CLL Live Vancouver 2026

What patients and care partners need to know about CLL

Diego Villa, MD MPH FRCPC

Centre for Lymphoid Cancer, BC Cancer

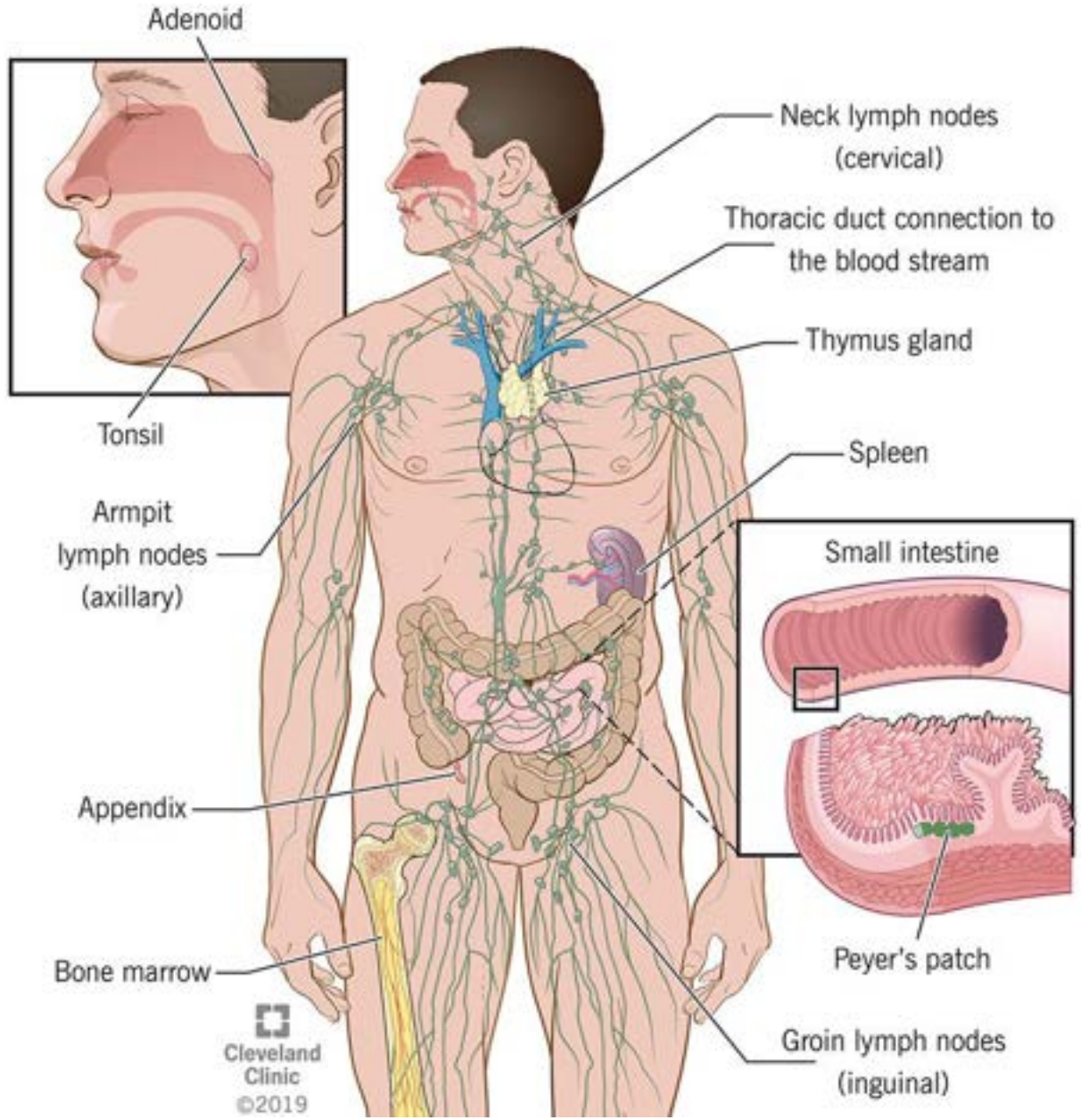
University of British Columbia, Vancouver BC, Canada

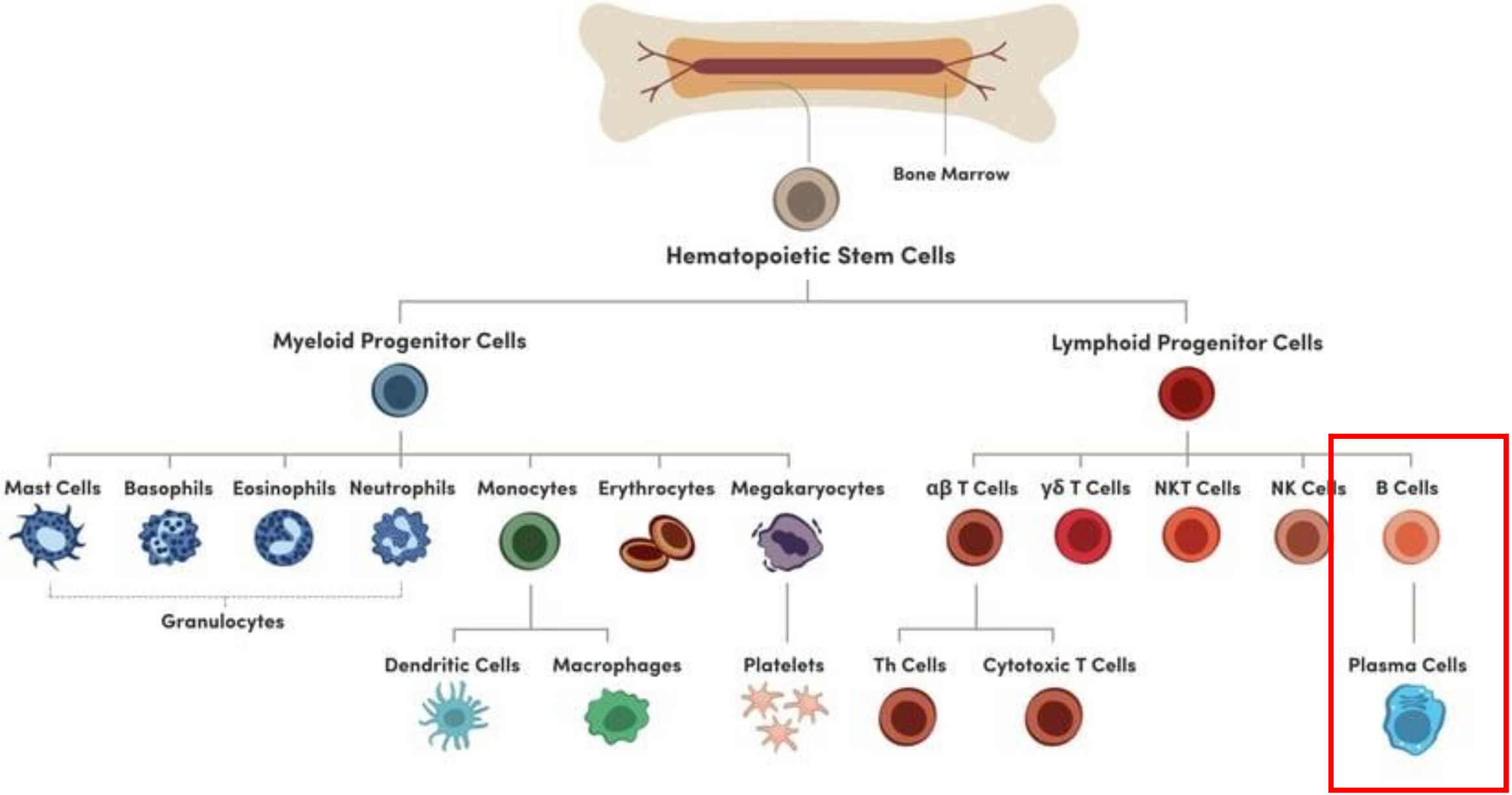
Disclosures

- I have partnered with multiple pharmaceutical companies
- Advisory boards
  - Roche, Abbvie, Janssen, AstraZeneca, BeOne, Kite/Gilead, BMS/Celgene, ONO therapeutics, Incyte, Eli Lilly, Kyowa Kirin.
- Research funding (to the institution)
  - Roche, AstraZeneca, BeOne

Objectives

- How is CLL diagnosed?
- What is the natural history of CLL?
- What tests need to be done? What tests do NOT need to be done?
- What genetic tests may inform prognosis?
- What does “active surveillance” mean and why won’t they treat me?
- When is the right time to initiate therapy?


