Global Leukemia Academy

Global Leukemia Academy

Evolving Treatment Landscape and Future Directions in Adult ALL Management

Focus: Latin America

Thursday, June 18, 2026
5.00 PM – 6.00 PM (Houston)
4.00 PM – 5.00 PM (Mexico City)

Meeting sponsors AMGEN Autolus APTITUDE HEALTH

Global Leukemia Academy

Welcome, Introductions, and Meeting Overview

Elias Jabbour, MD
MD Anderson Cancer Center,
Houston, TX, USA

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Meet the Faculty

Elias Jabbour, MD
The University of Texas MD Anderson Cancer Center, Houston, TX

Roberta Demichelis, MD
Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Program Objectives

- Gain insight into current treatment patterns for ALL in the Latin American region, including adoption of new technologies
- Discuss regional integration of genomic testing and its role in patient treatment
- Share the latest data on
  - Bispecifics and insights into their utility in ALL
  - Stem cell transplantation in ALL as a consolidation in first remission
  - The potential of MRD in monitoring and managing ALL
  - Promising novel and emerging therapies in ALL
- Discuss the opportunities for CAR T in leukemia: logistic barriers and challenges in the Latin American region
- Discuss future directions
  - Discuss the evolution of regional management algorithms for ALL

Virtual Meeting

Thursday, June 18, 2026

Time (Houston)	Time (Mexico City)	Title	Speaker/Moderator
5.00 PM – 5.05 PM 5 min	4.00 PM – 4.05 PM 5 min	Welcome, Meeting Overview, and Introductions	Elias Jabbour, MD
5.05 PM – 5.25 PM 20 min	4.05 PM – 4.25 PM 20 min	Global Progress in ALL (review of data from recent conferences and impact on SOC) 15-min presentation and 5-min Q&A	Elias Jabbour, MD
5.25 PM – 5.40 PM 15 min	4.25 PM – 4.40 PM 15 min	ALL Patient Case Discussion (with genomic testing)	Roberta Demichelis, MD
5.40 PM – 5.55 PM 15 min	4.40 PM – 4.55 PM 15 min	Opportunities and Challenges in Everyday Practice (Q&A session)	Roberta Demichelis, MD, and Elias Jabbour, MD
5.55 PM – 6.00 PM 5 min	4.55 PM – 5.00 PM 5 min	Conclusions and Wrap-Up	Roberta Demichelis, MD, and Elias Jabbour, MD

Global Leukemia Academy

Global Progress in ALL

Elias Jabbour, MD
MD Anderson Cancer Center,
Houston, TX, USA

APTITUDE HEALTH®

What Is New in B-ALL in 2026

Elias Jabbour, MD
Department of Leukemia
The University of Texas MD Anderson Cancer Center,
Houston, TX

