

# Incorporating Exercise Into the Cancer Treatment Paradigm

Barbara K. Haas, PhD, RN, Melinda Hermanns, PhD, RN-BC, CNE, and Gary Kimmel, MD



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**Background:** The benefits of exercise for patients with cancer are well documented. However, exercise is still not a standard of care for this population. Several factors contribute to the lack of exercise prescriptions for patients with cancer, including challenges posed by treatment-related side effects, lack of knowledge among healthcare providers and the laypeople, and inadequate resources.

**Objectives:** This article reviews the benefits of exercise in general and specifically to patients with cancer, discusses the specific challenges and considerations required in recommending exercise to this population, and provides specific recommendations for healthcare providers to incorporate exercise into treatment plans.

**Methods:** Using a case study exemplar, this article discusses the benefits and challenges to exercise while undergoing treatment for cancer and proposes specific solutions and recommendations.

**Findings:** Oncology practitioners can provide the opportunity for patients to safely engage in exercise with the appropriate resources and trained personnel using a successful model of delivering exercise to patients undergoing treatment for cancer. Exercise improves quality of life in all patients, including those with advanced-stage cancers and those actively receiving treatment.

Barbara K. Haas, PhD, RN, is the executive director and Melinda Hermanns, PhD, RN-BC, CNE, is an associate professor, both in the School of Nursing at The University of Texas; and Gary Kimmel, MD, is the founder and chairman emeritus of the Cancer Foundation for Life, all in Tyler, TX. The authors take full responsibility for the content of the article. The authors did not receive honoraria for this work. The content of this article has been reviewed by independent peer reviewers to ensure that it is balanced, objective, and free from commercial bias. No financial relationships relevant to the content of this article have been disclosed by the authors, planners, independent peer reviewers, or editorial staff. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the *Clinical Journal of Oncology Nursing* or the Oncology Nursing Society. Haas can be reached at [bhaas@uttyler.edu](mailto:bhaas@uttyler.edu), with copy to editor at [CJONEditor@ons.org](mailto:CJONEditor@ons.org). (Submitted July 2016. Revision submitted September 2016. Accepted for publication September 16, 2016.)

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**M**arjorie, a 71-year-old married woman, had been diagnosed with advanced stage breast cancer. Marjorie also had severe chronic obstructive pulmonary disease (COPD). Following a hospitalization for COPD, she required oxygen 24 hours per day at 2.5 liters. Given her pulmonary status, radiation and surgery were not planned as part of the breast cancer treatment. Marjorie was receiving oral hormonal therapy. Accompanied by her husband, Marjorie arrived at FitSTEPS for Life® (FSFL), a community-based exercise program for patients with cancer, using a walker. The only exercise that she was able to perform that day was walking into the center. Her long-term goal was to “walk without huffing and puffing.” Marjorie required a wheelchair to return to the car for the drive home.

Unfortunately, Marjorie’s presentation is not atypical. Many cancer survivors are inactive older adults who have

comorbidities. Coupled with the fatigue, depression, and side effects related to treatment, all of which are commonly experienced by cancer survivors, this population presents unique challenges to exercise engagement. This article will (a) review the benefits of exercise in general and specifically to patients with cancer, (b) discuss the specific challenges and considerations required in recommending exercise to this population, and (c) provide specific recommendations for healthcare providers to incorporate exercise into treatment plans.

## Physiology of Exercise

Although exercise induces a host of beneficial metabolic effects, the following discussion is confined to its influence on the behavior of cancer cells. A burgeoning amount of

