Breaking Down the Evidence: Updated Strategies for Initial ALL Treatment

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

- Describe the epidemiology, biology, and clinical presentation of ALL
- Differentiate treatment approaches for Philadelphia chromosome–positive versus Philadelphia chromosome–negative B-ALL
- Evaluate clinical evidence supporting the use of immunotherapy in the management of ALL

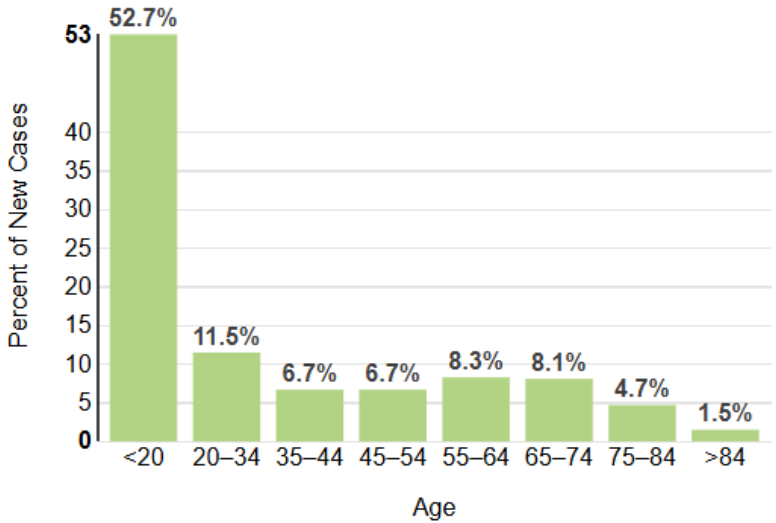
Abbreviation Key

- ALL: acute lymphoblastic leukemia
- ASA: aspirin
- AYA: adolescents and young adults
- CALGB: cancer and leukemia group B
- CAR-T: chimeric antigen receptor T-cell
- CBC: complete metabolic panel
- CHF: congestive heart failure
- CMR: complete molecular response
- CNS: central nervous system
- CR: complete response
- CVAD: cyclophosphamide, vincristine, anthracycline, dexamethasone
- CVD: cyclophosphamide, vincristine, dexamethasone
- DDI: drug-drug interactions
- DFS: disease free survival
- D5W: dextrose 5% in water
- ECOG: eastern cooperative oncology group performance status scale
- EFS: event free survival
- GI: gastrointestinal
- IT: intrathecal
- IV: intravenous
- LFT: liver function test
- Mg: milligrams
- MRD: minimal residual disease
- MTX: methotrexate
- NSAIDs: nonsteroidal anti-inflammatory drugs
- OS: overall survival
- PCR: polymerase chain reaction
- PFS: progression free survival
- Ph: Philadelphia
- PO: oral
- POMP: prednisone, oncovin, methotrexate, prednisone
- PPI: proton pump inhibitors
- RFS: relapse free survival
- R/R: relapse/refractory
- TKI: tyrosine kinase inhibitor
- WBC: white blood cell count
- ½ NS: one-half normal saline

Background

Epidemiology

- ALL diagnoses make up 0.3% of all new cancer cases
  - Estimated 6,100 new cases in the United States in 2025
- Most common in children, adolescents, and young adults
  - 52.7% of new cases occur in age < 20
- Median age at diagnosis: 17



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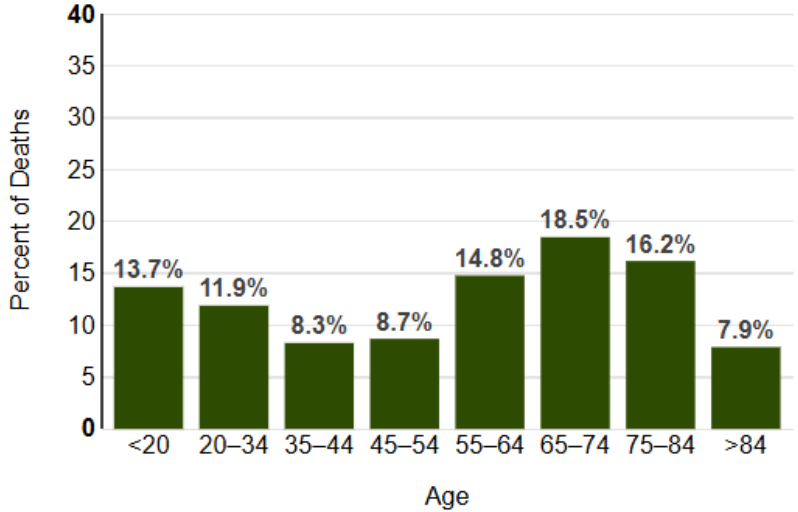
NCI SEER. Acute Lymphocytic Leukemia Stat Facts. 2025.

Epidemiology – Mortality

- Median age at death: 60
  - Largest share occurs in ages 65-74
- 5-year relative survival rate: 72.6%
  - Varies by age, and older adults contribute to a larger share of deaths



NCI SEER. Acute Lymphocytic Leukemia Stat Facts. 2025.

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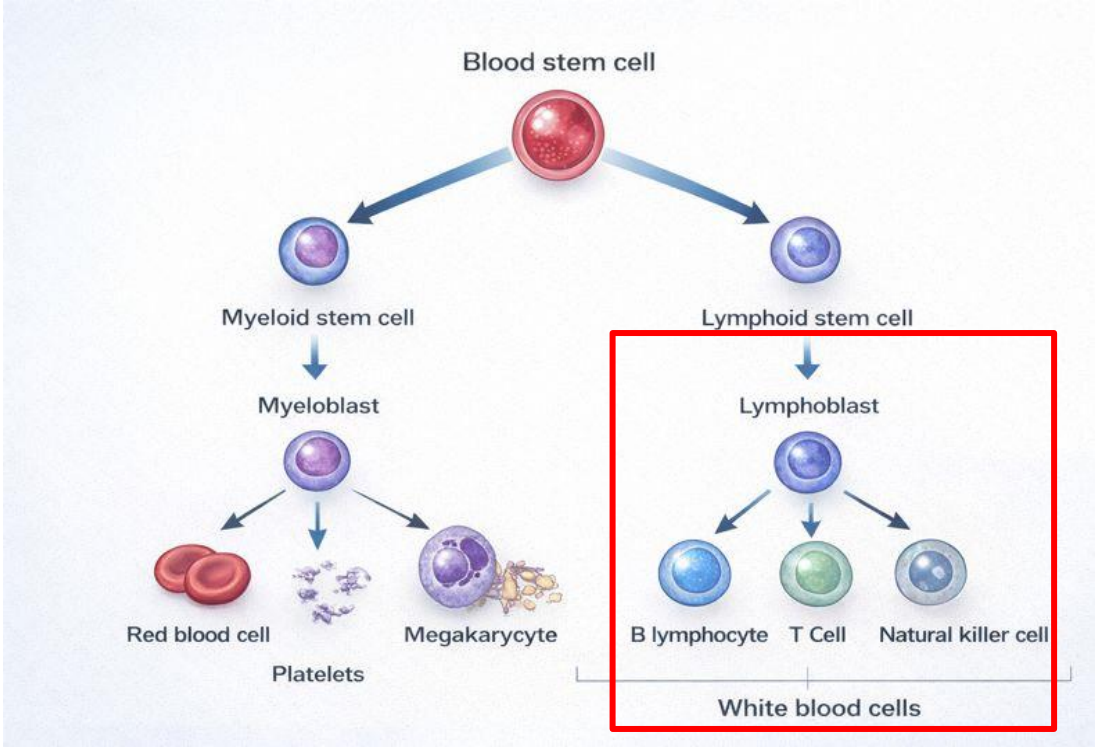
Pathophysiology



B-Cell	T-Cell
75%	25%

Malignant transformation of progenitor cells

Image: Microsoft Copilot – ALL Stem Cells, 2026.

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Clinical Presentation

- Unexpected weight loss
- Fatigue
- Fever or night sweats
- Easy bruising or bleeding
- Dyspnea
- Organ enlargement
- Pain in bones or joints

Puckett & Chan. Acute Lymphocytic Leukemia. StatPearls, 2023.

Risk Factors

Age > 70

Prior exposure to chemotherapy or radiation

Genetic disorders

- Li-Fraumeni Syndrome
- Down Syndrome
- Neurofibromatosis
- Klinefelter Syndrome

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Tebbi CK. Etiology of Acute Leukemia. *Cancers.* 2021.

Diagnosis

- CBC with differential
- Chemistry panel
- Fibrinogen and coagulation tests
- Evaluate for infection, tumor lysis
- Lumbar puncture
- Bone marrow biopsy and aspirate
  - Pathology and immunophenotyping
  - Cytogenetic studies
  - Molecular abnormalities

Puckett & Chan. Acute Lymphocytic Leukemia. StatPearls, 2023.

Diagnosis

- CBC with differential
- Chemis
- Fibrino
- Evalua
- Lumba
- Bone m
  - Patho
  - Cytogenetic studies
  - Molecular abnormalities

≥ 20% lymphoblasts within the bone marrow

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Puckett & Chan. Acute Lymphocytic Leukemia. StatPearls, 2023.

