Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

Support for this program provided by TEVA Oncology

Welcome and Overview

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www.LLS.org/CE

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Have no affiliations with commercial interests to disclose

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Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

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Acute Promyelocytic Leukemia (APL) Overview and Case Study

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Outline

- Leukemias and outcomes
- History of APL
- Epidemiology
- Treatment and outcomes in large trials
- What happens outside of a trial
- High mortality outside of a trial
- What is involved in our co-management

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Leukemias and Outcomes

Chronic Leukemias

- **Chronic myelogenous leukemia (CML)**
  - Imatinib (Gleevec) ≥90% survival
- **Chronic lymphocytic leukemia (CLL)**
  - Indolent disease in the elderly
  - Wide array of treatments is available

Acute Leukemias

- **Acute lymphoblastic leukemia (ALL)**
  - Generally pediatric disease with ≥80% cure rate
  - Cure rates are approximately 40%–50% in adults
- **Acute myelogenous leukemia (AML)**
  - Generally seen in older patients
  - M1 to M7: 50% cure rate across the spectrum
- **M3 – Acute promyelocytic leukemia (APL)**

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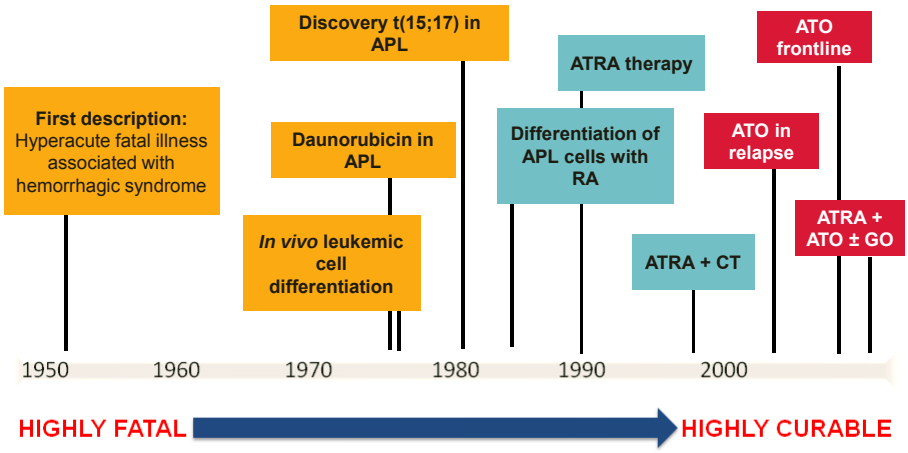
APL Therapy – History



ATO, arsenic trioxide; ATRA, all-trans retinoic acid; CT, chemotherapy; GO, gemtuzumab ozogamicin; RA, retinoic acid.
Chen Y, et al. *Cancer*. 2012;118(23):5811–5818.
Nowak D, et al. *Blood*. 2009;113(16):3655–3665.

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APL Diagnosis – Pathology

- Pancytopenia – low counts
- DIC common
- Bruising – typical complaint
- Bleeding – quite serious
  - Serious bleeds with normal lab findings
- CNS bleeds – common
  - Most likely reason for patient deaths due to bleeding

CNS, central nervous system; DIC, disseminated intravascular coagulation.
Sanz MA, et al. *Blood*. 2009;113(9):1875–1891.

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APL – Epidemiology

- APL is an uncommon disease with approximately 1000 new cases per year in the US
- Rare below 10 years of age
- Most common between the ages of 20 and 60 years
- Historically, this is the first disease for which targeted treatment was developed
- Highly effective and curable treatments
  - All-trans retinoic acid (ATRA), arsenic trioxide (ATO), and anthracyclines

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APL Treatment and Outcomes in Large Trials

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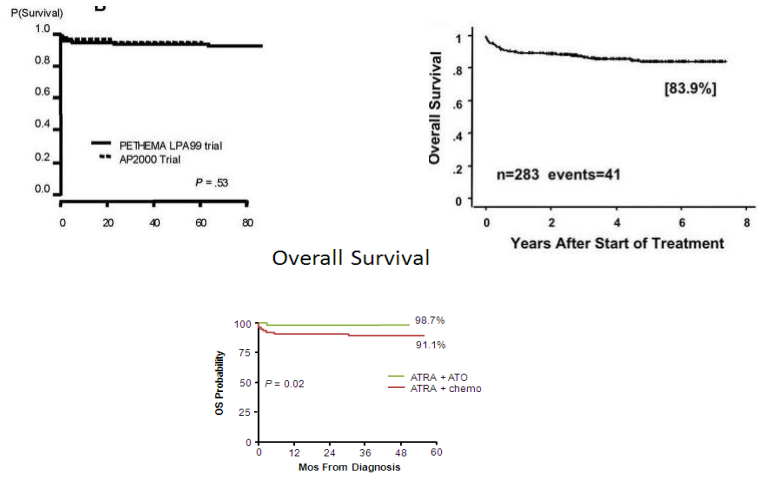
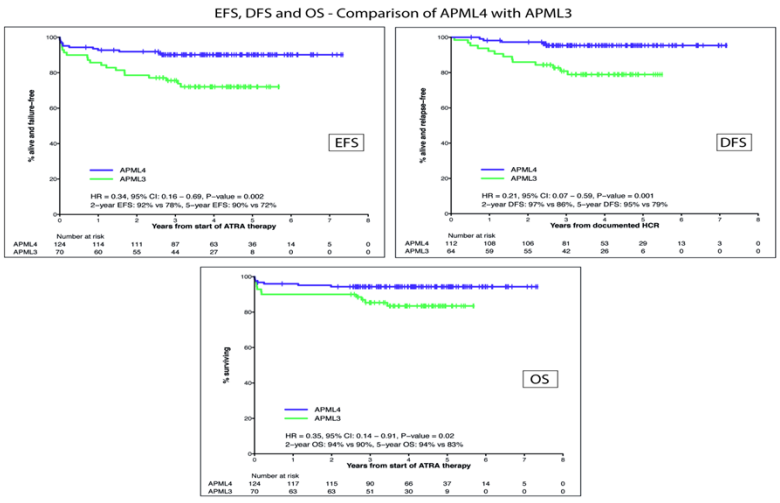
APL Survival in Large Cooperative Group Trials



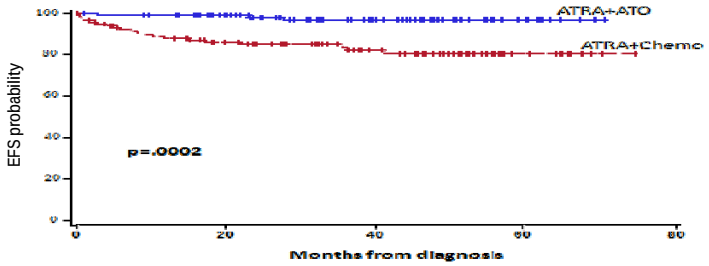
OS, overall survival.

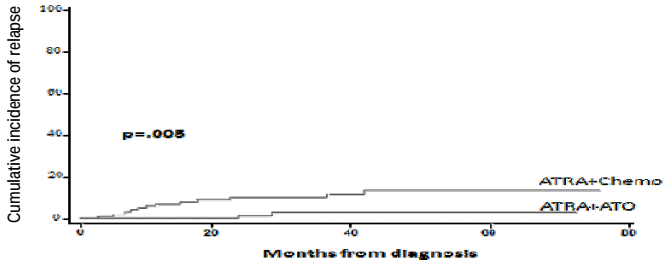
Australasian APML4 (adding ATO to ATRA/chemo)



CI, confidence interval; DFS, disease-free survival; EFS, event-free survival; HR, hazard ratio; OS, overall survival.

ATRA/ATO vs ATRA/Chemotherapy





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What Happens Outside of a Trial

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Case Study – Real-World Patient

- 56-year-old female; Jehovah's Witness
- Current diagnosis of flu, normal CBC (early December), treated with Tamiflu; DVT (late December), repeat CBC showing pancytopenia
- Subsequent work-up resulted in a diagnosis of APL
- Refused blood transfusions, so she was supported with cryoprecipitate, Aranesp, Procrit and G-CSF, which was approved by her congregation

CBC, complete blood count; DVT, deep vein thrombosis; G-CSF, granulocyte colony-stimulating factor.

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Population-Wide Survival in the US

- Survival of 90% in multicenter trials is not a reflection of the outcome in the general population. **Death rate of 5% to 10% is an underestimate**
- Recent analysis of US SEER data from 2000–2008 by investigators from MD Anderson showed 71% survival at 1 year and 64% at 5 years
- Current trials that are changing sequence, adding new drugs, and/or withholding maintenance will only have a minimal effect on the survival
- Biggest impact will be made by decreasing early deaths

Chen Y, et al. *Cancer*. 2012;118(23):5811–5818.

