**Tumor Markers in Common Use**

A tumor marker is anything present in or produced by cancer cells or other cells of the body in response to cancer or certain benign (noncancerous) conditions that provides information about a cancer, such as how aggressive it is, whether it can be treated with a targeted therapy, or whether it is responding to treatment. See the [Tumor Markers](https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet) fact sheet for more information.

Listed below are tumor markers that are in common use, mainly to determine treatment or to help make a diagnosis of cancer. New tumor markers frequently become available and may not be reflected on this list.

This list does not include the many tumor markers that are tested by [immunophenotyping](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000341450&version=Patient&language=English) and [immunohistochemistry](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000653117&version=Patient&language=English) to help diagnose cancer and to distinguish between different types of cancer. Some tumor markers listed below are targets for targeted therapy in multiple cancers but serve as tumor markers for only a subset of cancers.

***ALK* gene rearrangements and overexpression**

**Cancer types:** Non-small cell lung cancer and [anaplastic large cell lymphoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045552&version=Patient&language=English)  
**What's analyzed:** Tumor  
**How used:** To help determine treatment and prognosis

**Alpha-fetoprotein (AFP)**

**Cancer types:** Liver cancer and [germ cell tumors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045695&version=Patient&language=English)  
**What's analyzed:** Blood  
**How used:** To help diagnose liver cancer and follow response to treatment; to assess stage, prognosis, and response to treatment of germ cell tumors

**B-cell immunoglobulin gene rearrangement**

**Cancer type**: B-cell lymphoma  
**What's analyzed:** Blood, bone marrow, or tumor tissue  
**How used:** To help in diagnosis, to evaluate effectiveness of treatment, and to check for recurrence

**Beta-2-microglobulin (B2M)**

**Cancer types:** Multiple myeloma, chronic lymphocytic leukemia, and some lymphomas  
**What's analyzed:** Blood, urine, or [cerebrospinal fluid](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046483&version=Patient&language=English)  
**How used:** To determine prognosis and follow response to treatment

**Beta-human chorionic gonadotropin (Beta-hCG)**

**Cancer types:** [Choriocarcinoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046753&version=Patient&language=English) and germ cell tumors  
**What's analyzed:** Urine or blood  
**How used:** To assess stage, prognosis, and response to treatment

**Bladder Tumor Antigen (BTA)**

**Cancer types:** Bladder cancer and cancer of the kidney or [ureter](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046638&version=Patient&language=English)  
**What's analyzed:** Urine  
**How used:** As surveillance with [cytology](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000335081&version=Patient&language=English) and [cystoscopy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045988&version=Patient&language=English) of patients already known to have bladder cancer

***BRCA1* and *BRCA2* gene mutations**

**Cancer types:** Ovarian and breast cancers  
**What's analyzed:** Blood and/or tumor  
**How used:** To determine whether treatment with a particular type of targeted therapy is appropriate

**BCR-ABL fusion gene (Philadelphia chromosome)**

**Cancer types:** Chronic myeloid leukemia, acute lymphoblastic leukemia, and acute myelogenous leukemia  
**What's analyzed:** Blood or bone marrow  
**How used:** To confirm diagnosis, predict response to targeted therapy, determine whether treatment with a particular type of targeted therapy is appropriate, and monitor disease status

**BRAF V600 mutations**

**Cancer types:** Cutaneous melanoma, [Erdheim-Chester disease](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000791445&version=Patient&language=English), colorectal cancer, and non-small cell lung cancer  
**What's analyzed:** Tumor  
**How used:** To select patients who are most likely to benefit from treatment with certain targeted therapies

**C-kit/CD117**

**Cancer types:** [Gastrointestinal stromal tumor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044998&version=Patient&language=English), mucosal melanoma, acute myeloid leukemia, and [mast cell disease](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000789079&version=Patient&language=English)  
**What's analyzed:** Tumor, blood, or bone marrow  
**How used:** To help in diagnosing and determining treatment

**CA15-3/CA27.29**

**Cancer type:** Breast cancer  
**What's analyzed:** Blood  
**How used:** To assess whether treatment is working or if the cancer has recurred

**CA19-9**

**Cancer types:** Pancreatic, gallbladder, [bile duct](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000527370&version=Patient&language=English), and [gastric cancers](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000454513&version=Patient&language=English)  
**What's analyzed:** Blood  
**How used:** To assess whether treatment is working

**CA-125**

**Cancer type:** Ovarian cancer  
**What's analyzed:** Blood  
**How used:** To help in diagnosis, assessment of response to treatment, and evaluation of recurrence

**CA 27.29**

**Cancer type:** Breast cancer  
**What's analyzed:** Blood  
**How used:** To detect metastasis or recurrence

**Calcitonin**

**Cancer type:** [Medullary thyroid cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044550&version=Patient&language=English)  
**What's analyzed:** Blood  
**How used:** To aid in diagnosis, check whether treatment is working, and assess recurrence

**Carcinoembryonic antigen (CEA)**

**Cancer types:** Colorectal cancer and some other cancers  
**What's analyzed:** Blood  
**How used:** To keep track of how well cancer treatments are working and check if cancer has come back or spread

**CD20**

**Cancer type:** Non-Hodgkin lymphoma  
**What's analyzed:** Blood  
**How used:** To determine whether treatment with a targeted therapy is appropriate

**CD22**

**Cancer types:** [Hairy cell leukemia](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045159&version=Patient&language=English) and B-cell neoplasms  
**What's analyzed:** Blood and bone marrow  
**How used:** To help in diagnosis

**CD25**

**Cancer type:** Non-Hodgkin (T-cell) lymphoma  
**What's analyzed:** Blood  
**How used:** To determine whether treatment with a targeted therapy is appropriate

**CD30**

**Cancer types:** [Mycosis fungoides](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045794&version=Patient&language=English) and [peripheral T-cell lymphoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000405873&version=Patient&language=English)  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with a targeted therapy is appropriate

**CD33**

**Cancer type:** Acute myeloid leukemia  
**What's analyzed:** Blood  
**How used:** To determine whether treatment with a targeted therapy is appropriate

**Chromogranin A (CgA)**

**Cancer type:** [Neuroendocrine tumors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044904&version=Patient&language=English)  
**What's analyzed:** Blood  
**How used:** To help in diagnosis, assessment of treatment response, and evaluation of recurrence

**Chromosome 17p deletion**

**Cancer type:** Chronic lymphocytic leukemia  
**What's analyzed:** Blood  
**How used:** To determine whether treatment with a certain targeted therapy is appropriate

**Chromosomes 3, 7, 17, and 9p21**

**Cancer type:** Bladder cancer  
**What's analyzed:** Urine  
**How used:** To help in monitoring for tumor recurrence

**Circulating tumor cells of epithelial origin (CELLSEARCH®)**

**Cancer types:** Metastatic breast, prostate, and colorectal cancers  
**What's analyzed:** Blood  
**How used:** To inform clinical decision making, and to assess prognosis

**Cytokeratin fragment 21-1**

**Cancer type:** Lung cancer  
**What's analyzed:** Blood  
**How used:** To help in monitoring for recurrence

**Des-gamma-carboxy prothrombin (DCP)**

**Cancer type:** Hepatocellular carcinoma  
**What's analyzed:** Blood  
**How used:** To monitor the effectiveness of treatment and to detect recurrence

***DPD* gene mutation**

**Cancer types:** Breast, colorectal, gastric, and pancreatic cancers  
**What's analyzed:** Blood  
**How used:** To predict the risk of a toxic reaction to [5-fluorouracil](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000635764&version=Patient&language=English) therapy

***EGFR* gene mutation**

**Cancer type:** Non-small cell lung cancer  
**What's analyzed:** Tumor  
**How used:** To help determine treatment and prognosis

**Estrogen receptor (ER)/progesterone receptor (PR)**

**Cancer type:** Breast cancer  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with hormone therapy and some targeted therapies is appropriate

***FGFR2* and *FGFR3* gene mutations**

**Cancer type:** Bladder cancer  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with a certain targeted therapy is appropriate

**Fibrin/fibrinogen**

**Cancer type:** Bladder cancer  
**What's analyzed:** Urine  
**How used:** To monitor progression and response to treatment

***FLT3* gene mutations**

**Cancer type:** Acute myeloid leukemia  
**What's analyzed:** Blood  
**How used:** To determine whether treatment with certain targeted therapies is appropriate

**Gastrin**

**Cancer type:** Gastrin-producing tumor ([gastrinoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044239&version=Patient&language=English))  
**What's analyzed:** Blood  
**How used:** To help in diagnosis, to monitor the effectiveness of treatment, and to detect recurrence

**HE4**

**Cancer type:** Ovarian cancer  
**What's analyzed:** Blood  
**How used:** To plan cancer treatment, assess disease progression, and monitor for recurrence

***HER2/neu* gene amplification or protein overexpression**

**Cancer types:** Breast, ovarian, bladder, pancreatic, and stomach cancers  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with certain targeted therapies is appropriate

**5-HIAA**

**Cancer type:** [Carcinoid tumors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044233&version=Patient&language=English)  
**What's analyzed:** Urine  
**How used:** To help in diagnosis and to monitor disease

***IDH1* and *IDH2* gene mutations**

**Cancer type:** Acute myeloid leukemia  
**What's analyzed:** Bone marrow and blood  
**How used:** To determine whether treatment with certain targeted therapies is appropriate

**Immunoglobulins**

**Cancer types:** Multiple myeloma and Waldenström [macroglobulinemia](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044530&version=Patient&language=English)  
**What's analyzed:** Blood and urine  
**How used:** To help diagnose disease, assess response to treatment, and look for recurrence

***JAK2* gene mutation**

**Cancer type:** Certain types of leukemia  
**What's analyzed:** Blood and bone marrow  
**How used:** To help in diagnosis

***KRAS* gene mutation**

**Cancer types:** Colorectal cancer and non-small cell lung cancer  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with a particular type of targeted therapy is appropriate

**Lactate dehydrogenase**

**Cancer types:** Germ cell tumors, lymphoma, leukemia, melanoma, and [neuroblastoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045418&version=Patient&language=English)  
**What's analyzed:** Blood  
**How used:** To assess stage, prognosis, and response to treatment

**Microsatellite instability (MSI) and/or mismatch repair deficient (dMMR)**

**Cancer types:** Colorectal cancer and other solid tumors  
**What's analyzed:** Tumor  
**How used:** To guide treatment and to identify those at high risk of certain cancer-predisposing syndromes

**Neuron-specific enolase (NSE)**

**Cancer types:** Small cell lung cancer and neuroblastoma  
**What's analyzed:** Blood  
**How used:** To help in diagnosis and to assess response to treatment

