A Review on Precision Cancer Therapy

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ABSTRACT:

These days, cancer is the most lethal illness, and it's getting worse because of the way we live. The emergence of aberrant cells that have the capacity to invade and destroy healthy bodily tissues and divide uncontrollably is known as cancer. The most prevalent malignancies are those of the prostate, colon, lung, and breast. Nowadays, precision oncology focusses on matching the most precise and efficient treatment depending on the patient's unique situation as well as their disease and genetic profile. These treatments, which target cancer cells more precisely while protecting healthy cells, are typically based on the genetic profile of the tumour. Personalised medicine is another name for precision medicine. The cancer is treated based on the individual's medical history, condition, and type of cancer. This review aims to objectively evaluate how cancer treatment has changed, with a focus on the move towards more accurate techniques. An overview of the precision approach, personalised medicine for cancer, diagnosis and therapy, the benefits and drawbacks of precision medicine, and the successes and difficulties in applying precision cancer medicine are all covered in this review.

KEYWORDS: Cancer, Precision Therapy, Personalized medicine, Oncology, Immunotherapy, Biopsy.

INTRODUCTION:

In the realm of medicine, cancer is one of the most complicated and varied categories of illnesses; certain forms are readily curable, while others are still incurable. We cannot use a one-size-fits-all strategy for illnesses like cancer. Unfortunately, we have been treating many forms of cancer with the same strategy for decades due to a lack of technology. Even though these treatments have saved millions of lives worldwide, they still have drawbacks like side effects, recurrence, and in certain cases, death. However, as technology has advanced, cancer treatment has become more individualised, which has been a breakthrough [1].

Definition: "Any one of a wide range of diseases characterised by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue" is referred to as cancer. DNA alterations are the cause of cancer. The majority of DNA alterations that cause cancer take place in regions of DNA known as genes. Another name for these alterations is genetic alterations [2].

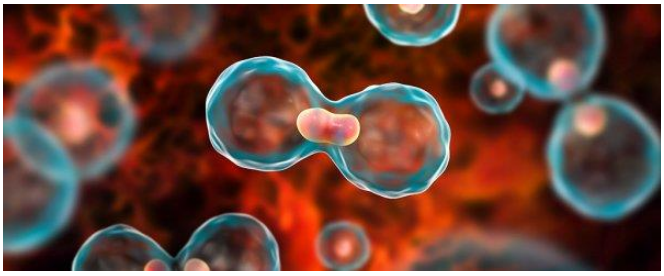

Fig.1 Cancer [3]

Prevalence of Cancer in India:

In 2022, there were a projected 1.4 million cancer cases in India, with lung cancer in men and breast cancer in women being the most prevalent forms. A major public health concern, cancer cases are expected to rise as a result of factors like air pollution, tobacco use, and lifestyle choices. Uttar Pradesh, Maharashtra, West Bengal, Bihar, and Tamil Nadu are the states having the highest estimated incidence of cancer.

Total estimated cases: In 2022, an estimated 1,413,316 new cases were reported. Incidence rate: Every year, about 100 out of every 100,000 persons receive a cancer diagnosis. Typical cancers: Lung cancer is most prevalent among men. Females: Breast cancer is the most common.

High-incidence states: The states with the greatest estimated numbers of cancer cases are Uttar Pradesh, Maharashtra, West Bengal, Bihar, and Tamil Nadu. Childhood cancers: For children aged 0 to 14, lymphoid leukaemia is the most common type [4].

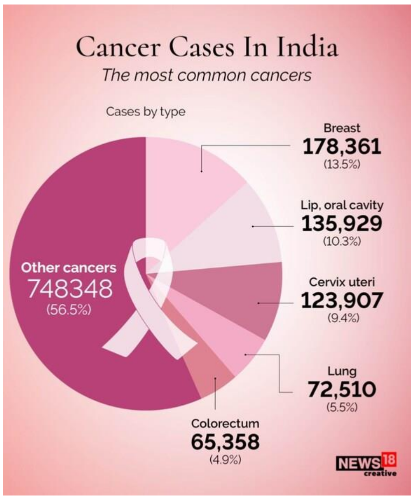

Fig.2 Cancer Cases in India [5]

CANCER, PRECISION ONCOLOGY AND PERSONALIZED MEDICINE

Precision oncology has developed into a field that focusses on matching the most precise and efficient treatments based on the patient's genetic profile and malignancy as well as other distinctive features that set each patient apart. Every patient has a distinct genome, proteome, epigenome, microbiome, lifestyle, diet, and other traits that interact to affect drug tolerance, remission, relapse, oncogenesis, disease progression, and viable therapy options.

There are variances between cancer cells from different patients as well as between cancer cells within a single patient because cancer is made up of several hundred heterogeneous diseases. No single medication has been successful in "curing" cancer since the disease is always evolving to avoid death. Immunotherapy and targeted medicines are now guided by a mix of each patient's distinct traits in precision oncology [6].

