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A REVIEW ON: "TARGETED CANCER THERAPY & THEIR DRUGS"

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ABSTRACT:

People with advanced and metastatic non-small cell lung cancer (NSCLC) that responds to targeted therapies or check point inhibitors now routinely survive for three or four years after diagnosis, and a lucky few live substantially longer. Chemotherapy and targeted therapy are both treatments that attacks cancer cells. Targeted therapy is less toxic to healthy cells than chemotherapy. Both options are often done in conjunction with other treatments, such as radiation. Before you have some types of targeted drugs you might need to have tests using some of your cancer cells or a blood sample. This is to find out whether the treatment is likely to work. These tests look for changes in certain proteins or genes. Your cancer specialist can tell you if this applies to your treatment.

Keywords: cancer, metastatic, chemotherapy, Targeted therapy, radiation.

INTRODUCTION:

"A Cancer is very Serious disease in which cell in one part of the body start growing and form lumps in a way that is not normal." [1]

Targeted cancer therapies are drugs that target specific part of cancer cells, such as proteins and genes, that help cancers growth and spread. They also may go after other type ofcells that help cancer growth and spread for some types of a cancer; targeted therapies may work better than other treatments.[2]

The FDA has approved targeted therapies for more than 15 types of cancer includingbut not limited to those of the breast, prostate, colon and lung, but they only work if your tumor has the right target and targeted therapies can often stop working if the target changes or your cancer finds a way around the treatment. [3,4]

Types of Targeted Therapies: [5, 20]

There are two main types of targeted therapies: small molecule medicines andmonoclonal antibodies.

Small molecule medicines are small enough to slip inside cancer cells and destroythem.

One can often spot small molecule medicines because their generic name endsin"-ib." For example, imatinib (Gleevec) treats chronic myelogenous leukemia (CML) and other cancers by blocking signals that are responsible for tumor cells growth.

Monoclonal antibodies are too big to get into cells. Instead, they attack targetson the outside of cells or right around them. Sometimes they are used to launch chemotherapy and radiation straight into tumors. You usually get them through an IVin a vein in your arm at a hospital or clinic.

Sometimes they're given as a shot.

The generic names of monoclonal antibodies end in "-mab." Bevacizumab is a monoclonal antibody that works by blocking blood vessels that feed tumors.

Scientists have come up with many small molecule meds and monoclonal antibodies that make use of different targets to treat cancer in different ways.

Hormone therapies [6]

Hormone therapies stop your body from making the hormones are needed forthe growth of some of breast and prostate cancers.

Breast cancer medicines like tamoxifen block the female hormone estrogen. Aromatase inhibitors lower the amount of estrogen in your body. For prostate cancer, doctors may prescribe meds that block male sex hormones or stop your body from making them.[7]

Hormone therapy also called hormonal therapy, hormone treatment, or endocrine therapy) slows or stops the growth of hormone-sensitive tumors by blocking the body's ability to produce hormones or by interfering with effects of hormones on breast cancer cells. [8] Tumors that are hormone insensitive do not havehormone receptors and do not respond to hormone therapy.[9]

Hormone therapy for breast cancer should not be confused with menopausal hormone therapy (MHT)—treatment with estrogen alone or in combination with progesterone to help relieve symptoms of menopause.[9] These two types of therapyproduce opposite effects: hormone therapy for breast cancer blocks the growth of HR- positive breast cancer, whereas MHT can stimulate the growth of HR-positive breast cancer. For this reason, when a woman taking MHT is diagnosed with HR-positive breast cancer she is usually asked to stop that therapy.[10]

TYPES OF HORMONE THERAPY ARE USED FOR BREAST CANCER

Blocking ovarian function: [11,12, 17, 18]

Because the ovaries are the main source of estrogen in premenopausal women, estrogen levels in these

women can be reduced by eliminating or suppressing ovarian function. Blocking ovarian function is called ovarian ablation.

Blocking ovarian function can be done surgically in an operation to remove the ovaries (called oophorectomy) or by treatment with radiation. This type of ovarian ablation is usually permanent.

