



EVOLVING TREATMENT STRATEGIES IN PEDIATRIC LEUKEMIA

June 12, 2024

Jointly provided by The Leukemia & Lymphoma Society and Postgraduate Institute for Medicine



WELCOME AND INTRODUCTIONS

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Senior Manager

Professional Education Programs
The Leukemia & Lymphoma Society
Rye Brook, NY

LEARNING OBJECTIVES

- Describe common childhood blood cancers, including ALL and AML
- Identify signs and symptoms of childhood blood cancers and diagnostic tests
- Explain treatments, including the role of clinical trials, and LLS PedAL, a precision medicine clinical trial for pediatric acute leukemia
- Describe strategies for management of short- and long-term side effects of treatment
- Explain the importance of following a care plan, including long-term follow-up and communication between the pediatrician/family physician and the pediatric oncologist
- Describe psychosocial concerns related to patients with pediatric cancer

CE DESIGNATION



JOINTLY ACCREDITED PROVIDER
ACCREDITATION COUNCIL FOR CONTINUING MEDICAL EDUCATION

Physician Continuing Medical Education

In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and The Leukemia & Lymphoma Society. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The Postgraduate Institute for Medicine designates this CME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.



Registered Nursing Credit Designation

Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under Provider Number CEP 5832 to award 1.0 continuing education contact hour through the California Board of Registered Nursing.



IPCE CREDIT[™]

Interprofessional Continuing Education

This activity was planned by and for the healthcare team, and learners will receive 1 Interprofessional Continuing Education (IPCE) credit for learning and change.



Continuing Physician Assistant Education

Postgraduate Institute for Medicine has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 1 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.



Social Worker Continuing Education

The Leukemia & Lymphoma Society (LLS) Provider Number 1105, is approved as an ACE provider to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Regulatory boards are the final authority on courses accepted for continuing education credit. ACE provider approval period: 12/10/2023-12/10/2026. Social workers completing this course receive 1.0 clinical continuing education credit.

The Leukemia & Lymphoma Society (LLS) is recognized by the New York State Education Departments State Board for Social Work as an approved provider of continuing education for licensed social workers #SW-0117. LLS maintains responsibility for the program. Social workers will receive 1.0 clinical CE contact hour for this activity.

SPEAKERS



Branko Cuglievan, MD
Assistant Professor, Pediatrics - Patient Care
Section Chief, Leukemia/Lymphoma
Children's Cancer Hospital
The University of Texas MD Anderson Cancer Center
Houston, TX



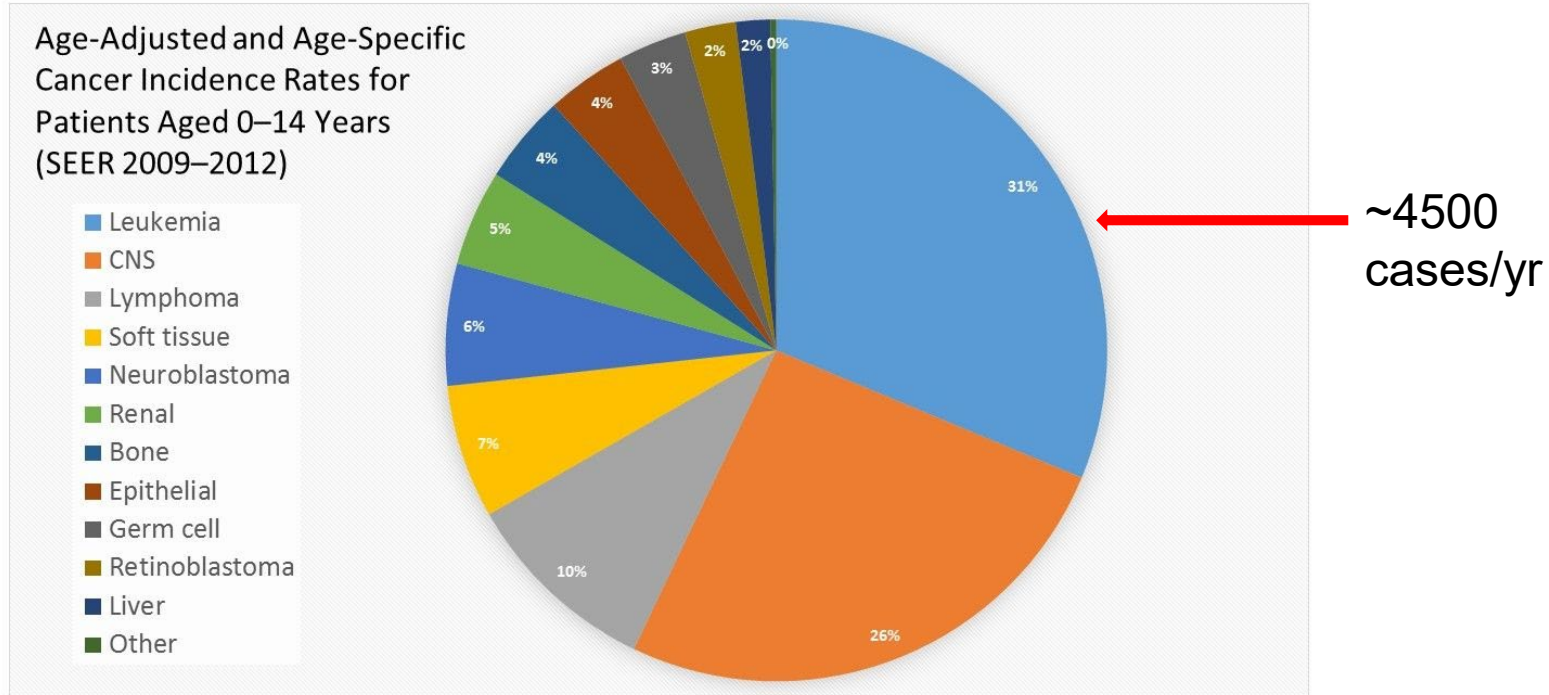
Romeo Torres, MSN, APRN, FNP-BC, CPHON
Pediatric Leukemia/Lymphoma
Children's Cancer Hospital
The University of Texas MD Anderson Cancer Center
Houston, TX

DISCLOSURES

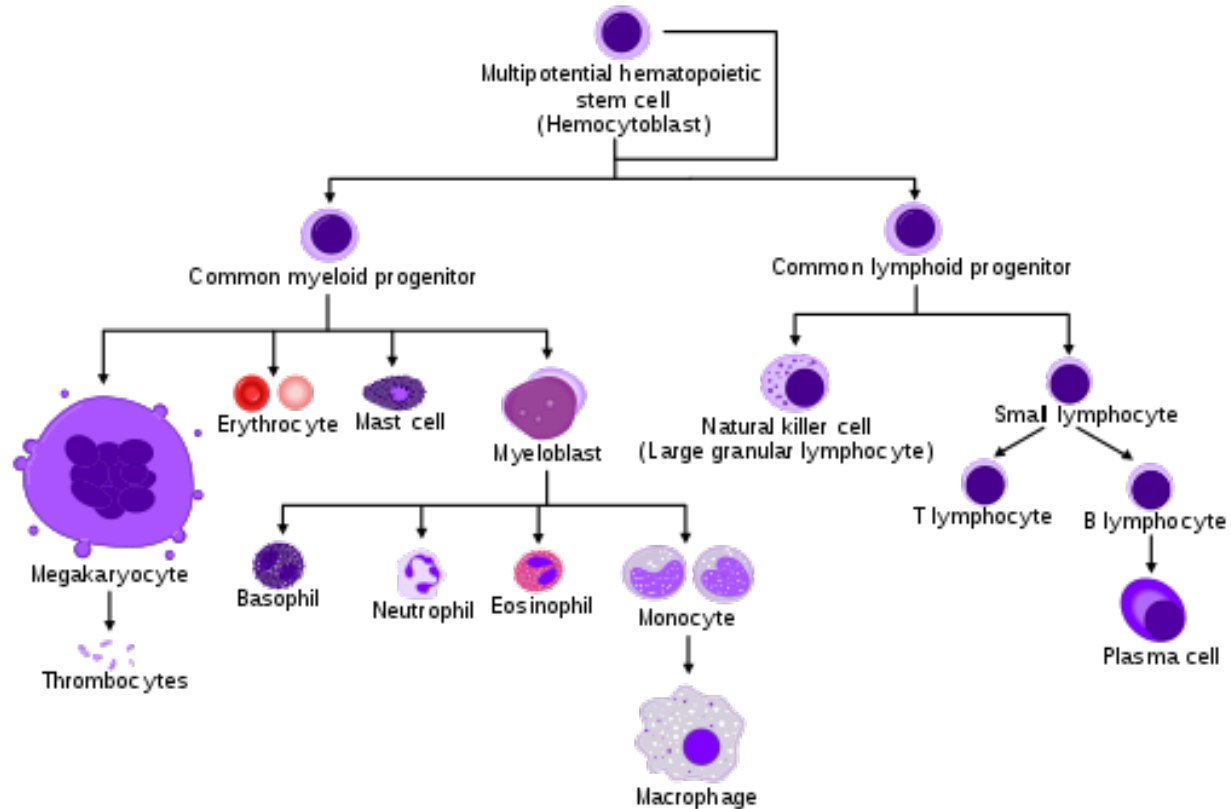
- **Branko Cuglievan, MD**
 - **Research Funding:** Astex, Kura Oncology, LLS, Octapharma, Syndax
 - **Travel/Accommodations:** Octapharma
- **Romeo Torres, MSN, APRN, FNP-BC, CPHON, has no disclosures**
- **Lesley Hoerst, BSN, RN, has no disclosures**