scientific research has demonstrated the influence of aerobic exercise on malignant tumors. Exercise exerts hormonal changes, such as reducing production of estrogen, androgen, and insulin-like growth factor 1 production. Preclinical studies demonstrate that exercise favorably influences microcellular functions that determine the activity of cancer, including apoptosis, DNA damage, and genomic aberrations (oncogene expression and mutation) (Davies, Batehup, & Thomas, 2011; Jones et al., 2013). Preclinical studies have demonstrated a number of metabolic pathways induced by exercise that directly affect cancer cell activity. Tumor microcirculation might be enhanced through increased vascular endothelial growth factor and changes in tumor endothelium, resulting in reduced tumor hypoxia by 50% and improved tumor blood flow by 200%, increasing delivery of chemotherapy to tumors (Betof et al., 2015; Vaccarezza & Vitale, 2015). Runqvist et al. (2013) demonstrated that serum taken from 10 individuals following 60 minutes of bicycle exercise resulted in a 43% reduction in epidermal growth factor and 35% increase in insulin-like growth factor-binding protein, inhibiting murine prostate cancer cell proliferation by 31%. Muscle is recognized as an endocrine organ that contains peptides known as myokines. These myokines, released by exercise, recruit natural killer cells that selectively inhibit tumor cell growth. In addition, physical activity activates AMP-activated protein kinase signaling that can inhibit the growth of cancer cells (Pedersen, Christensen, & Hojman, 2015). Another study by Pedersen et al. (2016) demonstrated a 60% reduction in tumor incidence and growth in five different murine tumor models by the release of epinephrine from muscles after exercise, causing interleukin-6 to mobilize natural killer cells to target and inhibit tumor growth. Emerging research identifies mitochondria, located in the cytoplasm of most cells, as a potential prominent influence on cancer development and growth. Modulation (syntheses and degradation) of mitochondria may arrest cell proliferation (Scatena, 2012). Aerobic exercise has demonstrated such activation of mitochondrial biogenesis (Viña et al., 2009). Telomeres are DNA protein structures found at both ends of each chromosome that protect the genome from degradation of the cell nucleus, unnecessary recombination, and fusion between chromosomes. Shortening of telomeres has been implicated in genome instability and enhanced oncogenesis. Exercise has been demonstrated to preserve telomere length reduction and reduce cancer risk (Shammas, 2011). In a study by Ornish et al. (2013), age-matched patients with prostate cancer were randomized to a three-month healthy lifestyle intervention versus usual care. At the end of five years, telomere length was significantly longer in the intervention group.

Exercise should be viewed as a therapeutic agent in cancer prevention and treatment. It is the only treatment with such a broad spectrum of benefit with minimal side effects and cost. From prevention to improvement of the adverse effects of cancer and its treatment to increased survival, exercise demonstrates exemplary benefit. Researchers are studying the amount of exercise required to improve outcomes in specific cancers; however, patients cannot and should not have to wait for clinicians to recommend or prescribe exercise.

If the maximal benefits of exercise are to be achieved, the dose and type of exercise prescribed must be titrated, like chemotherapy, to be compatible with the patient's physical condition and psychological motivation.

## Benefits of Exercise

Research consistently demonstrates that exercise enhances physical and psychosocial function with an improved quality of life (Galvão & Newton, 2005; Haas, Kimmel, Hermanns, & Deal, 2012; Mishra et al., 2012). Observational studies demonstrate a 50% increased survival rate with consistent exercise in patients with breast and colon cancers. Brisk walking for 150 minutes per week achieved this benefit in women with breast cancer, and more intense exercise of six hours per week of brisk walking was required to achieve survival benefit in patients with colon cancer (Holmes, Chen, Feskanich, Kroenke, & Colditz, 2005; Meyerhardt et al., 2006). In a study by Irwin et al. (2008), 900 patients with breast cancer who moderately exercised 2.5 hours per week were followed for six years. The researchers found that the risk of all-cause mortality of the women in the exercise group was reduced by 67% when compared to inactive women (Irwin et al., 2008). Men with prostate cancer who engaged in three hours of vigorous activity weekly (e.g., jogging, biking, swimming, weight training, tennis) experienced a 70% risk reduction in high-grade, advanced, or fatal prostate cancers (Giovannucci, Liu, Leitzmann, Stampfer, & Willett, 2005).

Cancer-related fatigue (CRF) is the most commonly reported side effect of cancer and its treatment. The literature is replete with studies demonstrating significant improvement in CRF with consistent exercise (McNeely & Courneya, 2010; Stricker, Drake, Hoyer, & Mock, 2004). Nausea, vomiting, anxiety, depression, and the integrity of bone and muscle mass are all favorably influenced by exercise during and following cancer treatment (Newton & Galvão, 2008). Patients with breast cancer who exercised during chemotherapy were more likely to complete the full dose of the prescribed chemotherapeutic regimen without treatment delay, potentially resulting in improved outcomes (Courneya et al., 2007). About 60% of patients with breast cancer gained weight after their diagnosis related to chemotherapy and inactivity. Proper nutrition and exercise can ameliorate this risk factor (Irwin et al., 2005).

