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Comprehensive Medicine Approach Towards Cancer Sufferers and Survivors: A Review

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ABSTRACT

Despite significant improvements in cancer diagnosis, prevention, and care, cancer is still expected to be the biggest cause of mortality worldwide. Cancer prevalence and fatality rates are both increasing. There are numerous cancer treatment options. The type of cancer and its stage determine the sort of treatment required. Surgery, chemotherapy, and radiation are examples of traditional therapeutic procedures. At the same time, significant advances have been made recently, including stem cell therapy, targeted therapy, natural antioxidants, radionics, chemodynamic therapy, and ferroptosis-based therapy. Most patients have a combined approach-surgery, chemotherapy, and radiation therapy. Current methods in oncology focus on developing safe cancer nanomedicines. To obtain novel diagnostic and therapeutic alternatives, stem cell treatment has demonstrated potential success. Cancer cell spread can be slowed by targeted treatment, which protects healthy cells from harm. The long-term cancer survivors suffered in terms of body image concerns, emotional and social, and spiritual/ philosophical issues leading to poor quality of life in these patients. The positive attribute of complementary medicine and alternative therapies is that they enable patients to help themselves while undergoing cancer treatment and afterward. This review explores recent comprehensive approaches for cancer and associated effects leading to psychological issues.

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INTRODUCTION

Cancer prevalence and fatality rates are increasing all over the world. Cancer is the top cause of death in 112 nations before the age of 70, and it ranks third or fourth in another 23. Cancer was responsible for around 19.3 million new cases and over 10 million deaths globally in 2020, with 28.4 million new cases projected in 2040.[1] There are numerous cancer treatment options. The type of cancer and its stage determine the sort of treatment required. Some cancer patients only receive one treatment. However, most patients have combined approach surgery, chemotherapy, and radiation therapy. Additionally, one might receive hormone therapy, targeted therapy, or immunotherapy. [2] The absence of local tumor cell infiltration and distant metastases are typically necessary conditions for surgical treatment to be successful. Cytotoxic chemicals are used in chemotherapy regimens to stop cancer cells from proliferating, invading, and metastasizing. The first anti-cancer medicine was mechlorethamine, a nitrogen mustard alkylating agent introduced to the market in 1949. Since then, steadily more anti-cancer medications have been introduced to the market.[3] Since 2022, oncology has remained the top indication for FDA-approved medications.[4] Drug efficacy and negative side effects are typically compared to assess the therapeutic effects. Target-based medications have gradually replaced conventional treatments as technology advanced into the twenty-first century. [5, 6] Effective cancer treatment and drug development are hampered by several factors, including the inability of the tumor site to be reached by the proper drug concentration, the debilitating adverse effects brought on by the non-selective tissue distribution of chemotherapeutic agents, and the occurrence of drug resistance, which results in cross-resistance to various drugs. [7, 8] Drugs that mark and eject cancer cells so chemotherapeutic agents cannot target

them are the most prevalent cause of drug resistance. Drug resistance to anti-cancer treatment comes from a variety of circumstances. Additionally, medication-induced apoptosis that is not sensitive to the drug, drug target alteration and mutation, and interference with or alteration of DNA replication are other major factors leading to treatment failure.[8, 9] Developing a revolution in neoplastic cancer or medications targeting specific tumor entities relies on those pathways and traits.[10] When used alone or in conjunction with radiotherapy, chemotherapy is thought to be the most efficient and often employed treatment option for cancer. Chemotherapy medications target tumor cells primarily by creating reactive oxygen species, which especially kill tumor cells.[11] Hormonal treatments are also often employed in the treatment of malignant malignancies. They are cytostatic because they suppress tumor growth by reducing hormonal growth factors that work through the hypothalamic-pituitary-gonadal axis, inhibiting hormone receptors and lowering the generation of adrenal steroid hormones.[12] Despite significant improvements in cancer diagnosis, prevention, and care, cancer is still expected to be the biggest cause of mortality worldwide.[9] This review explores recent comprehensive approaches for cancer and associated effects leading to psychological issues.

METHODS FOR SEARCHING

We explored the literature, the articles related to cancer, available therapeutic approaches, associated side effects with each therapy (chemotherapy, surgery, and radiation therapy), novel approaches to treat cancer, available comprehensive approaches to control the side effects, and their role in improving quality of life. We browsed Cochrane, PubMed, Scopus, Embase, and Google Scholar databases. Keywords used are (cancer) (tumor[MeSH Terms]) AND (Cancer[MeSH Terms])) AND (chemotherapy[All Fields]) OR (Surgery)) OR (radiation therapy[MeSH Terms])) OR (hormone therapy[MeSH Terms]), OR (immune therapy[MeSH Terms]), OR (target therapy[MeSH Terms]), OR (comprehensive approaches [MeSH Terms])) OR (adverse effects[MeSH Terms]) OR (quality of life) OR (complementary Therapy [MeSH Terms]) OR (Chiropractic therapy)) OR (Reflexology, massage) OR (Energy healing[MeSH Terms]), (Ayurvedic medicine [MeSH Terms])) OR (Naturopathic medicine [MeSH Terms]), OR (mind-body practice [MeSH Terms]),

Therapeutic modalities for cancer

There are numerous cancer treatment options. The type of cancer and its stage determine the sort of treatment. Only one treatment is given to certain cancer patients. However, most patients have a combination of therapies, such as surgery, chemotherapy, and radiation therapy. Other treatments are available, including hormone therapy, targeted therapy, and immunotherapy.[13]

Cancer Surgery

Surgery is a procedure used to remove or repair a physical part or diagnose an ailment. It is as popular as operation. Most malignancies are treated curatively and palliatively with surgery in nations of various income levels. Surgical excision offers conclusive locoregional control of the main tumor in high-income countries (HICs), where the most prevalent solid organ malignant tumors (breast and colon cancers) are more likely to be effectively diagnosed at an early stage. This strategy has substantial curative potential when used with well-chosen adjuvant systemic therapy, radiation, and other therapeutic measures. Surgical excision or debulking may be among the few methods accessible in low- and middle-income countries (LMICs), where locally progressed or metastatic cancer is frequently the primary illness presentation.[14]

Cancer control debates in LMICs have not given surgery enough consideration. [15, 16] Due to competing health goals and significant budgetary constraints, surgical procedures are assigned low priority under national health plans and receive inadequate resources from internal accounts or foreign development aid programs. [17, 18]

As a result, access to safe, ideal surgical services for cancer is generally limited in low-income countries (LICs) and many middle-income countries (MICs), and significant segments of the population cannot get even the most basic surgical care. [19]

Chemotherapy

Chemotherapy is a medical procedure that employs medications to destroy or restrict the division of cancer cells to stop the spread of the illness. Depending on the type and stage of the cancer being treated, chemotherapy can be given intravenously, orally, intramuscularly, topically, or by any combination of these methods. It can be used separately or with other therapies such as surgery, radiation, and biological treatment.[20, 21]