As it develops within a patient or in a subpopulation, cancer is a complex disease with a heterogeneous nature that is influenced by the population, environment, socioeconomic factors, and genetic or cellular abnormalities. Tumours are created by the aberrant and unchecked growth of cells that do not undergo apoptosis; these cells are known as neoplastic cells and are the source of cancer. A single tumour may contain a variety of cancer cells; the heterogeneous nature of these cells can be seen in heterogeneous diseases that are influenced by cell surface markers, growth rate, genetic, molecular, cellular, tissue, population, environmental, and socioeconomic factors. These tumours may coexist with other cells of stromal, endothelial, or immunological origin in the milieu of a complex system. Cancer can originate from any tissue or organ in the body, either from a somatic source (similar cell invasion at distant spread) or from a hereditary source (genetic abnormalities). Only a small percentage of the causes of cancer are known, and the majority of them are related to lifestyle choices, environmental factors, or infections.

Significant progress in the battle against cancer may result from the use of PM in cancer studies. The difficulties that healthcare professionals encounter when keeping an eye on patients include prolonged patient therapy, stage complexity, and interpatient variability (differences in response to cancer treatment). The development of personalised medicine has been greatly aided by the discovery of molecular changes as therapeutic targets. Numerous molecular changes that can be utilised for individualised treatment have been discovered by genomic, proteomic, and metabolomic investigations. These include mutations or fusions in PIK3CA, ERBB2, FGFR, BRAF, and NTRK. These findings have prompted the creation of targeted treatments that can precisely block these molecular changes, stopping the spread of cancer.

SYMPTOMATIC ORIGIN AND DEVELOPMENT OF CANCER

Uncontrolled and aberrant cell divisions spread quickly in cancer. Normal cells and the mechanism of apoptosis are identical to proliferating cells. Neoplastic cells are those that proliferate abnormally. Benign tumours and malignant tumours are the two distinct forms of cancer. Because benign tumours are found on the surface of cells, they are localised tumours. It is simple to eliminate from bodily parts. It is not transferable from one body part to another [10]. There are various kinds of benign tumours. The first is lipoma, which is an accumulation of fat cells in the body that appear as clusters in the skin and underlying muscle layer. —Myeloma: an increase in the body's muscle cells.

The first is lipoma, which is an accumulation of fat cells in the body that appear as clusters in the skin and underlying muscle layer. —Myeloma: Myeloma is the term for an increase of muscle cells in the body. A malignancy of the plasma cells is called myeloma. Multiple myeloma is another name for myeloma. Fibromass is an increase in the body's fibrous cells. It is mostly prevalent in the uterus of women. Malignant tumour: Due to its ability to spread, a malignant tumour is a hazardous type of cancer. It moves from one area of the body to another.

The cancer is not localised. There is a metastatic process. It comes in a variety of forms. Sarcomas, lymphomas, leukaemia, and carcinomas. Skin cancer is referred to as a carcinoma. Lymphomas: Lymphomas are cancers of the lymphatic system. The genesis of cancer is depicted in Fig 2.

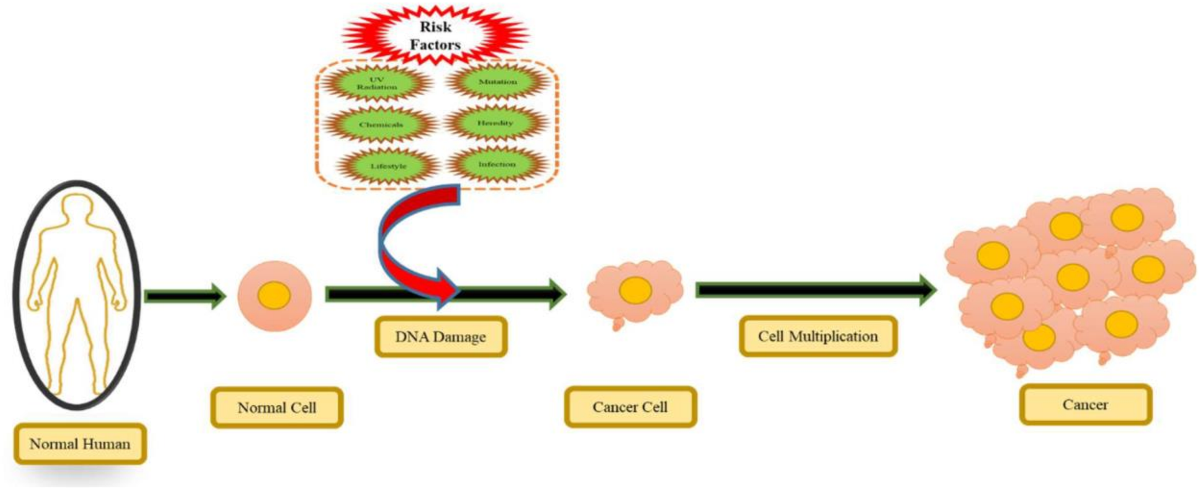

Fig.3 Diagrammatic representation showing the development process of cancer.