Alternatively, ovarian function can be suppressed temporarily by treatment with drugs called gonadotropin-releasing hormone (GnRH) agonists, which are also known as luteinizing hormone-releasing hormone (LHRH) agonists. By mimicking GnRH,

these medicines interfere with signals that stimulate the ovaries to produce estrogen.

Blocking estrogen production: [18]

Drugs called aromatase inhibitors are used to block the activity of an enzyme called aromatase, which the body uses to make estrogen in the ovaries and in other tissues. Aromatase inhibitors are used primarily in postmenopausal women because the ovaries in premenopausal women produce too much aromatase for the inhibitors to block effectively. However, these drugs can be used in premenopausal women if they are given together with a drug that suppresses ovarian function.

Examples of aromatase inhibitors approved by the FDA are anastrozole (Arimidex) and letrozole (Femara), both of which temporarily inactivate aromatase, and exemestane (Aromasin), which permanently inactivates aromatase.

Blocking estrogen's effects:[19]

Several types of drugs interfere with estrogen's ability to stimulate the growth of breast cancer cells:

Selective estrogen receptor modulators (SERMs) bind to estrogen receptors, preventing estrogen from binding. Examples of SERMs approved by the FDA for treatment of breast cancer are tamoxifen (Nolvadex) and toremifene (Fareston).

Because they bind to estrogen receptors, SERMs can potentially not only block estrogen activity (by preventing estrogen from binding to its receptor) but also mimic the effects of estrogen, depending on where they are expressed in the body. For example, tamoxifen blocks the effects of estrogen in breast tissue but acts like estrogen in the uterus and bone.

Other antiestrogen drugs:[20]

s fulvestrant (Faslodex), work in a somewhat different way to block estrogen's effects. Like SERMs, fulvestrant binds to the estrogen receptor and functions as an estrogen blocker. However, unlike SERMs, fulvestrant does not mimic estrogen. For this reason, it is called a pure antiestrogen. In addition, when fulvestrant binds to the estrogen receptor, the receptor is targeted for destruction.

Side effects

While hormone therapy can help managing breast cancer, it can also have adverse effects such as acne, bloating, indigestion, breast tenderness, swelling in the breasts or other parts of the body, abdominal or back pain, leg cramps, headaches, migraine, nausea, vaginal bleeding, mood changes, depression, lack of interest in sex.

Signal transduction inhibitors [21]

Signal transduction inhibitors are the most common targeted therapies.
They block signals that tell cells to divide too much and too fast.
One example is the breast cancer medication trastuzumab (Herceptin). A protein on theoutside of cells called HER2 receptor picks up signals telling the cell to grow and divide. HER2- positive breast cancers make too much of this protein, so the cancer keeps groeing. Trastuzumab can slow or stop this type of breast cancer by latching ontoHER2 receptor or proteins, like putting tinfoil over the windows. Signal transduction inhibitors target regulatory molecules that govern the fundamental processes of cell growth, differentiation, and survival. Most cancers have aberrant signal transduction elements (and often more than one), so they are logical targets for therapeutic intervention.[19]

signal transduction inhibitor function [22-23]

A substance that blocks signals passed from one molecule to another inside a cell. Blocking these signals can affect many functions of the cell, including cell division and cell death, and may kill cancer cells.
Signal transduction inhibitors drugs include dasatinib, erlotinib, gefitinib, imatinib, lapatinib, nilotinib, pazopanib, sorafenib, sunitinib. Signal transduction inhibitors (STIs) like imatinib, erlotinib and gefitinib bind to the ATP-binding site of tyrosine kinases.