**Nuclear matrix protein 22**

**Cancer type:** Bladder cancer  
**What's analyzed:** Urine  
**How used:** To monitor response to treatment

**PCA3 mRNA**

**Cancer type:** Prostate cancer  
**What's analyzed:** Urine (collected after digital rectal exam)  
**How used:** To determine need for repeat biopsy after negative biopsy

**PML/RARα fusion gene**

**Cancer type:** [Acute promyelocytic leukemia](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000444957&version=Patient&language=English) (APL)  
**What's analyzed:** Blood and bone marrow  
**How used:** To diagnose APL, to predict response to all-trans-retinoic acid or arsenic trioxide therapy, to assess effectiveness of therapy, to monitor minimal residual disease, and to predict early relapse

**Prostatic Acid Phosphatase (PAP)**

**Cancer type:** Metastatic prostate cancer  
**What's** **analyzed:** Blood  
**How used:** To help in diagnosing poorly differentiated carcinomas

**Programmed death ligand 1 (PD-L1)**

**Cancer types:** Non-small cell lung cancer, liver cancer, stomach cancer, [gastroesophageal junction](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000302458&version=Patient&language=English) cancer, classical Hodgkin lymphoma, and other aggressive lymphoma subtypes  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with a particular type of targeted therapy is appropriate

**Prostate-specific antigen (PSA)**

**Cancer type:** Prostate cancer  
**What's** **analyzed:** Blood  
**How used:** To help in diagnosis, to assess response to treatment, and to look for recurrence

***ROS1* gene rearrangement**

**Cancer type:** Non-small cell lung cancer  
**What's analyzed:** Tumor  
**How used:** To determine whether treatment with a particular type of targeted therapy is appropriate

**Soluble mesothelin-related peptides (SMRP)**

**Cancer type:** [Mesothelioma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044323&version=Patient&language=English)  
**What's** **analyzed:** Blood  
**How used:** To monitor progression or recurrence

**Somatostatin receptor**

**Cancer type:** [Neuroendocrine tumors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044904&version=Patient&language=English) affecting the pancreas or gastrointestinal tract ([GEP-NETs](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000792397&version=Patient&language=English))  
**What's** **analyzed:** Tumor (by diagnostic imaging)  
**How used:** To determine whether treatment with a particular type of targeted therapy is appropriate

**T-cell receptor gene rearrangement**

**Cancer type:** T-cell lymphoma  
**What's analyzed:** Bone marrow, tissue, body fluid, blood  
**How used:** To help in diagnosis; sometimes to detect and evaluate residual disease

**Thiopurine S-methyltransferase (TPMT) enzyme activity or *TPMT* genetic test**

**Cancer type:** Acute lymphoblastic leukemia  
**What's analyzed:** Blood and buccal (cheek) swab  
**How used:** To predict the risk of severe bone marrow toxicity ([myelosuppression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044173&version=Patient&language=English)) with thiopurine treatment

**Thyroglobulin**

**Cancer type:** Thyroid cancer  
**What's analyzed:** Blood  
**How used:** To evaluate response to treatment and to look for recurrence

**UGT1A1\*28 variant homozygosity**

**Cancer type:** Colorectal cancer  
**What's analyzed:** Blood and buccal (cheek) swab  
**How used:** To predict toxicity from irinotecan therapy

**Urine catecholamines: VMA and HVA**

**Cancer type:** Neuroblastoma  
**What's analyzed:** Urine  
**How used:** To help in diagnosis

**Urokinase plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1)**

**Cancer type:** Breast cancer  
**What's analyzed:** Tumor  
**How used:** To determine aggressiveness of cancer and guide treatment

**FoundationOne® CDx (F1CDx) genomic test**

**Cancer type:** Any solid tumor  
**What's analyzed:** Tumor  
**How used:** As a [companion diagnostic test](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000797062&version=Patient&language=English) to determine whether treatment with a particular type of targeted therapy is appropriate

**5-Protein signature (OVA1®)**

**Cancer type:** Ovarian cancer  
**What's analyzed:** Blood  
**How used:** To pre-operatively assess pelvic mass for suspected ovarian cancer

**17-Gene signature (Oncotype DX GPS test®)**

**Cancer type:** Prostate cancer  
**What's analyzed:** Tumor  
**How used:** To predict the aggressiveness of prostate cancer and to help manage treatment

**21-Gene signature (Oncotype DX®)**

**Cancer type:** Breast cancer  
**What's analyzed:** Tumor  
**How used:** To evaluate risk of distant recurrence and to help plan treatment

**46-Gene signature (Prolaris®)**

**Cancer type:** Prostate cancer  
**What's analyzed:** Tumor  
**How used:** To predict the aggressiveness of prostate cancer and to help manage treatment

**70-Gene signature (Mammaprint®)**

**Cancer type:** Breast cancer  
**What's analyzed:** Tumor  
**How used:** To evaluate risk of recurrence

**Targeted Cancer Therapies**

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**What are targeted cancer therapies?**

Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific [molecules](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045065&version=Patient&language=English) ("molecular targets") that are involved in the growth, [progression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044078&version=Patient&language=English), and spread of cancer. Targeted cancer therapies are sometimes called "molecularly targeted drugs," "molecularly targeted therapies," "precision medicines," or similar names.

Targeted therapies differ from standard [chemotherapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045214&version=Patient&language=English) in several ways:

* Targeted therapies act on specific molecular targets that are associated with cancer, whereas most standard chemotherapies act on all rapidly dividing normal and cancerous cells.
* Targeted therapies are deliberately chosen or designed to interact with their target, whereas many standard chemotherapies were identified because they kill cells.
* Targeted therapies are often [cytostatic](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000756173&version=Patient&language=English) (that is, they block tumor [cell proliferation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046479&version=Patient&language=English)), whereas standard chemotherapy agents are [cytotoxic](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044020&version=Patient&language=English) (that is, they kill tumor cells).

Targeted therapies are currently the focus of much anticancer drug development. They are a cornerstone of [precision medicine](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000741769&version=Patient&language=English), a form of medicine that uses information about a person’s [genes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045693&version=Patient&language=English) and [proteins](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046092&version=Patient&language=English) to prevent, diagnose, and treat disease.

Many targeted cancer therapies have been approved by the Food and Drug Administration (FDA) to treat specific types of cancer. Others are being studied in [clinical trials](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045961&version=Patient&language=English) (research studies with people), and many more are in preclinical testing (research studies with animals).

**How are targets for targeted cancer therapies identified?**

The development of targeted therapies requires the identification of good targets—that is, targets that play a key role in cancer cell growth and survival. (It is for this reason that targeted therapies are sometimes referred to as the product of "rational" drug design.)

One approach to identify potential targets is to compare the amounts of individual [proteins](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046092&version=Patient&language=en) in cancer cells with those in normal cells. Proteins that are present in cancer cells but not normal cells or that are more abundant in cancer cells would be potential targets, especially if they are known to be involved in cell growth or survival. An example of such a differentially expressed target is the [human epidermal growth factor receptor 2](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044570&version=Patient&language=en) [protein](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046092&version=Patient&language=en) (HER-2). HER-2 is expressed at high levels on the surface of some cancer cells. Several targeted therapies are directed against HER-2, including [trastuzumab](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045439&version=Patient&language=en) (Herceptin®), which is approved to treat certain breast and stomach cancers that [overexpress](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045812&version=Patient&language=en) HER-2.

Another approach to identify potential targets is to determine whether cancer cells produce mutant (altered) proteins that drive cancer [progression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044078&version=Patient&language=en). For example, the cell growth signaling protein BRAF is present in an altered form (known as BRAF V600E) in many [melanomas](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045135&version=Patient&language=en). [Vemurafenib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000702051&version=Patient&language=en) (Zelboraf®) targets this mutant form of the BRAF protein and is approved to treat patients with [inoperable](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000285970&version=Patient&language=en) or [metastatic](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044058&version=Patient&language=en) melanoma that contains this altered BRAF protein.

Researchers also look for abnormalities in [chromosomes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046470&version=Patient&language=en) that are present in cancer cells but not in normal cells. Sometimes these chromosome abnormalities result in the creation of a [fusion gene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000613509&version=Patient&language=en) (a gene that incorporates parts of two different genes) whose product, called a [fusion protein](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044591&version=Patient&language=en), may drive cancer development. Such fusion proteins are potential targets for targeted cancer therapies. For example, [imatinib mesylate](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044893&version=Patient&language=en) (Gleevec®) targets the [BCR-ABL fusion protein](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000641107&version=Patient&language=en), which is made from pieces of two genes that get joined together in some [leukemia](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045343&version=Patient&language=en) cells and promotes the growth of leukemic cells.

**How are targeted therapies developed?**

Once a candidate target has been identified, the next step is to develop a therapy that affects the target in a way that interferes with its ability to promote cancer cell growth or survival. For example, a [targeted therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000270742&version=Patient&language=English) could reduce the activity of the target or prevent it from binding to a [receptor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044958&version=Patient&language=English) that it normally activates, among other possible mechanisms.

Most targeted therapies are either small molecules or [monoclonal antibodies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046066&version=Patient&language=English). [Small-molecule compounds](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000653146&version=Patient&language=English) are typically developed for targets that are located inside the cell because such agents are able to enter cells relatively easily. Monoclonal antibodies are relatively large and generally cannot enter cells, so they are used only for targets that are outside cells or on the cell surface.

Candidate small molecules are usually identified in what are known as "high-throughput screens," in which the effects of thousands of test compounds on a specific target protein are examined. Compounds that affect the target (sometimes called "[lead compounds](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000754026&version=Patient&language=English)") are then chemically modified to produce numerous closely related versions of the lead compound. These related compounds are then tested to determine which are most effective and have the fewest effects on nontarget molecules.

Monoclonal antibodies are developed by injecting animals (usually mice) with purified target proteins, causing the animals to make many different types of [antibodies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044918&version=Patient&language=English) against the target. These antibodies are then tested to find the ones that bind best to the target without binding to nontarget proteins.

Before monoclonal antibodies are used in humans, they are "[humanized](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000470256&version=Patient&language=English)" by replacing as much of the mouse antibody molecule as possible with corresponding portions of human antibodies. Humanizing is necessary to prevent the human immune system from recognizing the monoclonal antibody as "[foreign](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000698772&version=Patient&language=English)" and destroying it before it has a chance to bind to its target protein. Humanization is not an issue for small-molecule compounds because they are not typically recognized by the body as foreign.