Adenoid
Tonsil
Neck lymph nodes
(cervical)
Thoracic duct connection to
the blood stream
Thymus gland
Spleen
Armpit
lymph nodes
(axillary)
Small intestine
Appendix
Peyer's patch
Bone marrow
Groin lymph nodes
(inguinal)
Cleveland
Clinic
©2019

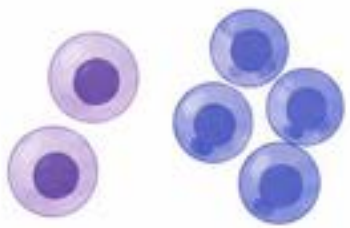

Bone Marrow
Hematopoietic Stem Cells
Myeloid Progenitor Cells
Lymphoid Progenitor Cells
Mast Cells
Basophils
Eosinophils
Neutrophils
Monocytes
Erythrocytes
Megakaryocytes
αβ T Cells
γδ T Cells
NKT Cells
NK Cells
B Cells
Granulocytes
Dendritic Cells
Macrophages
Platelets
Th Cells
Cytotoxic T Cells
Plasma Cells

1. Normal B cells

A healthy immune system

2. MBL (Monoclonal B-cell Lymphocytosis)

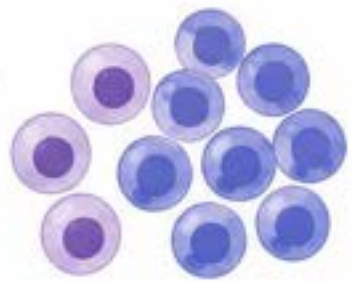
A small number of abnormal B cells is present **(< 5,000 cells/µL)**



No symptoms
Not cancer

3. High-count MBL

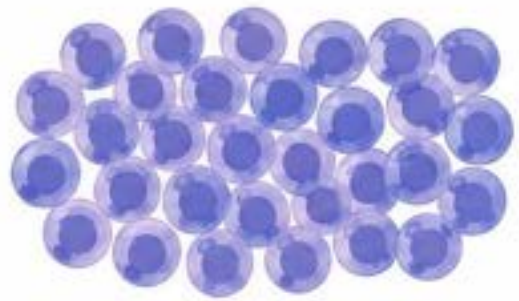
The number of abnormal B cells increases **(≥ 5,000 cells/µL)**



No symptoms
Not cancer

4. CLL (Chronic Lymphocytic Leukemia)

Many abnormal B cells accumulate and the disease can cause problems **(≥ 5,000 cells/µL with signs or symptoms)**



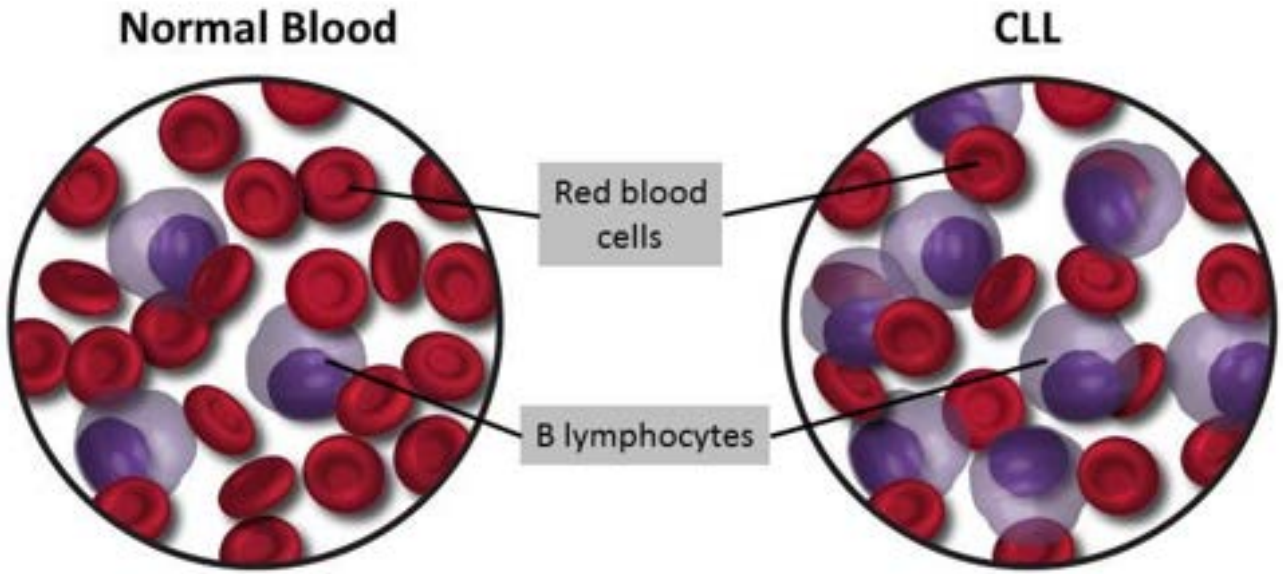
May have symptoms
This is cancer

Time (years)

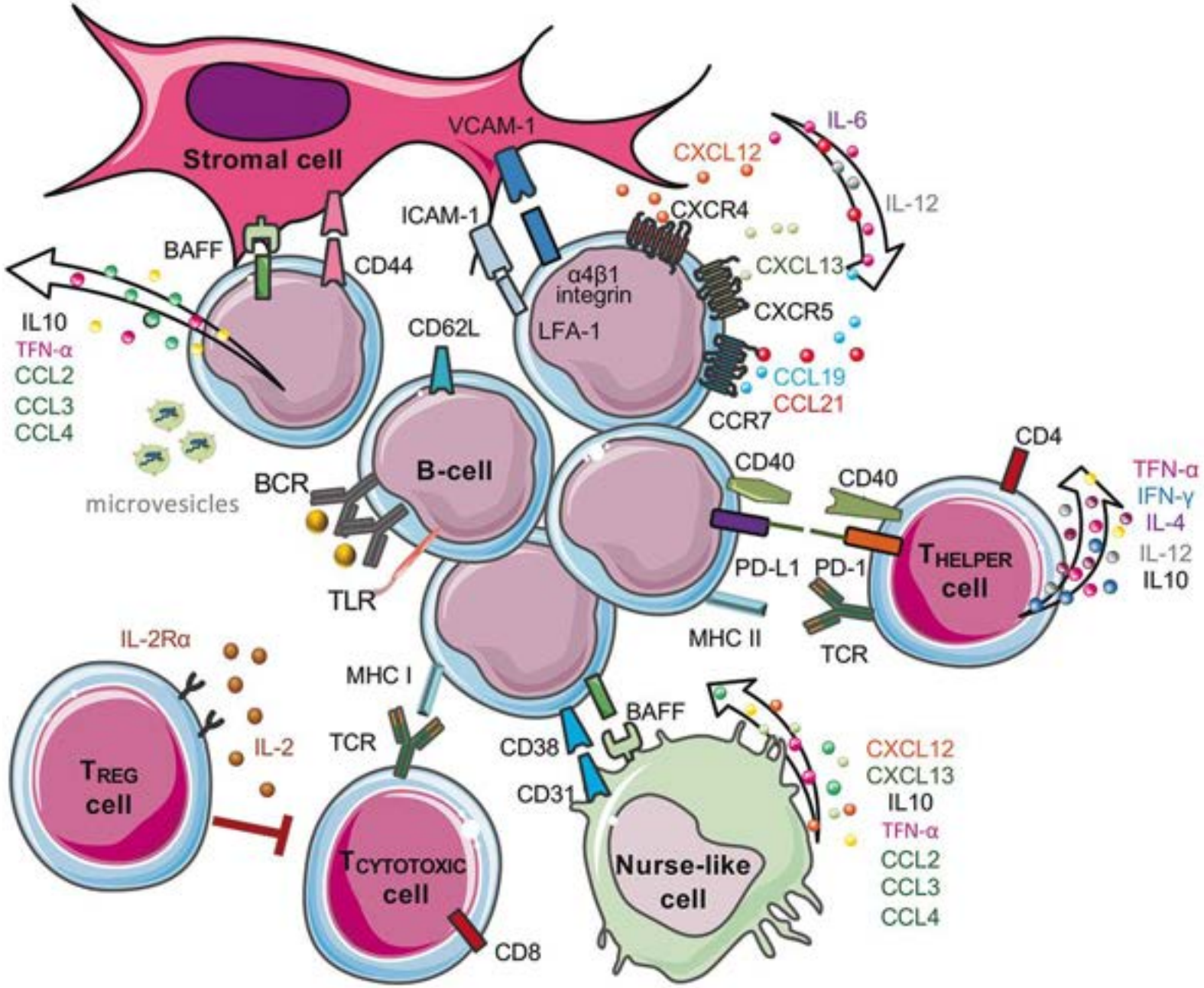
Progression is gradual and may take many years.

Diagnosis of CLL

Clonal expansion of abnormal B lymphocytes in PB
At least 5×10^9 B lymphocytes/L (5000/μL)
Lymphoid cells ≤ 55% atypical/immature
Low density of surface Ig (IgM or IgD) with κ or λ light chains
B-cell surface antigens (CD19, $CD20^{dim}$, CD23)
CD5 surface antigen



