Adult lymphoblastic lymphoma
Lymphoma Tumor Board
February 3, 2017

Diagnosis

- Lymphoblastic Lymphoma (LBL) is rare
- Sub-type of lymphoma that is generally of T-cell origin
- Comprises about 2% of all NHLs in adults
- Characteristics are almost identical to acute lymphoblastic leukemia (ALL)
- Patients with predominately nodal disease at presentation are classified as LBL whereas those with primarily disease in the marrow or peripheral blood are classified as ALL.
- Historically, no standard of care treatment specifically designed for LBL
- Pathology:
  - IHC panel: CD45 (LCA), CD19, CD20, CD79a, CD3, CD2, CD5, CD7, TdT, CD1a, CD10, or Cell surface marker analysis by flow cytometry: kappa/ lambda, CD45, CD3, CD5, CD19, CD10, TdT, CD13, CD33, CD1a, cytoplasmic CD3, CD22, myeloperoxidase

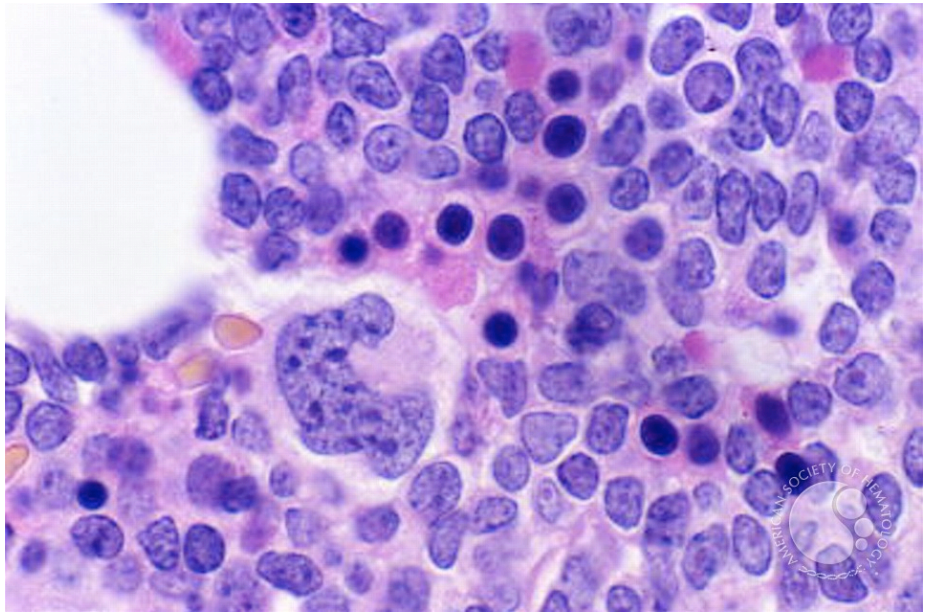
Classification

ALL – CLASSIFICATION WHO

- Uses immunophenotypic classification :
  - Acute lymphoblastic leukemia/lymphoma (Former Fab L1/L2)
    - **Precursor B** acute lymphoblastic leukemia/lymphoma.
      - Cytogenetic subtypes:
        - t(12;21)(p12,q22) TEL/AML-1
        - t(1;19)(q23;p13) PBX/E2A
        - t(9;22)(q34;q11) ABL/BCR
        - T(V,11)(V;q23) V/MLL
    - **Precursor T** acute lymphoblastic leukemia/lymphoma
  - Burkitt's leukemia/lymphoma (Former FAB L3) (mature B cell ALL)
  - Biphenotypic acute leukemia (2 to 5%)

Pathology

A.



B.

