IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2023 Vol.:28, Issue:1

A Brief Overview of the Risk Factors, Challenges, and Nanotechnology-Based Treatments for Cancer Diseases

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Submitted: 25 July 2023
Accepted: 18 August 2023
Published: 30 August 2023

Keywords: Cancer diseases, Epidemiology, Pathophysiology, Nanotechnology, Risk factors, Challenges

ABSTRACT

The most prevalent health problem in societies around the world is cancer. One of the leading causes of morbidity and mortality worldwide is cancer. According to GLOBOCAN (2012) findings, there were 14.1 million new cancer diagnoses and 8.2 million cancer-related deaths. By 2030, this is anticipated to increase by at least 70%. The category of diseases known as malignancies frequently exhibit uncontrolled cell proliferation and spread. If the metastasis, or spread of cancer cells, which characterizes this stage, is not prevented, death may result. Hereditary mutations, hormones, immunological diseases, radiation, cigarettes, toxins, and infectious organisms are only a few of the internal and external causes of cancer. There are a variety of complicated, poorly understood causes of cancer. Numerous things, including dietary problems, certain illnesses, a lack of exercise, obesity, and environmental toxins, are known to increase the risk of cancer. The goal of nanotechnology, which is the study of materials on atomic and molecular levels and often deals with groups in the nano (10-9) size range, is to develop materials or devices within that framework. The discovery of novel optical, electrical, magnetic, and structural properties in metals, semiconductors, and polymeric particles that are generally inaccessible from individual molecules and bulk materials is the basis for nanotechnology. Cancer nanotechnology has been intensively researched and used in cancer management and treatments due to its potential to dramatically enhance cancer diagnosis, detection, and treatment. Mainly We are interested in studying cancer, its risk factors, and challenges in India using nanotechnology as a therapeutic.

INTRODUCTION

Uncontrolled cell development and spread are common features of the group of diseases known as cancers. Death may occur if the metastasis, or spread of cancer cells, which marks this stage, is not stopped. Cancer is brought on by a variety of internal and external factors, including hereditary mutations, hormones, immunological disorders, radiation, cigarettes, chemicals, and infectious organisms. Cancer has many complex and poorly understood causes, which are diverse. There are a variety of factors known to raise the risk of cancer, such as dietary issues, specific illnesses, a lack of exercise, obesity, and environmental contaminants [(1)]. A variety of temporal and spatial physiologic alterations in cancer cells eventually result in malignant tumors. The biological hallmark of the condition is abnormal cell proliferation or neoplasia. For the majority of cancer patients, the primary cause of morbidity and mortality is tumor cell invasion of nearby tissues and distant organs. The biological mechanism by which healthy cells become cancerous has been the focus of extensive investigation in the biomedical sciences for many years [(2,3)]. The cancer's origin is a mystery. Paradoxes and contradictions have plagued the field. Formulating a clear strategy for efficient care of cancer is challenging without a comprehensive understanding of its causes. Although very specialized processes underpin malignant transformation, a wide range of general effects, such as radiation, chemicals, viruses, inflammation, etc., can cause the disease to manifest. In fact, it appears that long-term exposure to practically any environmental provocateur has the potential to cause cancer [(4)]. Global Cancer Observatory (GLOBOCAN) anticipates that 19.3 million new cases of cancer will occur globally in 2020 (5). Despite the extensive research and quick advancements over the previous ten years, cancer still kills lives globally. According to recent data, cancer is the second most common cause of death in the USA, accounting for around 23% of all fatalities, behind heart disease (6). Around 15 million new instances of cancer will be diagnosed and 12 million cancer sufferers will pass away by the year 2020, when the world's population is projected to reach 7.5 billion (7). Chemotherapy, radiation, and surgery are the only cancer treatments that are used most frequently. The early diagnosis and treatment of cancer, however, continue to be hampered by current technology. Cancer therapy is still far from ideal since it is afflicted by significant shortcomings, despite many advancements in conventional treatment choices like chemotherapy and radiation. The non-specific systemic distribution of anticancer drugs, insufficient drug concentrations reaching the tumour site, severe cytotoxicity, the inability to monitor therapeutic responses, and the emergence of multiple drug resistance are all frequent

problems with contemporary cancer treatments (8). Developing materials or devices within that framework is the focus of nanotechnology, which is the study of materials on atomic and molecular dimensions that typically deal with groupings in the nano (10^{-9}) size range. The fundamental basis for nanotechnology is the discovery of novel optical, electrical, magnetic, and structural features in metals, semiconductors, and polymeric particles that are typically not accessible from individual molecules and bulk materials. With the potential to significantly improve cancer diagnosis, detection, and treatment, cancer nanotechnology has been vigorously investigated and applied in cancer management and treatments (9). As with any cancer therapy, the main challenge is to deliver the desired therapeutic agent concentration to tumour sites, eliminating malignant cells while causing the least amount of harm to healthy cells. With this perspective, it is essential to develop single drugs that have a great deal of potential to significantly impact cancer prevention, detection, and therapy. As a result, a number of ligand-targeted therapeutic approaches, such as immunotoxins, radioimmuno-therapeutics, and drug immunoconjugates, are being developed to address the drawbacks of conventional chemotherapeutic agents and add to the toolbox of cancer therapy (10). Under the National Cancer Registry Programme (NCRP), National Centre for Disease Informatics and Research (NCDIR) of the Indian Council of Medical Research (ICMR-NCDIR), Bengaluru, systematic data collection on cancer has been conducted through PBCRs and hospital-based cancer registries since 1981.NCRP's main goal is to gather accurate information about the prevalence and patterns of cancer in India and to make projections for the future. In 2020, 1.39 million new (incident) cancer cases were predicted in our earlier study. In India, 14,61,427 new cases of cancer are anticipated in 2022 (about 100.4 new cases of cancer per 100,000 people). In India, one in nine persons will likely develop cancer at some point in their lives (11).

TYPES OF CANCER

According to information gathered by the Centers for Disease Control and Prevention (CDC) on the prevalence of cancer around the world, each year, 14.1 million new cases of the disease are reported, and an astounding 8.2 million people pass away from it. The estimated 19.3 million new cases of cancer were recorded in 2015. Globally, the most common malignancies diagnosed were lung cancer (13%), breast cancer (12%), colorectal cancer and other stomach cancers (17% combined), prostate cancer (8%), liver cancer (6%) and cervical cancer (4%) (5,12).