Pediatric Leukemias

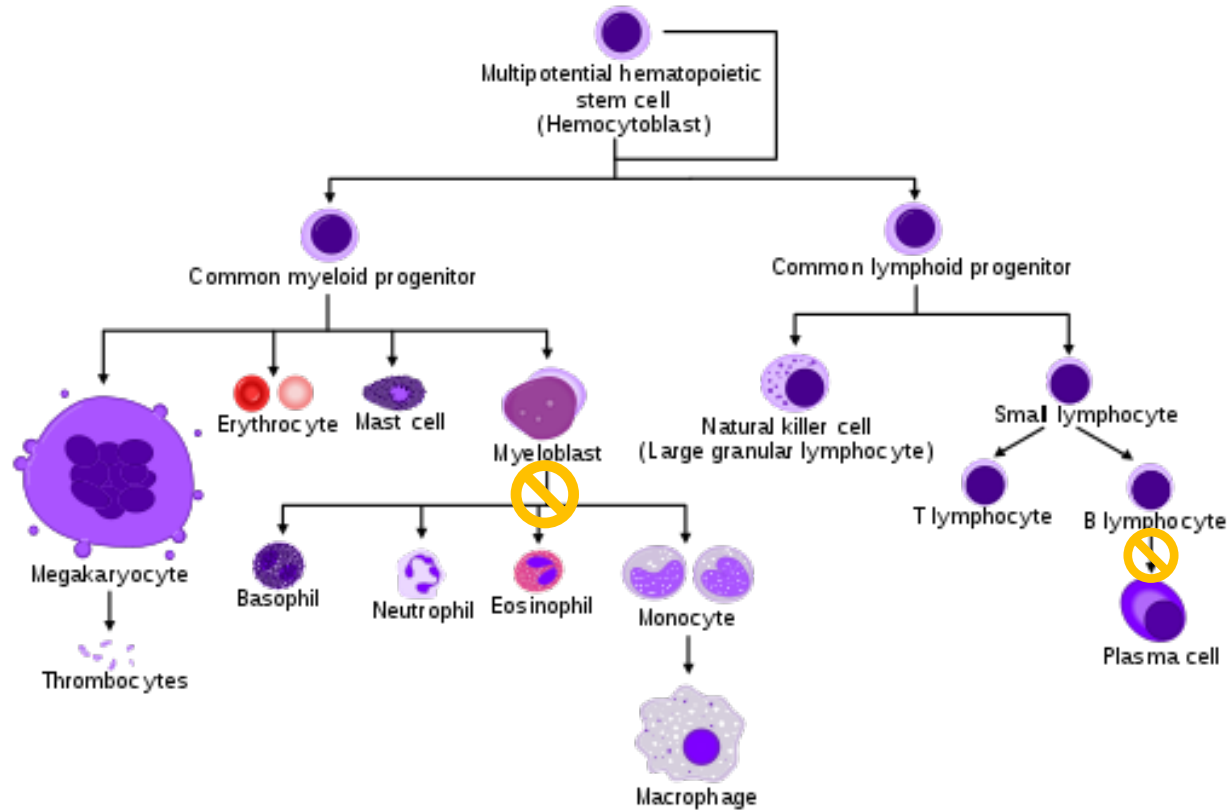
PEDIATRIC NEOPLASMS



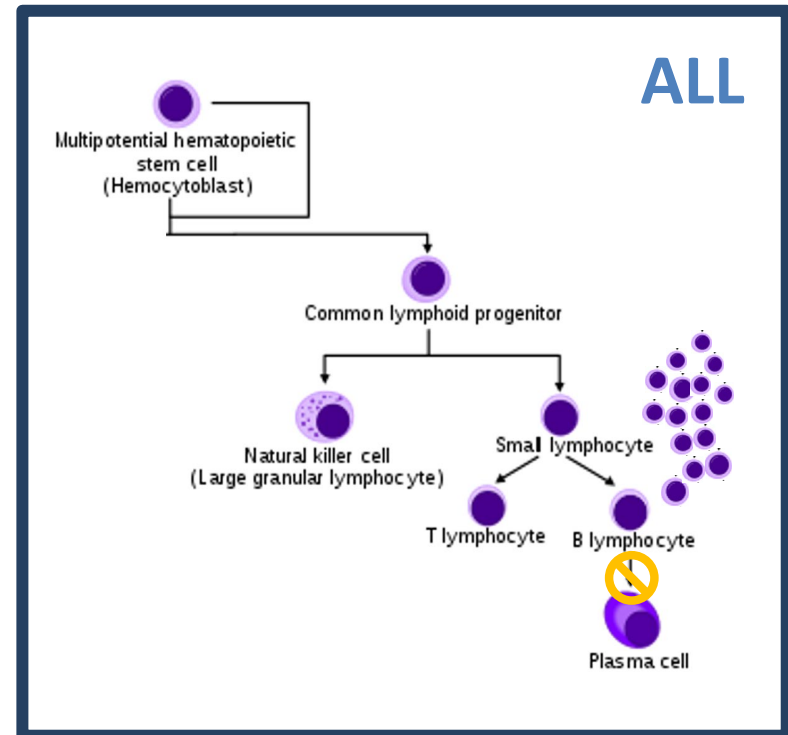
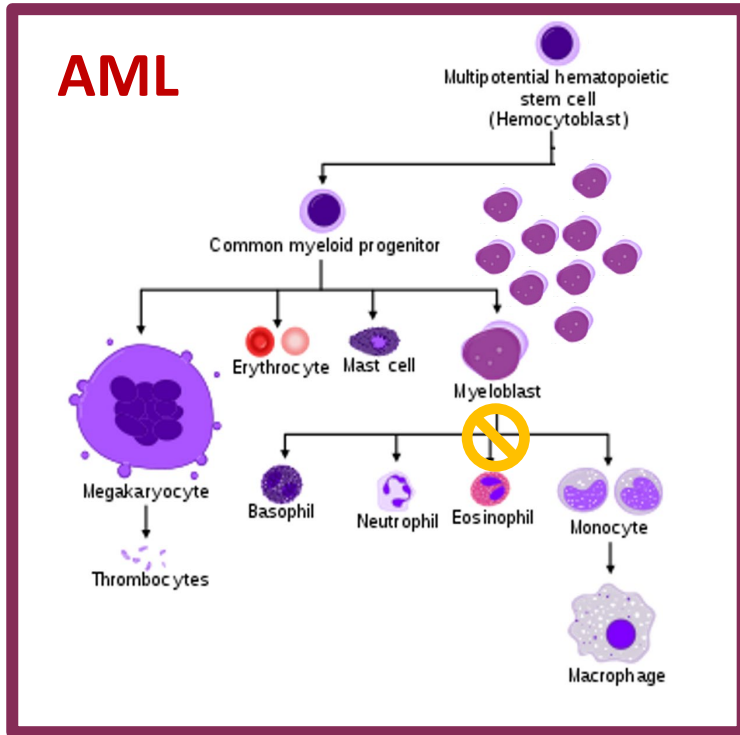
HEMATOPOIESIS