Chemotherapy slows the development and cell division of the tumor, reducing invasion and metastasis. Chemotherapy, on the other hand, can be hazardous since it also destroys healthy cells. Conventional chemotherapy medications considerably disturb malignant cells' macromolecular synthesis by interfering with the formation of DNA, RNA, or proteins or hindering the normal operation of the created molecule. Chemotherapeutic chemicals either directly kill cells or cause apoptosis due to a major macromolecular synthesis or activity interruption. Cell death may be postponed because traditional medications only kill a small fraction of the treated cells. As a result, the medicine may need to be administered a second time to elicit a reaction. Combination chemotherapy is routinely utilized to get good outcomes. They appear to do this by promoting cytotoxicity in resting and growing cells, preventing the formation of resistant clones. [22]

Following the release of the Lindskog article demonstrating nitrogen mustard's efficacy in treating lymphoma, particularly oral derivatives like chlorambucil and

cyclophosphamide, a significant early influence on cancer therapy development was made. [21] The discovery of actinomycin D sparked a search for more anti-cancer drugs, such as anthracyclines, mitomycin, and bleomycin. [23] Antimetabolites with the antifolate activity known as aminopterin, later methotrexate, were first demonstrated to be effective in treating pediatric leukemia. [24] The effectiveness of methotrexate in treating choriocarcinoma and leukemias encouraged further study into cancer therapies. Thiopurines, such as 6-mercaptopurine and 5-fluorouracil, also gained popularity as cancer treatments.[25]

Rituximab and trastuzumab received approval for treating lymphoma and breast cancer, respectively, in the late 1990s. [26] Molecular targeted therapy is a novel method of treating cancer. [21] Over the past ten years, the US FDA has approved several substances. Similarly, researchers are working on molecular targeted treatment, which selectively suppresses growth by focusing on cell signaling or angiogenesis, such as limiting protein breakdown. A different part is devoted to targeted therapy. Immune checkpoint inhibitors (PD1, CTLA 4, and PDL1) frequently activate the immune system against cancer cells. A separate discussion is given to immunotherapy from other subjects. [27] Chemotherapy drugs can be injected intrathecally, subcutaneously, intravenously, or intramuscularly. Some chemicals, like paclitaxel, must be mixed with solvents, such as cremophor, for better absorption. Doctors should be mindful of absorption factors such as surgery and stomach motility, especially in cancer patients using opioids. Chemotherapeutic substances are mostly processed and eliminated by the liver and kidneys. Some chemotherapy medications can harm the kidneys or liver. Toxic accumulations may induce organ failure in certain conditions. As a result, it is critical to consider dosage modifications in severe organ failure patients. Capecitabine doses vary for patients with renal impairment. [28]

Chemotherapy medications are frequently administered using the body surface area dose approach. The cytochrome P450 (CYP) enzyme is involved in the metabolism of several chemotherapy drugs. Bortezomib, docetaxel, etoposide, imatinib, sunitinib, sorafenib, and vinca alkaloids are all metabolized by CYP3A4/5. Some common medications have potent inducers, such as phenobarbital and phenytoin, and potent inhibitors, such as grapefruit juice and ketoconazole, of CYP enzymes, which can change the drug levels of chemotherapeutic agents and either reduce their efficacy or increase their toxicity. [20]

Chemotherapy substances

Nitrogen mustard, cyclophosphamide, lomustine, platinum analogs carboplatin, ifosfamide, carmustine, cisplatin, oxaliplatin, procarbazine, temozolomide, alkyl sulfonate, triazenes, dacarbazine, busulfan, and ethyleneimine are examples of alkylating agents. These drugs react with nucleophilic centers on proteins and nucleic acids to form R-CH2+, an unstable alkyl group. Impede transcription and DNA replication. [29]

Cytidine analogs include azacitidine, decitabine, gemcitabine, and cytarabine. Folate antagonists include methotrexate and pemetrexed. Purine analogs include cladribine, clofarabine, and nelarabine. Pyrimidine analogs include fluorouracil (5-FU) and capecitabine (a prodrug of 5-FU). These medications prevent DNA replication.[28, 29]

Antimicrotubular Agents are inhibitors of topoisomerase II: Anthracyclines (doxorubicin, daunorubicin, idarubicin, mitoxantrone), Topoisomerase I Inhibitors (irinotecan, topotecan), Taxanes (paclitaxel, docetaxel, cabazitaxel), Vinca Alkaloids (vinblastine, vincristine, vinorelbine), etc. [20,28]

Actinomycin D, bleomycin, and daunomycin are three antibiotics used in chemotherapy. These medicines prevent the production of RNA and DNA.

Hydroxyurea, Tretinoin, Arsenic Trioxide, and Proteasome Inhibitors are categorized as Miscellaneous.[28] **Table 1**

Table 1 Biological Cancer Treatment/Chemotherapy.

Therapy		Mechanism	Side effects
Chemotherapy	Cytostatic drugs	Interfere with cell proliferation	Grade 1-4
	Small molecule inhibitors	Targeted therapy: Interfere with oncogenic signal transduction	Grade 1-4
Biological cancer therapy	Antitumor MAbs	Targeted immunotherapy	Grade 1-3
	Anti-angiogenesis MAbs	Inhibit angiogenesis	Grade 1-3
	Checkpoint inhibitor MAbs	Immune regulation	Grade 1-4
	CAR-T cells	Targeted cytotoxic T lymphocytes	Grade 1-3
	Antitumor vaccines	Active specific vaccination	Grade 0-2
	Oncolytic viruses	Oncolysis, induction of immunogenic cell death	Grade 0-2
Note- Grade 1- mild, Grade 2- moderate, Grade 3- severe, Grade 4- or life-threatening Text is referenced. [30,31]			

The other medicines are biological, while cytostatic chemotherapy medications and SMIs are chemical therapies. Table 1 lists these medications' modes of action and negative effects.

According to the WHO categorization, its intensity can range from grade 1-4 (Mild, moderate, severe, life-threatening, or disabled). Skin, hair, bone marrow, blood, digestive systems, and kidneys are all affected immediately. All human organs, particularly critical ones such as the heart, lungs, and brain, are vulnerable to harm. Neurotoxicity in grades 3 and 4 can cause coma, paresthesia, paralysis, ataxia, spasms, and drowsiness. Infertility, carcinoma, and resistance to drugs are also long-term complications of chemotherapy.[31]

Radiation treatment

It uses high-energy radiation from x-rays, neutrons, gamma rays, and protons to kill and shrink tumors. Internal radiation treatment (Brachytherapy) delivers radiation to cancerous cells using radioactive material inserted within the body. External-beam radiation therapy uses a machine to administer radiation outside the body. In systemic radiation therapy, a radioactive substance penetrates tissues all over the body. They are commonly referred to as irradiation and radiotherapy.