**What types of targeted therapies are available?**

Many different targeted therapies have been approved for use in cancer treatment. These therapies include [hormone therapies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045110&version=Patient&language=English), [signal transduction inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044829&version=Patient&language=English), [gene expression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000537335&version=Patient&language=English) modulators, [apoptosis](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046524&version=Patient&language=English) inducers, [angiogenesis inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046739&version=Patient&language=English), [immunotherapies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045729&version=Patient&language=English), and [toxin](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046622&version=Patient&language=English) delivery molecules.

* **Hormone therapies** slow or stop the growth of hormone-sensitive tumors, which require certain [hormones](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045713&version=Patient&language=English) to grow. Hormone therapies act by preventing the body from producing the hormones or by interfering with the action of the hormones. Hormone therapies have been approved for both breast cancer and prostate cancer.
* **Signal transduction inhibitors** block the activities of molecules that participate in [signal transduction](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000597170&version=Patient&language=English), the process by which a cell responds to signals from its environment. During this process, once a cell has received a specific signal, the signal is relayed within the cell through a series of [biochemical reactions](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044124&version=Patient&language=English) that ultimately produce the appropriate response(s). In some cancers, the [malignant](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045772&version=Patient&language=English) cells are stimulated to divide continuously without being prompted to do so by external [growth factors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045705&version=Patient&language=English). Signal transduction inhibitors interfere with this inappropriate signaling.
* **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 is one method the body uses to get rid of unneeded or abnormal cells, but cancer cells have strategies to avoid apoptosis. Apoptosis inducers can get around these strategies to cause the death of cancer cells.
* **Angiogenesis inhibitors** block the growth of new [blood vessels](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045020&version=Patient&language=English) to tumors (a process called tumor angiogenesis). A blood supply is necessary for tumors to grow beyond a certain size because blood provides the [oxygen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000538149&version=Patient&language=English) and [nutrients](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044697&version=Patient&language=English) that tumors need for continued growth. Treatments that interfere with angiogenesis may block tumor growth. Some targeted therapies that inhibit angiogenesis interfere with the action of [vascular endothelial growth factor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044222&version=Patient&language=English) (VEGF), a substance that stimulates new blood vessel formation. Other angiogenesis inhibitors target other molecules that stimulate new blood vessel growth.
* **Immunotherapies** trigger the [immune system](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046356&version=Patient&language=English) to destroy cancer cells. Some immunotherapies are [monoclonal antibodies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046066&version=Patient&language=English) that recognize specific molecules on the surface of cancer cells. Binding of the monoclonal antibody to the target molecule results in the immune destruction of cells that express that target molecule. Other monoclonal antibodies bind to certain immune cells to help these cells better kill cancer cells.
* **Monoclonal antibodies that deliver toxic molecules** can cause the death of cancer cells specifically. Once the antibody has bound to its target cell, the toxic molecule that is linked to the antibody—such as a radioactive substance or a poisonous chemical—is taken up by the cell, ultimately killing that cell. The toxin will not affect cells that lack the target for the antibody—i.e., the vast majority of cells in the body.

[**Cancer vaccines**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044952&version=Patient&language=English) and [**gene therapy**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045353&version=Patient&language=English) are sometimes considered targeted therapies because they interfere with the growth of specific cancer cells. Information about cancer vaccines can be found in NCI's [Cancer Treatment Vaccines](https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/cancer-treatment-vaccines) page.

**How is it determined whether a patient is a candidate for targeted therapy?**

For some types of cancer, most patients with that cancer will have an appropriate target for a particular [targeted therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000270742&version=Patient&language=English) and, thus, will be candidates to be treated with that therapy. [CML](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044382&version=Patient&language=English) is an example: most patients have the [*BCR-ABL* fusion gene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000561237&version=Patient&language=English). For other cancer types, however, a patient’s tumor tissue must be tested to determine whether or not an appropriate target is present. The use of a targeted therapy may be restricted to patients whose tumor has a specific [gene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045693&version=Patient&language=English) [mutation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046063&version=Patient&language=English) that codes for the target; patients who do not have the mutation would not be candidates because the therapy would have nothing to target.

Sometimes, a patient is a candidate for a targeted therapy only if he or she meets specific criteria (for example, their cancer did not respond to other therapies, has spread, or is [inoperable](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000285970&version=Patient&language=English)). These criteria are set by the FDA when it approves a specific targeted therapy.

**What are the limitations of targeted cancer therapies?**

Targeted therapies do have some limitations. One is that cancer cells can become resistant to them. Resistance can occur in two ways: the target itself changes through [mutation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046063&version=Patient&language=en) so that the [targeted therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000270742&version=Patient&language=en) no longer interacts well with it, and/or the tumor finds a new pathway to achieve tumor growth that does not depend on the target.

For this reason, targeted therapies may work best in combination. For example, a recent study found that using two therapies that target different parts of the cell [signaling pathway](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000561720&version=Patient&language=en) that is [altered](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044643&version=Patient&language=en) in [melanoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045135&version=Patient&language=en) by the BRAF V600E [mutation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046063&version=Patient&language=en) slowed the development of resistance and [disease progression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045669&version=Patient&language=en) to a greater extent  than using just one targeted therapy ([1](https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#r1)).

Another approach is to use a targeted therapy in combination with one or more traditional [chemotherapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045214&version=Patient&language=en) drugs. For example, the targeted therapy [trastuzumab](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045439&version=Patient&language=en) (Herceptin®) has been used in combination with [docetaxel](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045382&version=Patient&language=en), a traditional chemotherapy drug, to treat women with metastatic [breast cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000444971&version=Patient&language=en) that [overexpresses](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045812&version=Patient&language=en) the protein [HER2/neu](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044945&version=Patient&language=en).

Another limitation of targeted therapy at present is that drugs for some identified targets are difficult to develop because of the target’s structure and/or the way its function is regulated in the cell. One example is Ras, a signaling protein that is [mutated](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044133&version=Patient&language=en) in as many as one-quarter of all cancers (and in the majority of certain cancer types, such as [pancreatic cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044521&version=Patient&language=en)). To date, it has not been possible to develop inhibitors of Ras signaling with existing drug development technologies. However, promising new approaches are offering hope that this limitation can soon be overcome.

**What are the side effects of targeted cancer therapies?**

Scientists had expected that targeted cancer therapies would be less toxic than traditional [chemotherapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045214&version=Patient&language=English) drugs because cancer cells are more dependent on the targets than are normal cells. However, targeted cancer therapies can have substantial [side effects](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046580&version=Patient&language=English).

The most common side effects seen with targeted therapies are [diarrhea](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000306496&version=Patient&language=English) and liver problems, such as [hepatitis](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046371&version=Patient&language=English) and elevated liver enzymes.  Other side effects seen with targeted therapies include:

* Skin problems (acneiform rash, dry skin, nail changes, hair depigmentation)
* Problems with [blood clotting](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000476017&version=Patient&language=English) and wound healing
* High blood pressure
* Gastrointestinal perforation (a rare side effect of some targeted therapies)

Certain side effects of some targeted therapies have been linked to better patient [outcomes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000467853&version=Patient&language=English). For example, patients who develop acneiform rash (skin eruptions that resemble [acne](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044183&version=Patient&language=English)) while being treated with the [signal transduction inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044829&version=Patient&language=English) [erlotinib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000508929&version=Patient&language=English) (Tarceva®) or [gefitinib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000258356&version=Patient&language=English) (Iressa®), both of which target the [epidermal growth factor receptor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045680&version=Patient&language=English), have tended to respond better to these drugs than patients who do not develop the rash ([2](https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#r2)). Similarly, patients who develop high blood pressure while being treated with the [angiogenesis inhibitor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046739&version=Patient&language=English) [bevacizumab](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046115&version=Patient&language=English) generally have had better outcomes ([3](https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#r3)).

The few targeted therapies that are approved for use in children can have different side effects in children than in adults, including [immunosuppression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045727&version=Patient&language=English) and impaired sperm production ([4](https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#r4)).

**What targeted therapies have been approved for specific types of cancer?**

The FDA has approved targeted therapies for the treatment of some patients with the following types of cancer (some targeted therapies have been approved to treat more than one type of cancer):

**Bladder cancer:**[Atezolizumab (Tecentriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/atezolizumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [durvalumab (Imfinzi™)](https://www.cancer.gov/about-cancer/treatment/drugs/durvalumab), [avelumab (Bavencio®)](https://www.cancer.gov/about-cancer/treatment/drugs/avelumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [erdafitinib (Balversa™)](https://www.cancer.gov/about-cancer/treatment/drugs/erdafitinib), [enfortumab vedotin-ejfv (Padcev™)](https://www.cancer.gov/about-cancer/treatment/drugs/enfortumabvedotin-ejfv)

**Brain cancer:** [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [everolimus (Afinitor®)](https://www.cancer.gov/about-cancer/treatment/drugs/everolimus)

**Breast cancer:** [Everolimus (Afinitor®)](https://www.cancer.gov/about-cancer/treatment/drugs/everolimus), [tamoxifen (Nolvadex)](https://www.cancer.gov/about-cancer/treatment/drugs/tamoxifencitrate), [toremifene (Fareston®)](https://www.cancer.gov/about-cancer/treatment/drugs/toremifene), [Trastuzumab (Herceptin®)](https://www.cancer.gov/about-cancer/treatment/drugs/trastuzumab), [fulvestrant (Faslodex®)](https://www.cancer.gov/about-cancer/treatment/drugs/fulvestrant), [anastrozole (Arimidex®)](https://www.cancer.gov/about-cancer/treatment/drugs/anastrozole), [exemestane (Aromasin®)](https://www.cancer.gov/about-cancer/treatment/drugs/exemestane), [lapatinib (Tykerb®)](https://www.cancer.gov/about-cancer/treatment/drugs/lapatinibditosylate), [letrozole (Femara®)](https://www.cancer.gov/about-cancer/treatment/drugs/letrozole), [pertuzumab (Perjeta®)](https://www.cancer.gov/about-cancer/treatment/drugs/pertuzumab), [ado-trastuzumab emtansine (Kadcyla®)](https://www.cancer.gov/about-cancer/treatment/drugs/ado-trastuzumab-emtansine), [palbociclib (Ibrance®)](https://www.cancer.gov/about-cancer/treatment/drugs/palbociclib), [ribociclib (Kisqali®)](https://www.cancer.gov/about-cancer/treatment/drugs/ribociclib), [neratinib maleate (Nerlynx™)](https://www.cancer.gov/about-cancer/treatment/drugs/neratinibmaleate), [abemaciclib (Verzenio™)](https://www.cancer.gov/about-cancer/treatment/drugs/abemaciclib), [olaparib (Lynparza™)](https://www.cancer.gov/about-cancer/treatment/drugs/olaparib), [talazoparib tosylate (Talzenna®)](https://www.cancer.gov/about-cancer/treatment/drugs/talazoparibtosylate), [atezolizumab (Tecentriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/atezolizumab), [alpelisib (Piqray®)](https://www.cancer.gov/about-cancer/treatment/drugs/alpelisib), [fam-trastuzumab deruxtecan-nxki (Enhertu®)](https://www.cancer.gov/about-cancer/treatment/drugs/famtrastuzumabderuxtecan-nxki), [tucatinib (Tukysa™)](https://www.cancer.gov/about-cancer/treatment/drugs/tucatinib), [sacituzumab govitecan-hziy (Trodelvy™)](https://www.cancer.gov/about-cancer/treatment/drugs/sacituzumabgovitecan-hziy), [pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo™)](https://www.cancer.gov/about-cancer/treatment/drugs/pertuzumabtrastuzumabandhyaluronidase-zzxf), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)

