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A Non-Systematic Review on Futuristic Approaches for Oncotherapy, Recent Innovations and Challenges

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ABSTRACT

Every year, Cancer is responsible for millions of Mortality worldwide and Even though many developments have been recorded in healthcare sector. For this reason, the broad field of oncotherapeutic researches still need much progress to be achieved in the medical field. A lot of issues are there to rectify and alleviate chronic side effects precipitated by conventional therapies. The various different technologies are currently under evaluation in clinical trials or have been already in therapy options. In this review, we focused on the pros and cons of the recent innovative therapeutic measures and discussed about the various ideologies to rectify the drawbacks as well as loopholes associated with the newer regimens.

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INTRODUCTION:

CANCER is the life threatening medical emergency, even though much progress achieved in medicine. Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread of cancer cells occurs, this stage is known as metastasis is not controlled, it can result in death. Carcinogens are a class of substances that are directly responsible for damaging DNA, and promoting or aiding cancer. Eg; tobacco, asbestos, arsenic, radiation, X-rays, sun and vehicle fumes.

The conventional therapies for cancer is a series of interventions includes psychosocial support, surgery, radiotherapy, chemotherapy which is aimed to cure the disease or prolonging patient's life considerably improving the patients Quality of Life.

As we said earlier, cancer is the second major death-causing disease next to heart diseases. In India, Nearly 2 to 2.5 million cancer cases are estimated, 7 lakh new cases and 3 lakhs deaths occur due to cancer. Cancer incidence worldwide is more than a fifth higher in men than in women. Globally, 15 milion people were diagnosed with cancer and this rate has been increase gradually with time.

During tumor progression, it becomes heterogeneous which creates mixed population of the cells by different molecular features and diverse response to the treatment.1 So, the deep understanding on this complexity is fundamental to design precise and efficient therapies.

In past decades, the research studies focused on finding new therapeutic measures to overcome side effects exerted by conventional therapies. Along with this, the recent researches focus on innovative immune surveillance, nano-medicine, targeted therapy, natural antioxidants, thermal ablation, gene therapy, radiomics, pathomics and personalized drug therapy on oncotherapy to reduce cancer prevalence as well as to eradicate the occurrence of cancer.

In this review, we will provide a general overview of the most advanced basic and applied cancer treatments as well as newly proposed therapy measures that are currently under investigation at research stage that should overcome the limitations of older conventional therapies.

NANOMEDICINE:

Nanoparticles are ranges between 1 -1000 nm in size but which exert versatile physiochemical properties due to their size and higher surface-to-volume ratio. The biocompatible nature of nanomedicine was used in recent research to overcome the low specificity and bioavailability related to conventional oncotherapy by encapsulating the active agents in nanoparticles will increase their solubility, stability, specificity and bioavailability in bodily fluids and retention time in tumor vasculature[1].

Table 1: Examples and Comments on Nano-Medicines

S.No	Example	Comments	Reference
1	ThermoDox	A liposomal formulation which release Doxorubicin as a response to an increment of temperature	[1]
2	Quantum dots coated with polyethelene glycol	It conjugates with anti- HER2 antibodies and is localized in specific tumor cells	[1]
3	Gold nanoparticles : Silica core Nano shell & gold shell coated with PEG (AURO SHELL, NANO SPECTRA)	It is used for the treatment of breast cancer by photodynamic therapy.	[1]
4	Doxorubicin-loaded PEGylated liposomes (DOXIL)	First approved nanoparticle by FDA(1995), This formulation drastically decreases the side effects exerted by doxorubicin; used to treat AIDS- associated Kaposi's sarcoma.	[1]
5	Albumin – Paclitaxel particles (ABRAXANE)	Approved by FDA for treating metastatic breast cancer and pancreatic ductal adenocarcinoma	[1]
6	An engineered protein combining interleukin – 2 and ditheria toxins (ONTAK)	Approved by FDA for the treatment of non – Hodgkin's peripheral T cell lymphomas	[1]

The nanoparticles show higher bioavailability, higher affinity and prolonged release compared toother systems; however, the encapsulation efficiency is comparatively low because of its high crystalinity[1]. In this type, many of the drugs have been either accepted or under clinical investigation, carry many advantages also contain fewer drawbacks, that have to be rectified on upcoming researches.

