Adult T-cell lymphoblastic leukemia/lymphoma

Lymphoma Tumor Board

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WHO / Revised European American Lymphoma (REAL) Classification

B-cell lymphomas(80% - 85%)	T-cell lymphomas (15% - 20%)
• Diffuse large B-cell lymphoma • **Follicular lymphoma** • **Chronic lymphocytic leukemia** /small lymphocytic lymphoma • Mantle cell lymphoma • Marginal zone B-cell lymphomas • Burkitt lymphoma • Lymphoplasmacytic lymphoma (Waldenstrom macroglobulinemia) • Hairy cell leukemia • Primary central nervous system (CNS) lymphoma	• Precursor T-lymphoblastic lymphoma/leukemia • Peripheral T-cell lymphomas • Cutaneous T-cell lymphomas (mycosis fungoides, Sezary syndrome, and others) • Adult T-cell leukemia/lymphoma • Angioimmunoblastic T-cell lymphoma • Extranodal natural killer/T-cell lymphoma, nasal type • Enteropathy-associated intestinal T-cell lymphoma (EATL) • Anaplastic large cell lymphoma (ALCL) • Peripheral T-cell lymphoma, unspecified

Diagnosis of T-cell lymphoblastic leukemia/lymphoma

- 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 very similar to acute lymphoblastic leukemia (ALL)
- *Patients with predominantly 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 – antigens usually evaluated at time of diagnosis:
  - CD45 (LCA), CD3, CD2, CD5, CD7, TdT, CD1a, CD10, CD19, CD20, CD79a, kappa/lambda, CD13, CD33, myeloperoxidase

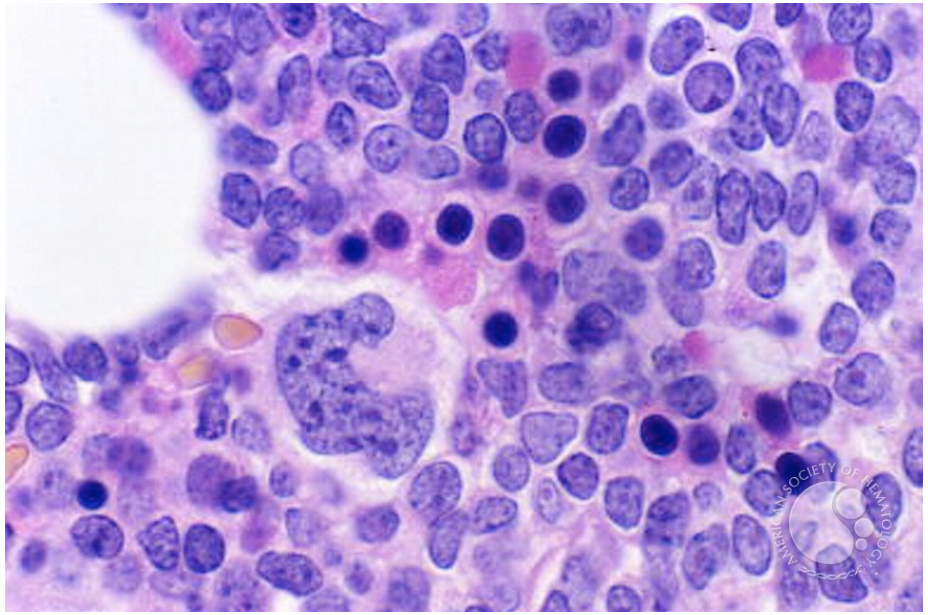
Classification of ALL

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 of T-cell lymphoblastic leukemia/lymphoma

A.



B.

