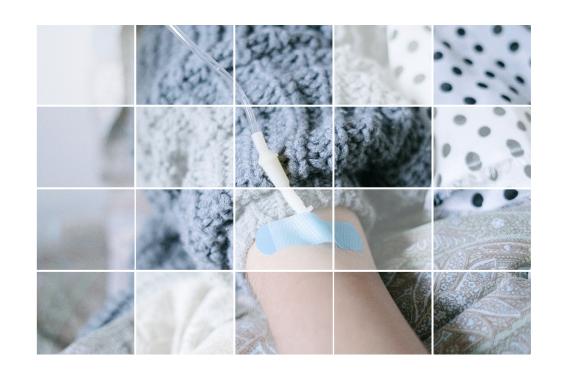
Cancer Treatmentsand Pipelines



Stella Dai 2021.11 Dragon Gate Investment Partners LLC

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Cancer Treatments



Biological Therapy for Cancer



Biological therapy is a type of cancer treatment that uses the **body's immune system** to **kill cancer cells**.



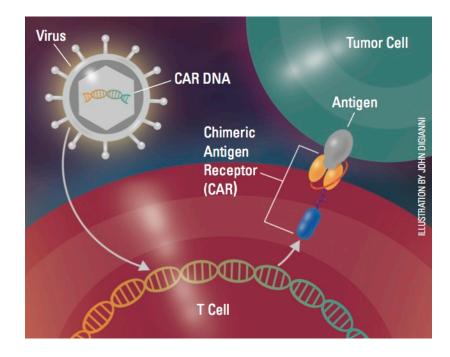
Biological therapy is used to treat many types of cancer, prevent or slow tumor growth, and prevent the spread of cancer.

Biological therapy often causes fewer toxic side effects when compared to other cancer treatments.



Types of Biological Therapies

- Adoptive cell transfer
- Angiogenesis inhibitors
- Bacillus Calmette-Guerin therapy
- Biochemotherapy
- Cancer vaccines
- Chimeric antigen receptor (CAR) T-cell therapy
- Cytokine therapy
- Gene therapy
- Immune checkpoint modulators
- Immunoconjugates
- Monoclonal antibodies
- Oncolytic virus therapy
- Targeted drug therapy



The process that goes into making CAR T cells. Source: Dana-Farber Cancer Institution.

Immunotherapy

Immune checkpoint
therapy helps cancerfighting immune cells, called
T cells, mount a longerlasting response against
cancer.

Adoptive cellular
therapy increases the
number and/or effectiveness
of immune cells, usually T
cells, which improves the
power of the immune
response against cancer.

Main Types of Adoptive Cellular Therapy

Chimeric Antigen Receptor (CAR) T cell therapy gives patients a large dose of T cells that are all genetically engineered to find and fight cancer. Chimeric Antigen Receptor (CAR) natural killer (NK) cell therapy is a promising new cellular immunotherapy that is still in clinical trials. NK cells are immune system cells that identify and kill abnormal cells, including some cancer cells. Many cancers are good at avoiding detection. This limits the NK cells ability to fight the disease naturally. In CAR NK cell therapy, NK cells are engineered to better recognize cancer, boosting their ability to find and kill cancer cells. Researchers do this by collecting NK cells from donated umbilical cord blood. They then add a molecule known as a chimeric antigen receptor, or CAR, to the NK cells. This CAR recognizes a molecule on the surface of cancer cells, enabling the CAR NK cells to better find and fight cancer. **Tumor infiltrating lymphocyte (TIL) therapy** uses a patient's T cells that are collected from a piece of the surgically-removed tumor. While these cells may recognize cancer, there are not enough of them to succeed. The number of these cells is increased substantially in the lab and then given back to the patient. **Endogenous T-cell (ETC) therapy** uses T cells from a patient's blood. From this diverse pool of T cells, doctors select only those that may recognize signatures specific to cancer. The number of these specific T cells is increased substantially and then given back to the patient.