**Cervical cancer:** [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)

**Colorectal cancer:** [Cetuximab (Erbitux®)](https://www.cancer.gov/about-cancer/treatment/drugs/cetuximab), [panitumumab (Vectibix®)](https://www.cancer.gov/about-cancer/treatment/drugs/panitumumab), [bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [ziv-aflibercept (Zaltrap®)](https://www.cancer.gov/about-cancer/treatment/drugs/ziv-aflibercept), [regorafenib (Stivarga®)](https://www.cancer.gov/about-cancer/treatment/drugs/regorafenib), [ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [encorafenib (Braftovi™)](https://www.cancer.gov/about-cancer/treatment/drugs/encorafenib), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)

**Dermatofibrosarcoma protuberans:** [Imatinib mesylate (Gleevec®)](https://www.cancer.gov/about-cancer/treatment/drugs/imatinibmesylate)

**Endocrine/neuroendocrine tumors:** [Lanreotide acetate (Somatuline® Depot)](https://www.cancer.gov/about-cancer/treatment/drugs/lanreotideacetate), [avelumab (Bavencio®)](https://www.cancer.gov/about-cancer/treatment/drugs/avelumab), [lutetium Lu 177-dotatate (Lutathera®)](https://www.cancer.gov/about-cancer/treatment/drugs/lutetiumlu177-dotatate), [iobenguane I 131 (Azedra®)](https://www.cancer.gov/about-cancer/treatment/drugs/iobenguanei131)

**Endometrial cancer:** [Pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [lenvatinib mesylate (Lenvima®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenvatinibmesylate)

**Esophageal cancer:** [Trastuzumab (Herceptin®)](https://www.cancer.gov/about-cancer/treatment/drugs/trastuzumab), [ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab)

**Head and neck cancer:** [Cetuximab (Erbitux®)](https://www.cancer.gov/about-cancer/treatment/drugs/cetuximab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab)

**Gastrointestinal stromal tumor:** [Imatinib mesylate (Gleevec®)](https://www.cancer.gov/about-cancer/treatment/drugs/imatinibmesylate), [sunitinib (Sutent®)](https://www.cancer.gov/about-cancer/treatment/drugs/sunitinibmalate), [regorafenib (Stivarga®)](https://www.cancer.gov/about-cancer/treatment/drugs/regorafenib), [avapritinib (Ayvakit™)](https://www.cancer.gov/about-cancer/treatment/drugs/avapritinib), [ripretinib (Qinlock™)](https://www.cancer.gov/about-cancer/treatment/drugs/ripretinib)

**Giant cell tumor:** [Denosumab (Xgeva®)](https://www.cancer.gov/about-cancer/treatment/drugs/denosumab), [pexidartinib hydrochloride (Turalio®)](https://www.cancer.gov/about-cancer/treatment/drugs/pexidartinib)

**Kidney cancer:** [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [sorafenib (Nexavar®)](https://www.cancer.gov/about-cancer/treatment/drugs/sorafenibtosylate), [sunitinib (Sutent®)](https://www.cancer.gov/about-cancer/treatment/drugs/sunitinibmalate), [pazopanib (Votrient®)](https://www.cancer.gov/about-cancer/treatment/drugs/pazopanibhydrochloride), [temsirolimus (Torisel®)](https://www.cancer.gov/about-cancer/treatment/drugs/temsirolimus), [everolimus (Afinitor®)](https://www.cancer.gov/about-cancer/treatment/drugs/everolimus), [axitinib (Inlyta®)](https://www.cancer.gov/about-cancer/treatment/drugs/axitinib), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [cabozantinib (Cabometyx™)](https://www.cancer.gov/about-cancer/treatment/drugs/cabozantinib-s-malate), [lenvatinib mesylate (Lenvima®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenvatinibmesylate), [ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [avelumab (Bavencio®)](https://www.cancer.gov/about-cancer/treatment/drugs/avelumab)

**Leukemia:** [Tretinoin (Vesanoid®)](https://www.cancer.gov/publications/dictionaries/cancer-drug/def/tretinoin), [imatinib mesylate (Gleevec®)](https://www.cancer.gov/about-cancer/treatment/drugs/imatinibmesylate), [dasatinib (Sprycel®)](https://www.cancer.gov/about-cancer/treatment/drugs/dasatinib), [nilotinib (Tasigna®)](https://www.cancer.gov/about-cancer/treatment/drugs/nilotinib), [bosutinib (Bosulif®)](https://www.cancer.gov/about-cancer/treatment/drugs/bosutinib), [rituximab (Rituxan®)](https://www.cancer.gov/about-cancer/treatment/drugs/rituximab), [alemtuzumab (Campath®)](https://www.cancer.gov/about-cancer/treatment/drugs/alemtuzumab), [ofatumumab (Arzerra®)](https://www.cancer.gov/about-cancer/treatment/drugs/ofatumumab), [obinutuzumab (Gazyva®)](https://www.cancer.gov/about-cancer/treatment/drugs/obinutuzumab), [ibrutinib (Imbruvica®)](https://www.cancer.gov/about-cancer/treatment/drugs/ibrutinib), [idelalisib (Zydelig®)](https://www.cancer.gov/about-cancer/treatment/drugs/idelalisib), [blinatumomab (Blincyto®)](https://www.cancer.gov/about-cancer/treatment/drugs/blinatumomab), [venetoclax (Venclexta™)](https://www.cancer.gov/about-cancer/treatment/drugs/venetoclax), [ponatinib hydrochloride (Iclusig®)](https://www.cancer.gov/about-cancer/treatment/drugs/ponatinibhydrochloride), [midostaurin (Rydapt®)](https://www.cancer.gov/about-cancer/treatment/drugs/midostaurin), [enasidenib mesylate (Idhifa®)](https://www.cancer.gov/about-cancer/treatment/drugs/enasidenibmesylate), [inotuzumab ozogamicin (Besponsa®)](https://www.cancer.gov/about-cancer/treatment/drugs/inotuzumabozogamicin), [tisagenlecleucel (Kymriah®)](https://www.cancer.gov/about-cancer/treatment/drugs/tisagenlecleucel), [gemtuzumab ozogamicin (Mylotarg™)](https://www.cancer.gov/about-cancer/treatment/drugs/gemtuzumabozogamicin), [rituximab and hyaluronidase human (Rituxan Hycela™)](https://www.cancer.gov/about-cancer/treatment/drugs/rituximabandhyaluronidasehuman), [ivosidenib (Tibsovo®)](https://www.cancer.gov/about-cancer/treatment/drugs/ivosidenib), [duvelisib (Copiktra™)](https://www.cancer.gov/about-cancer/treatment/drugs/duvelisib), [moxetumomab pasudotox-tdfk (Lumoxiti™)](https://www.cancer.gov/about-cancer/treatment/drugs/moxetumomabpasudotoxtdfk), [glasdegib maleate (Daurismo™)](https://www.cancer.gov/about-cancer/treatment/drugs/glasdegibmaleate), [gilteritinib (Xospata®)](https://www.cancer.gov/about-cancer/treatment/drugs/gilteritinibfumarate), [tagraxofusp-erzs (Elzonris™)](https://www.cancer.gov/about-cancer/treatment/drugs/tagraxofusp-erzs), [acalabrutinib (Calquence®)](https://www.cancer.gov/about-cancer/treatment/drugs/acalabrutinib)

**Liver and bile duct cancer:** [Sorafenib (Nexavar®)](https://www.cancer.gov/about-cancer/treatment/drugs/sorafenibtosylate), [regorafenib (Stivarga®)](https://www.cancer.gov/about-cancer/treatment/drugs/regorafenib), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [lenvatinib mesylate (Lenvima®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenvatinibmesylate), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [cabozantinib (Cabometyx™)](https://www.cancer.gov/about-cancer/treatment/drugs/cabozantinib-s-malate), [ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab), [ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [pemigatinib (Pemazyre™)](https://www.cancer.gov/about-cancer/treatment/drugs/pemigatinib), [atezolizumab (Tecentriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/atezolizumab), [bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab)

**Lung cancer:** [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [crizotinib (Xalkori®)](https://www.cancer.gov/about-cancer/treatment/drugs/crizotinib), [erlotinib (Tarceva®)](https://www.cancer.gov/about-cancer/treatment/drugs/erlotinibhydrochloride), [gefitinib (Iressa®)](https://www.cancer.gov/about-cancer/treatment/drugs/gefitinib), [afatinib dimaleate (Gilotrif®)](https://www.cancer.gov/about-cancer/treatment/drugs/afatinibdimaleate), [ceritinib (LDK378/Zykadia™)](https://www.cancer.gov/about-cancer/treatment/drugs/ceritinib), [ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [osimertinib (Tagrisso™)](https://www.cancer.gov/about-cancer/treatment/drugs/osimertinib), [necitumumab (Portrazza™)](https://www.cancer.gov/about-cancer/treatment/drugs/necitumumab), [alectinib (Alecensa®)](https://www.cancer.gov/about-cancer/treatment/drugs/alectinib), [atezolizumab (Tecentriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/atezolizumab), [brigatinib (Alunbrig™)](https://www.cancer.gov/about-cancer/treatment/drugs/brigatinib), [trametinib (Mekinist®)](https://www.cancer.gov/about-cancer/treatment/drugs/trametinib), [dabrafenib (Tafinlar®)](https://www.cancer.gov/about-cancer/treatment/drugs/dabrafenib), [durvalumab (Imfinzi™)](https://www.cancer.gov/about-cancer/treatment/drugs/durvalumab), [dacomitinib (Vizimpro®)](https://www.cancer.gov/about-cancer/treatment/drugs/dacomitinib), [lorlatinib (Lorbrena®)](https://www.cancer.gov/about-cancer/treatment/drugs/lorlatinib), [entrectinib (Rozlytrek™)](https://www.cancer.gov/about-cancer/treatment/drugs/entrectinib), [capmatinib hydrochloride (Tabrecta™)](https://www.cancer.gov/about-cancer/treatment/drugs/capmatinibhydrochloride), [ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [selpercatinib (Retevmo™)](https://www.cancer.gov/about-cancer/treatment/drugs/selpercatinib), [pralsetinib (Gavreto™)](https://www.cancer.gov/about-cancer/treatment/drugs/pralsetinib)