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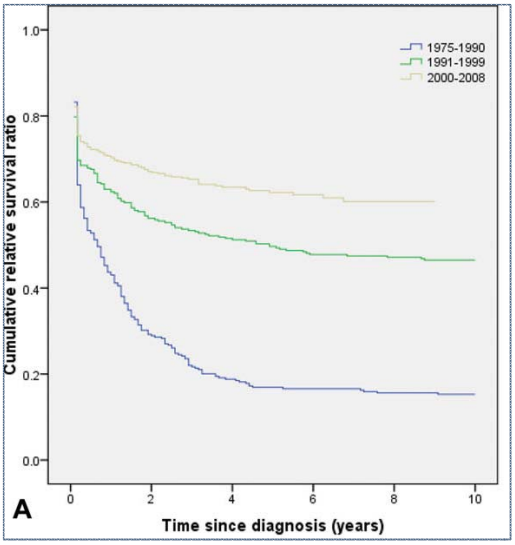
SEER Data (1975–2008)



Chen Y, et al. *Cancer*. 2012;118(23):5811–5818.

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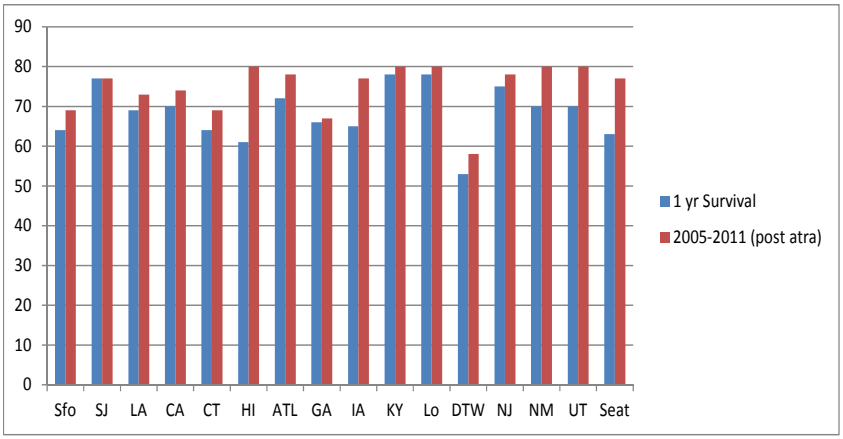
Survival Data From SEER Registries

Expected ~95%



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Early Deaths in APL (Days 1 to 30)

Study	Total patients	Patients died	Mortality rate	Percentage of patients with hemorrhage in early death
Brazil (2007)[4]	134	43	32%	66
Ankara & Samsun Turkey (2010)(12)	49	20	40%	65
Swedish registry (2011)[5]	105	30	29%	41
SEER data(2011)[6]	1400	238	17%(24% in >55yr)	Not discussed
AIIMS , India	33	6	18.1	58% in total patients during induction
Stanford (2012)[7]	70	19	26%	54
GRU (our center) ASCO 2012	19	7	37%	57
German, >60 years. (2013)	91	24	26%	Not discussed
Japan >65% years Hiroshima(2013)	32	7	21.3%	Not discussed

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Why Is There High Mortality Outside of a Trial?

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Possible Reasons

- Selection bias: possible reason
- Delayed treatment
  - Delay in ATRA treatment is commonly cited but not the case
- Decreased supportive care?
  - Probably the biggest reason
    - Prior to ATRA, early deaths in GIMEMA were <10
    - They have a network of treatment centers that follow written guidelines
    - MD Anderson had 5/44 early deaths in their clinical trial but 9/40 after the trial closed

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Can We Do Something Different?

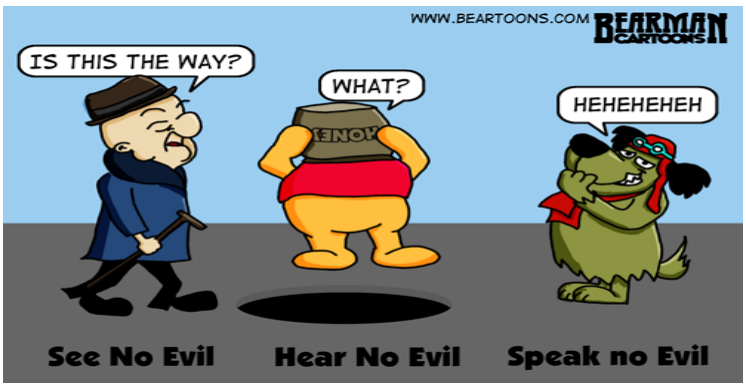

Image used with permission from Bearman Cartoons.

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Strategy (at GRU)

- Developed a simple 1.5-page treatment algorithm
- Quick diagnosis
- Ad hoc meeting and treatment planning
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- Prevention of differentiation syndrome; early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections
- Implemented in 2010

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Methods Used to Decrease Early Deaths

- Reviewed the literature
- Reviewed all patient charts
- Attended national meetings and talked to experts
- Attended the International APL meeting in Rome
- Obtained an external consultant to review our death charts
- Identified the three main causes of death in the first month: **BLEEDING, DIFFERENTIATION SYNDROME AND INFECTION**
- Implemented a proactive, simple program to decrease early deaths—at a point when the rest of the country did not recognize this as a problem

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What Is Involved in Our Co-Management

Treatment Outside Our Center

- Co-manage patients
- Text or email has worked very well
- Discuss day-to-day care in case they are more complicated
- Idea is to get them through induction

APL – Workup

- Quick diagnosis
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- Prevention of differentiation syndrome; early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections **(APL IS A MEDICAL EMERGENCY. TREATMENT WITH ATRA SHOULD BE STARTED ASAP)**
- Labs, BMBX, ECHO, PICC (no invasive procedures)

BMBX, bone marrow biopsy; ECHO, echocardiogram; PICC, peripherally inserted central catheter.

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Supportive Care

- Tumor lysis prophylaxis
- Antibacterial prophylaxis – Levofloxacin 500 mg QD
- Antifungal prophylaxis – Voriconazole 200 mg PO BID or posaconazole 200 mg PO TID
- Antiviral prophylaxis – Acyclovir 400 mg BID
- Keep hemoglobin in the 8 range
- **APL IS A MEDICAL EMERGENCY. TREATMENT WITH ATRA SHOULD BE STARTED ASAP**

BID, twice daily; PO, orally; QD, daily; TID, three times daily.

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Treatment of Coagulopathy

- Coagulopathy is a major problem. Procoagulants released by leukemia cells and fibrinolysis
- Intracranial, pulmonary and GI bleeding
- Treatment with ATRA should start ASAP
- Keep platelets above 50,000
- Keep fibrinogen above 150
- If there is clinical evidence of bleeding, give FFP twice a day as you are starting ATRA and chemotherapy until bleeding resolves
- After all clinical and lab coagulopathy resolves, blood product support is like any other leukemia

FFP, fresh frozen plasma; GI, gastrointestinal.

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Differentiation Syndrome

- Dyspnea, unexplained fever, weight gain, ARF, CHF, pleuropericardial effusions and interstitial pulmonary infiltrates
- Meticulous monitoring of intake and output. Daily weights
- Keep I/O matched (**SHOULD BE METICULOUS**)
- Diuretics should be used if there is evidence of fluid retention and weight gain
- Dexamethasone 10 mg BID should be started as soon as symptoms are noted
- In patients with a WBC >10,000, dexamethasone 10 mg BID could be started before initiating ATRA
- Temporary discontinuation of ATRA or ATO is indicated only in case of severe APL differentiation syndrome

ARF, acute renal failure; BID, twice daily; CHF, congestive heart failure; WBC, white blood count.

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Treatment: AIDA Regimen Example

- Induction
  - **Low-risk patients**
    - WBC <10,000 and platelet count >40,000
    - GIMEMA protocol. ATRA on day 1 followed by idarubicin 12 mg/m^2 on days 2, 4, 6 and 8 (**AIDA**)
  - **Intermediate-risk and high-risk patients**
    - WBC >10,000 and platelet count <40,000
    - ATRA to be started as soon as diagnosis is suspected
    - Idarubicin to be started on the same day and given per the GIMEMA protocol on days 1, 3, 5 and 7. Even if genetic results are unavailable, it is reasonable to give anthracycline
    - Older patients (individualized)

WBC, white blood count.

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Older Patients With APL

- Need to individualize
- Maybe begin with single-agent ATRA
- Dose reduction of ATO
- Meticulous supportive care

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Nursing Considerations

- Meticulous monitoring of patient during the first 10 days during which 70% of deaths occur
- Primary goal is to decrease early deaths within the first month; three main causes of death in the first month: BLEEDING, DIFFERENTIATION SYNDROME AND INFECTION
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- "Normal" laboratory values can still cause bleeding
- Prevention or early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections
- Outpatient consolidation, provide calendars, dialogue with patient and family

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Consolidation and Maintenance

- Generally depends on induction protocol
- If you pick a regimen, try to stick with the same follow-up treatments
  - Two to three cycles of anthracycline-based consolidation, given along with ATRA
  - ATO-based consolidation
- After completion of consolidation, a bone marrow evaluation should be done to demonstrate molecular remission
  - If molecular remission is achieved, maintenance with 1–2 years of oral ATRA + MTX and 6MP may be beneficial

6MP, 6-mercaptopurine; MTX, methotrexate.