Before the introduction of improved external beam radiation techniques and surgical approach developments in the twentieth century, Brachytherapy was critical in treating deep-seated tumors. [32, 33] Brachytherapy was often used as an adjuvant for soft-tissue sarcoma and breast cancer. Even though Brachytherapy no longer has as much of an impact as it formerly did, it is still a crucial component of the care of cervical cancer. Furthermore, Brachytherapy is supported by a committed but modest network of professionals. [34]

In the early years of Brachytherapy (1900e1955), source location was governed by a set of rules for geometry, source strength, and treatment duration. A regular form was used to estimate the objective volume, and treatment planning was carried out utilizing operating data previously obtained from tables. According to the rules, the target received an appropriate dose with an acceptable distribution. X-ray projection pictures taken from two different angles to verify and validate source placements allowed for some two-dimensional planning. Various predictive dosimetric systems, such as the Quimby, Paris, Manchester-Paterson-Parker, and Memorial systems for interstitial Brachytherapy and the Manchester, Stockholm, Fletcher, Manchester, Stockholm, Paris systems for intracavitary Brachytherapy, were developed based on clinical experience and simple dose calculations. [34]

Immunotherapy

To support the body's defenses against cancer, infections, and other diseases, immunotherapy is a treatment that either strengthens or weakens the immune system. Some immunotherapy treatments only target immune system cells. Others affect the immune system broadly. Examples of immunotherapy kinds include cytokines, vaccines, bacillus Calmette-Guerin (BCG), and specific monoclonal antibodies. [35, 36] Cancer is treated with immunotherapy in various ways. Immunological checkpoint inhibitors, which are medications that disable immunological checkpoints, are among them. These immune system checkpoints are typical components that prevent overly powerful immune responses. These medications avoid them, allowing immune cells to react forcefully to malignancy. [37]

T-cell transfer therapy is a procedure that improves T cells' innate capacity to combat cancer. Tumors' immune cells are removed to employ this therapy. The most potent ones are chosen or altered in the lab, generated in large numbers, and injected back into the body via a needle inserted into a vein. [38]

Immune cell treatment is another name for T-cell transfer therapy. Monoclonal antibodies, immune system proteins, are manufactured in a lab to attach to particular spots on cancer cells. Some monoclonal antibodies recognize cancer cells, allowing the immune system to detect and eliminate them more easily. The immunotherapy category includes these monoclonal antibodies. Monoclonal antibodies are another term for therapeutic antibodies. [39] Cancer immunizations boost the way the immune system reacts to cancer cells. Vaccines for treating diseases are distinct from those that aid in disease prevention.[40] Modulators of the immune system improve the body's defenses against cancer. Some substances impact certain resistant system components, while others have a broader impact. Immunotherapy can be administered orally, topically, intravenously, and orally, among other ways. [41]

Researchers at the National Cancer Institute have devised a unique immunotherapy strategy that has completely regressed breast cancer in a patient who had failed all conventional treatments. Immune check point inhibitors and CAR T cell treatments are new drugs that have produced significant and long-lasting impacts in some patients. Rarely people with advanced malignancies have experienced the total disappearance of their tumors after receiving immunotherapy.[36] Fig. 1

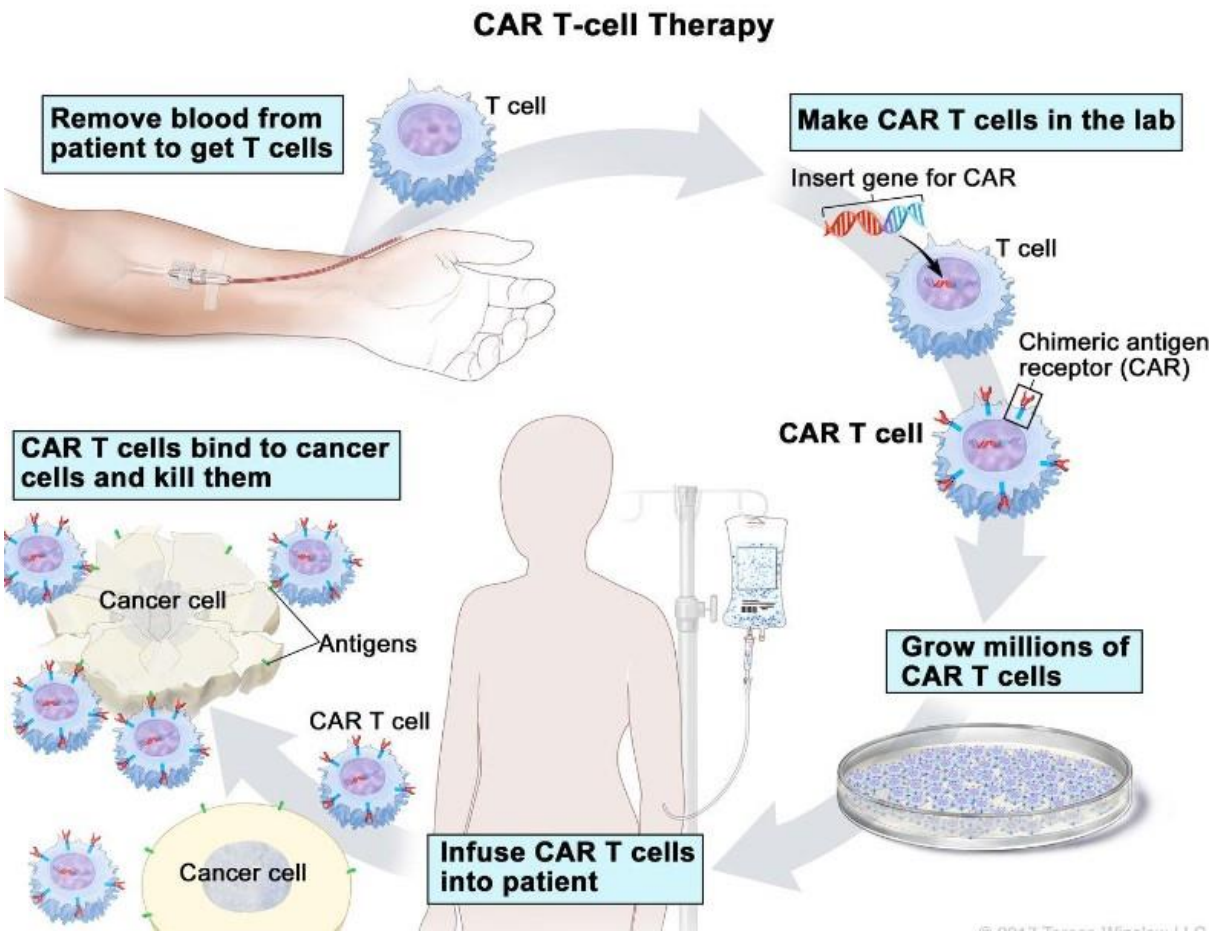

Fig. 1 CAR T-cell therapy [37]

Using a genome-wide DNA methylation study, Delacher et al. identified tissue-restricted Tregs. Tregs can adapt to specific tissue locations according to well-defined epigenetic mechanisms. Tissue-restricted Tregs, therefore, aid in organ homeostasis and self-tolerance. [42] Table 2 outlines the several self-tolerance routes in T and B cells. These data support the importance of immunological tolerance to self-antigens in immune system evolution. Table 2

The types of adverse effects an immunotherapy patient suffers will vary depending on the immunotherapy, the dose, the patient's health before treatment, the kind of cancer, and the stage of the illness.

