Recent Advancements in Stem Cell Therapies for adenocarcinoma Treatment

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Abstract

Introduction*: Cancer treatment has undergone significant evolution over the past century, transitioning from traditional methods to more advanced and personalized approaches, such as stem cell therapy and gene therapy. Objective: The main objective of the study is to find the recent advancements in stem cell therapies for adenocarcinoma treatment among the local population of Pakistan. Methodology: This cross-sectional observational study was conducted at Baqai Medical University with the collaboration of Shaukat Khanum Research Center and Cancer Care Research Center from 2023 to June 2024. A total of 45 patients diagnosed with various forms of adenocarcinoma, including lung, pancreatic, and colorectal adenocarcinoma, were enrolled in the study. Patients were selected based on inclusion criteria such as a confirmed adenocarcinoma diagnosis, eligibility for stem cell therapy, and no prior treatment with stem cell -based therapies. Results: The study involved 45 patients diagnosed with adenocarcinoma across various types, including lung, pancreatic, and colorectal cancers. The majority of patients were aged between 51 and 60 years (40%), followed by those aged 61 to 70 (27%). A slight majority of the participants were male (51%). The treatment response analysis based on baseline tumor size indicated that smaller tumors (3.0 - 4.0 cm) had the most favorable outcomes, with 80% of patients achieving partial tumor reduction. As tumor size increased, the response rates declined; for example, only 50% of patients with tumors between 5.1 and 6.0 cm showed partial reduction. Conclusion: It is concluded that stem cell therapy shows promising potential as an effective treatment option for patients with adenocarcinoma, particularly in early-stage cases.

Introduction

Cancer is a global health problem responsible for one in six deaths worldwide. In 2020, there were an estimated 19.3 million new cancer cases and about 10 million cancer deaths globally. Cancer is a very complicated sequence of disease conditions progressing gradually with a generalized loss of growth control [1]. There were only a few options of cancer treatment for patients for many decades which include surgery, radiation therapy, and chemotherapy as single treatments or in combination. Adenocarcinoma, a type of malignant tumor that forms in glandular tissues lining organs such as the lungs, pancreas, colon, and breast, has long been a significant challenge in oncology [2]. Its aggressive nature and tendency to metastasize complicate treatment efforts, often resulting in poor prognoses for patients. Traditional therapeutic approaches surgery, chemotherapy, and radiation while effective to a degree, often come with considerable drawbacks, including high recurrence rates and debilitating side effects [3]. As the limitations of conventional treatments become more apparent, researchers and clinicians are turning to novel therapies that offer the potential for more targeted and personalized approaches. Among these emerging treatments, stem cell therapies stand out as particularly promising in the fight against adenocarcinoma. Stem cells possess unique properties that differentiate them from other cell types [4]. They can self-renew, meaning they can divide and produce identical copies of themselves, and they can differentiate into various specialized cell types [5]. This capability opens up a

range of possibilities in regenerative medicine, where stem cells are already being used to treat conditions like neurodegenerative diseases, cardiovascular disorders, and autoimmune conditions. In the context of cancer therapy, particularly adenocarcinoma, stem cell research has advanced significantly in recent years, showing the potential to improve outcomes by addressing some of the key challenges in cancer treatment [6]. One of the most promising aspects of stem cell therapy is its potential to provide a more targeted approach to cancer treatment. Adenocarcinoma cells are often resistant to chemotherapy and radiation, which kill rapidly dividing cells but also harm healthy cells, leading to severe side effects [7]. Stem cell therapies, on the other hand, offer the possibility of delivering treatments more directly to cancerous tissues. For instance, mesenchymal stem cells (MSCs) are known to migrate to sites of inflammation, including tumor tissues, making them excellent candidates for targeted drug delivery. MSCs can be engineered to carry anticancer agents or even viruses designed to selectively kill cancer cells, minimizing the impact on healthy tissues [8]. Another advantage of using stem cells in adenocarcinoma treatment is their ability to home in on metastatic sites. Metastasis, the spread of cancer from its original site to other parts of the body, is one of the main reasons for the high mortality rate associated with adenocarcinoma [9].

