

How Chemotherapy Drugs Work

Many different kinds of chemotherapy or chemo drugs are used to treat cancer – either alone or in combination with other drugs or treatments. These drugs are very different in their chemical composition (what they are made of), how they are prescribed and given, how useful they are in treating certain types of cancer, and the side effects they might have.

- Chemotherapy works with the cell cycle
- Types of chemo drugs
- Other types of drugs used to treat cancer

It's important to know that not all medicines and drugs to treat cancer work the same way. Other drugs to treat cancer work differently, such as <u>targeted therapy</u>¹, hormone therapy, and <u>immunotherapy</u>². The information below describes how traditional or standard chemotherapy works.

Chemotherapy works with the cell cycle

Every time any new cell is formed, it goes through a usual process to become a fully functioning (or mature) cell. The process involves a series of phases and is called the **cell cycle**.

Chemotherapy drugs target cells at different phases of the cell cycle. Understanding how these drugs work helps doctors predict which drugs are likely to work well together. Doctors can also plan how often doses of each drug should be given based on the timing of the cell phases.

Cancer cells tend to form new cells more quickly than normal cells and this makes them a better target for chemotherapy drugs. However, chemo drugs can't tell the difference

between healthy cells and cancer cells. This means normal cells are damaged along with the cancer cells, and this causes side effects. Each time chemo is given, it means trying to find a balance between killing the cancer cells (in order to cure or control the disease) and sparing the normal cells (to lessen side effects).

The good news is that most normal cells will recover from the effects of chemo over time. But cancer cells are mutated (not normal) cells, and they usually do not recover from the effects of chemo. This is why chemo is good at killing many types of cancer cells.

Types of chemo drugs

Chemo drugs can be grouped by how they work, their chemical structure, and their relationships to other drugs. Some drugs work in more than one way, and may belong to more than one group. (Note: not all chemotherapy drugs are listed here.)

Knowing how the drug works is important in predicting side effects from it. This helps doctors decide which drugs are likely to work well together. If more than one drug will be used, this information also helps them plan exactly when each of the drugs should be given (in which order and how often).

Alkylating agents

Alkylating agents keep the cell from reproducing (making copies of itself) by damaging its DNA. These drugs work in all phases of the cell cycle and are used to treat many different cancers, including cancers of the lung, breast, and ovary as well as leukemia, lymphoma, Hodgkin disease, multiple myeloma, and sarcoma.

Because these drugs damage DNA, they can affect the cells of the bone marrow which make new blood cells. In rare cases, this can lead to leukemia. The risk of leukemia from alkylating agents is "dose-dependent," meaning that the risk is small with lower doses, but goes up as the total amount of the drug used gets higher. The risk of leukemia after getting alkylating agents is highest about 5 to 10 years after treatment.

Examples of alkylating agents include:

- Altretamine
- Bendamustine
- Busulfan
- Carboplatin
- Carmustine

- Chlorambucil
- Cisplatin
- Cyclophosphamide
- Dacarbazine
- Ifosfamide
- Lomustine
- Mechlorethamine
- Melphalan
- Oxaliplatin
- Temozolomide
- Thiotepa
- Trabectedin

Nitrosoureas

Nitrosoureas are a group of alkylating agents that have a special action. The other alkylating agents listed above cannot travel into the brain, but nitrosoureas are able to do so. They can enter the brain because they are able to cross through the area known as the blood-brain barrier, a special area that keeps most drugs out of the brain. This action makes these drugs useful in treating certain types of brain tumors.

Examples of nitrosoureas include:

- Carmustine
- Lomustine
- Streptozocin

Antimetabolites

Antimetabolites interfere with DNA and RNA by acting as a substitute for the normal building blocks of RNA and DNA. When this happens, the DNA cannot make copies of itself, and a cell cannot reproduce. They are commonly used to treat leukemias, cancers of the breast, ovary, and the intestinal tract, as well as other types of cancer.

Examples of antimetabolites include:

Azacitidine

- 5-fluorouracil (5-FU)
- 6-mercaptopurine (6-MP)
- Capecitabine (Xeloda)
- Cladribine
- Clofarabine
- Cytarabine (Ara-C)
- Decitabine
- Floxuridine
- Fludarabine
- Gemcitabine (Gemzar)
- Hydroxyurea
- Methotrexate
- Nelarabine
- Pemetrexed (Alimta)
- Pentostatin
- Pralatrexate
- Thioguanine
- Trifluridine/tipiracil combination

Anti-tumor antibiotics

These drugs are not like the antibiotics used to treat infections. They work by changing the DNA inside cancer cells to keep them from growing and multiplying.