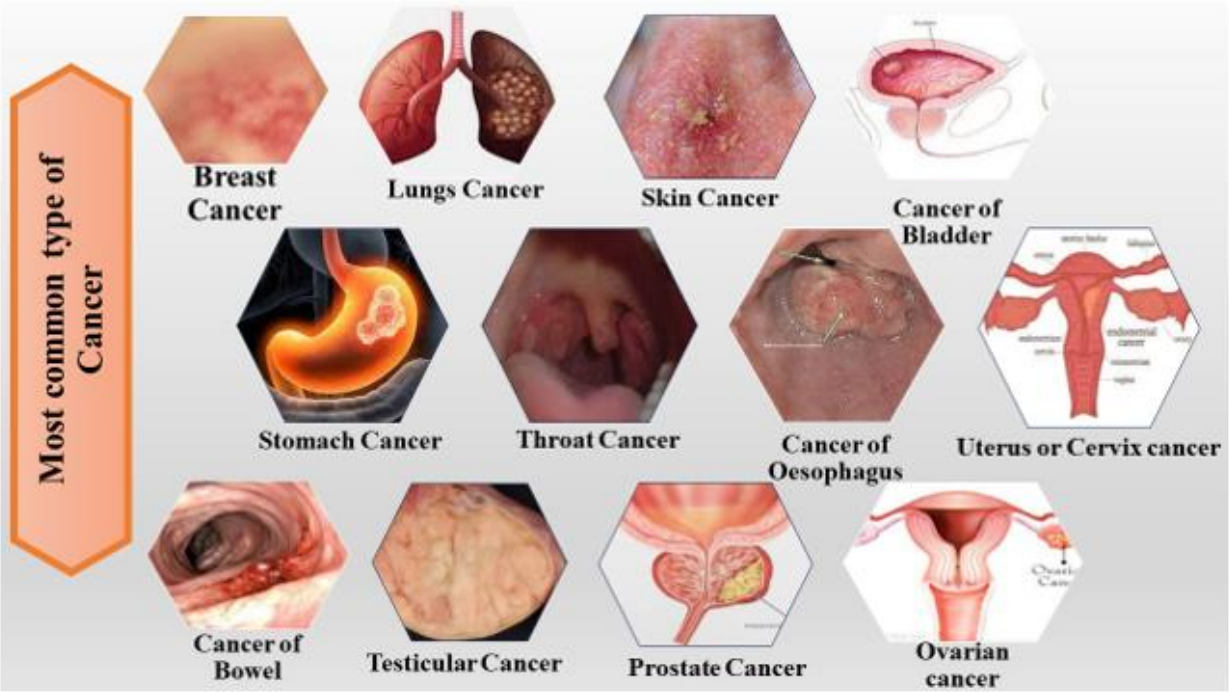

Fig.1: Cancer type that is most prevalent.

EPIDEMIOLOGY OF CANCER

The study of the factors influencing cancer is known as epidemiology, and it is done in order to deduce potential trends and causes. Finding the origin of cancer and identifying and developing better treatments are the goals of the study of cancer epidemiology. The issues of lead time bias and length time bias must be addressed in this field of study. Lead time bias is the idea that early diagnosis may artificially boost cancer survival rates without actually altering the disease's course (13). Infectious infections are the third-leading cause of cancer worldwide, behind dietary factors and tobacco smoking. The percentage of cancers that can be attributed to infectious and parasitic diseases, or the population attributable fraction, was estimated to be 10% in the US population in 1981, 10-20% in the UK population in 1998, 3.6% in the French population in 2000, 5% (acceptable estimates range from 4-15%) in the UK population in 2005, and 29.4% (31.7% in men and 25.3% in women) in the Chinese population in 2005. It was predicted to constitute 15.6% of the global population in 1990, 17.8% in 2002, and 16.1% in 2008. The most recent estimate translates to around 2 million new instances of infection-related malignancies identified globally in 2008 (14). Creating trustworthy statistics on the prevalence and trends of cancer in India and providing projections is one of NCRP's main goals. In 20205, we predicted that there would be 1.39 million new (incidental) cancer cases. Using the same datasets and methods, the current paper

aims to provide comprehensive estimates of cancer incidence in India by sex, age groups, and anatomical sites for the year 2022 and the anticipated increase in cases for 2025 (15).

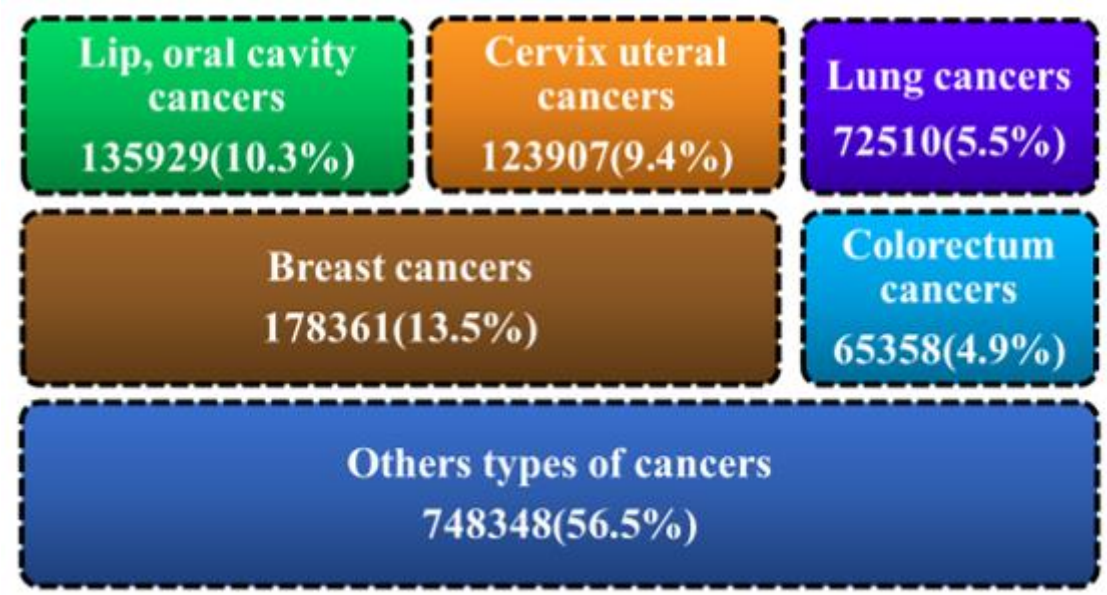

Fig.2: India Against Cancer's data on cancer (Source: Globocan 2020).

