Testing for Chronic Lymphocytic Leukemia

Diagnosing Chronic Lymphocytic Leukemia (CLL)

Doctors will use a series of tests to determine whether you have CLL and, if so, what the best course of treatment might be.[1,2] Many of these tests will be conducted in a laboratory with a blood or bone marrow sample.[1,2]

An accurate diagnosis of CLL is essential and can help your doctor or oncologist to decide the next steps.[1,2] In addition to diagnostic tests, your doctor will take into account your medical history, physical health, stage of disease, genetic markers, biomarkers, and other factors to help your doctor better understand your CLL and the potential outcomes for treatment.[1,2]

If your doctor suspects you may have cancer, they may:

TEST YOUR BLOOD TO:

- ✓ Measure the number of red cells, white cells, and platelets[3]
- ✓ Look for indicators, or biomarkers, that may suggest there is cancer activity[3]
- ✓ Check your body chemistry to examine how other parts of your body are functioning[3]

TEST YOUR BONE MARROW TO:

- ✓ See whether the cancer is affecting your blood or bone marrow[4]
- ✓ Check the extent of the disease[4]
- ✓ Find out if there is any cancer that shows up in the bone marrow that might not yet be present in routine blood samples[4]

What Are Genetic Markers and Biomarkers?

GENETIC MARKER
Refers to a specific sequence of DNA at a certain spot along a chromosome. Genetic markers and genes that are close to each other on a chromosome are usually inherited, which may help researchers find a gene near a marker that may cause a certain disease or trait within a family.[20]

BIOMARKER
A biological molecule found in the blood, other body fluids, or tissues that is a sign of a normal or abnormal process (eg, condition or disease). A biomarker may be used to see how well the body responds to treatment.[21]

Testing for CLL by Your Doctor

COMPLETE BLOOD COUNT TEST

- Usually **performed by a doctor through a blood draw** and when tested in a lab can show the number of red cells, white cells, and platelets in your blood[1,3]
- **A person with CLL often has increased numbers of lymphocytes, a type of white blood cell.** CLL can also cause low platelet counts and low red blood cell counts (anemia).[1,5,6]
- Having more than 10,000 lymphocytes/mm^3 of blood might suggest CLL, but other tests are needed to know for sure[1]

FLOW CYTOMETRY IMMUNOPHENOTYPING

- Flow cytometry immunophenotyping is an **important next step to confirm the diagnosis of CLL**[6-9]
- For this test, a doctor draws blood or bone marrow samples, which are "tagged" and passed through a laser in a laboratory test, which lights up the tagged cells and specific markers on the cell[9]
- If the abnormal lymphocytes are of the B-cell type (≥5,000 B lymphocytes/µL), then it might be CLL[6,9]

Flow Cytometry Immunophenotyping Can:

- See if the cells, or lymphocytes, are cancerous (known as a T-cell or B-cell malignancy) or from a noncancerous condition, such as an infection[9,10]
- Check the number of these cells[3,9]
- Identify any specific qualities of a cancerous cell, known as "tumor markers" which can help determine the course of the disease and treatment[3,9]

Tailoring Treatment for CLL

CLL is not one size fits all. In recent years, there has been **a great deal of progress made in understanding CLL and how to best treat it**. Certain genetic markers can point to which treatments may be most effective, which is why **predictive testing is important before you start treatment**.[1,3,8,9] In some cases, chemotherapy may not be the best course of treatment.[1,3,9,23] There are approved therapies that serve as preferred first-line treatments because they are efficacious in all types of CLL.[23]

Some people are surprised to know that **testing should be repeated throughout your journey with CLL**.[9]

FLUORESCENCE IN SITU HYBRIDIZATION (FISH)

- FISH is a test performed on your blood or bone marrow cells to detect chromosome changes (cytogenetic analysis) in blood cancer cells[1,3,9]
- This test provides clinicians with a **better idea of prognosis and response to specific treatments and is conducted at the time of diagnosis** to see whether a treatment is working[3]
- Approximately 80% of people with CLL carry at least one of these chromosomal changes: del13q, Trisomy 12, del11q, or del17p[9,12]

NEXT-GENERATION SEQUENCING (NGS) FOR TESTING DNA

- This lab test **uses blood or bone marrow samples to look for mutations in genes that can determine the potential outcome for a person living with CLL**, as well as if the disease will be responsive to chemoimmunotherapy treatments[1,9,24]
- DNA sequencing may be a gene-specific test or may include a panel of genes, including *IGHV, TP53*, *NOTCH1*, *ATM*, *BIRC3*, *SF381**[9,11,13,14]

CYTOSINE-PHOSPHATE-GUANINE (CpG)-STIMULATED METAPHASE KARYOTYPING

- Karyotyping is a test that **pairs and orders the chromosomes in a blood or bone marrow sample, allowing your doctor to determine if there are abnormalities** in the expected size, shape, or number of chromosomes[3,9,15,16]
- A "complex karyotype" is the presence of three or more defects in the chromosomes, which is associated with a poorer disease outcome. It affects up to 16% of people with CLL[9,17]
- Karyotyping in CLL is recommended at diagnosis or before treatment[6,9]

**IGHV, immunoglobulin heavy chain variable region gene; TP53, tumor protein p53 gene; NOTCH1, Notch homolog 1, translocation-associated gene; ATM, ataxia-telangiectasia mutated gene; BIRC3, baculoviral IAP repeat-containing protein 3 gene; SF381, splicing factor 381.*

Other Tests

SERUM MARKERS

- Elevated levels of certain components of the blood serum (the fluid portion that remains in the blood sample tube after clotting).[18] Your doctor may check for these as part of the blood test at diagnosis.

LYMPHOCYTE DOUBLING TIME (LDT)

- The length of time it takes the absolute lymphocyte count to double. This has also been found to help predict outcomes in patients with CLL.[6,7,19,22]

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