

Staging of NHL and CLL

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Staging

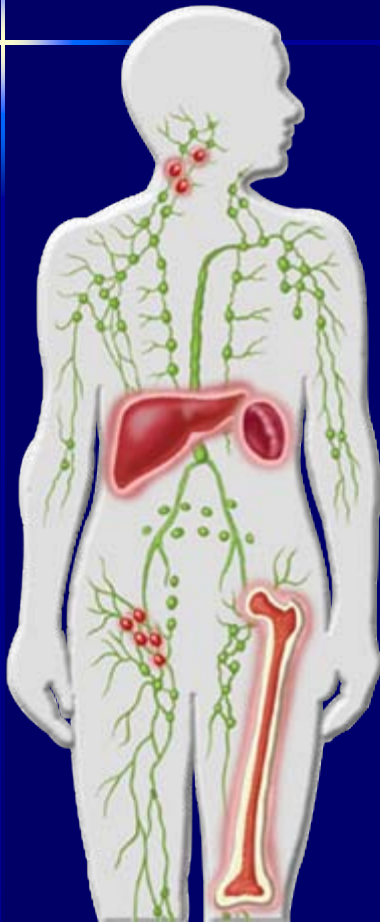
- Review of biopsy with a hematopathologist
- Detailed history and physical
- CT scan
- Bone marrow biopsy
- PET scan
- Labs
- ? laparotomy

Ann Arbor Staging

■ Stages I–IV

- Stage I
 - Single location
- Stage II
 - 2 or more locations
 - Same side of diaphragm
- Stage III
 - 2 or more locations
 - Both sides of diaphragm
- Stage IV
 - Disseminated

- Extranodal organ and/or spleen (E and/or S)
- Systemic symptoms (A or B)



Early Stage Indolent NHL

- A small percentage of patients are diagnosed with a low grade NHL as stage I or II
- Vigorous staging is required
 - CT scan, PET scan
 - PCR testing if possible
- 30-40% cure rate for those patients with Stage I indolent NHL using radiation
- Weigh risks and benefits

Treatment Options: Low Grade NHL

- Watch and wait

- External beam radiation

- Chemotherapy

 - Single agent
 - Combination

- Monoclonal antibody

 - Rituximab
 - alemtuzumab

- Interferon

- Stem cell transplant

 - Autologous

 - Allogeneic

- Radioimmunotherapy

 - 90Y Ibritumomab Tiuxetan

 - 131I Tositumomab

- Investigational therapies

Watch and Wait

- Indolent, low volume disease
 - Allows us to judge tempo of the disease
 - Treatment done in 2-5 years may be better or less toxic
 - It is rare, but spontaneous remissions may be as high as 10%
 - Does not affect the rate of transformation
 - It is not known that early treatment affects overall survival

The decision to treat

- Collaborative decision between Pt. and MD
- Enlarged lymph nodes that may soon cause a problem
- Blood counts that have been affected
- Paraneoplastic syndrome
- Symptoms
- Clinical trials
- Discuss all options and risks and benefits

Factors Contributing to decision

- Type of indolent NHL
- Patient preference
- Past therapies
- Age of patient
- Clinical trials available
- Comorbid illnesses
- Financial issues

CLL Staging: Rai and Binet

RAI SYSTEM

Stage	Description	Risk Status
0	Lymphocytosis, lymphocytes in blood $>15,000/\text{mcL}$ and $>40\%$ lymphocytes in the bone marrow	Good
I	Stage 0 with enlarged node(s)	Intermediate
II	Stage 0-I with splenomegaly, hepatomegaly, or both	Intermediate
III ^a	Stage 0-II with hemoglobin $<11.0 \text{ g/dL}$ or hematocrit $<33\%$	High
IV ^a	Stage 0-III with platelets $<100,000/\text{mcL}$	High

BINET SYSTEM

Stage	Description	Risk Status
A	Hemoglobin $\geq 10 \text{ g/dL}$ and platelets $\geq 100,000/\text{mm}^3$ and <3 enlarged areas	Low
B	Hemoglobin $\geq 10 \text{ g/dL}$ and platelets $\geq 100,000/\text{mm}^3$ and ≥ 3 enlarged areas	Intermediate
C ^a	Hemoglobin $<10 \text{ g/dL}$ and/or platelets $<100,000/\text{mm}^3$ and any number of enlarged areas	High

^a Immune-mediated cytopenias are not the basis for these stage definitions.

NCCN Clinical Practice Guidelines in Oncology. *Non-Hodgkin's Lymphomas*. V.3.2008

Binet JL, et al. *Cancer*. 1981;48:198-206;

Rai KR, et al. *Blood*. 1975;46:219-234.

NCCN Diagnosis Guidelines

■ Essential:

- Hematopathology review
- Immunophenotyping to establish diagnosis
- Cytogenetics or FISH* to detect del(17p), del(13q), +12, del(11q)

■ Useful under some circumstances:

- Molecular genetic analysis to detect antigen receptor gene rearrangements
- Determination of CD38 and/or Zap 70 expression by flow cytometry or immunochemistry

* FISH for the t(11:14) chromosomal translocation can help distinguish MCL from CLL

CLL Signs and Symptoms

- Fever
- Weight Loss
- Loss of Appetite
- Fatigue
- Anemia
- Leukopenia
- Thrombocytopenia
- Bone or Joint Pain
- Lymph Node Enlargement
- Enlarged Liver
- Enlarged Spleen
- Infections

Early CLL may have no signs or symptoms.