PATHOPHYSIOLOGY OF CANCER

In the developed world, cancer is one of the main causes of mortality. A physiological process called cell division takes place in tissues. Under normal conditions, a balance between proliferation and programmed cell death, typically manifested as apoptosis, is maintained by tightly controlling both processes. By interfering with the processes that regulate programming, certain DNA mutations cause cancer. The process through which healthy cells turn into cancerous ones is known as carcinogenesis. It is characterized by a series of genetic and cellular alterations that reprogram a cell to divide uncontrollably, resulting in the formation of a malignant mass (tumour) that can spread to other parts of the body (16). Dietary substances have been extracted and discovered in an effort to support both maintaining good health and preventing chronic diseases like cancer. Bioactive peptides, which have been described as "food derived components (naturally occurring or enzymatically generated) that, in addition to their nutritional value, exert a physiological effect in the body," have come under more attention (17).

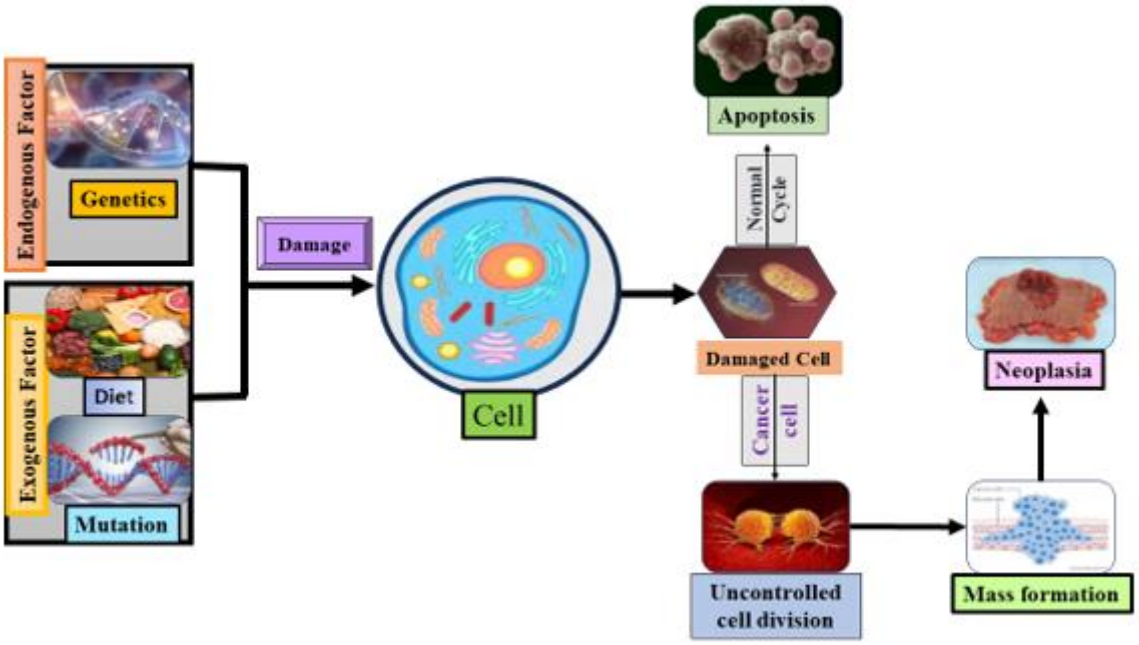

Fig.3: Cancer's pathophysiology (18)**.**

CANCER TREATMENT USING NANOTECHNOLOGY

Compared to conventional treatments, nanotechnology-based drug delivery methods for cancer treatment have many benefits, including extended drug shelf life, improved biodistribution, and administration of both hydrophilic and hydrophobic compounds (19). Through the gradual fusion of medicine and nanotechnology, an interdisciplinary subject known as "nanomedicine" has emerged, offering enormous potential for treating a number of human ailments. In general, nanomedicine is the process of employing molecular instruments and molecular understanding of the human body to identify, cure, and prevent disease and traumatic injury, as well as to reduce pain and preserve and enhance human health (20,21). Cancer drug-loaded nanocarriers differ from other cancer therapies in several ways, including the following: Nanocarriers can be made to carry a sizable therapeutic or diagnostic payload and are capable of carrying both therapeutic and diagnostic medicines. For high affinity and specificity in targeting cancer cells, multivalent targeting ligands can be coupled to nanocarriers. Combinatorial cancer therapy may be made possible by the ability to load and accommodate several different medications. Using nanocarriers, the conventional drug resistance mechanisms can be avoided. Nanocarriers were helped by passive and active targeting tactics to maximize drug accumulation in cancer cells while minimising damage in healthy cells. These techniques aid in enhancing the anticancer effects of cancer medications

while reducing systemic toxicity (22). Even though some of these methods were only speculatively proposed a few years ago, they are moving rather quickly towards dispelling translational certainties. Over a hundred different ways have made use of nanotechnology. We shall, however, briefly concentrate on a few of the most intriguing upcoming advancements and various research areas that are extremely close to completion, and their possible inclusion into useful clinical treatments or medical diagnostics by focusing on cancer (23,24).