There are known hereditary cancer syndromes of autosomal disorders caused by defective alleles, where mutations inherited from offspring by parent genes are frequently involved in the start or triggering of early cancer. In addition to being generated by certain genetic inheritance, cancer cells can also multiply as a result of an impacted lifestyle. Lifestyle choices (such as smoking or consuming carcinogens, eating habits, and exercise), environmental factors (such as exposure to certain chemicals or radiation), and mutations that occur during cellular division are all factors that contribute to the development of various conditions.

A person with cancer exhibits a variety of symptoms. The type of cancer a person has will often determine the signs and symptoms they experience. For example, breast cancer is indicated by a lump (mass of tissue) in the breast. Skin cancer is indicated by an unusual-looking mole. Excessive weight loss, blood in the urine or faeces, exhaustion, and tumours that appear anywhere on the body are common indicators of many types of cancer. The many forms of cancer and their typical symptoms are compiled in Fig. 4.

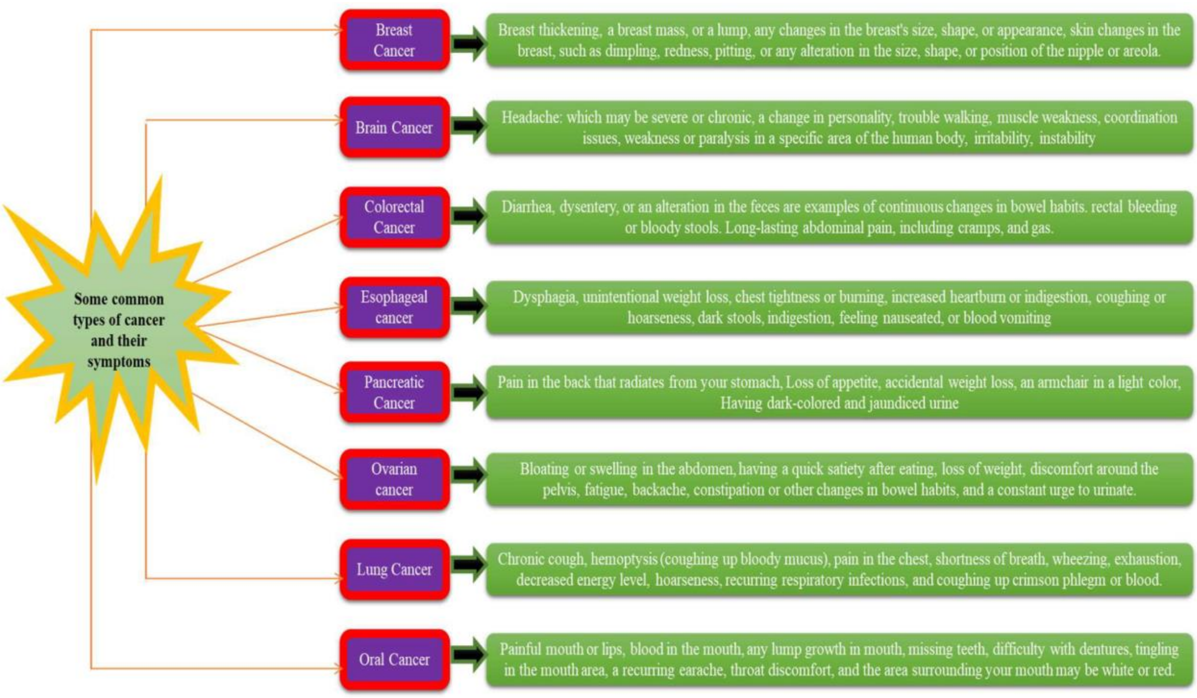

Fig.4 A systematic presentation depicting the common types of cancer and their common symptoms.

Genetic changes that allow normal cells to expand uncontrolled and develop into a mass or lump known as a tumour are the first step towards the development of cancer. Numerous causes, such as genetic predisposition, environmental influences, and exposure to carcinogens (such tobacco and certain chemicals), can result in these changes. The different sources of an individual's genetic alterations are systematically represented in Fig. 5 [7].