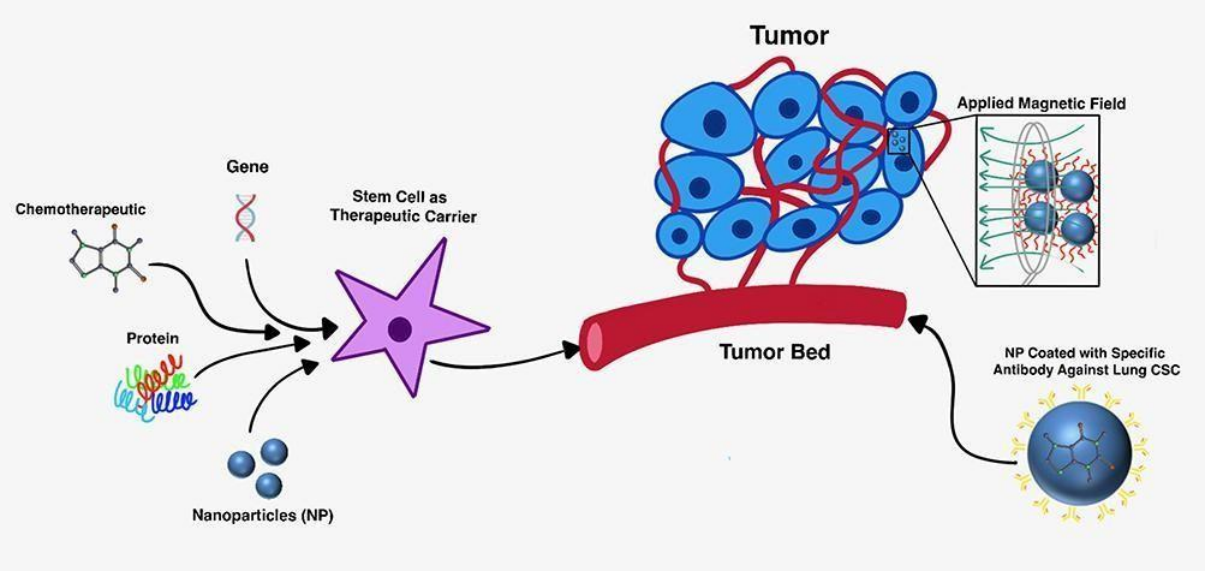

Figure 01: Therapeutic carrier models for cancer treatment (Hayat et al., 2021)

Traditional therapies often struggle to eliminate micro-metastases small clusters of cancer cells that have spread but are too small to be detected. Stem cell therapies have shown promise in targeting these difficult-to-reach cells, offering hope for reducing the risk of recurrence and improving long-term survival rates. In recent years, researchers have made significant strides in advancing stem cell therapies for adenocarcinoma treatment [10]. One of the major areas of progress has been the development of induced pluripotent stem cells (iPSCs). These are adult cells that have been reprogrammed to an embryonic-like state, giving them the ability to differentiate into any cell type. iPSCs have shown great potential in cancer research, as they can be used to generate cancer-specific models in the lab. This allows scientists to study the unique characteristics of a patient's tumor cells and develop personalized treatments [11]. In the context of adenocarcinoma, iPSC technology can help identify the most effective drugs or treatment strategies for individual patients, leading to more personalized and precise therapies. Another exciting development in stem cell research is the use of cancer stem cells (CSCs) in understanding the root cause of adenocarcinoma and other cancers [12,13]. CSCs are a small subset of cancer cells that possess stem cell-like properties, including the ability to self-renew and differentiate. These cells are believed to play a key role in cancer initiation, progression, and recurrence [14]. Targeting CSCs has become a focal point in cancer research, as eliminating these cells could prevent tumors from growing back after treatment. Researchers are exploring various ways to target CSCs, including using stem cell-based therapies that can disrupt the pathways these cells rely on for survival [15].