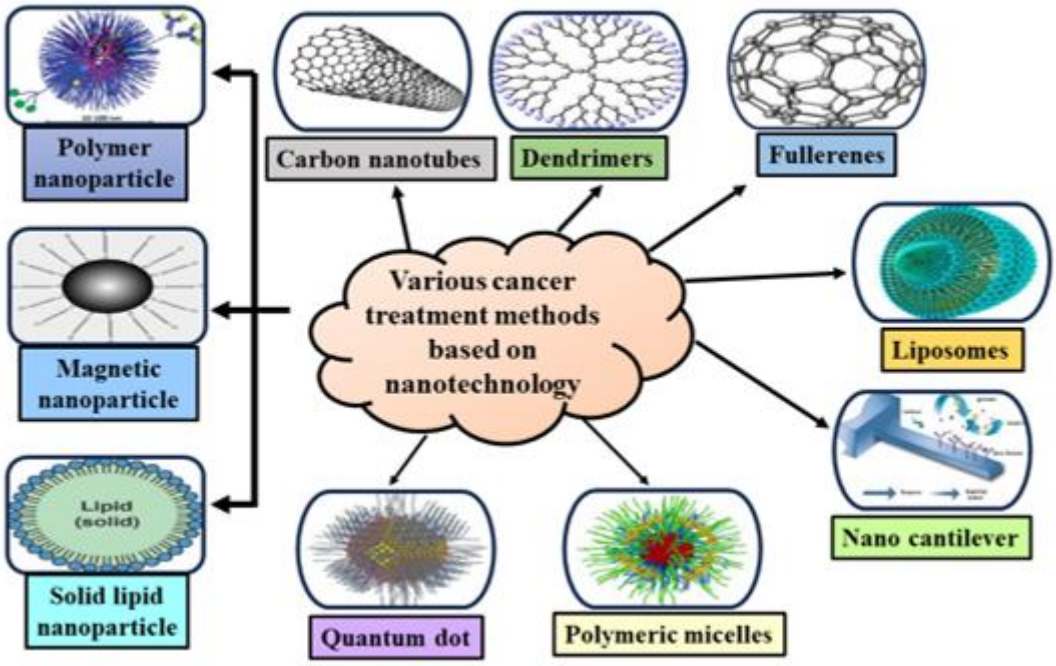

Fig.4: Several cancer treatment methods based on nanotechnology (25).

- **Carbon Nanotubes**

The carbon nanotube is a different kind of nanodevice for biomarker detection. In biology, carbon nanotubes-carbon cylinders made of benzene rings-have been utilized as diagnostic tools for differentiating between proteins in serum samples, as transporters for drugs, vaccines, and proteins, as well as sensors for detecting DNA and proteins (26). Carbon atoms with a diameter of 4 nm and a length of 100 µm make up carbon nanotubes, which have a network-like hydrophobic composition. It is made up of carbon molecules that have either one or two walls that are organized in a hexagonal arrangement by themselves. Due to its huge surface area, this possesses unique optical, electron emission, and mechanical properties and can support a big payload in a graphene cavity or on the surface. It has numerous biological uses as sensors for spotting DNA and proteins. It serves as carriers for the delivery

of drugs, vaccines, and proteins as well as diagnostic devices for the separation of various proteins from serum. Since it is insoluble in aqueous and organic solvents, its associated toxicity in biological fluid is its principal barrier to therapeutic application. This issue must be resolved (8,27).

- **Dendrimers**

A special family of repeatedly branched polymeric macromolecules known as dendrimers consists of a network of branches arranged around an inner core, the size and shape of which can be customized to produce a nearly flawless 3-D geometric pattern. Dendrimers' distinctive design allows for multivalent attachment of imaging probes and targeting moieties, making it possible to use them as a highly effective diagnostic tool for cancer imaging (28). Additionally, numerous researchers have effectively administered anticancer medications and investigated different dendrimers for efficient cancer therapy (29).

- **Fullerenes**

Any molecule that is fully made of carbon, whether it takes the shape of a hollow sphere, ellipsoid, or tube, is known as a fullerene. Fullerenes that are cylindrical or spherical are referred to as buckytubes or carbon nanotubes, respectively. Fullerenes have a structure that is similar to that of graphite and are made up of stacked sheets of connected hexagonal graphene, albeit they may also contain pentagonal (or occasionally heptagonal) rings. Graphite, diamond, and amorphous carbon, including soot and charcoal, were the only known carbon allotropes up until the discovery of fullerenes. Due to its unusual chemistry and potential technical uses, particularly in the fields of materials science, electronics, and nanotechnology, buckyballs and buckytubes have attracted a lot of investigation. Endohedral metallofullerenes nanoparticles that have been optimized as reactive oxygen species scavengers have been shown to limit the growth of tumours in a recent study (30).

- **Liposomes**

The innate ability of liposomes to target cancer is an intriguing characteristic. All healthy human blood arteries have endothelial walls that are enclosed by endothelial cells that are connected by tight junctions that prevent big blood particles from spilling out of the channel. Tumour vasculature are diagnostically leaky and do not maintain the same level of closure between cells. The improved permeability and retention effect refers to this property. Liposomes of a specific size, often less than 200 nm, can quickly enter tumour locations from

the blood, but they are prevented from doing so in healthy tissue vasculature by the endothelium wall (31,32). Doxorubicin (Doxil) and daunorubicin (Daunoxome), which are currently marketed as liposome delivery systems, are examples of drugs that can be delivered via liposomes.

The development of PEGylated Liposomes also shown a significantly prolonged circulation period and little contact with mononuclear phagocytes and plasma proteins. PEGylated liposomal formulations, specifically PEGylated liposomal doxorubicin, have been the most thoroughly researched (33).

- **Nanocantilever**

Nanometer-scale bending occurs in nanocantilevers as a result of environmental changes or surface modifications. They fall under the category of nanotechnology because of this bending at the nanoscale scale, and they can be employed as a part of biosensors (34). Due to the lack of expenditures involved with sample preparation, such as time and expensive materials, these have been referred to as a straightforward alternative to PCR processes and detection methods. The monitoring of multiple cancer indicators with nanocantilevers could increase the utility of microarray technologies. Protein, pH, and DNA/RNA-DNA/RNA hybridization events have all been detected using nano- and microcantilevers. An extensive evaluation of nanocantilevers used in biosensors has been published, revealing that these are a special tool for identifying important biomolecules (35).

- **Polymeric micelles**

A micelle is a grouping of amphiphilic surfactant molecules, and micelles are emerging as a crucial component of the therapies of the future. Genexol-PM (PEG-poly (d,l-lactide)-paclitaxel) was the first polymeric micelle formulation of paclitaxel that did not contain Cremophor-EL. Patients with advanced, resistant cancers participated in a Phase I and pharmacokinetic research. A number of polymeric PEG-micelle formulations have started clinical trials. For instance, a polymeric micelle loaded with doxorubicin that was tested in a Phase I clinical trial for solid tumours showed promising results in the treatment of restenosis caused by accumulation in vascular lesions (36–40). In vitro, anticancer antibody-conjugated polymeric micelles (immunomicelles) containing the water-insoluble medication paclitaxel have been developed by Torchilin et al. to recognize and bind to a variety of cancer cells. Curcumin-loaded methoxy PEG/poly--caprolactone diblock copolymeric micelles were

created by Mohanty et al. They used pancreatic cancer cell lines to demonstrate enhanced efficacy of the micellar system over the original medication (41,42).