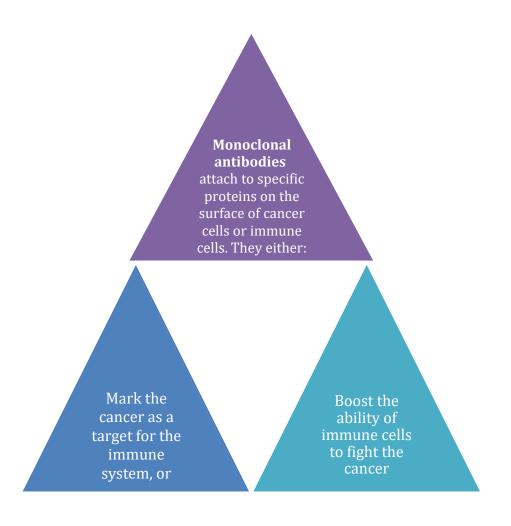
Source: "Immunotherapy", https://www.mdanderson.org/treatment-options/immunotherapy.html. Accessed Nov. 29.

Cancer Vaccines

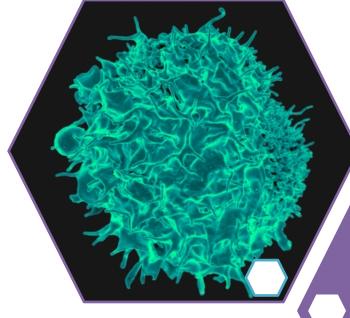
Cancer vaccines help the body recognize cancer cells and stimulate the immune system to destroy them. Cancer vaccines usually contain one of the following:

- Cancer cells taken from the patient's tumor
- Proteins designed to attach themselves to cancer cells
- Proteins specific to a patient's tumor

Monoclonal Antibodies



Cytokine therapy



Source: National Cancer Institute Center for Cancer Research

Cytokine therapy relies on proteins called interferons and interleukins to trigger an immune response. Interleukin-2 (IL-2) is used to treat kidney cancers and melanomas that have spread to other regions of the body. Interferon-alpha (IFN-alpha) is currently being used to treat melanoma, kidney cancer, and certain leukemias and lymphomas. These cytokine treatments are also being combined with other types of immunotherapies to increase their effectiveness.

Bone Marrow Transplant

A bone marrow transplant is a procedure that **infuses healthy blood-forming stem cells** into your body to **replace your damaged or diseased bone marrow**. A bone marrow transplant is also called a stem cell transplant.

You might need a bone marrow transplant if your bone marrow stops working and does not produce enough healthy blood cells.

Bone marrow transplants may use cells **from your own body (autologous transplant) or from a donor (allogeneic transplant)**.



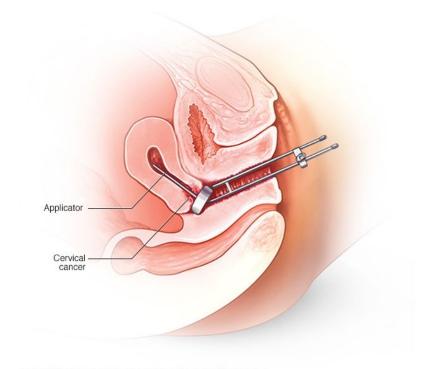
Brachytherapy

Brachytherapy (brak-e-THER-uh-pee) is a procedure that involves **placing radioactive material inside your body**.

Brachytherapy is one type of **radiation therapy** that's used to treat cancer. Brachytherapy is sometimes called **internal radiation**.

Brachytherapy allows doctors to deliver **higher doses of radiation** to more-specific areas of the body, compared with the conventional form of radiation therapy (external beam radiation) that projects radiation from a machine outside of your body.

Brachytherapy may cause **fewer side effects** when compared to external beam radiation, and the overall treatment time is **usually shorter** with brachytherapy.



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Source: Mayo Clinic.



Chemotherapy

Chemotherapy is a **drug treatment** that uses **powerful chemicals** to **kill fast-growing cells** in your body.

Chemotherapy is most often used to treat cancer since cancer cells grow and multiply much more quickly than most cells in the body.

Many different chemotherapy drugs are available. Chemotherapy drugs can be used alone or in combination to treat a wide variety of cancers.

