POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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Algoritmi terapeutici 2026: Leucemia Linfoblastica Acuta

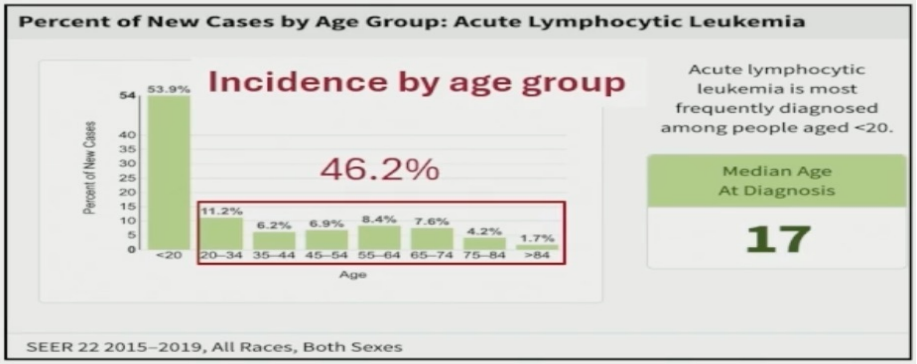
Direttore UOC Ematologia Ospedale Sant'Eugenio
Dipartimento di Biomedicina e Prevenzione, Università degli studi di Roma Tor Vergata

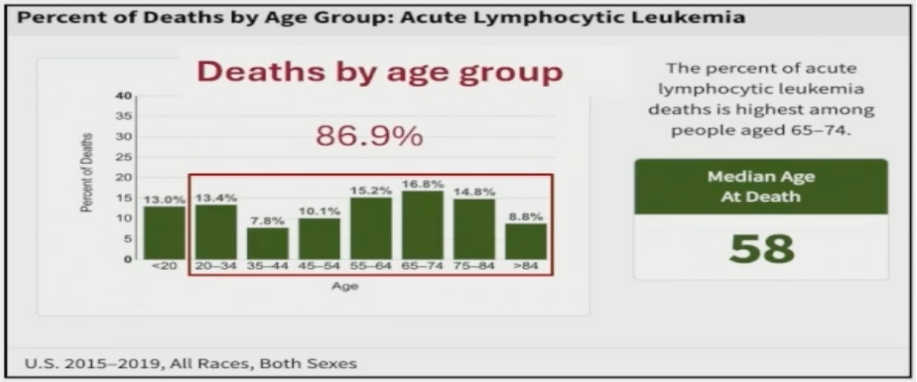
DICHIARAZIONE Maria Ilaria Del Principe

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Gilead Sciences	x					x	
Amgen						x	
Jhonson & Jhonson							x
Incyte							x
Abbvie							x

Estimated New Cases in 2025 (% of new cancer cases)	**6,550** (0.3%)
Estimated Deaths in 2025	**1,400**

- Highest incidence among patients <20 years
- Adults: 4 of every 10 diagnoses
  - Majority of deaths (4/5) occur in adults
- B-ALL accounts for 70-80% of ALL cases in adults
  - ~20% of cases of B-ALL are diagnosed in adults >55 years
  - Majority of deaths (4/5) occur in older adults
- T-ALL accounts for 20-30% of ALL cases in adults
  - Median age of diagnosis is 29 years
  - Higher incidence in male patients (2-3:1)
  - Modestly higher incidence in black patients
- Risk factors:
  - Down syndrome – 20-fold increase in risk
  - Prior chemo/radiation: estimated incidence of 3-7%

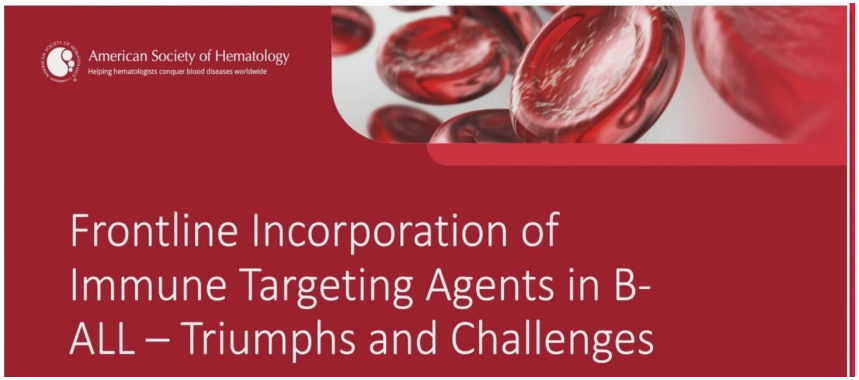




O'Dwyer KM. ASH Educational 2025

Goals of Therapy in 2026

- Personalize therapy based on risk and biology
- Achieve deep remission (MRD negativity)
- Reduce treatment-related toxicity
- Improve long-term survival and quality of life



Potential prognostic and predictive factors in adult ALL

	Risk factors	Annotations
Patient-related		
Age (y)	>30-60 y (continuous variable) >55 y (older adults and elderly)	Independent PF, usually not affecting risk model (age-adapted protocols)
Performance (ECOG)	>1	Retrospective data; relevance in older patients
Disease-related		
WBC ($\times 10^9$/L)	>30 (B), >100 (T)	Variably considered
Immunophenotype	Pro-B, CD20$^+$ (B), pro/pre-T, ETP, and mature-T (T)	Variably considered
Cytogenetics and fluorescence in situ hybridization	Ph$^+$, t(4;11), hypodiploidy, and complex*	Key prognostic elements; beside Ph$^+$ and KMT2Ar variably considered
Genetics	*BCR::ABL1*$^+$, *KMT2Ar*	Key prognostic elements
	Ph-like, mutated *CLRF2*/*TP53*/JAK-STAT, adverse CNA profile (B), unmutated *NOTCH1*/*FBWX7*, and abnormal *RAS*/*PTEN* (T)	Variably considered
Miscellaneous	CNS involvement	Occasionally considered
	Poor treatment compliance and undue treatment reductions and delay	Retrospective data, of greater concern with pediatric-type protocols
	Pharmacogenomics (affecting antimetabolite disposition)	Data in children, not usually assessed in adults
	Immune marrow microenvironment	Investigational, for research purposes
	Drug response profiling	Investigational, for research purposes
Treatment-response dynamics		
Corticosteroid sensitivity (prephase)	Poor prednisone response (PB count ≥1 × 10^9/L at the end of prephase)	Historical relevance, occasionally considered
Early/incomplete blast cell clearance (BM morphology)	Day 8-15 or end of induction BM blasts ≥5%	Variably considered
Time to CR (number of courses)	>1 cycle (late CR)	Variably considered
MRD (molecular/flow cytometry)	MRD positivity (from end of induction onwards): ≥0.1%/0.01% after induction ≥0.01%/positive after/during consolidation and pre/post-allogeneic SCT	Key and unifying factor predicting outcome