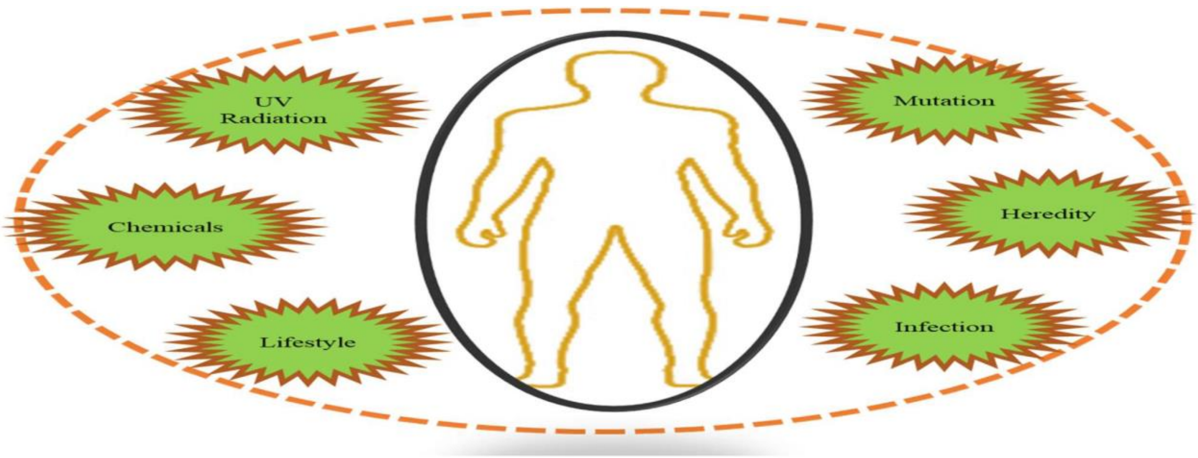

Fig.5 Major causes behind the genetic changes.

HOW CANCER IS DIAGNOSED?

Cancer cannot be diagnosed with a single, targeted test. To determine if a person has cancer or if an infection or other illness mimics the symptoms of cancer, numerous tests are required.

Laboratory tests, tumour biopsies, imaging, surgery, endoscopic examinations, and genetic testing are some of the methods used to diagnose cancer. Blood tests (CBC), urinalysis, and tumour markers are some of the frequently used procedures to examine the chemical components in physiological fluids and tissues. X-rays, computed tomography scans (often called CT scans, computer axial tomography, or CAT scans), bone scans, lymphangiograms (LAG), and mammograms are examples of diagnostic imaging. Ultrasound is a component of reflection imaging. MRI stands for magnetic resonance imaging.

Cystoscopy (also known as cystourethroscopy), colonoscopy, endoscopic retrograde cholangiopancreatography (ERCP), esophagogastroduodenoscopy (commonly known as EGD or upper endoscopy), and sigmoidoscopy are among the various endoscopic procedures that are performed to diagnose cancer. A biopsy is a procedure used to take tissue or cells from the body for examination under a microscope; there are numerous types of tumour biopsies used in the detection of cancer. Endoscopic biopsies, excisional or incisional biopsies, bone marrow biopsies, fine needle aspiration biopsies, punch biopsies, shave biopsies, and skin biopsies are some common forms of biopsies.

HOW CANCER IS TREATED?

The cancer is treated based on the individual's medical history, condition, and type of cancer. Chemotherapy and radiation therapy are the most often used treatments in the modern world. Other treatments include biological medicines and surgery.

There are some terms in treatment of cancer and they are:

1. Neoadjuvant therapy
2. Combined modality therapy
3. Adjuvant therapy

The common treatments include:

1) Radiation therapy
2) Chemotherapy
3) Hormone therapy
4) Bone marrow and blood transplant
5) Biologic therapy
6) Immunotherapy
7) Angiogenesis inhibitors [8]

TAILORED TREATMENT: A PRECISION APPROACH

The development of targeted treatments is a promising advancement in personalised cancer treatment. Chemotherapy kills rapidly dividing cells more or less randomly, whereas targeted medicines target particular chemicals or pathways that are active during the growth and survival of cancer cells. These treatments, which target cancer cells more precisely while protecting healthy cells, are typically based on the genetic profile of the tumour. Over time, a number of therapies and detection methods have developed to operate on the foundation of this strategy. Here are a few of them:

1- **Immunotherapy (using the immune system):** The development of immunotherapy, which further stimulates the human immune system to combat cancer cells, is an innovative concept that has arisen in personalised medicine for cancer treatment. Proteins that stop immune cells from attacking cancer cells are blocked by immunotherapy medications. By producing proteins that effectively suppress the immune response, some tumours even manage to evade the immune system. These proteins have been effectively suppressed by certain medications, enabling the immune system to recognise and eliminate the malignancy.

2- **Liquid biopsy (early diagnosis):** The development of biopsy is one of the most significant developments in cancer diagnosis. A type of biopsy known as "liquid biopsy" uses a patient's blood and bodily fluids to get an early, less invasive cancer diagnosis. It aids in comprehending the genetic mutation pattern. A more focused, individualised approach to cancer therapy has replaced a broad, one-size-fits-all strategy with personalised medicine. Personalised medicine is improving the accuracy, efficacy, and safety of cancer treatments through genetic testing, biomarkers, and novel treatments including immunotherapy and targeted therapies. The evolving personalisation of tumours promises to make their treatment more targeted, accessible, and effective than ever before, despite ongoing obstacles (Figure 6).