Table 2 Self-tolerance in T and B lymphocytes.

	B lymphocytes	**T lymphocytes**
Induction site	Bone marrow and periphery	The thymus (cortex) and periphery
Maturation stage	Immature IgM^+IgD^- B cell	$CD4^+CD8^+$ thymocyte
Stimuli	Recognition of multivalent antigens in the bone marrow (Central)	High-avidity recognition of antigens in the thymus (Central)
	Peripheral: Antigen recognition without T-cell help or second signals	Antigen presentation by antigen-presenting cells devoid of costimulators (peripheral)
Tolerance mechanism	Deletion or receptor editing (Central)	Deletion or regulatory T cells (Central)
	Block in signal transduction, failure to enter lymphoid follicles (Peripheral)	Energy, suppression, apoptosis (Peripheral)

Note- Above the text is referenced.[35]

The most frequent side effects for individuals receiving immunotherapy medications intravenously are skin reactions at the injection site, such as discomfort, swelling, and soreness. Although rare, some immunotherapy medications can potentially induce serious or fatal adverse responses. Compared to other cancer therapies, the timing of

immunotherapy-related side effects is less predictable. Immunotherapy patients may experience adverse effects right away after the first dose of a medication or months or years after the course of treatment has concluded. [36]

Hormone therapy

Hormonal therapy that alters, inhibits, or enhances hormones. To treat some diseases (such as diabetes or menopause), hormones raise low hormone levels. In addition, some malignancies, such as breast and prostate cancer, can be made to grow faster by hormones. It is possible to slow or stop the spread of cancer by using artificial hormones. These other drugs inhibit the body's natural hormones or surgical removal of the gland that makes a specific hormone—additionally referred to as hormone therapy, hormone treatment, and endocrine therapy. To stop or slow cancer progression, hormone therapy uses medications to block or reduce the amount of hormones in the body. Breast, prostate, ovarian, and womb cancer (also known as uterine or endometrial cancer) are among the cancers that can be hormone-sensitive.[43]

Hormone treatment is one sort of hormonal therapy used for the treatment of breast cancer. Tamoxifen is a drug that is used. Tamoxifen inhibits estrogen receptors, which is how it works. It prevents estrogen from instructing cancer cells to proliferate. People with a high risk of breast cancer may receive hormone therapy (tamoxifen or raloxifene). The term for this is chemoprevention. Both premenopausal and postmenopausal women are advised for tamoxifen. [44]

Anti-Aromatase Drugs

Aromatase inhibitors prevent aromatase from converting androgens into estrogen by blocking it. Aromatase inhibitors come in a few different varieties, such as exemestane (Aromasin), anastrozole (Arimidex), and letrozole (Femara). [45]

Agonists of the hormone-releasing luteinizing hormone (LHRH) or LH blockers

LH blockers stop the pituitary gland from sending signals to the ovaries. This medication won't assist because the ovaries stop producing hormones after menopause. Goserelin (Zoladex) is one variety that is used to treat breast cancer.[46]

Fulvestrant

By inhibiting estrogen receptors and limiting the number of cancer cells' receptors, fulvestrant (Faslodex) prevents estrogen from reaching the cancer cells. This might be taken in addition to other cancer medications. **[47]**

Therapy for prostate cancer

The amount of testosterone in the body is either blocked or reduced by hormone therapy.

Luteinizing hormone (LH) blockers

LH blockers are medications that prevent the luteinizing hormone from being produced. They do this by obstructing the signal from the pituitary to the testicles. Consequently, the testicles quit producing testosterone. Goserelin (Zoladex), leuprorelin (Prostap), and triptorelin (Decapetyl) are three different types of prostate cancer medications. [48]

Androgen blockers

Bicalutamide (Casodex), cyproterone acetate (Cyprostat), and flutamide (Drogenil) are a few examples of several anti-androgens. Anti-androgen medications function by binding to these receptors. By doing this, testosterone is prevented from getting to prostate cancer cells. [49]

Gonadotrophin-releasing hormone (GnRH) Blockers

The testicles are instructed to manufacture testosterone by luteinizing hormone. Therefore, inhibiting GnRH prevents the testicles from generating testosterone. Degarelix (Firmagon), a medication, inhibits GnRH. Gonadotrophin-releasing hormone (GnRH) blockers prevent the pituitary gland from producing luteinizing hormone by blocking impulses from the brain region's hypothalamus. [50]

Various hormone treatments

Other more recent hormonal therapies are available for prostate cancer. These treatments consist of enzalutamide, abiraterone, and darolutamide. [51]

Progesterone comes in various forms, including megestrol (Megace) and medroxyprogesterone acetate (Provera). [43]

The feminine hormones estrogen and progesterone influence the formation and operation of the cells lining the womb. Medical practitioners utilize progesterone therapy to treat larger or recurrent womb cancers.

Target therapy

A targeted treatment that employs medications or other substances to target specific compounds required for cancer cells to survive and proliferate. Targeted therapies treat cancer in various ways. Others prevent the signals that help blood vessels form, others avoid the signs that let cancer cells grow and divide, some deliver substances that kill cancer cells, and others deprive cancer cells of the hormones they need to succeed. Other specific medications either destroy cancer cells directly or work with the immune system to do so. Small-molecule drugs or monoclonal antibodies make up the majority of targeted therapies. Researchers are working on molecular targeted therapy along similar lines, which directly prevents cancer growth by targeting cell signaling or angiogenesis or preventing protein breakdown. [20]

Some targeted medicines can identify cancer cells to make it simpler for the immune system to locate and eradicate them. Immune checkpoints safeguard the body's healthy cells from being destroyed by an immune response that is too powerful. Immune checkpoints activate when partner proteins are recognized and bound by proteins on the surface of T cells. [35, 36]

By blocking the signals that allow cancer cells to divide and expand out of control, cancer cells can be prevented from spreading. [52]

Stop signs that support blood vessel development. Angiogenesis inhibitors are a group of specialized drugs that block these signals to prevent the growth of a blood supply.