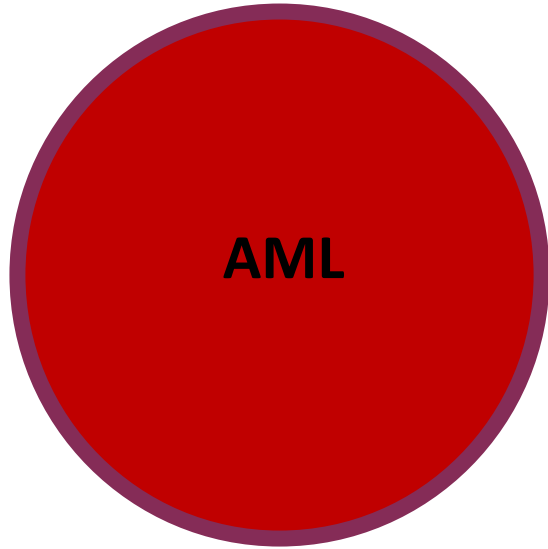
HEMATOPOIESIS



HEMATOPOIESIS

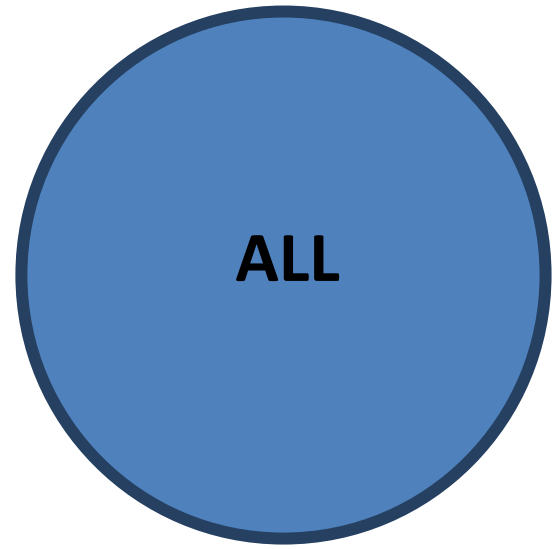


HEMATOPOIESIS



AML

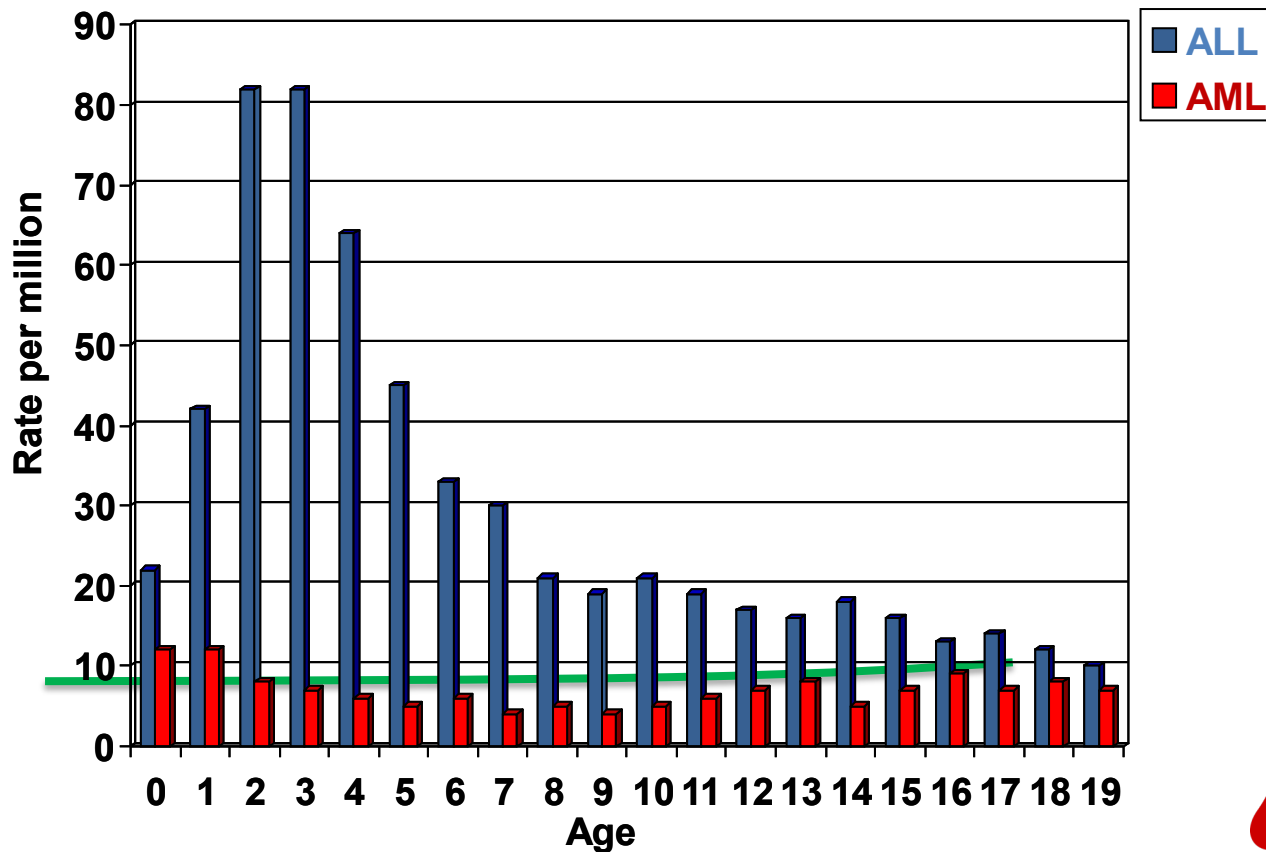
750
cases/year



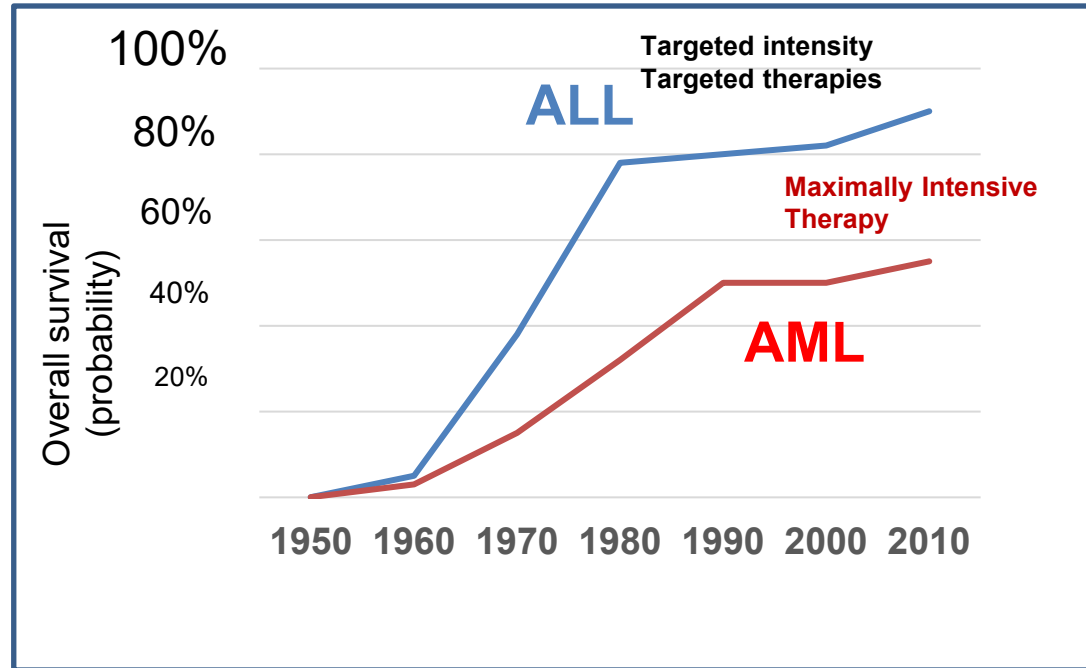
ALL

3,300
cases/year

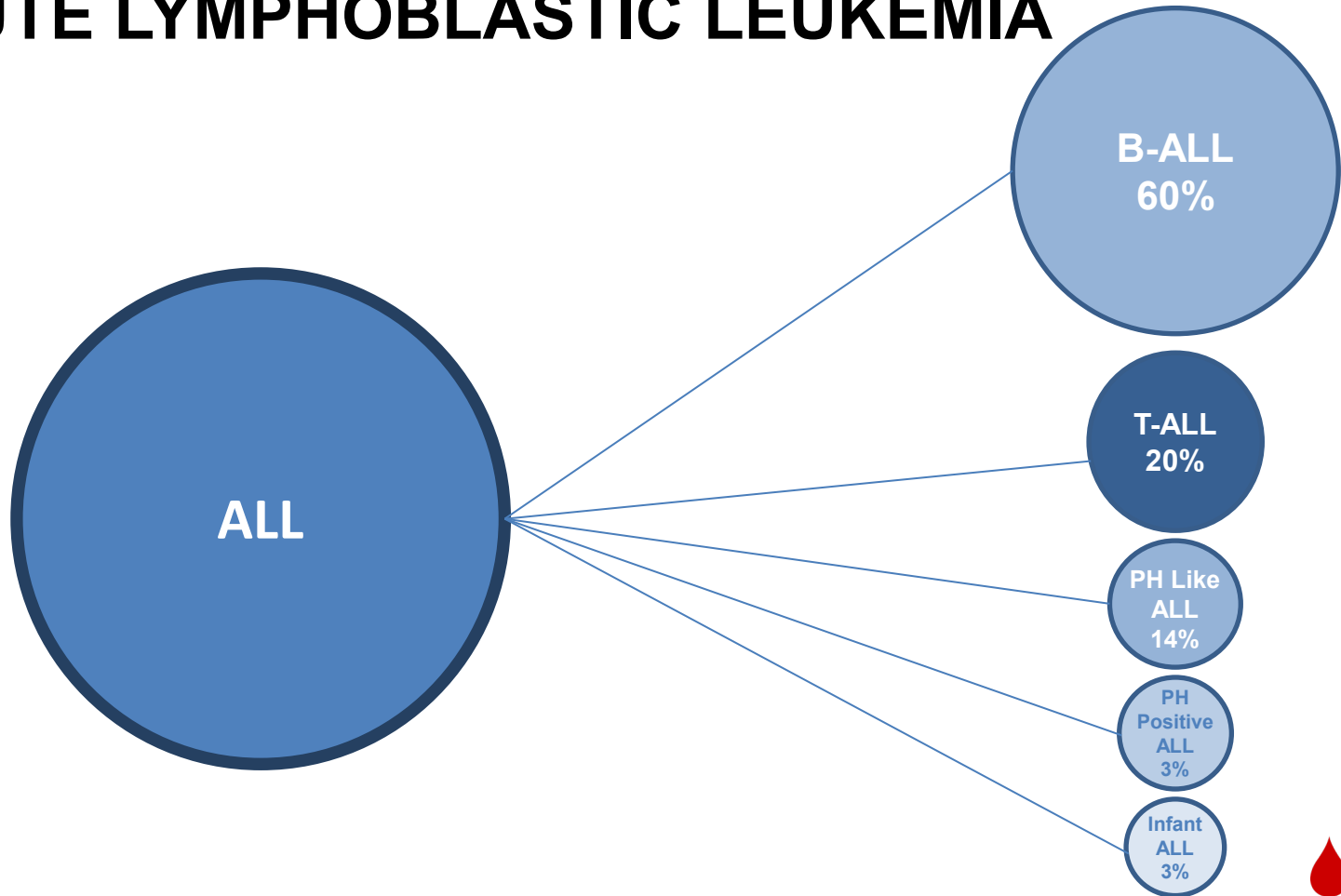
EPIDEMIOLOGY



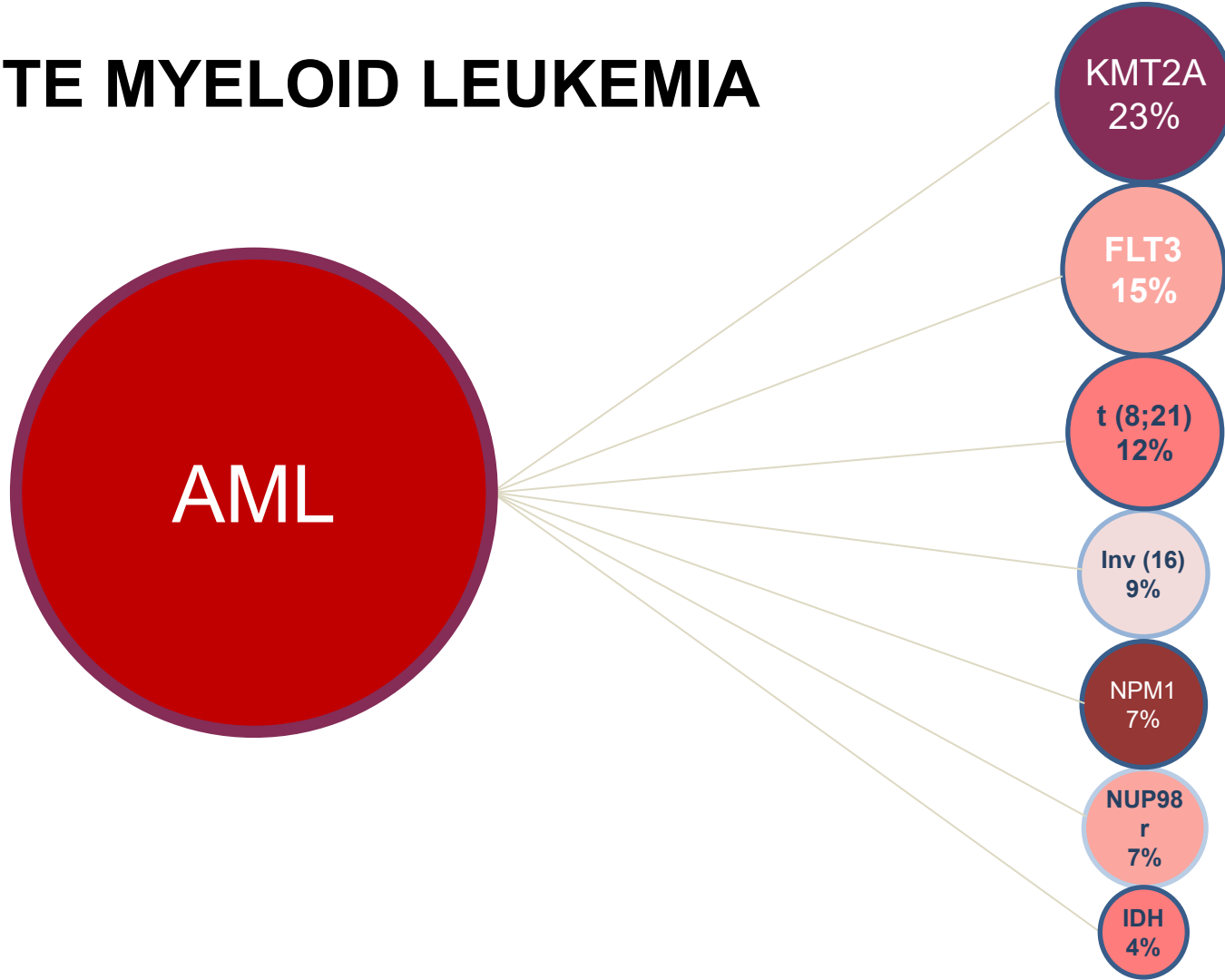
ALL VS. AML – THE HISTORICAL PERSPECTIVE



ACUTE LYMPHOBLASTIC LEUKEMIA

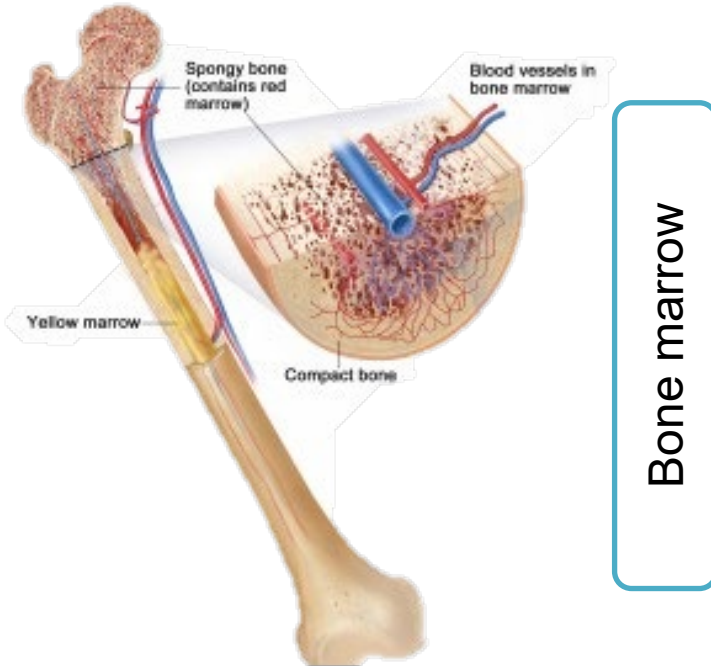


ACUTE MYELOID LEUKEMIA



Clinical Presentation

CLINICAL PRESENTATION: LEUKEMIA INFILTRATION



Lymphadenopathy

Hepatomegaly

Splenomegaly

Kidney lesions

TYPICAL ACUTE LEUKEMIA –PRESENTATION

Fatigue,
pallor, tachycardia

Easy bruising,
petechiae

Frequent
infections, fevers

Bone/Joint pains
(sometimes won't
want to walk
anymore)

Vague abdominal
pains, anorexia
(unexplained
weight loss)

Headaches,
vomiting, vision
changes

ACUTE LEUKEMIA – PRESENTATION ON EXAM

Lymphadenopathies

Hepatosplenomegaly

Cranial nerve palsies from CN involvement

Testicular Involvement (boys)

Chloromas (not as common) – seen in AML

Leukemia cutis (skin involvement)

Gingival infiltration



Petechiae¹



Leukemia Cutis²



Gingival Hyperplasia²

Acute Leukemia Workup

QUIZ QUESTION!

Which of the following is the accepted gold standard for diagnosing suspected leukemia?

- a) Flow cytometry on peripheral blood
- b) Next gen sequencing from peripheral blood
- c) Flow cytometry on bone marrow aspirate
- d) Urine catecholamine testing

QUIZ QUESTION!