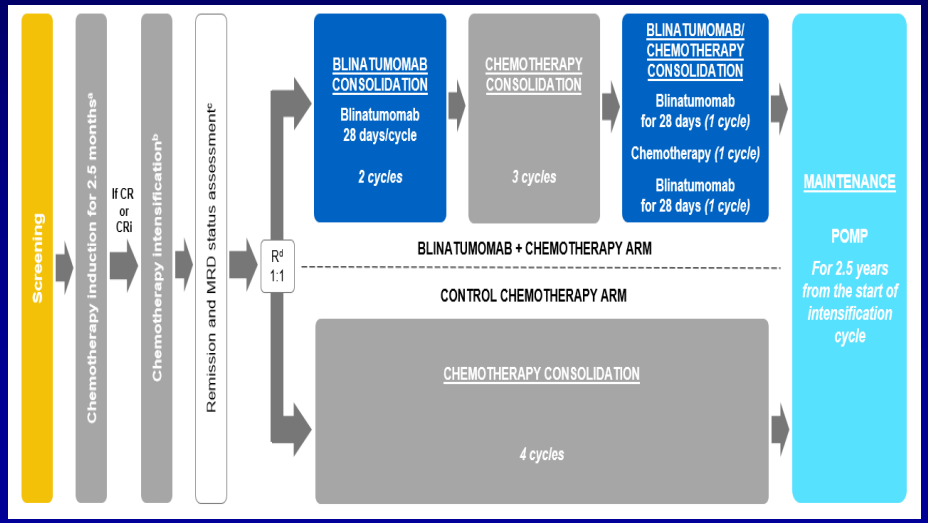
June 2026

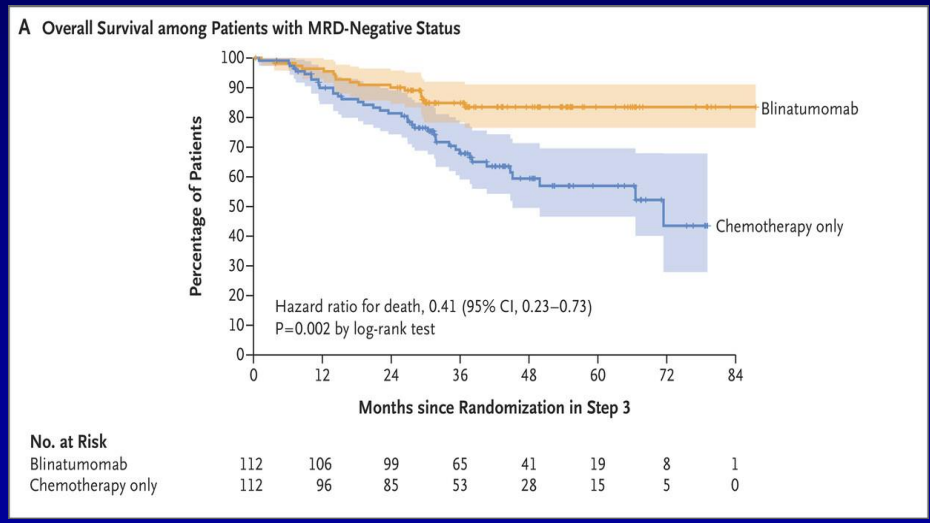
ALL: What Is New in 2026

- Philadelphia-negative ALL
- Philadelphia-positive ALL
- Measurable residual disease (MRD)
- Relapsed/refractory disease

E1910 Randomized Phase III Trial: Blina vs SOC as Consolidation in MRD-Negative CR

- 488 pts median age 51 yr (30–70)
- 224 MRD-neg CR randomized 1:1
- 22 pts (20%) Rx ASCT in each arm
- Median F/U 43 mo; median OS NR vs 71.4 mo (HR = 0.42; *P* = .003)
- No difference in OS if 1–2 cycles of blina vs control (HR: 0.62; *P* = .22)
- OS: 1–2 cycles vs 4 cycles (HR: 0.39; *P* = .07)

