

Infections and CLL: What to Know

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Why Are Infections a Concern in CLL?

Chronic lymphocytic leukemia (CLL) affects the immune system, which is the body's defense against germs. Even before any treatment begins, CLL weakens the ability to fight off infections in several ways:

1. The body may produce fewer antibodies (the proteins that help fight bacteria and viruses)
2. Other infection-fighting cells — including T cells, natural killer cells, monocytes/macrophages, and neutrophils — may not work as well as they should
3. These immune problems tend to get worse over time and may even be present before CLL is formally diagnosed

Because of this, people with CLL tend to get infections more often and more severely than people without CLL. Infections are the leading cause of death in CLL, accounting for 30% to 50% or more of all CLL-related deaths. This is why understanding and managing infection risk is so important.

BTK Inhibitors: Infection Risk That Improves Over Time

BTK inhibitors (pills taken daily that block a growth signal in cancer cells) can increase the risk of certain infections — particularly lung infections and, less commonly, fungal infections — especially early in treatment or in patients who have already received prior therapies. They can also lower neutrophils (white blood cells) counts.

Fortunately, infection risk tends to decrease over time as treatment continues. Studies show that immune function may actually improve during BTK inhibitor therapy, and the frequency and duration of infections may decline as patients remain on treatment.

BCL-2 Inhibitors: Watch for Low White Blood Cell Counts

BCL-2 inhibitors (pills that trigger cancer cells to self-destruct) may carry an important side effect: neutropenia, a drop in neutrophils (white blood cells) that are the body's first line of defense against bacterial and fungal infections.

The risk is usually even higher when BCL-2 inhibitors are combined with anti-CD20 antibody infusions.

This is why medical teams monitor blood counts closely during treatment and may:

- Temporarily pause or reduce your dose
- Give injections with growth factors to boost white blood cell production
- Prescribe preventive medications (e.g., antibiotics, antifungals)

Anti-CD20 Monoclonal Antibodies: The Long Effect After Treatment Ends

Anti-CD20 antibodies (infusions given through an IV that target immune cells called B cells) can be effective at helping control CLL, but they work by destroying B cells — the very immune cells the body needs to make antibodies and fight infections. The critical point to mention is that this damage may persist long after the final anti-CD20 infusion.

During this entire recovery period:

- Antibody levels may remain low
- Patients may be more vulnerable to bacterial infections, viral infections (including shingles), and potentially life-threatening hepatitis B reactivation
- Vaccines may be less effective
- Patients who get repeatedly exposed to anti-CD20 therapies may have progressively weakened B-cell reconstitution with each exposure

This is why your care team may:

- Continue antiviral medications for up to 12 months or longer after your last treatment
- Monitor blood counts and antibody levels during any treatment-free period
- Delay certain vaccinations until B cells have recovered
- Consider antibody replacement therapy called intravenous immunoglobulin (IVIG) if you develop recurrent infections

What Can You Do?

- Report any fever, chills, or signs of infection immediately to your care team because even a low-grade fever can be significant when the neutrophil count is low.
- Take all preventive medications exactly as prescribed, even after treatment ends, to potentially improve immune health
- Ask your care team about vaccines — some are recommended, but the timing may matter, especially if receiving anti-CD20 antibody treatments.
- Recommended vaccines include annual inactivated influenza, pneumococcal conjugate vaccine, recombinant shingles vaccine, RSV vaccine, and COVID-19 vaccine.
- Practice good hygiene: frequent handwashing, avoiding close contact with sick people, masking when appropriate, and safe food handling
- Talk to your doctor about antibody replacement therapy if infections are frequent or persist

Talk to Your Doctor About Infection Risk Before Starting Treatment

When it comes time to choose a treatment for your CLL, infection risk should be part of the conversation. Ask your doctor to consider your personal health history, your age, your disease biology and of course your past experience with infections when selecting a therapy. For example:

- If you have a history of frequent or severe infections, certain drug classes may carry more risk for you than others
- If you have a history of hepatitis B, anti-CD20 antibody therapy requires special precautions, including hepatitis B screening before starting treatment
- If you have low antibody levels even before treatment, your doctor may recommend antibody replacement therapy before or during treatment
- If you have other medical conditions (such as diabetes, lung disease, or kidney disease) that already increase your infection risk, this could factor into the treatment plan

Every patient is different. The best treatment plan is likely one that balances the effectiveness of the therapy against the infection risks — tailored to you.