- **Quantum Dots**

Nanocrystals with a diameter of less than 10 nm and composed of semiconductor particles are known as quantum dots (QD). It is made up of an inorganic element at its core and a metal shell around it that has unique optical and chemical characteristics. It had a variety of advantages over conventional organic fluorescent dyes and displayed several features that were advantageous for spectroscopy, including strong fluorescence intensity, a long lifetime, and good photobleaching resistance. A potential platform for multicolor imaging for the study of cancer behaviour is QD-based nanotechnology. They are a viable contender for in vivo fluorescent tagging and molecular cellular imaging due to their brightness, minimal photobleaching, and new physical, chemical, and optical features (43). Numerous studies have highlighted many crucial broad categories of QDs utilised in cancer diagnosis and medicine administration (44).

- **Nanoparticles**

These are submicron-sized colloidal particles with a therapeutic medication contained within their polymeric matrix, adsorbed on top of the surface, or conjugated on the surface (45). By altering their surfaces, nanoparticles can be directed to certain locations and interact biochemically with receptors produced on target cells. Additionally, it has the capacity to transport medications to the target area while bridging a number of biological barriers, including the blood-brain barrier. By being coated with polysorbates, the drug-loaded nanoparticles can pass the blood-brain barrier and improve the viability of brain targeting after an intravenous injection. Additionally, magnetic NPs have developed novel tiny sizes and magnetic characteristics that enable magnetic-mediated medication delivery to the cancer tissues. For specialized drug delivery, it can have its surface functionalized with various ligands. Solid-lipid nanoparticles, which are colloidal NPs produced from solid lipids and stabilized by surfactants, are another category of NPs. By evading RES clearance, these NPs have displayed a prolonged bioavailability in vivo. Numerous groups have thoroughly investigated the mentioned nanoparticles for various cancer treatments and drug delivery (46–48).

ALTERNATIVE CANCER TREATMENTS

- **Gene Therapy**

There are numerous initiatives involving cancer gene therapy in development. In one of these initiatives, researchers from Shanghai Second Medical University successfully inserted a gene into human tumour cells using a retrovirus, as described in the Chinese Medical Journal (2002). Most often, tumour cells have antigens on their surface that can distinguish them from healthy cells. Never-the less similar non-cancerous cells contain these antibodies, although on a far more minor scale. Because cancer cells are present, the likelihood of the retrovirus adhering to a noncancerous cell is minimal. If these cancer antigens are distinct, it may be possible to modify a retrovirus to include an antibody that will bind to the antigen, allowing the virus to attach to the cell and inject its viral DNA there. The team added a functioning tumour suppressor gene to the viral vector, and when the virus injected its DNA, it was incorporated into the. The tumour suppressor gene was ingested by the cell and incorporated into its DNA, restoring the cell's ability to self-regulate and undergo apoptosis (49).

- **Chemotherapy**

Chemotherapy (or "chemo") is the practise of treating cancer using drugs or medications. Many people find the idea of receiving chemotherapy terrifying. But understanding chemotherapy, how it works, and what to expect can frequently help allay your concerns. Additionally, it may help you feel more in charge of your cancer treatment (50).

- **Surgery**

In some circumstances, surgery can be used to detect, treat, or possibly assist prevent cancer. Most cancer patients will undergo some sort of surgery. When cancer has not progressed to other bodily parts, it frequently gives the best chance of recovery. Click here to read more about surgery (51).

- **Radiation Therapy**

High-energy particles or waves are used in radiation therapy to kill or harm cancer cells. Whether used alone or in conjunction with other treatments, it is one of the most popular cancer treatments. In this area, you may learn more about radiation therapy (52).

- **Hyperthermia**

Although the concept of using heat to cure cancer has been around for a while, early experiments yielded conflicting outcomes. More precise heat distribution is now possible thanks to better equipment, and hyperthermia is being researched as a potential treatment for several cancer types (53).

- **Immunotherapy**

Immunotherapy is a form of treatment that enlists the immune system to combat cancer. Learn more about the many forms of immunotherapy and the various cancers they are used to treat (54).

- **Targeted Therapy**

A more recent type of cancer treatment called targeted therapy employs medications or other chemicals to more precisely locate and kill cancer cells, typically with little harm to healthy cells. The use of targeted therapy in cancer treatment plans is on the rise (55).

- **Lasers in Cancer Treatment**

Blades (scalpels) can be replaced with lasers, which are extremely strong, focused beams of light, allowing extremely accurate surgical tasks, including the treatment of some tumours (56).

- **Photodynamic Therapy**

In order to cure cancer, a technique known as photodynamic therapy (PDT) employs special medications known as photosensitizing agents together with light. The medications only function after being "turned on" or activated by specific types of light (57).

RISK FACTORS OF CANCER

Smoking causes over 90% of lung cancers, along with a wide variety of other cancers, including cancers of the mouth, larynx, oesophagus, pancreas, stomach, colon, cervix, kidney, and bladder. Smoking also causes about 30% of all cancers in the developed world. A growing body of research connects smoking to an increased risk of leukaemia, liver, and prostate cancer. Tobacco certainly affects various stages of carcinogenesis; in addition to delivering a variety of carcinogens, it also induces irritation and inflammation and disrupts the body's defence mechanisms (58). Since 1964, when the US Surgeon General's Advisory

Commission Report identified smoking as the leading cause of lung cancer, attempts to limit tobacco usage have been made. At least 14 different cancers are more likely to occur as a result of tobacco smoking (59). According to estimates, eating played a role in between 30 and 35 percent of cancer fatalities in the USA. Depending on the type of cancer, the amount that nutrition affects cancer mortality varies greatly. For instance, nutrition may contribute to cancer deaths in as many as 70% of instances of colon cancer. There is still much to learn about how nutrition affects cancer risk. The majority of ingested carcinogens, such as nitrates, nitrosamines, pesticides, and dioxins, originate in food, food additives, or cooking (2). Blood type, genetics, gender, age, and ethnicity are the non-modifiable factors for cancer cousins. Cancer risk factors that can be modified include obesity, alcohol use, smoking, infections, and environmental factors including radiation and other substances that might cause cancer in humans (60).