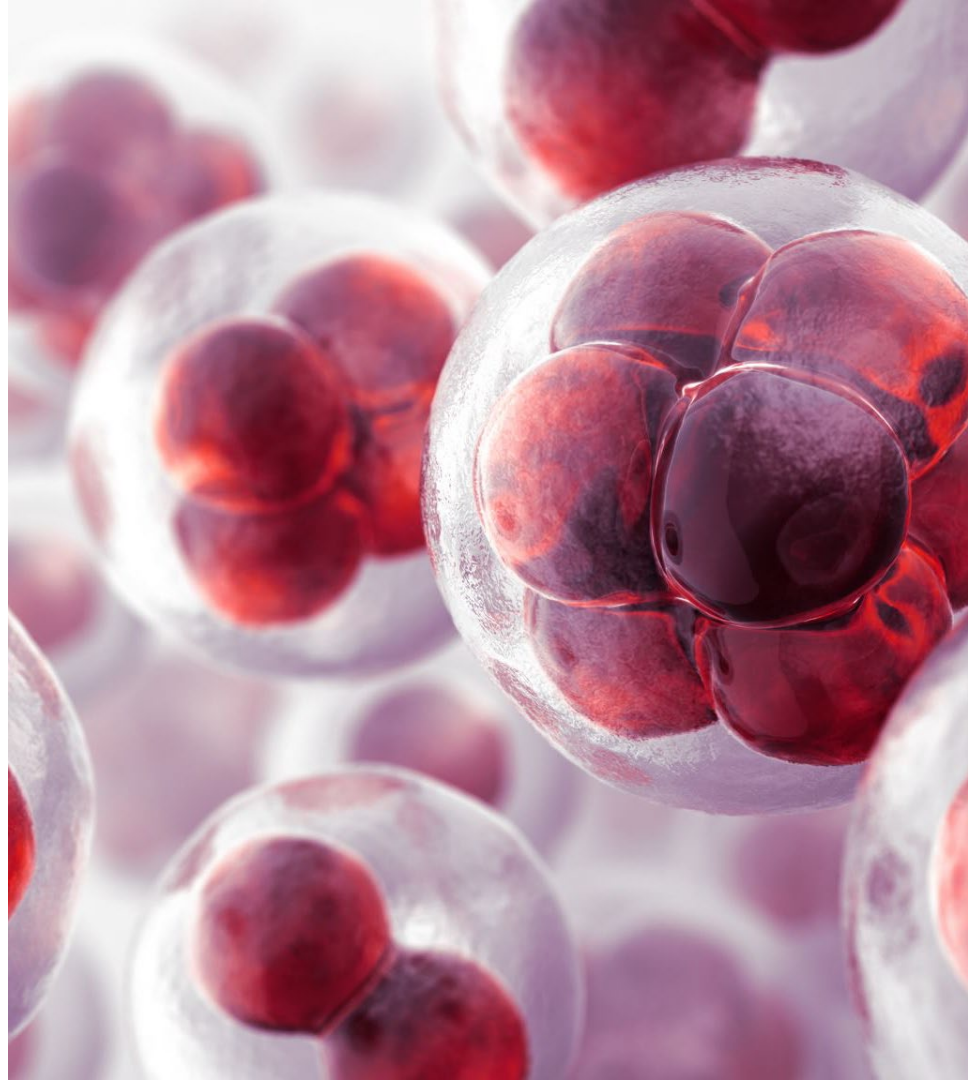
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- b) Next gen sequencing from peripheral blood
- c) Flow cytometry on bone marrow aspirate**
- d) Urine catecholamine testing

ACUTE LEUKEMIA WORKUP

Laboratory findings:

- CBC can be "normal"
- WBCs: varies – either high or low
- Hemoglobin and platelets: often low
- Differential – Neutropenia & blasts
- Can get preliminary diagnosis from peripheral blood, but not confirmatory
- Gold standard, confirmatory diagnosis is still from bone marrow biopsy & aspiration



ACUTE LEUKEMIA WORKUP

Chemistry panel:

- Can be normal in pre-treated disease
- Potassium & phosphorus ↑
- Uric Acid ↑
- Calcium (Inverse relationship with ↓ phosphorus)
- Creatinine ↑
- LDH ↑

Tumor lysis!

Coagulation studies:

- Risk for bleeding/clotting
- DIC could be present (APML)
 - PTT, PT/INR increased
 - Fibrinogen decreased
 - D-Dimer increased

ACUTE LEUKEMIA WORKUP

Infectious studies:

- Varicella (VZV)
- Herpes Simplex Virus (HSV)
- Cytomegalovirus (CMV)
- Hepatitis Studies (Hep A/Hep B)
- HIV
- Epstein-Barr (EBV)

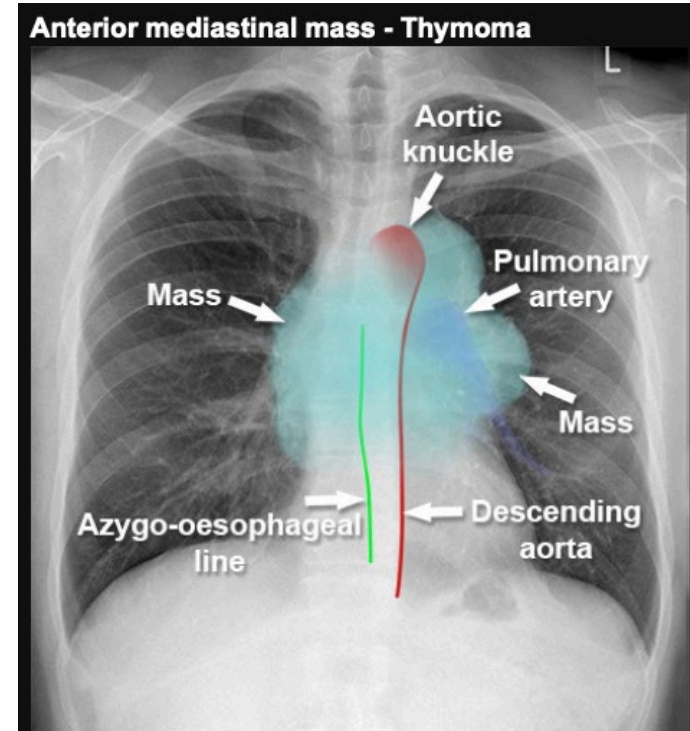
Others:

- Immunoglobulins (Ig)
 - IgG, IgA, IgM
- HLA Typing (Stem Cell)

ACUTE LEUKEMIA WORKUP

Chest X-ray³

- Performed to rule out mediastinal masses prior to sedation
- Present in 5–10% of ALL (often T-cell ALL)
- Masses can cause respiratory arrest or cardiac dysfunction
- Caution with sedation!



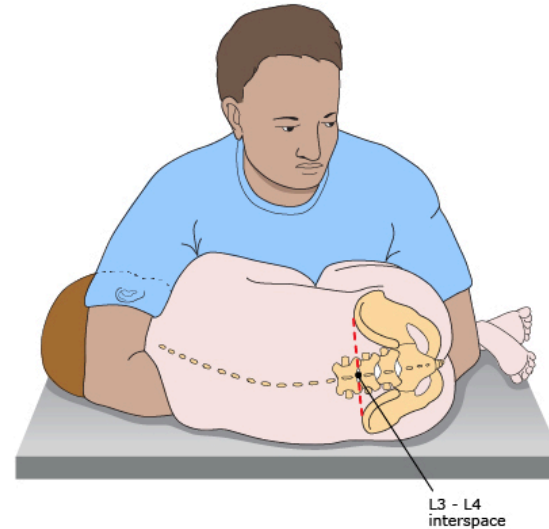
3

ACUTE LEUKEMIA WORKUP

Lateral recumbant position

Lumbar puncture⁴

- Standard for every patient at diagnosis
- Typically done with intrathecal chemotherapy as part of CNS “prophylaxis”
 - Cell count with differential
 - Cytology testing
 - Flow cytometry



The child is positioned near the edge of the examining table. The assistant places one arm around the posterior aspect of the child's neck and the other arm under the child's knees to hold the child in optimal position. The child's hips and shoulders should be kept perpendicular to the table in order to maintain spinal alignment without rotation. The assistant can maintain adequate restraint by holding onto his or her own wrists.

ACUTE LEUKEMIA WORKUP

Bone marrow aspiration and biopsy

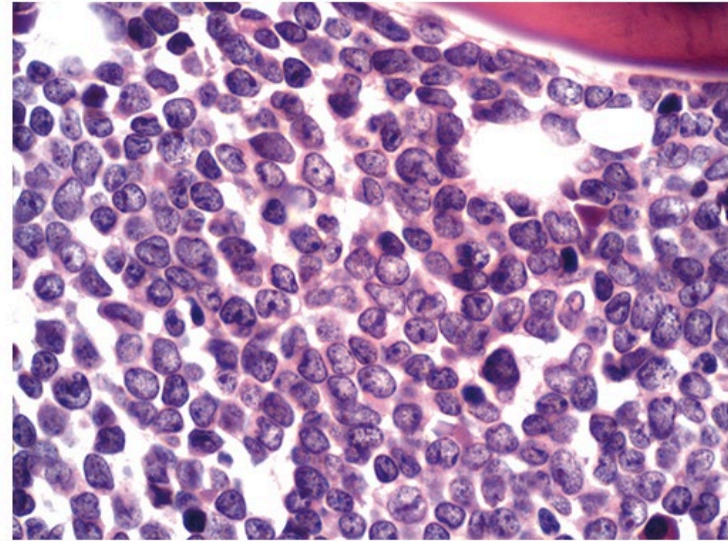
- Gold standard for diagnosis
- Typically done in bone of superior or anterior iliac crest
- Biopsy – Involves a large core needle to pull out a small piece of bone
- Aspiration – Pulls out liquid marrow for evaluation
- Sent for cytogenetics, flow cytometry, molecular diagnostics and "Next Gen" sequencing

ACUTE LEUKEMIA WORKUP

Bone marrow biopsy of a case of B cell acute lymphoblastic leukemia

Bone marrow analysis⁵

- Cellularity
- Hematopathology differential
- Morphology



Bone marrow biopsy shows total replacement of normal hematopoietic cells with lymphoblasts that shows convoluted or folded nuclei. Hematoxylin and eosin, 100x magnification.

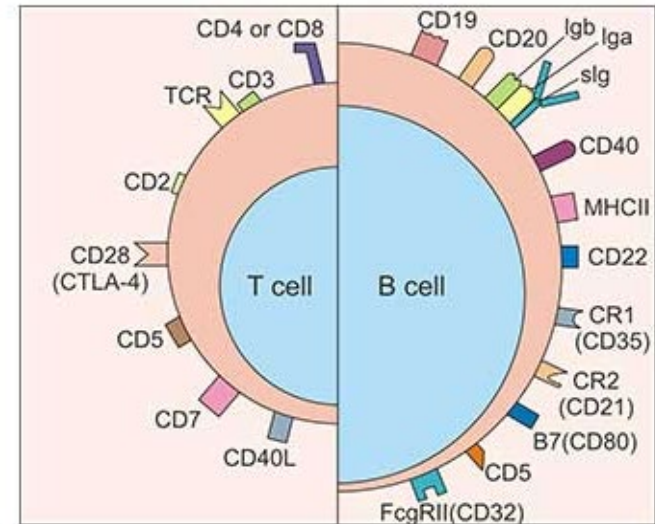
ACUTE LEUKEMIA WORKUP

Immunophenotyping⁶

- Identifies markers present on the cell surface
- Targeted therapies for specific markers exist now (Blinatumomab, Inotuzumab ozogamicin, Rituximab, CAR-T, etc.)
- These studies can also help differentiate lineage and subtypes

Cytogenetics

- Analyze the chromosomes inside the cell
- Identifies number of chromosomes (ploidy)
 - Diploid = 46 chromosomes



TREATMENTS

QUIZ QUESTION!

Which of the following has an overall highest rate of survivorship?