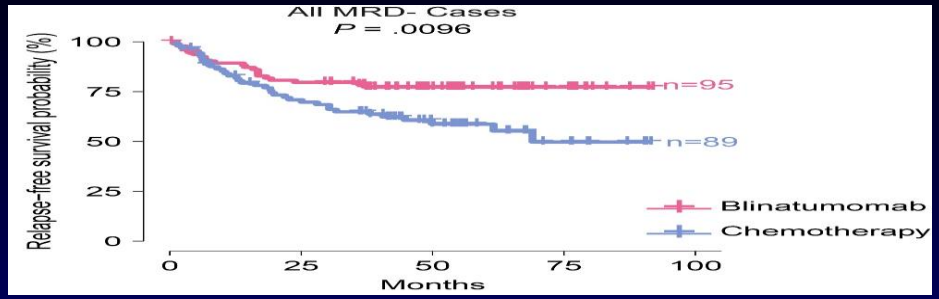


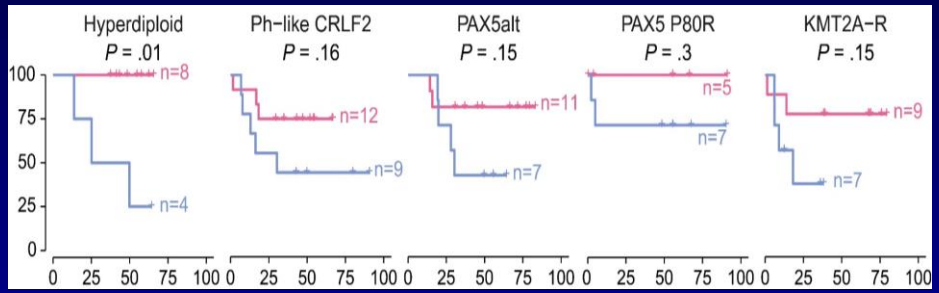


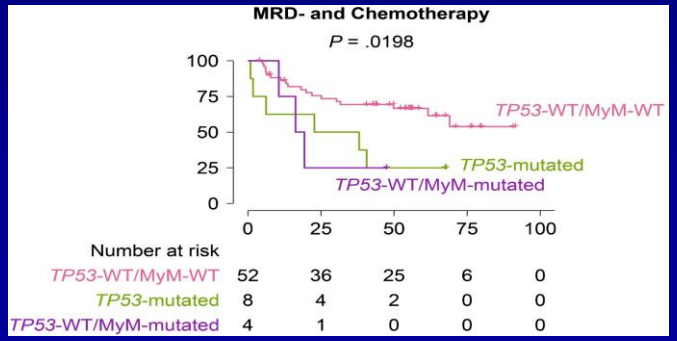
Litzow MR, et al. *N Engl J Med.* 2024;391:320-333.

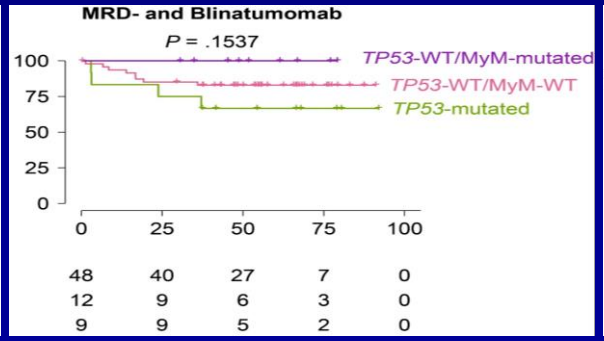
Genomics and Blina: Subsets Analysis E1910

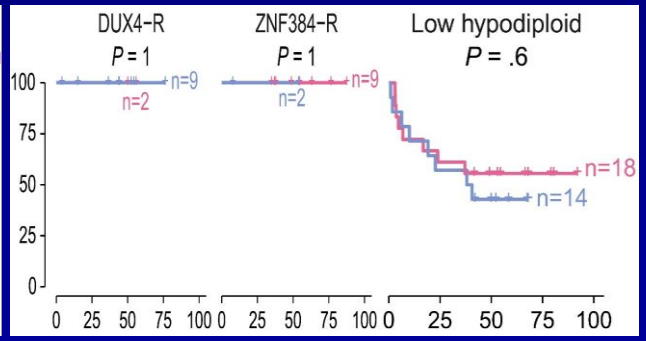
- Comprehensive genomic analysis of 569 adults with B-ALL
  - 22 molecular groups defined
  - Novel subgroup identified: *CEBP*-altered ALL (~3.5%)
- Pts for whom induction chemotherapy failed (n = 62) or were MRD-pos (n = 63) enriched
  - *BCR::ABL1*-like (30% vs 14%, *P* <.001), *KMT2A* (18% vs 9%, *P* = .03) and *BCL2/MYC* (5% vs 1%, *P* = .06)
- Pts who achieved MRD negativity enriched
  - *PAX5*alt (6% vs 18%, *P* = .002), *TCF3::PBX1* (0% vs 5%, *P* = .01), and *ZNF384* (2% vs 6%, *P* = .08)
- Blina (n = 93) improved RFS for pts with hyperdiploid, *PAX5*alt, *BCR::ABL1*-like, and *KMT2A*r ALL compared to chemotherapy alone (n = 90)
- *TP53* mutations (n = 65) associated with low hypodiploidy (n = 52)
- *CRLF2* rearrangements harbored the highest number of other CHIP gene mutations (n = 13), including *DNMT3A* (n = 4), *TET2* (n = 3), and *ASXL1* (n = 3)









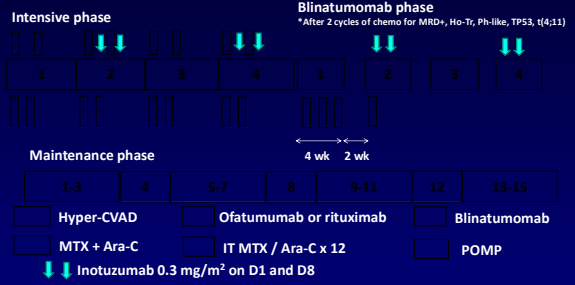


Zhong, et al. *Blood*. 2025;146(suppl 1):31.