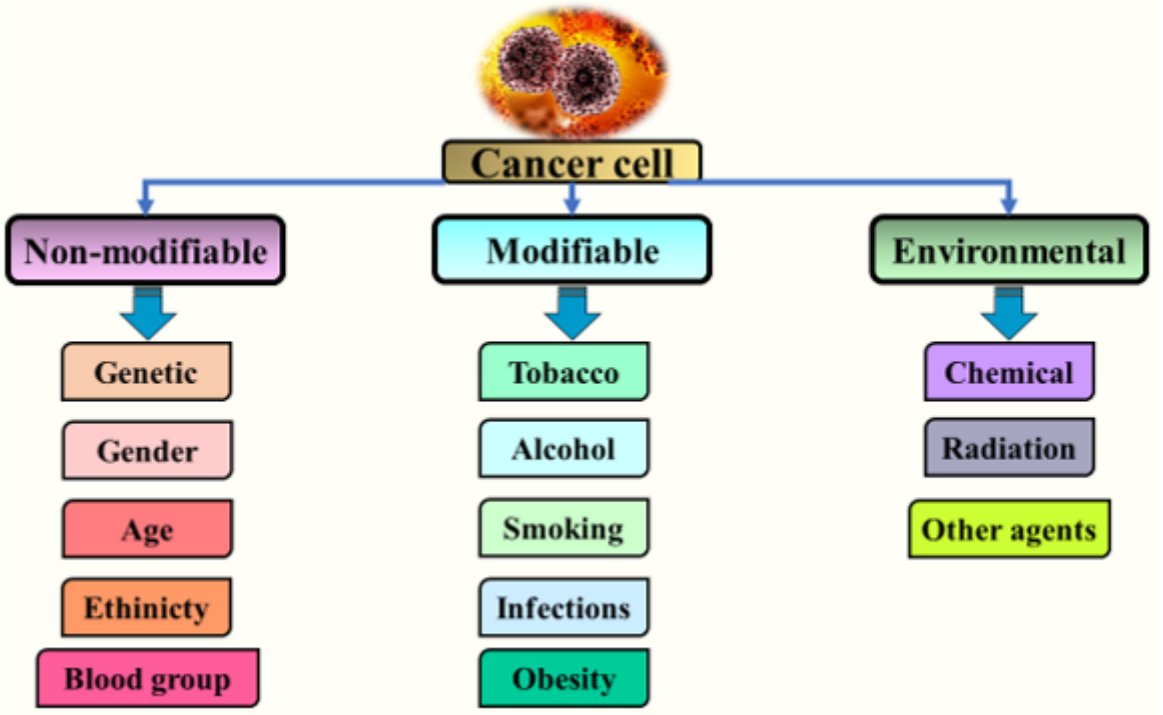

Fig.5: The reasons for cancer risk factors (61)**.**

CHALLENGES

Non-communicable illnesses have become serious health issues globally, particularly so in developing nations, as a result of changing lifestyles, increased lifespan, and improved management of infectious diseases. Cancer has become the second-leading cause of illness and mortality in India, behind heart diseases. 1.45 million instances of cancer were predicted

to be diagnosed in 2016, according to the Indian Council of Medical Research's (ICMR) National Centre for Disease Informatics and Research in Bengaluru, India. Within the next 20 years, this burden is probably going to double (11,62).

- **Distribution of various cancers in India:**

The National Cancer Registry Programme, which the ICMR launched in December 1981, is a key repository for data on the prevalence and trends of cancer in the nation. There are currently 29 hospital-based cancer registries and 29 population-based cancer registries (PBCRs). These represent 10% of all people in India. 11 of these PBCRs may be found in the North-East (NE) area. Male age-adjusted incidence (per 100,000) rates are greater in the West than in India (270.0 in Aizawl district and 149.4 in Delhi), with rates of 631.9 in Brazil and 493.9 in Michigan. Accordingly, the number of females per 100,000 is 474.6 in Brazil, 363.3 in the USA, 207.7 in Aizawl, and 144.8 in Delhi (India). Lung, head and neck (including the lips, tongue, and throat), prostate, and oesophageal cancer are the top five cancers in men. While the most prevalent cancers in women are those of the breast, cervix, ovary, oral cavity, and uterus. In Delhi, Chennai, Bengaluru, Bhopal, Mumbai, and Barshi PBCRs over the past three decades, the prevalence of cervical cancer has decreased. In these registries, the prevalence of colon/rectal, lung, breast, and prostate cancer is gradually increasing (63). In India, the prevalence of cancer varies significantly by region. For instance, India's NE area has the highest rate of cancer incidence for both sexes. Male instances where most prevalent in the Mizorami district of Aizawal, while female cases were more prevalent in the Arunachal Pradesh district of Papumpare. Different aetiological factors may be at play, such as environmental, dietary, lifestyle, and genetic factors, as evidenced by the higher incidence of gallbladder cancer in north India and the NE region compared to other areas, higher incidence of stomach cancer in Chennai and Bengaluru PBCRs, and higher incidence of oesophageal cancer in Kashmir and the NE region (64). The use of tobacco in various forms is linked to around 50% of cancers in men and 15% of cancers in women. These include pancreatic, renal, and urinary bladder tumours, as well as malignancies of the aerodigestive tract (head and neck, lung, and oesophagus) (64).

ACKNOWLEDGEMENT

Authors would like to thank, Goel Institute of Pharmacy & Sciences (GIPS), Lucknow, Uttar Pradesh, India for extending their facilities.

CONCLUSION AND FUTURE DIRECTION

Our review articles begin with a general overview of cancer diseases, including their types, epidemiology, pathophysiology, cancer treatments employing nanotechnology, complementary cancer treatments, risk factors for cancer, and obstacles. Our analysis leads us to the conclusion that while medication can help, it can also cause negative side effects (such kidney and liver damage) on the body. In contrast, non-pharmacological treatment can help, but it takes longer and has no adverse effects. There is a need for more randomized controlled studies on the topic of cancer treatment. Future study on cancer disorders is something we plan to do. To assess patients' physical and mental health and to provide better data on cancer diseases and its treatment, future counseling-based study will be carried out in our country or state with our colleague.

Table.1: Current status of clinical trials on Cancer.