Preclinical studies have suggested that the cardiotoxic effects of anthracyclines and trastuzumab (Herceptin<sup>®</sup>) may be mitigated by aerobic exercise (Scott et al., 2011; Wonders & Reigle, 2009). Lymphedema of the upper extremity following mastectomy with axillary node dissection may be prevented or reduced with appropriate prescribed exercise (Schmitz et al., 2009). Exercise has been demonstrated to activate the endocannabinoid system to reduce pain (Sparling, Giuffrida, Piomelli, Roszkopf, & Dietrich, 2003). Evidence from an increasing number of preclinical studies has demonstrated the remarkable inhibitory effect of exercise on cancer cell growth through a variety of physiologic pathways (Pedersen et al., 2016; Rundqvist et al., 2013). Therefore, exercise may be an effective therapeutic agent to treat cancer, in conjunction with conventional chemotherapy and radiation. The compelling evidence from scientific research has

demonstrated numerous benefits from exercise throughout the cancer care continuum and concludes that exercise should be incorporated as a routine component of treatment.

## Prevention of Cancer Using Exercise

Healthcare providers have been reluctant to acknowledge that cancer is a preventable disease. Prevention shifts the responsibility of wellness from the healthcare provider to the individual. One rationale for the lack of emphasis on prevention is the absence of revenue generated by the healthcare provider for such initiatives. In 2010, more than \$124 billion were spent on cancer care, with the total annual cost of cancer care estimated to reach nearly \$158 billion by 2020 (Mariotto, Yabroff, Shao, Feuer, & Brown, 2011). A healthy lifestyle, including tobacco abstinence, healthy diet, moderate alcohol, and consistent adequate physical activity, may reduce the risk of cancer by as much as 65% (Ford, Zhao, Tasai, & Li, 2011). Consistent exercise alone has demonstrated a 40% reduction in the incidence of cancer (Zhang, Sui, Hand, Hébert, & Blair, 2014). Numerous studies have demonstrated the protective role of exercise in multiple cancers, including breast, lung, kidney, colon, endometrial, and prostate cancers (Behrens & Leitzmann, 2013; Boyle, Keegel, Bull, Heyworth, & Fritschi, 2012; Giovannucci et al., 2005; Lynch, Neilson, & Friedenreich, 2011; Sun, Shi, Gao, & Xu, 2012; Voskuil, Monninkhof, Elias, Vlems, & van Leeuwen, 2007). Researchers predict that 50% of cancers are preventable based on scientific evidence (Colditz, Wolin, & Gehlert, 2012; Stewart & Wild, 2014). Despite compelling data, the proposed \$1 billion White House Cancer Moonshot Task Force initiative to cure cancer (Neugut & Gross, 2016) does not address the remarkable opportunity to reduce cancer mortality through prevention. A letter from 70 deans of Schools of Public Health across the United States was sent to Vice President Joe Biden (Association of Schools and Programs of Public Health, 2016) and included the following statement:

Since the beginning of the “War on Cancer,” the most notable successes have been due to the power and efficacy of prevention. The massive reductions in lung, cervical, colorectal, and gastric cancer mortality rates are almost entirely due to a focus on public health and prevention approaches (including screening). (p. 1)

Admittedly, achieving a healthy lifestyle through behavior modification in the United States’ sedentary society is not easily accomplished. However, much could be achieved over time with a more global initiative, starting with healthcare providers collaborating with the government to make prevention a priority. Although targeted therapy and designer drugs are at the forefront of cancer research, prevention will always play a seminal role in cost, effectively reducing cancer incidence and mortality.

## Exercise Challenges, Considerations, Recommendations, and Solutions

People receiving treatment for cancer or living after diagnosis and treatment often experience the lingering effects of

treatment and require special considerations when exercising. CRF and safety are primary risks to those not accustomed to exercising. In addition, external factors, such as healthcare provider lack of knowledge, lack of reimbursement, and the lack of standard-of-care models, contribute to difficulties in motivating people receiving cancer treatment to exercise. This section briefly describes these challenges and provides recommendations to address them (see Table 1).