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Algorithm

Work Up	• CBC, CMP, and DIC Panel to include Fibrinogen, D-Dimers, PT and PTT twice a day until all laboratory and clinical coagulopathy is completely resolved. • Echocardiogram. • Bone Marrow Examination. Aspirate, Biopsy, Flow cytometry, Cytogenetics, FISH for PML-RAR alpha and PML-RAR alpha by PCR. Tumor banking if available. • Baseline Chest X-ray • PICC Line. Do **NOT** attempt to put central lines or perform other surgically invasive procedures such as Bronchoscopy or Spinal Tap. • **DAY 14 Marrow is not necessary.**
Supportive care	• Tumor Lysis prophylaxis. • Antibiotic Prophylaxis with Levofloxacin 500 mg po qd or similar antibiotic. • Antifungal prophylaxis with Posaconazole 200 mg po tid, Voriconazole 200 mg po bid or another agent with similar efficacy • Anti-viral prophylaxis with Acyclovir 400 po bid or Valacyclovir 1000 mg PO daily • Red Cell transfusion is similar to other Leukemia Induction and suggested to transfuse at or below 7gm/dl. • **APL IS A MEDICAL EMERGENCY. TREATMENT WITH ATRA SHOULD BE STARTED ASAP.**
Coagulopathy	• Intracranial, Pulmonary and GI Hemorrhage. Risk of Bleeding is worse in patients with Active Bleeding, Hypofibrinogenemia, Increased levels of D-Dimers, prolonged PT and PTT, increased WBC, increased Peripheral Blasts, Renal Failure and poor PS • Treatment with ATRA should start ASAP • Keep platelets above 50,000 • If there is clinical evidence of bleeding at presentation from needle sticks, Bone Marrow Biopsy sites, give 4 units of FFP as you are starting the ATRA and Chemotherapy. Continue FFP support twice a day until clinical bleeding resolves. • Keep fibrinogen above 150. Use cryoprecipitate if needed • After all clinical and laboratory coagulopathy has resolved, the guidelines for blood product support are similar to management of other leukemias.
Differentiation Syndrome	• Meticulous monitoring of Intake and Output. • Daily weights • Keep I/O matched (**SHOULD BE METICULOUS**). • *Diuretics should be used if clinically there is evidence of fluid retention and weight gain.* • Dexamethasone at 10 mg BID should be started as soon as symptoms are noted. • In patients with a WBC >10,000, Dexamethasone 10 mg bid could be started before initiating ATRA • Temporary discontinuation of ATRA or Arsenic Trioxide (ATO) is indicated only in case of severe APL DS. • Dexamethasone should be maintained until complete disappearance of symptoms and ATRA or ATO should be restarted. Dexamethasone should be stopped 3 days after all DS symptoms have resolved.
Anthracycline based Induction	**INDUCTION OF LOW RISK PATEINTS** (WBC <10,000/ml and Platelets >40,000/ml) • GIMEMA protocol. ATRA on Day 1 followed by idarubicin 12 mg/m^2 on Days 2, 4, 6 and 8. **INDUCTION OF INTERMEDIATE RISK AND HIGH RISK PATIENTS** (WBC> 10,000 and Platelet count <40,000) • Idarubicin to be started on the same day and given per the GIMEMA protocol on days 1, 3, 5 and 7. Even if the genetic results are not available, it is reasonable to give the anthracycline. • Aggressive management of coagulopathy.
Arsenic trioxide based induction	Can be considered in the following patient groups a) Low and intermediate risk patients (WBC < 10,000/ml) b) Age >70 c) Not candidates for conventional chemotherapy for any reason. • Should be restricted to patients with confirmed PML-RAR alpha. • ATRA at 45 mg/m^2 in divided doses twice a day along with • Arsenic at 0.15 mg/kg daily, both continued till complete hematologic remission. • Watch for differentiation syndrome. • Follow for prolongation of QT interval. Keep Mg above 2.0 and K above 4.0. • Follow LFTs and for grade 2 to 4 Liver Dysfunction, HOLD Arsenic.
Hydroxyurea use for Leukocytosis: NO LEUCOPHERESIS	• WBC 5 - 10k – Hydroxyurea 500 mg q day • WBC 10 – 15k Hydroxyurea 500mg BID • WBC 15 – 20k – Hydroxyurea 500mg TID • WBC 20 – 50k – Hydroxyurea 500 mg QID • WBC > 50k – Hydroxyurea 1000 mg QID • Could also give a dose or two of Idarubicin 12mg/m2 if the Leukocytosis does not resolve or DS does not resolve in spite of using Dexamethasone.

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Experience in Other Diseases

- STEMI – Shorter door-to-balloon time improves survival
- In stroke patients, administration of TPA within 3 to 4.5 hours of symptom onset improves survival
- **THE GOAL IS TO STREAMLINE THE PROCESS**

STEMI, ST-segment elevation myocardial infarction; TPA, tissue plasminogen activator.

McNamara RL, et al. *J Am Coll Cardiol*. 2006;47(11):2180–2186.
Hacke W, et al. *N Engl J Med*. 2008;359(13):1317–1329.

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Strategy to Decrease Early Deaths at Main and Affiliate Sites

- Primary goal: prospectively assess 30-day mortality; Secondary goal: collect survival date
- Widespread education of hematologists, oncologists and nursing staff about early deaths and the need for rapid diagnosis and treatment
- At main sites: Ad hoc meeting at patients' admission with physicians, residents and nurses and rapid initiation of therapy
- At affiliate sites: An Investigator will help manage patients at affiliate sites using the same algorithm as outlined in the strategy we have used so far
- Decrease induction mortality to 5%–8%

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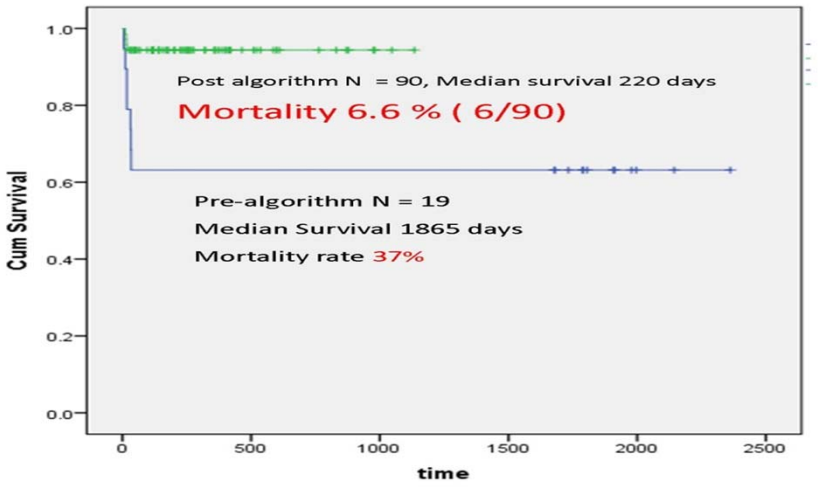
Survival Pre- and Post-Algorithm



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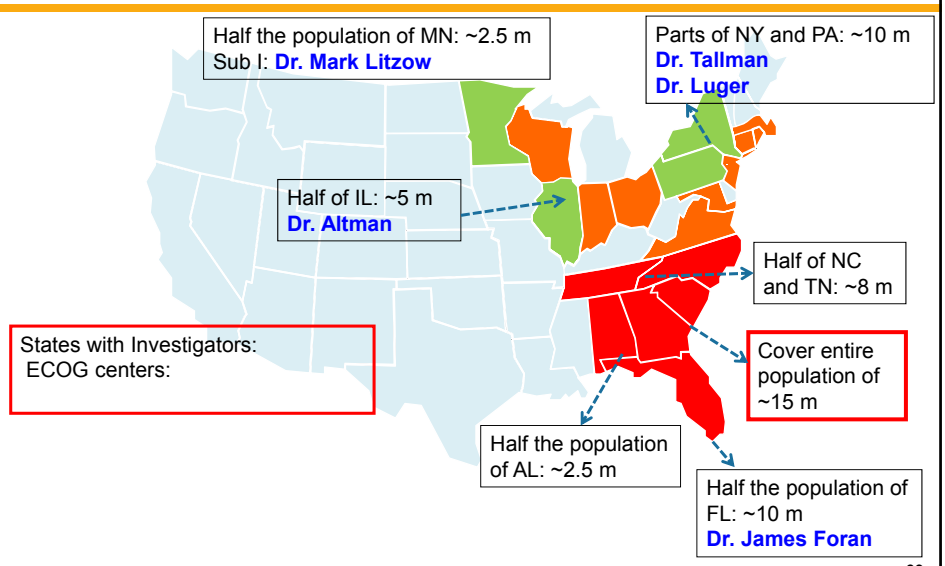
Planned Coverage on New NCI-ECOG Trial



ECOG, Eastern Cooperative Oncology Group; NCI, National Cancer Institute.

