Tumor-agnostic Drugs

For many years, drugs to treat cancer have been tested and Food and Drug Administration (FDA) approved based on where that cancer starts in the body. For example, a drug might be approved to treat breast cancer, prostate cancer, or lung cancer (or sometimes more than one type of cancer).

In recent years, much has been learned about the specific gene and protein changes in cells that drive them to grow out of control and become cancer cells. (These gene and protein changes are also called biomarkers.) Finding these specific changes in a person’s cancer cells can sometimes affect their treatment. For example, in people with lung cancer, the cancer cells are now tested for gene or protein changes to see if certain targeted therapy drugs might be helpful for them.

Taking this a step further, some drugs are now approved based mainly on if the cancer cells have specific gene or protein changes, regardless of where the cancer started in the body. Drugs approved for use in this way are called tumor-agnostic drugs or tissue-agnostic drugs.

Here is a list of drugs that are approved for cancer treatment based on a cancer’s protein or gene profile. A person’s cancer cells are typically tested for these changes before one of these drugs would be used.

Approved tumor-agnostic drugs

- Larotrectinib (Vitrakvi)
- Entrectinib (Rozlytrek)
- Pembrolizumab (Keytruda)
- Dostarlimab (Jemperli)
- Dabrafenib (Tafinlar) and trametinib (Mekinist)
- Selpercatinib (Retevmo)
Larotrectinib (Vitrakvi)

Some cancer cells can have changes in one of the $NTRK$ genes, which can lead to cancer growth. Larotrectinib is a targeted drug$^2$ that disables the proteins made by the abnormal $NTRK$ genes. This drug might be an option to treat people whose cancer:

- Has an abnormal $NTRK$ gene AND
- Has spread to distant parts of the body (stage 4 cancer) or cannot be removed with surgery AND
- Has grown while on other treatments or has no other available treatment options

This drug is a pill or liquid, typically taken twice a day.

Possible side effects of larotrectinib

Common side effects include muscle and joint pain, cough, dizziness, fatigue, nausea, vomiting, constipation, fever, abdominal pain, and diarrhea.

Other side effects can include abnormal liver test results, low red and white blood cell counts, and low blood calcium levels.

Entrectinib (Rozlytrek)

Some cancer cells can have changes in one of the $NTRK$ genes, which can lead to cancer growth. Entrectinib is a targeted drug$^3$ that disables the proteins made by the abnormal $NTRK$ genes. This drug might be an option to treat people whose cancer:

- Has an abnormal $NTRK$ gene AND
- Has spread to distant parts of the body (stage 4 cancer) or cannot be removed with surgery AND
- Has grown while on other treatments or has no other available treatment options

This drug is a pill, typically taken once a day.

Other approved uses of this drug: Entrectinib can also be used to treat people with metastatic (stage 4) non-small cell lung cancer (NSCLC) when the cancer cells have an abnormal $ROS1$ gene$^4$. 
Possible side effects of entrectinib

Common side effects include dizziness, fatigue, cough, nausea, vomiting, constipation, weight gain, joint pain, and diarrhea.

Less common but serious side effects can include abnormal liver tests, heart problems, shortness of breath, bone fractures, and confusion.

Pembrolizumab (Keytruda)

Pembrolizumab is a type of immunotherapy drug known as an immune checkpoint inhibitor. It works on PD-1, a protein on immune cells called T cells that normally helps keep them from attacking other cells in the body (including cancer cells). By blocking PD-1, pembrolizumab boosts the immune response against cancer cells. This can shrink some tumors or slow their growth.

This drug might be an option to treat some advanced cancers, typically after other treatments have been tried or when no other good treatment options are available, if the cancer cells have any of the following:

- A high level of microsatellite instability (MSI-H) or a defect in a mismatch repair gene (dMMR)
- A high tumor mutational burden (TMB-H), meaning the cancer cells have many gene mutations

This drug is an intravenous (IV) infusion, typically given every 3 or 6 weeks.

Other approved uses of this drug: Pembrolizumab can also be used to treat people with many other specific types of cancer, such as lung cancer and melanoma skin cancer.

Possible side effects of pembrolizumab

Common side effects include fatigue, muscle and joint pain, cough, rash, fever, nausea, abdominal (belly) pain, constipation, poor appetite, shortness of breath, low thyroid hormone levels, and diarrhea.

Infusion reactions: Some people might have an infusion reaction while getting this drug. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It’s important to tell your
doctor or nurse right away if you have any of these symptoms while getting a pembrolizumab infusion.