Though chemotherapy is an effective way to treat many types of cancer, chemotherapy treatment also carries **a risk of side effects**. Some chemotherapy side effects are **mild and treatable**, while others can **cause serious complications**.

Chemotherapy

There are a variety of settings in which chemotherapy may be used in people with cancer:

- **To cure cancer without other treatments.** Chemotherapy can be used as the primary or sole treatment for cancer.
- After other treatments, to kill hidden cancer cells. Chemotherapy can be used after other treatments, such as surgery, to kill any cancer cells that might remain in the body. Doctors call this adjuvant therapy.
- **To prepare you for other treatments.** Chemotherapy can be used to shrink a tumor so that other treatments, such as radiation and surgery, are possible. Doctors call this neoadjuvant therapy.
- **To ease signs and symptoms.** Chemotherapy may help relieve signs and symptoms of cancer by killing some of the cancer cells. Doctors call this palliative chemotherapy.

Chemotherapy for Conditions other than Cancer

Some chemotherapy drugs have proved useful in treating other conditions, such as:

diseases. Diseases that affect the bone marrow and blood cells may be treated with a bone marrow transplant, also known as a stem cell transplant.

Chemotherapy is often used to prepare for a bone marrow transplant.

Immune system disorders. Low doses of chemotherapy drugs can assist in controlling an overactive immune system caused by certain diseases, such as lupus and rheumatoid arthritis.



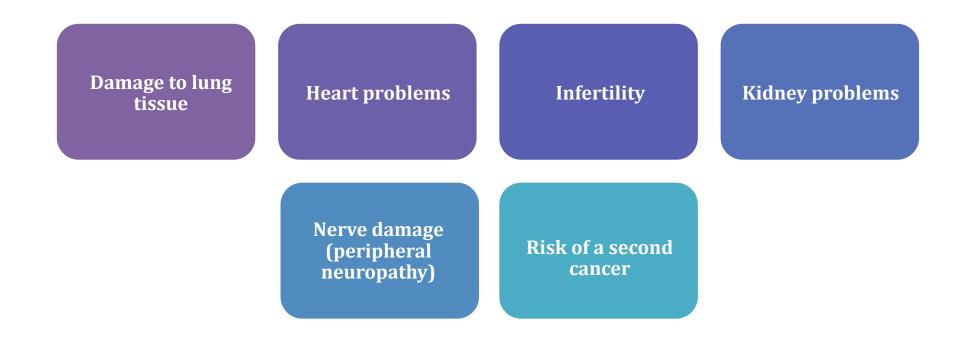
Side Effects of Chemotherapy Drugs

Common side effects of chemotherapy drugs include:

- Nausea
- Vomiting
- Diarrhea
- Hair loss
- · Loss of appetite
- Fatigue
- Fever
- Mouth sores
- Pain
- Constipation
- Easy bruising
- Bleeding
- Many of these side effects can be prevented or treated. Most side effects subside after treatment ends.

Long-Lasting and Late-Developing Side Effects

Chemotherapy drugs can also cause side effects that don't become evident until months or years after treatment. Late side effects vary depending on the chemotherapy drug but can include:



How Chemotherapy Drugs are Given

Chemotherapy drugs can be given in different ways, including:

Chemotherapy infusions. Chemotherapy is most often given as an infusion into a vein (intravenously). The drugs can be delivered intravenously through a tube attached to your arm or a device in your chest.

Chemotherapy pills. Some chemotherapy drugs come in pill or capsule form.

Chemotherapy shots. Chemotherapy drugs can be injected with a needle, the same as a shot.

Chemotherapy creams. Creams or gels containing chemotherapy drugs are applied to the skin to treat certain types of skin cancer.

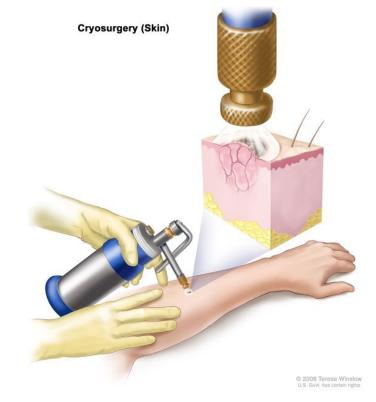
Chemotherapy drugs are used to treat one area of the body. Chemotherapy drugs can directly target one area of the body. For instance, chemotherapy drugs can be administered directly in the abdomen (intraperitoneal chemotherapy), chest cavity (intrapleural chemotherapy), or central nervous system (intrathecal chemotherapy). Chemotherapy can also be given through the urethra into the bladder (intravesical chemotherapy).