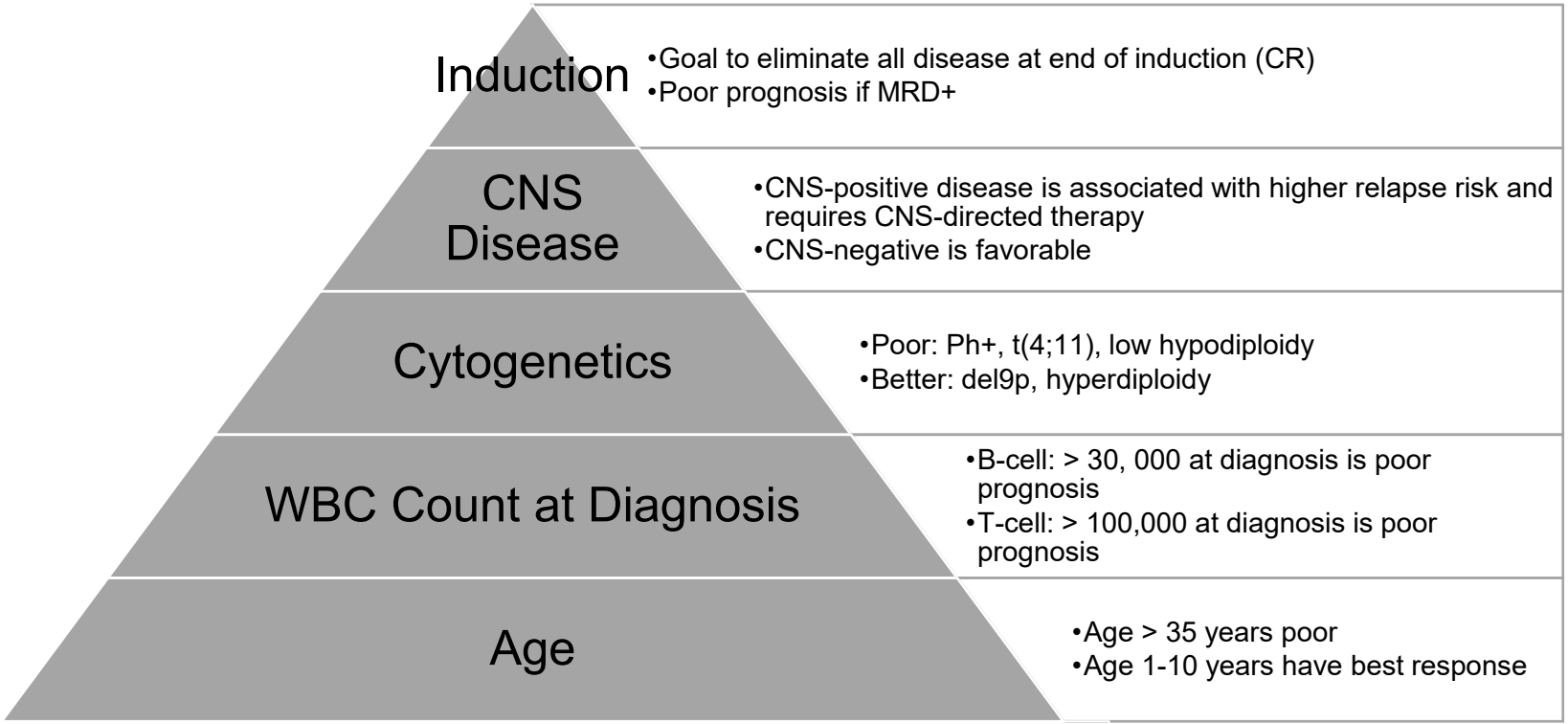
Risk Stratification

Risk Stratification

	Favorable	Unfavorable
Cytogenetics	Hyperdiploidy (> 50 chromosomes) t(12;21): ETV6::RUNX1	**t(9;22): BCR::ABL1 (Ph+)** Low hypodiploidy (30-39 chromosomes) KMT2A rearrangement
Age	< 35 years old	> 35 years old
WBC	B-cell ALL: < 30,000 T-cell ALL: < 100,000	B-cell ALL: > 30,000 T-cell ALL: > 100,000
Extramedullary disease	Negative	Positive
Induction response	Complete response (CR)	Primary refractory
MRD status	MRD negative	MRD positive

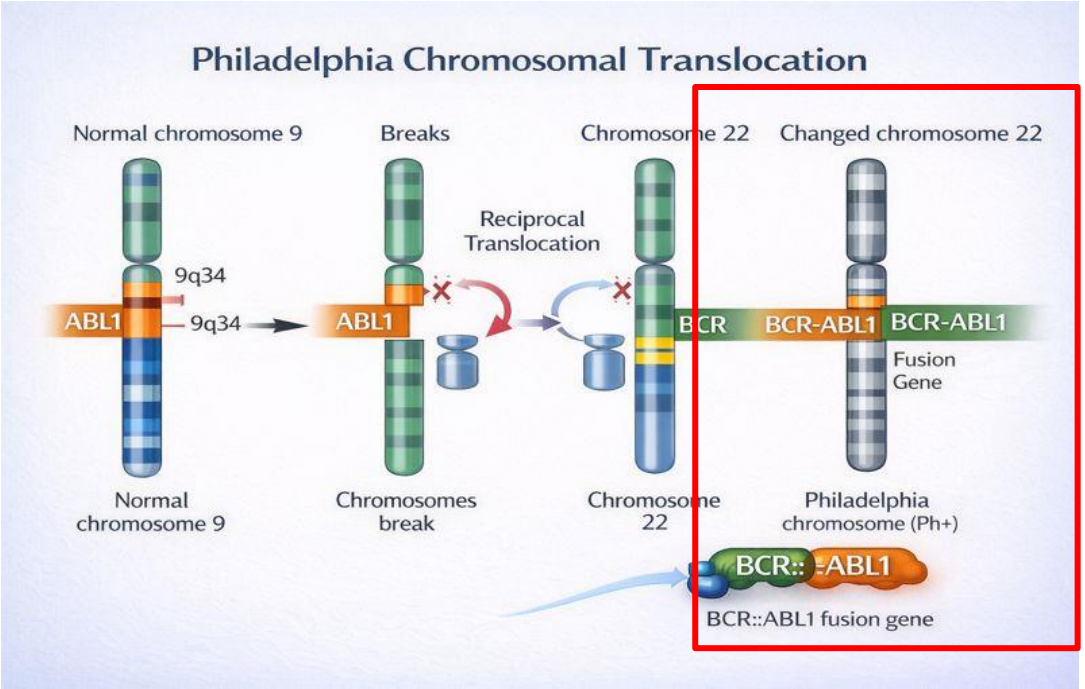
Moorman AV et al. Blood. 2010.
Brüggemann M et al. Blood. 2010.

Prognostic Factors



Gökbuget N et al. Blood. 2024.
Moorman AV et al. Blood. 2010.
Brüggemann M et al. Blood. 2010.

Philadelphia Chromosome



Chromosomal translocations drive cell division and proliferation impacting prognosis and treatment

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Image: Microsoft Copilot – Philadelphia Chromosome, 2026.

Assessment Question #1

Which of the following best describes acute lymphoblastic leukemia (ALL) and its typical clinical features?

A. A malignancy of mature lymphocytes that primarily presents with lymphadenopathy and normal blood counts

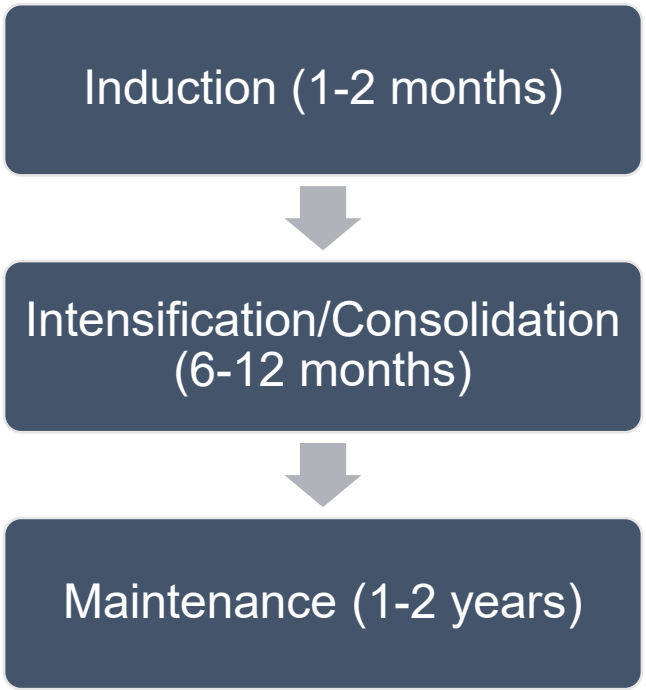
B. A disorder of immature lymphoid cells that commonly presents with cytopenias, fatigue, and infection

C. A myeloid stem cell disorder associated with splenomegaly and elevated platelets

D. A reactive process caused by viral infection that resolves spontaneously

Treatment Overview

General Treatment Course



+

CNS Prophylaxis: 8 to 15 doses of IT chemotherapy

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NCI PDQ®. Adult Acute Lymphoblastic Leukemia Treatment. 2025.