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Resources

- Difficult obtaining patient assistance for drug
- Very expensive
- No patient assistance programs for drug cost
- The Leukemia & Lymphoma Society's Information Resource Center (refer to support and financial assistance programs)
- Limited pharmaceutical assistance program
- Social work (prescription plans, financial, transportation)

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Conclusions

- Early deaths can and **SHOULD** be prevented in APL
- This concept was already validated in Latin America—Brazil, Chile, Uruguay and Mexico. Decreased early deaths from 32% to 15%
- Expedite diagnosis and treatment
- Proactively manage the three main causes of death
- Treating oncologists may be unaware of the problem
- Minimize complications from the presence of thrombocytopenia/ bleeding/infection
- APL is a **curable** disease amongst the leukemias

Rego EM, et al. *Blood*. 2013;121(11):1935–1943.

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Thank You

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Chronic Lymphocytic Leukemia (CLL) Overview and Case Study

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Outline

- Define disease
- Describe how CLL/SLL is different from leukemia: acute vs chronic leukemia
- Natural history of disease
- Epidemiology
- Rai staging
- Goal of treatment
- Case study

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What Is CLL?

- Chronic lymphocytic leukemia (CLL) is a cancer of the lymphocytes that normally work as immune cells to protect against infections

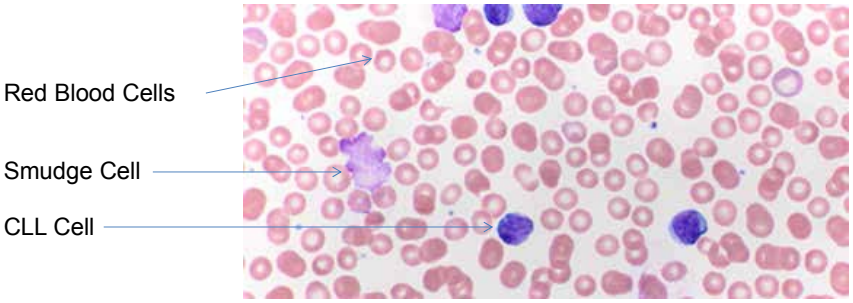

Image courtesy of JP Wilmot Cancer Institute; Chronic Lymphocytic Leukemia (CLL) Booklet.

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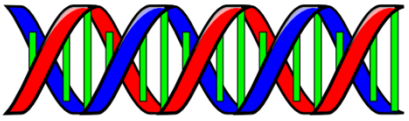
CLL

- CLL is caused when a single B lymphocyte becomes abnormal because of damage (mutation) to its DNA



- Once this occurs, the body no longer controls this cell, so it continues to divide and lives longer than it should
- This abnormal cell becomes CLL

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CLL vs SLL

- Small lymphocytic lymphoma (SLL) is a variant of the disease in which there are not a lot of abnormal lymphocytes in the blood
- World Health Organization (WHO) classification considers the two diseases to be identical—one disease at different stages

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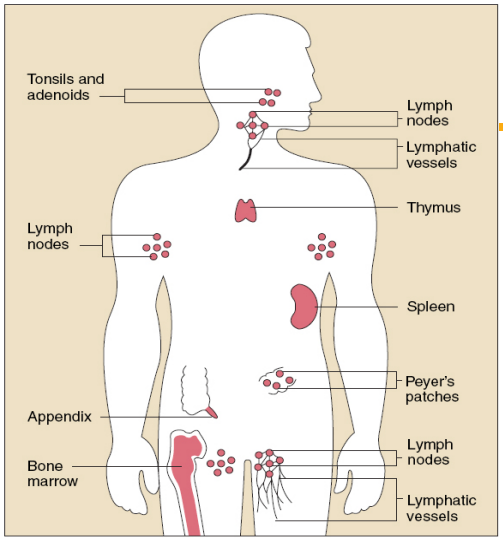

CLL – Lymphocyte dysfunction is in the bone marrow
SLL – There is more lymph node and lymphoid tissue involvement (vs bone marrow)

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CLL vs Acute Leukemia

- Chronic leukemias usually **progress slowly**, and there are a greater number of ***mature cells*** that can generally carry out normal function
- Acute leukemias are diseases that **progress rapidly** and affect cells that are ***not fully developed***

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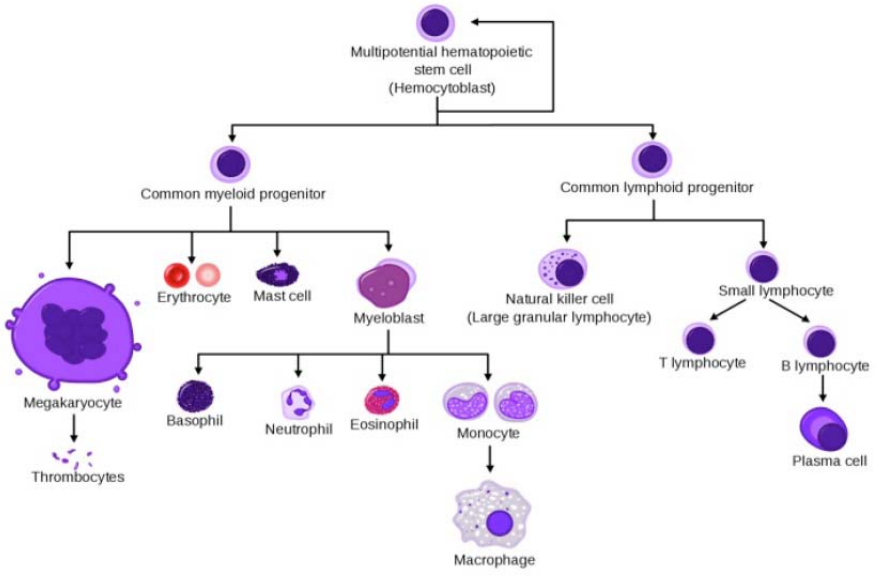

Image courtesy of JP Wilmot Cancer Institute; Chronic Lymphocytic Leukemia (CLL) Booklet.

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How Is CLL Diagnosed?

- Often found on random complete blood count (CBC) by primary
- Notice an elevated white blood count (WBC), specifically elevated lymphocytes

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Case Study: Maria S.

- 76-year-old widowed female in reasonably good heath; no other comorbidities
- Retired bus driver
- Lived in upstate NY
- March 2011: went to primary
  - Fatigue; "just did not seem right"
- Noted to have elevated WBC: 30 (normal 4–10)
- Was sent to local community oncologist

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Normal CBC

- WBC – normal 4–10
- Differential:
  - Neutrophils: 1.8–5.4 K/uL (ANC)
  - Lymphocytes: 1.3–3.6 K/uL (ALC)
  - Monocytes: 0.3–3.6 K/uL
  - Eosinophils: 0–0.5 K/uL

  ALC >5.0 **– criteria to meet CLL** (lymphocytosis) must show clonality on peripheral blood
- 2008 update of the National Cancer Institute guidelines

ALC, absolute lymphocyte count; ANC, absolute neutrophil count.

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Natural History of CLL

- Considered indolent (slow-growing) in nature
- Can watch for 5–10 years without intervening
- Life expectancy could be 10–20 years
- However, some patients need treatment quickly and aggressively
- How can we tell?

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Further Staging: FISH (fluorescent *in situ* hybridization)

- 13 q = favorable (17-year median OS)
- Trisomy 12 and 11 q = less favorable (9–11 years)
- **17p** – associated with mutated TP53
  - **Poor response rate**
  - Short duration of response with standard treatment
  - Most unfavorable prognosis (7-year median OS)

Example: Combined 11q + 17p = more unfavorable

OS, overall survival.
Wormsley SB, et al. *Blood*. 1990;76(1):123–130.

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Case Study: CBC at Presentation

- WBC: 30
- ALC: 6.0
- What else is needed when initially diagnosed?
- Obtain CT staging scans
  - Assess for organomegaly, extent of lymphadenopathy
  - Patient did not have
- Obtain bone marrow biopsy
  - Assess for evidence of disease; if so, how much?
  - Patient had 85% CLL in bone marrow

ALC, absolute lymphocyte count; CT, computed tomography.