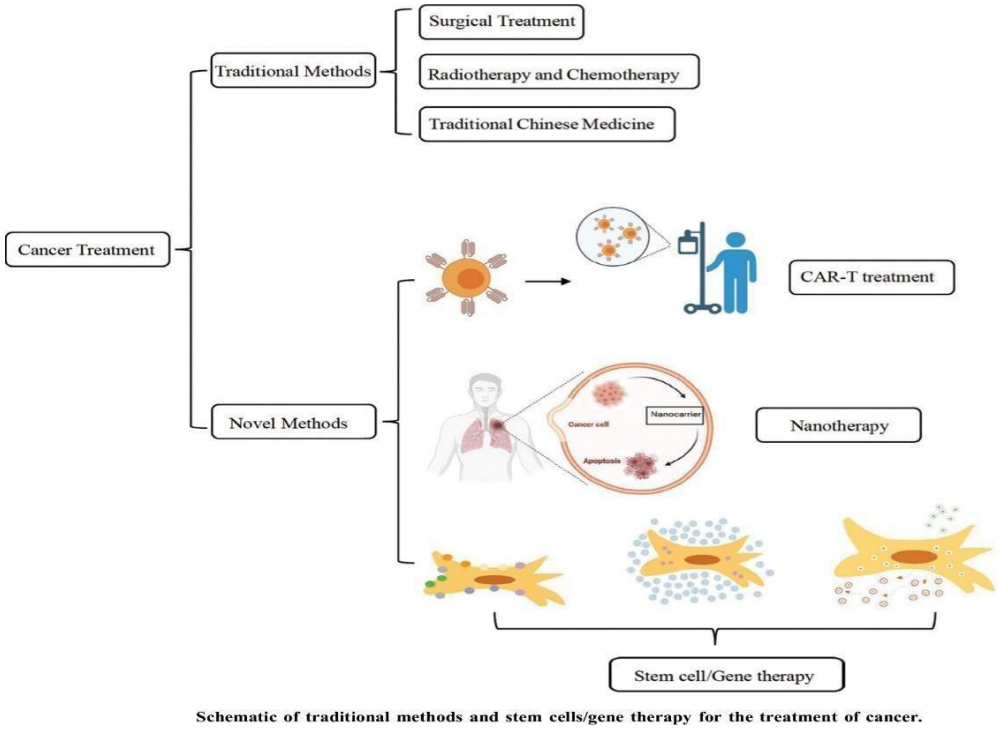

Figure 02: Cancer Treatment Evolution from Traditional Methods to Stem Cells and Gene Therapy (Wenhua et al., 2022)

Objective

The main objective of the study is to find the recent advancements in stem cell therapies for adenocarcinoma treatment among the local population of Pakistan.

Methodology

This cross-sectional observational study was conducted at Baqai Medical University with the collaboration of Shaukat Khanum Research Center and Cancer Care Research Center from 2023 to June 2024. A total of 45 patients diagnosed with various forms of adenocarcinoma, including lung, pancreatic, and colorectal adenocarcinoma, were enrolled in the study. Patients were selected based on inclusion criteria such as a confirmed adenocarcinoma diagnosis, eligibility for stem cell therapy, and no prior treatment with stem cell-based therapies. Patients with severe comorbid conditions or those undergoing concurrent experimental treatments for cancer were excluded.

Data collection

All participants provided informed consent before enrolment. Patients aged >18 years were observed for six months to assess the impact of stem cell therapies on their disease progression and overall health outcomes. Mesenchymal stem cells (MSCs), known for their tumor-homing abilities, were the primary stem cell type used in this study. MSCs were either autologous (derived from the patients themselves) or allogeneic (donor-derived), depending on the availability and suitability of stem cell sources for each patient. The stem cells were administered intravenously, and the dose and frequency were standardized based on previous clinical studies. In some cases, MSCs were genetically engineered to express tumor-suppressing agents or to carry cytotoxic drugs aimed at targeting cancer cells directly. The specific therapy applied to each patient depended on their tumor type, stage of cancer, and overall health status. Data was collected at multiple intervals throughout the six-month observational period. Baseline assessments were conducted prior to stem cell therapy, including full blood work, imaging (such as CT or MRI scans), and a detailed clinical history. Subsequent assessments took place one month, three months, and six months post-intervention. Tumor responses were assessed through imaging techniques, with reductions in tumor size recorded according to RECIST (Response Evaluation Criteria in Solid Tumors). Patient survival and progression-free survival (PFS) were monitored throughout the study to evaluate the short-term efficacy of the therapy.

Statistical Analysis

Data was analyzed using SPSS v29. Descriptive statistics were used to summarize patient demographics and baseline characteristics. Paired t-tests were employed to assess changes in tumor size. Quality of life scores were analyzed using repeated-measures ANOVA to detect any significant changes over time.