Difference between normal blood and CLL



CLL cell niche composition

B-cells

T-cells
T_{HELPER} / $T_{CYTOTOXIC}$ / $T_{REGULATORY}$

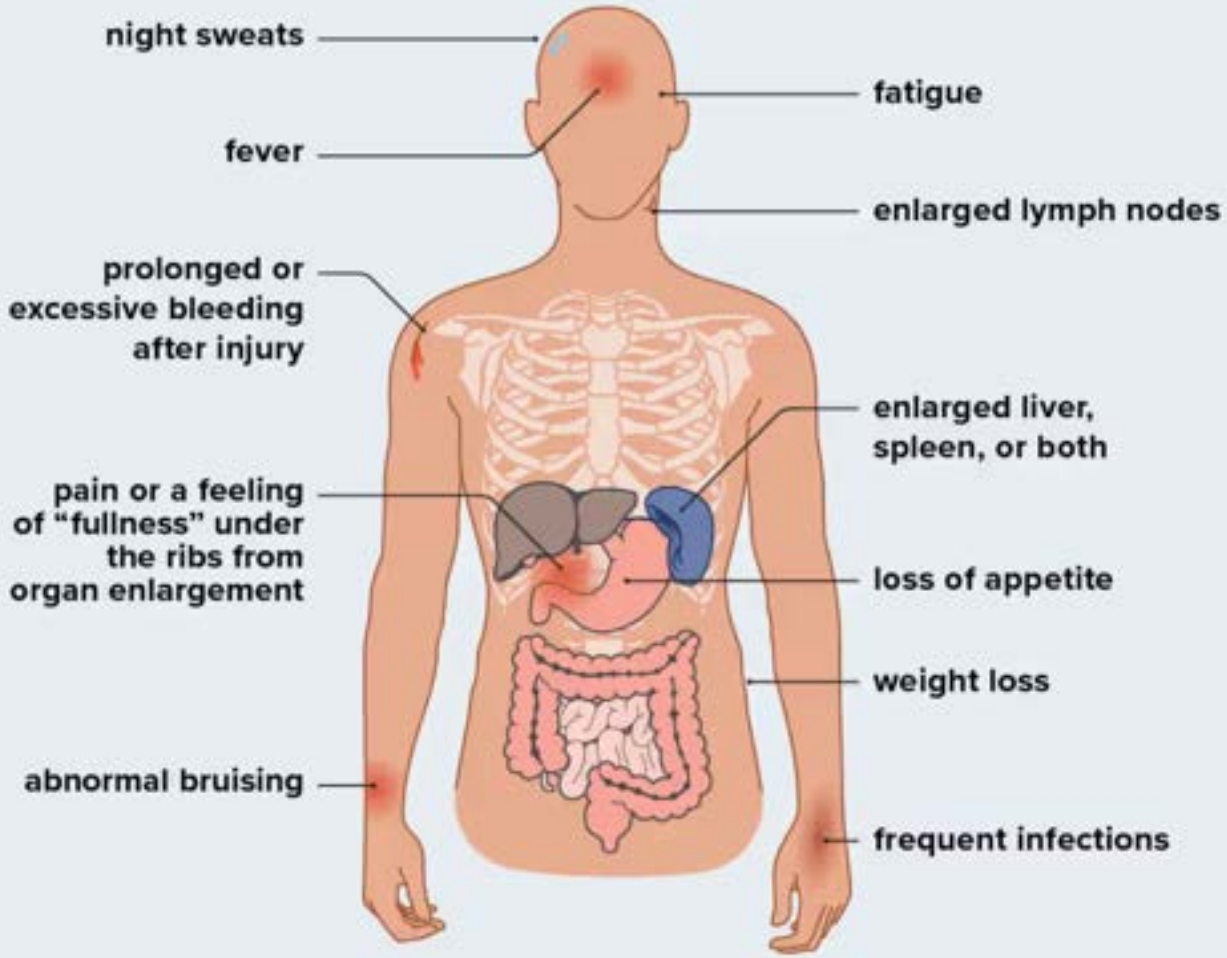
Stromal cells
MSC / FDC

Nurse-like cells

Survival
Homing
Migration
Drug resistance

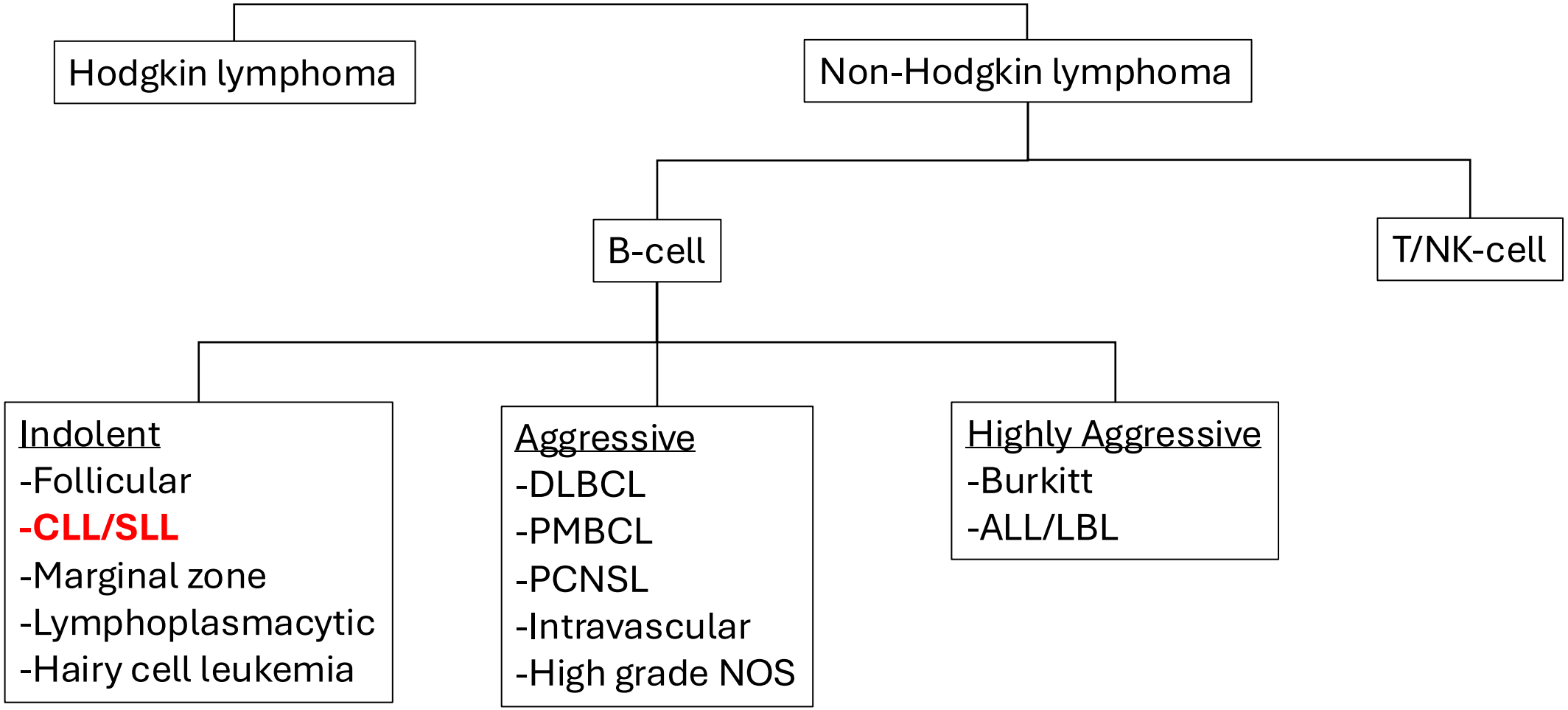
Delgado, Haematologica 2020

COMMON SYMPTOMS OF CLL

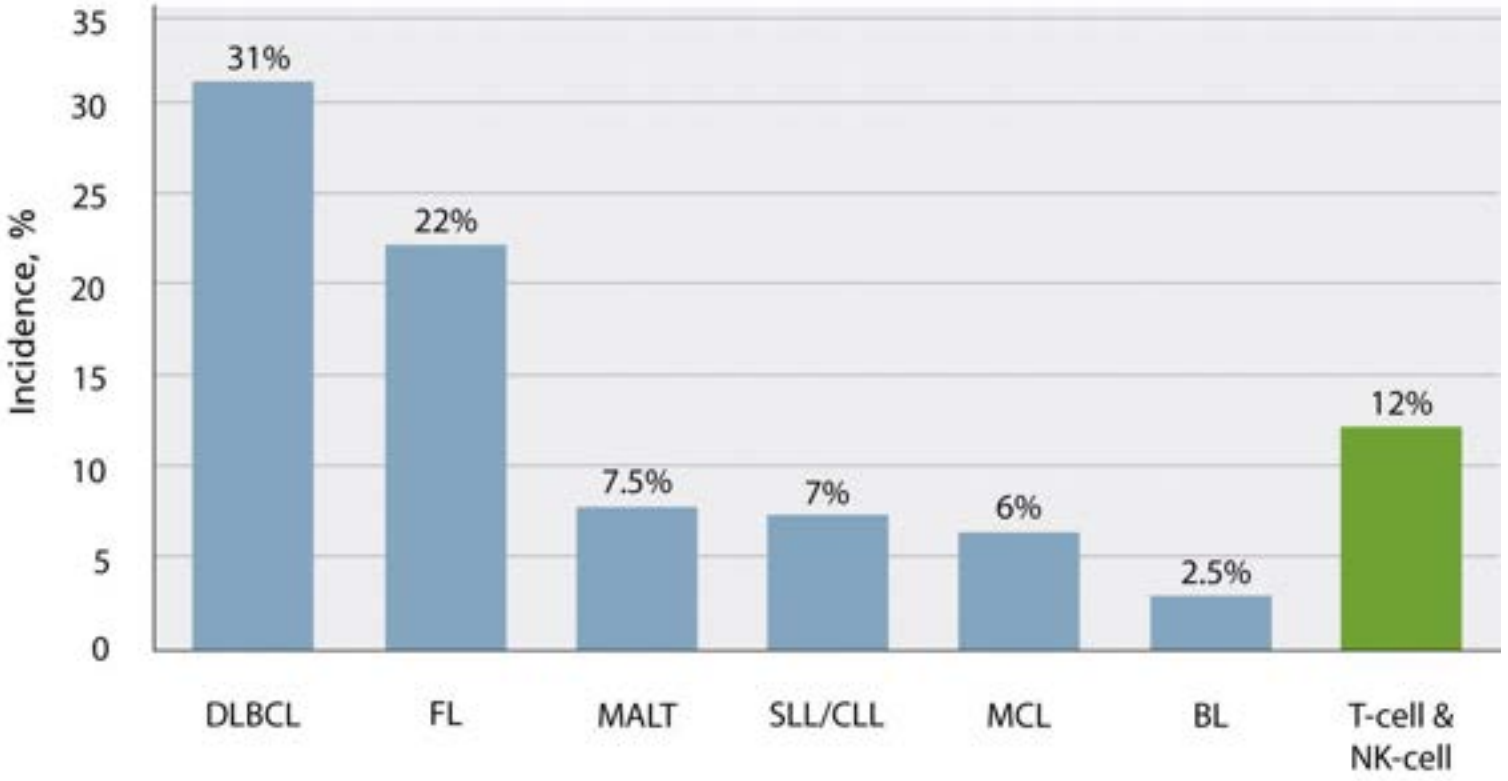


MEDICALNEWSTODAY

Classification of B-cell lymphomas



Most common lymphomas



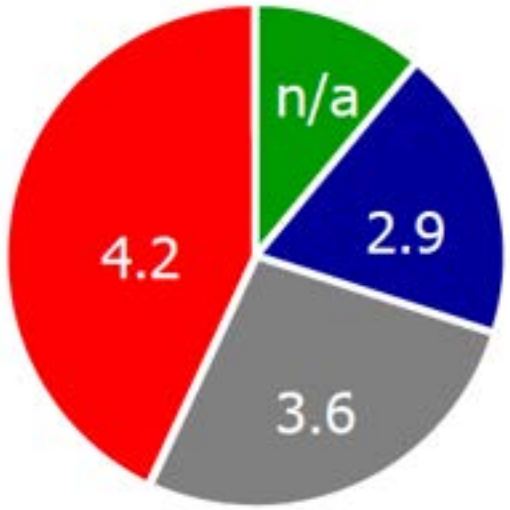
Canadian Cancer Society:

- 1585 people were diagnosed with CLL in Canada in 2022
- 3.8 people/100,000

Rummel, *JNCCN* 2010

Age distribution

- Median age at diagnosis 72 years
- Elderly may be fit or have comorbidities



Age at CLL diagnosis (years)	Patients[1] (%)	Mean comorbidities[2] (all cancer types, n)
≤ 54	11	n/a
55–64	19	2.9
65–74	27	3.6
75+	43	4.2

Ries, SEER Cancer Statistics Review 1975-2005

CLL/SLL is heterogeneous

<u>CHRONIC LYMPHOCYTIC LEUKEMIA</u>
Predominantly in blood and bone marrow
≥5,000 cells/uL

<u>SMALL LYMPHOCYTIC LYMPHOMA</u>
Predominantly in lymph nodes and spleen
<5,000 cells/uL

CLL/SLL is heterogeneous

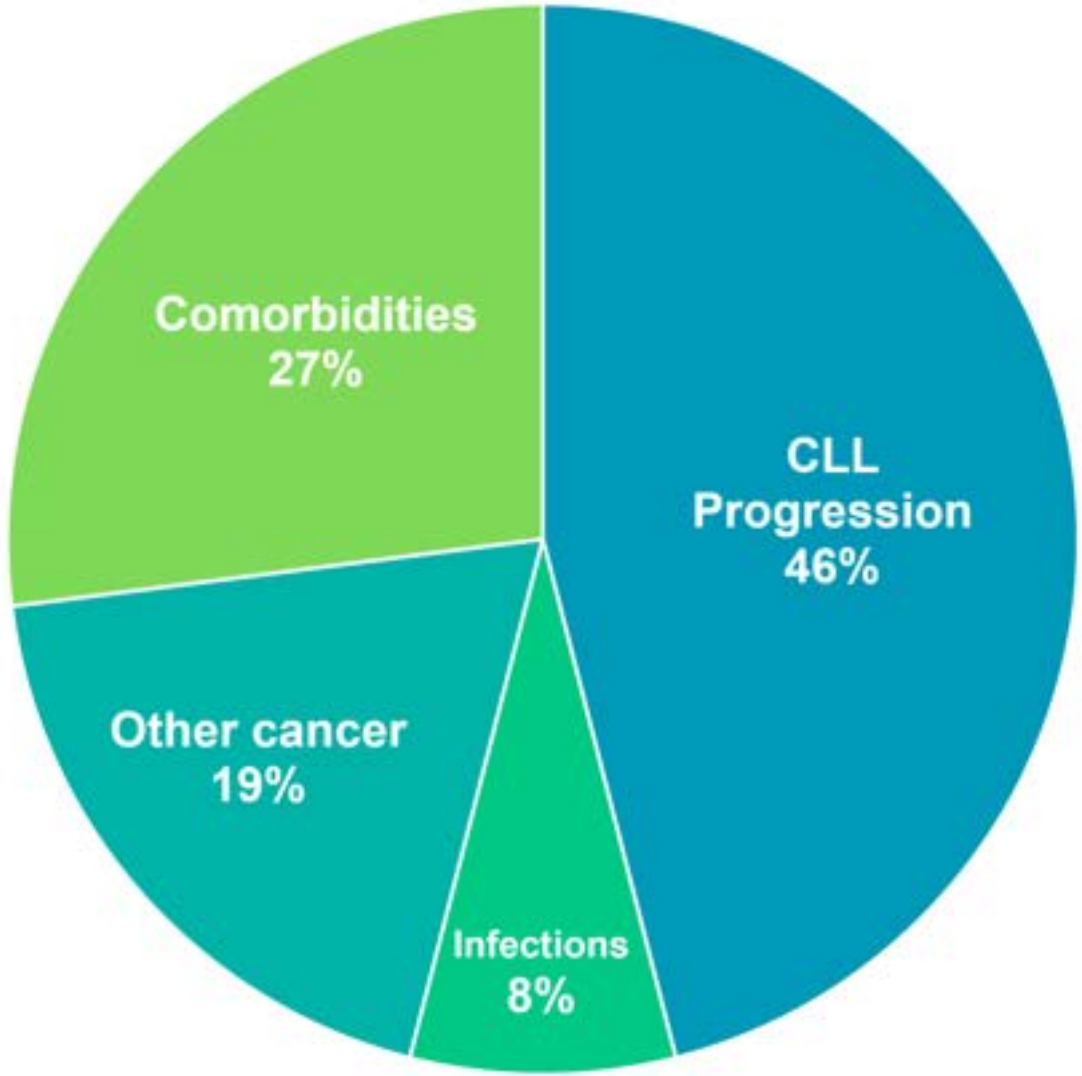
INDOLENT
May not require treatment
"Die with disease"

AGGRESSIVE
Requires treatment(s)
"Die of disease"

Causes of Death in CLL

Prospective cohort study 1143 newly diagnosed CLL patients

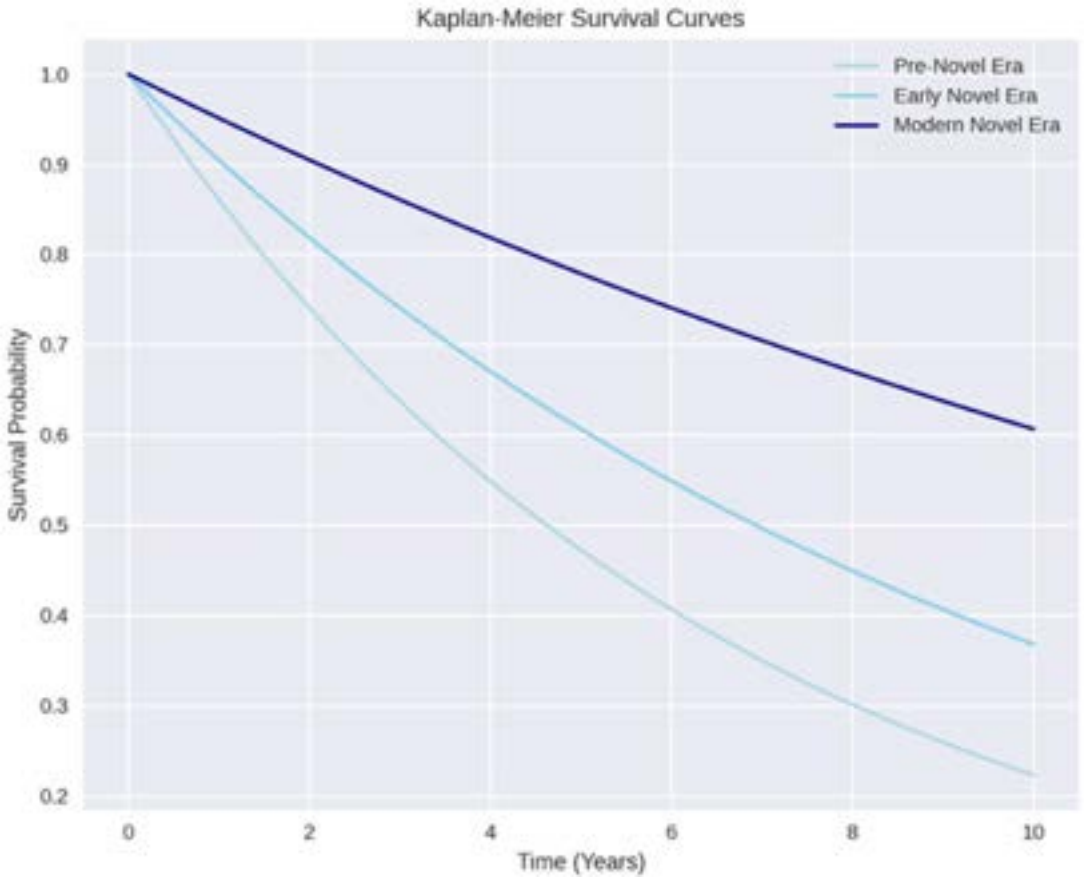
June 2002 – November 2014



Strati, BJH 2017

What is the survival of CLL/SLL in 2026?