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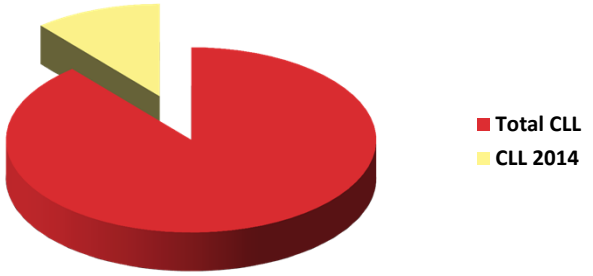
Epidemiology

- In 2013, an estimated **119,386** people in the United States were living with CLL
- **15,720** people were expected to be diagnosed with CLL in 2014



Total CLL expected in 2014: 120,000
New CLL cases in 2014: 15,720

The Leukemia & Lymphoma Society. *Chronic Lymphocytic Leukemia*. 2014.

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Epidemiology (cont'd)

- The most common type of leukemia in Western countries
- Considered disease of the elderly
- Median age at diagnosis is 70 years
- However, not unusual to make this diagnosis in younger individuals from 30–39 years of age

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Modified Rai Clinical Staging for CLL

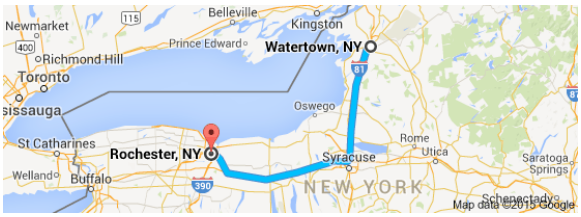
Risk	Stage	Description
Low	0	Lymphocytosis in blood or bone marrow
Intermediate	I	Lymphocytosis + enlarged lymph nodes
	II	Lymphocytosis + enlarged liver or spleen with/without lymphadenopathy
High	III	Lymphocytosis + anemia (Hgb <11), with/without enlarged liver, spleen or lymph nodes
	IV	Lymphocytosis + thrombocytopenia (<100) with/without anemia, enlarged liver, spleen or lymph nodes

Hgb, hemoglobin.
International Workshop on CLL. *Ann Intern Med*. 1989;110(3):236–238.

59

Case Study: Patient

- March 2011: Presented with intermediate Rai stage
- August 2011: Rituximab
- October 2011: Bendamustine/Rituximab
- January 2012: Increasing WBC, enlarging organomegaly
- Responded poorly: ALC from 30 to 100



- Referral made to CLL specialist at University of Rochester: clinical trial options

ALC, absolute lymphocyte count.

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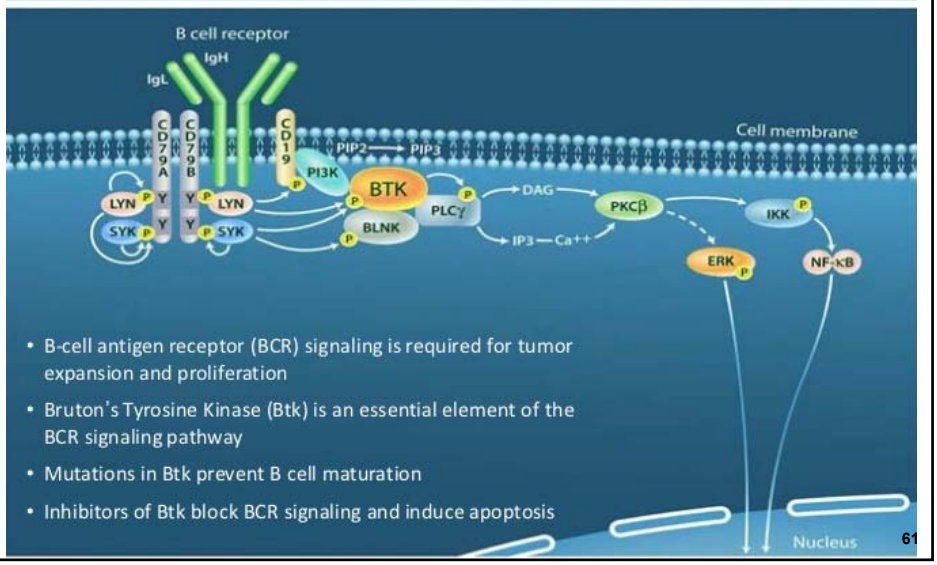
Bruton's Tyrosine Kinase (Btk)
A Critical B-Cell Signaling Kinase



- B-cell antigen receptor (BCR) signaling is required for tumor expansion and proliferation
- Bruton's Tyrosine Kinase (Btk) is an essential element of the BCR signaling pathway
- Mutations in Btk prevent B cell maturation
- Inhibitors of Btk block BCR signaling and induce apoptosis

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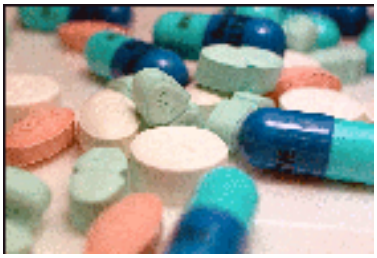
Ibrutinib: BTK

- 140-mg oral tablet:
  - CLL dose is 480 mg daily
  - FDA approved in 2014



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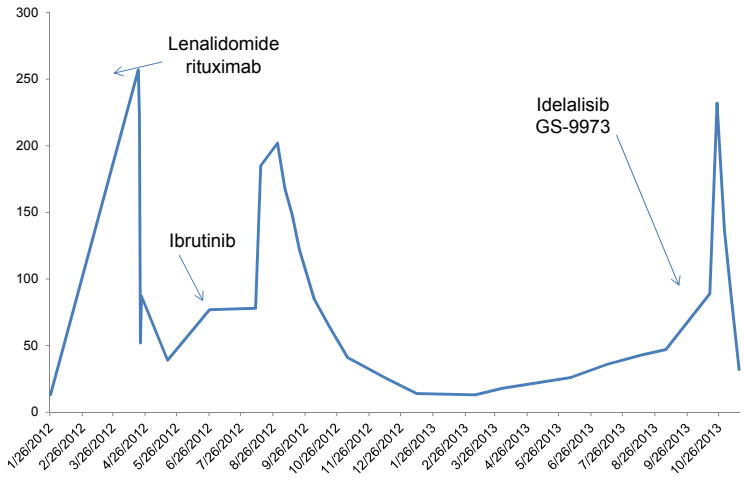
Case Study: Treatment Course



- Significant lymphocytosis: WBC spikes within first month of treatment
- Usually takes 2–3 months for WBC to return to normal

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Other Nursing Considerations

- Reasonably well tolerated
  - Not known to cause nausea
- Important side effect profile
- Bleeding and bruising
  - Should be considered “blood-thinning agent”
  - Hold 5–7 days prior to invasive procedure; restart 7 days after
- Known to cause some diarrhea
  - Typically can treat through; expect 1–2 bouts per day for first week. Patients usually recover quickly

64

Duration of Response

- Patients attain a complete remission
- How long will this last?
- Patients have been in remission for up to 3 years to date

65

Survivorship Issues

- Social workers and nursing: necessary to offer extensive emotional support
- During remission: often feel satisfied with response, but fearful of time because they wonder how long remission will last
- Secondly, ibrutinib is an expensive drug
  - Often need social work support to assist with financial assistance
  - Often turn to The Leukemia & Lymphoma Society for assistance with information gathering, as well as financial support

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Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

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Audience Discussion Question

Many oncologists consider any patient diagnosed with cancer a survivor, what makes a CLL survivor different? What special considerations are required in this population?

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Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

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Multiple Myeloma Overview and Case Study

Beth Finley-Oliver, RN, BSNc, OCN

Primary Nurse

Moffitt Cancer Center

Tampa, FL

This presentation was recorded in the studio following the ONS symposium

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Outline

- Understanding the Disease
  - Staging systems
  - Response criteria
- Case Study
- Treatment Strategy
  - Transplant vs non-transplant candidate
- Treatment Options
  - Newly diagnosed
- Nursing Considerations for Myeloma Patients
  - Bone health
  - Kidney health
  - Anemia
  - Preventing complications
- Multidisciplinary Team
  - Social worker
  - Physical and occupational therapist
    - Financial assistance

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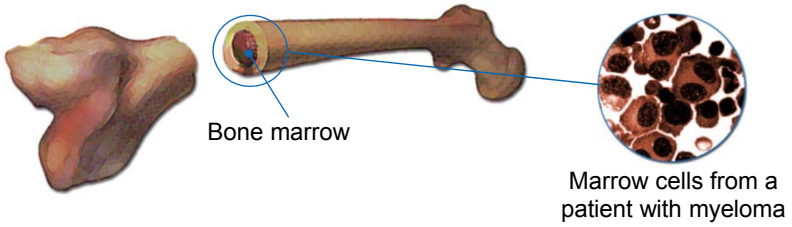
What Is Myeloma?

