CLL SOCIETY
Resource Library

STAGING

Staging in cancer is a process used to determine the extent to which cancer has spread in the body, predict its progression, and guide treatment decisions. By staging the disease, the healthcare team will be able to predict how the cancer might behave in the future and make informed treatment decisions. In most cancers, staging is based on the size of the tumor and how far the cancer has spread throughout the body. However, chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) do not typically form tumors. Instead, the cancerous cells are in the bone marrow, blood, and lymph nodes. Because of this, the outlook for a person with the disease is dependent on other information.

HOW IS STAGING IN CLL AND SLL PERFORMED?

In other cancers, it is necessary to obtain imaging tests such as a CT (computed tomography) or PET (positron emission tomography) scan at the time of diagnosis to look at the entire body to see how far the cancer has spread. CT and PET scans at the time of diagnosis are not necessary to assist with staging CLL and SLL. Instead, staging for the disease relies on blood tests and physical exams to determine a person's outlook.

IS THERE MORE THAN ONE WAY TO STAGE THE DISEASE?

Several tools can be used. But in the United States, the most commonly used is the Rai Staging System, which classifies the severity and progression of the disease based on clinical findings from blood tests and physical exams. There is also the CLL International Prognostic Index (CLL-IPI) which is a newer staging model that is not yet widely used. It combines genetic biomarker results with clinical parameters to categorize individuals into risk groups. In Europe, the most commonly used staging system is the Binet Staging System, which takes into consideration the extent of lymphoid tissue involvement. Additionally, there is the Ann Arbor Staging System, but it should not be used for staging CLL and SLL.

HOW DOES THE RAI STAGING SYSTEM WORK?

The Rai Staging System divides CLL and SLL into five stages (ranging from stage 0 to stage 4). Based on the staging criteria, individuals then fall into three risk categories (low, intermediate, and high). Each stage considers the extent of lymphocytosis, which is an elevated lymphocyte count. Lymphocytes are a type of white blood cells that are crucial in helping the body fight infections. Each stage of the Rai Staging System also considers to what degree the liver, spleen, and lymph nodes are involved. Here are the risk categories and criteria for each stage:

Low Risk:

- Rai Stage 0 – Indicates a low level of risk and is characterized by lymphocytosis alone, with no enlargement of the lymph nodes, spleen, or liver, and with near normal red blood cell and platelet counts.

Intermediate Risk:

- Rai Stage I – Occurs when a person has lymphocytosis plus enlarged lymph nodes. The spleen and liver are not enlarged, and the red blood cell and platelet blood counts remain normal or near normal or only slightly low.
- Rai Stage II – Occurs when a person has lymphocytosis plus an enlarged spleen (and possibly an enlarged liver), with or without enlarged lymph nodes. Red blood cell and platelet counts remain normal or are only slightly low.

High Risk:

- Rai Stage III – Occurs when a person has lymphocytosis plus anemia (low red blood cell count), with or without enlarged lymph nodes, spleen, or liver. The platelet count remains normal or only slightly low.
- Rai Stage IV – Occurs when a person has lymphocytosis plus thrombocytopenia (low platelet count), with or without a low red blood cell count, enlarged lymph nodes, spleen, or liver.

HOW DOES THE CLL INTERNATIONAL PROGNOSTIC INDEX STAGING SYSTEM WORK?

The CLL-IPI is a newer model that combines clinical, laboratory, and genetic characteristics of the disease into one single score that can be used to help estimate the amount of time until the first

treatment is needed, as well as overall survival. It assigns a point system to five independent risk factors and then calculates a total score (lower scores equal less risk). Adverse factors that result in higher scores include being age 65 or older, Rai Stage I-IV, the presence of deletion 17p and or TP53 mutation, mutated IGHV, and a serum beta-2 microglobulin level that is higher than 3.5 mg/L. Depending on total scores, individuals are assigned a level of risk which includes low, intermediate, high, and very high.

Here are the five independent factors that are assigned a score to help determine the level of risk:

- Age greater than 65: 1 point
- Rai Staging System Risk of Intermediate or High: 1 point
- Serum beta-2 microglobulin level greater than 3.5 mg/L: 2 points
- Unmutated IGHV: 2 points
- Presence of deletion 17p and/or TP53 mutation: 4 points

Here are the scoring system categories:

- Low risk: Scores = 0-1 point
- Intermediate risk: Scores = 2-3 points
- High risk: Scores = 4-6 points
- Very high risk: Scores = 7-10 points

The CLL-IPI was developed to better separate high-risk individuals in the era of therapies that are non-chemoimmunotherapy based options. Those with lower scores tend to have the longest amount of time before treatment is needed, while those with higher scores tend to have a shorter amount of time before treatment is needed.

HOW IS STAGING USED TO DETERMINE A PROGNOSIS AND GUIDE TREATMENT DECISIONS?

Many people with CLL and SLL have a slow-growing (indolent) form of the disease and will not require treatment for many years, while others will have a shorter time to wait until their first treatment is needed. The Rai Staging System is used as a prognostic indicator for CLL and SLL. People with a higher Rai Stage are likely to have a worse outcome compared to those with a lower Rai Stage if left untreated. It also may be utilized to determine the need for treatment. For example, someone with a Rai Stage III or IV may typically need to start treatment sooner, whereas someone with a Rai Stage of 0 is more likely to be closely monitored by their healthcare team using the active surveillance approach. The CLL-IPI Score incorporates the Rai Staging System to help predict overall survival and estimate the amount of time until the first treatment is needed. While both of these staging systems can be used to determine a prognosis (meaning the likely course of the disease) and predict when treatment may be needed for a group of people with similar disease features, it is important to remember that every person's CLL and SLL is unique. Both the Rai and CLL-IPI Staging Systems are only estimation tools, so individual outcomes will vary.

CLL SOCIETY MISSION

CLL Society is an inclusive, patient-centric, physician-curated nonprofit organization that addresses the unmet needs of the chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) community through patient education, advocacy, support, and research.