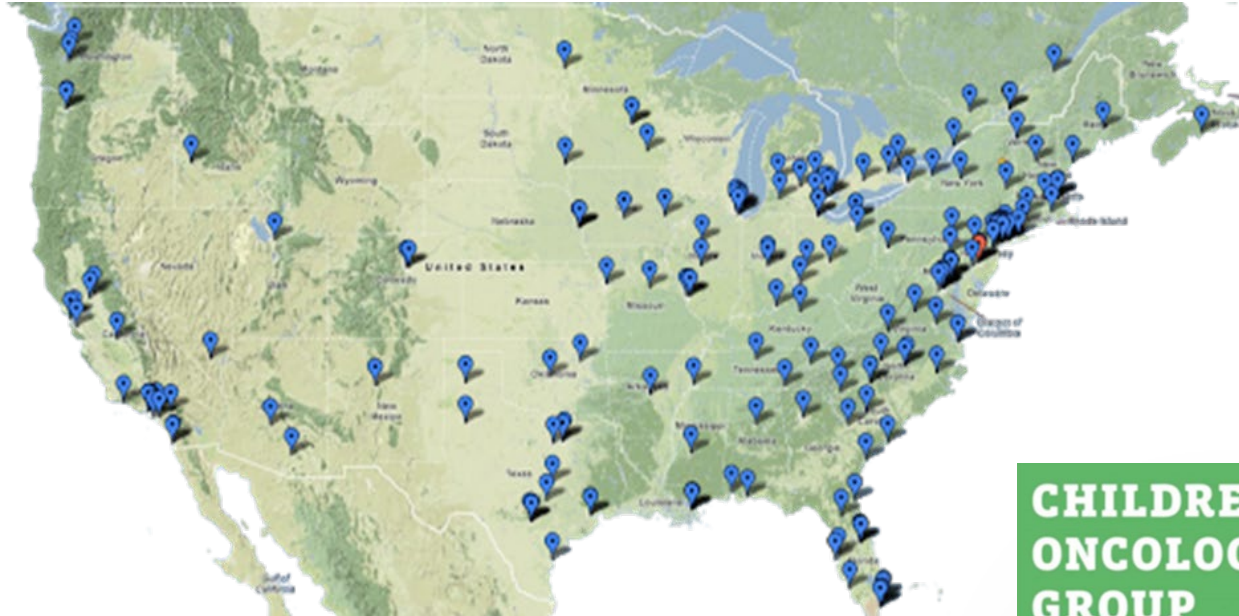
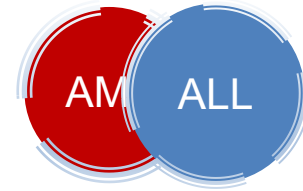
- a) Osteosarcoma
- b) Acute Lymphoblastic Leukemia
- c) Hodgkin Lymphoma
- d) Acute Myeloid Leukemia

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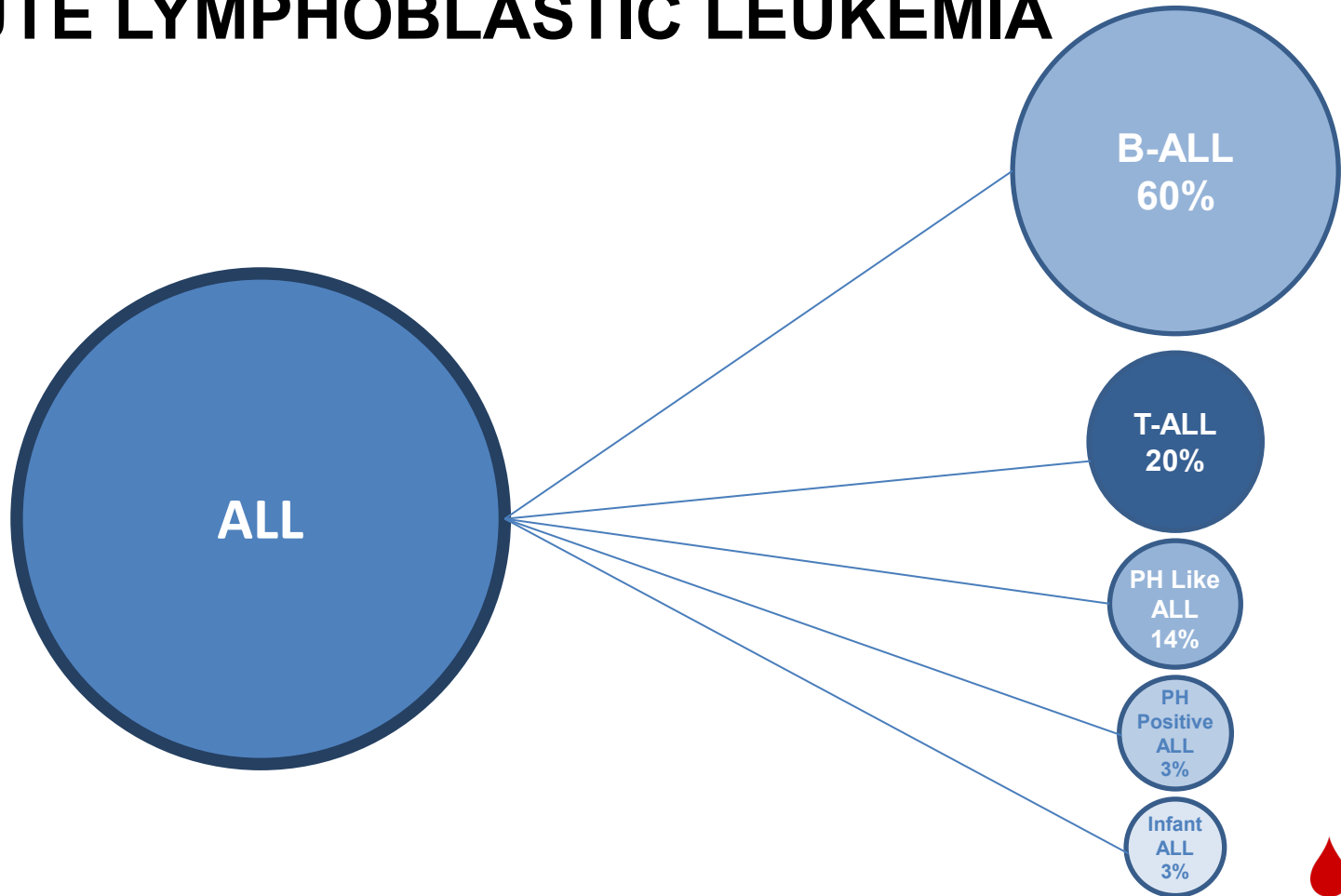
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- c) Hodgkin Lymphoma
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LEUKEMIAS IN CHILDREN



**CHILDREN'S
ONCOLOGY
GROUP**

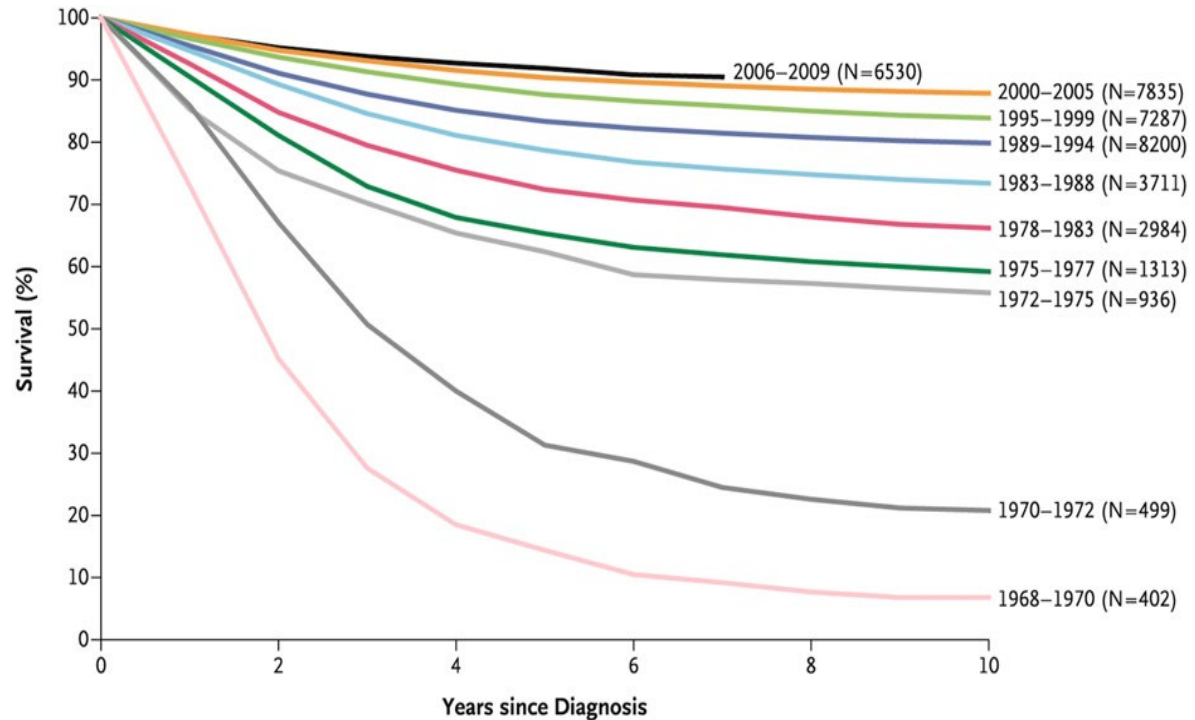
ACUTE LYMPHOBLASTIC LEUKEMIA



ALL EPIDEMIOLOGY AND SUCCESS

Attributed to the success of:

- A. Cooperative group trials
- B. IT chemotherapy
- C. Stratification and intensification
- D. Better drugs

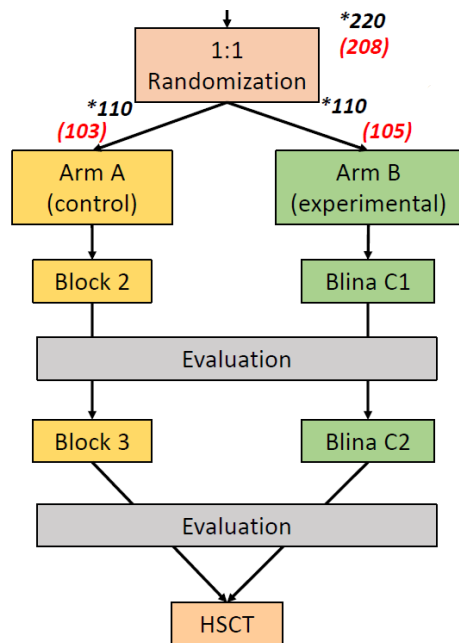


NCCN GUIDELINES

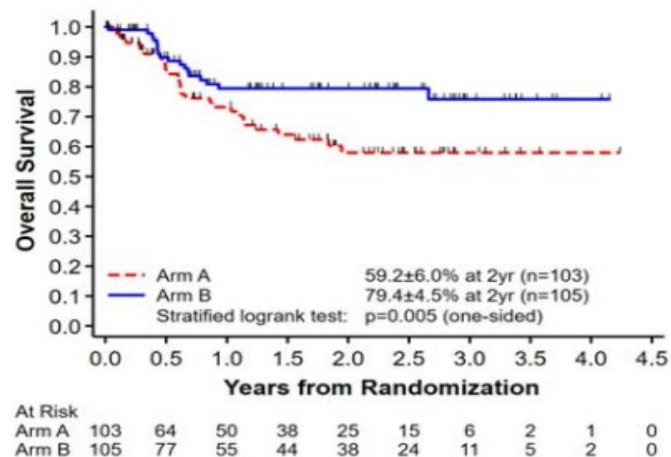
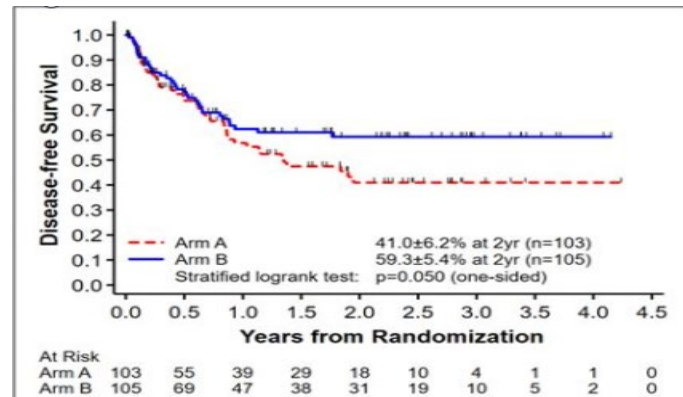
INITIAL RISK GROUP STRATIFICATION DEFINITIONS