Cancer of plasma cells

- An uncontrolled growth of plasma cells

Myeloma begins in the bone marrow

- Spongy tissue found in the center of bones



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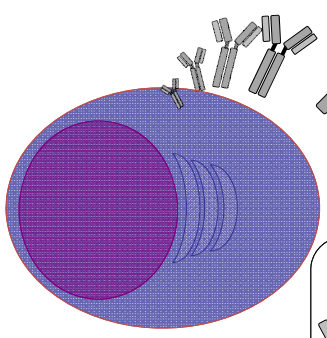
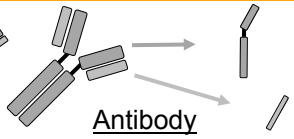
"M-spike"– Monoclonal Paraproteins



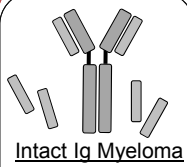
Myeloma Cell
- Produce Antibodies



Antibody
- Heavy and light chain components

Heavy Chain
- IgG >IgA >>IgD & IgE >> IgM

Light Chain
- Kappa (κ) > lambda (λ)



Intact Ig Myeloma
~80% MM
Eg, IgG kappa

Light Chain Myeloma
~15%–20% MM
Eg, kappa

Non-Secretory/ Oligosecretory
~0.5%–5% MM
Eg, kappa

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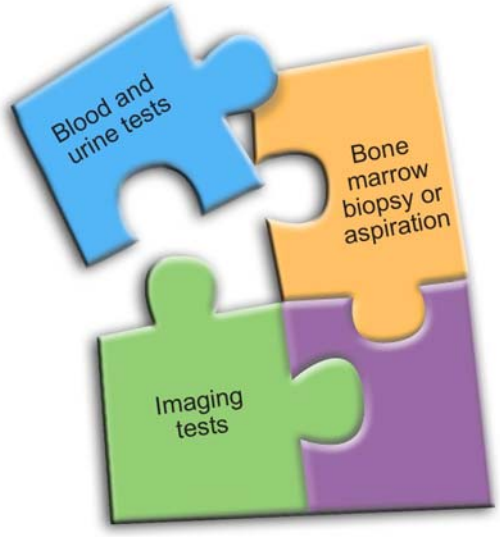
Ig, immunoglobulin; MM, multiple myeloma.

Diagnosing Myeloma



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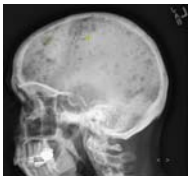
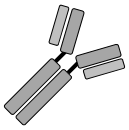
Diagnosis: "CRAB" Criteria

Presentation:

- Hypercalcemia (*C*)
- Renal Failure (*R*)
- Anemia (*A*)
  - Fatigue
- Fractures (*B*)
  - Bone pain
- Infections (I)



Ca^{++}



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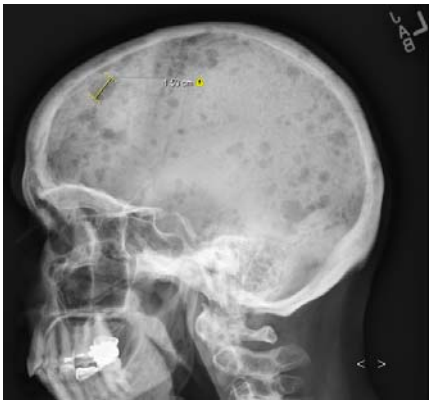
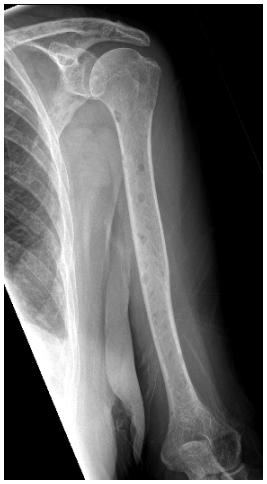
Durie BG, et al. *Leukemia.* 2006;20(9):1467–1473.

Lytic Lesions





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Durie-Salmon Staging System

Stage I	***All of the following:*** **Hemoglobin >10 g/dL** **Serum calcium normal (<12 mg/dL)** **Bone X-ray normal or solitary bone plasmacytoma only** **Low M-protein production (IgG <5 g/dL; IgA <3 g/dL)** **Bence-Jones protein <4 g/24 hours**
Stage II	**Fitting neither stage I nor III**
Stage III	***One or more of the following*:** **Hemoglobin <8.5 g/dL** **Serum calcium >12 mg/dL** **Advanced lytic bone lesions** **High M-protein production rates (IgG >7 g/dL; IgA >5 g/dL;** **Bence-Jones protein >12 g/24 hours)**

Durie-Salmon sub classifications (either A or B)
A: Relatively normal renal function (serum creatinine value <2.0 mg/dL)
B: Abnormal renal function (serum creatinine value =2.0 mg/dL)

Ig, immunoglobulin.
Durie BG, et al. *Cancer*. 1975;36(3):842–854.

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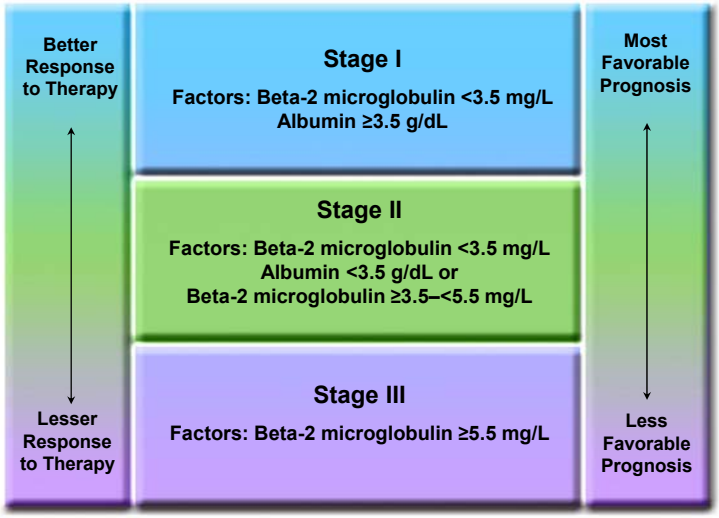
International Staging System (ISS)



Greipp PR, et al. *J Clin Oncol.* 2005;23(15):3412–3420.

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MM Risk Stratification

High Risk (25%)	Standard or Good Risk (75%)
t(4;14) by FISH t(14;16) or t(14;20) by FISH Deletion 17q13 by FISH Deletion 13 by metaphase analysis Aneuploidy by metaphase analysis Plasma cell labeling index >3.0 Beta-2 microglobulin >5.5 High-risk MyPRS™	Hyperdiploidy t(11;14) by FISH t(6;14) by FISH Beta-2 microglobulin <5.5 Labeling index <2.0

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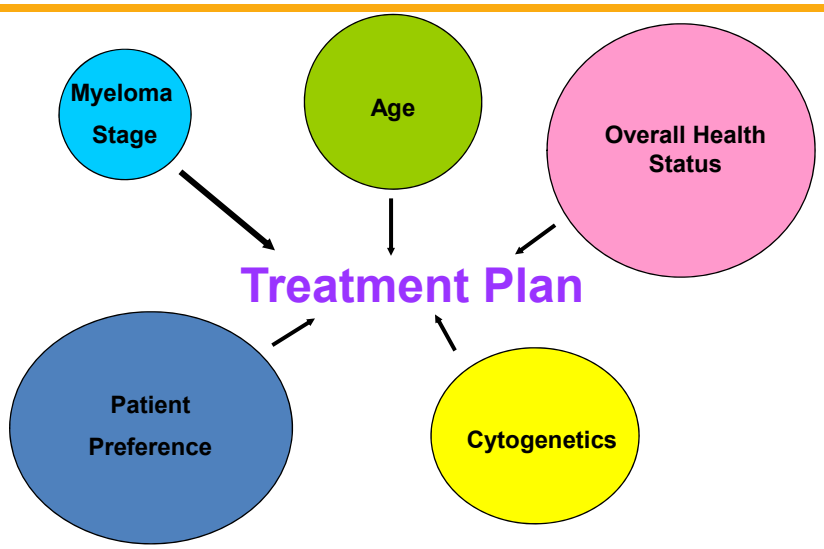
FISH, fluorescence in situ hybridization; MM, multiple myeloma; MyPRS, Myeloma Prognostic Risk Signature.

Factors Influencing Treatment Choice



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The Leukemia & Lymphoma Society. *Myeloma: A Guide for Patients and their Families.* March 2005.

Response Criteria

Response Type	M Protein	Plasma Cells in Bone Marrow	Other
Stringent complete response (sCR)	None (blood/urine)	No abnormal plasma cells	No free light chains
Complete response (CR)	None (blood/urine)	<5%	Disappearance of soft tissue plasmacytoma
Very good partial response (VGPR)	>90% reduction (blood)	NA	NA
Partial response (PR)	>50% reduction in serum and >90% reduction in urine	NA	>50% reduction in the size of soft tissue plasmacytoma
Minimal response (MR)	25%–49% reduction in blood and reduction of 50%–89% in urine	NA	25%–49% reduction in the size of soft tissue plasmacytoma
Stable disease (SD)	Does not meet criteria for response or progressive disease		
Progressive disease (PD)	>25% increase (blood or urine)	>10%	New bone lesions, soft tissue plasmacytoma, high calcium levels

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Durie BG, et al. *Leukemia*. 2006;20(9):1467–1473.