Autoimmune reactions: This drug basically removes one of the safeguards on the body's immune system. Sometimes this causes the immune system to attack other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, skin, or other organs.

It's very important to report any new side effects to your health care team right away. If you do have a serious side effect, treatment may need to be stopped and you may be given high doses of corticosteroids to suppress your immune system.

Dostarlimab (Jemperli)

Dostarlimab is a type of immunotherapy drug known as an immune checkpoint inhibitor. It works on PD-1, a protein on immune cells called T cells that normally helps keep them from attacking other cells in the body (including cancer cells). By blocking PD-1, dostarlimab boosts the immune response against cancer cells. This can shrink some tumors or slow their growth.

Dostarlimab might be an option for people with advanced or recurrent cancer if the cancer cells have a defect in a mismatch repair gene (dMMR), typically after other treatments have been tried and when no other good treatment options are available.

This drug is given as an intravenous (IV) infusion, typically every 3 weeks at first, and then every 6 weeks.

Other approved uses of this drug: Dostarlimab might also be used to treat advanced or recurrent endometrial cancer with a defect in a mismatch repair gene (dMMR), typically after other treatments have been tried.

Possible side effects of dostarlimab

Common side effects include fatigue, nausea, diarrhea, and anemia. Less common but possibly serious side effects can include low blood protein levels, low sodium levels, and low white blood cell counts.

Infusion reactions: Some people might have an infusion reaction while getting this drug. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It’s important to tell your doctor or nurse right away if you have any of these symptoms while getting a
dostarilizumab infusion.

**Autoimmune reactions:** This drug basically removes one of the safeguards on the body’s immune system. Sometimes this causes the immune system to attack other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, skin, or other organs.

It’s very important to report any new side effects to your health care team right away. If you do have a serious side effect, treatment may need to be stopped and you may be given high doses of corticosteroids to suppress your immune system.

**Dabrafenib (Tafinlar) and trametinib (Mekinist)**

In some cancers, the cells have changes in the *BRAF* gene, which causes them to make certain proteins that help the cells grow. Dabrafenib and trametinib are targeted drugs\(^\text{10}\) that affect some of these proteins. (Dabrafenib targets the BRAF protein, while trametinib affects the related MEK protein.) Combining these drugs might be an option to treat people whose cancer:

- Has a specific gene change known as a *BRAF V600E* mutation AND
- Has spread to distant parts of the body (stage 4 cancer) or cannot be removed with surgery AND
- Has grown while on other treatments and for which there are no other satisfactory treatment options

Dabrafenib and trametinib are not useful in people with colorectal cancer.

These drugs are pills, typically taken daily.

**Possible side effects of dabrafenib and trametinib**

Common side effects can include skin changes, rash, itching, sensitivity to the sun, headache, fever, chills, joint or muscle pain, fatigue, cough, hair loss, nausea, diarrhea, and high blood pressure.

Less common but serious side effects can include bleeding, heart rhythm problems, liver or kidney problems, lung problems, severe allergic reactions, severe skin or eye problems, and increased blood sugar levels.

Some people treated with these drugs develop skin cancers, especially squamous cell
skin cancers\textsuperscript{11}. Your doctor will want to check your skin often during treatment. You should also let your doctor know right away if you notice any new growths or abnormal areas on your skin.

**Selpercatinib (Retevmo)**

In a small percentage of cancers, the cells have certain changes in the \textit{RET} gene that cause them to make an abnormal form of the \textit{RET} protein, which helps the cells grow.

\textbf{Selpercatinib (Retevmo)} is a \textbf{targeted drug}\textsuperscript{12} known as a \textit{RET inhibitor}. It works by attacking the \textit{RET} protein.

This drug might be an option for people with advanced cancer if the cancer cells have a certain type of \textit{RET} gene change (known as a \textit{gene fusion}), typically after other treatments have been tried and when no other good treatment options are available.

This drug is taken by mouth as capsules, typically twice a day.

**Possible side effects of selpercatinib**

Common side effects can include swelling in the hands or feet, dry mouth, diarrhea or constipation, high blood pressure, feeling tired, skin rash, belly pain, nausea, headache, low white blood cell counts, and changes in certain other blood tests.

Less common but more serious side effects can include liver damage, lung damage, allergic reactions, changes in heart rhythm, bleeding easily, and problems with wound healing.

**Hyperlinks**

2. \url{www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html}
3. \url{www.cancer.org/treatment/treatments-and-side-effects/treatment-types/targeted-therapy.html}
5. \url{www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html}

References


Last Revised: September 22, 2022

Written by

The American Cancer Society medical and editorial content team (www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).