averages throughout a treatment or observation period.

Table 4 shows a uniform weight distribution of 0.25 across all criteria. This equal weighting indicates that each

evaluation factor Progression-Free Survival, Quality of Life Improvement, Reduction in Tumor Size, Side Effects, and Patient Compliance is considered equally important in assessing the effectiveness of treatments for metastatic breast cancer. Table 5 displays the Weighted Positive Distance from Average (PDA) for different metastatic breast cancer treatments, factoring in the equal weights assigned to each evaluation criterion. Hormone Therapy shows strong performance with notable weighted PDAs in Quality-of-Life Improvement (0.03829) and Patient Compliance (0.07075). Targeted Therapy has significant PDAs in Progression-Free Survival (0.04586) and Reduction in Tumor Size (0.03866), reflecting its effectiveness. Radiation Therapy stands out with high weighted PDA for Side Effects (0.11364), indicating substantial negative impact. Combination Therapy demonstrates high weighted PDAs in Reduction in Tumor Size (0.05928) and Side Effects (0.08333). This table helps evaluate how each treatment performs across the criteria, considering their relative importance.

Table 3. Negative Distance from Average (NDA) values for each treatment modality across all evaluation criteria.

Negative Distance from Average (NDA)					
	Progression-Free Survival	Quality of Life Improvement	Reduction in Tumor Size	Side Effects	Patient Compliance
Chemotherapy	0.053		0.000	0.273	0.000
Hormone Therapy	0.000	0.000	0.010	0.000	0.000
Targeted Therapy	0.000	0.000	0.000	0.000	0.019
Immunotherapy	0.000	0.000	0.000	0.515	0.396
Bone-directed Therapy	0.132	0.207	0.175	0.394	0.000
Radiation Therapy	0.369	0.423	0.258	0.000	0.094
Combination Therapy	0.000	0.000	0.000	0.000	0.019
Clinical Trial	0.000	0.000	0.093	0.000	0.245

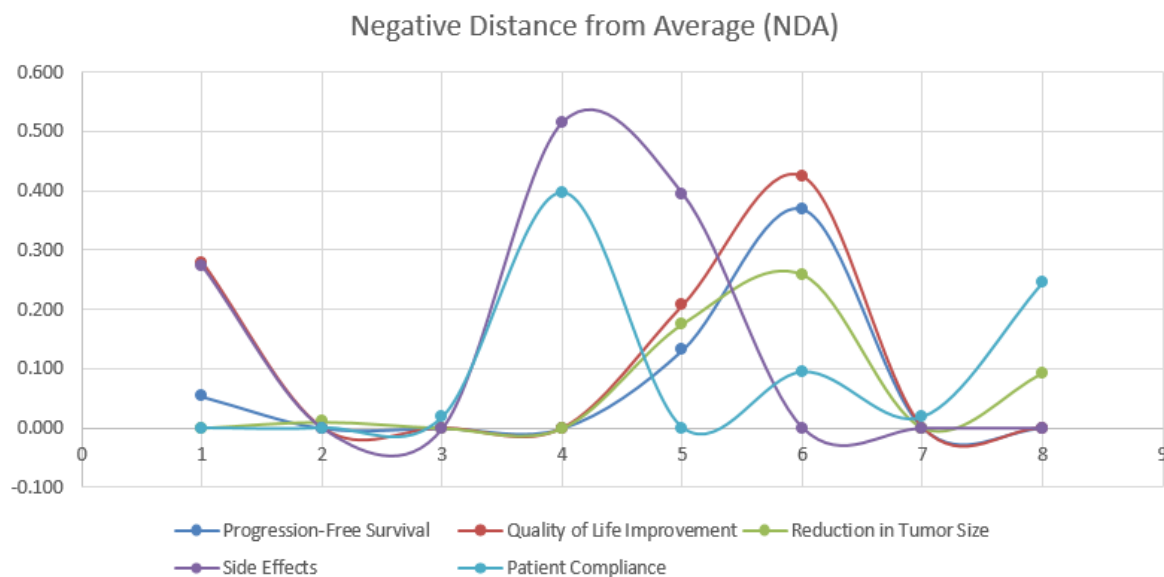


Fig. 3. Bar chart depicting the Negative Distance from Average (NDA) for each treatment modality across five evaluation criteria, indicating areas where treatments fall below the average performance.

Table 4. Uniform weight distribution (0.25) assigned to each evaluation criterion.

Weight					
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25
0.25	0.25	0.25	0.25	0.25	0.25

Table 5. Weighted Positive Distance from Average (SPi) values for each treatment modality across all evaluation criteria.