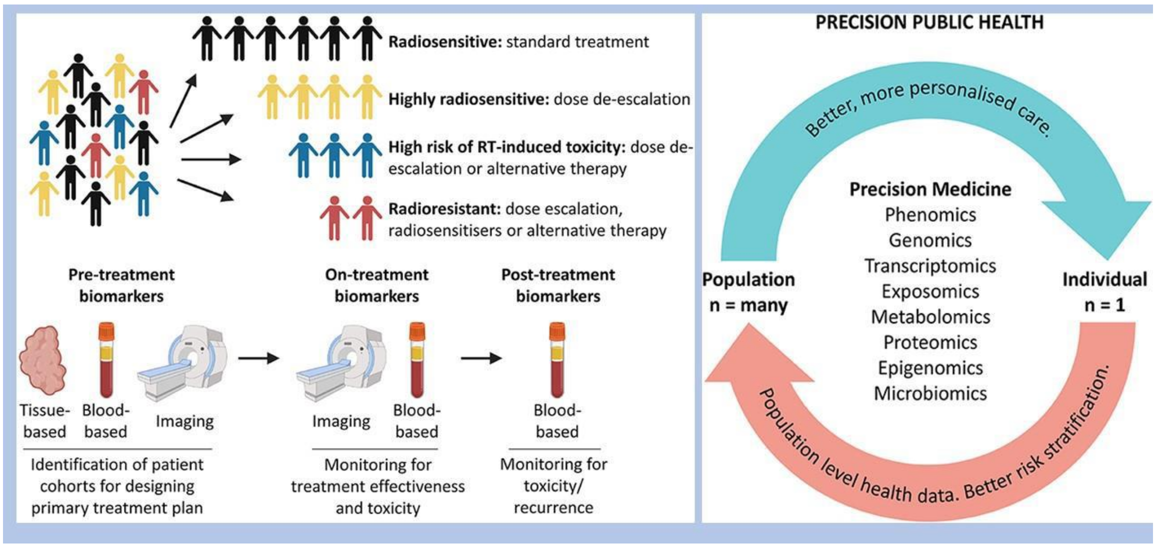

Fig.6 Review and importance of precision medicine in cancer treatment and individual health

WHAT IS PERSONALIZED MEDICINE FOR CANCER?

In the battle against cancer, something exciting is taking place. Physicians are developing novel approaches to each patient's cancer treatment. We refer to this strategy as personalised medicine. Doctors develop treatment strategies based on individual characteristics rather than administering the identical treatment to every patient. This blog will discuss personalised medicine in oncology, including its advantages, mechanisms, and effects on cancer patients. Although each patient is unique, doctors usually administer the same therapies to patients with the same type of cancer. Understanding these variations is the aim of personalised medicine. To choose the optimal course of action for you, it considers your health, lifestyle, and DNA.

To assist you choose the best course of action, doctors consider your genetic makeup. They accomplish this by examining your DNA, which functions as your body's instruction manual. Doctors can learn a lot about your cancer by reading it. This aids them in selecting the therapies that will be most effective for you.

HOW DOES PERSONALIZED MEDICINE WORK?

Initially, a tiny sample of your DNA is taken by doctors. After that, they look at this sample to find any distinctive features of your genes that might have an impact on your cancer. After learning this, they can select therapies that focus on those particular characteristics. Finding the correct key to stop cancer is similar to deciphering a secret code [1].

IMPORTANCE OF CLASSIFYING CANCER DIAGNOSIS AND TREATMENT

The most important step is cancer detection since it has a significant impact on patients' chances of survival. However, most cases of cancer are discovered at an advanced stage because of people's ignorance or carelessness. Furthermore, the majority of people from economically disadvantaged families may find it difficult to finance cancer therapies based on their type and stage, which could lead to a regression in the treatment of these illnesses. The evaluation of early-stage cancer detection and the development of cancer vaccines can be significantly improved by technological advancements in the understanding of biological processes, such as strong analytical molecular techniques, imaging, and histopathological methods with clinical trials (Fig. 7).

1. Early Detection and Diagnosis: Accurate diagnosis depends on determining the type of cancer and where it originated. Different screening techniques and diagnostic tests may be needed for different types of cancer. For example, colonoscopies are used to identify colorectal cancer, but mammograms are used to test for breast cancer.

2. Tailored Treatment: Every kind of cancer has distinct behaviours and reactions to therapies. Oncologists can create individualised treatment strategies by classifying malignancies according to their origin, such as breast, lung, or prostate. For instance, therapies that work for breast cancer may not work for lung cancer.

3. Research and Advancements: For continued research, it is crucial to comprehend the many forms of cancer. Scientists research various malignancies in order to create immunotherapies and targeted treatments that are specifically designed to address the distinctive features of each form of cancer.

4. Prognosis: The prognosis of a patient is greatly impacted by the type and stage of cancer. While some cancers advance slowly, others are more aggressive and spread quickly. Cancer classification offers important insights about how the disease is likely to progress.