Drug	Mode of administration	Disease	Enrolment	Allocation/Intervention model/Masking	Official Title of the study	Status	Clinical trial	Year
NA	Observational	Cancer	108	NA	COMPARATIVE EFFECTS OF PERIOPERATIVE AND ADJUVANT CHEMOTHERAPY ON OUTCOMES OF OPERABLE GASTRIC CANCER: EXPERIENCE FROM A CANCER CARE CENTER	NA	NCT04989764	2021
Anticoagulation treatment	Observational	Cancer	400	NA	Optimal Anticoagulation Strategy In Stroke Related to CANCER (OASIS-CANCER Study)	NA	NCT02743052	2016
NA	Observational	Cancer	60	NA	COMPLIANCE TO COMPRESSION GARMENTS AND RELATED FACTORS AMONG PATIENTS With BREAST CANCER-RELATED LYMPHEDEMA	NA	NCT04832386	2021
HEALTH FAITH MODEL GUIDED IN CANCER FREQUENTLY SEEN IN WOMEN	Interventional	Cancer	60	Randomized/Parallel Assignment/Double (Participant, Outcomes Assessor)	THE EFFECT OF CANCER EDUCATION BASED ON THE HEALTH BELIEF MODEL ON AWARENESS OF WOMEN WITH DISABILITIES AND THEIR PARTICIPATION IN SCREENING	NA	NCT05881902	2023

EARLY DIAGNOSIS AND SCREENING METHODS EDUCATION/ STANDART CANCER EDUCATİON								
Tivantinib/ Placebo	Interventional	Cancer	38	Non-Randomized/Single Group Assignment/Single (Participant)	A PHASE 1 SINGLE-BLIND, SINGLE-SEQUENCE STUDY ASSESSING THE EFFECT OF TIVANTINIB ON THE QTC INTERVAL IN CANCER SUBJECTS	Phase-1	NCT01699061	2019
Molecular Analysis of Cancer	Observational	Cancer	500	Case only	MOLECULAR TESTING OF CANCER BY INTEGRATED GENOMIC, TRANSCRIPTOMIC, AND PROTEOMIC ANALYSIS	NA	NCT02213822	2014
Observation	Observational	Cancer	4500	Case only	FALSE POSITIVE FINDINGS IN BREAST CANCER TOMOSYNTHESIS: An Analysis of Findings Leading to Recall and Work-up in ASL Avellino Screening	NA	NCT04259866	2020
SHR-1802	Interventional	Cancer	28	N/A/Single Group Assignment/None (Open Label)	Tolerability, Safety and Pharmacokinetic Characteristics of SHR-1802 in Patients With Advanced Malignancy: a Phase I Clinical Study	Phase-1	NCT04414150	2022
Observational /Survey	Observational	Cancer	5000	Cohort	SAVE THE BOTTOMS!!!: ASSESSING THE GAY MALE EXPERIENCE WITH ANAL CANCER PREVENTION STRATEGIES	NA	NCT05628194	2023
Retrospectively review of medical data in patients treated by focal HIFU for primary localized prostate cancer	Observational	Cancer	146	Cohort	FOCAL HIGH-INTENSITY FOCUSED ULTRASOUND FOR PRIMARY LOCALIZED PROSTATE CANCER: MIDTERM ONCOLOGICAL OUTCOMES	NA	NCT04602208	2020
Terahertz metamaterials	Observational	Cancer	520	Other	Terahertz Metamaterials for Tumour Marker Concentration Identification	NA	NCT04125524	2021

capecitabine (Xeloda), oxaliplatin and bevacizumab (Avastin)	Interventional	Cancer	60	Non-Randomized/Single Group Assignment/None (Open Label)	A Phase ll Study of Oxaliplatin, Capecitabine, and Bevacizumab in the Treatment of Metastatic Esophagogastric Adenocarcinomas	Phase-2	NCT00447330	2015
IXABEPILONE/ STEREOTACTIC BODY RADIATION THERAPY	Interventional	Cancer	0	N/A/Single Group Assignment/None (Open Label)	A Phase II Trial Of Ixabepilone and Stereotactic Body Radiation Therapy (SBRT) For Patients With Triple Negative Metastatic Breast Cancer	Phase-2	NCT01818999	202
Collection of blood and tumor samples	Interventional	Cancer	300	N/A/Single Group Assignment/None (Open Label)	PANCREATIC CANCER: DYNAMIC ASSESSMENT AT ALL STAGES OF TREATMENT: PANDORE-PANC-IPC 2021-082	NA	NCT05802485	2023
PD-0332991/Letrozole/Placebo/Letrozole	Interventional	Cancer	666	Randomized/Parallel Assignment/Quadruple (Participant Care ProviderInvestigatorOutcomes Assessor)	A RANDOMIZED, MULTICENTER, DOUBLE-BLIND PHASE 3 STUDY OF PD-0332991 (ORAL CDK 4/6 INHIBITOR) PLUS LETROZOLE VERSUS PLACEBO PLUS LETROZOLE FOR THE TREATMENT OF POSTMENOPAUSAL WOMEN WITH ER (+), HER2 (-) BREAST CANCER WHO HAVE NOT RECEIVED ANY PRIOR SYSTEMIC ANTI CANCER TREATMENT FOR ADVANCED DISEASE	Phase-3	NCT01740427	2022
Group continuous training at moderate intensity/Group high Intensity Interval Training/Group control	Interventional	Cancer	1573	Randomized/Crossover Assignment/Triple (Participant Care Provider Investigator)	MODERATE CONTINUOUS TRAINING VERSUS HIIT ON CARDIOMETABOLIC AND PSYCHOSOCIAL VARIABLES IN CANCER STADIUM II. CONTROLLED RANDOMIZED TRIAL	NA	NCT03915288	2019
Systematic symptom assessment	Interventional	Cancer	280	Randomized/Parallel Assignment/None (Open Label)	(Immunotherapy Symptom Capture) A RANDOMIZED CONTROLLED TRIAL OF SYSTEMATIC SYMPTOM ASSESSMENT	NA	NCT04929353	2021