Chemotherapy is given directly to cancer. Chemotherapy can be given directly to cancer or, after surgery, where the cancer once was. For example, thin disk-shaped wafers containing chemotherapy drugs can be placed near a tumor during surgery. The wafers break down over time, releasing chemotherapy drugs. Chemotherapy drugs may also be injected into a vein or artery that directly feeds a tumor.

Cryoablation for Cancer

Cryoablation for cancer is a treatment to **kill cancer cells** with **extreme cold**.

During cryoablation, a thin, wand-like needle (cryoprobe) is inserted through your skin and directly into the cancerous tumor. A gas is pumped into the cryoprobe in order to freeze the tissue. Then the tissue is allowed to thaw. The freezing and thawing process is repeated several times during the same treatment session.



Source: NIH. National Cancer Institute.

Cryoablation for Cancer

Cryoablation may be used to treat cancer when **surgery isn't an option**. Cryoablation is sometimes used as a **primary treatment** for:

- Bone cancer
- Cervical cancer
- Eye cancer
- Kidney cancer
- Liver cancer
- Lung cancer
- Prostate cancer
- Cryoablation is also used to **relieve the pain** and other symptoms caused by cancer that spreads to the **bone (bone metastasis) or other organs**.

Minimally Invasive Surgery

In minimally invasive surgery, doctors use a variety of techniques to operate, offering **reduced damage to the body** than with **open surgery**. In general, minimally invasive surgery is associated with **less pain**, **a shorter hospital stay**, and **fewer complications**.

Laparoscopy surgery is done through **small incisions**, using **small tubes**, **tiny cameras**, and **surgical instruments**.

Laparoscopy was one of the first types of minimally invasive surgery. Another type of minimally invasive surgery is **robotic surgery**. It provides a magnified, 3D view of the surgical site and helps the surgeon operate with precision, flexibility, and control.



Source: Colorectal Cancer Alliance.

Palliative Care



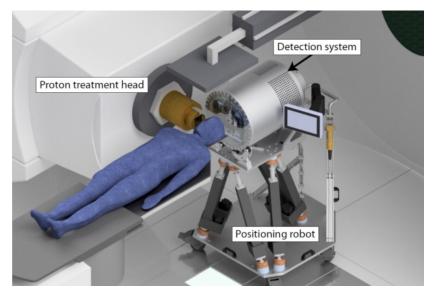
Palliative care is **specialized medical care** that focuses on providing patients **relief from pain and other symptoms** of a serious illness, **no matter the diagnosis or stage of the disease**. Palliative care teams aim to **improve the quality of life** for both patients and their families. This form of care is offered alongside curative or other treatments you may be receiving.

Palliative care is provided by a team of doctors, nurses, and other specially trained people. They work with you, your family, and your other doctors to provide an extra layer of support that complements your ongoing care.

Proton Therapy

Proton therapy is a form of **radiation therapy** that uses **high-powered energy** to treat cancer and certain noncancerous tumors. Radiation therapy using X-rays has long been used to treat these conditions. Proton therapy is a **newer type** of radiation therapy that uses **energy from positively charged particles (protons).**

Proton therapy has shown promise in treating several kinds of cancer. Studies have suggested that proton therapy **may cause fewer side effects** than traditional radiation since doctors can **better control where the proton beams deliver their energy**. But few studies have compared proton radiation and X-ray radiation, so it's **not clear** whether proton therapy is more effective at prolonging lives.



Source: Physics world.

Radiation Therapy

Radiation therapy is a type of cancer treatment that uses **beams of intense energy** to kill cancer cells. Radiation therapy most often uses **X-rays**, but **protons or other types of energy** are other treatment options.