Case Study

- 61-year-old male
- Presentation
  - SPEP: 3.6
  - IgG: 6791
  - Serum free light chain - Lambda: 89.56
  - Beta-2 microglobulin: 2.3
  - Albumin: 3.2 g/dL
  - Calcium: 8.2 mg/dL
  - Creatinine: 0.8 mg/dL
  - Hemoglobin: 9.3 g/dL
  - UPEP: 156 mg/24 hours
- BMBX 70%–80% plasma cells
- Survey + lytic lesions
  - Skull
  - 8th rib fracture
  - FISH results
    - Hyperdiploidy
    - 13q deletion
    - t(11;14)
  - **ISS II**
  - **Durie-Salmon Stage 2A**

BMBX, bone marrow biopsy; FISH, fluorescence in situ hybridization; Ig, immunoglobulin; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis.

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Treatment Options for Transplant-Eligible Patient

- Transplant
  - Avoid melphalan
  - RVD
    - Lenalidomide 25 mg, days 1–14
    - Bortezomib 1.3 mg/m^2, days 1, 4, 8, and 11
    - Dexamethasone 20 mg PO, days 1, 2, 4, 5, 8, 9, 11, and 12
  - VDC
    - Bortezomib 1.3 mg/m^2, days 1, 4, 8, and 11
    - Cyclophosphamide 500 mg PO, days 1, 8, and 15
    - Dexamethasone 20 mg PO, days 1, 2, 4, 5, 8, 9, 11, and 12

Bisphosphonate Monthly

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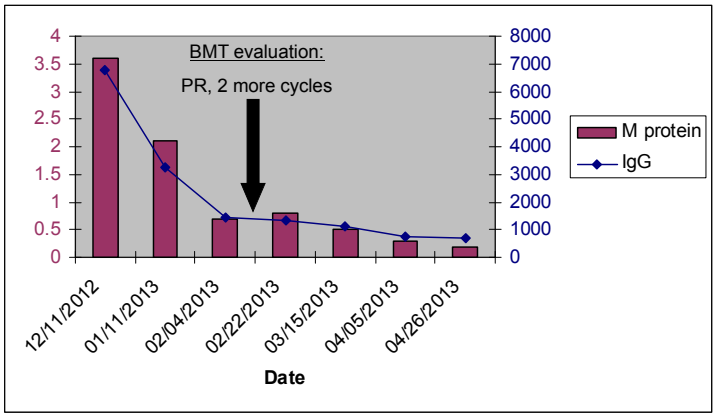
RVD, lenalidomide, bortezomib, and dexamethasone; VDC, bortezomib, dexamethasone, and cyclophosphamide.

Response: VGPR



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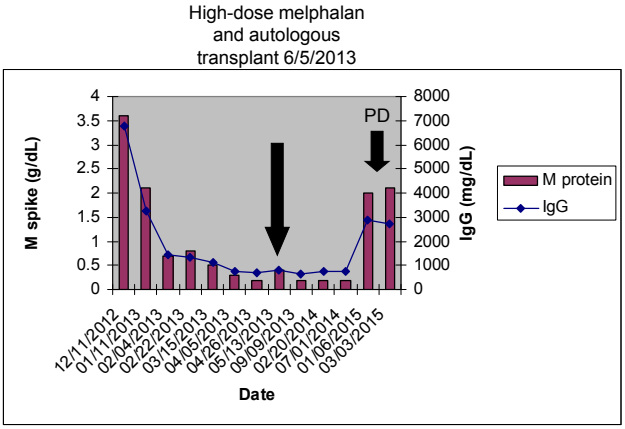
BMT, bone marrow transplant; Ig, immunoglobulin.

Disease Course



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Ig, immunoglobulin.

Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

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Nursing Considerations

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Managing Side Effects

Immunomodulatory Drugs (IMiDs)

	Thalidomide	Lenalidomide	Pomalidomide
Myelosuppression	Minimal	Yes	Yes
VTE	Yes	Yes	Yes
GI	Constipation	Diarrhea	Diarrhea
Rash	Yes	Yes	Yes
Sedation	Yes	No	No
Neuropathy	Yes	No	No

Teratogens!

GI, gastrointestinal; VTE, venous thromboembolism.

Proteasome Inhibitors

	Bortezomib	Carfilzomib
Schedule	Days 1, 4, 8, and 11 every 21 days	Days 1, 2, 8, 9, 15, and 16 every 28 days
Modes of administration	IV/SC	IV
Myelosuppression/ thrombocytopenia	Yes	Yes
Neuropathy	Yes	No
Zoster	Yes	Yes
Dyspnea	No	Yes
Fatigue	Yes	Yes
GI	Yes	No
Cardiac/pulmonary (RARE)	No	Yes

GI, gastrointestinal; IV, intravenous; SC, subcutaneous.

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Steroids (Dexamethasone/Prednisone)

- Mood Swings
- Insomnia
- Irritability
- Hyperactivity
- Edema
- Flushing
- Fatigue
- Blurry vision
- Cataracts
- Dyspepsia
  - PPI
- Muscle atrophy
- Hyperglycemia
- Acne
- Muscle cramping
- Taste changes
- Ulcer
- Weight gain
- Hair loss

PPI, proton pump inhibitor.

Faiman B, et al. *Clin J Oncol Nurs*. 2008;12(3):53–62.

88

Nurse's Role

- Education and support
  - Oral adherence to complex regimens
- Improving quality of life by helping to manage side effects
- Navigating patients and their caregivers throughout the disease process

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Bone Health

- Bisphosphonates
  - Avoid invasive dental procedures
  - Prevent pathological fractures
    - Orthopedist
    - Neurosurgeon
- Pain control
  - Avoid NSAIDs
  - Narcotic education

NSAID, non-steroidal anti-inflammatory drugs.
Miceli TS, et al. *Clin J Oncol Nurs.* 2011;15(4):9–23.

90

Renal Health

- Cast nephropathy (myeloma kidney)
- Hypercalcemia
  - Aggressive hydration and treatment
- Dehydration
  - IV fluids
- NSAIDS
- IV contrast
- Aminoglycoside antibiotics
  - Gentamycin, tobramycin, etc.
- Bisphosphonates

IV, intravenous; NSAID, non-steroidal anti-inflammatory drugs.
Faiman B, et al. *Clin J Oncol Nurs.* 2011;15(4):66–76.

91

Anemia

- Due to disease or treatment
- Supportive care
  - Erythropoietin-stimulating agents
    - Epoetin alfa
    - Darbepoetin alfa
  - PRBC transfusions
  - Fatigue
    - Treatment
    - Disease
    - Physical therapy

PRBC, packed red blood cell.

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Safety and Mobility

- Exercise
  - Physical/Occupational therapy
- Nutrition and hydration
  - Consult from nutritionist
- Psychosocial well-being
  - Support system
  - Fatigue
  - Sleep disturbances
  - Anxiety
  - Depression

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Rome SI, et al. *Clin J Oncol Nurs*. 2011;15(suppl):41–52.

Multidisciplinary Team Approach

- Social workers
  - Financial assistance programs
    - Non-profit organizations
      - The Leukemia & Lymphoma Society
      - Chronic Disease Fund
      - Patient Network Access
    - Pharmaceutical companies
- Physical and occupational therapists
- Dietician
- Pharmacist
- Dentist

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Summary

- Multiple myeloma is most often a chronic and complex disease
- Treatment decisions are individualized to the patient
- Managing side effects helps patients maintain quality of life
- A multidisciplinary team approach helps support patients and caregivers

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Thank You

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Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

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Follicular Lymphoma Overview and Case Study

Lynn Rich, ANP-BC, OCN
Nurse Practitioner
JP Wilmot Cancer Institute
University of Rochester
Rochester, NY

This presentation was recorded in the studio following the ONS symposium

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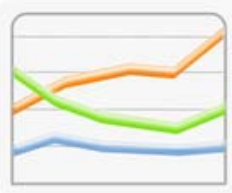
Outline



- Define disease
- Epidemiology
- Natural history of disease
  - Indolent vs curable
- Approved treatment options
  - Rituxan maintenance vs observation
- Use of idelalisib
- Communication strategies: support of social workers
- Resources: survivorship challenges

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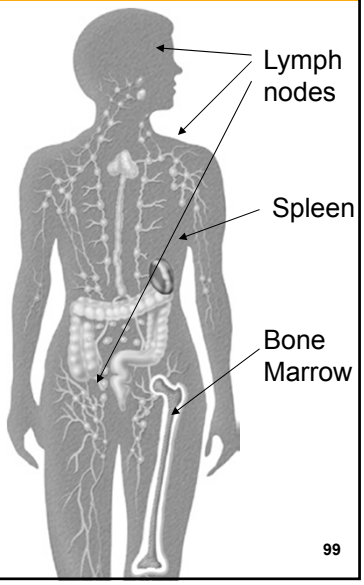
Lymphoma

General name given to a group of cancers that affect the lymphatic system

- Includes:
  - Lymph nodes
  - Plasma cells
  - Spleen
  - Lymphatic vessels
  - Bone marrow
  - Immunoglobulins
- Immune system helps protect against disease and infection



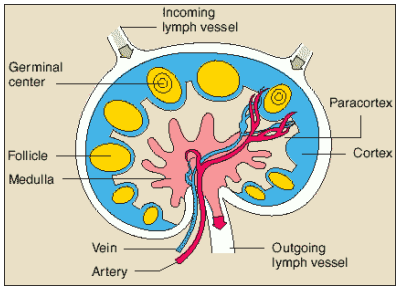
The Leukemia & Lymphoma Society. *Non-Hodgkin Lymphoma.* 2013.