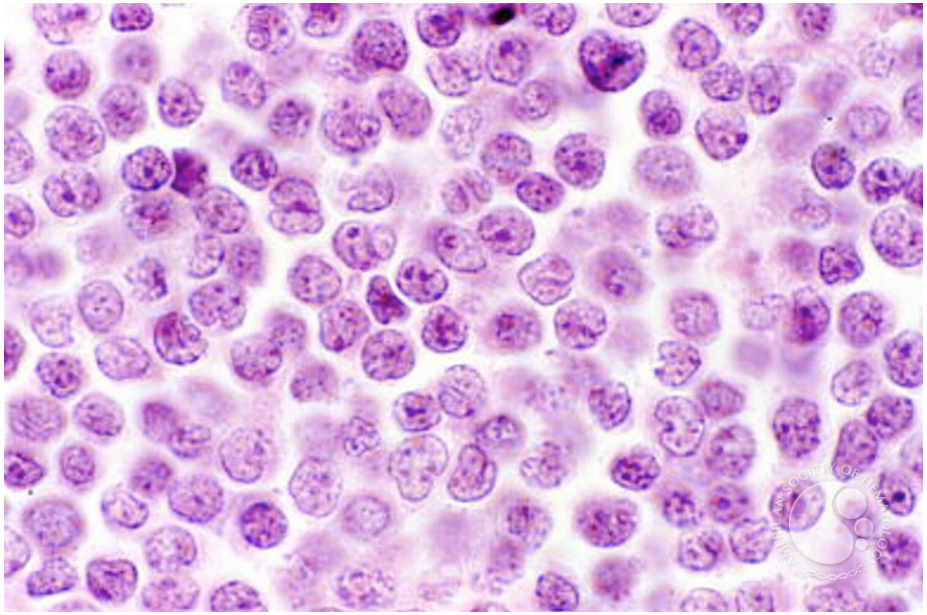


Image A. T-cell lymphoblastic lymphoma/leukemia in bone marrow biopsy. Neoplastic lymphocytes surround residual megakaryocytes and erythroid precursors. H&E section of formalin fixed tissue.

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.

Immunophenotype of T-cell leukemia/lymphoma

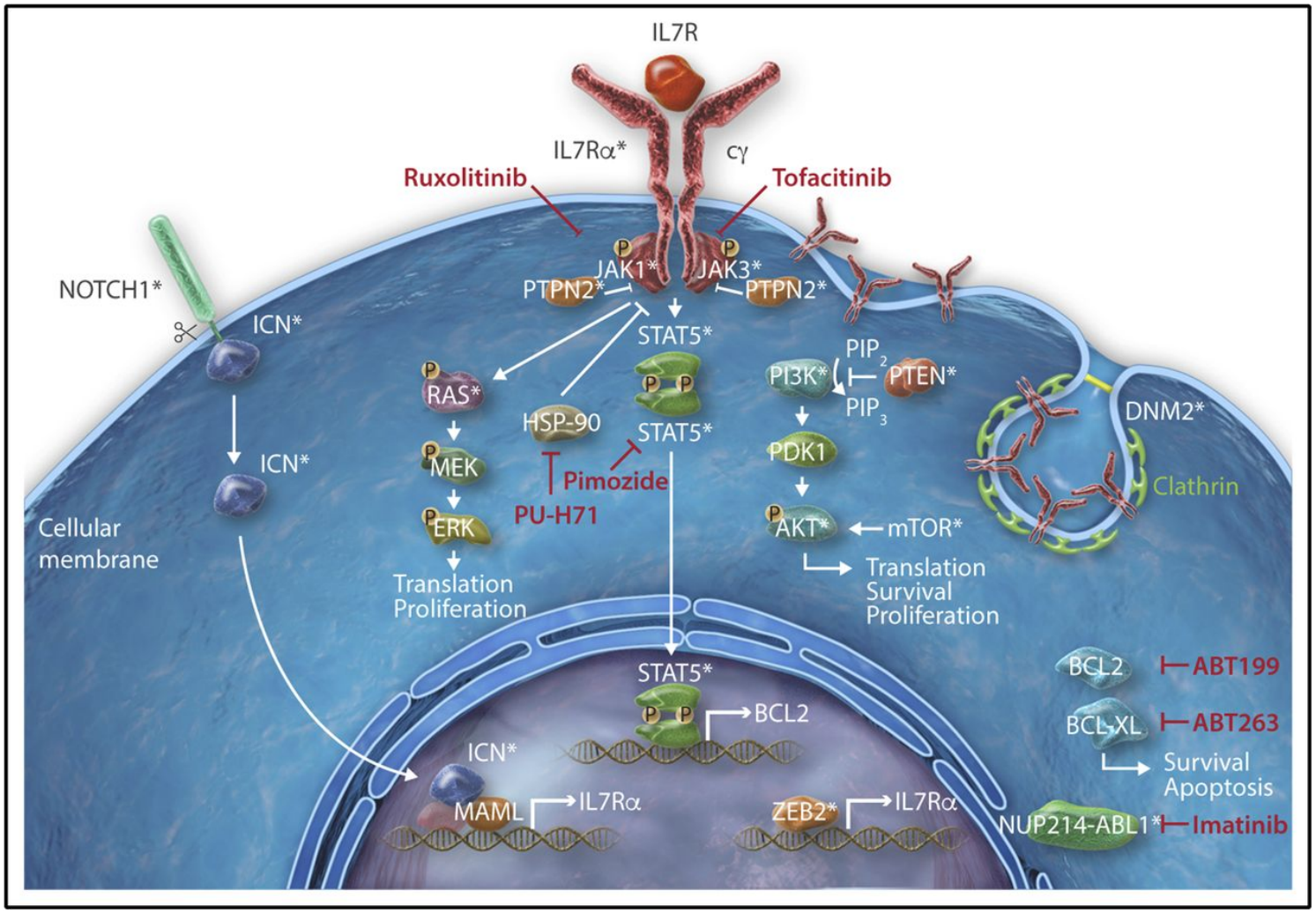
Table 1. T-cell CD antigen expression in pro-, pre-, cortical (thymic), and mature T-cell ALL cyCD3 indicates cytoplasmic CD3; sCD3, surface CD3

