IMMUNOTHERAPY FOR THE TREATMENT OF LUNG CANCER

BOOKLET SUPPLEMENT

Immunotherapy

Immunotherapy is one of the most exciting new approaches for treating several types of cancer, including lung cancer. Immunotherapies work by boosting your body's own natural defenses to fight cancer. Several immunotherapies are currently being developed and tested in clinical trials for a variety of lung cancer types and stages. At the time of this booklet's printing, the FDA has approved two immunotherapy drugs for the treatment of metastatic non-small cell lung cancer if chemotherapy is no longer working: nivolumab (Opdivo®) and pembrolizumab

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a partnership for lung cancer survival

(Keytruda®). Pembrolizumab has been approved only for patients with metastatic non-small cell lung cancer whose tumor has tested positive for the marker PD-L1. Other similar drugs are under development and are likely to be approved soon. For these treatments, patients with cancer that tests positive for EGFR or ALK mutations should receive targeted therapies specific for these mutations before immunotherapy is considered. Keep in mind that these treatments for lung cancer are still new, therefore more research must be done to understand which people are most likely to benefit and how best to use the treatments. Ask your doctor if there are any available immunotherapy treatments or clinical trials that might be right for you.

What is the Immune System and How Does It Work?

Your immune system is a network of specialized cells, tissues, and organs working together to defend your body from foreign invaders. It does this through its ability to recognize things that do not belong in the body, such as bacteria, viruses, or cancer cells. The frontline of the immune system includes cells circulating in your bloodstream — known as white blood cells. There are a number of different types of white blood cells, all of which attack foreign substances in different ways. Lymphocytes are one of the main cell types of the immune system, and they are particularly important in fighting cancer. One type of lymphocyte, called T-lymphocytes or T-cells, have specialized structures on their surface that can recognize when a cell is infected or is a cancer cell. When this happens, the T-cell starts a process leading to the destruction of the infected or cancerous cell. (Figure 1)

WHAT'S SUPPOSED TO HAPPEN

Figure 1A. Lymphocytes recognize the cancer cell as something that is not supposed to be there...

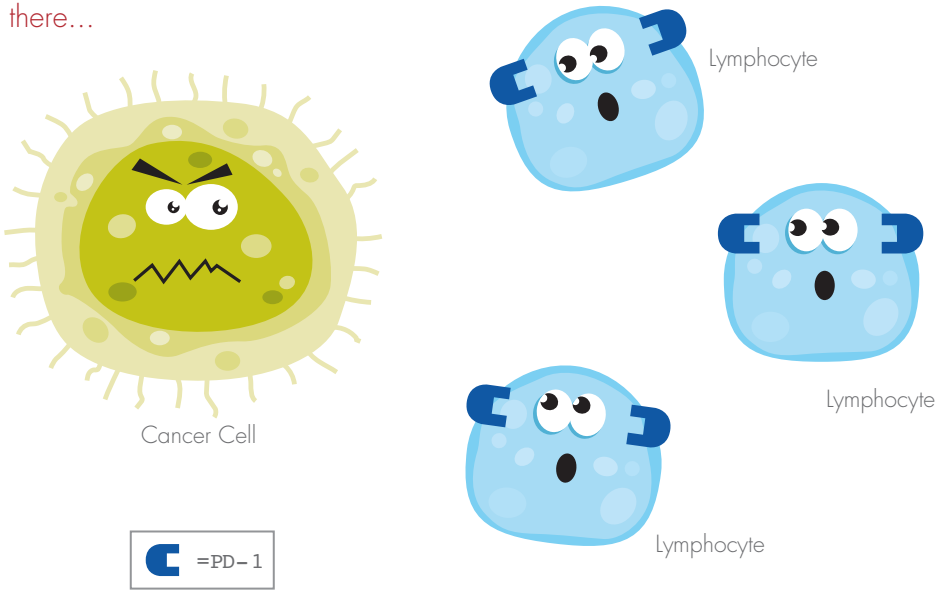
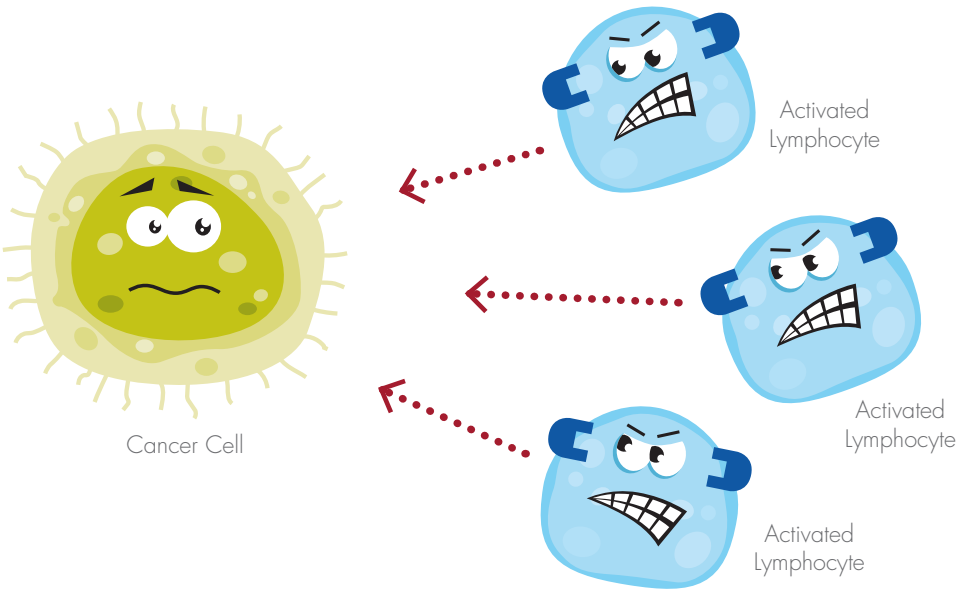