TARGETED THERAPY AND IMMUNOTHERAPY:

- Type of cancer treatment that helps your immune system fight cancer.
- Helps your body fight infections and other diseases.

- Made up of WBC and organs and tissues of the lymph system.
- Type of biological therapy.
- It is a type of treatment that uses substances made from living organisms to treat cancer.

Natural Killer Cells:

- A type of immune cell that has granules with enzymes that can kill tumor cells or cells infected with virus.
- Nk cells- Type of white blood cells
  - Innate immune cells
  - Tumor cells and virus-infected cells have strong cytolytic function.
  - Nk cells show a broad array of tissue distribution and phenotypic variability.
- Nk cells are complex compared to cytotoxic T-cells.
- Nk cells activation - Mature, bone marrow lymph nodes, spleen and thymus.
- Peripheral nk cell testing - To measure the percentage(%) and quantity of nk cells.
- The location of natural killer cells present in the body are bone marrow, lymphnodes, thymus, liver, uterus[7].

Mechanism of NK cell in cancer treatment:

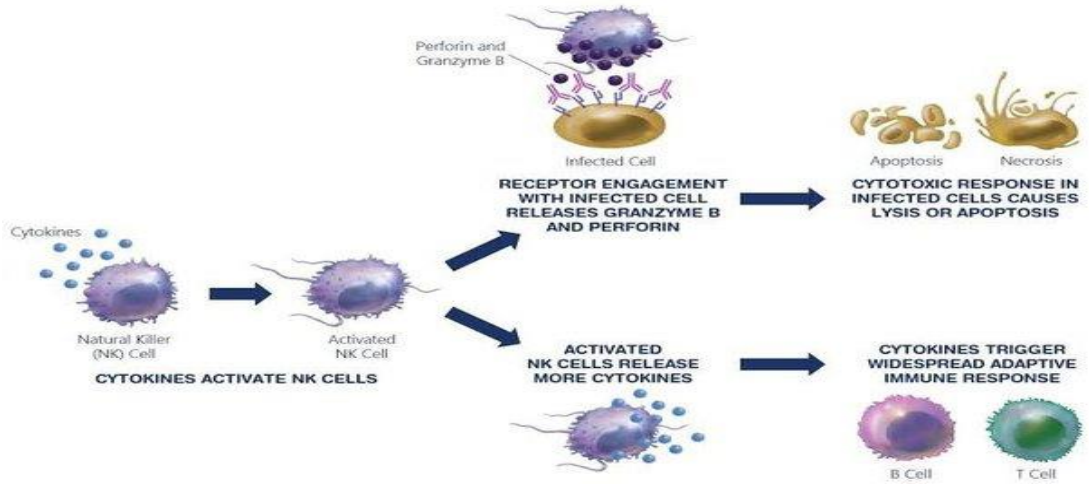

Table 2: Clinical trials for established NK cell-related therapies

Mechanism	Condition	Intervention	Phase	Reference
IL-15 signal pathway	Metastatic malignant melanoma, RCC	Recombinant human interleukin-15(rIL-15)	I (first-in-human)	[6]
	Advanced metastatic solid tumor	IL-15 by continuous infusion	I	[6]
	Refractory and relapsed adult T cell leukemia	IL-15 + alemtuzumab (anti-CD52)	I	[6]
	Refractory and relapsed chronic lymphocytic leukemia	IL-15+ obinutuzumab (anti-CD20)	I	[6]
	Hematologic malignancies recurring after transplantation	ALT-803 (IL-15 superagonist)	I (first-in-human)	[6]
	Metastatic NSCLC	ALT-803 + Nivolumab (anti-PD-1 antibody)	Ib	[6]
IL-21 signal pathway	Relapse/refractory low-grade B-cell LPD	Recombinant human interleukin-21 (rIL-21) + Rituximab (anti-CD20 antibody)	I	[6]
	Metastatic malignant melanoma, RCC	rIL-21	I	[6]
	Stage IV malignant melanoma without prior treatment	rIL-21	IIa	[6]
IL-12 signal pathway	Metastatic solid tumors	NHS-muIL12 (two IL12 heterodimers fused to the NHS76 antibody)	I (first-in-human)	[6]
	Murine mammary/subcutaneous tumors	NHS-muIL12+ Avelumab (anti-PD-L1 antibody)	Preclinical models	[6]
IL-2 signal pathway	Locally advanced or metastatic solid tumors	NKTR-214 (IL-2 pathway agonist)	I/II	[6]
	Advanced Solid Tumors (Japanese)	NKTR-214 + Nivolumab	I	[6]
Anti-KIR antibody	AML in FCR	IPH2101 (anti-KIR antibody)	I	[6]
	Relapsed/refractory MM	IPH2101	I	[6]
	Smoldering MM	IPH2101	II	[6]
	Relapsed/Refractory MM	IPH2101+ lenalidomide (immunomodulatory agent)	I	[6]
	AML	Lirilumab (2nd generation anti-KIR antibody))	II	[6]