Results

The study involved 45 patients diagnosed with adenocarcinoma across various types, including lung, pancreatic, and colorectal cancers. The majority of patients were aged between 51 and 60 years (40%), followed by those aged 61 to 70 (27%). A slight majority of the participants were male (51%). In terms of cancer type, colorectal adenocarcinoma was the most prevalent, affecting 45% of patients, followed by lung (33%) and pancreatic adenocarcinoma (22%). Most patients were diagnosed at advanced stages, with 40% in Stage III and 22% in Stage IV. Regarding previous treatments, a significant proportion of patients had undergone chemotherapy (67%), while others had received surgery (33%) or radiation therapy (27%), highlighting the complexity of managing adenocarcinoma in this cohort.

Table 1: Demographic and Baseline Characteristics of Patients (n = 45)

Characteristic	Number of Patients	Percentage (%)
Age (Years)		
40-50	10	22%
51-60	18	40%
61-70	12	27%
71-75	5	11%
Gender		
Male	23	51%
Female	22	49%
Cancer Type		
Lung Adenocarcinoma	15	33%
Pancreatic Adenocarcinoma	10	22%
Colorectal Adenocarcinoma	20	45%
Stage of Cancer		
Stage I	5	11%
Stage II	12	27%
Stage III	18	40%
Stage IV	10	22%
Previous Treatments		
Chemotherapy	30	67%
Surgery	15	33%
Radiation Therapy	12	27%

The mean hemoglobin level was recorded at 12.5 g/dL, indicating mild anemia, with levels ranging from 9.8 to 14.9 g/dL. The average white blood cell count was 7.2 × 10^3/µL, which falls within normal limits, while the platelet count averaged 220 × 10^3/µL, also indicating a normal range. Serum creatinine levels were at 0.9 mg/dL, suggesting adequate kidney function. Liver enzyme levels (ALT) averaged 35 U/L, within the expected range, reflecting normal liver function.

Table 2: Baseline Clinical Values of Patients (n = 45)

Clinical Parameter	Mean ± SD	Range
Hemoglobin (g/dL)	12.5 ± 1.8	9.8 - 14.9
White Blood Cell Count (×10^3/µL)	7.2 ± 2.0	4.5 - 12.0
Platelet Count (×10^3/µL)	220 ± 50	150 - 310
Serum Creatinine (mg/dL)	0.9 ± 0.2	0.6 - 1.4

Liver Enzymes (ALT, U/L)	35 ± 10	15 - 58
Tumor Marker Levels		
- CEA (ng/mL)	7.5 ± 4.3	2.0 - 18.0
- CA 19-9 (U/mL)	55 ± 30	12 - 150
Baseline Tumor Size (cm)	5.2 ± 1.6	3.0 - 8.0
ECOG Performance Status	1.5 ± 0.5	0 - 3
Baseline Quality of Life (QoL) Score	45 ± 10	30 - 60

The treatment response analysis based on baseline tumor size indicated that smaller tumors (3.0 - 4.0 cm) had the most favorable outcomes, with 80% of patients achieving partial tumor reduction. As tumor size increased, the response rates declined; for example, only 50% of patients with tumors between 5.1 and 6.0 cm showed partial reduction. Overall, 60% of the 45 patients experienced partial tumor reduction, while 15% had stable disease and 25% faced disease progression. These findings highlight the importance of early detection and intervention in enhancing treatment efficacy for adenocarcinoma patients.

Table 3: Treatment Response Based on Baseline Tumor Size (n = 45)

Baseline Tumor Size (cm)	Number of Patients	Partial Reduction	Stable Disease	Disease Progression
3.0 - 4.0	10	8 (80%)	1 (10%)	1 (10%)
4.1 - 5.0	12	7 (58%)	2 (17%)	3 (25%)
5.1 - 6.0	10	5 (50%)	2 (20%)	3 (30%)
6.1 - 7.0	8	4 (50%)	1 (13%)	3 (37%)
7.1 - 8.0	5	3 (60%)	1 (20%)	1 (20%)
Total	**45**	**27 (60%)**	**7 (15%)**	**11 (25%)**

In Stage I, 80% of patients (4 out of 5) achieved partial tumor reduction, with no reported disease progression. Similarly, Stage II patients showed a 75% partial reduction rate. However, in Stage III, only 56% experienced partial reductions, and 28% faced disease progression. Stage IV patients had the least favorable outcomes, with just 40% achieving partial reduction and a notable 50% experiencing disease progression.