Figure 1B. ...and become activated to help destroy the cancer cell.



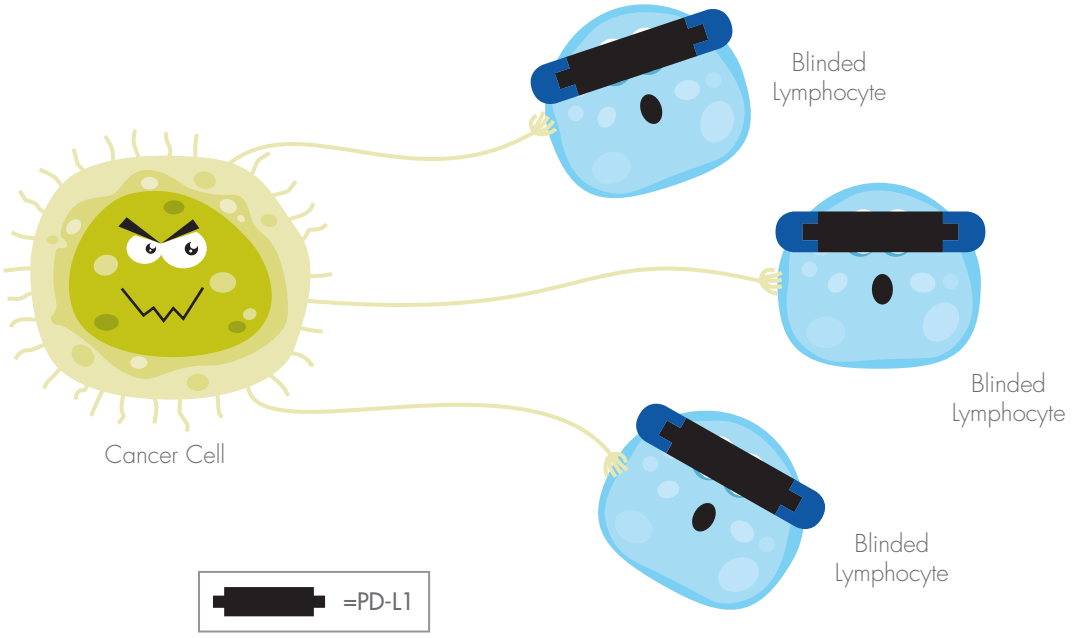
How Does Immunotherapy Work?