Hyper-CVAD-InO → Blina in ND Adult ALL

- 75 pts (38 no InO, 37 InO); median age 33 yr (18–59); median F/U 48 mo (13–90)
- CR rate 100% (84% post-C1); MRD-neg 95% (66% at CR); NGS MRD-neg 79%; 60-day mortality 0%; 24 (32%) allo-SCT

Hyper-CVAD + Blinatumomab in B-ALL. Regimen



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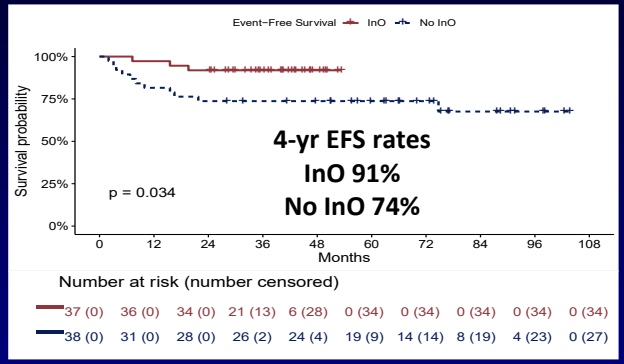
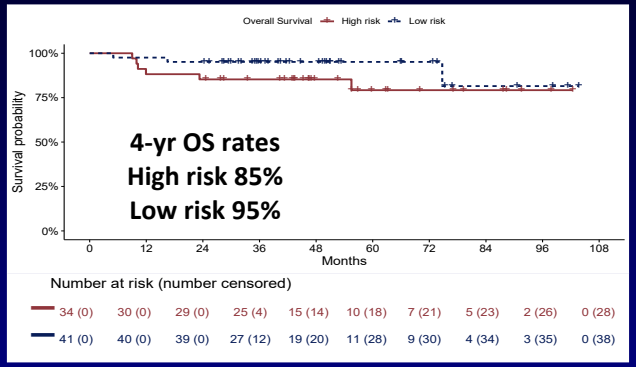
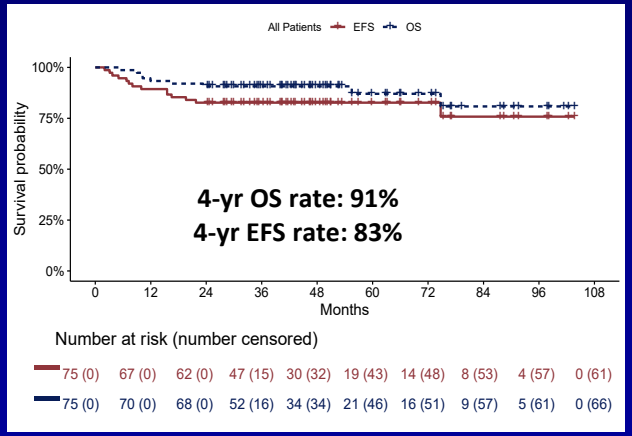


OS by risk





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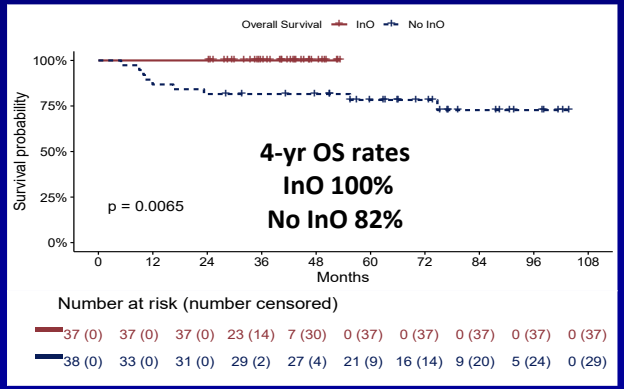
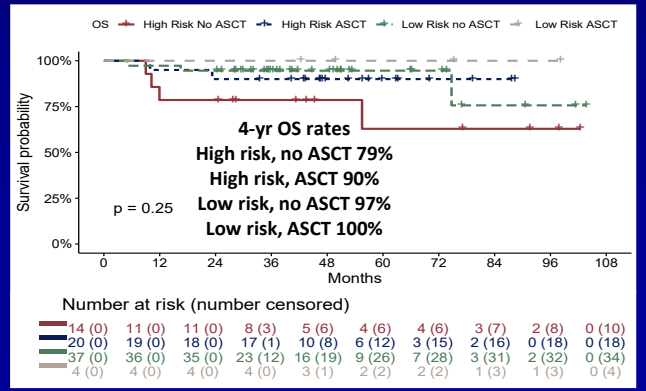