Response Criteria

Complete Response

- No circulating blasts or extramedullary disease
- Bone marrow: < 5% blasts
- No recurrence for at least 4 weeks

MRD +

- Flow cytometry: > 0.01%
- PCR: > ~10^{-5}
- Next-generation sequencing: > 10^{-6}

Progressive Disease

- Increase in absolute number of circulating blasts in peripheral blood
- Increase in bone marrow blasts by 25% or more
- Development of extramedullary disease

Refractory Disease

- Failure to achieve CR at the end of induction

Relapse

- Reappearance of blasts in blood or bone marrow > 5%
- Any extramedullary site after achievement of CR

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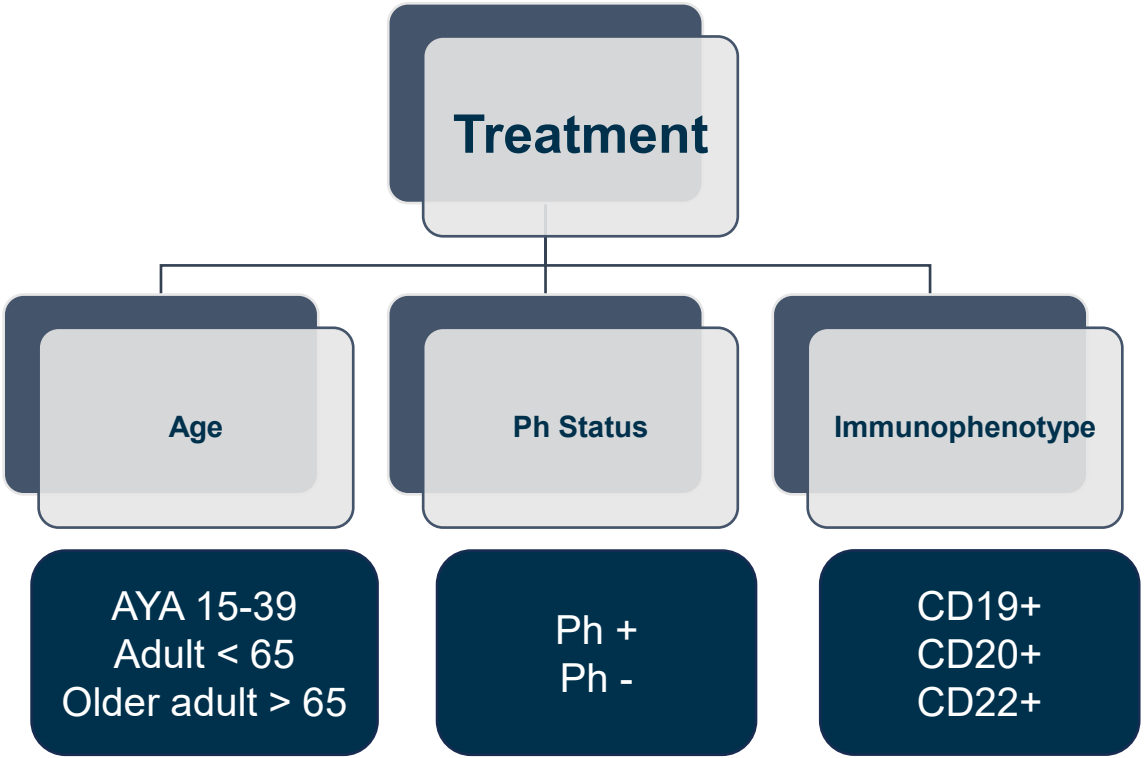
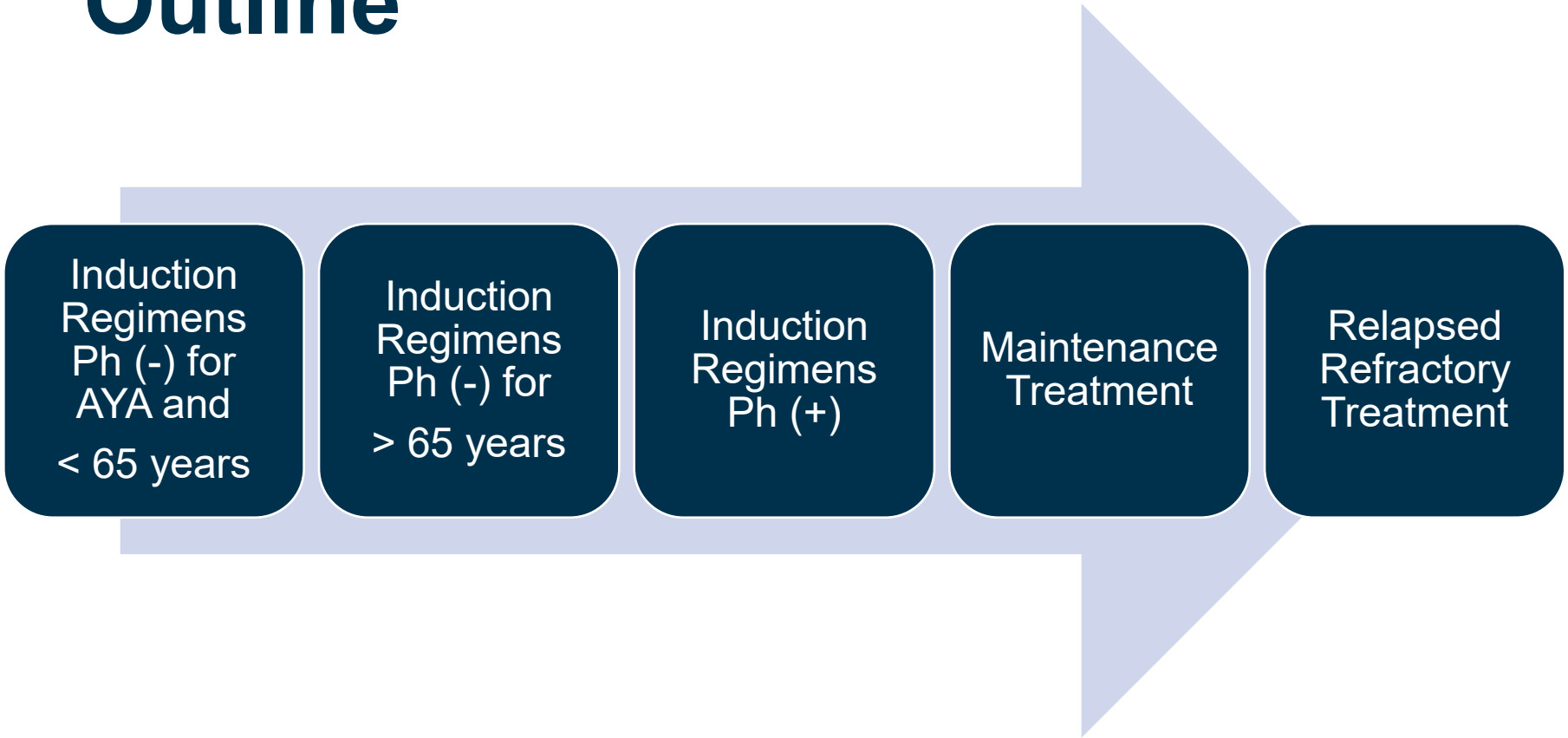
Short et al. Blood. 2025.

Treatment Selection Factors



Outline


Induction Regimens Ph (-) for AYA and < 65 years
Induction Regimens Ph (-) for > 65 years
Induction Regimens Ph (+)
Maintenance Treatment
Relapsed Refractory Treatment

Induction Ph (-)

Induction Treatment

Clinical trial preferred for all ages

Induction Treatment: Ph (-)*

AYA without comorbidities	Both AYA and adults < 65 years without comorbidities	Adults
• CALGB 10403	• ECOG 1910 • HyperCVAD	• Inotuzumab + mini-HyperCVAD

*Selected regimens

Stock W, et al. Blood. 2019.
DeAngelo DJ, et al. Blood. 2007.
Litzow MR, et al. N Engl J Med. 2024.
Kantarjian HM, et al. J Clin Oncol. 2000.
Geyer MB, et al. Blood. 2019.
Kantarjian H, et al. Lancet Oncol. 2018.

Drug Components

Regimen	Drug Component
CALGB 10403	Daunorubicin, pegaspargase, prednisone, vincristine
ECOG 1910	Cyclophosphamide, cytarabine, daunorubicin, dexamethasone, mercaptopurine, pegaspargase, vincristine, rituximab (CD20+)
HyperCVAD	Cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with methotrexate, cytarabine, rituximab (CD20+)
Inotuzumab ozogamicin + mini-HyperCVD	Cyclophosphamide, vincristine, dexamethasone, inotuzumab ozogamicin alternating with cytarabine, methotrexate, inotuzumab ozogamicin

Stock W, et al. Blood. 2019.
Litzow MR, et al. N Engl J Med. 2024.
Geyer MB, et al. Blood. 2019.
DeAngelo DJ, et al. Blood. 2007.
Kantarjian HM, et al. J Clin Oncol. 2000.
Kantarjian H, et al. Lancet Oncol. 2018.

Drug Components

Regimen	Drug Component
CALGB 104	
ECOG 19	opurine,
HyperCVA	with
Inotuzum ozogamic HyperCV	n

In fit patients, backbone of therapy includes vinca alkaloid, anthracycline, and steroid with the addition of asparaginase in our AYA population

Stock W, et al. Blood. 2019.
Litzow MR, et al. N Engl J Med. 2024.
Geyer MB, et al. Blood. 2019.
DeAngelo DJ, et al. Blood. 2007.
Kantarjian HM, et al. J Clin Oncol. 2000.
Kantarjian H, et al. Lancet Oncol. 2018.

Clinical Pearls

Drug	Clinical Pearls
Pegaspargase	• MOA: depletes circulating asparagine, which leukemic lymphoblasts cannot synthesize → selective cytotoxicity • Supportive care includes glucose monitoring for risk of hyperglycemia • Adverse events include hepatotoxicity, pancreatitis, thrombosis, and hypersensitivity reactions

Pegaspariginase [PI]. DailyMed.

Induction Treatment: Ph (-)*

Adults ≥ 65 years or adults with comorbidities

- Low intensity:
  - Vincristine + prednisone
  - POMP
- Moderate intensity:
  - ALLIANCE A041703
  - Inotuzumab ozogamicin + mini-hyperCVD
  - Mini-hyperCVD
- High intensity:
  - ECOG 1910

*Selected regimens

Larson RA, et al. Blood. 1998.
Rambaldi A, et al. Cancer. 2020.
DeAngelo DJ, et al. Blood. 2007.
Kantarjian H, et al. Blood. 2018.
Litzow MR, et al. N Engl J Med. 2024.
Larson RA, et al. J Clin Oncol. 1998.
Wieduwilt MJ, et al. Blood. 2023.
Kantarjian H, et al. Lancet Oncol. 2018.
Jain N, et al. Blood. 2019.

Drug Components

Regimen	Drug Component
POMP	Mercaptopurine, vincristine, methotrexate, prednisone
ALLIANCE A041703	Inotuzumab ozogamicin, blinatumomab, intrathecal methotrexate, dexamethasone
Inotuzumab ozogamicin + mini-hyperCVD	Hyperfractionated cyclophosphamide, vincristine, dexamethasone alternating with high-dose methotrexate, dose-adjusted cytarabine

Larson RA, et al. J Clin Oncol. 1998.
Rambaldi A, et al. Cancer. 2020.
DeAngelo DJ, et al. Blood. 2007.
Wieduwilt MJ, et al. Blood. 2023.
Kantarjian H, et al. Lancet Oncol. 2018.