	cyCD3	CD7	CD5	CD2	CD1a	sCD3	CD34
Pro-T	+	+	—	—	—	—	±
Pre-T	+	+	+	+	—	—	±
Cortical (thymic)	+	+	±	±	+	±	—
Mature	+	+	±	+	—	+	—

The landscape of genetic alterations in T-ALL

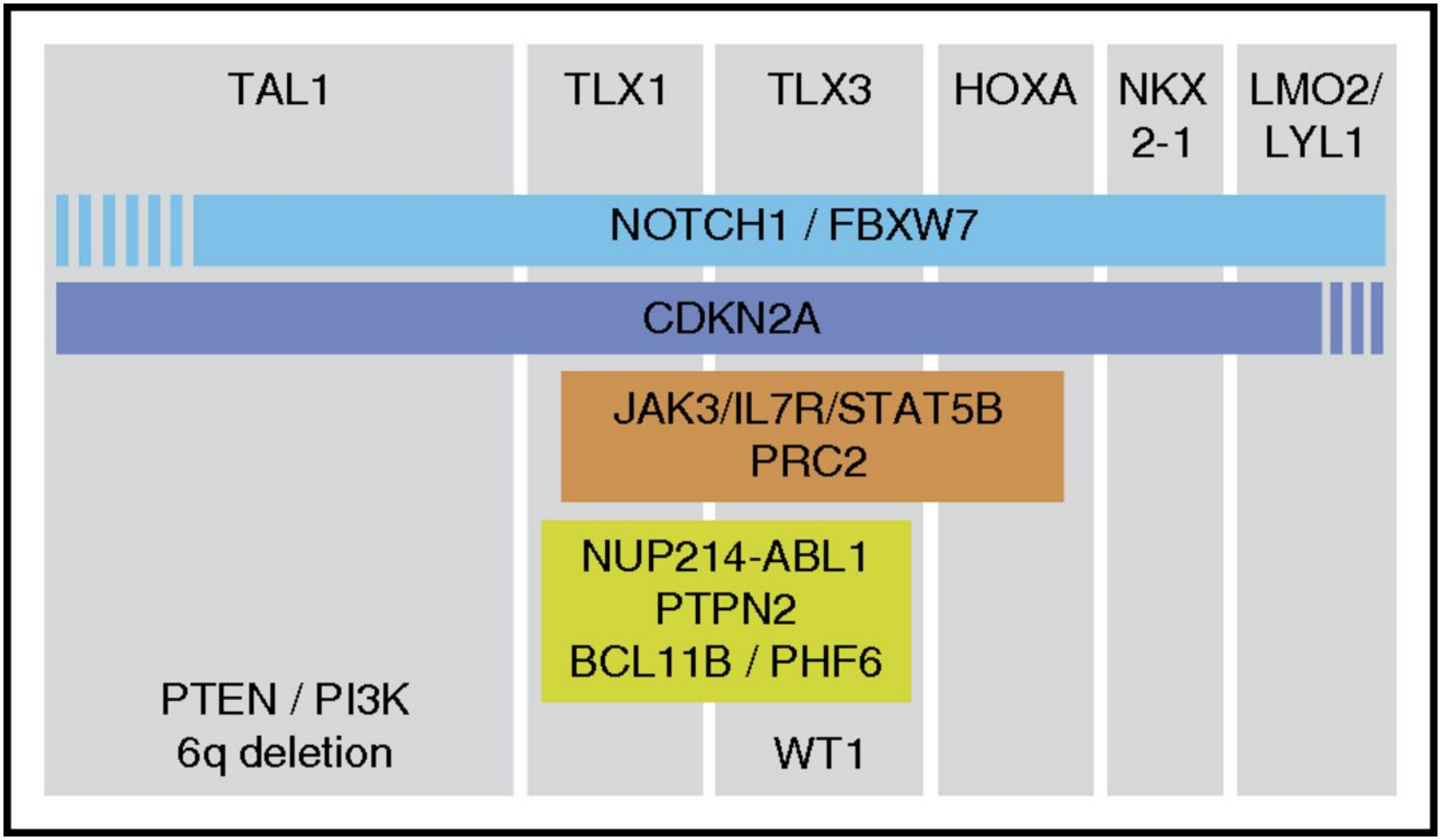
Mark R. Litzow, and Adolfo A. Ferrando Blood 2015;126:833-841