OS by risk and ASCT

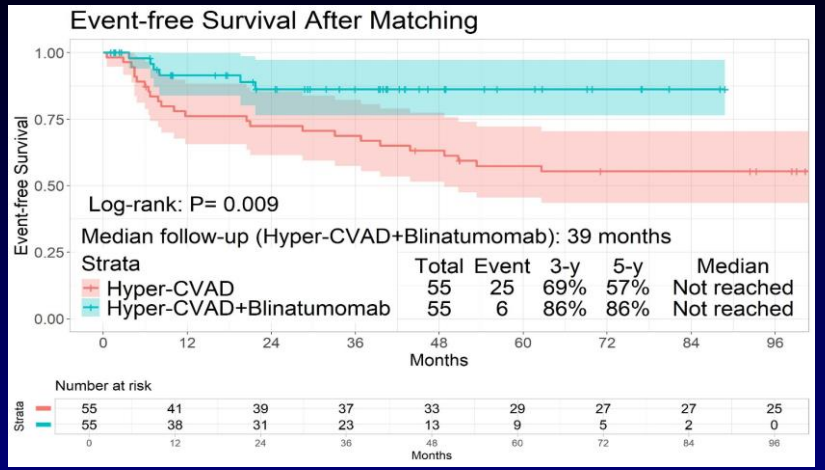


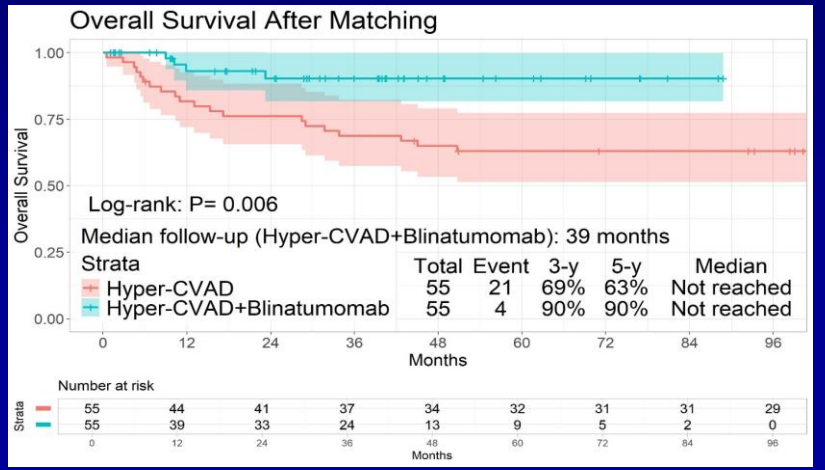
Goulart N, et al. *Blood*. 2025;146(suppl 1):1567.

Hyper-CVAD vs Hyper-CVAD-Blina ± InO in ND Ph-Neg B-ALL: Propensity Score Analysis

- 241 pts Rx with either Hyper-CVAD (n = 161) or Hyper-CVAD + blina ± InO (n = 80)
- Propensity score matching: 55 pts in each
- Median age 37 yr for Hyper-CVAD vs 35 yr for Hyper-CVAD + blina ± InO
- Median F/U: Hyper-CVAD 153 mo vs Hyper-CVAD + blina ± InO 36 mo
- No compromise in outcomes despite reduction in duration/amount of intensive chemotherapy

Outcome	Hyper-CVAD	Hyper-CVAD + Blina	*P* Value
AYA 3-yr EFS	77%	89%	.116
AYA 3-yr OS	77%	96%	.042
Ph-like 3-yr EFS	63%	83%	.271
Ph-like 3-yr OS	77%	96%	.042
High risk 3-yr EFS	57%	81%	.013
High risk 3-yr OS	57%	84%	.014





Goulart N, et al. *Blood*. 2025;146(suppl 1):1567.