Drug Components

Regimen	Drug Component
POMP	
ALLIANC	
Inotuzum + mini-hy	

Compared to younger patients, older adults are commonly initiated on chemotherapy with dose reductions and immunotherapy-based regimens

Larson RA, et al. J Clin Oncol. 1998.
Rambaldi A, et al. Cancer. 2020.
DeAngelo DJ, et al. Blood. 2007.
Wieduwilt MJ, et al. Blood. 2023.
Kantarjian H, et al. Lancet Oncol. 2018.

Evolution of Treatment Regimens

CALGB 10403

Primary Objective	• To determine whether a pediatric-inspired ALL regimen improves event-free survival (EFS) in adolescents and young adults with newly diagnosed Ph (-) ALL • Endpoints: induction response rate, EFS, DFS, OS
Design	• November 2007 to September 2012, newly diagnosed ALL patients were enrolled with an ECOG score of 0-2, and no prior treatment of ALL
Population	• 318 patients aged 17-39 (median 24 years) newly diagnosed with Ph (-) B-cell (76%) and T-cell (24%) ALL

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Stock W et al. Blood. 2019.

CALGB 10403

Intervention

- Pediatric-inspired multi-agent chemotherapy regimen
- Vincristine, pegaspargase, anthracyclines, cyclophosphamide, cytarabine, IT chemotherapy with cytarabine or methotrexate, 6-mercaptopurine, thioguanine, prednisone/dexamethasone

Outcomes

- CR: ~90% after induction
- Median EFS: ~78 months compared to prior 30 months
- Median DFS: ~82 months
- 3-year OS: ~73%, previously ~58%

Clinical Significance

- Demonstrated that AYA patients benefit from pediatric-inspired therapy
- Changed standard of care as pediatric-style regimens are now recommended for fit AYA patients

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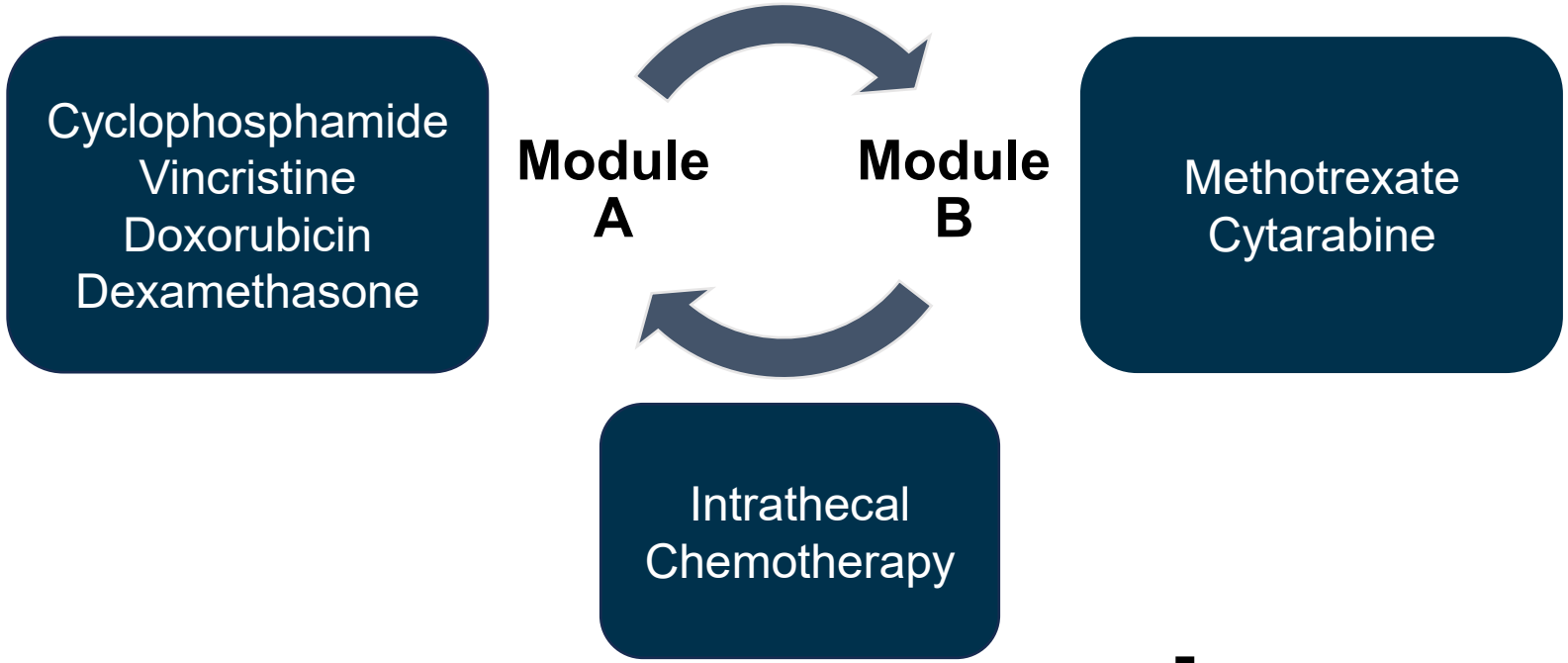
Stock W et al. Blood. 2019.

HyperCVAD Regimen

Alternating Module A and B every 21 days for up to 4 cycles of each module



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Kantarjian H et al. Lancet Oncol. 2018.

Clinical Pearls

Drug	Clinical Pearls
High-dose Methotrexate	• Provide adequate hydration using D5W or 1/2NS with added sodium bicarbonate, typically infused at 150 mL/hr • Initiate methotrexate when urine pH ≥ 8 • DDI: avoid proton pump inhibitors, NSAIDs, penicillin, ASA, trimethoprim • Toxicity prevention: IV leucovorin starts 36 hours after initiation of MTX infusion then transitioned into PO leucovorin
High-dose Cytarabine	• Keratoconjunctivitis: Dexamethasone eye drops given 4 times daily during treatment and 48 hours after • Assess for cerebellar toxicity prior to administration
Cyclophosphamide	• Hemorrhagic cystitis risk: aggressive hydration with NS and initiation of IV mesna for prevention

Methotrexate injection [PI]. DailyMed.
Cytarabine injection [PI]. DailyMed.
Cyclophosphamide [PI]. DailyMed.

Clinical Pearls

Drug	Clinical Pearls
Vincristine	• Never administer intrathecally as this is fatal • Maximum 2mg per dose • Adverse events include neurotoxicity including peripheral neuropathy, ileus, and constipation • DDI: CYP3A inhibitors increase toxicity such as azole antifungals
Doxorubicin	• Cardiotoxicity is dose limiting with higher cumulative doses (> 400 mg/m²) • Dexrazoxane can be considered for cardio-protection in selected patients • Use central access as there is a risk of extravasation

Vincristine injection [PI]. DailyMed.
Doxorubicin injection [PI]. DailyMed.

Rituximab

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Rituximab

Targets CD20 on the surface of the B-cell to activate complement-mediated cytotoxicity and anti-body dependent cell-mediated cytotoxicity

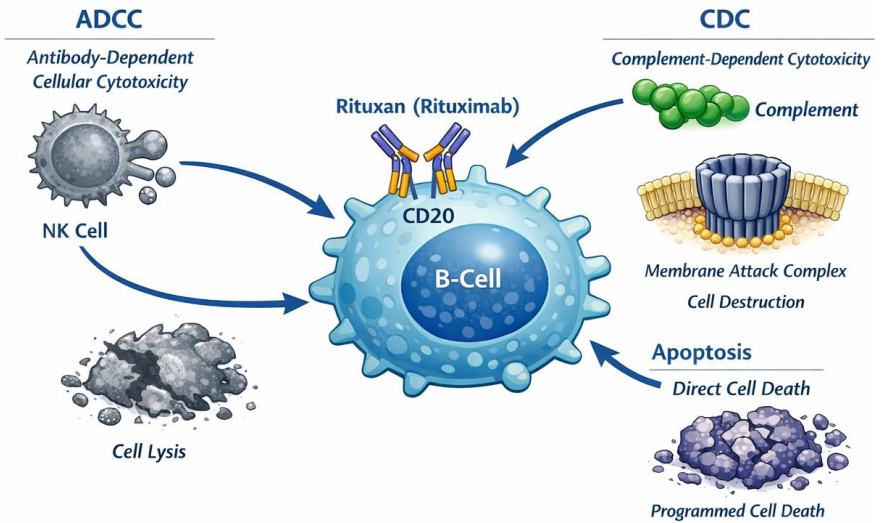

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Image: Microsoft Copilot – Rituximab, 2026.

Rituximab

Place in therapy

- May be added to multiagent chemotherapy in CD20+ B-ALL

Dose

- 375 mg/m^2 over 2-6 hours on D1, 11 of hyper-CVAD and D2, D8 of MTX + Cytarabine

Adverse events

- Hypersensitivity reactions, reactivation of Hepatitis B, tumor lysis syndrome

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Rituximab injection [PI]. DailyMed.

HyperCVAD + Rituximab

Primary Objective

- Evaluate the efficacy of adding rituximab to hyper-CVAD in adults with CD20 positive Burkitt's Lymphoma or B-ALL

Design

- Single-center, single-arm Phase II study conducted at MD Anderson Cancer Center, with outcomes compared to a historical control cohort treated with hyper-CVAD alone

Population

- 31 adults who were newly diagnosed Burkitt Lymphoma or B-ALL (45%) with ECOG ≤ 3
- Patients with organ dysfunction, HIV infection, or old age were not excluded, allowing for inclusion of higher-risk patients

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Thomas DA et al. *Cancer*. 2006.