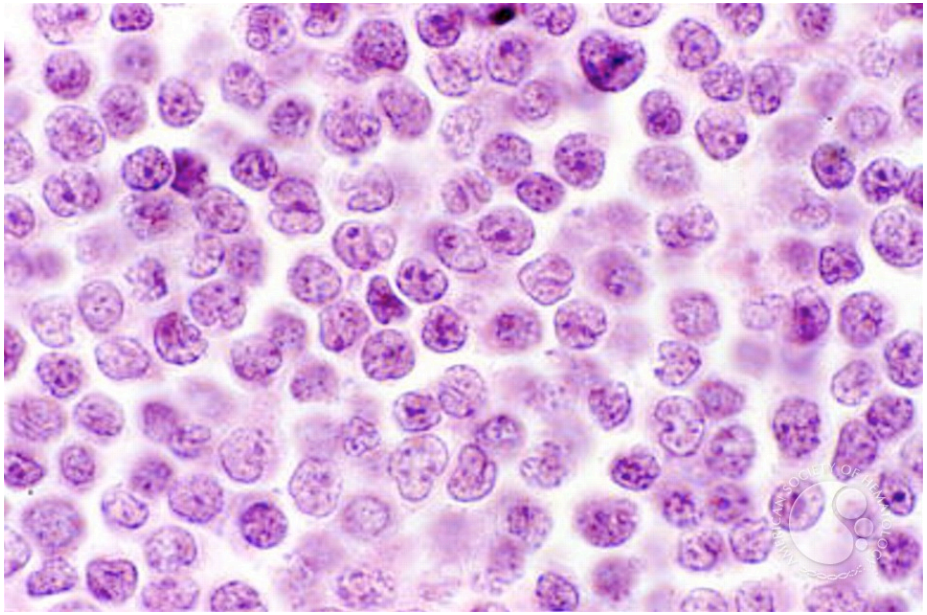


Image A. T-cell lymphoblastic lymphoma/leukemia in bone marrow biopsy. Neoplastic lymphocytes surround residual megakaryocytes and erythroid precursors. H&E section of formalin fixed tissue.

Image B. T-cell lymphoblastic lymphoma/leukemia. Cytology of lymphoblasts reveals medium sized cells with delicate unclumped chromatin, convoluted nuclear membrane and small but distinct nucleoli.

Treatment

- Adaptation of pediatric protocols of intensive chemotherapy and CNS prophylaxis has led to marked improvements in outcomes in adults

- Numerous chemotherapy/radiotherapy regimens are simila r in dose and schedule to ALL regimens

- Common features of these regimens include:
  - Induction therapy
  - CNS prophylaxis
  - Consolidation therapy
  - Subsequent maintenance therapy for 12 to 18 months

- Long-term disease-free survival rates between 40-70%

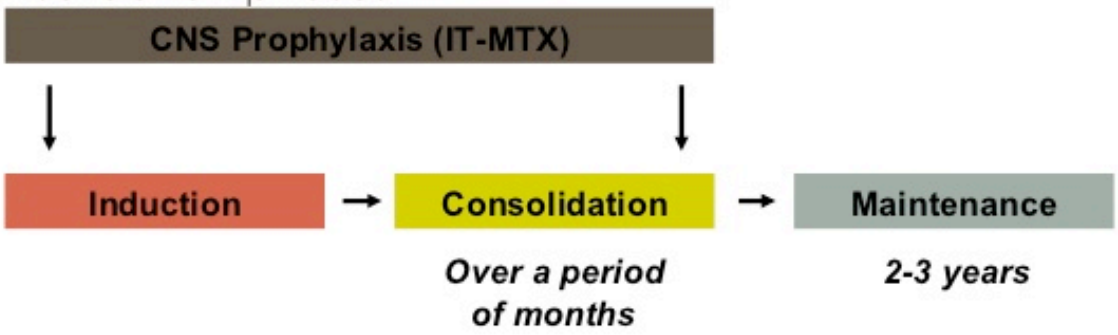
The landscape of genetic alterations in T-ALL

Mark R. Litzow, and Adolfo A. Ferrando Blood 2015;126:833-841

Treatment

ALL: TYPICAL TREATMENT

- Primary objective : to achieve and maintain a complete remission (CR)
- Induction, consolidation, maintenance phases
  - CNS prophylaxis with IT-MTX during induction and consolidation phases