Weighted PDA				
Progression-Free Survival	Quality of Life Improvement	Reduction in Tumor Size	Side Effects	Patient Compliance
0.00000	0.00000	0.01804	0.00000	0.05189
0.02613	0.03829	0.00000	0.05303	0.07075
0.04586	0.05631	0.03866	0.02273	0.00000
0.02613	0.07432	0.01804	0.00000	0.00000
0.0000	0.00000	0.0000	0.00000	0.07075
0.00000	0.00000	0.00000	0.11364	0.00000
0.03402	0.05631	0.05928	0.08333	0.00000
0.00641	0.00225	0.00000	0.02273	0.00000

Table 6 presents the Weighted Negative Distance from Average (NDA) for various metastatic breast cancer treatments, incorporating the equal weight given to each evaluation criterion. Radiation Therapy has the highest weighted NDA for Progression-Free Survival (0.09221) and Quality of Life Improvement (0.10586), indicating significant performance shortfalls. Immunotherapy shows substantial weighted NDA for Side Effects (0.12879) and Patient Compliance (0.09906), reflecting considerable negative impacts. Bone-directed Therapy and Combination Therapy exhibit moderate weighted NDAs across several criteria, indicating some performance issues but not as severe. This table highlights areas where treatments fall short of average performance, guiding potential improvements.

Table 7 summarizes the effectiveness of various metastatic breast cancer treatments based on three metrics: Weighted Positive Distance from Average (Spi), Weighted Negative Distance from Average (Sni), and the Average Score (ASi), along with their overall Rank. Combination Therapy ranks highest (Rank 1) with the highest ASi of 0.99176, indicating superior performance across the criteria. It has the highest Spi (1.00000) and a high Sni (0.98351), suggesting it performs well above average while having

minimal shortcomings. Hormone Therapy and Targeted Therapy follow, with ranks 2 and 3, respectively. Hormone Therapy shows a high ASi (0.89948) due to its strong performance in Quality-of-Life Improvement and Patient Compliance. Targeted Therapy excels in Progression-Free Survival and Reduction in Tumor Size, reflected in its ASi (0.84281). Clinical Trial is ranked 4th, with a moderate ASi (0.41966), reflecting its balanced performance but less impressive compared to the top three therapies. Chemotherapy and Bone-directed Therapy rank 5th and 7th, showing intermediate ASi values, indicating moderate effectiveness but also some areas of concern. Radiation Therapy and Immunotherapy have the lowest ranks, 8 and 6 respectively, due to significant performance issues reflected in their lower ASi and high negative distances (Sni). This table provides a comprehensive overview of each treatment's relative effectiveness and overall suitability for managing metastatic breast cancer.

Figure 4 Spi and sni and asi Shows the Chemotherapy Spi 0.30020, Sni 0.47108, ASi 0.38564 and Hormone Therapy Spi 0.80796, Sni 0.99099, ASi 0.89948 and Targeted Therapy Spi 0.70211, Sni 0.98351, ASi 0.84281 and Immunotherapy Spi 0.50871, Sni 0.20357, Asi 0.35614

and Bone-directed Therapy Spi 0.30374, Sni 0.20604, ASi 0.25489 and Radiation Therapy Spi 0.48783, Sni 0.00000, ASi 0.24392 and Combination Therapy Spi 1.00000, Sni 0.98351, ASi 0.99176 and Clinical Trial Spi 0.13475, Sni 0.70457, ASi 0.41966. **Figure 5.** Rank Shows the

Chemotherapy is in 5th Rank, Hormone Therapy is in 2nd Rank, Targeted Therapy is in 3rd Rank, Immunotherapy is in 6th Rank, Bone-directed Therapy is in 7th Rank, Radiation Therapy is in 8th Rank, Combination Therapy is in 1st Rank and Clinical Trial is in 4th Rank.

Table 6. Weighted Negative Distance from Average (S_{Ni}) values for each treatment modality across all evaluation criteria.

Weighted NDA				
Progression-Free Survival	Quality of Life Improvement	Reduction in Tumor Size	Side Effects	Patient Compliance
0.01331	0.06982	0.00000	0.06818	0.00000
0.00000	0.00000	0.00258	0.00000	0.00000
0.00000	0.00000	0.00000	0.00000	0.00472
0.00000	0.00000	0.00000	0.12879	0.09906
0.03304	0.05180	0.04381	0.09848	0.00000
0.09221	0.10586	0.06443	0.00000	0.02358
0.00000	0.00000	0.00000	0.00000	0.00472
0.00000	0.00000	0.02320	0.00000	0.06132

Table 7. Summary of weighted positive distance (S_{Pi}), weighted negative distance (S_{Ni}), appraisal scores (A_{Si}), and final rankings for all treatment alternatives.