HyperCVAD + Rituximab

Intervention

- 8 alternating courses every 21 days of HyperCVAD and high dose methotrexate + cytarabine
  - Rituximab 375 mg/m² given on D1, D11 of hyper-CVAD and D2, D8 of MTX + Cytarabine for a total of 8 doses over 4 courses

Outcomes

- CR: 86%
- 3-year OS: 89% compared to historical 53%
- 3-year DFS: 88% compared to historical 60%
- 3-year EFS: 80% compared to historical 52%

Clinical Significance

- Demonstrated meaningful survival improvement vs historical hyper-CVAD alone
- Established rituximab + intensive chemotherapy as a standard approach

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Thomas DA et al. Cancer. 2006.

Blinatumomab

Bispecific Antibody – Blinatumomab

Bispecific T-cell engager (BiTE) that binds to CD19 expressed on the surface of malignant B-cells and to the CD3 receptor expressed on T-cell surfaces, resulting in T-cell activation and proliferation, cytokine secretion, and lysis of B-cells

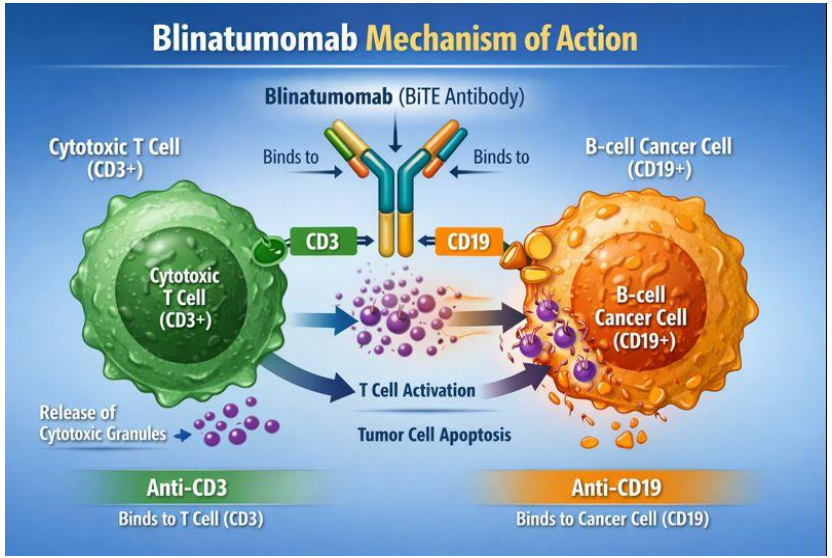

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Image: Microsoft Copilot – Bispecific Antibody Blinatumomab, 2026.

Blinatumomab

Place in therapy

- Initially used in R/R phase, but increasingly used in consolidation

Dose

- Consolidation and MRD+: D1-28 28 mcg/day
- R/R: D1-7: 9 mcg/day, D8-28: 28 mcg/day

Adverse events

- Cytokine release syndrome, neurotoxicity, infection, fever

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Blinatumomab [PI]. DailyMed.

HyperCVAD and Blinatumomab

Population

- Newly diagnosed B-ALL patients aged 18 to 65 years fit for intensive chemotherapy

Interventions

- Treatment strategy changed over time: initially Hyper-CVAD+ blinatumomab, then amended to incorporate inotuzumab followed by blinatumomab

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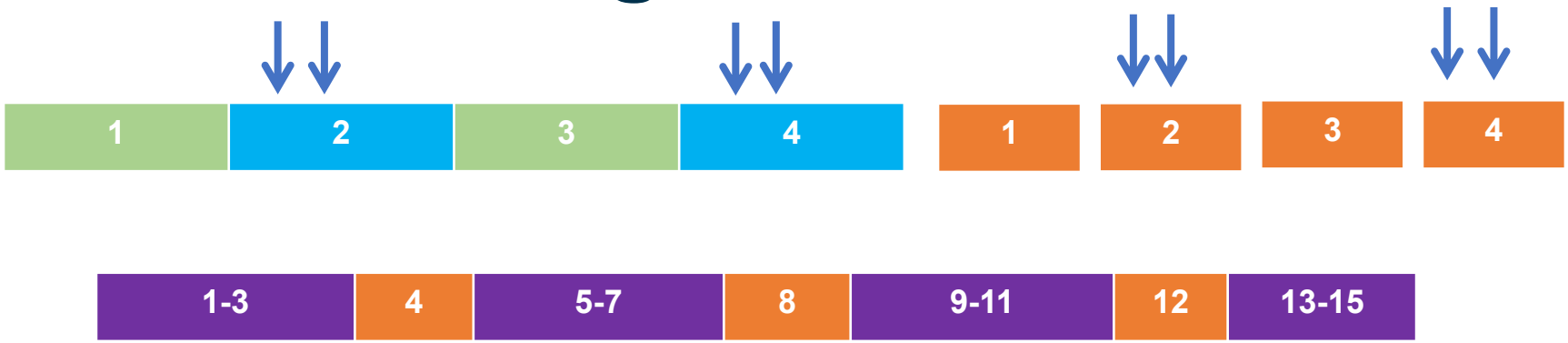
Kantarjian Het al., Am J Hematol. 2025.

Treatment Algorithm



Legend
Hyper-CVAD
MTX
Blinatumomab
POMP
Inotuzumab

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Kantarjian Het al., Am J Hematol. 2025.

HyperCVAD and Blinatumomab

Population

- Newly diagnosed B-ALL patients aged 18 to 65 years fit for intensive chemotherapy

Interventions

- Treatment strategy changed over time: initially Hyper-CVAD+ blinatumomab, then amended to incorporate inotuzumab followed by blinatumomab

Results

- Hyper-CVAD + blinatumomab:
  - CR~95%
  - 3-yr OS ~82%
  - 3-yr RFS ~74%
- Hyper-CVAD + inotuzumab → blinatumomab:
  - CR ~98–100%
  - 3-yr OS ~100%
  - 3-yr RFS ~90%

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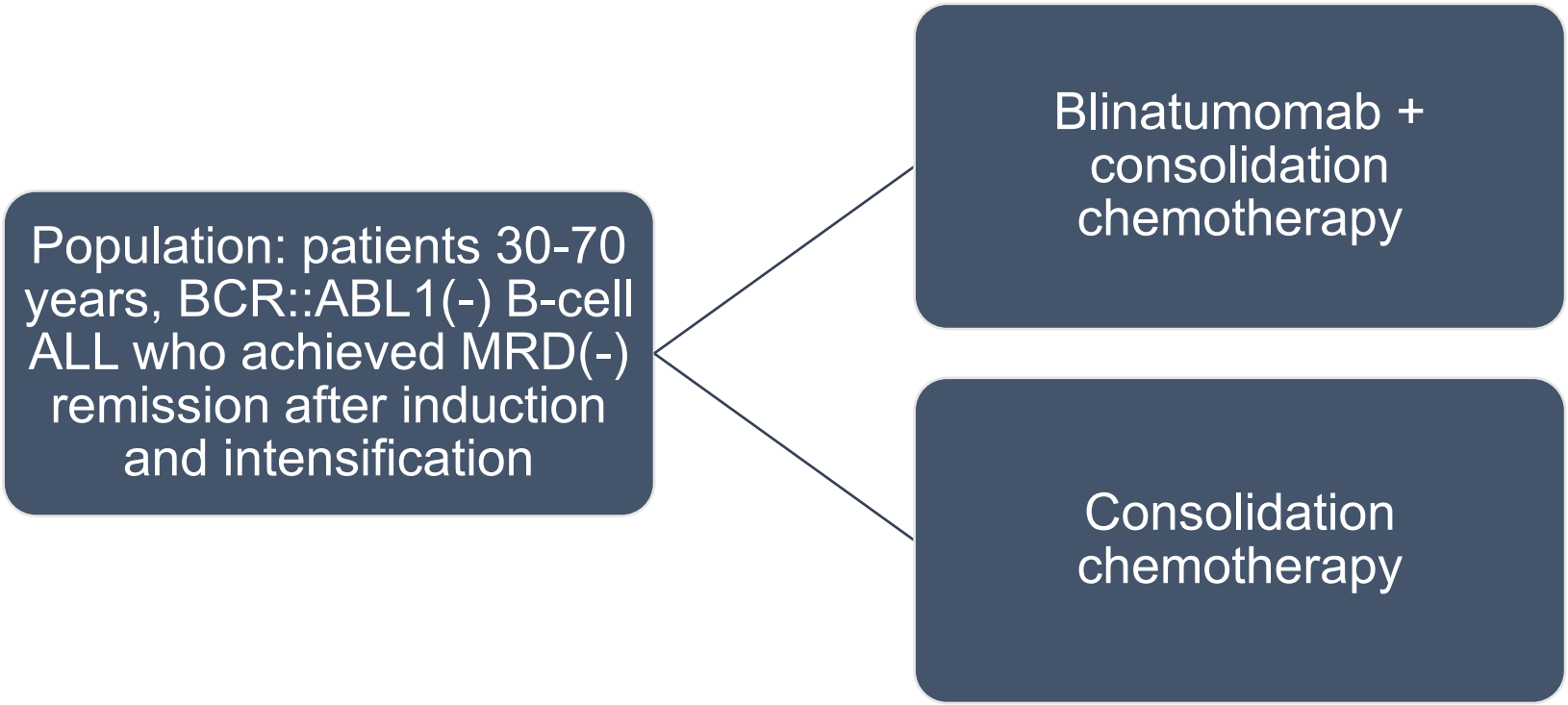
Kantarjian H et al., Am J Hematol. 2025.

ECOG 1910



ADVOCATE HEALTH

Litzow MR et al. N Engl J Med. 2024.