	SCCHN	Lirilumab + Nivolumab	II	[6]
	Cisplatin-ineligible muscle-invasive bladder cancer	Lirilumab + Nivolumab	Ib	[6]
Anti-NKG2A	Advanced gynecologic malignancies	Monalizumab (IPH2201, anti-NKG2A antibody)	I	[6]
	metastatic microsatellite- stable	Monalizumab + durvalumab	First-in human	[6]

antibody	colorectal cancer			
	recurrent or metastatic head and neck cancer	Monalizumab + cetuximab	I	[6]
TNF pathway	Advanced solid tumors	BMS-986156 (glucocorticoid-induced TNF Receptor-Related Protein Agonist) +/− Nivolumab	I/IIa	[6]
Cell adoptive therapy	Canine sarcomas	Radiotherapy+ intra-tumoral autologous NK transfer	first-in-dog	[6]
	Recurrent medulloblastoma and ependymoma (children)	ex-vivo-expanded NK cells	I	[6]
	Metastatic gastrointestinal carcinoma	Adoptive transferred autologous NK cells + cetuximab	I	[6]
	HER2-positive cancers	Adoptive transferred autologous NK cells + trastuzumab	I	[6]
	Locally advanced colon carcinoma	Adoptive transferred autologous NK cells + chemotherapy	I	[6]
	Malignant lymphoma or advanced solid tumors.	Adoptive transferred allogeneic NK cells	I	[6]
	Myeloid leukemia	Adoptively transferred memory-like NK cells induced by IL-12, IL-15, and IL-18	I (first-in human)	[6]
	High-risk AML, MDS, CML	MbIL21 ex vivo-expanded donor-derived NK cells	I	[6]
	MDS, AML.	Fludarabine/cyclophosphamide + total lymphoid irradiation + adoptive transferred IL2-activated haploidentical NK cells	I	[6]
	Older AML patients	Transferred umbilical cord blood CD34 hematopoietic stem + progenitor-derived NK Cells	I (first-in human)	[6]
	Non-Hodgkin lymphoma	Haploidentical donor NK cells + rituximab+ IL-2	II	[6]
	Myeloma	α-galactosylceramide-loaded monocyte-derived dendritic cells + low-dose lenalidomide (mediate antigen-specific co-stimulation of human iNKT cells)	I	[6]
CAR-NK therapy	CD19-positive lymphoid tumors	NK cells expressing anti-CD19 CAR, IL-15 and inducible caspase 9	I/II	[6]

Drawbacks of NK cell therapy:

The areas needed to be re assessment in natural killer cell therapy to promote effectiveness of this type of treatment are as follows[8]:

1. **Limited persistence:** NK cells have a relatively short lifespan in the body, which can limit their long-term effectiveness. The infused NK cells may not persist in sufficient

numbers to provide sustained anti-tumor activity over an extended period of time.

2. **Immune evasion mechanisms:** Tumors can employ various immune evasion mechanisms to evade NK cell recognition and attack. For example, tumors may down-regulate the expression of ligands that activate NK cells or up-regulate inhibitory receptors that dampen NK cell function. These mechanisms can reduce the efficacy of NK cell therapy.