Gökbuget N et al. Blood. 2024;143(19):1903-1930

WHO Classification

Precursor B-cell neoplasms	
B-cell lymphoblastic leukaemias/lymphomas	
B-lymphoblastic leukaemia/lymphoma, NOS	(Same)
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy	B-lymphoblastic leukaemia/lymphoma with hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy	(Same)
B-lyr	
B-lyr	
B-lyr feat	
B-lyr rear	
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1*-like features	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with *TCF3::PBX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
B-lymphoblastic leukaemia/lymphoma with *IGH::IL3* fusion	B-lymphoblastic leukaemia/lymphoma with t(5;14)(q31.1;q32.1); *IGH/IL3*
B-lymphoblastic leukaemia/lymphoma with *TCF3::HLF* fusion	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with other defined	(Same)

Alaggio R et al. Leukemia. 2022;36(7):1720-1748

ICC Classification

B-ALL
- B-ALL with recurrent genetic abnormalities
- B-ALLwith t(9;22)(q34.1;q11.2)/*BCR::ABL1*
  - with lymphoid only involvement
  - with multilineage involvement
- B-ALLwith t(v;11q23.3)/*KMT2A* rearranged
- B-ALL with t(12;21)(p13.2;q22.1)/*ETV6::RUNX1*
- B-ALL, hyperdiploid
- B-ALL, hypodiploid
- B-ALL, near haploid
- B-ALL with t(5;14)(q31.1;q32.3)/*IL3::IGH*
- B-ALL with *HLF* rearrangement
- B-ALL with *UBTF::ATXN7L3/PAN3,CDX2* ("CDX2/UBTF")
- B-ALL with mutated *IKZF1* N159Y
- B-ALL with mutated *PAX5* P80R
- Provisional entity: B-ALL, *ETV6::RUNX1*-like
- Provisional entity: B-ALL, with *PAX5* alteration
- Provisional entity: B-ALL, with mutated *ZEB2* (p.H1038R)/ IGH::*CEBPE*
- Provisional entity: B-ALL, *ZNF384* rearranged-like
- Provisional entity: B-ALL, *KMT2A* rearranged-like
- B-ALL, NOS

T-ALL
- Early T-cell precursor ALLwith *BCL11B* rearrangement
- Early T-cell precursor ALL, NOS
- T-ALL, NOS
  - Provisional entities (see supplemental Table 7)

Provisional entity: natural killer cell ALL

Arber DA et al. Blood. 2022;140(11):1200-1228

2024 ELN recommendations

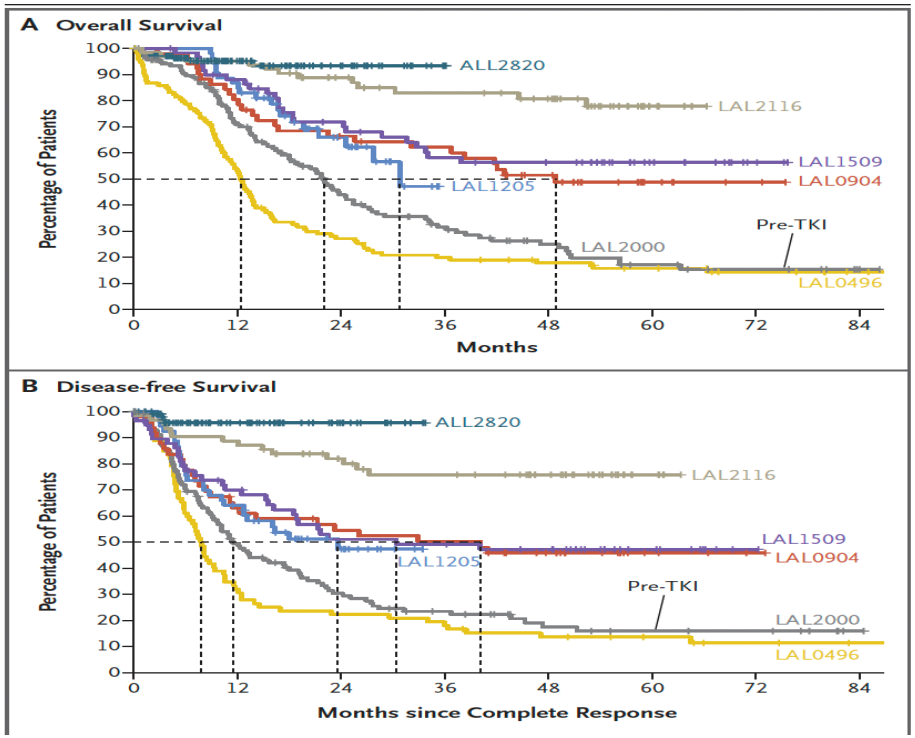
Molecular genetics	Mandatory	t(9;22)/Ph$^+$/*BCR::ABL1* t(4;11)$^+$/*KMT2Ar* t(1;19)$^+$/*TCF3::PBX1* Other high-risk cytogenetics

Gökbuget N et al. Blood. 2024;143(19):1903-1930

Ph+ B-ALL: a reversal of fortune for older adults

Table 1. The GIMEMA Frontline Strategy without Chemotherapy from 2000 to 2025 in Patients with Ph-Positive ALL.*

Study Protocol	Age	Induction Therapy	Complete Remission
	yr		*% of patients*
LAL0201-B[30]	>60	Imatinib	100
LAL1205[31]	>18	Dasatinib	100
LAL0904, 3rd amendment[20]	16–60	Imatinib followed by chemotherapy (with or without HSCT)	96
LAL1408[32]	>60 or unfit	Nilotinib and imatinib	94
LAL1509[33]	18–60	Dasatinib and total therapy†	97
LAL1811[34]	>60 or unfit	Ponatinib	95
LAL2116[35,36]	>18	Dasatinib plus blinatumomab	98
ALL2820[37,38]	>18	Ponatinib plus blinatumomab	95



Foà R. N Engl J Med . 2025 May 15;392(19):1941-1952

Trials in progress for pediatric Ph+ ALL:

AALL2131/EsPhALL 2022 (NCT061241157)

Age	≥1 year– 24 years
Design	Pilot study, single arm
Treatment	Chemotherapy backbone: AALL0232 + TKI Addition of blina (3 cycles) and removal of consolidation chemotherapy (8 weeks).
TKI	Dasatinib
Primary Endpoint	3-year EFS

- Ph+ ALL is rare in children
  - 5% of total cases
- Intensive chemotherapy the SOC
  - Significant infections complications
  - High-rates of relapse (~24%)
  - 5-year EFS estimated at 60%
  - Potential long-term treatment-related toxicities
- Adult trials are beginning to inform treatment strategies in children with Ph+ ALL