Treatment Algorithm

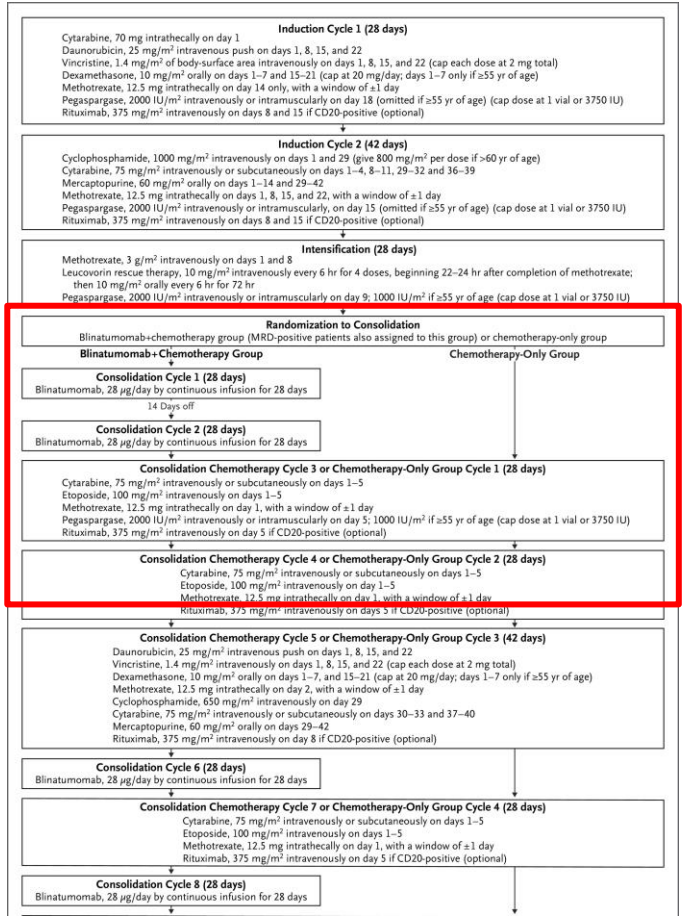


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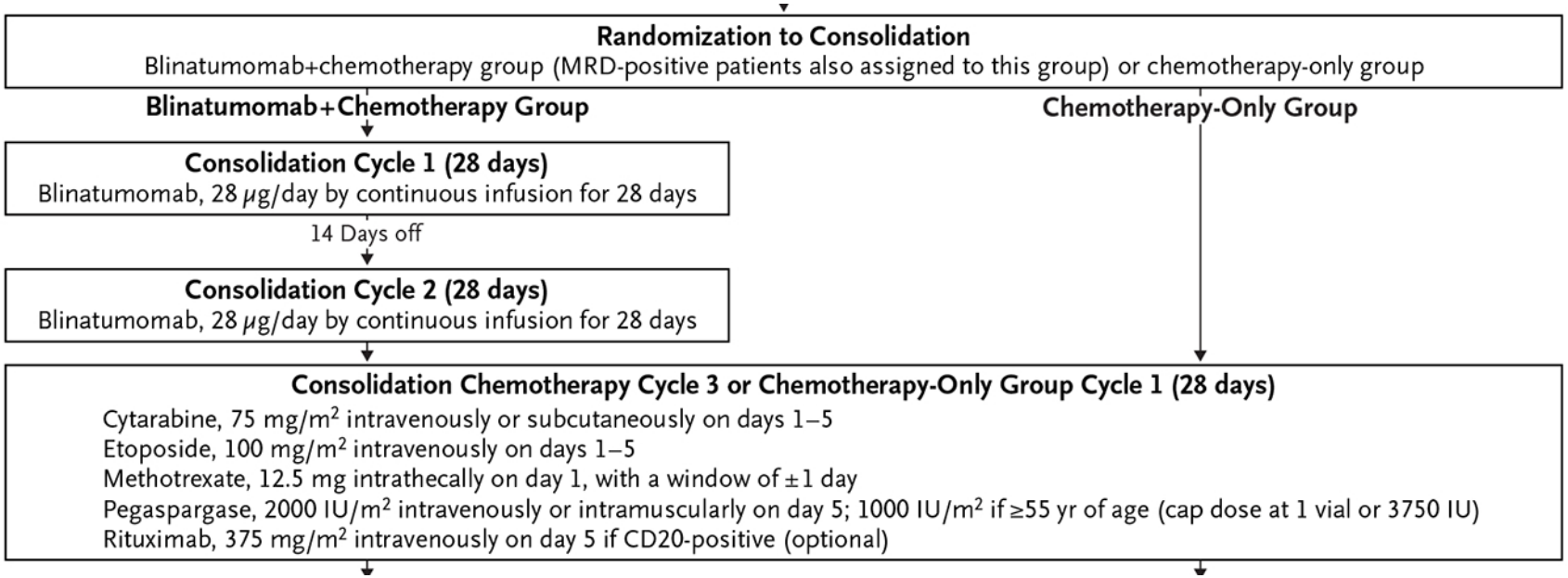
Image: Microsoft Copilot – HyperCVAD and Blinatumomab Treatment Algorithm, 2026.

Treatment Algorithm



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ECOG 1910 Results

	Blinatumomab + Consolidation chemotherapy (n=112)	Consolidation chemotherapy (n=112)
3-year OS	85% (CI 0.23 to 0.73; p value 0.002)	68%
3-year RFS	80% (CI 0.32 to 0.87)	64%
Safety (Grade 4)		
Neutropenia	55%	86%
Infection	1%	1%
Neurologic events	23%	5%

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Litzow MR et al. N Engl J Med. 2024.

Inotuzumab Ozogamicin

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Inotuzumab Ozogamicin

CD22 directed antibody-drug conjugate, gets internalized by the cell and leads to double-strand DNA breaks, cell cycle arrest and apoptosis

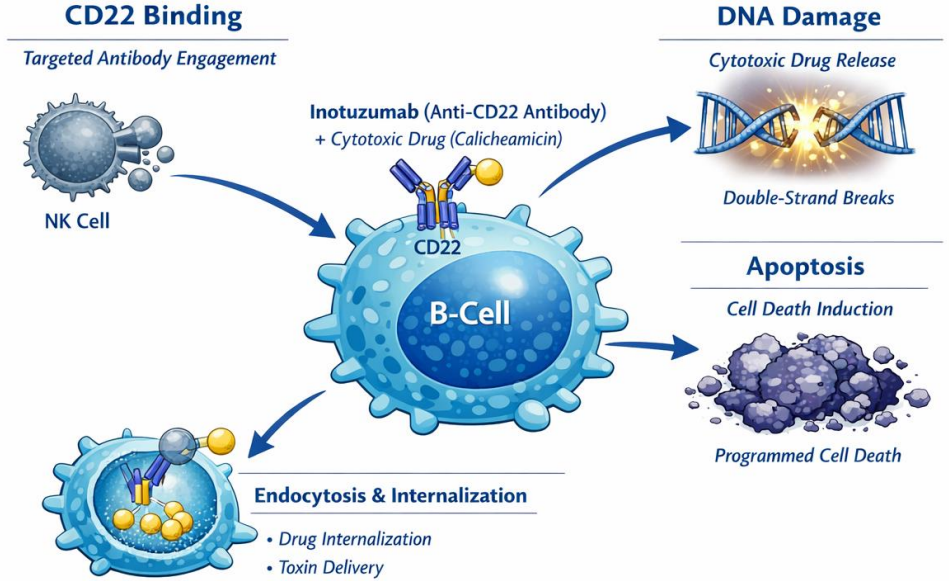

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Image: Microsoft Copilot – Inotuzumab Ozagamicin, 2026.

Inotuzumab Ozogamicin

Place in therapy

- May be added to mini-hyperCVD for induction in less fit adults or used in relapsed/refractory cases for CD22+

Dose

- Fractionated schedule:
  - C1 0.6 mg/m^2 D2 + 0.3 mg/m^2 D8
  - C2-4 0.3 mg/m^2 D2 + 0.3 mg/m^2 D8 of 21-day cycles

Adverse events

- Boxed warning: hepatic veno-occlusive disease
- Hypersensitivity reactions, myelosuppression, hemorrhage, QTc prolongation

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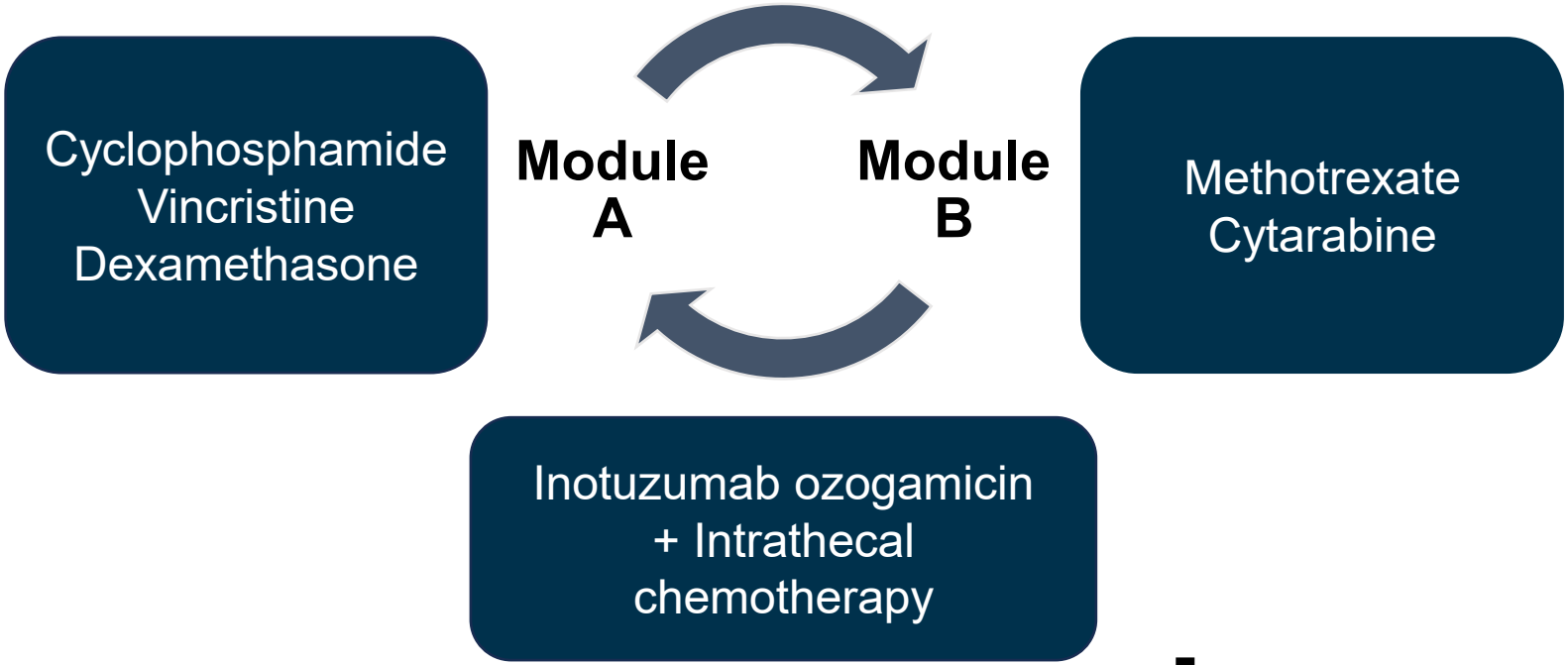
Inotuzumab ozogamicin [PI]. DailyMed.