Because the immune system can be so powerful, the body has control mechanisms in place to prevent it from accidentally attacking normal, healthy tissues, such as the joints, bowels, or skin. One way this happens is through proteins found on the cells of the body called "checkpoint proteins." PD-1 is a type of checkpoint protein that is found on T-cells and helps to regulate the immune response. Under normal circumstances, PD-1 binds to another protein called PD-L1, which helps "turn off" the T-cells so that they don't attack normal body organs and tissues.

In some cases, cancer cells can find ways to use these control mechanisms to trick the immune system into thinking that they are "normal" and should not

WHAT'S SOMETIMES HAPPENS

Cancer cell secretes proteins that make lymphocytes and other immune cells unable to "see" the cancer cells.



be attacked. One way they do this is by producing their own PD-L1. If a cancer cell produces this protein and that PD-L1 binds to PD-1 (Figure 2), the T-cell no longer recognizes the cancer cell as something foreign. The T-cell becomes inactivated and will no longer attack, making the cancer cells "invisible" to the patrolling T-cells, allowing them to escape. This allows cancer cells to continue to grow and spread.

Researchers have developed several strategies for strengthening the immune system against tumors. One such strategy is to prevent cancer cells from making themselves "invisible." Drugs that use this strategy, such as nivolumab (Opdivo®) and pembrolizumab (Keytruda®), are sometimes called "checkpoint inhibitors."

Nivolumab and pembrolizumab work by binding to the PD-1 on T-cells so that they are no longer available to bind with PD-L1 (Figure 3A). That reduces the cancer cell's ability to trick the immune system. Some immunotherapies under development work by binding to PD-L1 instead of to PD-1 (Figure 3B), but in either case, the result is the same: PD-L1 and PD-1 can no longer bind to each other, allowing the T-cells to recognize the tumor cells and destroy them. Your doctor may recommend testing your tumor for PD-L1 before prescribing one of these treatments. Some studies suggest that this test may help your doctor determine if immunotherapy is right for you.

It is important to remember that immunotherapies work differently from chemotherapy. When a patient receives chemotherapy, changes in the size of a tumor can be measured quickly, often within days. With immunotherapy, the benefits can take much longer to recognize. Researchers aren't sure exactly why this happens, but it may be because the immune response takes a little while to become fully active. In some patients, immunotherapy causes T-cells and other immune cells to flock to the tumor, making it appear to actually get larger before it begins to shrink. Your doctor will work with you to determine how to best monitor your progress while you are on an immunotherapy.

WITH IMMUNOTHERAPY, THE GOOD GUYS WIN

Figure 3A. Immunotherapy agents such as nivolumab and pembrolizumab stick to PD-1 so it can't interact with PD-L1.