Tumors remain tiny in the absence of blood supply. However, if a tumor already has blood circulation, these treatments may

decrease the malignancy by destroying the blood vessels that support it. [53]

It distributes chemicals that attack cancer cells. Some monoclonal antibodies are combined with substances that can kill cells, like toxins, chemotherapy drugs, or radiation. These monoclonal antibodies bind to particular regions of the cancer cell's surface, causing the cancer cells to take up the cell-killing substances and die. Cells won't be harmed without the target. [54]

Healthy cells naturally die when they are damaged or no longer needed, killing malignant cells in the process. Cancer cells, however, can avoid this form of death. Some targeted medications can cause cancer cells to undergo apoptosis, which kills them. [55]

It deprives the cancer of the hormones it needs to thrive. Some malignancies, such as prostate and breast cancer, require particular hormones to grow. Hormone treatments inhibit the production of specific hormones in the body. Cancerous cells belong to those that inhibit hormone action on cells. [43]

Side effects frequently accompany the use of chemotherapeutic drugs. In cancer, cytotoxic therapy often targets the synthesis of DNA and proteins. Most chemotherapy drugs act on quickly proliferating cells; they hit cells that multiply immediately. Toxicities associated with such chemicals include myelosuppression, mucositis, infertility, nausea, vomiting, alopecia, diarrhea, infusion reactions, fatigue, and sterility. Furthermore, immunosuppression raises the chance of infection. **[56- 58]**

Cancer patients may experience life-threatening side effects from chemotherapy, which frequently happen at home. [56] Chemotherapy's physical side effects have generally been well-documented. Bone marrow suppression, neuropathies, gastrointestinal issues, hair loss, exhaustion, and skin conditions are some of chemotherapy's most typical adverse reactions. Also included are several negative effects, particularly on certain medications. [59-61] For instance, bleomycin and anthracyclines are linked to pulmonary and cardiotoxicity, respectively.[62]

Patients taking oral anti-cancer medications who are younger and have concomitant illnesses may experience more severe symptoms. The possibility of chronic diseases being included in symptom attribution increased with more comorbidities and the absence of concurrent IV chemotherapy. Patients said that the use of oral anti-cancer medications made it difficult to control coexisting conditions.[63] However, after treatment regimens, patients had various degrees of symptom intensity. Greater symptom severity and number were linked to female gender, older age, advanced cancer stage, low socioeconomic level, and total gastrectomy. [64] It is alarming how common adverse effects from chemotherapy are among local patients. Clinical chemists may find the results of their perceptions and informational requirements useful when managing side effects. Therefore, oncology healthcare providers must be able to identify the side effects that their patients are experiencing and, if possible, assist in resolving these issues. [65-67] It is significant to note that people who took chemotherapy had more advanced cancer, had completed various forms of treatment, and may have experienced more symptoms and had a greater impact on daily living. [65] It should be highlighted that some innovative medications, in addition to cytostatic agents over the past ten years, can potentially cause serious adverse effects (AEs). [30] According to the study analysis, the occurrence of chemotherapy side effects in advanced colorectal cancer is a reliable and independent predictive factor for survival and response. [68]

Not only can targeted therapy approaches have adverse consequences, but many patients also experience multidrug resistance, which lowers their quality of life. The primary reason cancer chemotherapy fails is multidrug resistance (MDR). Antitumor medication development that can resist MDR is progressing quickly, demonstrating how highly the scientific community values this area of biomedical research. [69] Examining the MDR-modulating characteristics of diverse groups of natural substances and their analogs has yielded encouraging findings. The primary methods for overcoming MDR have been shown to include inhibiting P-gp or decreasing its expression. To overcome treatment resistance, researchers now consider using hybrid compounds that can interact with two or more cancer cell targets concurrently. This tactic is based on creating hybrid combinations, which can be made by combining the structural components of different medications or by conjugating two pharmaceuticals or pharmacophores using cleavable/non-cleavable linkers. The method is promising since it can achieve better pharmacokinetic and pharmacodynamic results than if the two components were administered separately. It should be emphasized, nonetheless, that developing effective multivalent medications is an extremely difficult process. [70]

The knowledge of the mechanisms behind the development of medication resistance has improved recently. [71, 72] These have created brand-new tactics to avoid or defeat known drug resistance pathways. These tactics include tweaking the anti-cancer medications already on the market to improve their capacity to target tumor cells, which has always been a key goal in the fight against cancer MDR. Even though these symptoms influence patients' psychosocial well-being, they are very common. To improve patient's quality of life (QOL), which could ultimately affect their willingness to complete the course of treatment, it is crucial to control the side effects of chemotherapy effectively. [66, 67] Chemotherapy side effects are a significant and frequently unnoticed clinical barrier in cancer treatment. They may harm a patient's quality of life and the course of their therapy. Positive support networks, asking for assistance, healthcare provider interventions, and self-management techniques were the four themes that arose while discussing symptom control techniques. Building social support networks, enhancing health literacy, enhancing continuity of treatment, receiving assistance from healthcare professionals, engaging in health-seeking activities, and

addressing unmet supportive care requirements were suggested to obtain external support. [65]

Complementary and Alternative medicine

Cancer patients may use complementary and alternative medicine (CAM) to manage the treatment side effects such as fatigue, nausea, and pain, as well as to comfort themselves and lessen their anxiety about the disease and its care, feel like they are participating in their care, and try to treat or cure their cancer. [73] Integrative medicine is a patient-centered approach that integrates traditional medical treatment with complementary and alternative medicine (CAM) methods that have been scientifically proven safe and effective. This approach addresses wellness's mental, physical, and spiritual elements while emphasizing the patient's preferences. [74] In traditional medicine, doctors treat symptoms and diseases with drugs, radiation, or surgery. In addition to physicians and nurses, chemists, physician assistants, and therapists also practice it. Other titles for it include biomedicine, Western, mainstream, or orthodox medicine. Some medical experts who practice CAM also provide traditional medical care. Standard medical care refers to practices regularly used by healthcare professionals and accepted as effective treatments for a particular ailment category. Sometimes referred to as best practice, traditional therapy, and standard of care. [75] Complementary medicine is not viewed as a kind of care in and of itself, despite being utilized in conjunction with traditional medical care. One example is acupuncture, to help relieve some side effects of cancer treatment. Most complementary medical practices have not gotten much scientific scrutiny. Alternative medicine is used in place of conventional medical therapy. One example is substituting a certain diet for cancer treatments prescribed by an oncologist. Less research has been done on the bulk of alternative medicine practice. [76]

Types of Alternative and Complementary Medicine

Researchers discover new things about CAM treatments every day, but there is still plenty to learn. This list is not a recommendation; it serves as an introduction to the many CAM practices. The efficacy of a few therapies described below still requires further study. [76]

Mind Body Therapies

These help to relax the body and mind by combining mental attention, breathing, and physical movement. There are various therapies, for instance, meditation, b*iofeedback, hypnosis, imagery, yoga, and tai chi.*

Meditation, quieting the mind, and reducing unpleasant thoughts and feelings through concentrated breathing or word or phrase repetition.

Biofeedback is utilizing specialized equipment, and the patient learns how to regulate some bodily processes (including heart rate and blood pressure) that are typically unconscious.

Hypnosis is a trance-like state where a person is more focused on specific emotions, thoughts, visions, and sensations. It helps patients to feel more open to express aid in their healing.

Yoga is an age-old method of exercise that uses controlled breathing, stretches, and positions to balance the mind and body.

Tai chi is a moderate meditation exercise incorporating controlled breathing and slow body movements.