Mini-HyperCVD + Inotuzumab

Alternating Module A and B every 28 days for up to 4 cycles of each module



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Kantarjian H et al. Lancet Oncol. 2018.

Mini-HyperCVD + Inotuzumab

Primary Objective	• Evaluate progression-free survival (PFS) at 2 years with inotuzumab ozogamicin plus low-intensity chemotherapy in older patients with newly diagnosed Ph-negative ALL.
Design	• Single-center, single-arm Phase II trial at MD Anderson Cancer Center
Population	• 52 patients who were ≥ 60 years of age, newly diagnosed Ph (-) ALL, ECOG ≤ 3 • Majority were treatment naïve (48/52)

ADVOCATE HEALTH

Kantarjian H et al. Lancet Oncol. 2018.

Mini-HyperCVD + Inotuzumab

Intervention	• Mini-HyperCVD: no anthracycline to reduce toxicity risk in older/unfit patients • Inotuzumab ozogamicin: given during cycles 1–4 for CD22+
Outcomes	• CR: 85% • 2-year OS: 66% • 2-year EFS: 59%
Clinical Significance	• Established inotuzumab-based low-intensity regimens as a frontline option for older adults • Provided foundation for later chemo-free or sequential immunotherapy strategies

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Kantarjian H et al. Lancet Oncol. 2018.

Alliance Study 041703

Population

≥ 60 years, newly diagnosed Philadelphia(-), CD22(+) B-cell ALL

Intervention

Up to 2 cycles of Inotuzumab ozogamicin followed by 4-5 cycles of Blinatumomab with IT methotrexate

Results

CR 85% after 2 cycles of inotuzumab ozogamicin and 97% by the end of 2 cycles of blinatumomab

1-year EFS 75% (CI 61 to 92), OS 85% (CI 73 to 98)

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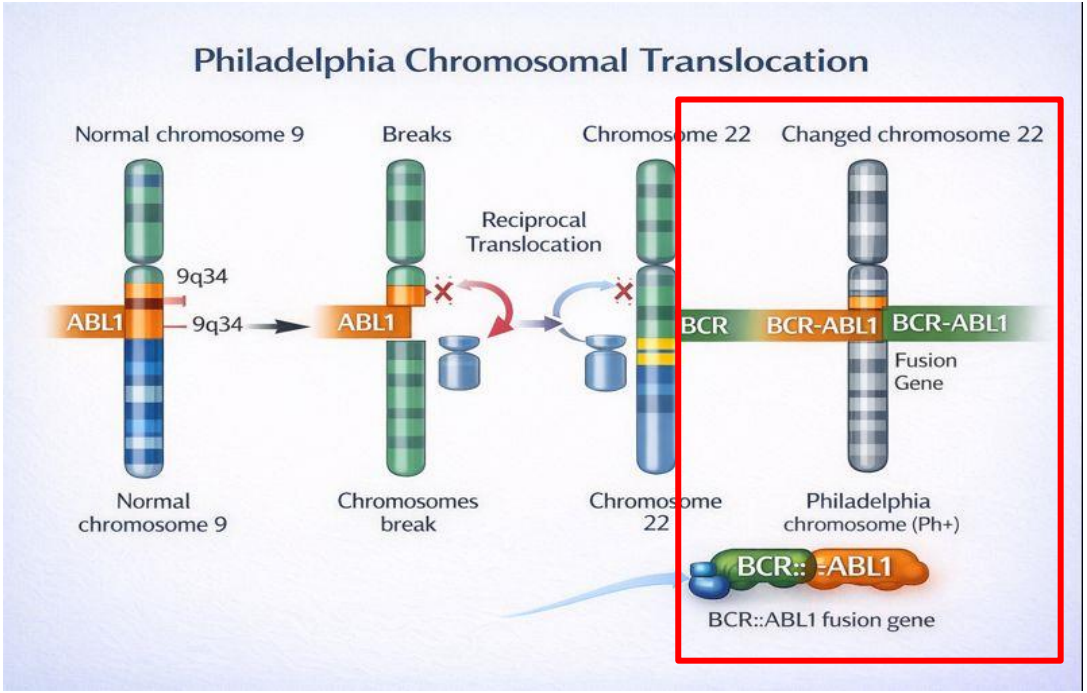
Wieduwilt MJ et al. J Clin Oncol. 2023;41(suppl 16):7006.

Induction Ph (+)

Philadelphia Chromosome



Induction Treatment: Ph (+)*

Both AYA and adults < 65 years without comorbidities	Adults ≥ 65 years or adults with comorbidities

• TKI + blinatumomab
• TKI + HyperCVAD
	• Low intensity
	  • TKI + blinatumomab
	  • TKI + corticosteroid
	• Moderate Intensity
	  • TKI + Mini-HyperCVD

*Selected regimens

Jabbour E, et al. Blood. 2020.
Jabbour E, et al. N Engl J Med. 2018.
Foà R, et al. N Engl J Med. 2020.
Foà R, et al. Blood. 2011.
Rousselot P, et al. Blood. 2016.

Tyrosine Kinase Inhibitors

Mechanism of action

- Bind to ATP-binding site of tyrosine kinase enzymes, preventing phosphorylation and subsequent activation of signaling pathways

Dose

- Imatinib: 400-800mg PO daily
- Dasatinib: 100-180mg PO daily
- Ponatinib: 15-45mg PO daily
- Nilotinib: 400mg PO BID

Hallmark Adverse events

- Dasatinib: pleural effusions, pulmonary hypertension
- Ponatinib: arterial thrombotic events, hypertension (boxed warning)
- QT prolongation: imatinib, nilotinib

Imatinib [PI]. DailyMed. Dasatinib [PI]. DailyMed.
Ponatinib [PI]. DailyMed. Nilotinib [PI]. DailyMed.
Bosutinib [PI]. DailyMed.

Ponatinib + Blinatumomab

Primary Objective

- Evaluate the rate of complete molecular response (CMR) with a chemotherapy-free regimen of ponatinib plus blinatumomab in patients with Ph+ ALL

Population

- Adults ≥ 18 years, ECOG ≤ 2, 40 newly diagnosed Ph+ ALL, 14 R/R Ph+ ALL

Intervention

- Blinatumomab D1-28, 28mcg over 24 hours every 6 weeks for 5 cycles + Ponatinib PO 30mg daily during cycle 1, then decrease to 15mg after CMR
- After completion of Blinatumomab, Ponatinib monotherapy for 5 years
- 12 doses of IT chemotherapy for CNS prophylaxis

Results

- Newly diagnosed: CMR 87%, 1-year OS 95%, ES 95%
- R/R: 79% CMR, 92% CR

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Jabbour E et al. Lancet Haematol. 2023.

Ponatinib + Blinatumomab Update

Primary Objective

- Assess the rate of complete molecular response (CMR) with frontline ponatinib + blinatumomab in newly diagnosed Ph (+) ALL

Population

- Newly diagnosed Ph (+) ALL with median age of ~55

Intervention

- Blinatumomab 28mcg over 24 hours + Ponatinib PO 30mg then decrease to 15mg after CMR
- After completion of Blinatumomab, Ponatinib monotherapy
- 12 to 15 doses of IT chemotherapy for CNS prophylaxis

Results

- 3-year OS 91%
- 3-year EFS 77%

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Kantarjian H et al. J Clin Oncol. 2024.

Assessment Question #2

Which treatment strategy is most appropriate for a patient with newly diagnosed Philadelphia chromosome–positive (Ph+) B-ALL?

A. Pediatric-inspired multiagent chemotherapy alone
B. Hyper-CVAD without targeted therapy
C. Tyrosine kinase inhibitor–based therapy combined with immunotherapy
D. Chemotherapy followed by routine allogeneic stem cell transplant in first remission

Maintenance Treatment

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Maintenance Regimens

Ph (-)

- POMP
- Blinatumomab alternating with POMP

Ph (+)

- POMP
- TKI + Vincristine + Prednisone
- TKI monotherapy

Larson RA, et al. J Clin Oncol. 1998.
Short NJ, et al. Blood. 2020.
Ottmann OG, et al. Cancer. 2007.
Litzow MR, et al. J Clin Oncol. 2023.
Rousselot P, et al. Blood. 2016.

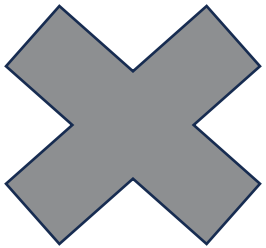
POMP Regimen

Prednisone
- 60 mg/m^2 daily on D1-5

Vincristine
- 2mg IV on D1 of each cycle

Methotrexate
- 20 mg/m^2 on D1, 8, 15 and 22

Mercaptopurine (6-MP)
- 60 mg/m^2 daily on D1-28



Given in variable cycles for up to 2 years after consolidation

Doses and cycles vary based on protocol

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Advani AS et al. J Clin Oncol. 2022.