99

Lymphoma

Two distinct types:

- Non-Hodgkin lymphoma (NHL)
  - Approx. 50 different subtypes
- Hodgkin lymphoma (HL)
  - Approx. 5 different subtypes



100

Follicular Lymphoma (FL)

- B-cell NHL (vs T/NK-cell NHL)
- Damage to DNA of one of the parent B cells causes a malignant transformation resulting in uncontrolled and exaggerated growth of the lymphocyte

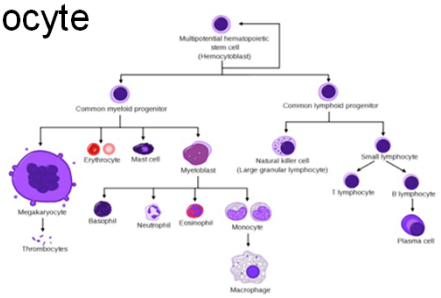


Image courtesy of JP Wilmot Cancer Institute; Chronic Lymphocytic Leukemia (CLL) Booklet.

101

Follicular Lymphoma (FL)

- **2nd** most common subtype of NHL
- Average age at diagnosis is 60 years
- Indolent: slow-growing disease
- Treatable, but not curable
  - Impact of deciding treatment

The Leukemia & Lymphoma Society. *Non-Hodgkin Lymphoma.* 2013.

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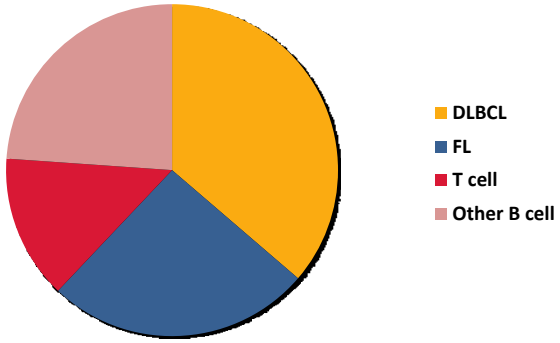
NHL: Epidemiology

Approximately 70,800 new cases of NHL in 2014

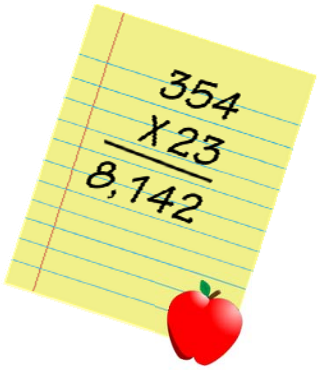


DLBCL, diffuse large B-cell lymphoma.
The Leukemia & Lymphoma Society. *Non-Hodgkin Lymphoma*. 2013.

103

Case Study: MB

- 57-year-old married female
  - 3rd-grade elementary teacher
  - Symptom profile
    - Abdominal fullness
    - Sweats
    - Fatigue
    - Lymphadenopathy
  - Next step, stage?



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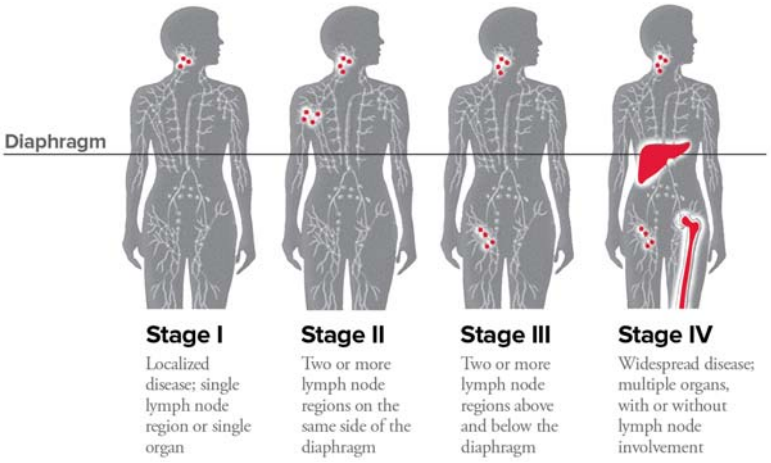
Ann Arbor Staging System



The Leukemia & Lymphoma Society. *Non-Hodgkin Lymphoma.* 2013.

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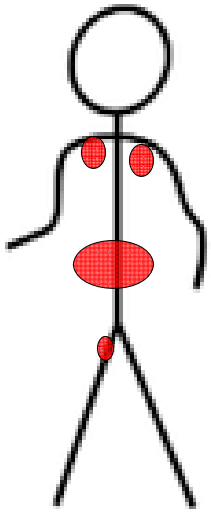
Case Study: MB

- Stage III
  - Bilateral axillary – small
  - Abdominal – 10-cm mass
  - Small inguinal node (groin node)
  - Bone marrow negative (would have been stage IV)



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Treatment

- Watch and wait?
- Grade 1, 2, or 3?

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Ready to Treat

- Criteria includes:
  - >3 sites of disease, 3 cm or more
  - 1 node measuring 7 cm
  - Cytopenias – refractory thrombocytopenia disease
  - Effusions
  - Symptoms of disease, or B symptoms
  - Threatened organ involvement
  - Elevated LDH

LDH, lactate dehydrogenase.

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Case Study: MB

- Treated with R-CHOP – completed 2007
  - Attained complete remission
- Consider maintenance with rituximab vs observation
  - Upfront vs consolidation
  - Things to consider:
    - Expected response
    - Impact on overall survival
    - Quality of life
    - Financial impact

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

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Case Study: MB

- No maintenance rituximab
- Relapsed in 5/2008
  - Concerning?

- What we did:
  - Salvage RICE × 2, then autologous stem cell transplant
  - Complete remission 9/2008

RICE, rituximab, ifosfamide, carboplatin, and etoposide.

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Case Study: MB

- Relapsed 12/2014
  - Essentially asymptomatic – mild abdominal fullness
  - However, CT of abdomen showed increased disease
- Is she ready for treatment?
  - What are the treatment options?

CT, computed tomography.

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Idelalisib – What Is It?

- PI3K inhibitor
  - Phosphoinositide 3-kinase delta

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Idelalisib

- Oral agent
- FDA approved in 2014
- Used for CLL/SLL or FL
- In relapsed setting

CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma.

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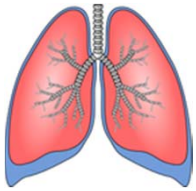
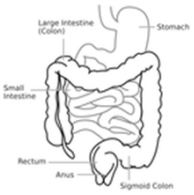
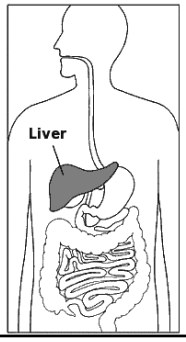
Side Effect Profile



- Concern for pneumonitis or colitis
  - What to look for
  - When concerned
  - How to follow



- Concern for evolution of liver function abnormalities
  - What to look for
  - When concerned
  - How to follow



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Things to Consider

- Is this patient a good candidate?
  - Why wouldn't she be?
  - Why would she be?

- Bring in social worker
  - Help to assess medical literacy (implications)
  - Help with financial assistance
    - What are potential sources of assistance?

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Communication Strategies

- Create a calendar with details
  - When to take pills, get blood drawn, etc.
- Dialogue with patient
  - Check in by phone
    - At least weekly initially
    - Consider MyChart®

- Eventually evolve to monthly visits, if tolerated

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What Happened to MB?

- Began idelalisib 150 mg BID
- Well tolerated
- Held after 2 months for elevated LFTs
- Update to date…

BID, twice daily; LFTs, liver function tests.

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Resources – Survivorship Issues

- The Leukemia & Lymphoma Society
  - www.LLS.org
  - Explore local chapter support groups
- YMCA – Exercise program
  - Explain cancer survivor
  - Describe health and fitness programs
- Look for specific related survivor support groups
  - www.LLS.org/survivorship

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Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies

LEUKEMIA & LYMPHOMA SOCIETY® fighting blood cancers

someday is today®

Thank You