Imagery concentrates on uplifting mental images, such as conjuring up pictures or experiences to aid in the body's recovery; creative outlets: pursuits in music, dance, or other artistic endeavors [77]

Biologically based practices

This kind of CAM makes use of natural resources. Vitamins are one type of nutrition the body needs in small amounts to function and be healthy. Dietary supplements are another nutrient-rich food that may be added to the diet. Plants or plant parts are known as botanicals. Cannabis is one kind. Herbs & seasonings. [78]

Manipulative and body-based practices

These are based on manipulating one or more bodily parts. Examples include massage therapy, which involves massaging the body's soft tissues using kneading, tapping, and stroking; Chiropractic therapy manipulates the skeleton, joints, and spine. [79] Reflexology is a massage in which pressure is administered to certain places on the hands or feet that correspond with certain bodily parts. [80]

Energy healing

The objective and foundation of energy healing is a life force that permeates the body. It balances the patient's energy flow. The available data do not sufficiently support the presence of energy fields. However, no negative consequences have been noticed in the application of this therapy. [81] Reiki, for instance, is softly placing hands on or just above the subject to direct energy to support the individual's healing reaction. [82] Therapeutic touch: passing hands over a person's body's energy fields or lightly touching them. [83]

Integrative medicine

Although a placebo effect couldn't be ruled out, there were only modest improvements in pain. These belief systems and healing methods have developed in various societies and civilizations. [84] These are ayurvedic, traditional Chinese, and naturopathic medicine**.**

Ayurvedic medicine: an Indian system that aims to purify the body and restore harmony to the body, mind, and soul. It uses dietary restrictions, natural remedies, physical activity, breathing exercises, and other techniques.

Traditional Chinese medicine is predicated on the idea that qi, the body's life force, travels along meridian channels and maintains equilibrium in a person's physical, mental, emotional, and spiritual well-being. It seeks to reestablish the harmony between the yin and yang energies in the body. Surgery and medications are not used in naturopathic medicine. Its premise is that the body can heal through natural

components, including air, water, light, heat, and massage. In addition, it might use acupuncture, diet, herbal remedies, and aromatherapy. [85]

CONCLUSION

Surgery, chemotherapy, and radiation have all been utilised as traditional treatments. Recent examples of significant improvements include using stem cells, customized therapy, naturally occurring antioxidants, chemodynamic therapy, radionics, and ferroptosis-based therapy. The majority of patients use a combination of radiation therapy, chemotherapy, and surgery. Today's oncology practices are focused on developing safe cancer nanomedicines. Stem cell treatment has shown promise in developing new diagnostic and therapeutic approaches. Targeted treatment can slow or stop the spread of certain cancer cells while shielding healthy cells from harm. Long-term cancer survivors experience poor quality of life due to body image, emotional and social problems, and spiritual/philosophical issues. Complementary and alternative therapies empower patients to care for themselves during and after cancer treatment.

REFERENCES

I. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A. et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71:209–49.

II. Kifle ZD, Tadele M, Alemu E, Gedamu T, Ayele AG. Recent development of new therapeutic agents and novel drug targets for cancer treatment. SAGE Open Med. 2021;9:20503121211067083.

III. Pourquier P. [Alkylating agents] Bull Cancer. 2011;98:1237–51.

IV. de la Torre BG, Albericio F. The Pharmaceutical Industry in 2022: An Analysis of FDA Drug Approvals from the Perspective of Molecules. Molecules. 2023. 28.

V. Berdigaliyev N, Aljofan M. An overview of drug discovery and development. Future Med Chem. 2020;12:939–47.

VI. Eder J, Herrling PL. Trends in Modern Drug Discovery. Handb Exp Pharmacol. 2016;232:3–22.

VII. Assaraf YG, Brozovic A, Gonçalves AC, Jurkovicova D, Linē A, Machuqueiro M, Saponara S, Sarmento-Ribeiro AB, Xavier CPR, Vasconcelos MH. The multi-factorial nature of clinical multidrug resistance in cancer. Drug Resist Updat. 2019 Sep;46:100645.

VIII. Li YJ, Lei YH, Yao N, Wang CR, Hu N, Ye WC, Zhang DM, Chen ZS. Autophagy and multidrug resistance in cancer. Chin J Cancer. 2017 Jun 24;36(1):52.

IX. Kifle ZD, Tadele M, Alemu E, Gedamu T, Ayele AG. Recent development of new therapeutic agents and novel drug targets for cancer treatment. SAGE Open Med. 2021 Dec 23;9:20503121211067083.

X. Abbas Z, Rehman S. An overview of cancer treatment modalities. *Neoplasm* 2018; 1: 139–157.

XI. El-Hussein A, Manoto SL, Ombinda-Lemboumba S, et al. A review of chemotherapy and photodynamic therapy for lung cancer treatment. *Anti-cancer Agents Med Chem* 2021; 21(2): 149–161.

XII. Ghanghoria R, Kesharwani P, Tekade RK, et al. Targeting luteinizing hormone-releasing hormone: a potential therapeutics to treat gynecological and other cancers. *J Control Release* 2018; 269: 277–301.

XIII. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, Kitui SK, Manyazewal T. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Med. 2021 Aug 12;9:20503121211034366.

XIV. Dare AJ, Anderson BO, Sullivan R, Pramesh CS, Andre I, Adewole IF, et al. Surgical Services for Cancer Care. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. Cancer: Disease Control Priorities, Third Edition (Volume 3) [Internet]. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2015 [cited 2023 Jul 31]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK343623/

XV. Goss PE, Strasser-Weippl K, Lee-Bychkovsky BL, Fan L, Li J, Chavarri-Guerra Y. et al. Challenges to effective cancer control in China, India, and Russia. Lancet Oncol. 2014 Apr;15(5):489-538.

XVI. Purushotham AD, Lewison G, Sullivan R. The state of research and development in global cancer surgery. Ann Surg. 2012 Mar;255(3):427-32.

XVII. Bae JY, Groen RS, Kushner AL. Surgery as a public health intervention: common misconceptions versus the truth. Bull World Health Organ. 2011 Jun 1;89(6):394.

XVIII. Farmer PE, Kim JY. Surgery and global health: a view from beyond the OR. World J Surg. 2008 Apr;32(4):533-6.

XIX. Funk LM, Weiser TG, Berry WR, Lipsitz SR, Merry AF, Enright AC, Wilson IH, Dziekan G,

Gawande AA. Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. Lancet. 2010 Sep 25;376(9746):1055-61.

XX. Cancer Chemotherapy - StatPearls - NCBI Bookshelf [Internet]. [cited 2023 Jul 31]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564367/

XXI. DeVita VT, Chu E. A history of cancer chemotherapy. Cancer Res. 2008 Nov 01;68(21):8643-53.

XXII. Baserga R. The cell cycle. N Engl J Med. 1981 Feb 19;304(8):453-9.

XXIII. PINKEL D. Actinomycin D in childhood cancer; a preliminary report. Pediatrics. 1959 Feb;23(2):342-7.

XXIV. Farber S, Diamond LK. Temporary remissions in acute leukemia in children produced by folic acid antagonist, 4-aminopteroyl-glutamic acid. N Engl J Med. 1948 Jun 3;238(23):787-93.