### Fatigue

The most common side effect of cancer and its treatment, estimated to occur in nearly 100% of patients, is CRF (Bower, 2014). Exercise has been demonstrated to be effective in alleviating CRF (Cramp & Byron-Daniel, 2012; Pearson, Morris, di Stefano, & McKinstry, 2016) unless anemia is present, in which case iron supplements may be helpful. The adverse effects (e.g., joint and muscle pain, diarrhea, dizziness, unusual weakness) associated with drugs, such as epoetin alfa (Epogen®) and darbopoetin alfa (Aranesp®), often precludes them from incorporation into regimens to treat anemia (Minton, Richardson, Sharpe, Hotopf, & Stone, 2010). To combat CRF, small, frequent episodes of exercise tailored to patient needs are recommended (Office of Disease Prevention and Health Promotion, 2016; Schmitz et al., 2010). For example, exercising for five minutes three times per day may be all that a patient can tolerate. The amount and intensity of exercise can be gradually increased over time.

### Safety Concerns

In general, patients with cancer should not be exercising in a crowded gym with the general population. Unlike other patient populations, patients with cancer need special consideration when embarking on an exercise program (Kimmel, Haas, & Hermanns, 2014; Schmitz, Ahmed, Hannan, & Yee, 2005). Cancer and its treatment may render patients susceptible to infection, bleeding, and inadequate oxygenation. Peripheral neuropathy as a result of treatment puts this population at risk for losing balance and falling. Patients with primary or metastatic bone cancer have an increased risk of fractures as a result of improper lifting or high-impact exercise. Studies have repeatedly demonstrated the safety of supervised aerobic and resistance exercise (Adamsen et al., 2009; Rajotte et al., 2012; Schmitz et al., 2005, 2010). Despite demonstrated efficacy and safety, concerns about whether exercise during cancer treatment is safe persist (Blaney, Lowe-Strong, Rankin-Watt, Campbell, & Gracey, 2013; Sabatino et al., 2007).

Ideally, centers designed specifically for cancer or home-based exercise programs are recommended (Kimmel et al., 2014). Without specially trained staff who are aware of the risks associated with cancer treatment, a patient receiving treatment for cancer may experience complications related to exercise rather than benefits (American Cancer Society, 2014). Several appropriate measures should be used to ensure safety of patients with cancer participating in an exercise program.

### Healthcare Provider Misconceptions

Unfortunately, many practicing physicians and healthcare providers are not familiar with the benefits that an exercise

**TABLE 1. Exercise Challenges, Considerations, and Recommendations for Patients Receiving Treatment for Cancer**

Challenge	Considerations	Recommendations
Cancer-related fatigue	<ul style="list-style-type: none"> <li>Anemia may contribute to or worsen fatigue.</li> </ul>	<ul style="list-style-type: none"> <li>Evaluate for anemia, and treat if indicated.</li> <li>Create an individualized exercise treatment plan.</li> <li>Recommend small episodes of exercise several times per day.</li> <li>Monitor oxygen saturation levels during exercise.</li> </ul>
Healthcare provider misconceptions	<ul style="list-style-type: none"> <li>Healthcare providers may not be aware of exercise benefits or know how or where to refer patients.</li> </ul>	<ul style="list-style-type: none"> <li>Educate professionals, providers, and laypeople on the benefits of exercise.</li> <li>Use inservices for professional training.</li> <li>Educate using articles in local newspapers, television interviews, or the local news.</li> <li>Become a navigator in cancer treatment centers.</li> </ul>
Lack of reimbursement	<ul style="list-style-type: none"> <li>Cost of care is often prohibitive, even for those with insurance.</li> <li>Lack of reimbursement is a disincentive for physicians to include exercise in a treatment plan.</li> </ul>	<ul style="list-style-type: none"> <li>Conduct a community assessment to determine potential support; provide in-kind space.</li> <li>Make use of existing resources (e.g., churches, community centers, university centers).</li> <li>Develop a strong volunteer support system to supplement professional care.</li> <li>Use grants and fundraising to pay for exercise staff.</li> <li>Advocate for changes in healthcare provision and reimbursement.</li> </ul>
Lack of standard-of-care model	<ul style="list-style-type: none"> <li>Standard physical therapy referral for 6–8 weeks is not long enough to ensure a life-style change.</li> <li>Standard physical therapy preparation may not include exercise considerations for patients with cancer.</li> </ul>	<ul style="list-style-type: none"> <li>Ensure that potential models are supported by physicians and nurses.</li> <li>Train staff in the risks of exercise to patients with cancer and undergoing treatment.</li> <li>Evaluate each patient and individualized treatment prescription.</li> <li>Set goals with patients.</li> <li>Encourage a lifestyle change or lifetime approach to exercise.</li> </ul>
Safety	<ul style="list-style-type: none"> <li>Neutropenia puts patients at risk for infection.</li> <li>Thrombocytopenia precludes high-impact exercise and increases risk for bleeding.</li> <li>Peripheral neuropathy may contribute to balance issues.</li> <li>Bone metastases may put patients at risk for fractures.</li> </ul>	<ul style="list-style-type: none"> <li>Train staff to be aware of risks of exercise to patients with cancer.</li> <li>Check temperature prior to exercise, particularly if receiving chemotherapy; delay exercise if fever is present.</li> <li>Avoid high-impact exercise that could stimulate bleeding.</li> <li>Observe and check oxygen saturation periodically.</li> <li>Use a safety belt or stool that fits over a treadmill to sit down, if needed.</li> <li>Use stabilizing rings for the stability balls to prevent movement of the balls.</li> <li>Be aware of primary or metastatic bone disease, and avoid twisting, impact, overexertion, or stressing.</li> <li>Take note of peripheral neuropathy spatial awareness. Use flex bands for motor neuropathy and flex balls for sensory neuropathy.</li> <li>Recommend balancing exercises, such as tai chi.</li> <li>Acquire physician approval to exercise.</li> <li>Recommend appropriate footwear.</li> </ul>