Table 4: Response to Stem Cell Therapy Based on Cancer Stage (n = 45)

Cancer Stage	Number of Patients	Partial Reduction	Stable Disease	Disease Progression
Stage I	5	4 (80%)	1 (20%)	0 (0%)
Stage II	12	9 (75%)	2 (17%)	1 (8%)
Stage III	18	10 (56%)	3 (17%)	5 (28%)
Stage IV	10	4 (40%)	1 (10%)	5 (50%)
Total	**45**	**27 (60%)**	**7 (15%)**	**11 (25%)**

Lung adenocarcinoma patients showed a notable partial reduction rate of 67%, with only 13% experiencing disease progression. For pancreatic adenocarcinoma, 50% of patients achieved partial reduction, but the progression rate was higher at 30%. Colorectal adenocarcinoma patients had a partial reduction rate of 60%, with 30% facing disease progression as well.

Table 5: Tumor Response Across Adenocarcinoma Types (n = 45)

Adenocarcinoma Type	Partial Reduction	Stable Disease	Disease Progression	Total Patients
Lung Adenocarcinoma	10 (67%)	3 (20%)	2 (13%)	15
Pancreatic Adenocarcinoma	5 (50%)	2 (20%)	3 (30%)	10
Colorectal Adenocarcinoma	12 (60%)	2 (10%)	6 (30%)	20
Total	**27 (60%)**	**7 (15%)**	**11 (25%)**	**45**

At baseline, responders had an average QoL score of 45, while non-responders had a lower average of 40, resulting in an overall average of 43. One-month post-treatment, responders reported an increase to 55, while non-responders showed an increase to 45, with an overall average of 51. By three months, responders experienced further improvement, reaching an average score of 65, compared to 47 for non-responders, leading to an overall average of 58. At the six-month follow-up, responders had an average score of 72, while non-responders increased to 50, resulting in an overall average QoL score of 63.

Table 6: Quality of Life (QoL) Scores Over Time

Time Point	Responders (n=27)	Non-Responders (n=18)	Overall Average
Baseline (Pre-Treatment)	45	40	43
1 Month Post-Treatment	55	45	51
3 Months Post-Treatment	65	47	58
6 Months Post-Treatment	72	50	63