XXV. Elion GB, Singer S, Hitchings GH. Antagonists of nucleic acid derivatives. VIII. Synergism in combinations of biochemically related antimetabolites. J Biol Chem. 1954 Jun;208(2):477-88.

XXVI. McLaughlin P, Grillo-López AJ, Link BK, Levy R, Czuczman MS, Williams ME, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol. 1998 Aug;16(8):2825-33.

XXVII. Chidharla A, Parsi M, Kasi A. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 8, 2022. Cetuximab.

XXVIII. Chemotherapeutic agent - an overview | ScienceDirect Topics [Internet]. [cited 2023 Aug 3]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/chemotherapeutic-agent

XXIX. Colvin M. Alkylating Agents. In: Holland-Frei Cancer Medicine 6th edition [Internet]. BC Decker; 2003 [cited 2023 Aug 3]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK12772/

XXX. Schirrmacher V. From chemotherapy to biological therapy: A review of novel concepts to reduce the side effects of systemic cancer treatment (Review). Int J Oncol. 2019 Feb;54(2):407-419.

XXXI. Seeber S, Schütte J, editors. *Therapiekonzepte Onkologie.* Springer-Verlag; Berlin, Heidelberg: 1993.

XXXII. Brachytherapy - an overview | ScienceDirect Topics [Internet]. [cited 2023 Jul 31]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/brachytherapy

XXXIII. External Beam Radiotherapy - an overview | ScienceDirect Topics [Internet]. [cited 2023 Jul 31]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/external-beam-radiotherapy

XXXIV. Gerbaulet A, Potter R, Mazeron JJ, Meertens H, Van € Limbergen E. The GEC ESTRO handbook of Brachytherapy. Brussels: ESTRO; 2002. Available at: http://books.google.at/books?id¼qALMHAAACAAJ.

XXXV. Abbas KA, Lichtman AH, Pillai S, editors. *Cellular and Molecular Immunology.* 6th Edition. Saunders Elsevier; Oxford: 2010. p. 261.

XXXVI. Immunotherapy for Cancer - NCI [Internet]. 2015 [cited 2023 Aug 1]. Available from: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy

XXXVII. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012 Mar 22;12(4):252-64.

XXXVIII. Park TS, Rosenberg SA, Morgan RA. Treating cancer with genetically engineered T cells. Trends Biotechnol. 2011 Nov;29(11):550-7.

XXXIX. Zahavi D, Weiner L. Monoclonal Antibodies in Cancer Therapy. Antibodies (Basel). 2020 Jul 20;9(3):34.

XL. Liu J, Fu M, Wang M, Wan D, Wei Y, Wei X. Cancer vaccines as promising immuno-therapeutics: platforms and current progress. J Hematol Oncol. 2022 Mar 18;15(1):28.

XLI. Waldman AD, Fritz JM, Lenardo MJ. A guide to cancer immunotherapy: from T cell basic science to clinical practice. Nat Rev Immunol. 2020 Nov;20(11):651–68.

XLII. Delacher M, Imbusch CD, Weichenhan D, Breiling A, Hotz-Wagenblatt A, Träger U, Hofer AC, Kägebein D, Wang Q, Frauhammer F, et al. Genome-wide DNA-methylation landscape defines specialization of regulatory T cells in tissues. *Nat Immunol.* 2017;18:1160–1172.

XLIII. Mitra S, Lami MS, Ghosh A, Das R, Tallei TE, Fatimawali, Islam F, Dhama K, Begum MY, Aldahish A, Chidambaram K, Emran TB. Hormonal Therapy for Gynecological Cancers: How Far Has Science Progressed toward Clinical Applications? Cancers (Basel). 2022 Feb 1;14(3):759.

XLIV. Nazarali SA, Narod SA. Tamoxifen for women at high risk of breast cancer. Breast Cancer (Dove Med Press). 2014 Feb 17;6:29-36.

XLV. Chumsri S, Howes T, Bao T, Sabnis G, Brodie A. Aromatase, aromatase inhibitors, and breast cancer. J Steroid Biochem Mol Biol. 2011 May;125(1-2):13-22.

XLVI. Tolkach Y, Joniau S, Van Poppel H. Luteinizing hormone-releasing hormone (LHRH) receptor agonists vs antagonists: a matter of the receptors? BJU Int. 2013 Jun;111(7):1021-30.

XLVII. Osborne CK, Wakeling A, Nicholson RI. Fulvestrant: an oestrogen receptor antagonist with a novel mechanism of action. Br J Cancer. 2004 Mar;90 Suppl 1(Suppl 1):S2-6.

XLVIII. Msaouel P, Diamanti E, Tzanela M, Koutsilieris M. Luteinising hormone-releasing hormone antagonists in prostate cancer therapy. Expert Opin Emerg Drugs. 2007 May;12(2):285-99.

XLIX. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012–. Anti-androgens. 2014 Jun 10.

L. Shore ND. Experience with degarelix in the treatment of prostate cancer. Ther Adv Urol. 2013 Feb;5(1):11-24.

LI. Cattrini C, Caffo O, De Giorgi U, Mennitto A, Gennari A, Olmos D, Castro E. Apalutamide, Darolutamide and Enzalutamide for Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC): A Critical Review. Cancers (Basel). 2022 Mar 31;14(7):1792.

LII. Cooper GM. The Development and Causes of Cancer. In: The Cell: A Molecular Approach 2nd edition [Internet]. Sinauer Associates; 2000 [cited 2023 Aug 3]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/

LIII. Lopes-Coelho F, Martins F, Pereira SA, Serpa J. Anti-Angiogenic Therapy: Current Challenges and Future Perspectives. Int J Mol Sci. 2021 Apr 5;22(7):3765.

LIV. Zahavi D, Weiner L. Monoclonal Antibodies in Cancer Therapy. Antibodies (Basel). 2020 Jul 20;9(3):34.

LV. Wong RS. Apoptosis in cancer: from pathogenesis to treatment. J Exp Clin Cancer Res. 2011 Sep 26;30(1):87.

LVI. Chan HK, Ismail S. (2014). Side effects of chemotherapy among cancer patients in a Malaysian General Hospital: experiences, perceptions and informational needs from clinical pharmacists. *Asian Pac J Cancer Prev*, 15(13):5305–9.

LVII. Wochna Loerzel V. (2015). Symptom Experience in Older Adults Undergoing Treatment for Cancer. *Oncol Nurs Forum*, 42(3): E269–78. [

LVIII. Russo S, Cinausero M, Gerratana L, et al. (2014). Factors affecting patient's perception of anti-cancer treatments side-effects: an observational study. *Expert Opin Drug Saf*, 13(2): 139–50.