3. **Tumor microenvironment:** The tumor microenvironment can create an immunosuppressive milieu that hampers NK cell function. Factors such as hypoxia, high levels of inhibitory cytokines, and the presence of immunosuppressive cells like regulatory T cells can impair NK cell activity and limit their anti-tumor effects.

4. **Limited homing and infiltration:** NK cells may face challenges in homing to tumor sites and infiltrating solid tumors. The tumor vasculature and stromal components can create physical barriers that restrict NK cell access to tumor cells. This can limit the effectiveness of NK cell therapy in solid tumors.

5. **Off-target effects:** While NK cells are generally considered safe, there is a potential risk of off-target effects. NK cells can recognize and attack healthy tissues that express low levels of activating ligands or aberrantly express inhibitory ligands. This can lead to unintended tissue damage and adverse effects.

6. **Manufacturing challenges**: Generating a sufficient number of functional NK cells for therapy can be challenging. The expansion and activation of NK cells ex vivo require specialized techniques and can be time-consuming and costly. Ensuring the quality, purity, and consistency of the manufactured NK cell products is also crucial for their therapeutic efficacy.

TARGETED THERAPY:

- Treatment that targets proteins that control how cancer cells grow, divide, and spread, it acts as the foundation of precision medicine.
- Most targeted therapies are either small-molecule drugs or Monoclonal antibodies.
- **Small-molecule drugs** are small enough to enter cells easily, so they are used for targets that are inside cells[1].

- **Monoclonal antibodies,** also known as therapeutic antibodies, are proteins produced in the lab. These proteins are designed to attach to specific targets found on cancer cells[1].

TUMOR MICROENVIRONMENT:

Tumor Microenvironment (TME) is the cellular environment in which the tumor exists in the human system. It includes the blood vessels, fibroblasts, cells that contribute to immunity, bone marrow-derived inflammatory cells, lymphocytes, signaling and the extracellular matrix (ECM)[2].

The development or role of TME:

Tumor Microenvironment plays several functions in the growth and progression of cancer. Some of the functions of TME are[4]:

1. Promoting angiogenesis: TME can promote the formation of new blood vessels, which can supply nutrients and oxygen to the tumor cells, allowing them to grow and spread**.**

2. Suppressing the immune system: TME can suppress the immune system, making it difficult for the body to fight cancer cells.

3. Modulating extracellular matrix: TME can modulate the extracellular matrix, which can affect the behavior of cancer cells and their response to therapy.

4. Promoting metastasis: TME can promote the spread of cancer cells to other parts of the body, leading to metastasis.

5. Providing a supportive environment: TME can provide a supportive environment for cancer cells to grow and survive, including factors such as growth factors, cytokines, and chemokines. Understanding the functions of TME is important for developing effective cancer treatments that can target the tumor microenvironment and improve patient outcomes.

Understanding the functions of TME is important for developing effective cancer treatments that can target the tumor microenvironment and improve patient outcomes.

Future directions:

The tumor microenvironment is newly emerging once-therapeutic measures, varies researches were going on as the future directions. They are as follows:

- Identification of the new targets.
- Combination therapies
- Personalized medicines.
- Introduction of new technologies.
- Conducting clinical trials on new therapies

EXTRACELLULAR VESICLES:

Extracellular vesicles (EVs) are lipid bilayer-enclosed structures that are released from cells into the extracellular environment[9]. They are proposed to be tailor-made specialized mini-maps of their cell of origin and are transported in the bloodstream and other body fluids. EVs are involved in cell-to-cell communication and can contain a variety of biomolecules, including proteins, lipids, and nucleic acids. EVs can be sub-grouped based on size and cellular origin, with exosomes being ~30 nm–120 nm and of endosomal origin, and microvesicles/ectosomes being > 120-1000 nm and from the cell membrane[9-11].