					IN CANCER PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS			
mFOLFOX6	Interventional	Cancer	1980	Randomized/Parallel Assignment/None (Open Label)	CIRCULATING TUMOR DNA BASED DECISION FOR ADJUVANT TREATMENT IN COLON CANCER STAGE II	Phase-3	NCT04120701	2021
Periodic ARV7 and miRNA evaluation	Observational	Cancer	46	Case-only	CIRCULATING MICRO-RNA (miRNA) AND AR-V7 MUTATIONAL STATUS IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (CRPC): PRIMERA+ STUDY (PROSTATE CANCER INNOVATING MARKERS OF EXPECTED RESPONSE TO AGONIST LHRH+ ANDROGEN RECEPTOR INHIBITION	NA	NCT04188275	2019
ZN-c5	Interventional	Cancer	12	Non-Randomized/Parallel Assignment/None (Open Label)	A PHASE 1B STUDY TO ASSESS THE SAFETY AND TOLERABILITY OF ZN-C5 IN CHINESE SUBJECTS WITH ADVANCED BREAST CANCER	Phase-1	NCT04852419	2022
NA	Observational	Cancer	60	Cohort	COLONIC RESECTION FOR CANCER AS DIABETOGENIC RISK FACTOR - A Study of the Pathophysiological Effects of Colon Resection on Glucose Homeostasis	NA	NCT04649567	2020
Metformin	Interventional	Cancer	150	Randomized/Single Group Assignment/Single (Participant)	BLADDER CANCER SCREENING AMONG DIABETIC PATIENTS ON METFORMIN THERAPY IN A WEST AFRICA SUB-REGION	Early Phase-1	NCT02505516	2015
Liquid nitrogen spray cryotherapy with the truFreeze device	Interventional	Cancer	1	N/A/Single Group Assignment/None (Open Label)	A Phase II, Multi-Center Study of Interventional Spray Cryotherapy for Early-Stage Esophageal Cancer (ICE-CANCER)	NA	NCT01868139	2022
Organ Preservation	Interventional	Cancer	30	N/A/Single Group Assignment/None (Open Label)	ORGAN PRESERVATION AFTER NEOADJUVANT TREATMENT FOR LOCALLY ADVANCED RECTAL CANCER	NA	NCT03064646	2018

HPV vaccine, Merck	Interventional	Cancer	1200	N/A/Single Group Assignment/None (Open Label)	ERADICATING CERVICAL CANCER IN KENYA: Benefits of Community-based Prevention, and the Effects of Aflatoxin on HPV Vaccination	NA	NCT04774887	2021
Tumor and blood sample	Interventional	Cancer	24	N/A/Single Group Assignment/None (Open Label)	PROTEOGENOMIC SIGNATURES ANALYSIS IN OVARIAN CANCER: LONGITUDINAL MODIFICATION ON TUMOR TISSUE BEFORE AND AFTER PLATINUM-BASED NEOADJUVANT CHEMOTHERAPY	NA	NCT05953883	2023
NA	Observational	Cancer	652	cohort	TREATMENT PATTERNS AND CLINICAL OUTCOMES AMONG PATIENTS RECEIVING PALBOCICLIB COMBINATIONS FOR HR+/HER2- ADVANCED/METASTATIC BREAST CANCER IN REAL WORLD SETTINGS	NA	NCT03159195	2022
Questionnaire	Observational	Cancer	75	Case-only	THERAPEUTIC PATIENT EDUCATION AND CANCER PAIN	NA	NCT02391740	2016
hypnosis	Interventional	Cancer	40	N/A/Single Group Assignment/None (Open Label)	PSYCHOLOGICAL CARE AND HYPNOSIS IN PATIENTS WITH CANCER	NA	NCT03971773	2019
Dietary Supplement: Vitamin C, E and Zinc	Interventional	Cancer	60	Randomized/Parallel Assignment/Double (Participant Investigator)	SUPPLEMENTATION OF VITAMIN E, C and ZINC IN PATIENTS WITH NON-MELANOMA SKIN CANCER: INFLUENCE ON OXIDATIVE STRESS AND INFLAMMATORY STATE	NA	NCT02248584	2014
Excision of sentinel node(s)	Interventional	Cancer	115	N/A/Single Group Assignment/None (Open Label)	IDENTIFICATION OF SENTINEL NODE(S) BY SENTIMAG® /SIENNA+ IN BREAST CANCER: FEASIBILITY STUDY	NA	NCT01790399	2014
Capecitabine/ radiotherapy/ TME resection/TEM surgery	Interventional	Cancer	55	N/A/Single Group Assignment/None (Open Label)	CHEMORADIOTHERAPY FOR RECTAL CANCER IN THE DISTAL RECTUM FOLLOWED BY ORGANSPARING TRANSANAL ENDOSCOPIC	Phase-2	NCT01273051	2017

					MICROSURGERY: CARTS Study CApecitabine, Radiotherapy and Tem Surgery. A PHASE II, FEASIBILITY TRIAL			
Nilotinib and Paclitaxel	Interventional	Cancer	34	N/A/Single Group Assignment/None (Open Label)	Rapid Analysis and Response Evaluation of Combination Anti-Neoplastic Agents in Rare Tumors (RARE CANCER) Trial: RARE 1 Nilotinib and Paclitaxel	Phase-2	NCT04449549	2023
Planned Visual Education Based on Health Belief Model	Interventional	Cancer	116	Randomized/ Parallel Assignment/ Single (Participant)	DOES PLANNED VISUAL EDUCATION AFFECT UNIVERSITY STUDENTS' ATTITUDES AND BELIEFS ABOUT SKIN CANCER?	NA	NCT05788939	2023
PF-06939999 dose escalation/PF-06939999 monotherapy/ PF-06939999 in combination with docetaxel	Interventional	Cancer	54	Non-Randomized/Parallel Assignment/ None (Open Label)	A PHASE 1 STUDY TO EVALUATE THE SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF ESCALATING DOSES OF PF-06939999 (PRMT5 INHIBITOR) IN PARTICIPANTS WITH ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER, HEAD AND NECK SQUAMOUS CELL CARCINOMA, ESOPHAGEAL CANCER, ENDOMETRIAL CANCER, CERVICAL CANCER AND BLADDER CANCER	Phase-1	NCT03854227	2022
Lirilumab/Nivolumab/ Ipilimumab	Interventional	Cancer	337	Randomized/Parallel Assignment/ Triple (Participant Care ProviderInvestigator)	A Phase 1/2 Study of the Combination of Lirilumab (Anti-KIR) Plus Nivolumab (Anti-PD-1) or Lirilumab Plus Nivolumab and Ipilimumab in Advanced Refractory Solid Tumors	Phase-1 & 2	NCT01714739	2023
Lirilumab/ Ipilimumab	Interventional	Cancer	22	Non-Randomized/ Single Group Assignment/ None (Open Label)	A Phase 1 Study of BMS-986015, an Anti-KIR Monoclonal Antibody, Administered With Ipilimumab, an Anti-CTLA4 Monoclonal Antibody, in Subjects With Select Advanced Solid Tumors	Phase-1	NCT01750580	2015

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