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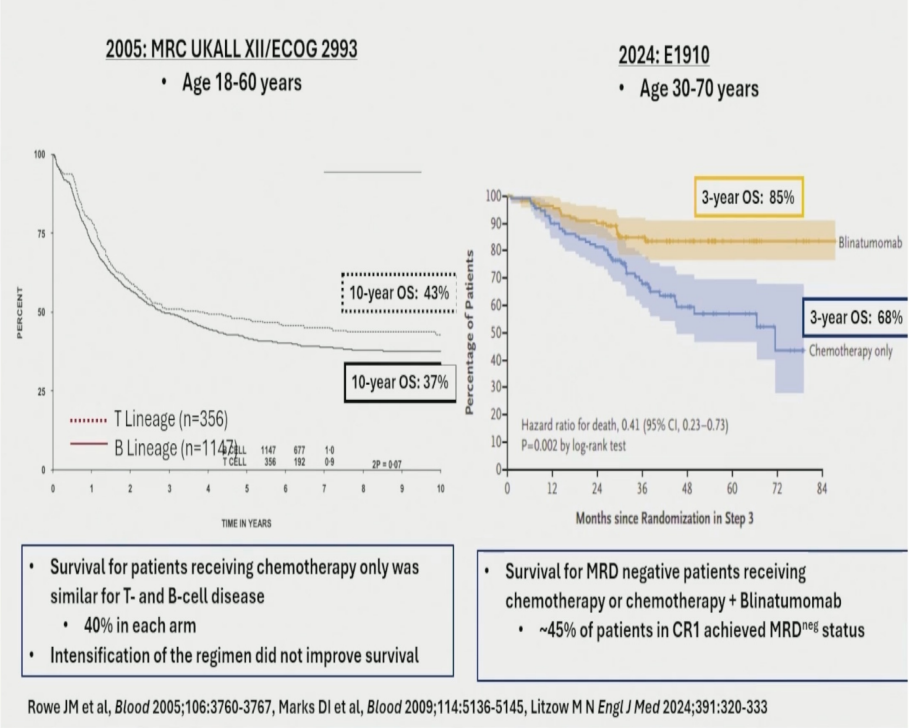
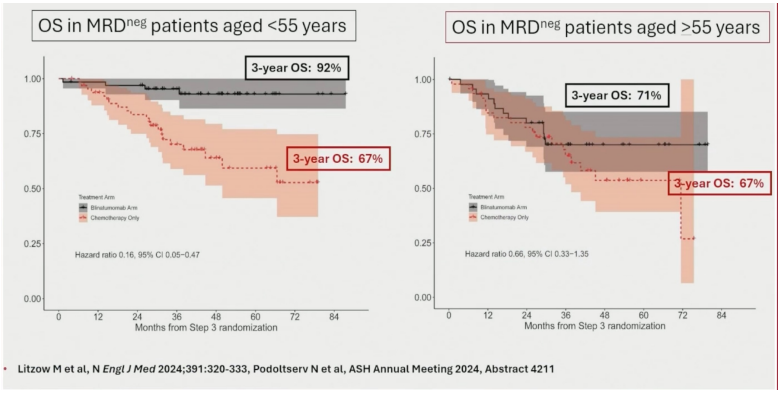
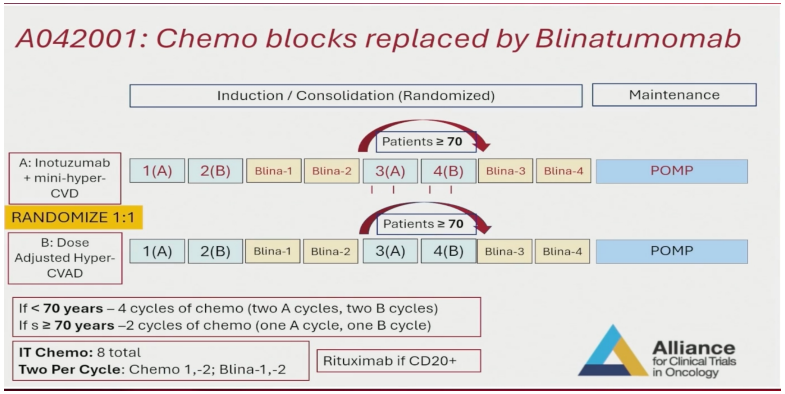
20 years of progress in adult Ph- B ALL



Rowe JM et al, *Blood* 2005;106:3760-3767, Marks DI et al, *Blood* 2009;114:5136-5145, Litzow M N *Engl J Med* 2024;391:320-333

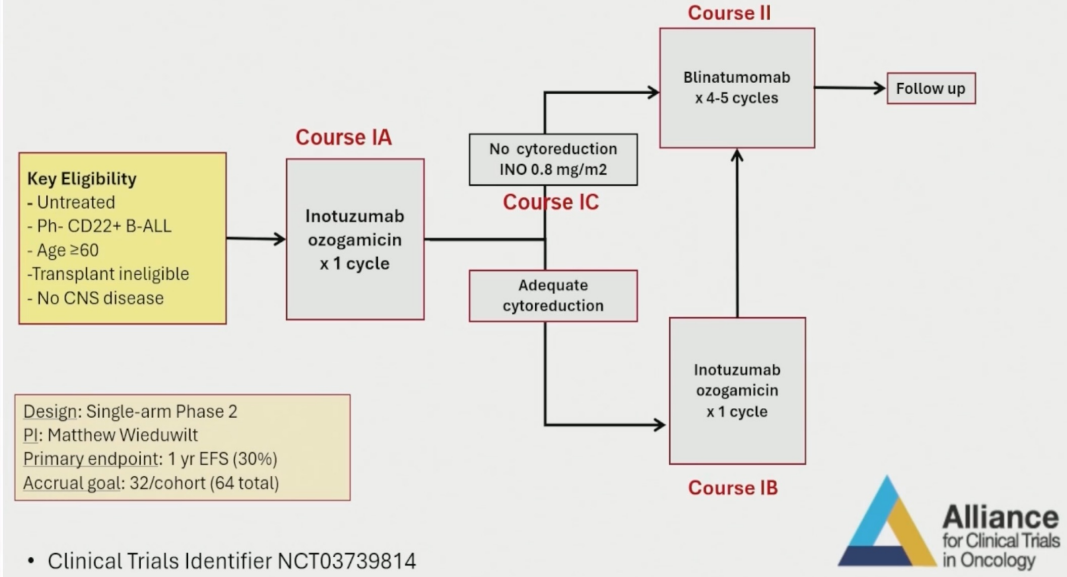


• Litzow M et al, N *Engl J Med* 2024;391:320-333, Podoltserv N et al, ASH Annual Meeting 2024, Abstract 4211



O'Dwyer KM. ASH Educational 2025

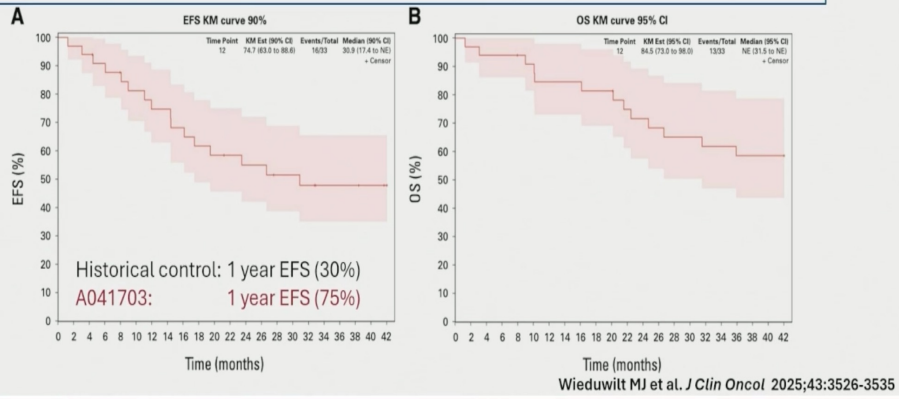
A041703: InO + Blin for Ph^{neg} B-ALL in older adults