Radiation therapy most often refers to **external beam radiation therapy**. During this treatment, a machine outside of your body emits high-energy beams at a precise point on your body. Another type of radiation treatment is called brachytherapy (brak-e-THER-uh-pee), where radioactive material is placed inside your body.

Radiation therapy works by damaging cells and **destroying the genetic material** that controls how cells grow and divide. While both healthy and cancerous cells are damaged by radiation therapy, the goal is to **destroy as few normal, healthy cells as possible**. Normal cells can often repair much of the damage caused by radiation.



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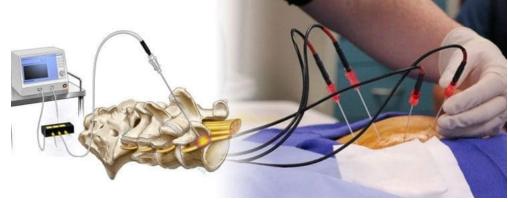
Source: Mayo Clinic.

Radiofrequency Ablation for Cancer

Radiofrequency ablation for cancer is a **minimally invasive procedure** that uses **electrical energy and heat** to destroy cancer cells.

The radiologist uses imaging tests to guide a thin needle through the skin or through an incision and into the cancer tissue. High-frequency energy passes through the needle and causes the surrounding tissue to heat up, killing the nearby cells.

Radiofrequency ablation is most commonly used to treat **a spot of cancer** that is causing problems such as **pain or other discomfort** and is generally not used as the primary treatment for most cancers.



Source: Spinomax Pain & Spine Clinic.

Radiofrequency Ablation for Cancer

Radiofrequency ablation is sometimes used to treat cancers in the:

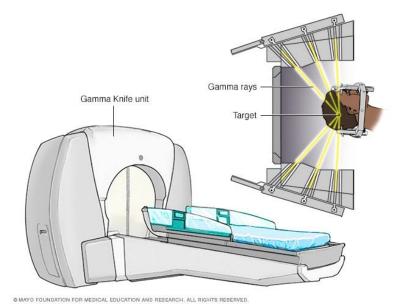
- Adrenal gland
- Breast
- Bone
- Kidney
- Liver
- Lung
- Pancreas
- Thyroid
- Radiofrequency ablation is typically considered a treatment option only if you're **not** a **good candidate for surgery for some reason,** such as your **overall health** or **the presence of many small tumors** in an organ.
- Radiofrequency ablation may also be an option for treating **precancerous cells** in the esophagus that are associated with Barrett's esophagus. Radiofrequency ablation is one of several types of ablation therapy used to treat **a wide range of conditions**.

Stereotactic Radiosurgery (SRS)

Stereotactic radiosurgery (SRS) uses **many precisely focused radiation beams** to treat tumors and other problems in the **brain, neck, lungs, liver, spine, and other areas** in the body.

It is not surgery in the traditional sense because there's no incision. Instead, stereotactic radiosurgery uses **3D imaging** to **target high doses of radiation** to the affected area with minimal impact on the surrounding healthy tissue.

Like other forms of radiation, stereotactic radiosurgery works by **damaging the DNA of the targeted cells**. The affected cells then lose the ability to reproduce, which causes **tumors to shrink**.



Source: Mayo Clinic.

Cancer Pipelines Keywords



ALK inhibitor



ALK inhibitors are <u>anti-cancer drugs</u> that act on tumors with variations of <u>anaplastic lymphoma kinase</u> (ALK) such as an <u>EML4-ALK translocation</u>. They fall under the category of <u>tyrosine kinase inhibitors</u>, which work by inhibiting proteins involved in the abnormal growth of tumor cells. All the current approved ALK inhibitors function by <u>binding to the ATP pocket of the abnormal ALK protein, blocking its access to energy and deactivating it.</u>



Anti EGFR

Anti-EGFR (epidermal growth factor receptor) therapies, including tyrosine kinase inhibitors (TKIs) and monoclonal antibodies, demonstrate activity in **a variety of tumor types**. While both inhibit the EGFR pathway, they act via different mechanisms. Monoclonal antibodies bind to the extracellular domain of EGFR, **preventing ligand binding and interrupting the signaling cascade**.