	S _{Pi}	S _{Ni}	A _{Si}	Rank
Chemotherapy	0.30020	0.47108	0.38564	5
Hormone Therapy	0.80796	0.99099	0.89948	2
Targeted Therapy	0.70211	0.98351	0.84281	3
Immunotherapy	0.50871	0.20357	0.35614	6
Bone-directed Therapy	0.30374	0.20604	0.25489	7
Radiation Therapy	0.48783	0.00000	0.24392	8
Combination Therapy	1.00000	0.98351	0.99176	1
Clinical Trial	0.13475	0.70457	0.41966	4

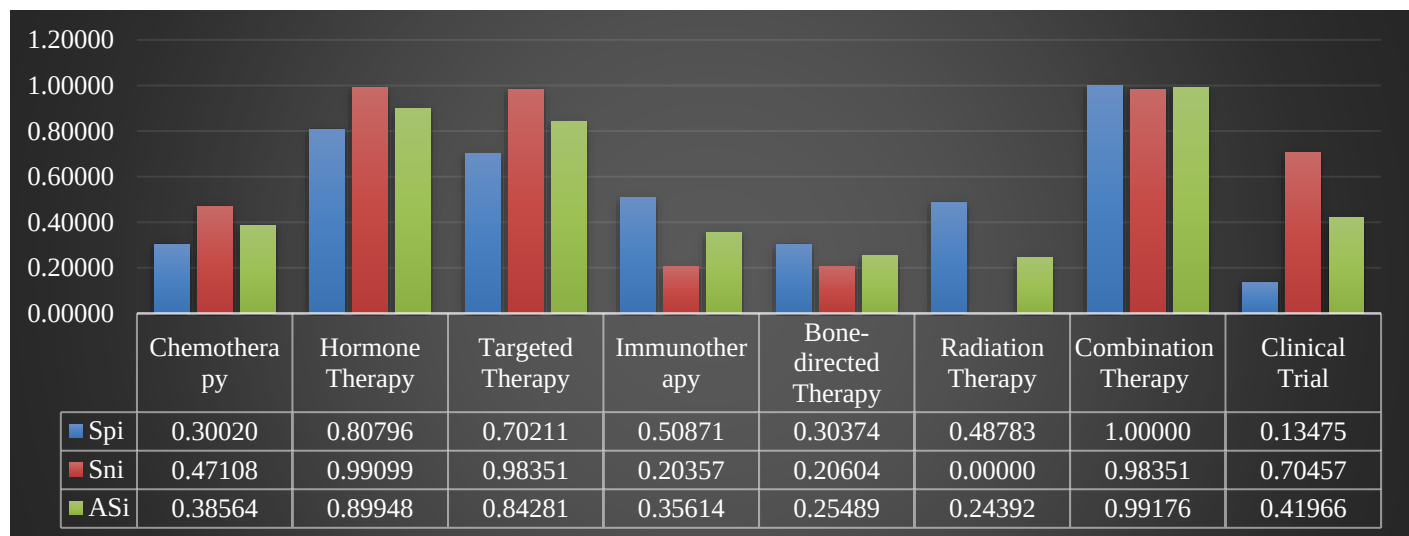


Fig. 4. Comparative bar chart of weighted positive distance (S_{Pi}), weighted negative distance (S_{Ni}), and appraisal scores (A_{Si}) for all eight treatment alternatives in metastatic breast cancer.

