



# INTERLEUKIN-2

## **WHAT IS INTERLEUKIN-2?**

Interleukin-2 (IL-2) is a protein made by the body. T-helper cells, a kind of white blood cell, produce IL-2 when they are stimulated by an infection. IL-2 makes infection-fighting cells multiply and mature. Patients who use IL-2 have large increases in their T-cell (CD4+ cell) counts. IL-2 is called an immune modulator.

Interleukin-2 has been approved by the FDA to treat some types of cancer, but is not approved for use in HIV disease. Based on negative results of two major international studies, research on the use of IL-2 in patients with HIV has stopped.

Using gene splicing, the Chiron Corporation developed a way to manufacture IL-2. Their version is called Proleukin. It was bought by Novartis. It is used in the treatment of some kinds of cancer.

## **WHO SHOULD TAKE IL-2?**

IL-2 stimulates the immune system and increases the number of CD4+ cells. People who started with higher CD4 cell counts got larger CD4+ cell increases.

Scientists did not agree on the value of the new CD4 cells generated by IL-2. In 2009, two major international studies were completed. They showed that a CD4 count based on taking IL-2 is not as good as a CD4 count based on successful antiretroviral therapy (ART). The difference has to do with how many different types of CD4 cells you have.

Before HIV disease attacks your immune system, you have millions of different types of CD4 cells. An easier way to think about them is like the letters of the alphabet. Each letter is programmed to respond to one particular type of infection. With a healthy immune system, you have many copies of each letter. As your CD4 cell count goes down, you have fewer copies of each letter, and you might run out of some letters.

Let's say that you need to spell the word "zebra" in order to fight pneumonia. If you

lose all your copies of the letter "z," you can't spell zebra and you might develop pneumonia.

IL-2 makes more copies of "letters" (types of CD4 cells) that still exist, but it doesn't bring back missing "letters." There could still be gaps in the immune defenses. The major IL-2 research studies showed that CD4 counts were increased significantly. However, these CD4 increases did not result in any improvement in patient health.

Researchers also used IL-2 to try to clear infected "resting" CD4 cells from the blood. These experiments were not successful.

## **HOW IS IL-2 TAKEN?**

IL-2 has been given as an intravenous infusion and as twice-daily subcutaneous (below the skin) injections. Early research showed that the largest increases in CD4 cells occur when IL-2 is given every day for 5 days, once every 8 weeks. If the CD4 cell count climbs enough after the first few cycles, future cycles can occur less frequently.

The best dosage of IL-2 has not been determined. The dosage is stated as "millions of international units," or MIU. Some patients taking IL-2 have been followed for six years or more. After initially using IL-2 every 2 months, they increased the time between cycles to as much as 3 years. They still had significantly higher CD4 cell counts.

## **WHAT ARE THE SIDE EFFECTS?**

Without ART, IL-2 can increase HIV viral load up to six times its pre-treatment level. These increases disappear within one month. ART controls these "spikes" in viral load. You should not use IL-2 unless you are taking ART. However, based on recent research, there is no reason for people with HIV to take IL-2.

When IL-2 is given by intravenous infusion, the most common side effect is called capillary leak syndrome. This causes weight gain, swelling, low blood pressure, and other problems.

At lower doses, people taking IL-2 get flu-like symptoms, including fever, chills, and muscle aches. Because IL-2 stimulates the immune system, it can make some immune disorders get worse, including arthritis, psoriasis, and diabetes. It can also reduce the number of neutrophils, a type of infection-fighting cell, and can cause low levels of thyroid.

When IL-2 is given by subcutaneous injection, the side effects are usually milder than with intravenous infusions. There is the added side effect of irritation where the injection is given. Side effects show up from 2 to 6 hours after injection of IL-2, and disappear soon after the end of each cycle.

IL-2 can cause mood changes including irritability, insomnia, confusion, or depression. These can continue for several days after IL-2 is stopped.

## **HOW DOES IL-2 REACT WITH OTHER DRUGS?**

The body naturally produces IL-2. No serious interactions with antiviral medications have been noted. Also, there is no evidence that the body develops resistance to IL-2 when it is given in cycles.

## **THE BOTTOM LINE**

IL-2 stimulates the immune system and can lead to large increases in the number of CD4+ (T-helper) cells. Unfortunately, these increases in CD4 cells do not produce any improvement in health in people with HIV.

Based on major research results, there is no reason to take IL-2 as a way to enhance ART.

*Reviewed May 11, 2011*