www.NCCN.org

PHASE III STUDY OF BLINATUMOMAB IN PEDIATRIC RELAPSED B-ALL

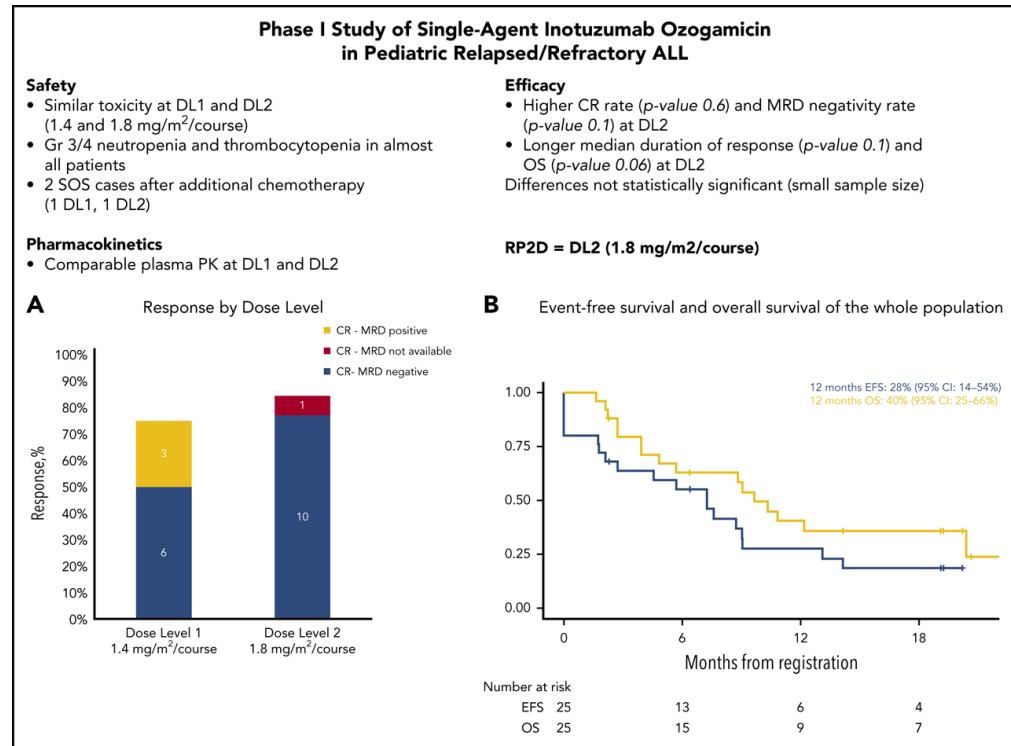


Parameter	Blina	Chemo	p
%2-yr DFS	59	41	.05
%2-yr OS	79	59	.005
% SCT	73	49	<.001
% MRD clearance	79	21	<.001



PHASE II STUDY OF INOTUZUMAB IN R-R PEDIATRIC ALL

- The recommended phase 2 dose established at 1.8 mg/m² per course
- 85% reached CR after 1 course, 100% of whom had MRD negativity



CHILDREN'S ONCOLOGY GROUP

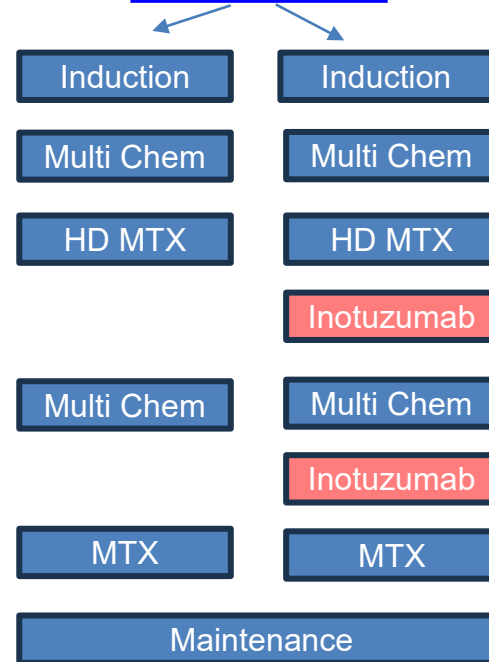
Blinatumomab

AALL1731



Inotuzumab

AALL1732



SEQUENTIAL IMMUNOTHERAPY

> Clin Lymphoma Myeloma Leuk. 2024 Apr;24(4):e168-e173. doi: 10.1016/j.clml.2023.12.016.
Epub 2023 Dec 30.

Dose-Dense Mini-Hyper-CVD, Inotuzumab Ozogamicin and Blinatumomab Achieves Rapid MRD-Negativity in Philadelphia Chromosome-Negative B-cell Acute Lymphoblastic Leukemia

Nicholas J Short ¹, Elias Jabbour ², Trevor Jamison ², Shilpa Paul ³, Branko Cuglievan ⁴,
David McCall ⁴, Amber Gibson ⁴, Nitin Jain ², Fadi G Haddad ², Lewis F Nasr ², Kayleigh R Marx ³,
Caitlin Rausch ³, J Michael Savoy ³, Rebecca Garriss ², Farhad Ravandi ², Hagop Kantarjian ²

Affiliations + expand

PMID: 38212207 DOI: 10.1016/j.clml.2023.12.016

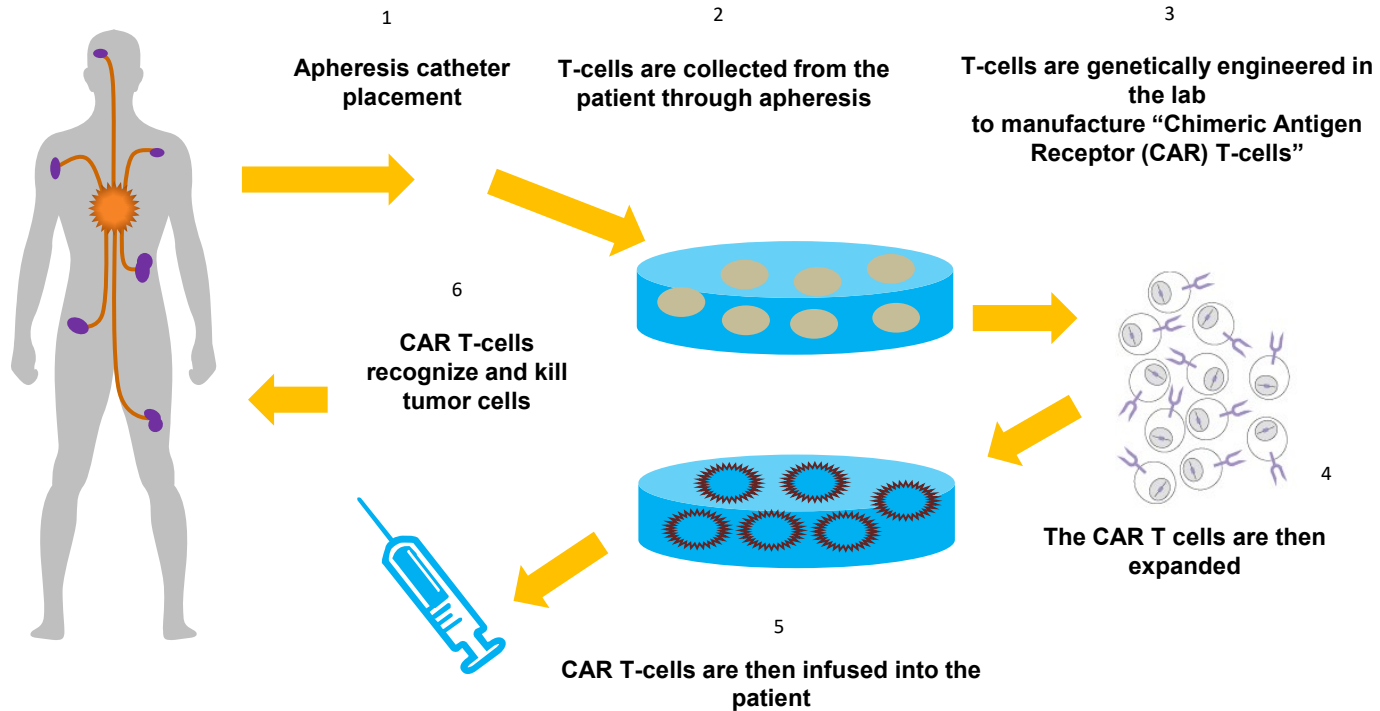
Mini-hyper CVD + CRIB (condensed rituximab, inotuzumab ozogamicin, and blinatumomab) for refractory pediatric B-acute lymphoblastic leukemia

David McCall ¹, Elias Jabbour ², Michael Roth ¹, Cesar Nunez ¹, Branko Cuglievan ¹

Affiliations + expand

PMID: 36031729 DOI: 10.1002/psc.29939

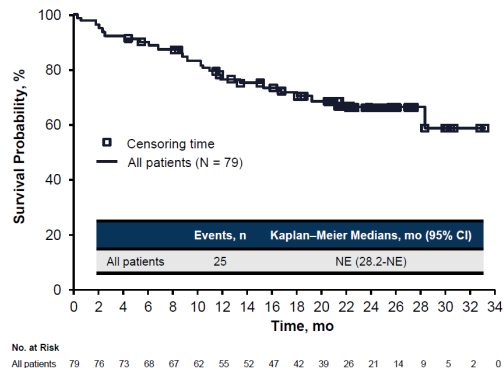
CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY: HOW IT WORKS



CAR T-CELL THERAPY IN ALL: PRESENT AND FUTURE CHALLENGES

- 75 patients
- 3-month remission rate of 81% and all MRD negative
- 6-month EFS: 73% OS: 90%
- 12-month EFS: 50% OS 76%
- CRS 73% and ICANS 40%