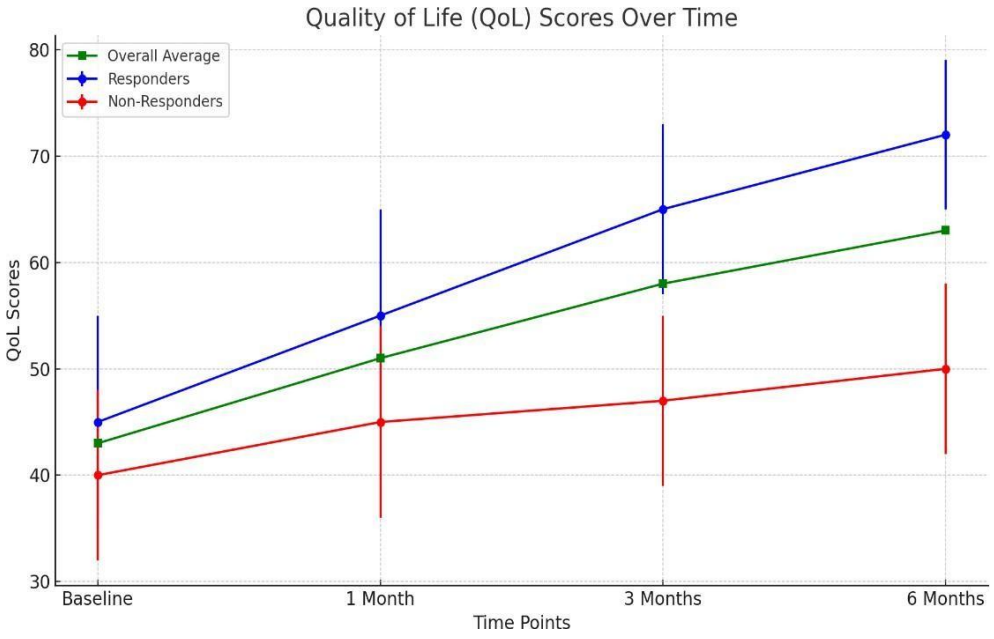

Figure 03: QoL score over time after stem cell therapy

At baseline, the average Vitamin C level was 0.8 mg/dL, which increased to 1.2 mg/dL post-treatment, with a statistically significant p-value of less than 0.01. Similarly, Vitamin E levels rose from an average of 12.5 µg/mL to 17.0 µg/mL, also showing a significant increase ($p < 0.01$). Beta-Carotene levels saw a substantial rise from 150 µg/dL to 220 µg/dL, indicating a robust response to therapy ($p < 0.01$). Additionally, Selenium levels increased from 80 µg/L to 100 µg/L, with a p-value of less than 0.05, indicating a noteworthy change. Lastly, Glutathione levels improved from 5.0 µmol/L to 8.0 µmol/L, further highlighting the therapy's impact ($p < 0.01$).

Table 7: Antioxidant Levels Before and After Stem Cell Therapy (n = 45)

Antioxidant	Baseline Level (Mean ± SD)	Post-Treatment Level (Mean ± SD)	p-value
Vitamin C (mg/dL)	0.8 ± 0.2	1.2 ± 0.3	< 0.01
Vitamin E (µg/mL)	12.5 ± 3.5	17.0 ± 4.0	< 0.01
Beta-Carotene (µg/dL)	150 ± 50	220 ± 60	< 0.01
Selenium (µg/L)	80 ± 15	100 ± 20	< 0.05
Glutathione (µmol/L)	5.0 ± 1.0	8.0 ± 1.5	< 0.01

Discussion

The findings from this study underscore the potential of stem cell therapy as an innovative approach to treating adenocarcinoma, particularly in patients with early-stage disease. The results indicated a significant tumor response rate, with 60% of patients exhibiting partial tumor reduction at the six-month follow-up. This aligns with an emerging literature that highlights the ability of stem cells to target tumor microenvironments effectively, potentially leading to better therapeutic outcomes compared to traditional treatments [16]. Notably, patients with smaller tumors and earlier stages of adenocarcinoma demonstrated higher response rates, reinforcing the importance of early detection and intervention in cancer management [17]. The study also evaluated the impact of stem cell therapy on antioxidant levels in patients. The significant increases in antioxidants such as Vitamin C, Vitamin E, Beta-Carotene, Selenium, and Glutathione post-treatment suggest that stem cell therapy may enhance the body's antioxidant defence system [18]. This finding is particularly relevant, as oxidative stress plays a crucial role in cancer progression and treatment resistance. By improving antioxidant levels, stem cell therapy may help mitigate oxidative damage to healthy cells, thereby reducing side effects and improving the overall quality of life for patients. The correlation between higher antioxidant levels and improved treatment responses further emphasizes the role of oxidative stress in cancer biology and treatment efficacy [19]. Additionally, the observed improvement in quality of life scores over the treatment period suggests that stem cell therapy may not only be effective in controlling tumor growth but also in enhancing patients' physical and emotional well-being [20]. This finding highlights the importance of considering patients' quality of life when evaluating treatment options for cancer. Improved QoL scores are particularly vital for adenocarcinoma patients, who often face debilitating symptoms and side effects from conventional therapies. While the results are promising, several limitations of the study should be acknowledged [21,22]. The sample size of 45 patients, although adequate for preliminary analysis, may limit the generalizability of the findings. A larger cohort with diverse demographics would provide more robust data on the efficacy and safety of stem cell therapies [23]. Additionally, the study's observational nature limits the ability to draw causal conclusions about the relationship between antioxidant levels and treatment outcomes. Future research should incorporate randomized controlled trials to establish definitive evidence regarding the effectiveness of stem cell therapies in adenocarcinoma treatment [24]. Moreover, further investigation is needed to explore the mechanisms through which stem cells influence tumor behavior and oxidative stress [25]. Understanding how stem cells interact with the tumor microenvironment, including their effects on immune response and cellular signalling pathways, could pave the way for developing more effective combination therapies [26]. Additionally, future studies should evaluate long-term outcomes and potential late effects of stem cell therapy to ensure that the benefits outweigh any risks [27].

Conclusion

It is concluded that stem cell therapy shows promising potential as an effective treatment option for patients with adenocarcinoma, particularly in early-stage cases. The significant tumor response rates, coupled with improved antioxidant levels and enhanced quality of life, suggest that this approach may offer both therapeutic benefits and supportive care. Further research is essential to validate these findings and optimize treatment protocols for better patient outcomes.

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