- Clinical Trials Identifier NCT03739814

A041703: Outcomes with chemotherapy-free regimen

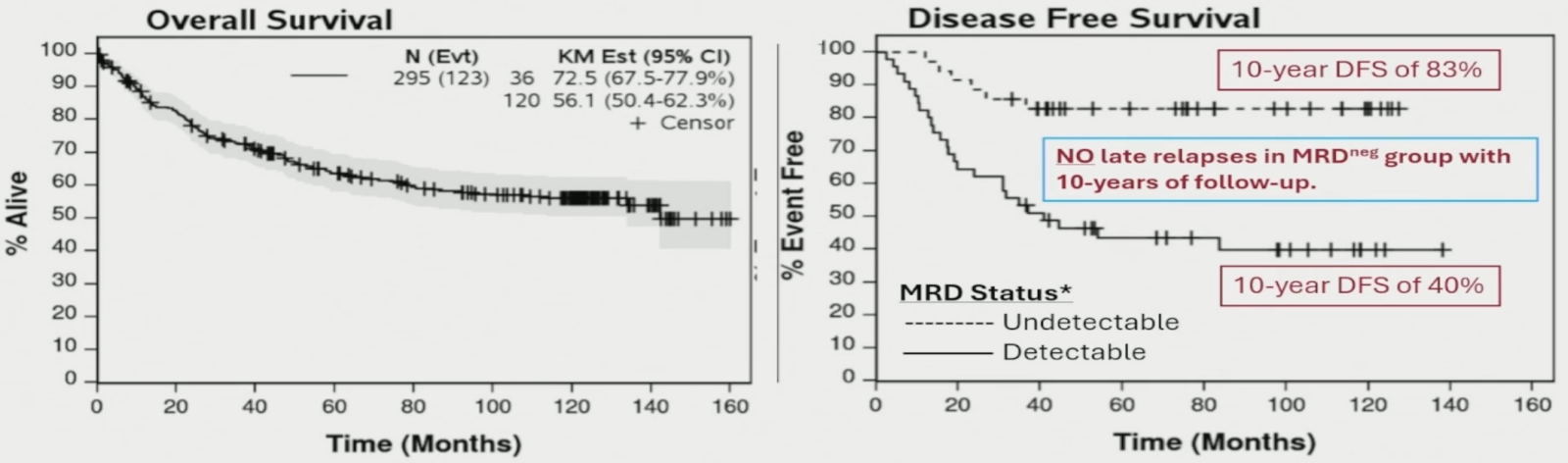
Best Cumulative Response	By End of Course IB or IC	By End of Course II
Hematologic response (N = 33), No. (%)		
Composite CR (CR + CRh + CRi)	28 (85)	32 (97)
CR	15 (45)	19 (58)
CRh	11 (33)	12 (36)
CRi	2 (6)	1 (3)
Refractory	3 (9)	1 (3)
Undetermined[a]	2[a] (6)	0 (0)
MRD undetectable. No. (%)	12/12 (100)	10/11 (91)



Wieduwilt MJ et al. *J Clin Oncol* 2025;43:3526-3535

O'Dwyer KM. ASH Educational 2025

Young adult B-ALL in 2025: 10-year outcomes C10403

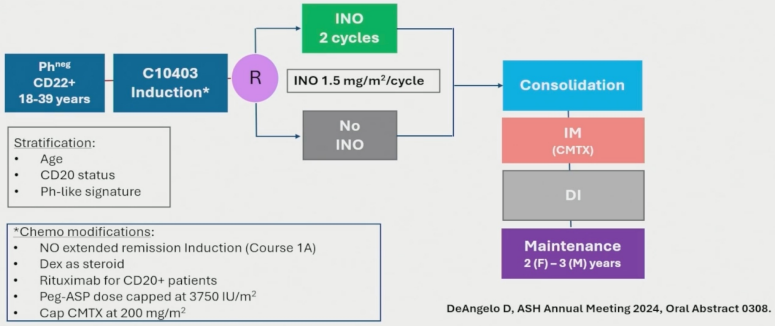


Stock W et al. HemaSphere 2025;9(51):S118

O'Dwyer KM. ASH Educational 2025

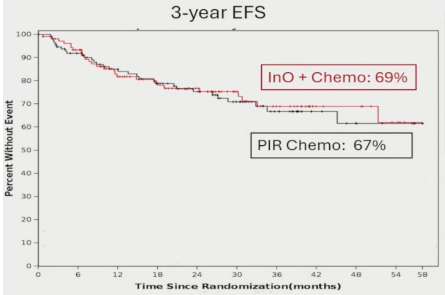
Phase 3 Trial Alliance A041501: InO in Young Adults with Ph^{neg} B-cell ALL

Alliance for Clinical Trials in Oncology



DeAngelo D, ASH Annual Meeting 2024, Oral Abstract 0308.

A041501: Initial results of randomized cohorts



	Chemo (N=116)	InO (N=111)	Total (N=227)
Event, n (%)			
Censor	85 (73.3%)	82 (73.9%)	167 (73.6%)
Death	4 (3.4%)	14 (12.6%)	18 (7.9%)
Progression	27 (23.3%)	15 (13.5%)	42 (18.5%)

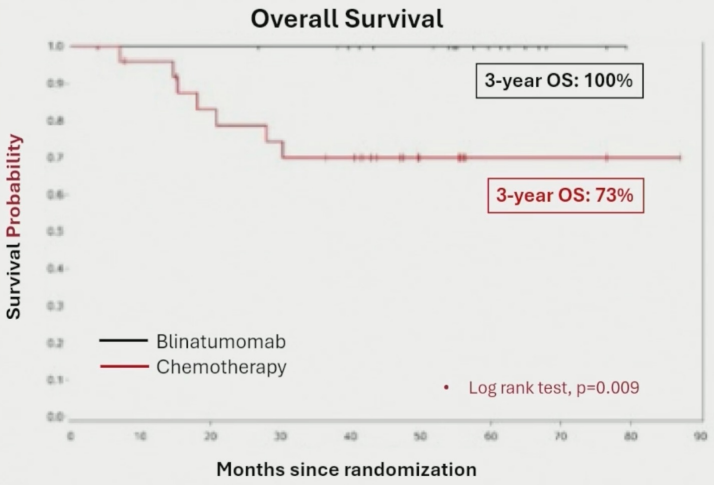
- Causes of the events are different

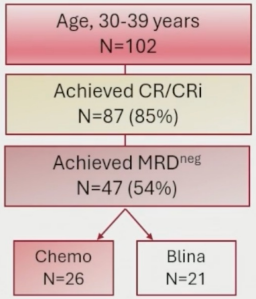
Outcome	C10403	A041501
3-year EFS	59%	69%
3-year OS	73%	80%

Historical CALGB OS: 46%

DeAngelo D, ASH Annual Meeting 2024, Oral Abstract 0308.