**Lymphoma:** [Ibritumomab tiuxetan (Zevalin®)](https://www.cancer.gov/about-cancer/treatment/drugs/ibritumomabtiuxetan), [denileukin diftitox (Ontak®)](https://www.cancer.gov/about-cancer/treatment/drugs/denileukindiftitox), [brentuximab vedotin (Adcetris®)](https://www.cancer.gov/about-cancer/treatment/drugs/brentuximabvedotin), [rituximab (Rituxan®)](https://www.cancer.gov/about-cancer/treatment/drugs/rituximab), [vorinostat (Zolinza®)](https://www.cancer.gov/about-cancer/treatment/drugs/vorinostat), [romidepsin (Istodax®)](https://www.cancer.gov/about-cancer/treatment/drugs/romidepsin), [bexarotene (Targretin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bexarotene), [bortezomib (Velcade®)](https://www.cancer.gov/about-cancer/treatment/drugs/bortezomib), [pralatrexate (Folotyn®)](https://www.cancer.gov/about-cancer/treatment/drugs/pralatrexate), [ibrutinib (Imbruvica®)](https://www.cancer.gov/about-cancer/treatment/drugs/ibrutinib), [siltuximab (Sylvant®)](https://www.cancer.gov/about-cancer/treatment/drugs/siltuximab), [idelalisib (Zydelig®)](https://www.cancer.gov/about-cancer/treatment/drugs/idelalisib), [belinostat (Beleodaq®)](https://www.cancer.gov/about-cancer/treatment/drugs/belinostat), [obinutuzumab (Gazyva®)](https://www.cancer.gov/about-cancer/treatment/drugs/obinutuzumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [rituximab and hyaluronidase human (Rituxan Hycela™)](https://www.cancer.gov/about-cancer/treatment/drugs/rituximabandhyaluronidasehuman), [copanlisib hydrochloride (Aliqopa™)](https://www.cancer.gov/about-cancer/treatment/drugs/copanlisibhydrochloride), [axicabtagene ciloleucel (Yescarta™)](https://www.cancer.gov/about-cancer/treatment/drugs/axicabtageneciloleucel), [acalabrutinib (Calquence®)](https://www.cancer.gov/about-cancer/treatment/drugs/acalabrutinib), [tisagenlecleucel (Kymriah®)](https://www.cancer.gov/about-cancer/treatment/drugs/tisagenlecleucel), [venetoclax (Venclexta™)](https://www.cancer.gov/about-cancer/treatment/drugs/venetoclax), [mogamulizumab-kpkc (Poteligeo®)](https://www.cancer.gov/about-cancer/treatment/drugs/mogamulizumabkpkc), [duvelisib (Copiktra™)](https://www.cancer.gov/about-cancer/treatment/drugs/duvelisib), [polatuzumab vedotin-piiq (Polivy™)](https://www.cancer.gov/about-cancer/treatment/drugs/polatuzumabvedotin-piiq), [zanubrutinib (Brukinsa](https://www.cancer.gov/about-cancer/treatment/drugs/zanubrutinib)[™](https://www.cancer.gov/about-cancer/treatment/drugs/elotuzumab)[)](https://www.cancer.gov/about-cancer/treatment/drugs/zanubrutinib), [tazemetostat hydrobromide (Tazverik™)](https://www.cancer.gov/about-cancer/treatment/drugs/tazemetostathydrobromide), [selinexor (Xpovio™)](https://www.cancer.gov/about-cancer/treatment/drugs/selinexor), [tafasitamab-cxix (Monjuvi®)](https://www.cancer.gov/about-cancer/treatment/drugs/tafasitamab-cxix), [brexucabtagene autoleucel (Tecartus™)](https://www.cancer.gov/about-cancer/treatment/drugs/brexucabtageneautoleucel)

**Malignant mesothelioma:** [Ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab)

**Microsatellite instability-high or mismatch repair-deficient solid tumors**: [Pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)

**Multiple myeloma:** [Bortezomib (Velcade®)](https://www.cancer.gov/about-cancer/treatment/drugs/bortezomib), [carfilzomib (Kyprolis®)](https://www.cancer.gov/about-cancer/treatment/drugs/carfilzomib), [panobinostat (Farydak®)](https://www.cancer.gov/about-cancer/treatment/drugs/panobinostat), [daratumumab (Darzalex™)](https://www.cancer.gov/about-cancer/treatment/drugs/daratumumab), [ixazomib citrate (Ninlaro®)](https://www.cancer.gov/about-cancer/treatment/drugs/ixazomibcitrate), [elotuzumab (Empliciti™)](https://www.cancer.gov/about-cancer/treatment/drugs/elotuzumab), [selinexor (Xpovio™)](https://www.cancer.gov/about-cancer/treatment/drugs/selinexor), [isatuximab-irfc (Sarclisa®)](https://www.cancer.gov/about-cancer/treatment/drugs/isatuximab-irfc), [*daratumumab and hyaluronidase-fihj (Darzalex Faspro™)*](https://www.cancer.gov/about-cancer/treatment/drugs/daratumumabandhyaluronidase-fihj)*,* [*belantamab mafodotin-blmf (Blenrep)*](https://www.cancer.gov/about-cancer/treatment/drugs/belantamabmafodotin-blmf)

**Myelodysplastic/myeloproliferative disorders:** [Imatinib mesylate (Gleevec®)](https://www.cancer.gov/about-cancer/treatment/drugs/imatinibmesylate), [ruxolitinib phosphate (Jakafi®)](https://www.cancer.gov/about-cancer/treatment/drugs/ruxolitinibphosphate), [fedratinib hydrochloride (Inrebic®)](https://www.cancer.gov/about-cancer/treatment/drugs/fedratinibhydrochloride)

**Neuroblastoma:** [Dinutuximab (Unituxin™)](https://www.cancer.gov/about-cancer/treatment/drugs/dinutuximab)

**Ovarian epithelial/fallopian tube/primary peritoneal cancers:** [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab), [olaparib (Lynparza™)](https://www.cancer.gov/about-cancer/treatment/drugs/olaparib), [rucaparib camsylate (Rubraca™)](https://www.cancer.gov/about-cancer/treatment/drugs/rucaparibcamsylate), [niraparib tosylate monohydrate (Zejula™)](https://www.cancer.gov/about-cancer/treatment/drugs/niraparibtosylatemonohydrate)

**Pancreatic cancer:** [Erlotinib (Tarceva®)](https://www.cancer.gov/about-cancer/treatment/drugs/erlotinibhydrochloride), [everolimus (Afinitor®)](https://www.cancer.gov/about-cancer/treatment/drugs/everolimus), [sunitinib (Sutent®)](https://www.cancer.gov/about-cancer/treatment/drugs/sunitinibmalate), [olaparib (Lynparza™)](https://www.cancer.gov/about-cancer/treatment/drugs/olaparib)

**Plexiform neurofibroma:** [Selumetinib sulfate (Koselugo™)](https://www.cancer.gov/about-cancer/treatment/drugs/selumetinibsulfate)

**Prostate cancer:** [Cabazitaxel (Jevtana®)](https://www.cancer.gov/about-cancer/treatment/drugs/cabazitaxel), [enzalutamide (Xtandi®)](https://www.cancer.gov/about-cancer/treatment/drugs/enzalutamide), [abiraterone acetate (Zytiga®)](https://www.cancer.gov/about-cancer/treatment/drugs/abirateroneacetate), [radium 223 dichloride (Xofigo®)](https://www.cancer.gov/about-cancer/treatment/drugs/radium-223-dichloride), [apalutamide (Erleada™)](https://www.cancer.gov/about-cancer/treatment/drugs/apalutamide), [darolutamide (Nubeqa®)](https://www.cancer.gov/about-cancer/treatment/drugs/darolutamide), [rucaparib camsylate (Rubraca™)](https://www.cancer.gov/about-cancer/treatment/drugs/rucaparibcamsylate), [olaparib (Lynparza™)](https://www.cancer.gov/about-cancer/treatment/drugs/olaparib)

**Skin cancer:** [Vismodegib (Erivedge®)](https://www.cancer.gov/about-cancer/treatment/drugs/vismodegib), [sonidegib (Odomzo®)](https://www.cancer.gov/about-cancer/treatment/drugs/sonidegib), [ipilimumab (Yervoy®)](https://www.cancer.gov/about-cancer/treatment/drugs/ipilimumab), [vemurafenib (Zelboraf®)](https://www.cancer.gov/about-cancer/treatment/drugs/vemurafenib), [trametinib (Mekinist®)](https://www.cancer.gov/about-cancer/treatment/drugs/trametinib), [dabrafenib (Tafinlar®)](https://www.cancer.gov/about-cancer/treatment/drugs/dabrafenib), [pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab), [nivolumab (Opdivo®)](https://www.cancer.gov/about-cancer/treatment/drugs/nivolumab), [cobimetinib (Cotellic™)](https://www.cancer.gov/about-cancer/treatment/drugs/cobimetinib), [alitretinoin (Panretin®)](https://www.cancer.gov/publications/dictionaries/cancer-drug/def/alitretinoin), [avelumab (Bavencio®)](https://www.cancer.gov/about-cancer/treatment/drugs/avelumab), [encorafenib (Braftovi™)](https://www.cancer.gov/about-cancer/treatment/drugs/encorafenib), [binimetinib (Mektovi®)](https://www.cancer.gov/about-cancer/treatment/drugs/binimetinib), [cemiplimab-rwlc (Libtayo®)](https://www.cancer.gov/about-cancer/treatment/drugs/cemiplimab-rwlc), [atezolizumab (Tecentriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/atezolizumab)

**Soft tissue sarcoma:**[Pazopanib (Votrient®)](https://www.cancer.gov/about-cancer/treatment/drugs/pazopanibhydrochloride), [alitretinoin (Panretin®)](https://www.cancer.gov/publications/dictionaries/cancer-drug/def/alitretinoin), [tazemetostat hydrobromide (Tazverik™)](https://www.cancer.gov/about-cancer/treatment/drugs/tazemetostathydrobromide)

**Solid tumors that are tumor mutational burden-high (TMB-H):** [Pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)

**Solid tumors with an *NTRK* gene fusion:** [Larotrectinib sulfate (Vitrakvi®)](https://www.cancer.gov/about-cancer/treatment/drugs/larotrectinibsulfate), [entrectinib (Rozlytrek™)](https://www.cancer.gov/about-cancer/treatment/drugs/entrectinib)