Anthracyclines: Anthracyclines are anti-tumor antibiotics that interfere with enzymes involved in copying DNA during the cell cycle. They bind with DNA so it cannot make copies of itself, and a cell cannot reproduce. (Enzymes are proteins that start, help, or speed up the rate of chemical reactions in cells.) They are widely used for a variety of cancers.

Examples of anthracyclines include:

- Daunorubicin
- Doxorubicin (Adriamycin)
- Doxorubicin liposomal
- Epirubicin
- Idarubicin
- Valrubicin

A major concern when giving these drugs is that they can permanently damage the heart if given in high doses. For this reason, lifetime dose limits (also called *cumulative dose*) are often placed on these drugs.

Anti-tumor antibiotics that are not anthracyclines include:

- Bleomycin
- Dactinomycin
- Mitomycin-C
- Mitoxantrone (also acts as a topoisomerase II inhibitor, see below)

Topoisomerase inhibitors

These drugs are also called *plant alkaloids*. They interfere with enzymes called *topoisomerases*, which help separate the strands of DNA so they can be copied. (Enzymes are proteins that cause chemical reactions in living cells.) Topoisomerase inhibitors are used to treat certain leukemias, as well as lung, ovarian, gastrointestinal, colorectal, and pancreatic cancers.

Topoisomerase inhibitors are grouped according to which type of enzyme they affect:

Topoisomerase I inhibitors (also called *camptothecins*)include:

- Irinotecan
- Irinotecan liposomal
- Topotecan

Topoisomerase II inhibitors (also called *epipodophyllotoxins*) include:

- Etoposide (VP-16)
- Mitoxantrone (also acts as an *anti-tumor antibiotic*)
- Teniposide

Topoisomerase II inhibitors can increase the risk of a second cancer.

Mitotic inhibitors

Mitotic inhibitors are also called *plant alkaloids*. They are compounds derived from natural products, such as plants. They work by stopping cells from dividing to form new cells, but can damage cells in all phases by keeping enzymes from making proteins needed for cell reproduction.

Examples of mitotic inhibitors include the taxanes and vinca alkaloids.

- Taxanes include: CabazitaxelDocetaxelNab-paclitaxelPaclitaxel
- Vinca alkaloids include: VinblastineVincristineVincristine liposomalVinorelbine

They are used to treat many different types of cancer including breast, lung, myelomas, lymphomas, and leukemias. These drugs may cause <u>nerve damage</u>³, which can limit the amount that can be given.

Corticosteroids

Corticosteroids, often simply called *steroids*, are natural hormones and hormone-like drugs that are useful in the treatment of many types of cancer, as well as other illnesses. When these drugs are used as part of cancer treatment, they are considered chemotherapy drugs.

Examples of corticosteroids include:

- Prednisone
- Methylprednisolone
- Dexamethasone

Steroids are also commonly used to help prevent nausea and vomiting caused by chemo. They are used before some types of chemo to help prevent severe allergic reactions, too.

Other chemotherapy drugs

Some chemotherapy drugs act in slightly different ways and do not fit well into any of the other categories. Here are some examples:

- All-trans-retinoic acid
- Arsenic trioxide
- Asparaginase
- Eribulin

- Hydroxyurea
- Ixabepilone
- Mitotane
- Omacetaxine
- Pegaspargase
- Procarbazine
- Romidepsin
- Vorinostat

Other types of drugs used to treat cancer

Other drugs and biological treatments are used to treat cancer, but aren't considered chemotherapy. They often have different side effects than chemotherapy. Many are used along with surgery, chemo, or radiation therapy.

Targeted therapies

Targeted therapies work by finding specific substances called *proteins* or *receptors* that some cancer cells have. The protein or receptor is precisely targeted by the drug, so normal cells are not affected by the drugs. This is different from how traditional chemotherapy drugs work. Targeted drugs can be used as the main treatment for a cancer, or they may be used after treatment to keep the cancer under control or keep it from coming back.

To learn more, see <u>Targeted Therapy</u>⁴.

Hormone therapy

Drugs in this category work on different actions of hormones that make some cancers grow. These drugs are used to slow the growth of certain breast, prostate, and endometrial (uterine) cancers, which normally grow in response to natural sex hormones in the body. They work by making the cancer cells unable to use the hormone they need to grow, or by preventing the body from making the hormone.

Immunotherapy

Immunotherapy is a type of treatment that uses drugs to boost or alter a person's immune system. These drugs are used with certain types of cancer to help a patient's

immune system recognize and attack cancer cells.

To learn more, see <u>Immunotherapy</u>⁵.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects/pain/peripheral-neuropathy.html</u>
- 4. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 5. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html</u>

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