Source: "Anti-EGFR therapies: clinical experience in colorectal, lung, and head and neck cancers", https://pubmed.ncbi.nlm.nih.gov/16736979/. Accessed Nov. 10.

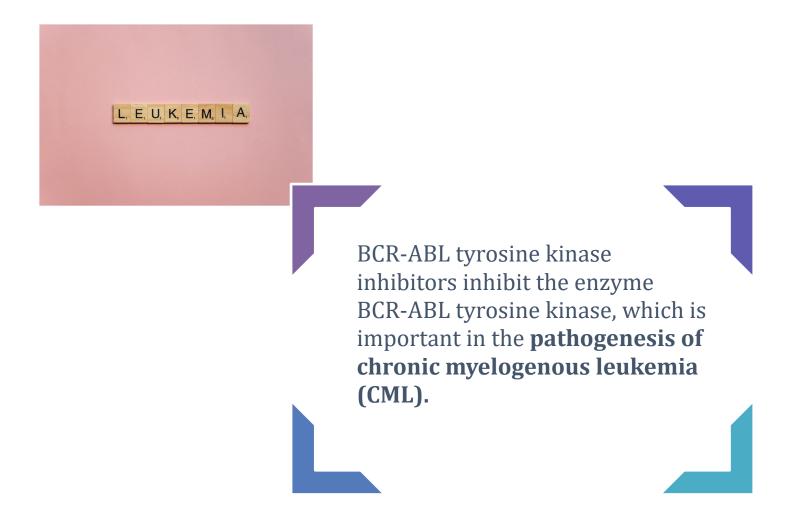
BCMA-CD3 Bispecific Antibody

BCMA/CD3-targeting bispecific antibodies (BsAb) are a recently developed immunotherapy class that shows potent tumor killing activity in **multiple myeloma**.





BCR-ABL inhibitor





BRAF kinase inhibitor

A substance that blocks a protein is called BRAF. BRAF is a kinase enzyme that helps **control cell growth and signaling**. BRAF may be found in a mutated (changed) form in some types of cancer, including **melanoma and colorectal cancer**. Blocking mutated BRAF kinase proteins may help **keep cancer cells from growing**. Some BRAF kinase inhibitors are used to treat cancer.





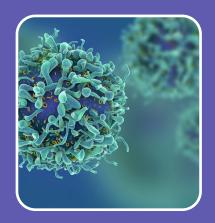
c-MET inhibitor

C-MET inhibitors can be classified into three groups: **small-molecule** tyrosine kinase inhibitors of the c-MET receptor (crizotinib, tivantinib, cabozantinib, foretinib), as well as **monoclonal antibodies** against c-MET (onartuzumab) and against the HGF ligand (ficlatuzumab, rilotumumab). The efficacy and safety of these agents is assessed both in monotherapy and in combination with other molecularly targeted agents. Furthermore, the toxicity profile of c-MET inhibitors is **completely different** from that of standard chemotherapy.



Source: "C-MET inhibitors in the treatment of lung cancer", https://pubmed.ncbi.nlm.nih.gov/25266653/. Accessed Nov. 17.

IL-15 Agonist



IL-15 is an immunostimulatory cytokine trans-presented with the IL-15 receptor α chain to the shared IL-2/IL-15R β and common γ chains displayed on the surface of **T cells and NK cells.** To further define the functionally important regions of this cytokine, activity and binding studies were conducted on human IL-15 muteins generated by site-directed mutagenesis.