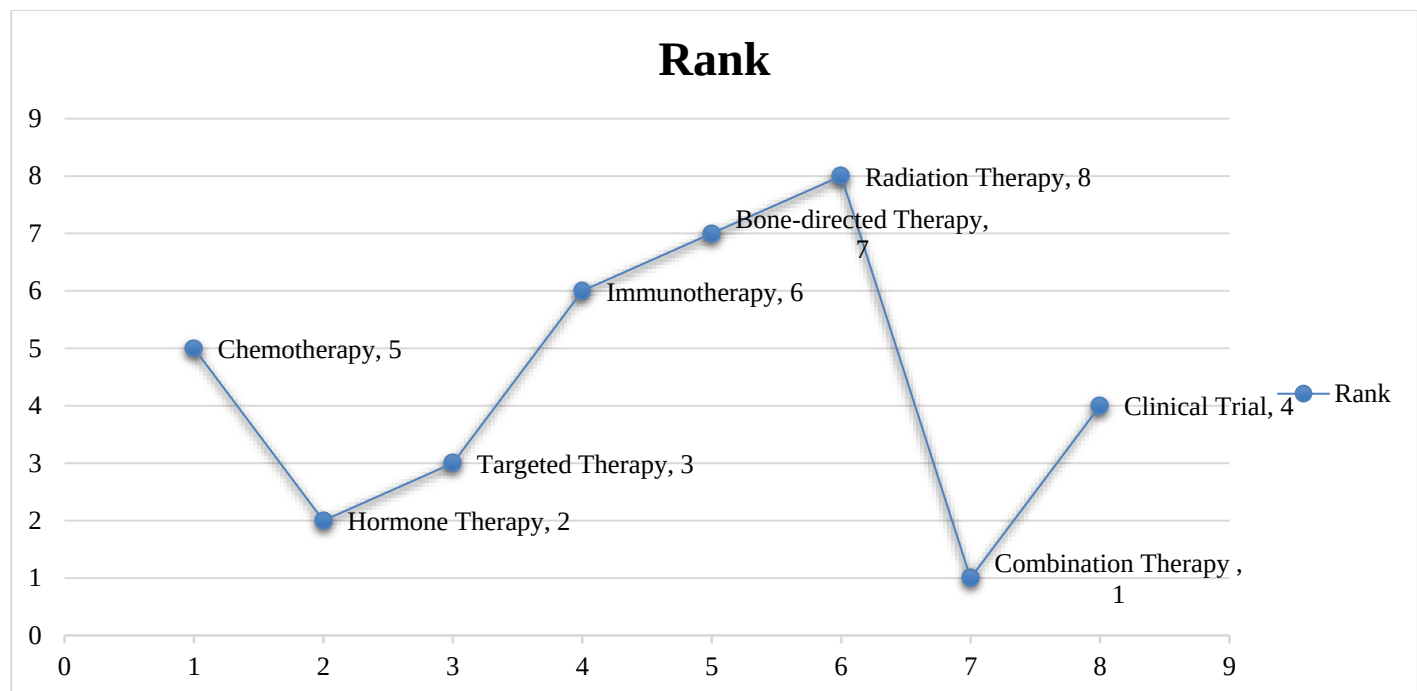


Fig. 5. Final ranking of all treatment alternatives based on appraisal scores (ASi), with Combination Therapy ranked highest and Radiation Therapy ranked lowest.

5. CONCLUSION

Metastatic breast cancer, or stage IV Breast cancer is a complicated disease that affects patient survival and quality of life, making it a major oncology problem. At this stage of progression, cancer cells have moved from the original tumor to distant organs such the liver, lungs, bones and brain. This progression changes the treatment focus from a curative approach to a palliative one, aimed at prolonging life & raising the standard of living. Research into metastatic breast cancer is crucial for several reasons. Understanding the molecular and genetic mechanisms behind metastasis helps in identifying new biomarkers and therapeutic targets. As a result, tailored treatments that target cancer cells precisely have been developed, minimizing damage to normal cells, reducing side effects, and increasing effectiveness. For instance, advances in individuals with HER2-positive metastatic breast cancer, HER2-targeted treatments have greatly improved outcomes. Additionally, studying drug resistance mechanisms is important. Many patients initially respond to treatments, but resistance often develops over time, leading to disease progression. Research into the pathways involved in resistance can guide the development of new drugs or combination therapies to overcome these challenges. Exploring how the tumor microenvironment supports metastatic growth can also uncover strategies to disrupt the interaction between cancer cells and surrounding tissues. Early detection of metastases is another vital research area. Techniques like Compared to conventional imaging techniques, liquid biopsies, which examine circulating tumor

DNA in blood samples, may provide earlier detection. Timely actions resulting from early identification may improve patient outcomes.

Moreover, the advent of personalized medicine, which tailors treatments based on the genetic and molecular profile of individual tumors, is transforming treatment approaches. This personalized approach aims to maximize therapeutic benefits while minimizing unnecessary side effects. Despite these advancements, metastatic breast cancer remains a major challenge with no definitive cure available yet. Ongoing research is essential for advancing treatment options, improving patient survival, and striving towards a cure. The commitment of researchers, combined with technological advancements and a better comprehension of the biology of cancer, offers hope for more effective treatments and better outcomes for those metastatic breast cancer. In summary, research in metastatic breast cancer is critical for advancing treatment strategies, enhancing patient care, and seeking future breakthroughs in combating this aggressive disease.

DECLARATIONS

Ethical Approval

We affirm that this manuscript is an original work, has not been previously published, and is not currently under consideration for publication in any other journal or conference proceedings. All authors have reviewed and approved the manuscript, and the order of authorship has

been mutually agreed upon.

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Availability of data and material

All of the data obtained or analyzed during this study is included in the report that was submitted.

Conflicts of Interest

The authors declare that they have no financial or personal interests that could have influenced the research and findings presented in this paper. The authors alone are responsible for the content and writing of this article.

Authors' contributions

All authors contributed equally in the preparation of this manuscript.

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