Data from SEER, n=49,056



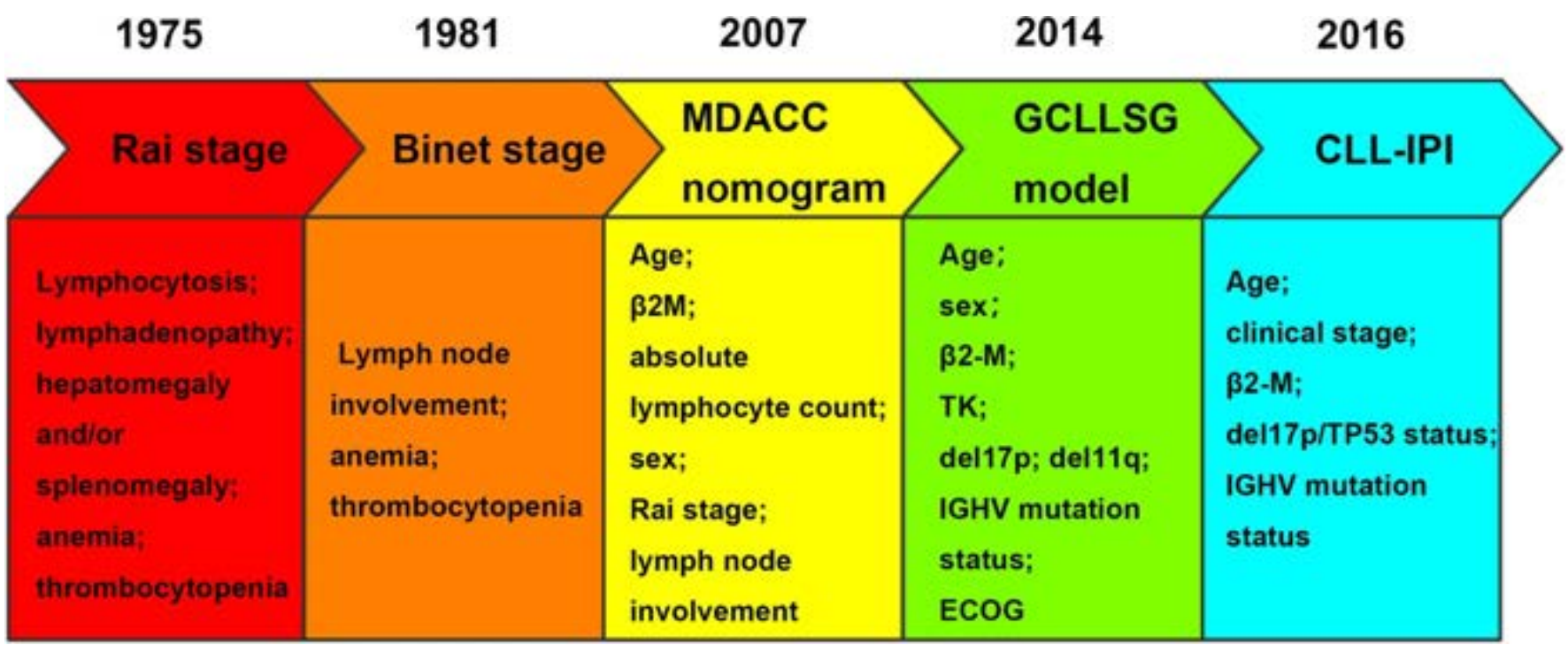
2015-2020: modern novel era, median survival 12 years

2005-2014: early novel era, median survival 7 years

1995-2004: pre-novel era, median survival 4.5 years

Modi, CLML 2026

Estimating Prognosis

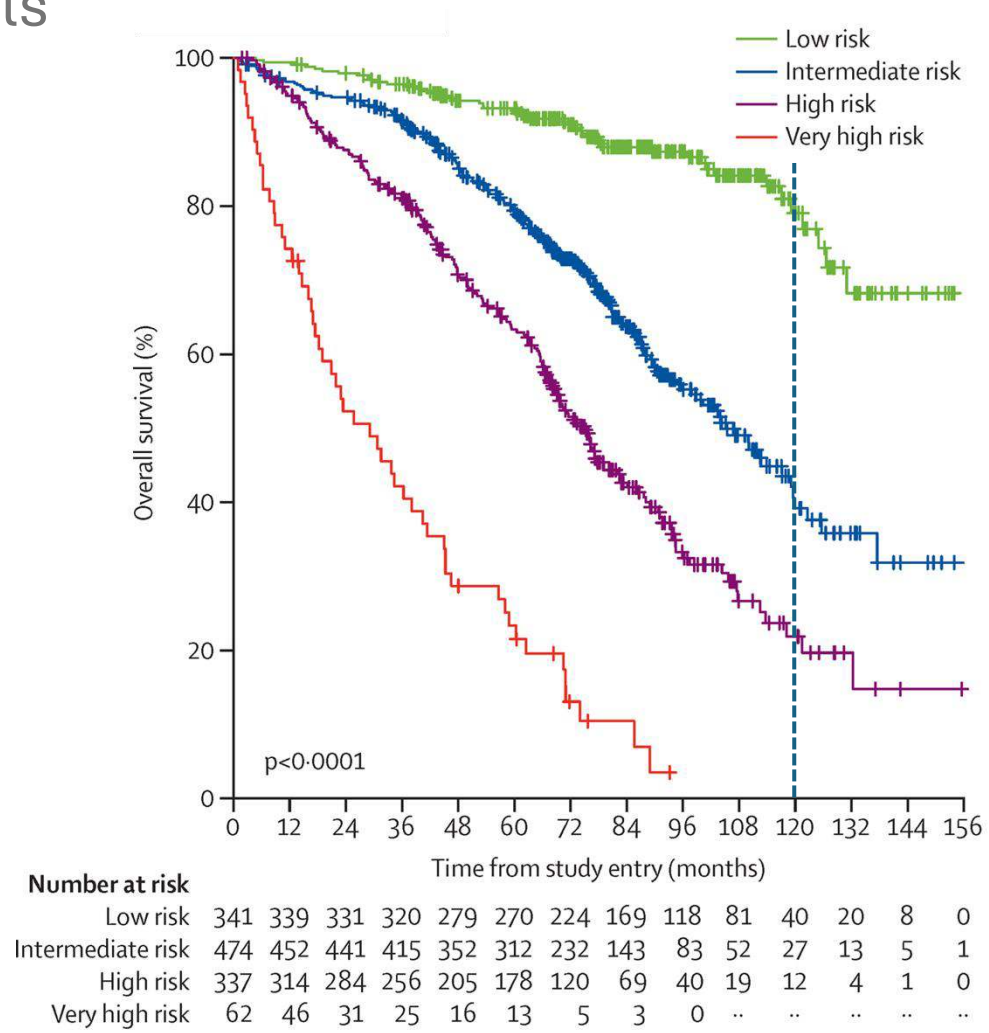


Yun, Biomarker Research 2020

CLL-IPI to estimate overall survival

Used n=3472 from 8 clinical trials

Prognostic Factor
Del17p on FISH or *TP53* mutation
Unmutated *IGHV* genes
Serum β2 microglobulin >3.5 mg/L
Rai Stage I-IV
Age >65 years



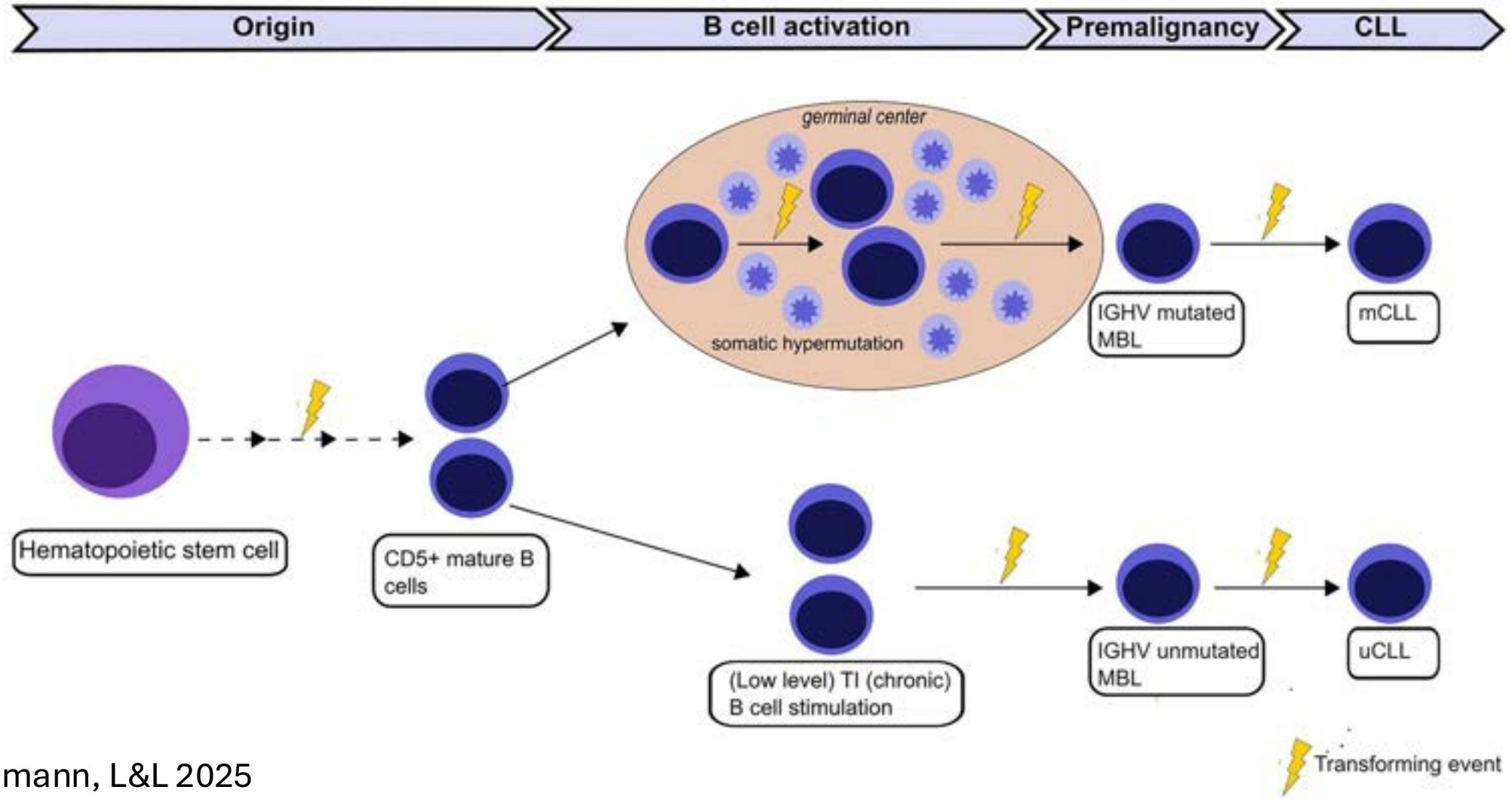
Lancet 2016

Two types of CLL based on IGHV mutation

- ~60% cases
- Indolent/slower progression
- Often with low-risk genetics
- Longer time to 1L therapy
- Deeper and durable response
- Longer survival

- ~40% cases
- Aggressive/faster progression
- Often with high-risk genetics
- Shorter time to 1L therapy
- Shorter duration of response
- Shorter survival