LIX. Meirow D, Nugent D (2001). The effects of radiotherapy and chemotherapy on female reproduction. Hum Reprod Update, 7, 535-43.

LX. Arslan FT, Basbakkal Z, Kantar M (2013). Quality of life and chemotherapy-related symptoms of Turkish cancer children undergoing chemotherapy. Asian Pac J Cancer Prev, 14, 1761-8.

LXI. Partridge AH, Burstein HJ, Winer EP (2001). Side effects of chemotherapy and combined chemohormonal therapy in women with early-stage breast cancer. J Natl Cancer Inst Monogr, 30, 135-42.

LXII. Ismail F, Mohamed AK, Lim KH (2011). Systemic Therapy of Cancer, 3rd edition. The Ministry of Health, Kuala Lumpur pp 75-8.

LXIII. Spoelstra SL, Given CW, Sikorskii A, Majumder A, Schueller M, Given BA. Treatment with oral anti-cancer agents: symptom severity and attribution, and interference with comorbidity management. Oncol Nurs Forum. 2015 Jan;42(1):80-8.

LXIV. Lin Y, Docherty SL, Porter LS, Bailey DE. Common and Co-Occurring Symptoms Experienced by Patients With Gastric Cancer. Oncol Nurs Forum. 2020 Mar 1;47(2):187-202.

LXV. Parthipan M, Feng G, Toledano N, Donison V, Breunis H, Sudharshan A, Emmenegger U, Finelli A, Warde P, Soto-Perez-de-Celis E, Krzyzanowska M, Matthew A, Clarke H, Mina DS, Alibhai SMH, Puts M. Symptom experiences of older adults during treatment for metastatic prostate cancer: A qualitative investigation. J Geriatr Oncol. 2023 Jan;14(1):101397.

LXVI. Carelle N, Piotto E, Bellanger A, et al. (2002). Changing patient perceptions of the side effects of cancer chemotherapy. Cancer, 95, 155-63.

LXVII. Kayl AE, Meyers CA (2006). Side-effects of chemotherapy and quality of life in ovarian and breast cancer patients. Curr Opin Obstet Gynecol, 18, 24-8.

LXVIII. Schuell B, Gruenberger T, Kornek GV, Dworan N, Depisch D, Lang F, Schneeweiss B, Scheithauer W. Side effects during chemotherapy predict tumour response in

advanced colorectal cancer. Br J Cancer. 2005 Oct 3;93(7):744-8.

LXIX. Mansoori B, Mohammadi A, Davudian S, Shirjang S, Baradaran B. The Different Mechanisms of Cancer Drug Resistance: A Brief Review. Adv Pharm Bull. 2017 Sep;7(3):339-348.

LXX. Dallavalle S, Dobričić V, Lazzarato L, Gazzano E, Machuqueiro M, Pajeva I, Tsakovska I, Zidar N, Fruttero R. Improvement of conventional anti-cancer drugs as new tools against multidrug resistant tumors. Drug Resist Updat. 2020 May;50:100682.

LXXI. Assaraf YG, Brozovic A, Gonçalves AC, Jurkovicova D, Linē A, Machuqueiro M, Saponara S, Sarmento-Ribeiro AB, Xavier CPR, Vasconcelos MH. The multi-factorial nature of clinical multidrug resistance in cancer. Drug Resist Updat. 2019 Sep;46:100645.

LXXII. Li YJ, Lei YH, Yao N, Wang CR, Hu N, Ye WC, Zhang DM, Chen ZS. Autophagy and multidrug resistance in cancer. Chin J Cancer. 2017 Jun 24;36(1):52.

LXXIII. Singh P, Chaturvedi A. Complementary and alternative medicine in cancer pain management: a systematic review. Indian J Palliat Care. 2015 Jan-Apr;21(1):105-15.

LXXIV. Satija A, Bhatnagar S. Complementary Therapies for Symptom Management in Cancer Patients. Indian J Palliat Care. 2017 Oct-Dec;23(4):468-479.

LXXV. Ng JY, Dhawan T, Fajardo RG, Masood HA, Sunderji S, Wieland LS, et al. The Brief History of Complementary, Alternative, and Integrative Medicine Terminology and the Development and Creation of an Operational Definition. Integrative Medicine Research. 2023 Jul;100978

LXXVI. Tabish SA. Complementary and Alternative Healthcare: Is it Evidence-based? Int J Health Sci (Qassim). 2008 Jan;2(1):V-IX.

LXXVII. Tokumoto J, Abrams DI. CHAPTER 47 - Complementary and Alternative Medicine. In: Volberding PA, Sande MA, Greene WC, Lange JMA, Gallant JE, Walsh CC, editors. Global HIV/AIDS Medicine [Internet]. Edinburgh: W.B. Saunders; 2008 [cited 2023 Aug 3]. p. 547–53. Available from: https://www.sciencedirect.com/science/article/pii/B9781416028826500514

LXXVIII. Gerik S, Maypole J. Chapter 10 - Overview of Biologically Based Therapies in Rehabilitation. In: Deutsch JE, Anderson EZ, editors. Complementary Therapies for Physical Therapy [Internet]. Saint Louis: W.B. Saunders; 2008 [cited 2023 Aug 3]. p. 156–75. Available from: https://www.sciencedirect.com/science/article/pii/B9780721601113500166

LXXIX. Vickers A, Zollman C, Reinish JT. Massage therapies. West J Med. 2001 Sep;175(3):202–4.

LXXX. Calcagni N, Gana K, Quintard B. A systematic review of complementary and alternative medicine in oncology: Psychological and physical effects of manipulative and body-based practices. PLoS One. 2019 Oct 17;14(10):e0223564.

LXXXI. Agdal R, von B Hjelmborg J, Johannessen H. Energy healing for cancer: a critical review. Forsch Komplementmed. 2011;18(3):146-54.

LXXXII. McManus DE. Reiki Is Better Than Placebo and Has Broad Potential as a Complementary Health Therapy. J Evid Based Complementary Altern Med. 2017 Oct;22(4):1051-1057.

LXXXIII. O'Mathúna DP. WITHDRAWN: Therapeutic touch for healing acute wounds. Cochrane Database Syst Rev. 2016 Sep 1;9(9):CD002766.

LXXXIV. Ge L, Wang Q, He Y, Wu D, Zhou Q, Xu N, Yang K, Chen Y, Zhang AL, Hua H, Huang J, Hui KK, Liang F, Wang L, Xu B, Yang Y, Zhang W, Zhao B, Zhu B, Guo X, Xue CC, Zhang H; International Trustworthy traditional Chinese Medicine Recommendations (TCM Recs) Working Group. Acupuncture for cancer pain: an evidence-based clinical practice guideline. Chin Med. 2022 Jan 5;17(1):8.

LXXXV. Marsden E, Nigh G, Birdsall S, Wright H, Traub M. Oncology Association of Naturopathic Physicians: Principles of Care Guidelines. Curr Oncol. 2019 Feb;26(1):12-18.