Deregulation of the JAK-STAT signaling cascade in T-ALL



Tiziana Girardi et al. Blood 2017;129:1113-1123

Representation of the cooperation of oncogenic events

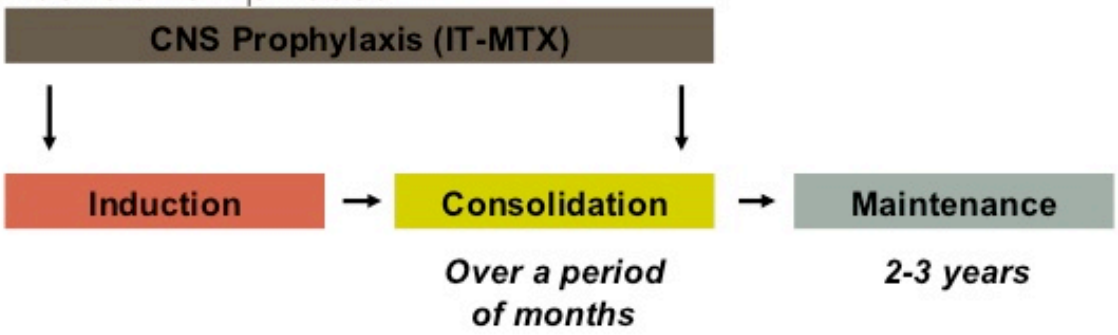


Tiziana Girardi et al. Blood 2017;129:1113-1123

Treatment of ALL - general principles

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 of T-cell lymphoblastic leukemia/lymphoma

- Adaptation of pediatric protocols of intensive chemotherapy and CNS prophylaxis has led to marked improvements in outcomes in adults
- Numerous chemotherapy/radiotherapy regimens are similar 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%