*Note.* Based on information from American College of Sports Medicine, 2016; Kimmel et al., 2014; National Comprehensive Cancer Network, 2014; Office of Disease Prevention and Health Promotion, 2016; Oncology Nursing Society, 2016; Schmitz et al., 2010.

program may have for a patient with cancer and are reluctant to recommend exercise (Brown & Schmitz, 2014; Sabatino et al., 2007). Educating professionals and laypeople on the benefits of exercise is critical to changing the current cancer treatment paradigm. Nurses, in particular, play a pivotal role in encouraging and recommending treatment modalities for optimal patient care to physicians (Rieger & Yarbrow, 2003). Nurses' keen assessments are critical in conveying the physiologic (Rieger & Yarbrow, 2003) and psychological health status of the patient (Hendrick & Cobos, 2010) to the physician and/or nurse practitioner. Nurse navigators are effective and influential advocates for patients and can increase awareness of the importance of exercise in this population (Dang, 2015; McMullen, 2013). Interdisciplinary collaboration can help facilitate this process (Gagnon et al., 2013). With increased awareness and education, healthcare providers can make referrals to appropriate exercise centers.

## Cost

One particularly difficult challenge to incorporating exercise into the cancer treatment paradigm is the lack of reimbursement (Blaney, Lowe-Strong, Rankin-Watt, Campbell, & Gracey, 2010; Cheville & Tchou, 2007; Haas & Kimmel, 2011). Although some patients may be prescribed a six- to eight-week physical therapy regimen, the typical physical therapy department is not geared to work with the cancer population. In addition, exercise should be a permanent lifestyle change, and that is rarely accomplished in two months (Kimmel et al., 2014). Even for patients who have insurance and could typically afford to pay for an exercise trainer, the out-of-pocket costs associated with expensive drug therapies are a burden to patients. Because exercise is often not billable, there is a disincentive for healthcare providers to prescribe it or incorporate it into a patient's treatment plan. However,

low-cost exercise centers specifically designed for patients with cancer exist.