Monitoring for CLL

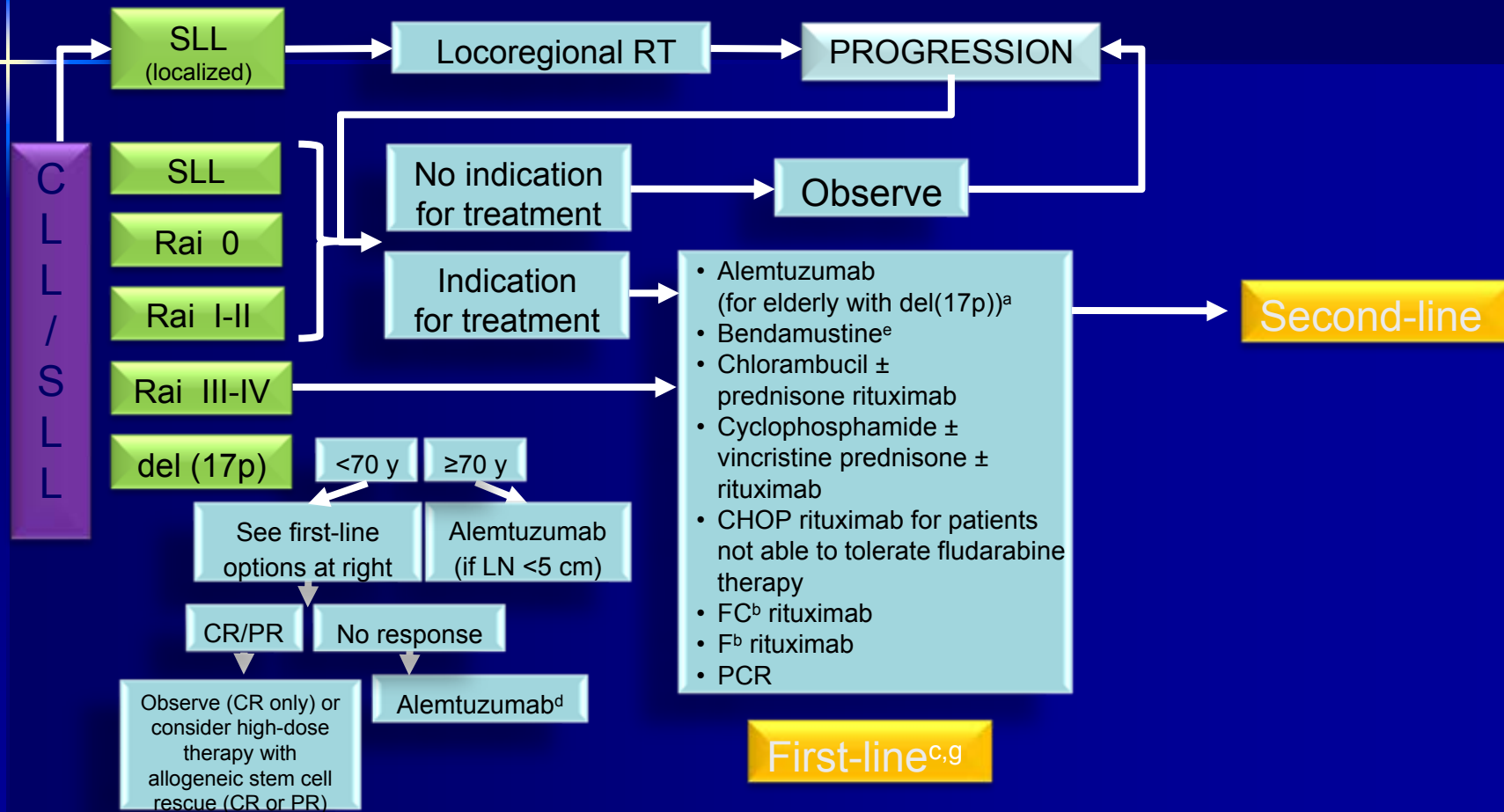
- Blood counts every 6-12 weeks
- Physical assessment every 6-12 weeks
 - Assess liver and spleen size
 - Assess for enlarged lymph nodes
- Assess for recurrent infections and organ function
- Assess for development of other cancers
- Assess for changes in the disease

CLL : Indications for Treatment

- Active disease should be confirmed prior to initiating treatment
- ≥ 1 of the following **symptoms** must be present:
 - Weight loss 10% within previous 6 months
 - Extreme fatigue
 - Fevers $>100.5^{\circ}\text{F}$ for ≥ 2 weeks without evidence of infection
 - Night sweats without evidence of infection
- Evidence of progressive marrow failure as manifest by the development or **worsening of anemia** and/or **thrombocytopenia**
- **Autoimmune anemia** and/or **thrombocytopenia** poorly responsive to corticosteroid therapy
- **Massive spleen** (i.e., $>6\text{cm}$ below the left coastal margin) or progressive splenomegaly
- **Massive nodes** or clusters (i.e., 10 cm in longest diameter) or progressive lymphadenopathy
- **Progressive lymphocytosis**
 - $>50\%$ over a 2-month period
 - Lymphocyte doubling time of <6 months

NCCN Practice Guidelines for CLL Updated in 2008

Use of specific drugs is reflective of NCCN guidelines, but not necessarily approved indications



^a Must be aware of high risk of CMV reactivation.

^b Autoimmune hemolytic anemia (AIHA) should not preclude the use of combination therapy containing fludarabine and patients should be observed carefully.

^c Consider prophylaxis for tumor lysis syndrome.

^d If response, consider high dose therapy with allogeneic stem cell rescue

^e NCCN Drugs and Biologics Compendium, 2008.

^f Rituximab and alemtuzumab should be used in combination only when there is existing literature to support its use in combination.

^g Prophylactic therapy for shingles and pneumocystis should be considered in purine analog-based combination therapy

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