Role of EVs in cancer treatment:

Extracellular vesicles (EVs) have been implicated in various aspects of cancer, including drug resistance. EVs can transfer drug-efflux pumps from drug-resistant cancer cells to drug-sensitive cells, leading to the acquisition of drug resistance. Additionally, EVs can transfer oncogenic molecules, such as mRNAs, to recipient cells, promoting tumor growth and metastasis. However, EVs also have potential as drug delivery vehicles, as they can be engineered to target specific cells and tissues. Researchers are exploring the use of EVs as a means of delivering anti-cancer drugs directly to tumor cells, potentially increasing drug efficacy and reducing side effects. The roles of EVs, or extracellular vesicles, are diverse and complex. In the context of cancer, tumor-secreted EVs play a critical role in intercellular communication between tumor cells and stromal cells in local and distant microenvironments. They can orchestrate multiple systemic pathophysiological processes, such as coagulation, vascular leakiness, and reprogramming of stromal recipient cells to support pre-metastatic niche formation and subsequent metastasis. EVs contain bioactive molecules, such as nucleic acids, proteins, and lipids, that can redirect the function of a recipient cell and promote angiogenesis, coagulation, and immune modulation, among other

effects. In addition to their role in cancer, EVs have been implicated in a variety of physiological and pathological processes, such as blood coagulation, immune regulation, and neurodegenerative diseases[9-11].

GENE THERAPY:

Gene therapy is intended as the introduction of a normal copy of a defective gene in the genome in order to cure specific diseases. The first application dates back to 1990 when a retroviral vector was exploited to deliver the adenosine deaminase (ADA) gene to T-cells in patients with severe combined immunodeficiency (SCID). Further research demonstrated that gene therapy could be applied in many human rare and chronic disorders and, most importantly, in cancer treatment. Approximately 2,900 gene therapy clinical trials are currently ongoing, 66.6% of which are related to cancer[1].

The emerging field of cancer gene therapy offers a number of exciting potential treatments. The term gene therapy encompasses a wide range of treatment types that all use genetic material to modify cells (either *in vitro* or *in vivo*) to help effect a cure. Numerous *in vitro* and preclinical animal models, testing a wide variety of gene therapy agents, have shown remarkable efficacy[3].

In this section, we focus on the gene therapy trials that have progressed beyond the preclinical stage and are now in clinical trials. In order to explain these treatments, we have broken the field of cancer gene therapy treatments into three broad categories are as follows:

- Immunotherapy,
- Oncolytic virotherapy
- Gene transfer.

Each section includes a brief history of the gene therapy category and a discussion of the state of current clinical trials and the future directions for the therapy.

Traditional immunotherapy has achieved limited success because tumor cells tend to evolve mechanisms that evade immune detection. A wide array of gene therapy techniques are being used to overcome this limitation. Currently, gene therapy is being used to create recombinant cancer vaccines. Unlike vaccines for infectious agents, these are meant to cure or contain it by training the patient's immune system to recognize the cancer cells by

presenting it with highly antigenic and immune-stimulatory cellular debris. Some of the advancements are as follows[3]:

Table 3: Advancements of Gene therapy

Cancer	Stimulating genes	Clinical trials.gov identifier	Description	Phase
Prostate	Murine α(1,3)-galactosyltransferase	NCT00105053	Mouse protein-sugar are expressed on allogeneic prostate cells to induce a hyperacute rejection response	II
Pancreatic	CEA and MUC^{-1}	NCT00088660	Replication incompetent vaccinia and fowlpox viruses engineered to produced CEA and MUC-1 given subcutaneously to produce an immune response to pancreatic cancer	III
Prostate	GM-CSF	NCT00122005	Allogeneic prostate cells expressing the GM-CSF gene are used to induce immune response following chemotherapy and peripheral blood mononuclear cells infusion	VII
Lymphoma	GM-CSF and CD40L	NCT00101101	Autologous tumor cells are combined with allogeneic cells that express GM-CSF and CD40L and incorporated into a vaccine with low doses of IL-2	II
Melanoma	IL-2	NCT00059163	Autologous tumor cells engineered to express IL-2 are incorporated into a vaccine	II
Kidney	CD-80	NCT00040170	A modified replication incompetent adenovirus containing the tumor antigen CD-80 is injected subcutaneously along with the cytokine IL-2 to produce an immune response to prostate cancer	II

As with any cancer monotherapy, combination therapy using vaccines may be more effective than vaccine therapy alone. With the current round of ongoing clinical trials, the potential of gene therapy cancer vaccines is close to being fulfilled.