Gene expression modulators [23]

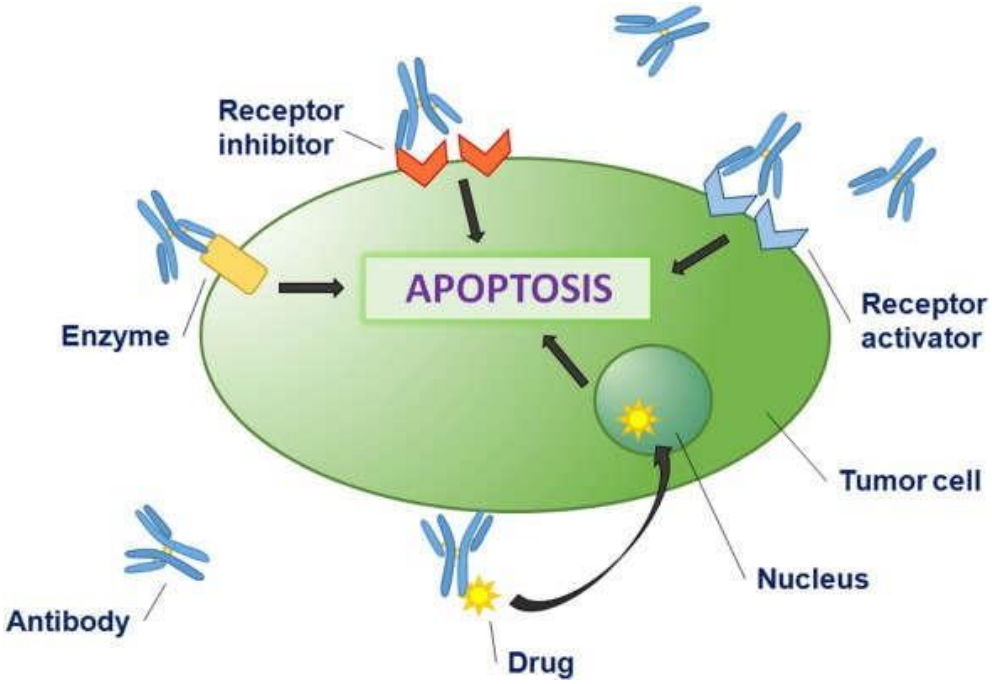
This type of targeted therapy works to change the proteins that control the waythe instructions of genes in cancer cells get carried out, or are expressed, because it's abnormal.
Gene expression modulators modify the function of proteins that play a role in controlling gene expression. Apoptosis inducers cause cancer cells to undergo a process of controlled cell death called apoptosis.

Apoptosis inducers [24]

Cancer cells often find a way around the natural process of apoptosis, where healthy cells die when they're old or damaged. Apoptosis inducers cause cancer cells to go through normal cell death.
Bortezomib (Velcade) is a drug of choice that does this to lymphoma and multiple myeloma,a blood cancer. Scientists are also studying plant compounds like resveratrol (found in red wine) to see if they might trigger cancer cell death.

Apoptosis inducer drugs [24]

Targeting IAP-family members **XIAP, cIAP1, Survivin, or Apollon** can induce apoptosis in tumor cell lines in culture or sensitize cells to cytotoxic anticancer drugs. Endogenous antagonists of IAPs keep these apoptosis suppressors in check, promoting apoptosis.



Angiogenesis inhibitors [25]

Angiogenesis inhibitors are the drugs that block the growth of blood vessels from which cancer cells form to get their nutrients and oxygen. Some target a substance called vascular endothelial growth factor (VEGF). Others go after different substances that trigger blood vessel growth. If a tumor already has a blood supply, targeted therapies can get rid of it.

Classification of angiogenesis inhibitors [25]

Growth of newly formed vessels in tumor micro-environment can be inhibited directly by targeting endothelial cells in the growing vasculature or indirectly by targeting either tumour cells or the other tumor-associated stromal cells. Therefore, angiogenesis inhibitors can be classified into direct and indirect inhibitors

Treatment rationales of angiogenesis inhibitors [25]

Angiogenesis inhibitors are used as either monotherapy or in combination with other anti- tumor drugs. Monotherapy using anti-angiogenic agents is mostly intended for prevention of cancer in susceptible individuals or for delaying disease progression in patients with cancer who have previously treated with first-line/second-line regimens. In combined therapy, anti- angiogenic drugs may be added to treatment regimens to increase their efficacy or to reduce developing drug resistance.