E1910, subgroup analysis young adults 30-39 years





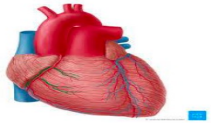
Dinner S et al. HemaSphere 2025;9(51):26-28

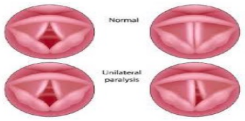
O'Dwyer KM. ASH Educational 2025

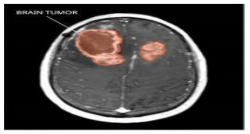
Children and adolescents with B-ALL

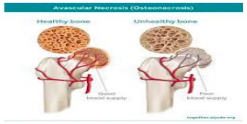
Severe toxicity free survival: physician-derived definitions of unacceptable long-term toxicities following acute lymphocytic leukaemia

*Liv Andrés-Jensen, Andishe Attarbaschi, Edit Bardi, Shlomit Barzilai-Birenboim, Deepa Bhojwani, Melanie M Hagleitner, Christina Halsey, Arja Harila-Saari, Raphaele R L van Litsenburg, Melissa M Hudson, Sima Jeha, Motohiro Kato, Leontien Kremer, Wojciech Mlynarski, Anja Möricke, Rob Pieters, Caroline Piette, Elizabeth Raetz, Leila Ronceray, Claudia Toro, Maria Grazia Valsecchi, Lynda M Vrooman, Sigal Weinreb, Naomi Winick, Kjeld Schmiegelow, on behalf of the Ponte di Legno Severe Toxicity Working Group**









Disease free survival (DFS) → Severe toxicity free survival (STFS)

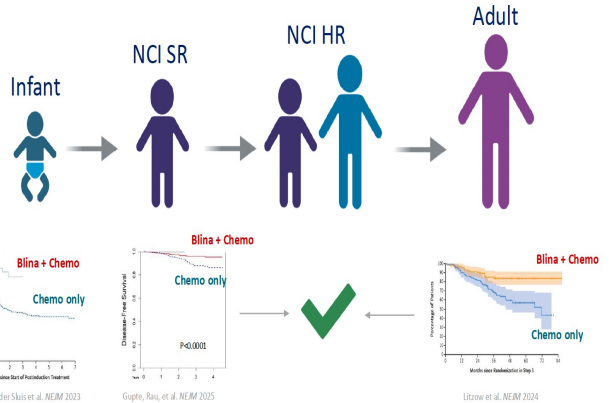
Abstract 13888 – Karen Arane

Courtesy of Gupta S. ASH Educational 2025

Children and adolescents with B-ALL

Blinatumomab benefits across age and risk groups

SickKids THE HOSPITAL FOR SICK CHILDREN



van der Sluis et al. *NEJM* 2023 — Gupte, Rau, et al. *NEJM* 2025 — Litzow et al. *NEJM* 2024

- None of the above studies removed any blocks of chemotherapy from standard backbones

What elements of chemo do we take away?

SickKids THE HOSPITAL FOR SICK CHILDREN

Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

J Clin Oncol. 2022 Jan 10;40(5):956–967. doi: 10.1200/JCO.21.01693

Phase II Trial of Inotuzumab Ozogamicin in Children and Adolescents With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia: Children's Oncology Group Protocol AALL1621

Maureen M O'Brien, Lingyun Ji, Nirali N Shah, Susan R Rheingold, Deepa Bhojwani, Constance M Yuan, Xinxin Xu, Joanna S Yi, Andrew C Harris, Patrick A Brown, Michael J Borowitz, Olga Militano, John Kairalla, Meenakshi Devidas, Elizabeth A Raetz, Lia Gore, Mignon L Loh

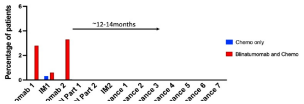
308 Addition of Inotuzumab to a Pediatric Inspired Chemotherapy Regimen in Young Adult Patients with B-Cell Acute Lymphoblastic Leukemia: Findings from the Alliance A041501 Phase 3 Randomized Trial

Program: Oral and Poster Abstracts
Type: Oral
Session: 615. Acute Lymphoblastic Leukemias: Therapies Excluding Allogeneic Transplantation: Clinical Trials in Pediatric and Young Adult Patients
Hematology Disease Topics & Pathways:
Clinical trials, Research, Clinical Research

Saturday, December 7, 2024: 4:15 PM

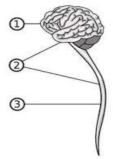
Daniel J. DeAngelo, MD, PhD, Jun Yin, Anjali S. Advani, MD, Selina Luger, MD, FRCPC, Jill Fulcher, MS, PhD, FRCPath, Michaela Liedtke, MD, Geoffrey L. Uy, MD, Shira N. Dinner, MD, Lindsay Wide, MD, Marlise R. Luskin, MD, Carer Saygin, MD, Ella Peeters, Noreen Fulton, Richard C. Harvey, PhD, Gabe E Perez Barbano, MS, Rebecca Teske, Harry P. Erba, MD, PhD

Grade 3+ sepsis/catheter related infections SR-Avg



What elements of chemo do we take away?

SickKids THE HOSPITAL FOR SICK CHILDREN



A diagram showing the CNS:
1. Brain
2. Central nervous system (brain and spinal cord)
3. Spinal cord

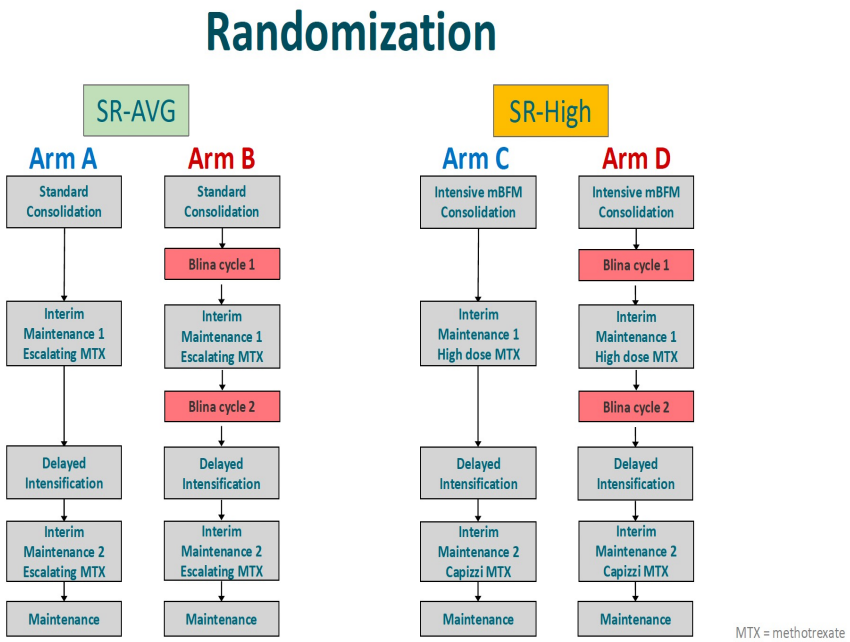
	Acute toxicity	CNS coverage	Late effects	Burden on family and quality of life	Other comments
Induction	+++	+++	+	++++	• Response to traditional Induction therapy is a key component of contemporary risk stratification. • There is some late effect risk associated with anthracycline in 4-drug induction.
SR Consolidation	+	+++		++	
HR Consolidation	+++	+++	+	++++	
SR Interim Maintenance 1*	+	++		++	
HR Interim Maintenance 1#	++	++++		+++	
Delayed Intensification	+++	+++	++	+++	• HR Delayed Intensification includes 1 additional dose of long-acting asparaginase with consequent additional risk of toxicity and burden on families.
Interim Maintenance 2*	+	++		++	• HR Interim Maintenance 2 includes 2 additional doses of long-acting asparaginase with consequent additional risk of toxicity and burden on families.
Maintenance	+	+		++	