Assessment Question #3

Which statement best describes the current role of immunotherapy in the management of acute lymphoblastic leukemia (ALL)?

A. Immunotherapy is reserved only for relapsed or refractory ALL after failure of all chemotherapy options
B. Immunotherapy has largely replaced the need for CNS prophylaxis in ALL
C. Immunotherapy is increasingly incorporated into frontline and consolidation therapy, often reducing reliance on intensive chemotherapy
D. Immunotherapy is used exclusively in Philadelphia chromosome–positive ALL

Relapsed or Refractory

Relapsed Refractory Treatment

- Tyrosine kinase inhibitors
- Blinatumomab
- CAR-T
  - Tisagenlecleucel
  - Brexucabtagene Autoleucel
  - Obecabtagene autoleucel
- Allogeneic transplant
- Retreatment with initial regimen

Kantarjian H et al. Cancer. 2010
Short NJ et al. Lancet Haematol. 2021

Guideline Updates Summary

AYA Ph (-)

- Pediatric inspired regimens preferred

Adults Ph (-)

- Early integration of immunotherapy in all age groups
- Inotuzumab-based regimens for older/unfit patients

Ph (+) ALL

- Shift toward chemo-free or chemo-minimized regimens

Summary

- Acute lymphoblastic leukemia (ALL) is a malignant disorder characterized by clonal proliferation of immature lymphoid precursor cells
- Management of ALL is guided by patient age, comorbidities, Philadelphia chromosome status, and molecular markers that inform targeted and immunotherapy selection
- Recent advances in immunotherapy and targeted agents have transformed frontline treatment strategies
- Emerging clinical trial data support chemo-sparing strategies that are reshaping standards of care

References

- Advani AS, Moseley A, O'Dwyer KM, et al. SWOG 1318: a Phase II trial of blinatumomab followed by POMP maintenance in older patients with newly diagnosed Philadelphia chromosome–negative B-cell ALL. J Clin Oncol. 2022;40(14):1574–1582.
- Blinatumomab for injection [package insert]. DailyMed. Updated December 2024. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Bosutinib tablet [package insert]. DailyMed. Updated June 2023. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Brüggemann M, Raff T, Kneba M, et al. Clinical significance of minimal residual disease quantification in adult patients with standard-risk acute lymphoblastic leukemia. Blood. 2010;115(18):3730-3738. doi:10.1182/blood-2009-07-234492
- Cytarabine injection [package insert]. DailyMed. Updated July 18, 2024. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- DeAngelo DJ, et al. A multicenter study of a dose-intensive pediatric regimen in adult acute lymphoblastic leukemia (Dana-Farber Cancer Institute ALL Consortium). Blood. 2007;109(9):3675-3680.
- Dasatinib tablet [package insert]. DailyMed. Updated October 2023. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Foà R, Bassan R, Vitale A, et al. Dasatinib–blinatumomab for Ph-positive acute lymphoblastic leukemia in adults. N Engl J Med. 2020;383(17):1613-1623. doi:10.1056/NEJMoa2016272
- Foà R, Vitale A, Vignetti M, et al. Dasatinib as first-line treatment for adult patients with Philadelphia chromosome–positive acute lymphoblastic leukemia. Blood. 2011;118(25):6521-6528. doi:10.1182/blood-2011-05-351403
- Geyer MB, et al. Pediatric-inspired therapy in adults with newly diagnosed acute lymphoblastic leukemia: a Memorial Sloan Kettering Cancer Center experience. Blood. 2019;134(18):1548-1559.
- Gökbuget N, Dombret H, Ribera JM, et al. Central nervous system involvement in adult acute lymphoblastic leukemia: risk factors and outcome. Blood. 2012;120(16):3214-3221. doi:10.1182/blood-2012-04-423020
- Imatinib mesylate tablet [package insert]. DailyMed. Updated March 2019. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Inotuzumab ozogamicin injection [package insert]. DailyMed. Updated August 2024. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Jain N, Stevenson K, Winer ES, et al. A multicenter phase I study combining venetoclax with mini-hyper-CVD in older adults with untreated and relapsed/refractory acute lymphoblastic leukemia. Blood. 2019;134(Suppl 1):3867. doi:10.1182/blood-2019-129988

References

- Jabbour E, Short NJ, Jain N, et al. Ponatinib and blinatumomab for Philadelphia chromosome–positive acute lymphoblastic leukaemia: a US, single-centre, single-arm, phase 2 trial. Lancet Haematol. 2023;10(1):e24-e34. doi:10.1016/S2352-3026(22)00319-2
- Kantarjian HM, O'Brien S, Smith TL, et al. Results of treatment with Hyper-CVAD, a dose-intensive regimen, in adult acute lymphocytic leukemia. J Clin Oncol. 2000;18(3):547-561.
- Kantarjian H, Ravandi F, Short NJ, et al. Inotuzumab ozogamicin in combination with low-intensity chemotherapy for older patients with Philadelphia chromosome–negative acute lymphoblastic leukemia: a single-arm, phase 2 study. Lancet Oncology. 2018;19(2):240-248. doi:10.1016/S1470-2045(18)30011-1
- Kantarjian H, Short NJ, Haddad FG, et al. Results of the simultaneous combination of ponatinib and blinatumomab in Philadelphia chromosome–positive acute lymphoblastic leukemia. J Clin Oncol. 2024;42(36):4246-4251. doi:10.1200/JCO.24.00272
- Larson RA, Dodge RK, Buckley JD, et al. A Pediatric Treatment Regimen in Adults With Acute Lymphoblastic Leukemia (CALGB 9111): A Randomized Trial of Sequential Intensification With and Without Filgrastim. J Clin Oncol. 1998;16(3):1050-1058. doi:10.1200/JCO.1998.16.3.1050
- Larson RA, Dodge RK, Linker CA, Stone RM, Powell BL, Lee EJ, Schulman P, Davey FR, Frankel SR, Bloomfield CD, George SL, Schiffer CA. A randomized controlled trial of filgrastim during remission induction and consolidation chemotherapy for adults with acute lymphoblastic leukemia: CALGB study 9111. Blood. 1998;92(5):1556-1564.
- Litzow MR, Sun Z, Mattison RJ, et al. Blinatumomab for measurable residual disease–negative acute lymphoblastic leukemia in adults. N Engl J Med. 2024;391(4):320-333. doi:10.1056/NEJMoa2312948
- Methotrexate injection [package insert]. DailyMed. Updated July 15, 2025. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Molina JC, Carraway HE. Treatment of Relapsed Acute Lymphocytic Leukemia in Adult Patients. Curr Treat Options Oncol. 2024;25(8):993-1010. doi:10.1007/s11864-024-01213-4
- Moorman AV, Harrison CJ, Buck GAN, et al. Cytogenetic abnormalities in adult acute lymphoblastic leukemia: prognostic significance and clinical implications. Blood. 2010;115(2):206-214. doi:10.1182/blood-2009-07-232843

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References

- Nilotinib capsule [package insert]. DailyMed. Updated February 2024. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Ottmann OG, Wassmann B, Pfeifer H, et al. Imatinib compared with chemotherapy as front-line treatment of elderly patients with Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ALL). Cancer. 2007;109(10):2068-2076.
- PDQ® Adult Treatment Editorial Board. PDQ adult acute lymphoblastic leukemia treatment. Bethesda, MD: National Cancer Institute; updated March 17, 2025. Accessed January 19, 2026. Available at: https://www.cancer.gov/types/leukemia/patient/adult-all-treatment-pdq
- Ponatinib hydrochloride tablet [package insert]. DailyMed. Updated July 2024. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- Puckett Y, Chan O. Acute Lymphocytic Leukemia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated August 26, 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459149/
- Rambaldi A, Ribera JM, Kantarjian HM, Dombret H, Ottmann OG, Stein AS, Tuglus CA, Zhao X. Blinatumomab compared with standard of care for the treatment of adult patients with relapsed/refractory Philadelphia chromosome–positive B-precursor acute lymphoblastic leukemia. Cancer. 2020;126(2):304-310. doi:10.1002/cncr.32558
- Rousselot P, Coudé MM, Gokbuget N, et al. Dasatinib and low-intensity chemotherapy in elderly patients with Philadelphia chromosome–positive ALL. Blood. 2016;128(6):774-782. doi:10.1182/blood-2016-02-700153
- Rituximab injection [package insert]. DailyMed. Updated January 6, 2025. Accessed January 19, 2026. Available at: https://dailymed.nlm.nih.gov
- National Cancer Institute. SEER Cancer Stat Facts: Acute Lymphocytic Leukemia. Published 2025. Accessed January 2, 2026. https://seer.cancer.gov/statfacts/html/alyl.html
- Short NJ, Aldoss I, DeAngelo DJ, et al. Clinical use of measurable residual disease in adult ALL: recommendations from a panel of US experts. Blood Adv. 2025;9(6):1442-1451. doi:10.1182/bloodadvances.2024015441

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References

- Stock W, Luger SM, Advani AS, et al. A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: results of CALGB 10403. Blood. 2019;133(14):1548-1559. doi:10.1182/blood-2018-10-881961
- Tebbi CK. Etiology of Acute Leukemia: A Review. Cancers (Basel). 2021;13(9):2256. Published 2021 May 8. doi:10.3390/cancers13092256
- Thomas DA, Faderl S, O'Brien S, et al. Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. Cancer. 2006;106(7):1569-1580. doi:10.1002/cncr.21776
- Wieduwilt MJ, Advani AS, Wang ES, et al. Inotuzumab ozogamicin followed by blinatumomab for older adults with newly diagnosed Philadelphia chromosome–negative B-cell acute lymphoblastic leukemia: Alliance A041703. J Clin Oncol. 2024;42(suppl):abstr 7004.

Questions?

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Pause here! After questions, your moderator will then stop the recording prior to presenting the CE Text Code