IGHV mutations



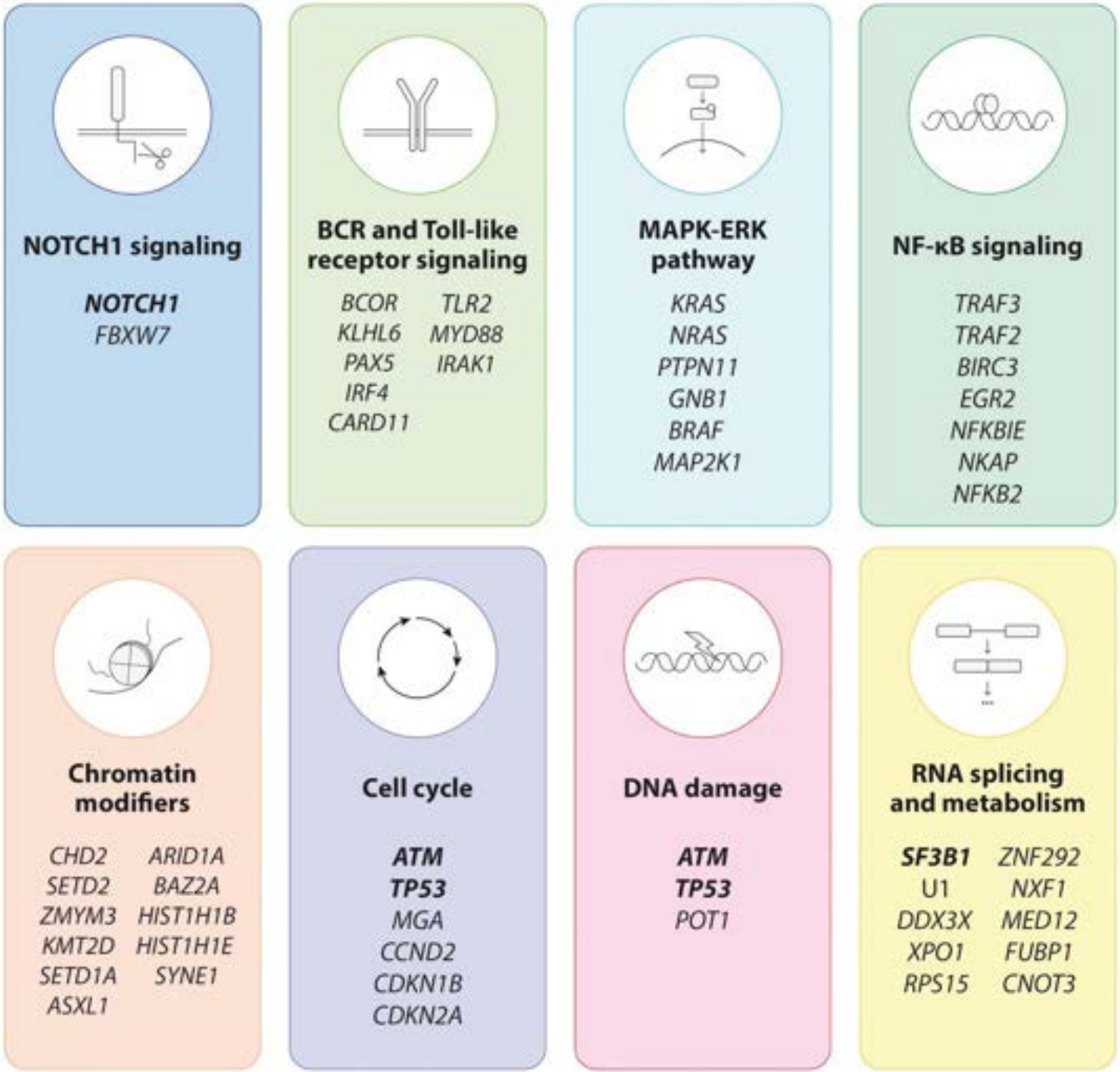
Dampmann, L&L 2025

Two types of CLL based on IGHV mutation

- ~60% cases
- Indolent/slower progression
- Often with low-risk genetics
- Longer time to 1L therapy
- Deeper and durable response
- Longer survival

- ~40% cases
- Aggressive/faster progression
- Often with high-risk genetics
- Shorter time to 1L therapy
- Shorter duration of response
- Shorter survival

Recurrent Mutations in CLL



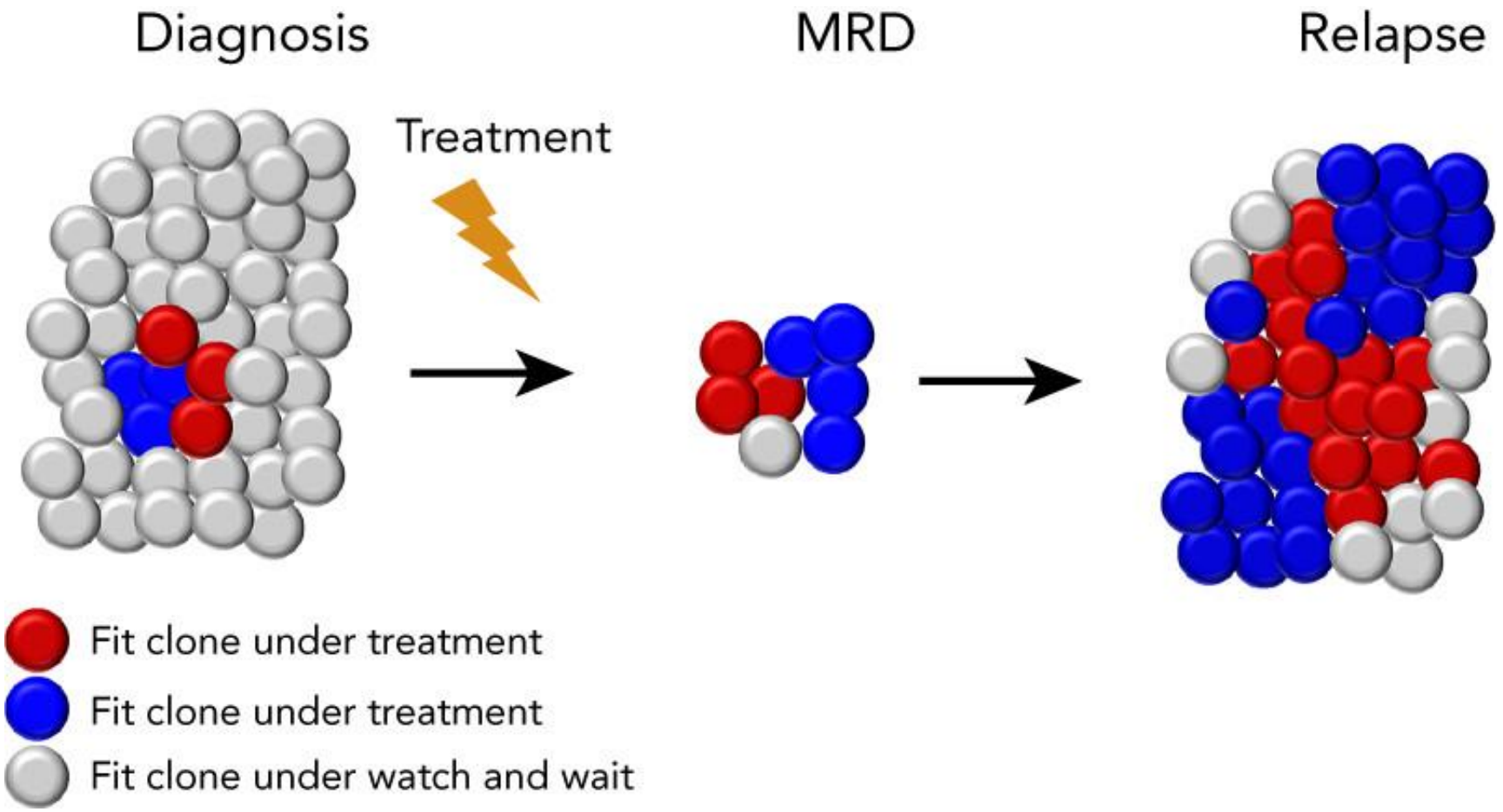
Delgado, Haematologica 2020

CLL/SLL is heterogeneous

INDOLENT
May not require treatment
“Die with disease”

AGGRESSIVE
Requires treatment(s)
“Die of disease”