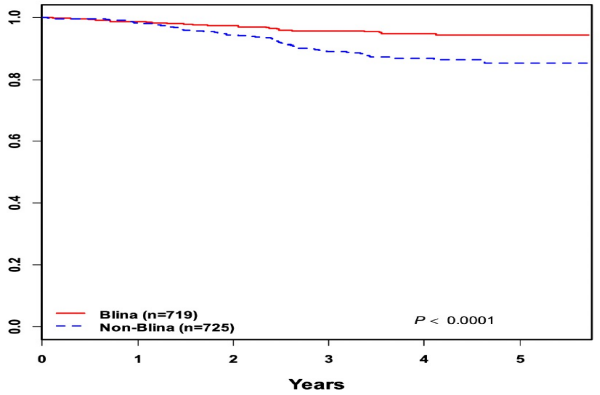
CNS – Central nervous system; HR – High risk; SR – Standard risk
*Escalating methotrexate
#High-dose methotrexate

…and how much?

Courtesy of Gupta S. Educational 2025

Updated results of the COG trial AALL1731



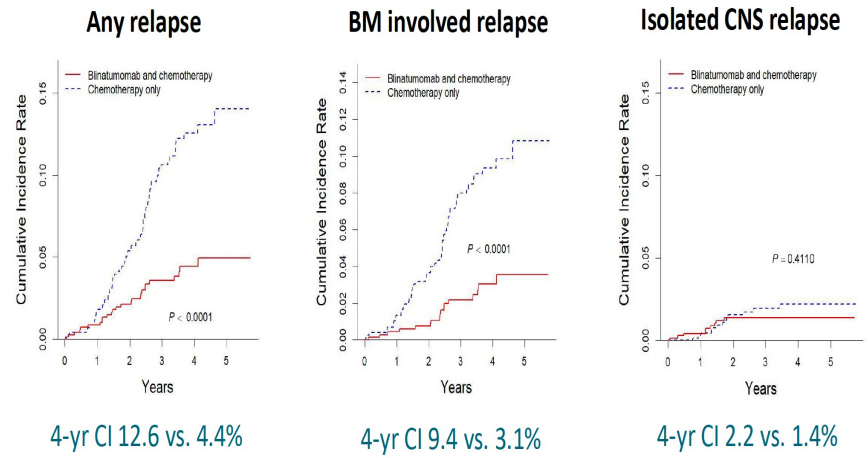


4-yr DFS 86.9 vs 94.8%
HR 0.41

Courtesy of Gupta S

Updated results of the COG trial AALL1731

Updated Overall Results



4-yr CI 12.6 vs. 4.4%

4-yr CI 9.4 vs. 3.1%

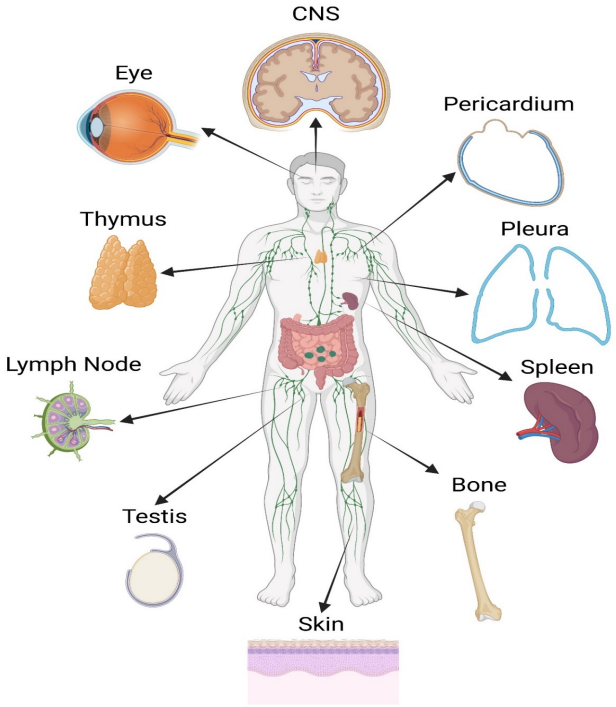
4-yr CI 2.2 vs. 1.4%

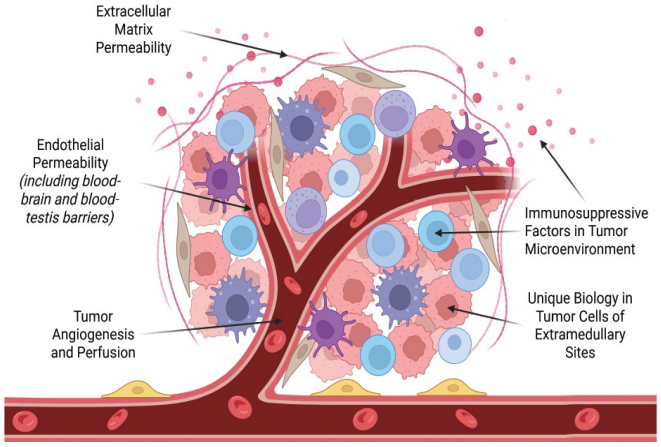
Changes in prognostic value

	Chemotherapy			Blinatumomab and Chemotherapy		
	HR	95CI	p	HR	95CI	p
Cytogenetics			**0.007**			0.10
Favorable	Ref	Ref	Ref	Ref	Ref	Ref
Neutral	1.76	0.97-3.18	0.06	2.58	0.89-7.48	0.08
Unfavorable	**3.49**	**1.61-7.55**	**0.002**	**4.09**	**1.10-15.24**	**0.04**
Cytogenetic lesion						
ETV6::RUNX1	0.66	0.27-1.63	0.37		NE	
Double trisomy	0.51	0.25-1.02	0.05	0.58	0.20-1.65	0.30
iAMP21	1.50	0.60-3.72	0.38	0.69	0.09-5.06	0.72
KMT2A-R	2.02	0.50-8.23	0.33	3.15	0.75-13.19	0.12
Hypodiploid	**3.69**	**1.49-9.14**	**0.005**	3.17	0.76-13.28	0.11
TCF3::HLF	-	-	-	-	-	-
CNS status						
CNS1	Ref	Ref	Ref	Ref	Ref	Ref
CNS2	1.51	0.78-2.94	0.22	0.58	0.14-2.43	0.46
Day 29 bone marrow mpFC MRD						
<0.01%	Ref	Ref	Ref	Ref	Ref	Ref
≥0.01%	**1.85**	**1.17-2.91**	**0.008**	1.87	0.92-3.78	0.08