5. Support and Awareness: Raising awareness of particular cancer kinds is aided by cancer classifications. In order to find treatments and assist patients, this information is crucial for public education, support systems, and fundraising initiatives.

Description of different treatment methods for Cancer (Table 1).

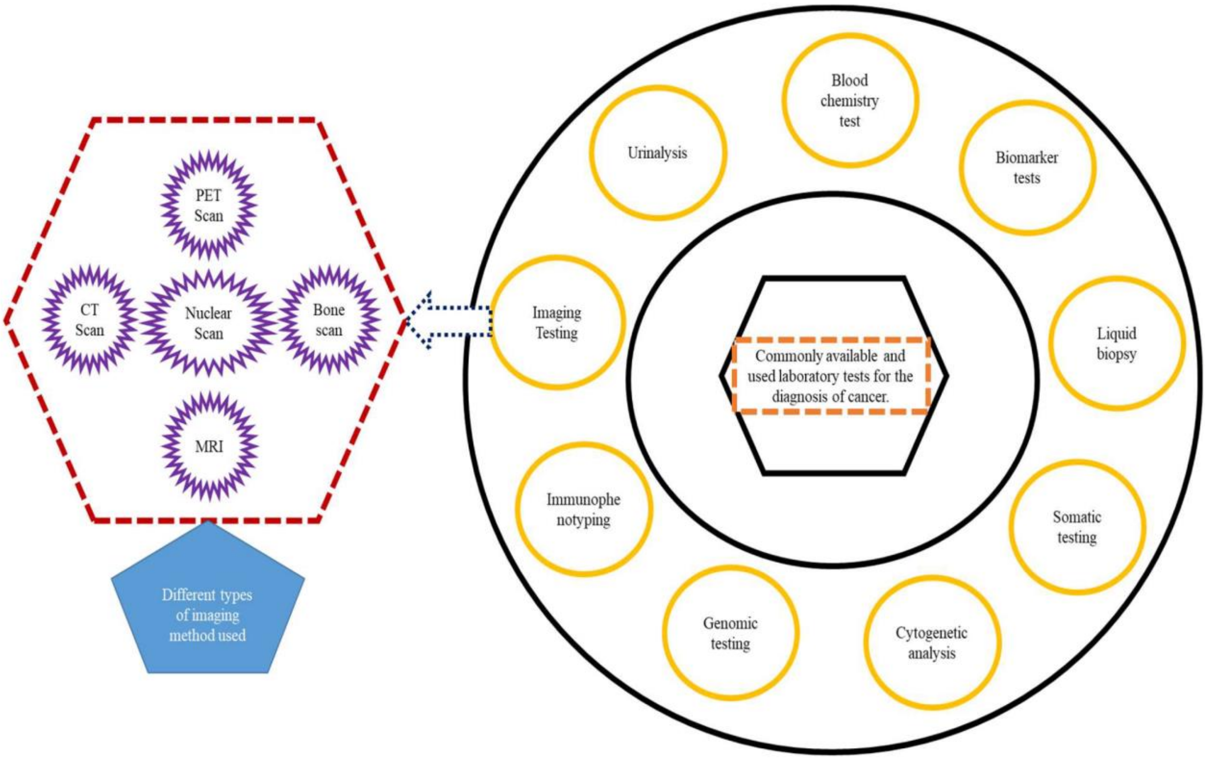

Fig.7 Various types of tests which are commonly used for the diagnosis of cancer.

Table 1 The treatment type along with the medication.

Treatment Type	**Description**	**Common Medications**
Surgery	Removal of cancerous tissue, tumors, or organs to eliminate or reduce the cancer.	- N/A (Procedure-based)
Chemotherapy	Uses drugs to kill or slow down cancer cells' growth and division.	-Doxorubicin: Adriamycin-Cisplatin: Platinol-Paclitaxel: Taxol Fluorouracil: 5-FU
Radiation Therapy	Uses high-energy rays to target and kill cancer cells or shrink tumors.	- Radium-223: Xofigo-Iodine-131: Iotrex- Cobalt-60: Radioactive cobalt source
Immunotherapy	It boosts the body's immune system to recognize and destroy cancer cells.	- Pembrolizumab: Keytruda-Nivolumab: Opdivo-Ipilimumab: Yervoy- CAR T-cell Therapy: Kymriah,

		Yescarta
Targeted Therapy	Targets specific molecules involved in cancer growth, preventing the cancer from growing and spreading.	- Trastuzumab: Herceptin Imatinib: Gleevec- Rituximab: Rituxan- Erlotinib: Tarceva
Hormone Therapy	Interferes with the body's hormone production to slow or stop the growth of hormone-sensitive cancers.	Tamoxifen: Nolvadex- Letrozole: Femara- Anastrozole: Arimidex- Leuprolide: Lupron
Stem Cell Transplant	It replaces damaged bone marrow with healthy stem cells and is commonly used after high- dose chemotherapy or radiation.	Filgrastim: Neupogen- Plerixafor: Mozobil- Tacrolimus: Prograf- Cyclophosphamide: Cytoxan
Precision Medicine	Tailor's treatment is based on the genetic makeup of the cancer, identifying specific genetic changes for targeted therapies.	Larotrectinib: Vitrakvi- Entrectinib: Rozlytrek- Olaparib: Lynparza- Trifluridine/Tipiracil: Lonsurf
Palliative Care	It focuses on symptom management, providing relief, and improving the quality of life for patients with serious illnesses.	Morphine: MS Contin- Dexamethasone: Decadron Ondansetron: Zofran Haloperidol: Haldol