**Stomach (gastric) cancer:** [Pembrolizumab (Keytruda®)](https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab)**,** [trastuzumab (Herceptin®)](https://www.cancer.gov/about-cancer/treatment/drugs/trastuzumab), [ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab)

**Systemic mastocytosis:** [Imatinib mesylate (Gleevec®)](https://www.cancer.gov/about-cancer/treatment/drugs/imatinibmesylate), [midostaurin (Rydapt®)](https://www.cancer.gov/about-cancer/treatment/drugs/midostaurin)

**Thyroid cancer:** [Cabozantinib (Cometriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/cabozantinib-s-malate), [vandetanib (Caprelsa®)](https://www.cancer.gov/about-cancer/treatment/drugs/vandetanib), [sorafenib (Nexavar®)](https://www.cancer.gov/about-cancer/treatment/drugs/sorafenibtosylate), [lenvatinib mesylate (Lenvima®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenvatinibmesylate), [trametinib (Mekinist®)](https://www.cancer.gov/about-cancer/treatment/drugs/trametinib), [dabrafenib (Tafinlar®)](https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/Dabrafenib%20Mesylate), [selpercatinib (Retevmo™)](https://www.cancer.gov/about-cancer/treatment/drugs/selpercatinib)

**Where can I find information about clinical trials of targeted therapies?**

Both FDA-approved and experimental targeted therapies for specific types of cancer are being studied in clinical trials. Descriptions of ongoing clinical trials that are testing types of targeted therapies in cancer patients can be accessed by searching NCI’s [list of cancer clinical trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search). NCI’s list of cancer clinical trials includes all NCI-supported clinical trials that are taking place across the United States and Canada, including the NIH Clinical Center in Bethesda, MD.  For information about other ways to search the list, see [Help Finding NCI-Supported Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search/help).

Alternatively, call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) for information about clinical trials of targeted therapies.

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[[PubMed Abstract]](https://www.ncbi.nlm.nih.gov/pubmed/23369685)

**Angiogenesis Inhibitors**

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[How do angiogenesis inhibitors work?](https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/angiogenesis-inhibitors-fact-sheet" \l "how-do-angiogenesis-inhibitors-work)

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**What is angiogenesis?**

Angiogenesis is the formation of new blood vessels. This process involves the migration, growth, and [differentiation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046445&version=Patient&language=English) of [endothelial cells](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044203&version=Patient&language=English), which line the inside wall of blood vessels.

The process of angiogenesis is controlled by chemical signals in the body. Some of these signals, such as [vascular endothelial growth factor (VEGF)](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044222&version=Patient&language=English), bind to [receptors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044958&version=Patient&language=English) on the surface of normal endothelial cells. When VEGF and other endothelial growth factors bind to their receptors on endothelial cells, signals within these cells are initiated that promote the growth and survival of new blood vessels.Other chemical signals, called [angiogenesis inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046739&version=Patient&language=English), interfere with blood vessel formation.

Normally, the angiogenesis stimulating and inhibiting effects of these chemical signals are balanced so that blood vessels form only when and where they are needed, such as during growth and healing. But, for reasons that are not entirely clear, sometimes these signals can become unbalanced, causing increased blood vessel growth that can lead to abnormal conditions or disease. For example, angiogenesis is the cause of age-related wet [macular degeneration](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000642150&version=Patient&language=English).

**Why is angiogenesis important in cancer?**

Angiogenesis plays a critical role in the growth of cancer because [solid tumors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045301&version=Patient&language=English) need a blood supply if they are to grow beyond a few millimeters in size. Tumors can actually cause this blood supply to form by giving off chemical signals that stimulate angiogenesis. Tumors can also stimulate nearby normal cells to produce angiogenesis signaling molecules.

The resulting new blood vessels “feed” growing tumors with oxygen and nutrients, allowing the tumor to enlarge and the cancer cells to invade nearby tissue, to move throughout the body, and to form new colonies of cancer cells, called metastases.

Because tumors cannot grow beyond a certain size or spread without a blood supply, scientists have developed drugs called angiogenesis inhibitors, which block tumor angiogenesis. The goal of these drugs, also called antiangiogenic agents, is to prevent or slow the growth of cancer by starving it of its needed blood supply.

**How do angiogenesis inhibitors work?**

Angiogenesis inhibitors are unique cancer-fighting agents because they block the growth of [blood vessels](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045020&version=Patient&language=English) 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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046066&version=Patient&language=English) that specifically recognize and bind to [VEGF](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044474&version=Patient&language=English). When VEGF is attached to these drugs, it is unable to activate the VEGF [receptor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044958&version=Patient&language=English). Other angiogenesis inhibitors bind to VEGF and/or its receptor as well as to other receptors on the surface of [endothelial cells](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044203&version=Patient&language=English) 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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046356&version=Patient&language=English)—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.

**What angiogenesis inhibitors are being used to treat cancer in humans?**

The [U.S. Food and Drug Administration](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000454785&version=Patient&language=English) (FDA) has approved a number of angiogenesis inhibitors to treat cancer. Most of these are [targeted therapies](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000270742&version=Patient&language=English) that were developed specifically to target VEGF, its receptor, or other specific molecules involved in angiogenesis. Approved angiogenesis inhibitors include:

* [Axitinib (Inlyta®)](https://www.cancer.gov/about-cancer/treatment/drugs/axitinib)
* [Bevacizumab (Avastin®)](https://www.cancer.gov/about-cancer/treatment/drugs/bevacizumab)
* [Cabozantinib (Cometriq®)](https://www.cancer.gov/about-cancer/treatment/drugs/cabozantinib-s-malate)
* [Everolimus (Afinitor®)](https://www.cancer.gov/about-cancer/treatment/drugs/everolimus)
* [Lenalidomide (Revlimid®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenalidomide)
* [Lenvatinib mesylate (Lenvima®)](https://www.cancer.gov/about-cancer/treatment/drugs/lenvatinibmesylate)
* [Pazopanib (Votrient®)](https://www.cancer.gov/about-cancer/treatment/drugs/pazopanibhydrochloride)
* [Ramucirumab (Cyramza®)](https://www.cancer.gov/about-cancer/treatment/drugs/ramucirumab)
* [Regorafenib (Stivarga®)](https://www.cancer.gov/about-cancer/treatment/drugs/regorafenib)
* [Sorafenib (Nexavar®)](https://www.cancer.gov/about-cancer/treatment/drugs/sorafenibtosylate)
* [Sunitinib (Sutent®)](https://www.cancer.gov/about-cancer/treatment/drugs/sunitinibmalate)
* [Thalidomide (Synovir, Thalomid®)](https://www.cancer.gov/about-cancer/treatment/drugs/thalidomide)
* [Vandetanib (Caprelsa®)](https://www.cancer.gov/about-cancer/treatment/drugs/vandetanib)
* [Ziv-aflibercept (Zaltrap®)](https://www.cancer.gov/about-cancer/treatment/drugs/ziv-aflibercept)

**Do angiogenesis inhibitors have side effects?**

Side effects of treatment with VEGF-targeting angiogenesis inhibitors can include [hemorrhage](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000373015&version=Patient&language=English), clots in the arteries (with resultant stroke or heart attack), [hypertension](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044038&version=Patient&language=English), impaired wound healing, reversible posterior leukoencephalopathy syndrome (a brain disorder), and protein in the urine. Gastrointestinal perforation and [fistulas](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000463712&version=Patient&language=English) also appear to be rare side effects of some angiogenesis inhibitors.

Antiangiogenesis agents that target the VEGF receptor have additional side effects, including fatigue, diarrhea, biochemical [hypothyroidism](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044547&version=Patient&language=English), [hand-foot syndrome](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044825&version=Patient&language=English), cardiac failure, and hair changes.

**Immune System Modulators**

When inserted directly into the bladder, BCG can cause an immune response against bladder cancer cells.

Credit: iStock

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**How do immune system modulators work against cancer?**

Immune-modulating agents are a type of immunotherapy that enhance the body’s immune response against cancer.

Types of immune-modulating agents include:

* **Cytokines**, which are proteins made by [white blood cells](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045993&version=Patient&language=en). They play important roles in your body’s normal immune responses and in the immune system’s ability to respond to cancer.

Cytokines that are sometimes used to treat cancer include:

* + [**Interferons**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045324&version=Patient&language=en) **(INFs)**. Researchers have found that one type of interferon, called INF-alfa, can enhance your immune response to cancer cells by causing certain white blood cells, such as [natural killer cells](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044062&version=Patient&language=en) and dendritic cells, to become active. INF-alfa may also slow the growth of cancer cells or promote their death.
  + [**Interleukins**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046069&version=Patient&language=en) **(ILs)**. There are more than a dozen interleukins, including IL-2, which is also called T-cell [growth factor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045705&version=Patient&language=en). IL-2 boosts the number of white blood cells in the body, including killer T cells and natural killer cells. Increasing these cells can cause an immune response against the cancer. IL-2 also helps B cells (another type of white blood cell) produce certain substances that can target cancer cells.

Hematopoietic growth factors are cytokines that are used to reduce side effects from cancer treatment by promoting the growth of blood cells that are damaged by chemotherapy. They include:

* + **Erythropoietin**, which increases the production of red blood cells
  + **IL-11**, which increases the production of platelets
  + **Granulocyte-macrophage colony-stimulating factor (GM-CSF) and** [**granulocyte colony-stimulating factor**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046749&version=Patient&language=en) **(G-CSF)**, which both increase the number of white blood cells. Boosting white blood cells reduces the risk of infections. G-CSF and GM-CSF can also enhance the immune system response against cancer by increasing the number of cancer-fighting T cells.
* **BCG** is a weakened form of the bacteria that causes tuberculosis. It does not cause disease in humans. BCG is used to treat bladder cancer. When inserted directly into the bladder with a catheter, BCG causes an immune response against cancer cells. It is also being studied in other types of cancer. BCG stands for Bacillus Calmette-Guérin.
* **Immunomodulatory drugs (also called** [**biological response modifiers**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045616&version=Patient&language=en)**)** stimulate the immune system. They include:
  + [Thalidomide](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045458&version=Patient&language=en) (Thalomid®)
  + [Lenalidomide](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000393761&version=Patient&language=en) (Revlimid®)
  + [Pomalidomide](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000589401&version=Patient&language=en)(Pomalyst®)
  + [Imiquimod](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045080&version=Patient&language=en) (Aldara®, Zyclara®)

Thalidomide, lenaliodomide, and pomalidomide cause cells to release IL-2. They also stop tumors from forming new blood vessels. Tumors need to form new blood vessels to grow beyond a certain size. These three drugs may also be called angiogenesis inhibitors.