ELIANA: Median Overall Survival Not Reached¹



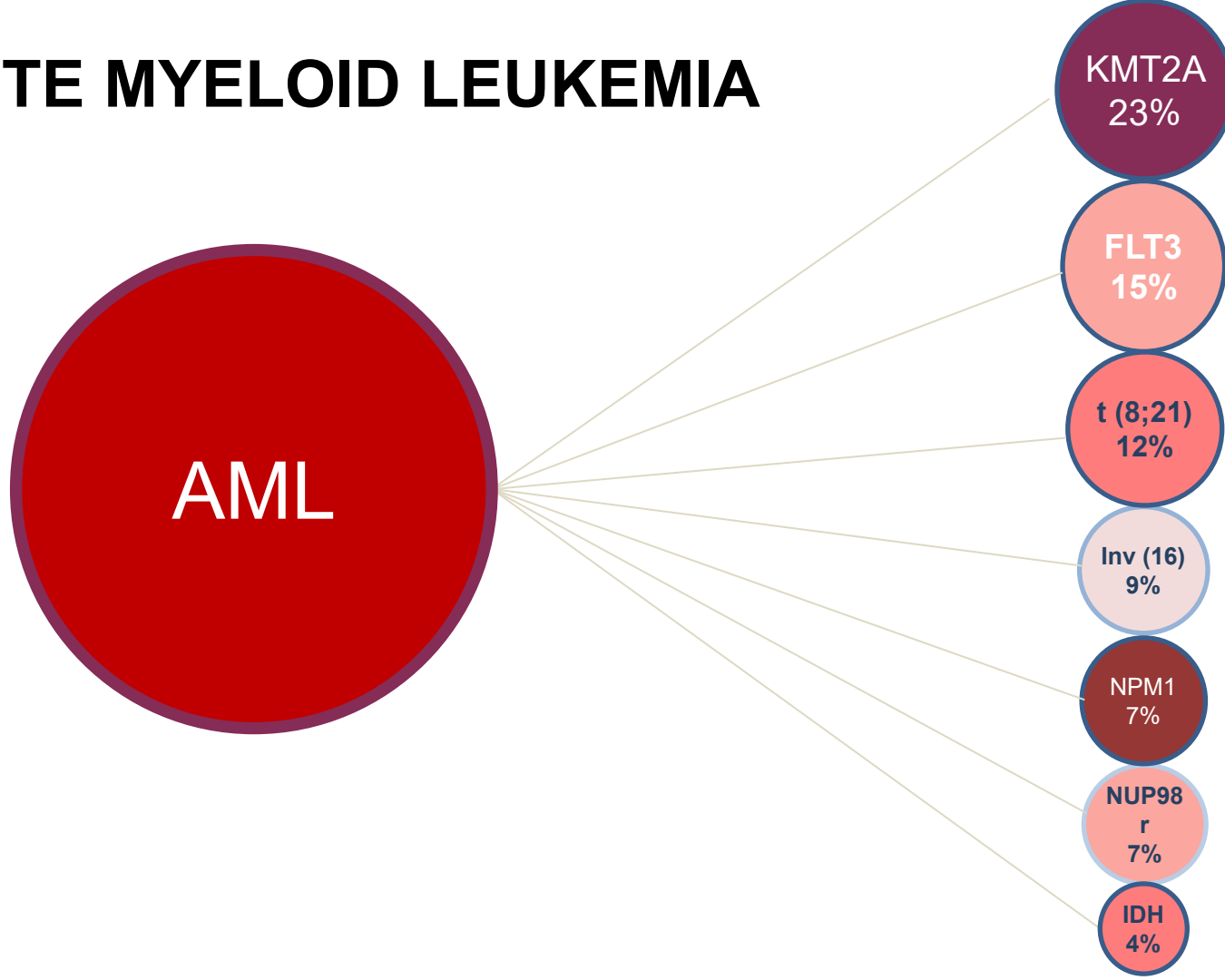
OS Rates Among Infused Patients

- **12 month:** 76% (95% CI, 65-85)
- **18 month:** 70% (95% CI, 58-79)
- **24 month:** 66% (95% CI, 54-76)

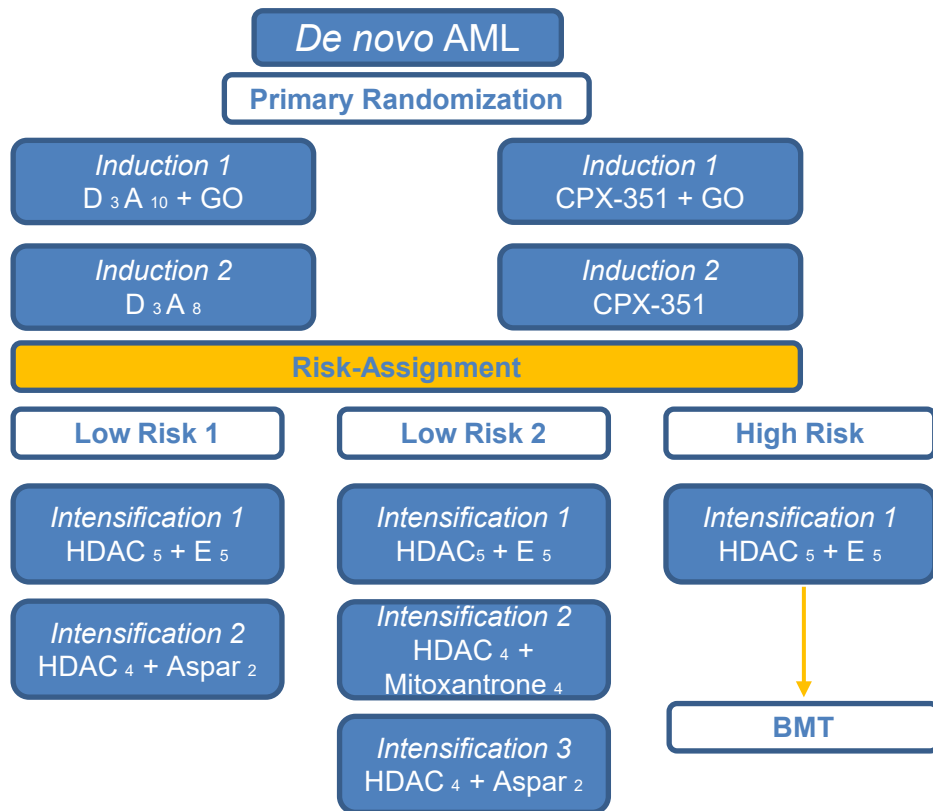
Note: All patients infused with tisagenlecleucel were included. Time is relative to infusion.
1. Grupp SA et al. ASH 2018. Abstract 895.

PeerView.com

ACUTE MYELOID LEUKEMIA



PEDI AML THERAPY IN US (COG)

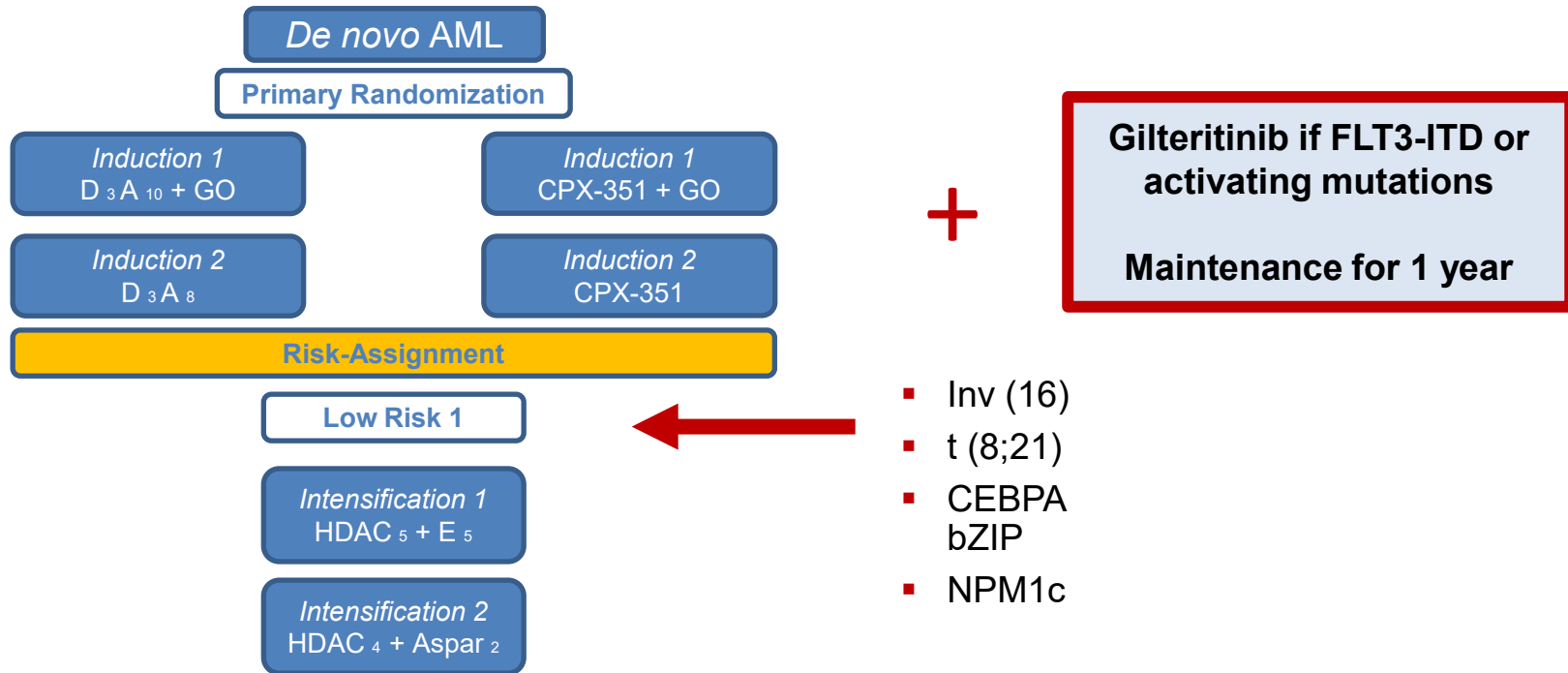


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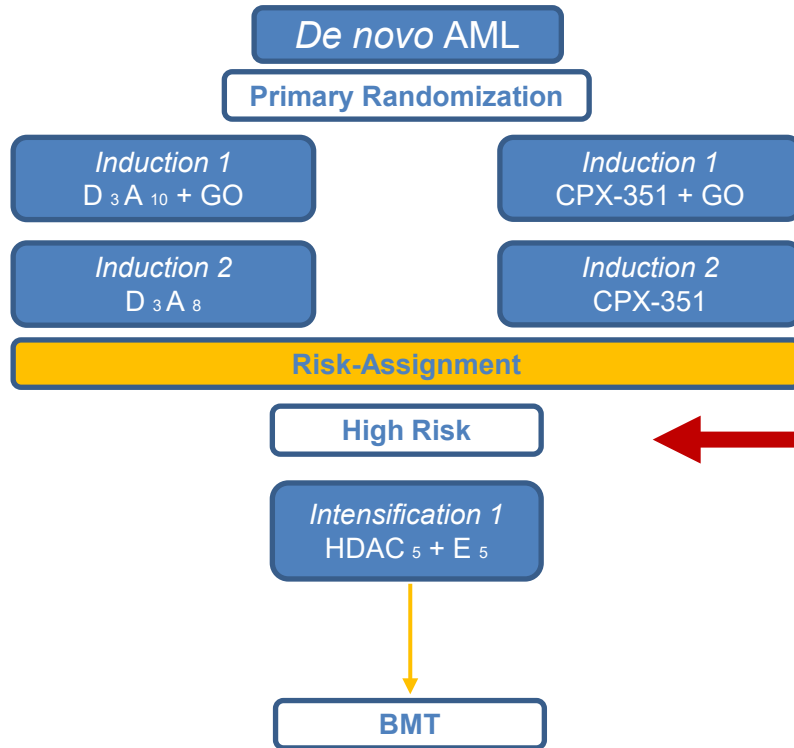
Gilteritinib if FLT3-ITD or activating mutations

Maintenance for 1 year

PEDI AML THERAPY IN US (COG)



PEDI AML THERAPY IN US (COG)



+

Gilteritinib if FLT3-ITD or activating mutations

Maintenance for 1 year

- KMT2Ar*
- NUP98r
- ETV6r or loss
- CBFA2T3-GLIS2
- Monosomy 5/Del (5q) or 7
- RAM phenotype
- MECOMr
- NPM1-MLF1
- DEK-NUP214
- KAT6A-CREBBP
- FUS-ERG



IMPORTANCE OF COMMUNICATION AND A PLAN

- Parents will instill a lot of trust with the medical team; therefore, it is of utmost importance to ensure a trusting and healing relationship not only with the patient, but also with the parents (when age appropriate).
- A lot of the anxiety of treatment comes from the unknown, taking the time to go over what side effects to expect at home and long-term effects will help ease a lot of this anxiety.
- Explain that once in survivorship, long-term follow-up is recommended to monitor for lifelong effects of chemotherapy (such as screening echocardiograms with anthracycline use).
- Reach out to Adolescent & Young Adult (AYA) groups to assist teens transitioning into adulthood and to provide college assistance.

Short- and Long-term Side Effects

QUIZ QUESTION!

Which of the following is the most common adverse effect of immunotherapies?

- a) Urinary frequency
- b) Alopecia
- c) Infusion-related reactions
- d) Altered mental status

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QUIZ QUESTION!

Which of the following is the typical recommended lifetime maximum anthracycline dosing?