Courtesy of Gupta S

CNS is the Most Important Extramedullary Site in ALL





- Concept is not new for ALL
  - CNS has blood-brain barrier
  - Testis has blood-testis barrier
- Patterns of relapse after HCT[1]
  - Some sites have seemingly less GVL
  - Ex.: skin, visceral organs
- Sanctuary sites → extramedullary relapse
- Relatively infrequent historically
  - *Post hoc* analysis of UKALL12/ECOG 2993[2]
  - Of 609 relapses, 45 (8%) had isolated EMD
  - Most common site was CNS (n = 22)

Courtesy of Cassaday RD. ASH Educational 2025

Recent Rates of Extramedullary Relapse: Ph- B-ALL

- Summary of Prospective Trials Incorporating Immunotherapy into Frontline Treatment for Adults

Treatment	Chemo Intensity*	Patient Age: Median (Range), y	N	Overall Survival	Relapses		
					Total	EMD, n (%)	Sites/Comments
S1318: Blin followed by POMP[1]	Absent	75 (66-84)	29	37% @ 3 y	13	2 (15%)	NR
A041703: InO followed by Blin[2]	Absent	71 (60-84)	33	85% @ 1 y	12	2 (17%)	Both EMD relapses involved CNS
Mini-hyperCVD + InO ± Blin[3]	Reduced	68 (60-87)	80	46% @ 5 y	12	5 (42%)	All included CNS, with 2 isolated to CNS
INITIAL-1: InO followed by Chemo[4]	Reduced	64 (56-80)	43	73% @ 3 y	11	4 (36%)	All involved CNS
EWALL-InO[5]	Reduced	68 (55-84)	131	55% @ 2 y	49	4 (8%)	1 each: CNS, testis, skin, and bone
E1910: Chemo + Blin[6]	Full	51.5 (30-69)	112	85% @ 3 y	NR	NR	NR
E1910: Chemo only[6]		50 (30-70)	112	68% @ 3 y	NR	NR	NR

Abbreviations: Blin, blinatumomab; CNS, central nervous system; EMD, extramedullary disease; InO, inotuzumab ozogamicin; NR, not reported; NE, not estimable.

*Based on authors' description or relative comparison of cytotoxic chemotherapy during induction and maintenance phases (i.e., not maintenance)

Courtesy of Cassaday RD. ASH Educational 2025

Recent Rates of Extramedullary Relapse: Ph+ B-ALL

- Summary of Prospective Trials Incorporating Immunotherapy into Frontline Treatment for Adults

Treatment	Chemo Intensity*	Patient Age: Median (Range), y	N	Overall Survival	Relapses		
					Total	EMD, n (%)	Sites/Comments
D-ALBA: Dasatinib + Blin[1]	Absent	54 (24-82)	63	81% @ 53 mo	9	5 (55%)	4 involved CNS, 1 nodal only
S1318: Dasatinib + Blin[2]	Absent	73 (65-87)	24	87% @ 3 y	7	2 (29%)†	2 involved CNS
Ponatinib + Blin[3]	Absent	50 (18-83)	76	88% @ 3 y	10	6 (60%)	5 isolated CNS, 1 peritoneum and lymph nodes
EWALL PH-01: Chemo + Dasatinib[4]	Reduced	69 (59-83)	71	36% @ 5 y	36	1 (3%)†	1 involved CNS
PhALLCON: Chemo + Imatinib[5]	Reduced	52 (19-75)	81	Median NE @ 20 mo	9‡	NR	NR
PhALLCON: Chemo + Ponatinib[5]		54 (19-82)	164	Median NE @ 18 mo	6‡	NR	NR
HyperCVAD + Ponatinib[6]	Full	46 (21-80)	86	65% @ 6 y	15	NR	No CNS relapses after increased IT chemo; rate prior not reported

†Only reported EMD relapses involving CNS, so potentially an understatement. ‡Described as "loss-of-response" events with no other details.

[1]Foà, et al. *N Engl J Med.* 2020;383:1613-23. [2]Advani, et al. *Blood Adv*. 2023;7:1279-85. [3]Short, et al. *J Hematol Oncol*. 2025;18:55.
[4]Rousellot, et al. *Blood*. 2016;128:774-82. [5]Jabbour, et al. *JAMA*. 2024;331:1814-23. [6]Kantarjian, et al. *Am J Hematol*. 2023;98:493-501

Courtesy of Cassaday RD. ASH Educational 2025

Activity of Immunotherapy Against CNS Disease

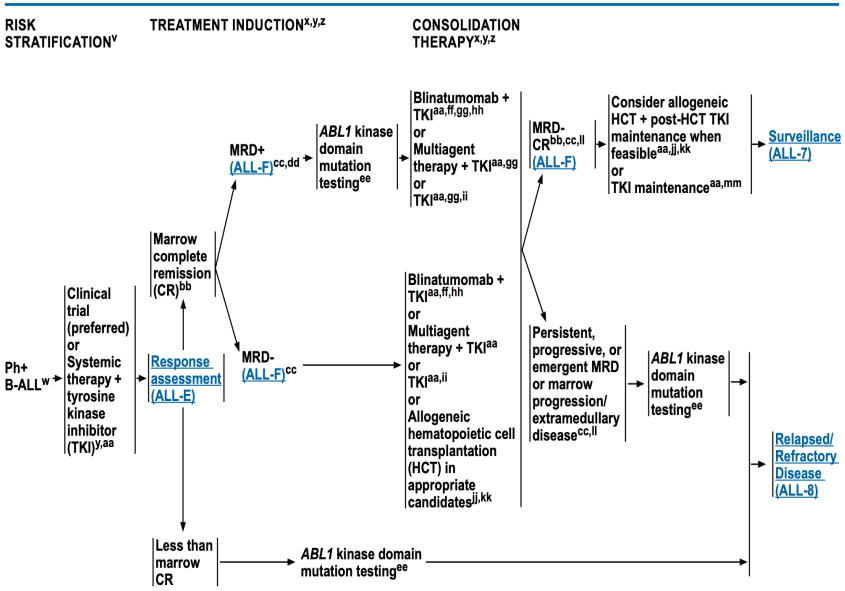
- Evidence is Emerging that Support the Use of Some of these Agents