Treatment

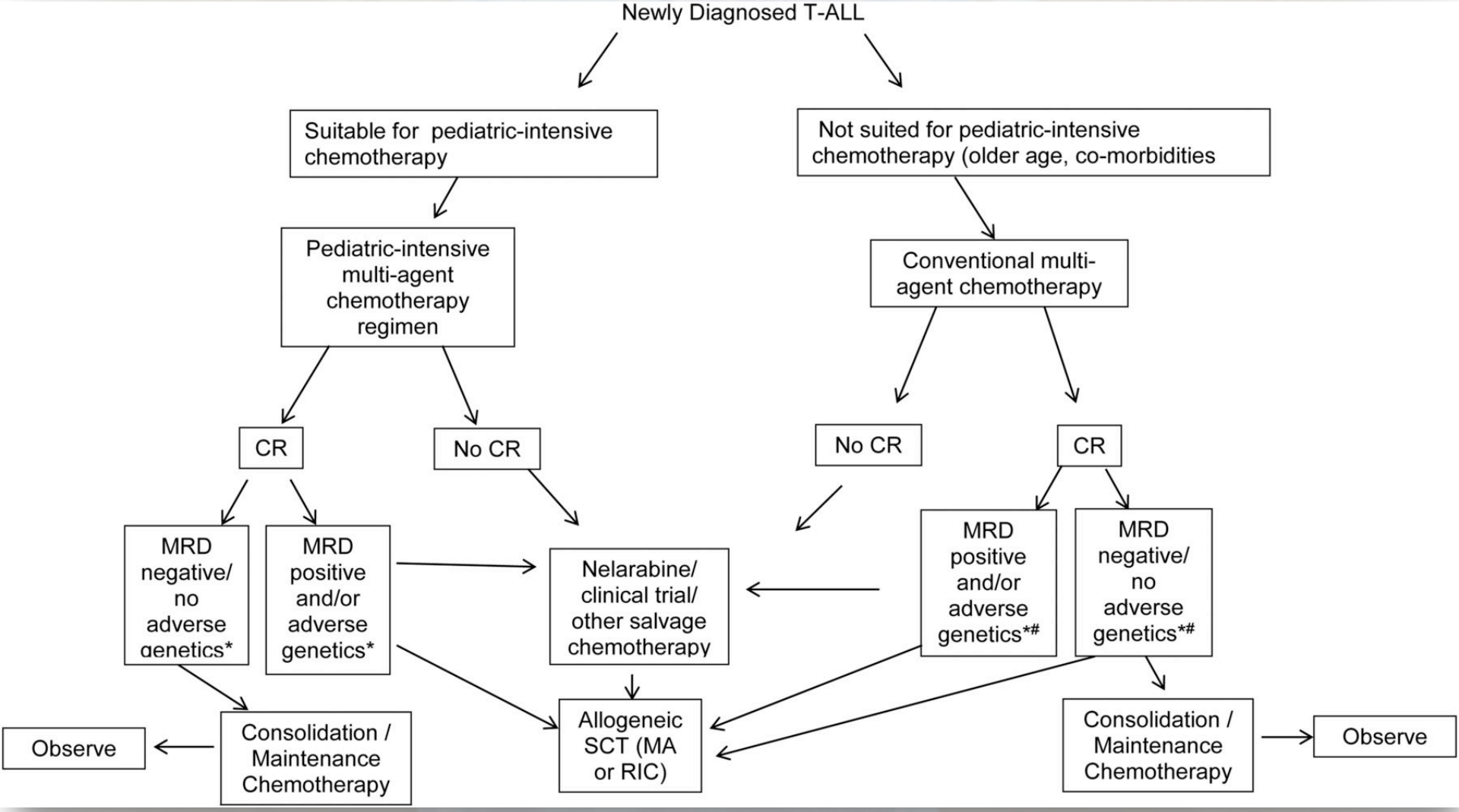
Table 1

Intensive Induction Regimens for Adult Lymphoblastic Lymphoma

Author	Regimen	N	Response Rate	Failure-Free Survival/ Relapse-Free Survival	Overall Survival
Coleman et al [11]	Two ALL-type protocols with intensified CNS	44	100%	3-yr FFS = 56%	NA
Slater et al [12]	Various ALL protocols	51	80% CR for "nonleukemic"; 77% CR for leukemic	NA	5-yr actuarial OS = 45%
Bernasconi et al [13]	Various ALL protocols	31	77% OR	3-yr RFS = 45%	3-yr OS = 59%
Levine et al [16]	Modified LSA_2L_2	15	73% CR; 27% PR	5-yr actuarial FFS = 35%	5-yr actuarial OS = 40%
Weinstein et al [17]	APO	21	95% CR	3-yr actuarial FFS = 58%	5-yr actuarial OS = 69%
Hoelzer et al [18]	Two ALL-type protocols, both including CNS and	45	93% CR	7-yr actuarial DFS = 62%	7-yr actuarial OS = 51%
Thomas et al [19]	HyperCVAD	33	91%	3-yr PFS = 66%	3-yr OS = 70%
Jabbour et al [20]	LMT-89 (ALL-type induction regimen derived	27	85% OR	5-yr FFP = 44%	5-yr OS = 63%
Song	"Hybrid" NHL/ALL regimen	34	100% OR	4-yr EFS = 68%	4-yr OS = 72%

ALL = acute lymphoblastic leukemia; APO = doxorubicin (Adriamycin), prednisone, vincristine (Oncovin); CHOP = cyclophosphamide, hydroxydaunomycin, vincristine, prednisone; CNS = central nervous system; CR = complete response; DFS = disease-free survival; EFS = event-free survival; FFP = freedom from progression; FFS = failure-free survival; HyperCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytarabine, methotrexate; IPI = International Prognostic Index; NA = not available; NHL = non-Hodgkin lymphoma; OR = overall response; PR = partial response; RFS = relapse-free survival; SCT = stem cell transplantation.