PM FOR CANCER TREATMENT OF VARIOUS ALIGNMENTS

Herbal, Ayurvedic, and allopathic medicines have been administered in customised forms to ailing patients in India since ancient times. These alignments, which take the shape of foods with plant and animal origins that are blended differently for the immunised body, are a component of daily cultural practices. The layout of the PM workflow is depicted in Fig. 8. Personalised medications were based on herbs that are beneficial for certain symptomatic disorders and also immunised the immune system as a nontoxic adjuvant [7].

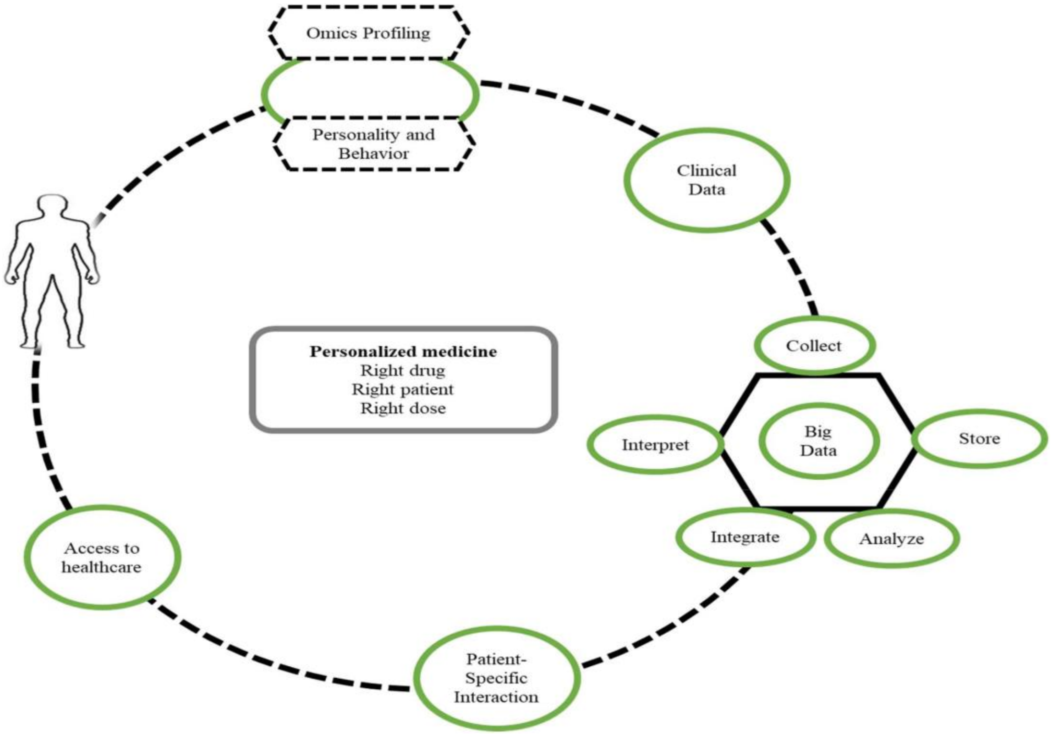

Fig.8 A fundamental structure for personalized healthcare.

ADVANTAGES AND DISADVANTAGES OF PRECISION MEDICINE [9]