Treatment

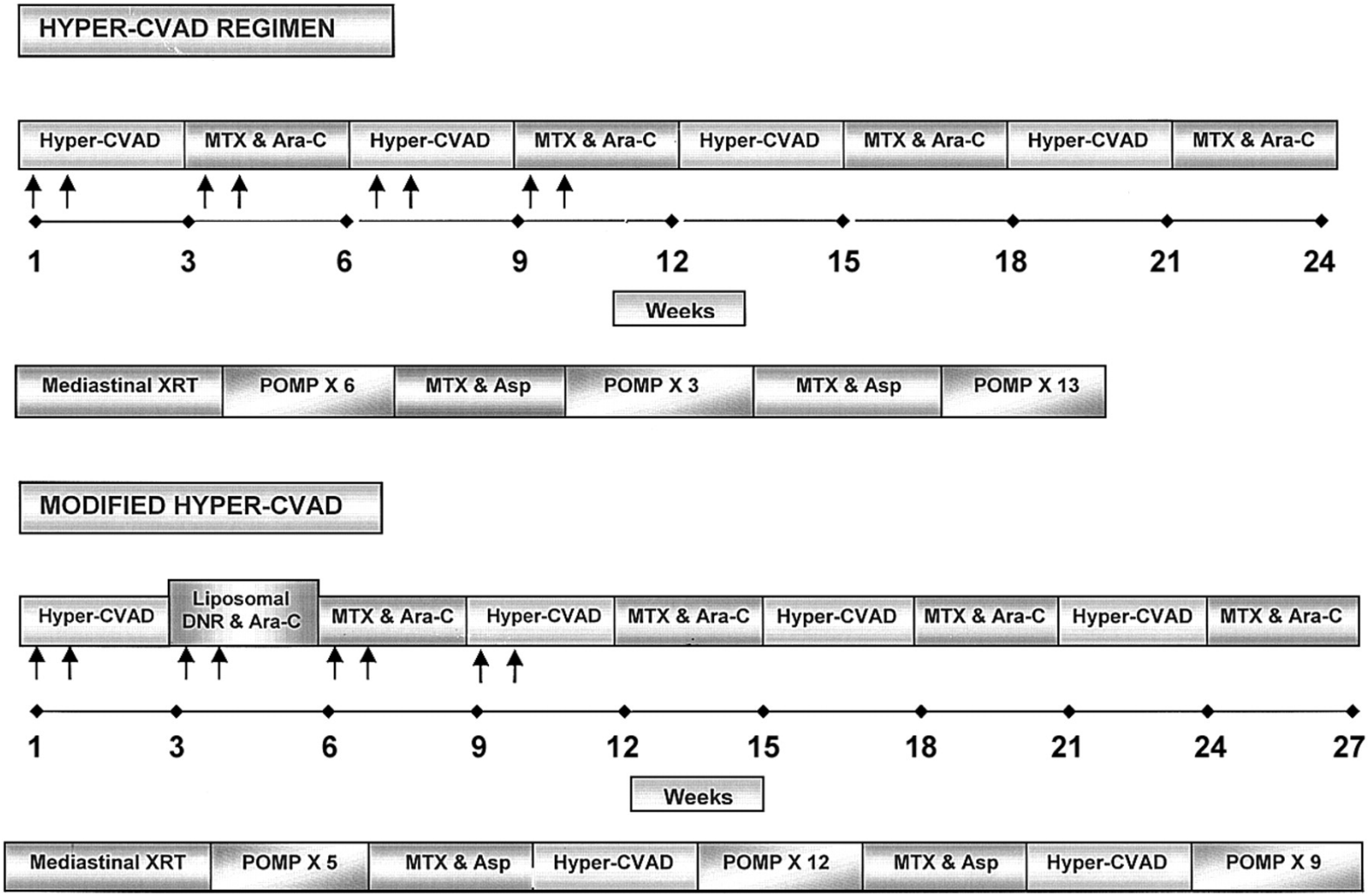
Table 1

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%

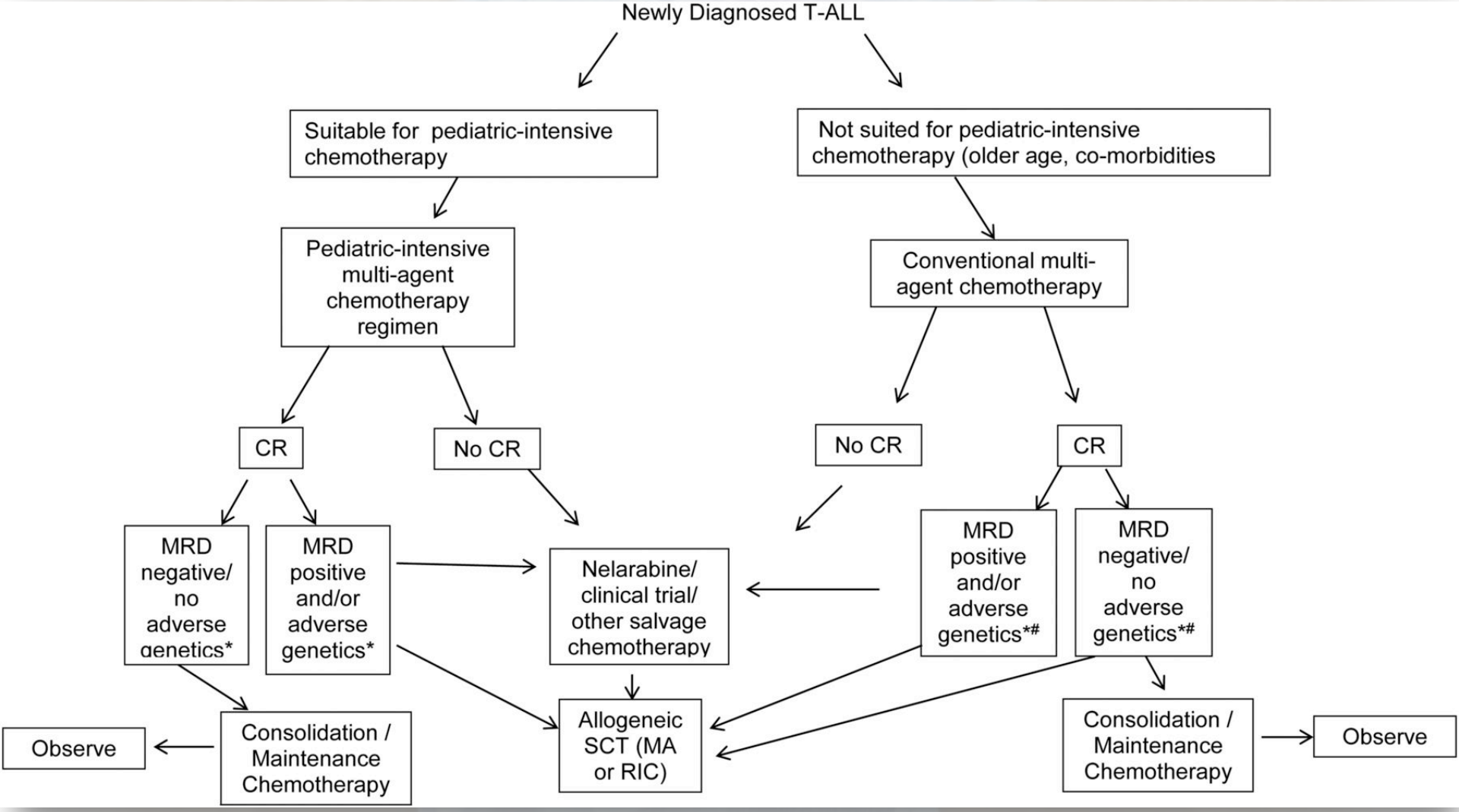
ALL = acute lymphoblastic leukemia; APO = doxorubicin (Adriamycin), prednisone, vincristine (Oncovin); CHOP = cyclophosphamide, hydroxydaunomycin, vincristine, prednisone; CNS = central nervous system; CR = complete response; DFS = disease-free survival; EFS = event-free survival; FFP = freedom from 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.