Blina + ChemoRx Improves DFS and Mitigates Adverse Prognostic Factors in Childhood ALL (AALL1731)

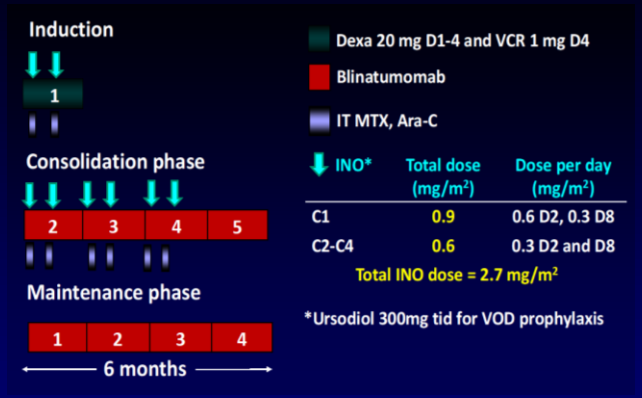
- 1440/2245 SR; median age 4.3 yr (1–10)
- Median F/U 3.5 yr; Rx chemoRx ± 2 BLINA

Parameter	ChemoRx (n = 722)	ChemoRx + Blina (n = 718)	*P* Value
4-yr DFS, %	87	95	<.0001
4-yr CIR, %	12.6	4.4	<.0001
BM relapse	9.4	3.1	<.0001
CNS relapse	2.2	1.4	.41

- Traditional adverse prognosticators lose significance with blina
- Unfavorable genetics (iAMP21, *KMT2A* rearrangement, t[17;19], hypodiploidy) adverse impact
- Addition of blina associated with improved outcomes in pts with unfavorable genetics: 4-yr DFS Arm C 77% vs Arm D 92%

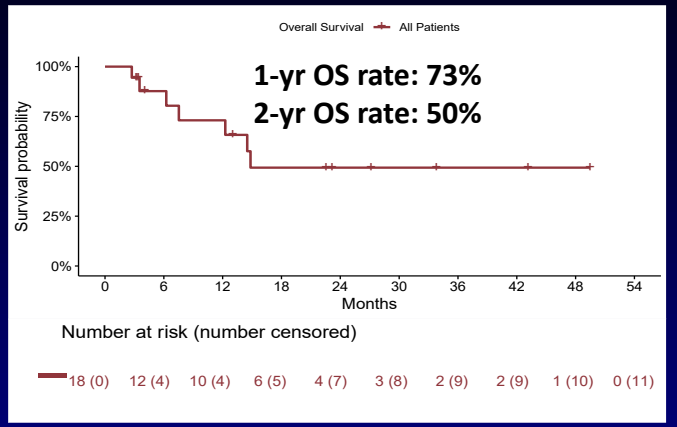
Gupta S, et al. *Blood*. 2025;146(suppl 1):758; Gupta S, et al. *N Engl J Med*. 2025;392(9):875-891.

Chemo-Free Rx With InO/Blina in Older Ph-Negative B-ALL



- N = 18, median age 76 (65–83), 94% >70 yr
- 38% high-risk cytogenetics, 50% with *TP53*mut
- No secondary MDS/AML
- No VOD
- Median F/U 24 mo
- 10 (55%) alive in CR without ASCT
- 2 relapsed (11%)

OS



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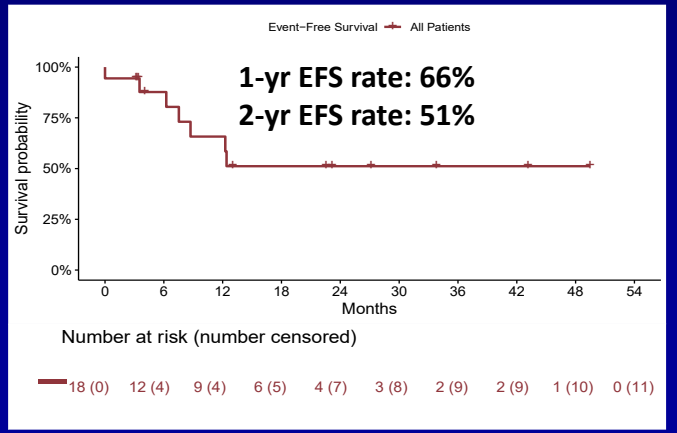