- a) 1 gm/m²
- b) 450 mg/m²
- c) 0.5 g/m²
- d) 100 mg/m²

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TRADITIONAL CHEMOTHERAPIES: METHOTREXATE

Adverse effects from methotrexate:

- Acute kidney injury
- Mucositis
- Methotrexate toxicity
- Lower blood counts (neutropenia risk!)
- Nausea/abdominal pain
- Watch for medication interactions

Long-term adverse effects from methotrexate:

- Decline in neurocognitive function
- Relatively normal renal function
- Relatively normal bone mineral density

TRADITIONAL CHEMOTHERAPIES: VINCA ALKALOIDS

Vinca alkaloid side effects:

- Constipation
- Neuropathy
- Poor blink reflex
- Jaw pain
- Vinblastine typically has less neurotoxicity than Vincristine

Vinca alkaloid long-term side effects:

- Neuropathy, and neuropathic complaints, but reversible with time
- Motor function alterations
- Ocular and vocal cord palsies

TRADITIONAL CHEMOTHERAPIES: ANTHRACYCLINES

Anthracyclines:

- Cardiac toxicity
- Nausea
- Skin changes or hair loss

Anthracycline long-term effects:

- Cardiomyopathies (lifetime dose max)!
- Coronary artery disease & atherosclerosis

TRADITIONAL CHEMOTHERAPIES: CYCLOPHOSPHAMIDE

Side effects:

- Hemorrhagic cystitis
- Liver toxicity
- Kidney injury with or without hematuria
- Altered taste
- Nausea

Cyclophosphamide long-term effects:

- Increased risk of secondary malignancy
- Cardiotoxicities
- Fertility function
- Renal and liver dysfunction

TRADITIONAL CHEMOTHERAPIES: ASPARAGINASE

Asparaginase:

- Risk of infusion reaction
- Pancreatitis
- Hyperglycemia
- Hyperlipidemia
- Coagulopathy

Long-term effects of asparaginase:

- Chronic pancreatitis
- Dysregulation of glucose
- Dysregulation of lipids
- Chronic abdominal pain
- Growth changes

IMMUNOTHERAPY SIDE EFFECTS

Blinatumomab:

- Risk of infusion reaction
- Monitor for cytokine release syndrome
- Neurotoxicity can develop
- Encourage daily handwriting testing while admitted inpatient after initiating blina to evaluate for neurotoxicity.
- Neuro exams

Inotuzumab:

- Risk of infusion reaction
- Prolonged QT
- Alterations in liver function studies
- Ursodiol prophylaxis indicated
- Hepatic veno-occlusive disease

LONG-TERM SIDE EFFECTS

- Vaccinations – Check titers and revaccinate per institution policy/CDC
- HEENT – Routine dental visits, and routine eye exams
- CNS – Developmental/Learning delays, seizures
- CV – Cardiomyopathies (secondary to anthracycline use, the ‘rubicin’ medications)
- Endocrine – Growth, diabetes, bone health/density, thyroid studies if radiated
- Pulm – Pulmonary function testing if received chest radiation or underwent stem cell transplant
- Secondary Malignancies – MDS, therapy-associated AML

LONG-TERM SIDE EFFECTS

- Fertility concerns
- Psychosocial – Cancer and cancer treatment imparts lifelong trauma, ensure they are being followed with the appropriate mental health professionals for depression, PTSD, chronic pain, anxiety, etc.
 - Job prospects – Some jobs may discriminate against cancer survivors, survivorship clinics can assist with this
 - School & college – A lot of grants/scholarships available for cancer patients, additionally these may require learning accommodations due to treatment

QUIZ QUESTION!

Which of the following is a common long-term adverse effect of prolonged steroid use?

- a) Hearing changes
- b) Mood changes
- c) Allergic reactions
- d) Glucose dysregulation

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Future



Transforming treatment and care for kids with blood cancer.

LLS PedAL

**LLS PedAL: The First-of-its-Kind Global
Master Clinical Trial for Pediatric Acute Leukemia**

CANCER CLINICAL TRIAL ELIGIBILITY CRITERIA: MINIMUM AGE CONSIDERATIONS FOR INCLUSION OF PEDIATRIC PATIENTS



Guidance for Industry and IRBs

Additional copies are available from:

Office of Communications, Division of Drug Information

Center for Drug Evaluation and Research

Food and Drug Administration

10001 New Hampshire Ave., Hillandale Bldg., 4th Floor Silver Spring, MD 20993-0002

Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353;

*Email: druginfo@fda.hhs.gov <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>
and/or*

Office of Communication, Outreach, and Development

Center for Biologics Evaluation and Research

Food and Drug Administration

10903 New Hampshire Ave., Bldg. 71, rm. 3128 Silver Spring, MD 20993-0002

Phone: 800-835-4709 or 240-402-8010;

Email: ocod@fda.hhs.gov <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>

U.S. Department of Health and Human Services

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Center for Drug Evaluation and Research (CDER)

Center for Biologics Evaluation and Research (CBER)

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Adult Leukemia

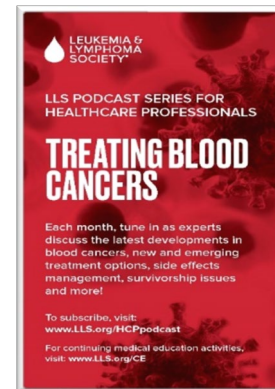
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 - Staying Connected: www.LLS.org/StayingConnected
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
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- ❑ LLS Research Grant Programs: www.LLS.org/Research or email researchprograms@LLS.org



Facts About Blood Cancer Survivorship Treatment and Ongoing Patient Care

Facts About Pediatric Acute Leukemia

Facts About Acute Myeloid Leukemia (AML)

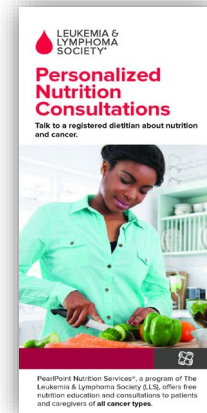
**STAYING CONNECTED:
FACILITATING THE LEARNING EXPERIENCE
DURING AND AFTER CANCER TREATMENT**

LEUKEMIA & LYMPHOMA SOCIETY



FREE LLS RESOURCES FOR PATIENTS

- ❑ **Information Specialists** (IRC) – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges.
- ❑ **Clinical Trial Nurse Navigators** (CTSC) – provide personalized service for patients seeking treatment in a clinical trial, sift through and provide information to bring back to the HC team www.LLS.org/CTSC
- ❑ **Nutrition Education Services Center** (NESC) – one-on-one **free** nutrition education and consultations to patients of all cancer types with RDs who have expertise in oncology nutrition www.LLS.org/Nutrition
- ❑ **Reach out Monday–Friday, 9 am to 9 pm ET**
 - Phone: 800.955.4572
 - Live chat: www.LLS.org/IRC
 - Email: LLS.org/ContactUs
 - HCP Patient Referral Form: www.LLS.org/HCPreferral



FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

❑ www.LLS.org/ChildhoodCancer

❑ **Webcasts, Videos, Podcasts, booklets:**

- www.LLS.org/Webcasts
- www.LLS.org/EducationVideos
- www.LLS.org/Podcast
- www.LLS.org/Booklets

❑ **Support Resources**

- Financial Assistance: www.LLS.org/Finances
 - Urgent Need
 - Patient Aid
 - Travel Assistance
- Other Support: www.LLS.org/Support
 - LLS Regions
 - Online Weekly Chats Facilitated by Oncology SW
 - LLS Community Social Media Platform
 - First Connection Peer to Peer Program

CHILDHOOD BLOOD CANCER

CHILDREN AND YOUNG ADULTS

- Childhood Blood Cancer
 - Coping With Cancer
 - What to Tell Your Child
 - Blood Cancer and Treatment Options
 - Caring for Your Child During Treatment
 - School
 - Helping Siblings Cope
 - Coping Tips for Parents
 - Just for Teens
- + Young Adults
 - Caring For Kids And Adolescents Workbook
 - + Long-Term And Late Effects Of Treatment For Childhood Cancer Survivors

Hearing that your child has cancer is terrifying. Today, however, most childhood blood cancer patients can expect to have full and productive lives. Thanks to new and improved therapies, survival rates for childhood blood cancer have improved significantly over the past several decades. In addition, doctors, nurses and researchers continue to search for the causes of childhood leukemia and lymphoma to develop even better treatments and labor therapies to decrease toxic side effects. Social workers, psychologists, psychiatrists and other health professionals are also working to understand how to help children and families manage cancer and its treatment and maintain a good quality of life.

What Does Caring for a Child with Blood Cancer Look Like?

As a parent or guardian, you already provide for your child in many ways, but caring for a child with cancer brings new challenges. You will be spending a lot of time with your child at medical appointments and working closely with the members of your child's healthcare team to ensure your child is getting the best possible care.

Depending on the treatment plan, your child may need to stay at the hospital overnight (or even for weeks) to receive treatment. You may have to deal with an emergency situation, such as a medical crisis requiring a trip to the emergency room. After your child's cancer treatment is completed, you will need to be vigilant about follow-up care and watch for long-term and late effects of treatment. You will also have to help your child when he or she returns to school.

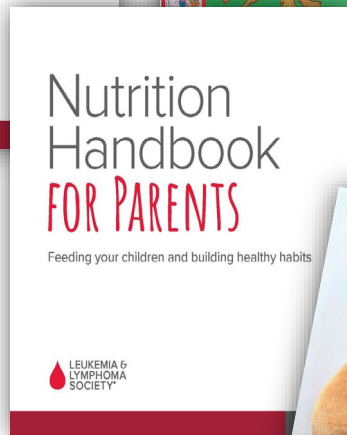
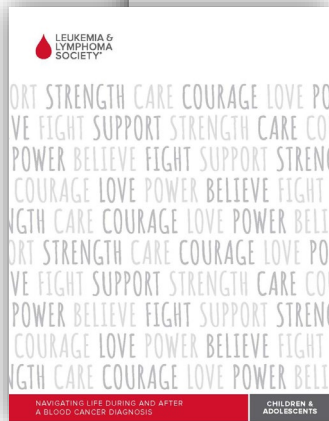
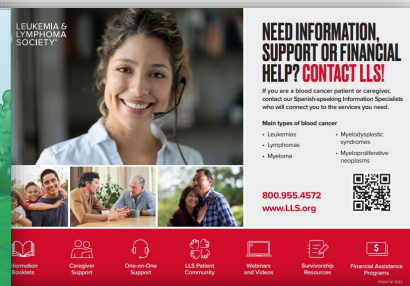
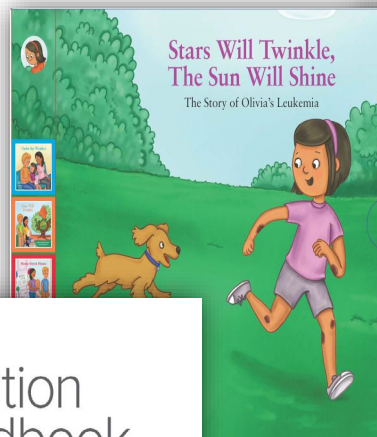
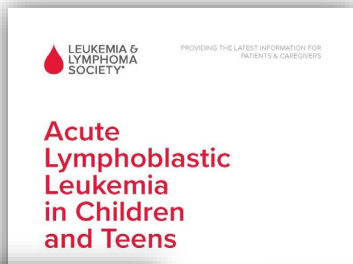
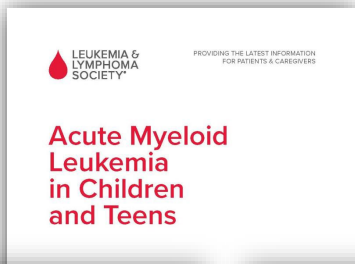
In addition to caring for a child who has cancer you may have other children, as well as other family members, who need your time and support too.

Equally important, you need to look after yourself during this difficult time.

Caregiving Strategies



FREE LLS RESOURCES FOR YOUR PATIENTS AND CAREGIVERS



BOOKLETS AND FACT SHEETS

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Spanish – www.LLS.org/Materiales

Q & A

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