Oncolytic Agents

Another growing area of gene therapy treatment for cancer is the use of oncolytic vectors for cancer destruction. Even in this early stage, oncolytic viral therapy has demonstrated some success. Both adenovirus and herpes virus agents have ongoing clinical trials for intractable cancers. The most notable adenoviral therapy is the ONYX-015 viral therapy. ONYX-015 is an adenovirus that has been engineered to lack the viral E1B protein.44 Without this protein, the virus is unable to replicate in cells with a normal pathway. In addition, the E1B protein is essential for RNA export during viral replication.45 Cancer cells often have deficiencies in the p53 pathway due to mutations and thus, allow ONYX-015 to replicate and lyse the cells. The second type of oncolytic virotherapy undergoing clinical trials uses herpes simplex virus type 1 (HSV-1). Two vectors, G207 and NV1020, are currently in phase I and phase II trials for the treatment of intractable cancers.

Future Directions:

Oncolytic gene therapy is not yet developed technology, because there is only few number of oncolytic vectors were identified. The combination of the powerful killing nature of these vectors combined with the selectivity makes them an exciting avenue for lowering the number of cancer deaths.

Gene Transfer

One of the most vital range of treatments to emerge from the concept of gene therapy is that of gene transfer or insertion. This is a radically new treatment paradigm involving the introduction of a foreign gene into the cancer cell or surrounding tissue. For example, suicide genes (genes that cause cellular death when expressed), anti-angiogenesis genes and cellular stasis genes. Initial attempts to implement gene transfer therapy have highlighted its promise, as well as some delivery difficulties.

Table 4: Ongoing trials involved in Gene transfer therapy

Cancer	Transferred genes	Clinicaltrials.gov identifier	Description	Phase	Reference
Pancreatic	Rexin-G	NC00121745	A cytocidal cyclin G1 construct accumulates preferentially in the tumor cells to block the action of cyclin G1 and initiate cell death	I	[3]
Glioblastoma	HSVtk	NC00001328	The HSVtk gene is introduced into glioblastoma cells via a mouse retrovirus. Glioblastoma cells with the HSVtk gene are then sensitive to the drug ganciclovir which is administered	I	[3]
Head and Neck	p53	NC00041613	Transfer of the p53 gene via a replication incompetent adenovirus to tumor cells to inhibit cell growth and induce apoptosis	III	[3]
Melanoma	MDA-7	NC00116363	MDA-7 a novel tumor suppressor molecule is introduced into the melanoma cells and over expression inhibits cellular proliferation and induces apoptosis	II	[3]
Pancreatic	TNF-α	NC00051467	The TNF-α gene under the control of a radiation-inducible promoter is introduced into tumor cells and in combination with the radiation therapy induces cell death	II	[3]

Gene transfer, while a radically new type of treatment, is also the only gene therapy product to obtain regulatory approval in any global market, as demonstrated by China's 2003 approval of Gendicine for clinical use. Medicine is a modified adenovirus that delivers the p53 gene to cancer cells and is approved for the treatment of head and neck squamous cell carcinoma. Since approval, thousands of patients have been treated in China; some with repeated injections. As yet, large-scale efficacy trial results have not been published; the results of which are eagerly awaited. Current gene transfer trials have demonstrated

statistically significant survival improvements and provided very encouraging signs that current research is on the right path. New delivery methods and more sophisticated gene expression cassettes will create better therapeutic alternatives to make the goal of cancer treatment and eradication achievable.

THERMAL ABLATION:

Thermal ablation includes techniques called hyperthermia or hypothermia to destroy neoplastic tissues. The cell necrosis occurs at temperatures lower than -40°C or higher than 60°C. Long exposures to temperatures between 41°C and 55°C are also effective for tumor cell damage. Moreover, it has been shown that cancer cells are more sensitive to high temperatures than healthy ones[1].