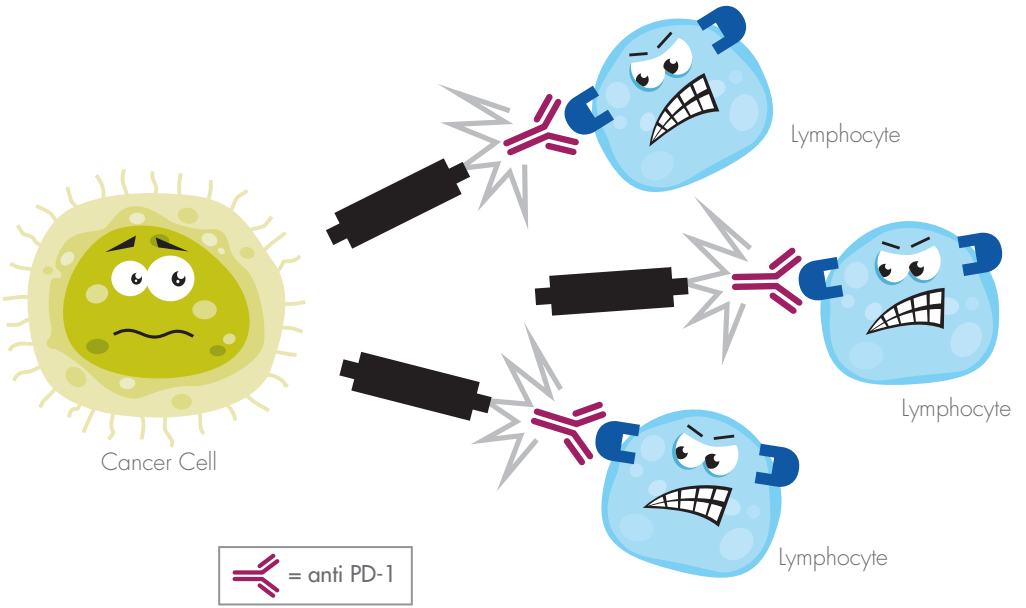
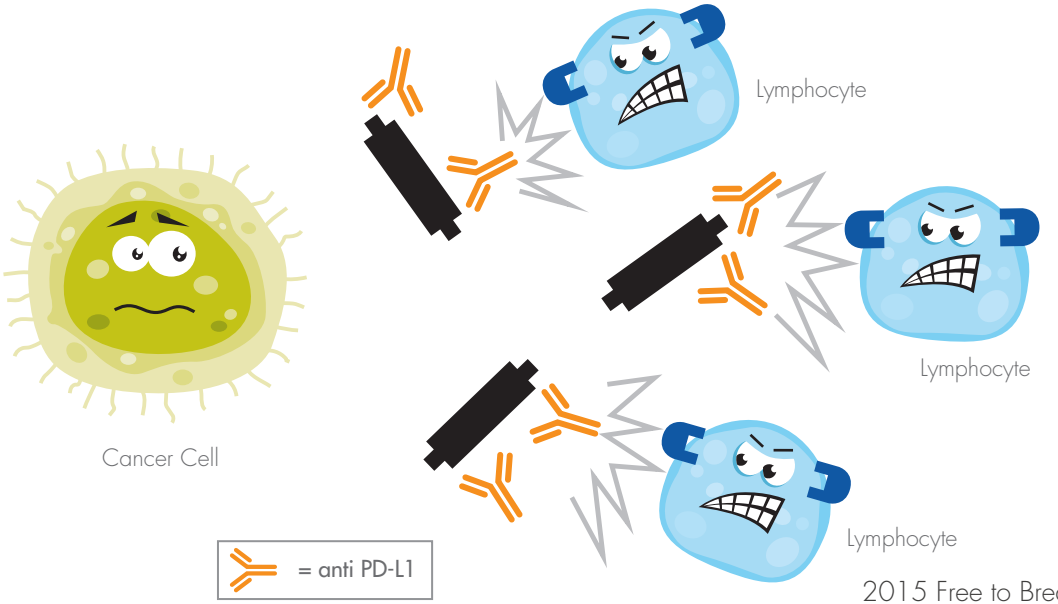


Figure 3B. Other immunotherapies are in development that bind to PD-L1 and also inhibit PD-1 from binding to PD-L1.



What Side Effects Can Occur With Immunotherapy?

Because immunotherapies work by enhancing or turning on the immune system, they can sometimes cause your immune system to become overactive and attack normal tissues or organs. This can be a particular concern in patients who have had an organ transplant or who already have immune system problems such as Crohn's disease, ulcerative colitis, or lupus. You should discuss with your doctor if you have experienced any of these before starting an immunotherapy. The most common side effects patients experience with immunotherapies are mild and can include fatigue, itching, skin rashes, muscle, joint or bone pain, and nausea. In rare cases, the immune system over-reacts, which can cause more serious side effects if they result in your body's own defenses attacking normal organs. This is most commonly seen in the lungs, liver, intestines, kidney or hormone glands. When this happens, conditions such as pneumonitis, a lung problem with symptoms of cough, chest pain, or shortness of breath, or colitis, an intestinal problem that can result in diarrhea or tears or holes in the intestine, can occur. **Be sure you talk to your doctor about any concerns or side effects you experience during your treatment.**