Side effects of angiogenesis inhibitors [26]

Many of the body's normal functions depend on angiogenesis. Therefore, angiogenesis inhibitors can cause a wide range of side effects including:

- High blood pressure
- A rash or dry, itchy skin
- Hand-foot syndrome. This causes tender, thickened areas on the palms and soles.

Sometimes, it causes blisters.

- Diarrhea
- Fatigue
- Low blood counts
- Problems with wound healing or cuts reopening

Although common, these side effects do not happen with every drug or every person. And medicines can help manage these side effects.

Rare side effects are:

- Serious bleeding
- Heart attacks
- Heart failure
- Blood clots
- Holes in the intestines, called bowel perforations

Talk with your health care team about the risks and benefits of angiogenesis inhibitors. And ask about ways to prevent serious side effects.

Angiogenesis inhibitors working [25]

Angiogenesis inhibitors are unique cancer-fighting agents because they block the growth of blood vessels that support tumor growth rather than blocking the growth of tumor cells themselves.

Angiogenesis inhibitors interfere in several ways with various steps in blood vessel growth. Some are monoclonal antibodies that specifically recognize and bind to VEGF. When VEGF is attached to these drugs, it is unable to activate the VEGF receptor. Other angiogenesis inhibitors bind to VEGF and/or its

receptor as well as to other receptors on the surface of endothelial cells or to other proteins in the downstream signaling pathways, blocking their activities. Some angiogenesis inhibitors are immunomodulatory drugs—agents that stimulate or suppress the immune system—that also have antiangiogenic properties.

In some cancers, angiogenesis inhibitors appear to be most effective when combined with additional therapies. Because angiogenesis inhibitors work by slowing or stopping tumor growth without killing cancer cells, they are given over a long period.

Immunotherapies [27]

immunotherapies use your immune system to destroy cancer cells. Some boostour immune system so it does a better job of hunting down cancer. Others mark tumor cells so it's easier for your immune system to find them. Immunotherapy is a form of cancer treatment that uses the power of the body's immune system to prevent, control, and eliminate cancer. From the preventive vaccine for cervical and liver cancer to the first therapy ever proven to extend the lives of patients with metastatic melanoma, immunology has already led to major treatment breakthroughs for a number of cancers. Every cancer type is unique, though, and immunology and immunotherapy are impacting each cancer in different ways.

Side Effects:[28]

Targeted therapies can cause serious side effects. Common ones are diarrhea,liver problems like hepatitis, and changes to your skin, hair, and nails.

- A rash that looks like acne on your scalp, face, neck, chest, and back. It may itch, burn, sting, or hurt. Sometimes it can get infected. It usually lasts the whole time you're treated but goes away after treatment stops.

- Feeling like you have bad sunburn. This may start even before you see anychanges in your skin.

- Extreme sensitivity to sunlight.

- Dry skin. Nearly everyone on targeted therapy has it. Your skin may crack open,especially on your hands and feet, making it hard to use your hands or walk.

- Swollen, painful sores on your finger nails and toenails.

- Sores on your scalp and hair loss or baldness. Your hair may turn an odd coloror not grow back after treatment.

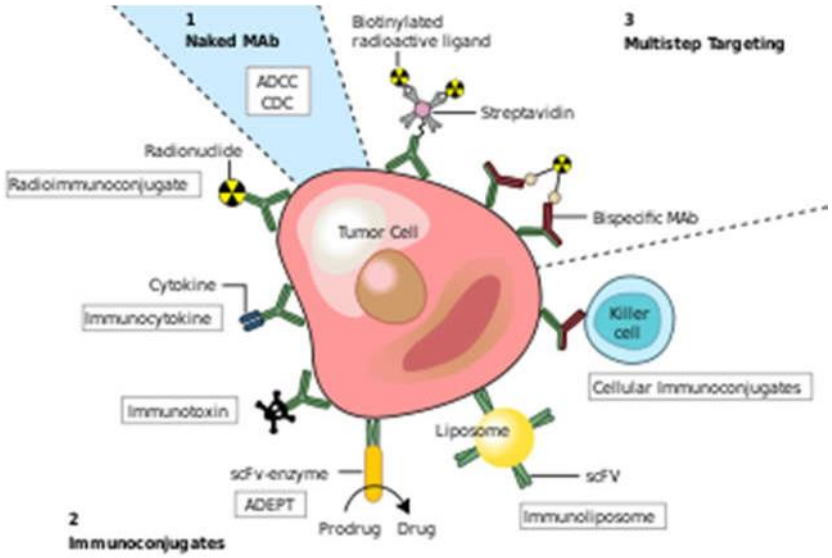
- Eyelids may be red, swollen, and turn inward or down ward. This coulddamage the clear layer on the front of your eye called the cornea.