Imiquimod is a cream that you rub on the skin. It causes cells to release cytokines.

**Which cancers are treated with immune system modulators?**

Most immune-modulating agents are used to treat [advanced cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000478743&version=Patient&language=en). Some are used to help manage side effects.

**What are the side effects of immune system modulators?**

Immune-modulating agents can cause side effects, which affect people in different ways. The side effects you may have and how they make you feel will depend on how healthy you are before treatment, your type of cancer, how advanced it is, the type of immune-modulating agent you are getting, and the dose.

Doctors and nurses cannot know for sure when or if side effects will occur or how serious they will be. So, it is important to know which signs to look for and what to do if you start to have problems.

Immune-modulating agents can cause flu-like [symptoms](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045022&version=Patient&language=en), which include:

* [Fever](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000450108&version=Patient&language=en)
* Chills
* Weakness
* Dizziness
* [Nausea or vomiting](https://www.cancer.gov/about-cancer/treatment/side-effects/nausea)
* Muscle or joint aches
* [Fatigue](https://www.cancer.gov/about-cancer/treatment/side-effects/fatigue)
* Headache

Learn more about [flu-like symptoms caused by cancer treatment](https://www.cancer.gov/about-cancer/treatment/side-effects/flu-symptoms).

Cytokines can also cause many serious side effects, such as:

* Trouble breathing
* Low or high blood pressure
* Severe allergic reactions
* Lowered blood counts, which can raise the risk of infections and cause [bleeding problems](https://www.cancer.gov/about-cancer/treatment/side-effects/bleeding-bruising)
* Blood clots
* Problems with mood, behavior, thinking, and [memory](https://www.cancer.gov/about-cancer/treatment/side-effects/memory)
* Skin problems, such as rash, burning at injection site, and ulcers
* Organ damage

BCG can also cause urinary side effects.

Thalidomide, lenalidomide, and pomalidomide can cause:

* Blood clots
* [Nerve problems](https://www.cancer.gov/about-cancer/treatment/side-effects/nerve-problems) that lead to pain, numbness, tingling, swelling, or muscle weakness in different parts of the body.
* Birth defects, if used during pregnancy

Imiquimod can cause skin reactions.

**Hormone Therapy for Breast Cancer**

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**What are hormones and hormone receptors?**

Hormones are substances that function as chemical messengers in the body. They affect the actions of cells and tissues at various locations in the body, often reaching their targets through the bloodstream.

The hormones [estrogen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046076&version=Patient&language=en) and [progesterone](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045158&version=Patient&language=en) are produced by the ovaries in [premenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045268&version=Patient&language=en) women and by some other tissues, including fat and skin, in both premenopausal and [postmenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045269&version=Patient&language=en) women and in men. Estrogen promotes the development and maintenance of female sex characteristics and the growth of long bones. Progesterone plays a role in the menstrual cycle and pregnancy.

Estrogen and progesterone also promote the growth of some breast cancers, which are called hormone-sensitive (or hormone-dependent) breast cancers. Hormone-sensitive breast cancer cells contain proteins called [hormone receptors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044359&version=Patient&language=en) ([estrogen receptors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046409&version=Patient&language=en), or ERs, and [progesterone receptors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000423248&version=Patient&language=en), or PRs) that become activated when hormones bind to them. The activated receptors cause changes in the expression of specific genes, which can stimulate cell growth.

To determine whether breast cancer cells contain hormone receptors, doctors test samples of tumor tissue that have been removed by surgery. If the tumor cells contain estrogen receptors, the cancer is called [estrogen receptor positive](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045270&version=Patient&language=en) (ER positive), estrogen sensitive, or estrogen responsive. Similarly, if the tumor cells contain progesterone receptors, the cancer is called [progesterone receptor positive](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045273&version=Patient&language=en) (PR or PgR positive). Breast tumors that contain estrogen and/or progesterone receptors are sometimes called [hormone receptor positive](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000788029&version=Patient&language=en) (HR positive). Most ER-positive breast cancers are also PR positive.

Breast cancers that lack ERs are called [ER negative](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044403&version=Patient&language=en), and if they lack both ER and PR they may be called HR negative.

Approximately 67%–80% of breast cancers in women are ER positive ([1](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r1), [2](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r2)). Approximately 90% of breast cancers in men are ER positive and approximately 80% are PR positive ([3](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r3)).

**What is hormone therapy?**

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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045713&version=Patient&language=en) or by interfering with effects of hormones on breast cancer cells. Tumors that are hormone insensitive do not have [hormone receptors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044359&version=Patient&language=en) and do not respond to hormone therapy.

Hormone therapy for breast cancer should not be confused with [menopausal hormone therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000304725&version=Patient&language=en) (MHT)—treatment with estrogen alone or in combination with progesterone to help relieve symptoms of [menopause](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046296&version=Patient&language=en). These two types of therapy produce 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.

**What types of hormone therapy are used for breast cancer?**

Several strategies are used to treat hormone-sensitive breast cancer:

**Blocking ovarian function:** Because the [ovaries](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046687&version=Patient&language=en) are the main source of [estrogen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046076&version=Patient&language=en) in [premenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045268&version=Patient&language=en) women, estrogen levels in these women can be reduced by eliminating or suppressing ovarian function. Blocking ovarian function is called [ovarian ablation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045811&version=Patient&language=en).

Ovarian ablation can be done surgically in an operation to remove the ovaries (called [oophorectomy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045438&version=Patient&language=en)) 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) agonist](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000306500&version=Patient&language=en)s, which are also known as [luteinizing hormone-releasing hormone (LHRH) agonist](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046304&version=Patient&language=en)s. By mimicking [GnRH](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000306531&version=Patient&language=en), these medicines interfere with signals that stimulate the ovaries to produce estrogen.

Examples of [ovarian suppression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044445&version=Patient&language=en) drugs that have been approved by the U.S. Food and Drug Administration (FDA) are [goserelin](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045289&version=Patient&language=en) (Zoladex) and [leuprolide](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000595341&version=Patient&language=en) (Lupron).

**Blocking estrogen production:** Drugs called [aromatase inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044232&version=Patient&language=en) 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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045269&version=Patient&language=en) 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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045504&version=Patient&language=en) (Arimidex) and [letrozole](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045421&version=Patient&language=en) (Femara), both of which temporarily inactivate aromatase, and [exemestane](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045445&version=Patient&language=en) (Aromasin), which permanently inactivates aromatase.

**Blocking estrogen’s effects:** Several types of drugs interfere with estrogen’s ability to stimulate the growth of breast cancer cells:

* [**Selective estrogen receptor modulators (SERMs)**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044229&version=Patient&language=en) bind to estrogen receptors, preventing estrogen from binding. Examples of SERMs approved by the FDA for treatment of breast cancer are [tamoxifen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000509341&version=Patient&language=en) (Nolvadex) and [toremifene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045338&version=Patient&language=en) (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](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046645&version=Patient&language=en) and bone.
* **Other** [**antiestrogen**](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044813&version=Patient&language=en) **drugs**, such as [fulvestrant](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000306498&version=Patient&language=en) (Faslodex), work in a somewhat different way to block estrogen’s effects. Like SERMs, fulvestrant binds to the [estrogen receptor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046409&version=Patient&language=en) and functions as an [estrogen blocker](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000648588&version=Patient&language=en). 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.

**How is hormone therapy used to treat breast cancer?**

There are three main ways that hormone therapy is used to treat hormone-sensitive breast cancer:

**Adjuvant therapy for early-stage breast cancer:** [Tamoxifen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000509341&version=Patient&language=en) is FDA approved for [adjuvant hormone treatment](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045587&version=Patient&language=en) of [premenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045268&version=Patient&language=en) and [postmenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045269&version=Patient&language=en) women (and men) with ER-positive [early-stage breast cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000446564&version=Patient&language=en), and the [aromatase inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044232&version=Patient&language=en) [anastrozole](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045504&version=Patient&language=en), [letrozole](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045421&version=Patient&language=en), and [exemestane](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045445&version=Patient&language=en) are approved for this use in postmenopausal women.

Research has shown that women who receive at least 5 years of adjuvant therapy with tamoxifen after having surgery for early-stage ER-positive breast cancer have reduced risks of breast cancer [recurrence](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045861&version=Patient&language=en), including a new [breast cancer in the other breast](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044169&version=Patient&language=en), and reduced risk of death at 15 years ([4](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r4)).

Until recently, most women who received adjuvant hormone therapy to reduce the chance of a breast cancer recurrence took tamoxifen every day for 5 years. However, with the introduction of newer hormone therapies (i.e., the aromatase inhibitors), some of which have been compared with tamoxifen in [clinical trials](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045961&version=Patient&language=en), additional approaches to hormone therapy have become common ([5](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r5)–[7](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r7)).

For example, some women may take an aromatase inhibitor, instead of tamoxifen, every day for 5 years. Other women may receive additional treatment with an aromatase inhibitor after 5 years of tamoxifen. Finally, some women may switch to an aromatase inhibitor after 2 or 3 years of tamoxifen, for a total of 5 or more years of hormone therapy. Research has shown that for postmenopausal women who have been treated for early-stage breast cancer, adjuvant therapy with an aromatase inhibitor reduces the risk of recurrence and improves [overall survival](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000655245&version=Patient&language=en), compared with adjuvant tamoxifen ([8](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r8)).

Some premenopausal women with early-stage ER-positive breast cancer may have [ovarian suppression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044445&version=Patient&language=en) plus an aromatase inhibitor, which was found to have higher rates of freedom from recurrence than ovarian suppression plus tamoxifen or tamoxifen alone ([9](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r9)).

Men with early-stage ER-positive breast cancer who receive adjuvant therapy are usually treated first with tamoxifen. Those treated with an aromatase inhibitor usually also take a [GnRH agonist](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000753541&version=Patient&language=en).

Decisions about the type and duration of adjuvant hormone therapy are complicated and must be made on an individual basis in consultation with an oncologist.

**Treatment of advanced or metastatic breast cancer:** Several types of hormone therapy are approved to treat [metastatic](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044058&version=Patient&language=en) or [recurrent](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045862&version=Patient&language=en) hormone-sensitive breast cancer. Hormone therapy is also a treatment option for ER-positive breast cancer that has come back in the breast, [chest wall](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044996&version=Patient&language=en), or nearby [lymph nodes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045762&version=Patient&language=en) after treatment (also called a locoregional recurrence).