Schema for the hyper-CVAD and modified hyper-CVAD regimens



Deborah A. Thomas et al. Blood 2004;104:1624-1630

Treatment

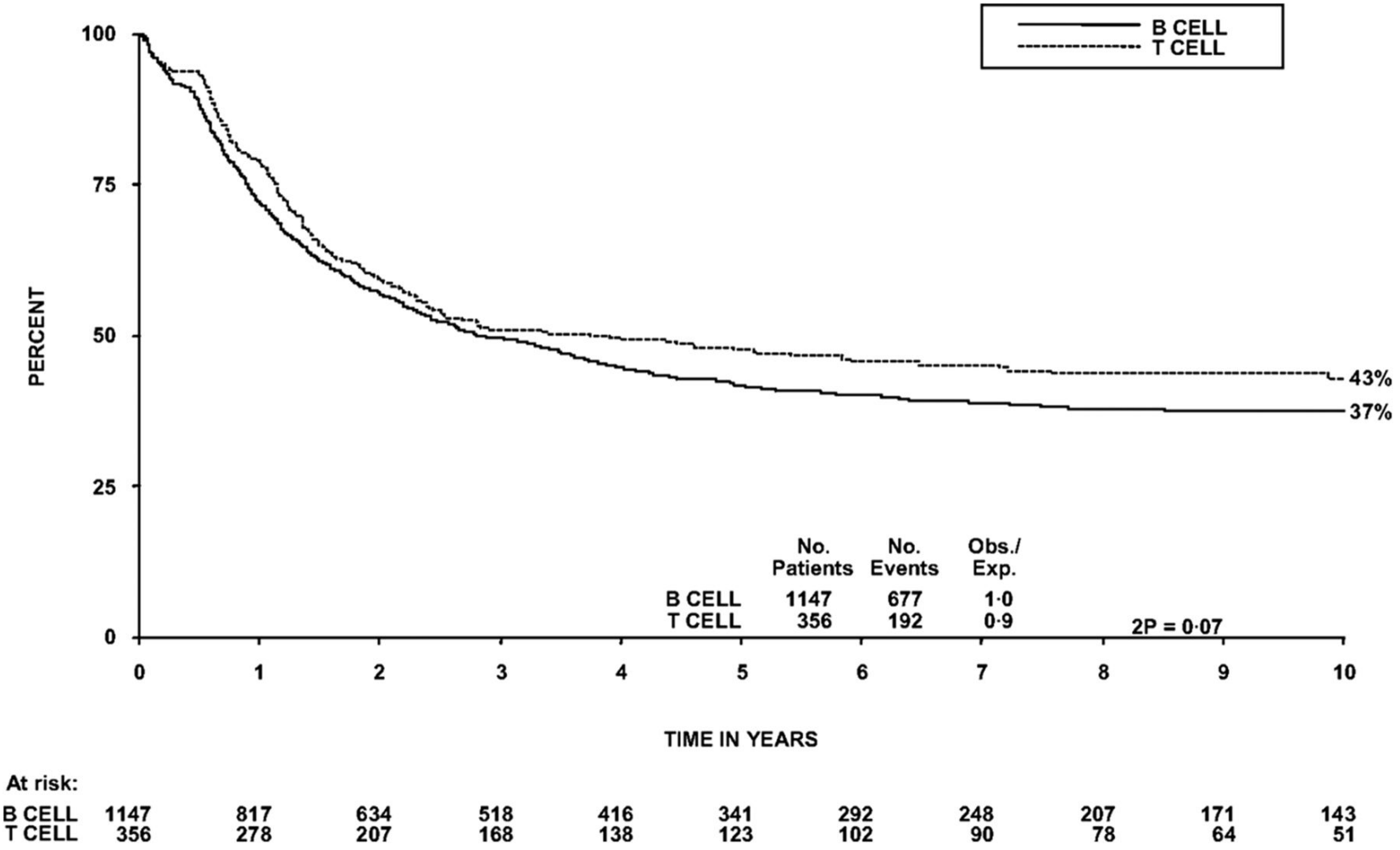


Blood 2015 126:833-841; doi: https://doi.org/10.1182/blood-2014-10-551895

Supportive care

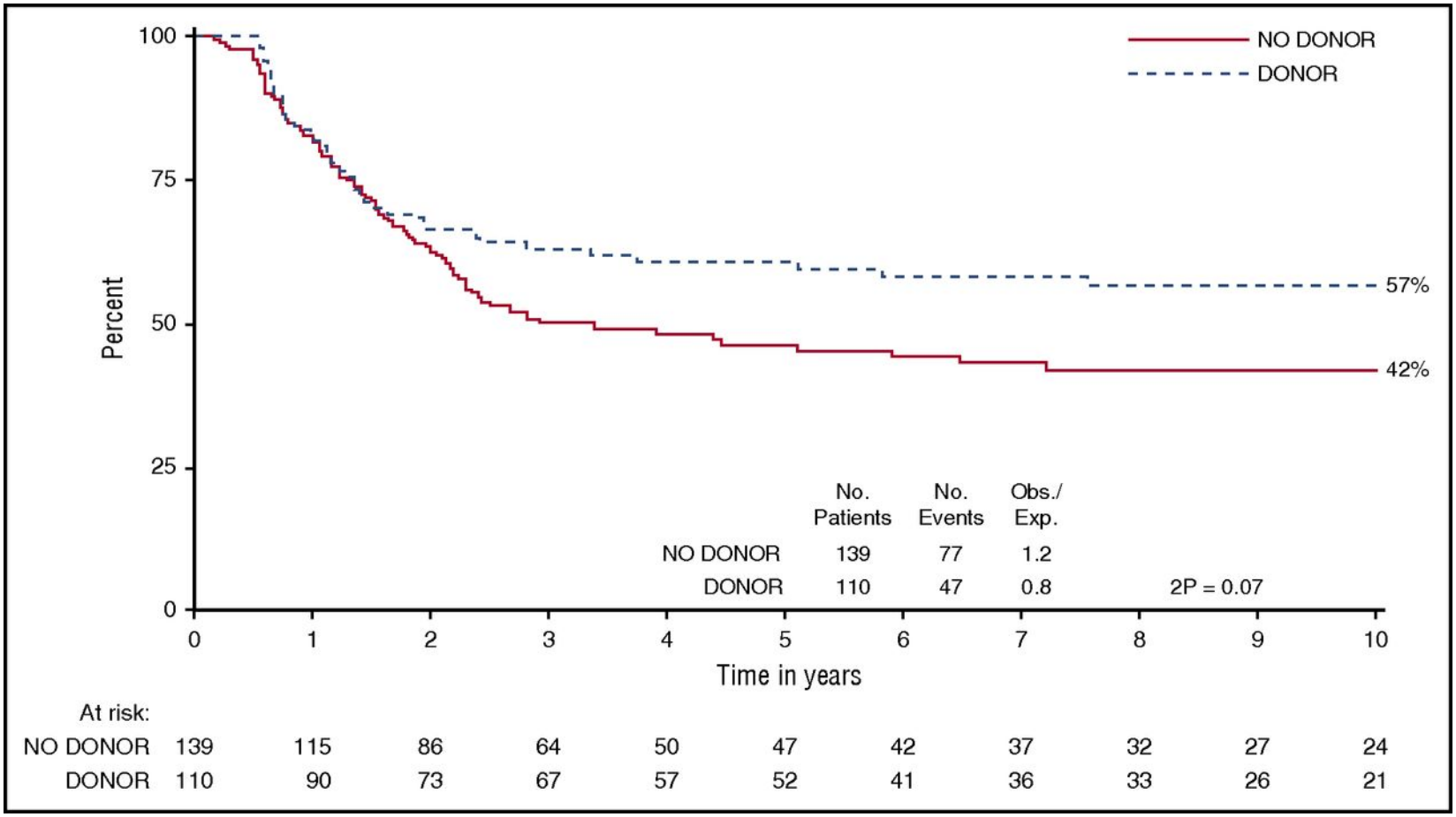
- Allopurinol is recommended for the first 10 days of induction therapy to prevent hyperuricemia.
- Antimicrobial prophylaxis, antiviral and *Pneumocystis jiroveci* pneumonia prophylaxis throughout treatment.
- Fungal prophylaxis should include mold coverage throughout induction therapy.
  - Broader 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