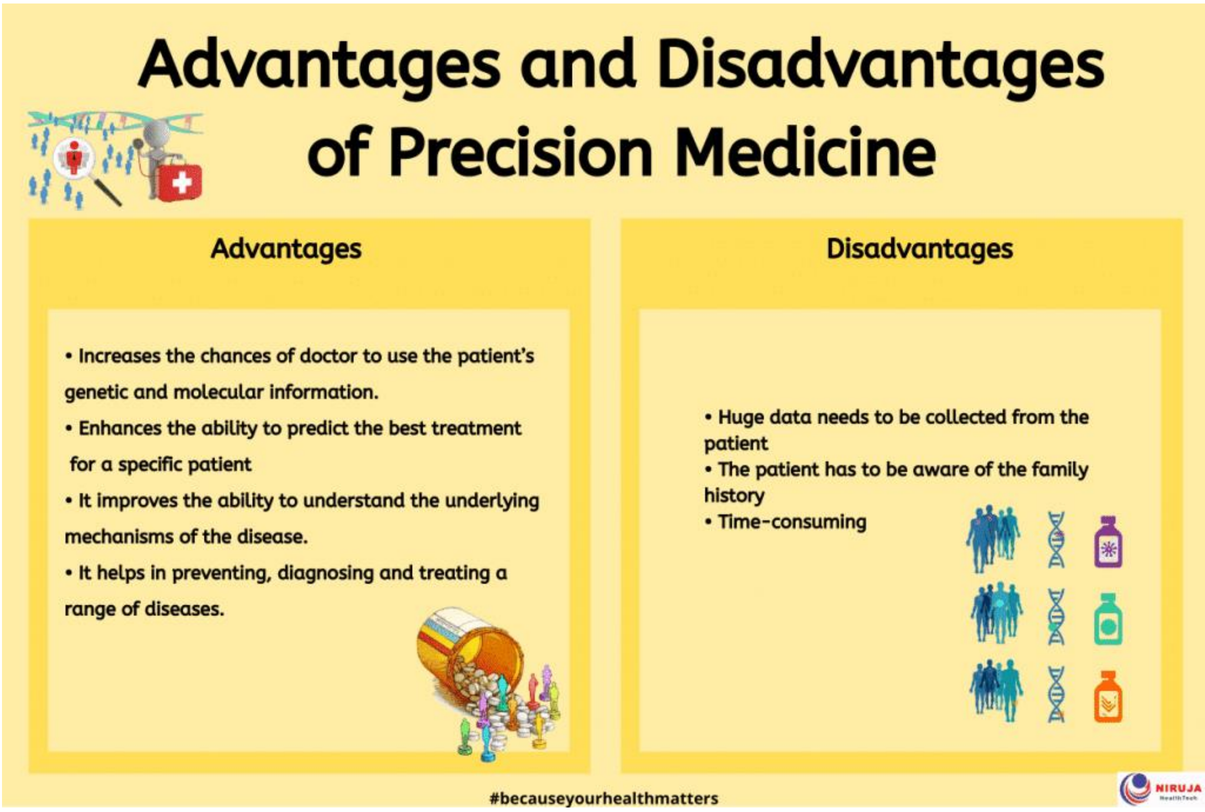

Fig.9 Advantages and Disadvantages of Precision Medicine[9]

ACHIEVEMENTS AND CHALLENGES IN IMPLEMENTING PRECISION CANCER MEDICINE

1. Diagnostics

Achievements

- Identification of biomarker/signatures
- Development of high-throughput sequencing technologies
- Decreasing of turn-around-time of sequencing
- Integration of further omics (e.g., transcriptomics and proteomics)

Challenges

- Highly dynamic diagnostic needs and technologies
- Increasing complexity
- Development of AI tools
- Integration of drug testing by model systems
- Longitudinal tracking of disease (e.g., monitoring and resistance mechanisms) Standardized EQA schemes for comprehensive genomic profiling

2. Therapy recommendation

Achievements

- Molecular tumor boards (MTB)
- Evidence-based therapy recommendations
- Harmonized evidence levels for variant interpretation

Challenges

- Integration of complex data and interaction
- Further standardization and harmonization of variant interpretation and therapy recommendations

3. Drugs

Achievements

- Increasing drug portfolio for stratified treatment
- Novel trial designs accelerating drug approval

Challenges

- Access to drugs governed by HTA bodies
- Development of smart and fast clinical trials
- Use of RWD/RWE in drug development

4. Financing

Achievements

- Long-term cost-reduction of sequencing
- Basic funding by national networks

Challenges

- Sustainable funding/reimbursement for the entire diagnostics process including MTB
- Short innovation cycles requiring continuous investments
- Financing academia-industry-driven clinical trials
- Financing a digital ecosystem allowing sharing, processing, analyzing data
- Financing data collection (follow-up/monitoring) in registry-based studies

5. **Data**

Achievements

- First achievements in data harmonization
- Setup of prospective registry trials

Challenges

- Big data/interpretation of data
- Harmonization of data structures/establishing data infrastructure
- Follow-up/response monitoring
- Robust analysis of real-world data

6. **Health professionals**

Achievements

- High interdisciplinarity
- Regional/national/international networks

Challenges

- Education and training of multidisciplinary teams
- Lifelong learning in an innovative and highly dynamic environment

7. **Legal and ethical aspects**

Achievements

- Modular templates for patient information
- Implementation of trust centers
- Data use and access committees

Challenges

- Informed consent
- Data sharing/use and privacy protection
- Handling of incidental findings
- Access to off-label treatments

8. **Patient involvement**

Achievements

- Involvement of patient representatives

Challenges

- More patient empowerment
- Public visibility (e.g., access and data safety) [10]

Conclusion:

Personalized treatments based on a tumor's distinct molecular profile have replaced general chemotherapy in the field of precision cancer therapy, resulting in better results and fewer side effects. Modern oncology is greatly impacted by precision cancer therapy, which creates previously unheard-of possibilities for tailored, efficient therapies.

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