Source: Memorial Sloan Kettering Cancer Center

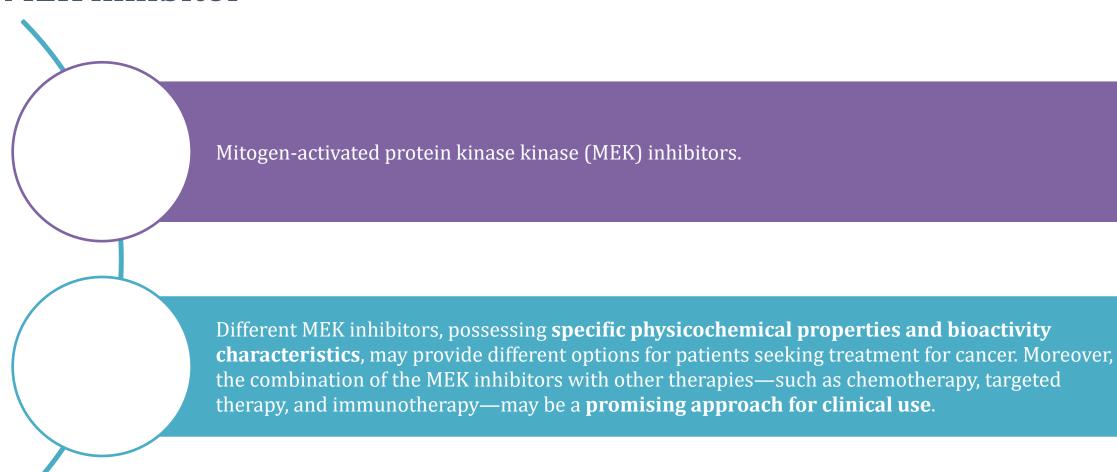


JAK1 inhibitor

Four JAKs exist in humans: JAK1, JAK2, JAK3, and nonreceptor tyrosine-protein kinase TYK2. These kinases bind to types I and II cytokine receptors and transmit extracellular cytokine signals to **activate various signal transducers and activators of transcription**, which **drive the proinflammatory machinery of the cellular immune response**.



MEK inhibitor



PARP inhibitor



PARP inhibitors are a type of cancer drug. PARP stands for poly adenosine diphosphate-ribose polymerase, a type of enzyme that helps repair DNA damage in cells. PARP inhibitors work by preventing cancer cells from repairing, allowing them to die. These drugs are a type of targeted therapy.

Radioligand Therapy

Radioligand therapy is an innovative approach to treating certain types of cancer. It delivers radiation to cancer cells in a targeted and precise way, with a minimal effect on healthy cells, which allows for greater efficiency.

Radioligand therapy has evolved from targeted radioisotope therapies, well established as a treatment option for **thyroid cancer and bone metastases due to prostate cancer, among other clinical indications**. While targeted radioisotope therapies offer organ-level precision, radioligand therapy **enables precision at the cellular level**.

Radioligands bind to certain types of cancer cells wherever they are in the body and can be used for **diagnosis and treatment**. Radioligand therapy is currently licensed for use for **certain types of neuroendocrine neoplasms and lymphoma**. It also looks promising in other cancers, such as **metastatic castration-resistant prostate cancer**, **as well as non-cancer conditions**.



Source: Radioligand therapy



SHP2 tyrosine phosphatase Inhibitor

Shp2 is a nonreceptor protein tyrosine phosphatase (PTP) encoded by the PTPN11 gene. It is involved in growth factor-induced activation of mitogen-activated protein (MAP) kinases Erk1 and Erk2 (Erk1/2) and has been implicated in the pathogenicity of the oncogenic bacterium Helicobacter pylori. Moreover, gain-of-function Shp2 mutations have been found in childhood leukemias and Noonan syndrome.



Thrombopoietin receptor (TPO-R) Agonist



Thrombopoietin receptor (Tpo R), also known as myeloproliferative leukemia protein (c-Mpl), is a type I transmembrane protein that is a member of the hematopoietin/cytokine receptor superfamily. As a consequence of alternative splicing, there are four identified mRNA variants. The functional receptor is encoded by the P isoform of mRNA. The human and mouse receptors share approximately 81% amino acid sequence identity. Tpo R is expressed at low levels in various cell types, including hematopoietic progenitor cells, megakaryocytes, and platelets.

Tyrosine kinase inhibitor

A substance that blocks the action of enzymes is called tyrosine kinases. Tyrosine kinases are a part of many cell functions, including **cell signaling**, **growth**, **and division**. These enzymes may be too active or found at high levels in some types of cancer cells and blocking them may help keep cancer cells from growing. Some tyrosine kinase inhibitors are used to treat cancer. They are a type of **targeted therapy**.



Thanks!



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