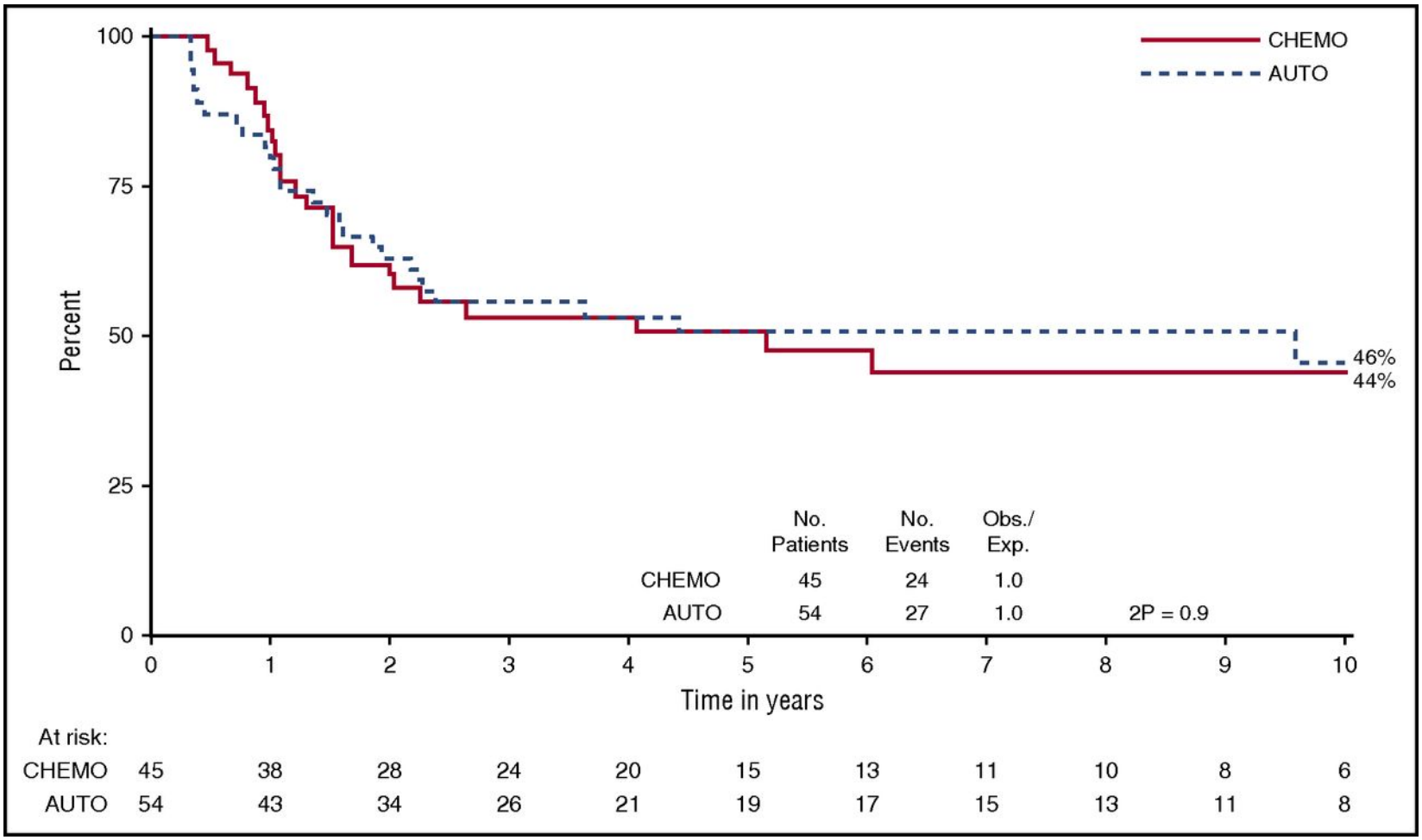
Mark R. Litzow, and Adolfo A. Ferrando Blood 2015;126:833-841

Comparison of OS in patients with T-cell ALL who had a matched sibling donor vs those without a donor within the UKALL XII/E2993 trial



David I. Marks, and Clare Rowntree Blood 2017;129:1134-1142

Comparison of OS in patients with T-cell ALL treated with autologous stem cell transplantation (auto) or chemotherapy (chemo) within the UKALL XII/E2993



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