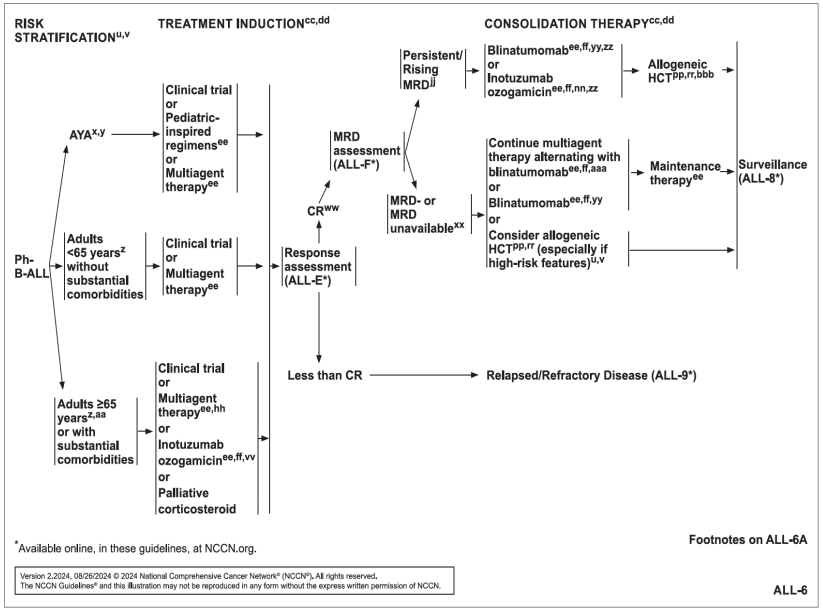
Agent	Mechanism of Action	Evidence of CNS Activity
Blinatumomab	CD3-CD19 Bispecific T-cell Engager	**Limited**: 1 retrospective series
Inotuzumab Ozogamicin	CD22 Antibody-Drug Conjugate	**None**
Tisagenlecleucel	CD19 CAR-T Cells	**Moder** prospe series
Brexucabtagene autoleucel	CD19 CAR-T Cells	**Moder** experie
Obecabtagene autoleucel	CD19 CAR-T Cells	**None** (yet…)

Modified from: Kopmar & Cassaday. *Blood.* 2023;141:1379-88.
*Muhsen, Roloff, et al. *Blood Adv*. 2025;9:4081-9.

Courtesy of Cassaday RD. ASH Educational 2025

Allogeneic Stem Cell Transplantation





NCCN. Acute Lymphoblastic Leukemia, Version 2.2024

CAR-T Cell Therapy in 2026

PRINCIPLES OF SYSTEMIC THERAPY

REGIMENS FOR RELAPSED OR REFRACTORY Ph-POSITIVE B-ALL[a,b]

Other Recommended Regimens
• TKI[c] (dasatinib,[1,2] imatinib,[3] ponatinib,[4] nilotinib,[5] or bosutinib[6]) ‣ The TKIs noted above may also be used in combination with any of the regimens noted on ALL-D 3 of 27 that were not previously given. • Asciminib + dasatinib[7] • Blinatumomab ± TKI[8,9] • Inotuzumab ozogamicin ± TKI[10,11] • Tisagenlecleucel (patients aged <26 years and with refractory disease or ≥2 relapses and following therapy that has included 2 TKIs)[12] • Brexucabtagene autoleucel (following therapy that has included TKIs)[13] • Obecabtagene autoleucel (following therapy that has included TKIs)[14] • The regimens listed on ALL-D 26 of 27 for Ph-negative B-ALL may be considered for Ph-positive B-ALL refractory to TKIs.

PRINCIPLES OF SYSTEMIC THERAPY

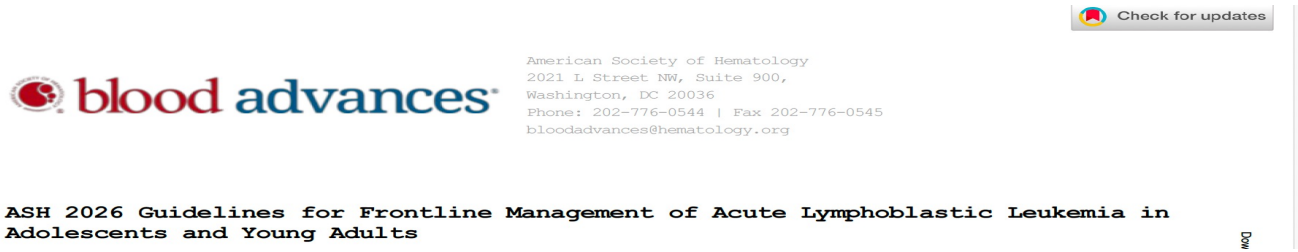
REGIMENS FOR RELAPSED OR REFRACTORY Ph-NEGATIVE B-ALL[a,b,c,d]

Preferred Regimens
• **Blinatumomab (CD19 antigen directed) (category 1)[1] ± multiagent therapy** • **Inotuzumab ozogamicin (CD22 antigen directed) (category 1)[2]** • **Tisagenlecleucel (CD19 antigen directed) (patients aged <26 years and with refractory disease or ≥2 relapses)[3]** • **Brexucabtagene autoleucel (CD19 antigen directed)[4]** • **Obecabtagene autoleucel (CD19 antigen directed)[5]**
Other Recommended Regimens[e]
• **Inotuzumab ozogamicin + mini-hyperCVD with or without sequential blinatumomab** (hyperfractionated cyclophosphamide, vincristine, dexamethasone, alternating with methotrexate, cytarabine)[6,7] • **Augmented HyperCVAD:** hyperfractionated cyclophosphamide, intensified vincristine, doxorubicin, intensified dexamethasone, pegaspargase; alternating with high-dose methotrexate, cytarabine[8] • **Clofarabine alone[9-12] or in combination** (eg, clofarabine, cyclophosphamide, etoposide)[10,13,14] • **MOpAD regimen:** methotrexate, vincristine, pegaspargase, dexamethasone; with rituximab for CD20-positive disease[15] • **Fludarabine-based regimens** ‣ **FLAG-IDA:** fludarabine, cytarabine, G-CSF ± idarubicin[16] ‣ **FLAM:** fludarabine, cytarabine, mitoxantrone[17] • **Cytarabine-containing regimens:** eg, high-dose cytarabine, idarubicin, IT methotrexate[18] • **Alkylator combination regimens:** eg, etoposide, ifosfamide, mitoxantrone[19] • **Revumenib (*KMT2A* rearranged)[f,20]**

NCCN. Acute Lymphoblastic Leukemia, Version 2.2024

Key Take-Home Messages

- Immunotherapy is central across disease phases
- Ongoing clinical trials remain essential



- ✓ *suggests* that empiric dose capping and dose reductions of asparaginase are reasonable strategies…
- ✓ *suggests* against routinely proceeding with allo-HSCT as consolidation
- ✓ *suggests* the addition of rituximab to standard chemotherapy
- ✓ *suggests* the addition of blinatumomab

Novità dal Meeting della Società Americana di Ematologia

Torino, 19-21 Febbraio 2026

Thank you