Many targeted therapies work better combined with other treatments like chemo and radiation, so you could be dealing with those side effects as well.[29]

Monoclonal antibodies: [28,29]

Monoclonal antibodies are immune system proteins that are created in the lab. Antibodies are produced naturally by your body and help the immune system recognize germs that cause disease, such as bacteria and viruses, and mark them for destruction. Like your body's own antibodies, monoclonal antibodies recognize specific targets.

Many monoclonal antibodies are used to treat cancer. They are a type of targeted cancer therapy, which means they are designed to interact with specific targets.



Monoclonal antibodies are designed to function in different ways. A particular drug may actually function by more than one means. The role of the drug in helping the immune system may include the following:[27]
Flagging cancer cells.
Triggering cell-membrane destruction.Blocking cell growth.
Preventing blood vessel growth. development of new blood vessels. Blocking immune system inhibitors. Directly attacking cancer cells.
Delivering radiation treatment. Delivering chemotherapy Binding cancer and immune cells.

Monoclonal antibody treatments have been developed for some but not all cancers, andcertain types of cancer cells are more vulnerable than others to monoclonal antibody interventions. Nonetheless, treatments have been approved for a number of cancers, including brain cancer, breast cancer, chronic lymphocytic leukemia, colorectal cancer, head and neck cancers, Hodgkin's lymphoma, lung cancer, melanoma, non-Hodgkin's lymphoma, prostate cancer, stomach cancer.

FDA approved drugs for cancer treatment: [25, 27, 28]

Agent	Target(s)	FDA-approvedindication(s)
Olaparib (Lynparza)	PARP	Ovarian cancer (with BRCAmutation)
Olaratumab (Lartruvo)	PDGFRα	Soft tissue sarcoma
Osimertinib(Tagrisso)	EGFR	Non-small cells lung cancer (withEGFR T790M mutation)
Palbociclib (Lbrance)	CDK4, CDK6	Breast cancer (HR+, HER2-)

Different kinds of chemo therapy or chemo drugs are used to treat cancer-eitheralone or in combination with other drugs or treatments.

Examples of alkylating agents include:[7]

- Altretamine.
- Bendamustine.
- Busulfan.
- Carboplatin.
- Carmustine.
- Chlorambucil.
- Cisplatin.
- Cyclophosphamide.

Conclusion:

Targeted therapy is a cancer treatment that use drugs to target specific genesand proteins that are involved in the growth and survival of cancer cell. Targeted therapy can affect the tissue environment that helps a cancer grow and survive or it can target cells related to cancer growth, like blood vessel cells.

According to Ayurveda avoidance of a food and lifestyle that causes imbalance in tridosha (vata, pitta,

kapha) recovery of healthy digestive power (JATHARAGNI) Elimination of toxins through panch karma… Vaman for kapha, Virechana for pitta, Raktmokshana through jaluaka, Shriga, siravdh for Raktdrushtij, Vikara and Basti for Vata.

Therapeutic activities like yoga can complement cancer-fighting medical treatment to help the body, mind and spirit in the midst of the cancer battle.

"Several studies have demonstrated that yoga can combat fatigue and improve strength and range of motion for patient undergoing cancer treatment."

Oncology yoga build strength and flexibility strength the immune system andthe lymphatic function.

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