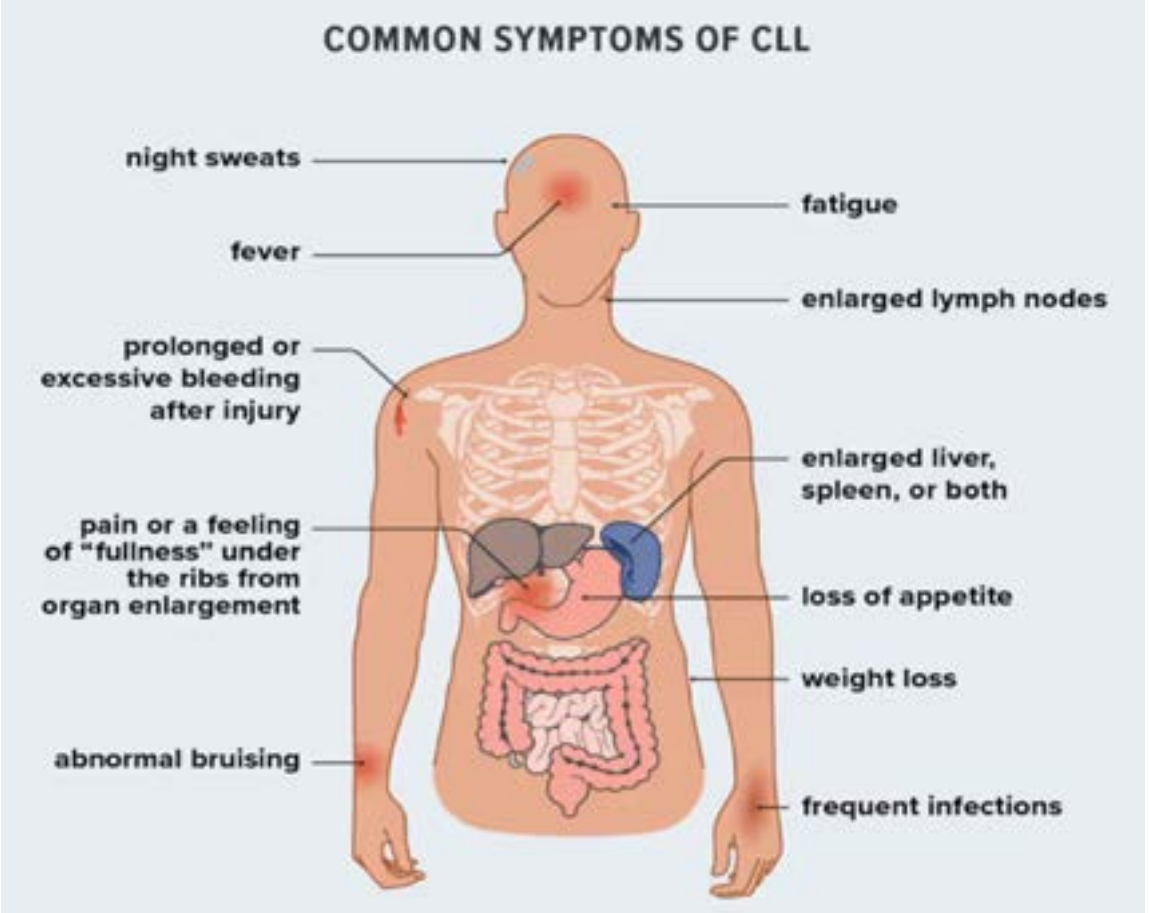
Clonal Evolution



Condoluci, JNCCN 2020

Clinical evaluation at diagnosis and/or before treatment initiation

- History and physical
- General blood tests
- Prognostic markers
  - Cytogenetics (FISH)
  - IGHV mutation status
  - *TP53* mutation status
- Biopsy (marrow, node)?
- Imaging investigations?

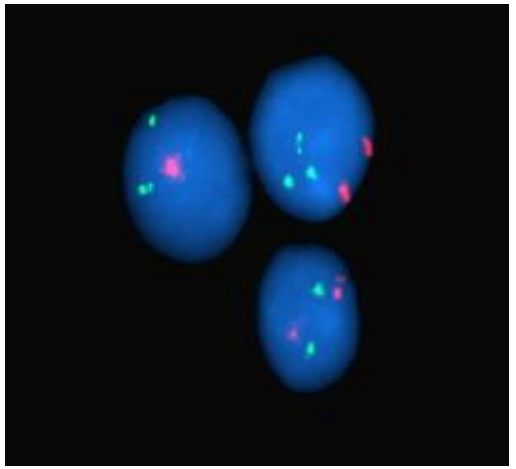


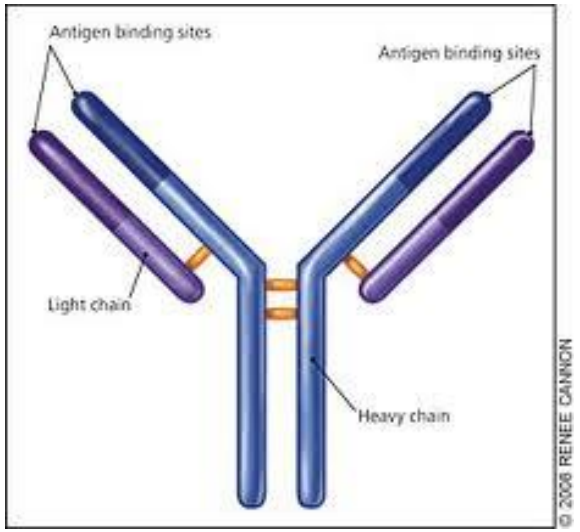
Diagnostic test	General practice	Clinical trial
Tests to establish the diagnosis		
CBC and differential count	Always	Always
Immunophenotyping of peripheral blood lymphocytes	Always	Always
Assessment before treatment		
History and physical, performance status	Always	Always
CBC and differential count	Always	Always
Marrow aspirate and biopsy	Sometimes	Desirable
Serum chemistry, serum immunoglobulin, DAT	Always	Always
Chest radiograph	Always	Always
Infectious disease status	Always	Always
Additional tests before treatment		
FISH for del(13q), del(11q), del(17p), add(12)	Always	Always
TP53 mutation	Always	Always
IGHV mutational status	Always	Always
Serum β_2-microglobulin	Desirable	Always
CT scan of chest, abdomen, and pelvis	Sometimes	Desirable
MRI, PET scans	Sometimes	Sometimes

Cytogenetics and genomic testing

- Cytogenetic abnormalities by FISH
  - Deletion 17p, Del 11q, Trisomy 12, Del 13q
- Gene sequencing (Sanger or Next generation sequencing)
  - *TP53* mutation – poor prognosis
  - IGHV mutational status
    - Unmutated – worse prognosis
    - Mutated – better prognosis
  - Karyotyping, gene panels (*NOTCH*, *SF3B1*)

Access to these tests is limited in many centres

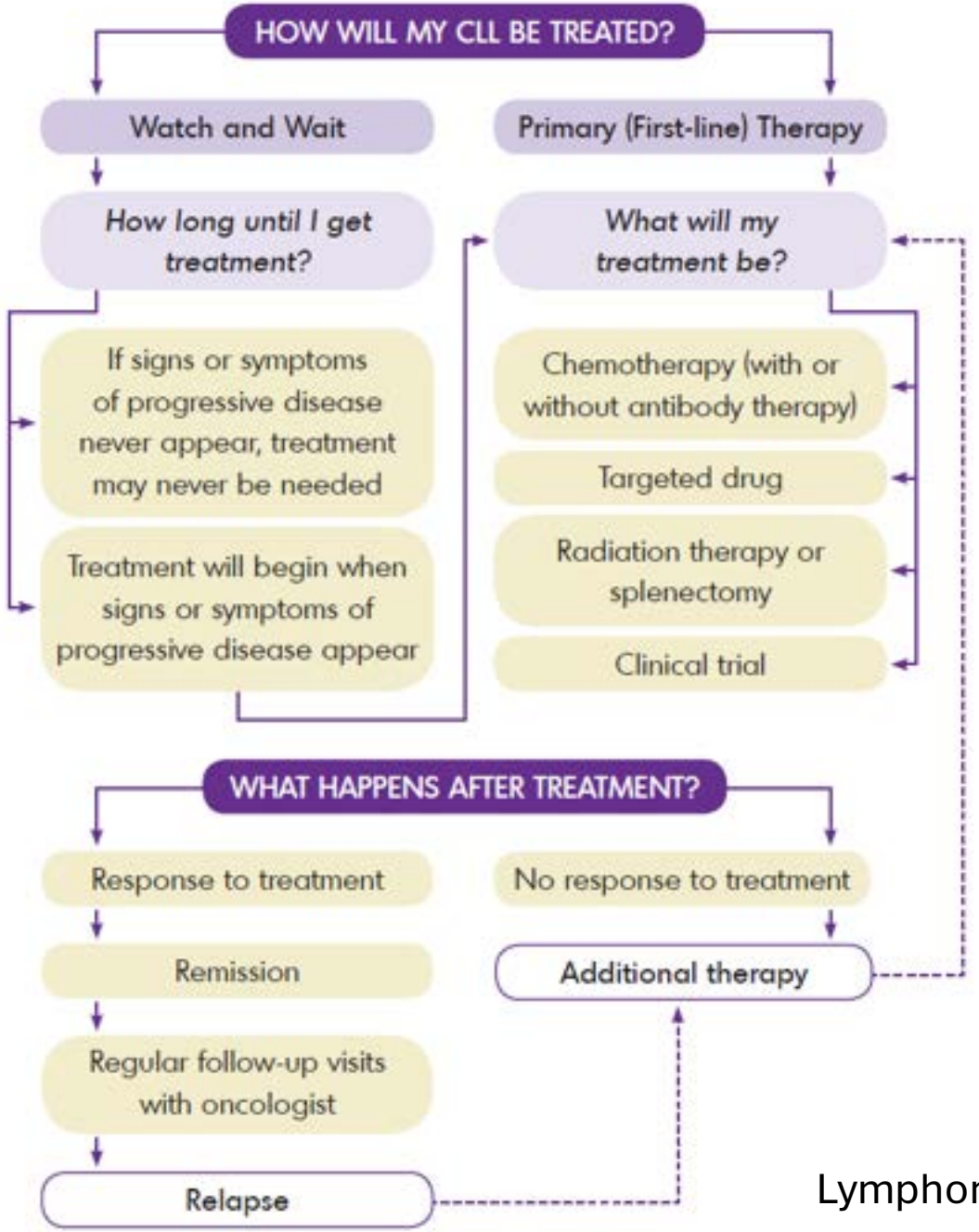




Principles of CLL/SLL Treatment

Goals of therapy

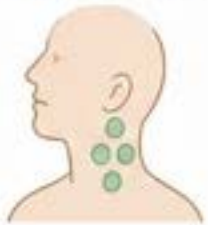
- Prolong survival
- Improve quality of life



Lymphoma.ca

Indications to Initiate Therapy in CLL (IWCLL Guidelines)

1. Significant lymph node enlargement



Nodes are very large (≥10 cm) or causing pressure or symptoms.

2. Enlarged spleen or liver

Spleen or liver is enlarged significantly (≥6 cm below the rib cage) or causing discomfort or symptoms.

3. Low blood counts due to CLL

- Hemoglobin < 10 g/dL (anemia)
- Platelets < 100,000/µL (low platelets)
- Neutrophils < 1,500/µL (low infection-fighting cells)

and due to CLL in the bone marrow.