Two [SERMs](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044230&version=Patient&language=en), tamoxifen and toremifene, are approved to treat metastatic breast cancer. The antiestrogen [fulvestrant](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000306498&version=Patient&language=en) is approved for postmenopausal women with metastatic ER-positive breast cancer that has spread after treatment with other antiestrogens ([10](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r10)). Fulvestrant is also approved for postmenopausal women with HR-positive, [HER2-negative](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000774531&version=Patient&language=en) [locally advanced](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045955&version=Patient&language=en) or metastatic breast cancer who have not previously been treated with hormone therapy ([11](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r11)). In addition, it may be used in premenopausal women who have had [ovarian ablation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045811&version=Patient&language=en).

The aromatase inhibitors anastrozole and letrozole are approved to be given to postmenopausal women as initial therapy for metastatic or locally advanced hormone-sensitive breast cancer ([12](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r12), [13](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r13)). Both of these drugs and the aromatase inhibitor exemestane are also approved to treat postmenopausal women with advanced breast cancer whose disease has worsened after treatment with tamoxifen ([14](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r14)). Men with advanced breast cancer who are treated with an aromatase inhibitor also receive a GnRH agonist.

Some women with advanced breast cancer are treated with a combination of hormone therapy and one of several targeted therapies:

* [Palbociclib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000768872&version=Patient&language=en) (Ibrance), is approved for use in combination with letrozole as initial therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women. Palbociclib inhibits two cyclin-dependent kinases (CDK4 and CDK6) that appear to promote the growth of hormone receptor–positive breast cancer cells ([15](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r15)).  
    
  Palbociclib is also approved to be used in combination with fulvestrant for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer whose cancer has gotten worse after treatment with another hormone therapy ([16](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r16)).
* [Abemaciclib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000791149&version=Patient&language=en) (Verzenio), another CDK4 and CDK6 inhibitor, is approved to be used in combination with fulvestrant for postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer whose disease has [progressed](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044078&version=Patient&language=en) after treatment with hormone therapy ([17](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r17)).  
    
  Abemaciclib is also approved to be used alone for women and men with HR-positive, HER2-negative advanced or metastatic breast cancer whose disease got worse after treatment with hormone therapy and previous chemotherapy given for metastatic disease ([18](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r18)).
* [Ribociclib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000787678&version=Patient&language=en) (Kisqali), another CDK4/6 inhibitor, is approved to be used in combination with an aromatase inhibitor in postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer that has not been treated with hormone therapy ([19](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r19), [20](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r20)).  
    
  Ribociclib is also approved to be used in combination with fulvestrant in postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer who have not been treated with hormone therapy or whose disease got worse during treatment with hormone therapy ([21](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r21)).
* [Lapatinib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000539453&version=Patient&language=en) (Tykerb) is approved to be used in combination with letrozole to treat hormone receptor–positive, HER2-positive metastatic breast cancer in postmenopausal women for whom hormone therapy is indicated. It is a small-molecule inhibitor of the HER2 and EGFR tyrosine kinases.
* [Alpelisib](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000798365&version=Patient&language=en) (Piqray) is approved to treat breast cancer that is HR positive and HER2 negative and has a mutation in the [*PIK3CA* gene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000798600&version=Patient&language=en). It is used with fulvestrant to treat postmenopausal women, and men, whose breast cancer is advanced or metastatic and has gotten worse during or after treatment with hormone therapy ([22](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r22)).
* Some women with advanced breast cancer that is HER2 and HR positive may receive hormone therapy plus [trastuzumab](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045439&version=Patient&language=en) with or without [pertuzumab](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000340934&version=Patient&language=en) ([23](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r23)).

**Neoadjuvant treatment of breast cancer:** The use of hormone therapy to treat breast cancer to reduce tumor size before surgery ([neoadjuvant therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045800&version=Patient&language=en)) has been studied in clinical trials ([24](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r24)). These trials have shown that neoadjuvant hormone therapy—in particular, with aromatase inhibitors—can be effective in reducing the size of breast tumors in postmenopausal women, but it is not yet clear how effective it is in premenopausal women.

Hormone therapy is sometimes used for the neoadjuvant treatment of HR-positive breast cancer in postmenopausal women who cannot tolerate chemotherapy or when surgery needs to be delayed.

**Can hormone therapy be used to prevent breast cancer?**

Yes. Most breast cancers are [ER positive](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044404&version=Patient&language=en), and clinical trials have tested whether hormone therapy can be used to prevent breast cancer in women who are at increased risk of developing the disease.

A large NCI-sponsored [randomized clinical trial](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045858&version=Patient&language=en) called the Breast Cancer Prevention Trial found that [tamoxifen](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000509341&version=Patient&language=en), taken for 5 years, reduces the risk of developing [invasive breast cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000537695&version=Patient&language=en) by about 50% in postmenopausal women who were at increased risk ([25](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r25)). Long-term follow-up of another randomized trial, the International Breast Cancer Intervention Study I, found that 5 years of tamoxifen treatment reduces the [incidence](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046145&version=Patient&language=en) of breast cancer for at least 20 years ([26](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r26)). A subsequent large randomized trial, the Study of Tamoxifen and Raloxifene, which was also sponsored by NCI, found that 5 years of [raloxifene](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000572250&version=Patient&language=en) (a [SERM](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044230&version=Patient&language=en)) reduces breast cancer risk in such women by about 38% ([27](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r27)).

As a result of these trials, both tamoxifen and raloxifene have been approved by the FDA to reduce the risk of developing breast cancer in women at high risk of the disease. Tamoxifen is approved for this use regardless of menopausal status. Raloxifene is approved for use only in postmenopausal women.

Two [aromatase inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044232&version=Patient&language=en)—[exemestane](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045445&version=Patient&language=en) and [anastrozole](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045504&version=Patient&language=en)—have also been found to reduce the risk of breast cancer in postmenopausal women at increased risk of the disease. After 3 years of follow-up in a randomized trial, women who took exemestane were 65% less likely than those who took a [placebo](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046688&version=Patient&language=en) to develop breast cancer ([28](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r28)). After 7 years of follow-up in another randomized trial, women who took anastrozole were 50% less likely than those who took a placebo to develop breast cancer ([29](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r29)). Both exemestane and anastrozole are approved by the FDA for treatment of women with ER-positive breast cancer. Although both are also used for breast cancer prevention, neither is approved for that [indication](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000348991&version=Patient&language=en) specifically.

**What are the side effects of hormone therapy?**

The side effects of hormone therapy depend largely on the specific drug or the type of treatment ([7](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r7)). The benefits and harms of taking hormone therapy should be carefully weighed for each person. A common switching strategy used for [adjuvant therapy](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045587&version=Patient&language=en), in which patients take tamoxifen for 2 or 3 years, followed by an [aromatase inhibitor](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044232&version=Patient&language=en) for 2 or 3 years, may yield the best balance of benefits and harms of these two types of hormone therapy ([30](https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#r30)).

[Hot flashes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000256567&version=Patient&language=en), [night sweats](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000454810&version=Patient&language=en), and [vaginal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044308&version=Patient&language=en) dryness are common side effects of all hormone therapies. Hormone therapy also may disrupt the [menstrual cycle](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045784&version=Patient&language=en) in [premenopausal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045268&version=Patient&language=en) women.

Less common but serious side effects of hormone therapy drugs are listed below.

**Tamoxifen**

* Risk of [blood clots](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000476017&version=Patient&language=en), especially in the lungs and legs
* [Stroke](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000439425&version=Patient&language=en)
* [Cataracts](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000440102&version=Patient&language=en)
* [Endometrial cancer](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000444987&version=Patient&language=en) and [uterine sarcoma](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000445097&version=Patient&language=en)
* Bone loss in premenopausal women, but no increased risk of fracture
* Mood swings, depression, and loss of [libido](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000467845&version=Patient&language=en)
* In men: headaches, nausea, vomiting, skin rash, [impotence](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000321376&version=Patient&language=en), and loss of [libido](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000467845&version=Patient&language=en)

**Raloxifene**

* Risk of blood clots, especially in the lungs and legs
* Stroke in certain subgroups

**Ovarian suppression**

* Bone loss
* Mood swings, depression, and loss of libido

**Aromatase inhibitors**

* Risk of heart attack, angina, heart failure, and hypercholesterolemia
* Bone loss
* Joint pain
* Mood swings and depression

**Fulvestrant**

* [Gastrointestinal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045692&version=Patient&language=en) symptoms, including nausea, vomiting, and [constipation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000407757&version=Patient&language=en)
* Weakness and fatigue
* Pain, including bone pain, back pain, [musculoskeletal](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044938&version=Patient&language=en) pain, joint pain, and in the extremities
* Headache
* Hot flashes
* Breathing problems, including painful breathing, shortness of breath, and cough
* Loss of appetite

**Can other drugs interfere with hormone therapy?**

Certain drugs, including several commonly prescribed [antidepressants](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000044105&version=Patient&language=en) (those in the category called [selective serotonin reuptake inhibitors](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000335507&version=Patient&language=en), or SSRIs), inhibit an enzyme called CYP2D6. This enzyme plays a critical role in the body's use of tamoxifen because CYP2D6 metabolizes, or breaks down, tamoxifen into molecules, or metabolites, that are much more active than tamoxifen itself.

The possibility that SSRIs might, by inhibiting CYP2D6, slow the [metabolism](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046173&version=Patient&language=en) of tamoxifen and reduce its effectiveness is a concern given that as many as one-fourth of breast cancer patients experience clinical [depression](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000430479&version=Patient&language=en) and may be treated with SSRIs. In addition, SSRIs are sometimes used to treat [hot flashes](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000256567&version=Patient&language=en) caused by hormone therapy.

Many experts suggest that patients who are taking antidepressants along with tamoxifen should discuss treatment options with their doctors. For example, doctors may recommend switching from an SSRI that is a potent inhibitor of CYP2D6, such as [paroxetine hydrochloride](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045553&version=Patient&language=en) (Paxil), to one that is a weaker inhibitor, such as [sertraline](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000335513&version=Patient&language=en) (Zoloft), or that has no inhibitory activity, such as [venlafaxine](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000046117&version=Patient&language=en) (Effexor) or [citalopram](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000450095&version=Patient&language=en) (Celexa). Or they may suggest that their postmenopausal patients take an aromatase inhibitor instead of tamoxifen.

Other medications that inhibit CYP2D6 include the following:

* Quinidine, which is used to treat abnormal heart rhythms
* [Diphenhydramine](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000449930&version=Patient&language=en), which is an [antihistamine](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000468794&version=Patient&language=en)
* [Cimetidine](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000045184&version=Patient&language=en), which is used to reduce stomach acid

People who are prescribed tamoxifen should discuss the use of all other medications with their doctors.

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