Hyperthermia includes Radiofrequency (RF), Microwave and Laser ablation. An alternated current of RF waves is applied to a target zone by an insulated electrode tip, while a second electrode, needed to close the circuit, is placed on the skin surface[1]. The interaction with the current causes the oscillation of ions in the extracellular fluid, which, in turns, produces heat. RF is used in clinics due to its effectiveness and safety. The medium plays a vital role in their effectiveness. So, RF ablation works better in the liver than in lungs because of water and ion content.

Microwave ablation works based on the principle of electromagnetic interaction which acts between microwaves and polar molecules (Tissues present in water). This interaction produces oscillation and increases the temperature. MA allows high temperatures to be reached in a shorter period of time.

Laser therapy is a more precise and very effective therapy. It exploits the properties of laser beams of very narrow and extremely focused at a specific wavelength. The absorption of the light emitted by the laser results in the heating and subsequent damage of the targeted area[1].

RADIOMICS AND PATHOMICS:

Radiomics and Pathomics are two promising and innovative fields based on accumulating quantitative image features from radiology and pathology screenings as therapeutic and prognostic indicators of disease outcomes. Many artificial intelligence technologies, such as machine learning applications, have been introduced to manage and elaborate the massive amount of collected datasets and to accurately predict the treatment efficacy, the clinical

outcome, and the disease recurrence. Prediction of the treatment response can help in finding an *ad hoc* adaptation for the best prognosis and outcome. Nowadays, personalized medicine requires an integrated interpretation of the results obtained by multiple diagnostic approaches, and biomedical images are crucial to provide real-time monitoring of disease progression, being strictly correlated to cancer molecular characterisation[1].

Radiomics is intended as the high throughput quantification of tumor properties obtained from the analysis of medical images. Pathomics, on the other side, relies on the generation and characterization of high-resolution tissue images. Many studies are focusing on the development of new techniques for image analysis in order to extrapolate information by quantification and disease characterization. Flexible databases are required to manage big volumes of data coming from gene expression, histology, 3D tissue reconstruction (MRI) and metabolic features (positron emission tomography, PET) in order to identify disease phenotypes[1].

PERSONALISED CANCER MEDICINE:

Personalized medicine is an emerging approach to patient care in which an individual's characteristics, It plays vital role in cancer therapy to on prevention and where significant short-term toxicities and long-term functional implications are associated with oncotherapy. In this we included some recent molecular targets for particular personalized cancer treatments are as follows[5]:

Table 5: Molecular Targets for Personalized Cancer Treatment

S.NO	CANCER TYPE	CELLULAR TARGET	TARGET AGENT	CATEGORY
1	Colorectal	KRAS	Cetuximab	Monoclonal antibody against EGFR
2	Breast	HER2	Trastuzumab	Monoclonal antibody against HER2/ Neu (EGFR2)
3	Chronic myeloid leukaemia	BCR-ABL fusion protein	Imatinib	Receptor tyrosine kinase inhibitor
4	Gastrointestinal stromal Tumours	c KIT	Imatinib	Receptor tyrosine kinase inhibitor
5	Non-small cell lung cancer	EGFR	Erlotinib and gefitinib	Receptor tyrosine kinase inhibitor
6		EML4-ALK fusion protein	Crizotinib	Receptor tyrosine kinase inhibitor
7	Metastatic malignant Melanoma	BRAF V600E	Vemurafenib	B-raf/MEK/ERK pathway inhibitor
8	Ovarian, breast and prostate cancer (under investigation)	BRCA1, BRCA2	Olaparib	Poly(adp-ribose) polymerase (parp) Inhibitor

CONCLUSION:

In recent years research in oncology, has been taken remarkable steps towards more effectiveness, precise, less invasive, cost-effective and cost beneficial therapy. The above recent innovations in cancer treatment shows the promising results in the database of the clinical trials. The current scenario of cancer research considers not only patient recovery and well being during treatment period but also to eradicate or to prevent the occurrence of the cancer. However, some cons still have to be overcome much more progress to likely to come in future.

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