4. Rapid or progressive disease

- Lymph nodes or spleen getting larger quickly
- Lymphocyte count rising quickly (e.g., doubling in < 6 months)

5. CLL-related symptoms

- Unexplained weight loss (≥10% in 6 months)
- Significant fatigue
- Fevers ≥ 100.4°F (38°C) for ≥ 2 weeks without infection
- Night sweats for ≥ 1 month without infection

6. Autoimmune complications not controlled with standard therapy

Autoimmune anemia or low platelets caused by CLL that does not improve with steroids or other standard treatments.

7. Symptomatic or progressive disease

Symptoms or problems caused by CLL that are getting worse and affecting quality of life.

8. Transformation to aggressive lymphoma

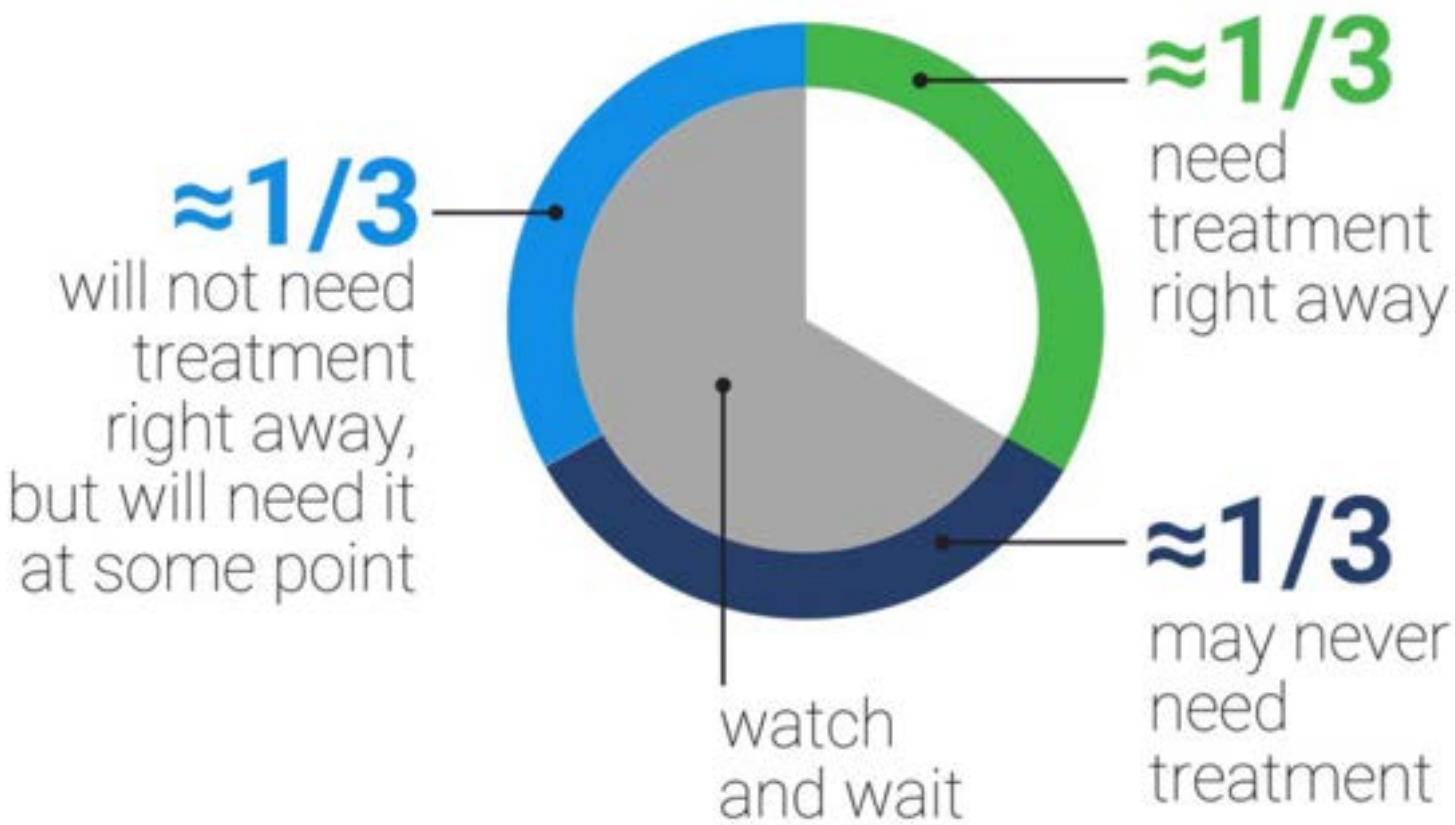
If CLL changes into a more aggressive type of lymphoma (Such as Richter transformation).

“I have a blood cancer and you’re just going to sit on it?”

Role for active surveillance in CLL/SLL

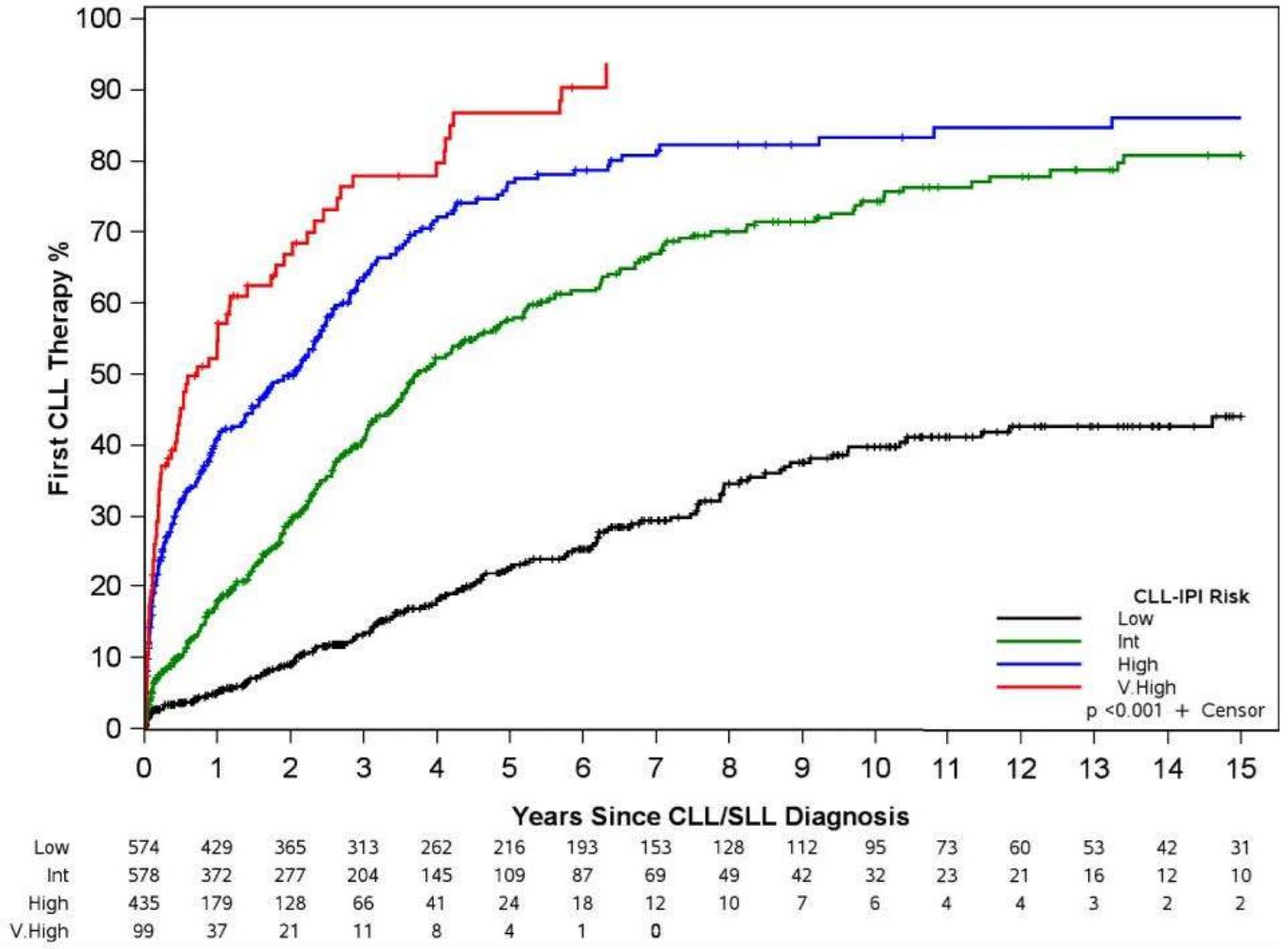
- CLL/SLL is incurable (today).
- Studies have shown that early treatment *does not* prolong survival and may worsen quality of life due to side effects.
- May develop resistance to drugs and would not be able to use them when the disease progresses.
- Potential access to better 1st line therapy in the future.

Role for active surveillance in CLL/SLL



CLL-IPI to estimate time to 1L therapy

Prognostic Factor
Del17p on FISH or *TP53* mutation
Unmutated *IGHV* genes
Serum β2 microglobulin >3.5 mg/L
Rai Stage I-IV
Age >65 years



Hampel, Blood Cancer Journal 2022

What does Active Surveillance mean?

- Review by medical professional every 3-12 months
  - History and physical examination
  - Monitor blood counts
  - Monitor for treatment indications
  - Promote healthy lifestyle: exercise, nutrition, mental health, preventative medicine including cancer screening
- If symptoms appear → treatment may be necessary

Conclusions

- CLL/SLL is a heterogeneous immune system malignancy.
  - Leukemic vs. nodal presentation
  - Indolent vs. aggressive forms
  - Clonal evolution
- The clinical evaluation remains relatively straightforward and there are well validated prognostic markers.
- CLL/SLL remains incurable in 2026 although multiple novel therapies have significantly improved survival in the last decade.