## Lack of Standard-of-Care Models

Traditional treatments have not consisted of prescribing exercise as a treatment modality in cancer care. A vast amount of research has confirmed the benefits of exercising, necessitating the need for exercise as a vital component to the standard of care for patients with cancer (Schmitz et al., 2005). At this time, no standard amount of exercise is recommended (Blaney et al., 2013; Brown & Schmitz, 2014; Kimmel et al., 2014). General exercise recommendations for patients with cancer are based on those recommended for the general population and include 150 minutes of moderate aerobic exercise or 75 minutes of vigorous aerobic exercise weekly (American Cancer Society, 2016; Office of Disease Prevention and Health Promotion, 2016; Oncology Nursing Society [ONS], 2016; Schmitz et al., 2010). Research is required to establish specific and individualized guidelines for the different cancer types and stages (Brown & Schmitz, 2014). In addition, consideration must be given to factors such as age, access, and comorbidities. A paradigm shift is needed, and a standard-of-care model for patients with cancer is necessary to ensure appropriate and maximum health outcomes for patients in the cancer treatment continuum. A standard-of-care model would not only benefit the healthcare community as a whole, but also empower patients to advocate for and become experts in their own health and increase their health benefits. To implement a program, such as FSFL, structured and individualized exercise for each patient should be appropriately prescribed based on the patient's condition, needs, and abilities. A standard-of-care model should include resistance training (e.g., dumbbells, stretch bands), flexibility exercise to prevent injury (e.g., stretching), core-strengthening exercises (e.g., stability ball, squat machine, side walking, standing on one leg), and aerobic exercises (e.g., treadmill, elliptical, cycling). Trained staff with degrees in exercise science are critical to ensure that the exercise is individualized, safe, and administered for optimal benefit. An added benefit of a standardized model is that it enables collection of data to advance exercise science in the cancer population. A customized software program created by FSFL tracks program activity and monitors each participant's exercise sessions by recording specifics, such as intensity, duration, and monitored metrics, will help advance exercise science. Customized software can use real-time texting to provide patients with reminders to enhance consistent exercise adherence. Software also provides a resource for research data collection from multiple locations without geographic boundaries.

If a targeted exercise program for patients with cancer does not exist in a geographic area, several measures can be taken to help establish such a center. First, a needs assessment should be done to identify available resources and determine what is needed in the community. If resources are limited, plans to expand resources can be instituted. The specific exercise plans should be made in consultation with a clinical exercise physiologist, according to the guidelines

provided by organizations, such as the ONS (2014) Get Up, Get Moving campaign and the *Healthcare Providers' Action Guide* developed by the Exercise is Medicine® (2016) initiative. Once resources are in place, increasing awareness of healthcare professionals and the community is paramount. Staying abreast of practice changes is important to provide optimal care for the patient. Nurses play a key role in recommending exercise to patients and cancer care providers until a standard-of-care model is adopted and exercise becomes a part of treatment paradigm.

## Case Study Revisited

At the initial visit for Marjorie, a thorough assessment at FSFL was completed. Marjorie's goal was to walk without "huffing and puffing" on oxygen. The staff prescribed daily visits to the center initially. After one week in the program, Marjorie no longer required oxygen during exercise and was able to walk for nine minutes at 0.8 mph on a treadmill.

During the next seven months, Marjorie continued to attend the FSFL center three days per week. Her treadmill time and intensity were gradually increased, and additional exercises were added to improve strength and balance. At the end of 210 days, Marjorie was completing 30 minutes on the treadmill at 1 mph off oxygen, in addition to her strength and balance exercises. After seven months, Marjorie's cancer progressed. Because Marjorie came to the center with stage IV breast cancer, cure was never an expectation. However, an individual program of exercise provided Marjorie with a significant improvement in quality of life. She met her goal of walking without "huffing and puffing" and was able to enjoy her remaining time with her children, grandchildren, and great-grandchildren. Although it was not measured, healthcare costs (e.g., oxygen, hospitalizations, care providers) were likely reduced significantly as a result of her exercise program.

## Conclusion

Marjorie's story is one exemplar of the impact that exercise can have on the lives of patients with cancer. The research that supports the benefits of exercise for the general population has also demonstrated that exercise is effective in the population of patients receiving treatment for cancer. Exercise provides numerous benefits to patients with cancer, and

### Implications for Practice

- ▶ Serve as patient advocates by heightening awareness about the benefits of exercise to patients throughout the cancer continuum.
- ▶ Use available resources to incorporate exercise recommendations into treatment plans.
- ▶ Perform individual patient assessment prior to recommending a specific program of exercise.

it may also prevent occurrence and recurrence of cancer. It is now up to healthcare providers from all disciplines, including oncology nurses, to translate this science into practice and make exercise a standard of care in cancer treatment.

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