Treatment

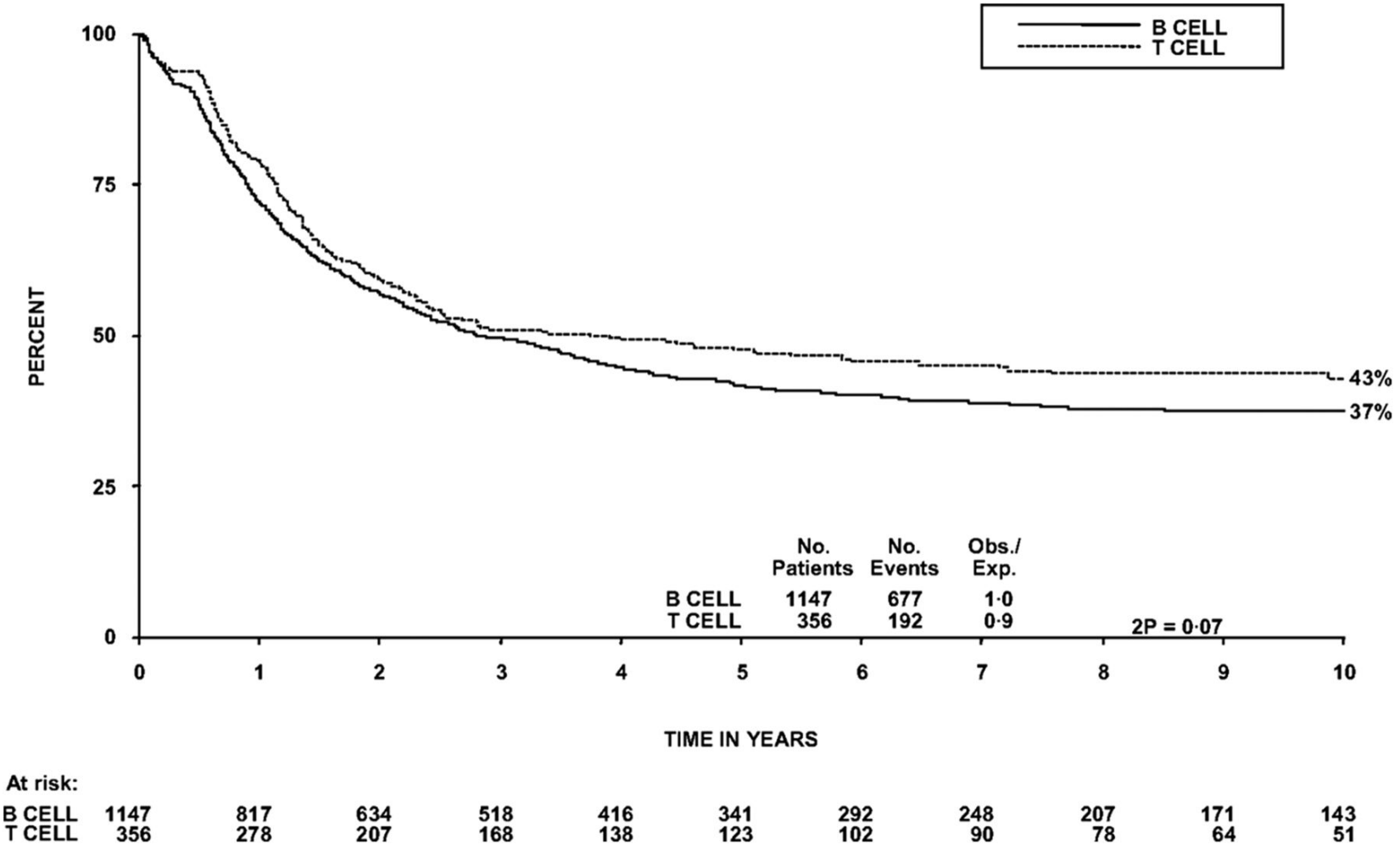


Blood 2015 126:833-841; doi: https://doi.org/10.1182/blood-2014-10-551895

Supportive care

- Allopurinol is recommended for the first 10 days of induction therapy to prevent hyperuricemia.
- Antimicrobial prophylaxis, antiviral and *Pneumocystis jiroveci* pneumonia prophylaxis throughout treatment.
- Fungal prophylaxis should include mold coverage throughout induction therapy.
  - Broader spectrum azole antifungals should be used with caution when using vincristine.
- Asparaginase-related toxicities
  - Asparaginase-related hypersensitivity reactions can occur in 20% of children and adults.

OS from the diagnosis of patients with B- vs T-ALL in the UKALLXII/E2993 trial



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