Parameter	N (%)
ORR (CR/CRi)	**17 (94)**
Complete remission	**16 (89)**
MRD-Negative CR/CRi	
MRD-neg by FCM (any time)	**16 (89)**
MRD-neg by FCM (postinduction)	**12 (67)**
MRD-neg by NGS (any time)	**10 (67)**
MRD-neg by NGS (postinduction)	**5 (33)**
Day 14 Evaluation (prior to receipt of blina)	
CR/CRi	**10 (82)**
MRD-neg by FCM	**4 (40)**

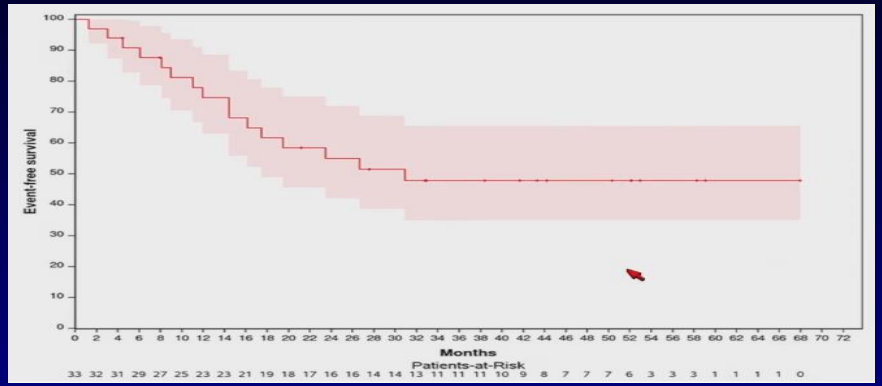
5 deaths in CR (28%): MI, PNA, resp failure, hospice, multiorgan failure post-ASCT

Goulart H, et al. *Blood*. 2025;146(suppl 1):5131.

Chemo Rx-Free InO + Blina in Pre–B-ALL (Alliance A 041703): Long-Term Follow-Up

- InO 0.8 mg/m^2 D1, 0.5 mg/m^2 D8 and 15; × 1–2; then blina × 2–3; IT MTX × 8
- 33 pts; median age 71 yr (60–84). Median F/U 45 mo
- CR-CRi post-Ino 85%; post-blina 97%
- 3-yr EFS 48% – median 31 mo; 12 relapses, 1 ED, 3 deaths in CR
- 3-yr OS 59% – median NR; 5 allo SCT, no CNS relapses
- Among relapses: 40% CD19 neg; 42% *TP53+*; 13 deaths
- MRD-neg post-course 1A better EFS (52% vs 0%, median NR vs 8 mo) and better OS (100% vs 0%; median NR vs 20 mo)
- 1 SOS (3% G5). Blina neurotoxicity: 3 pts (2 G3, 1 G5)

EFS



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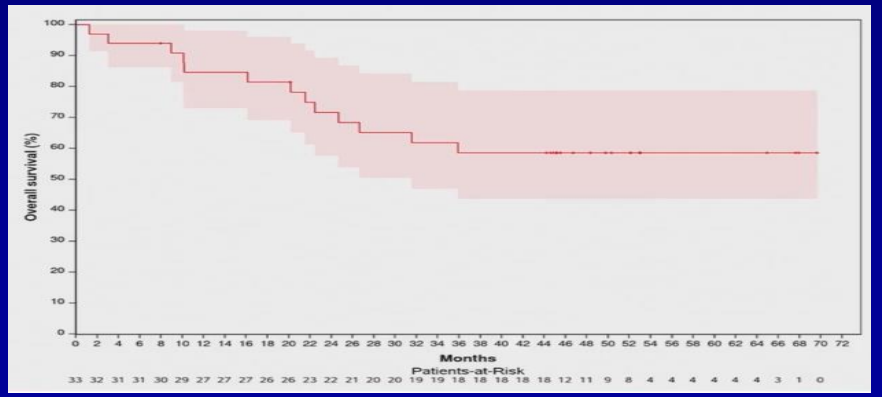
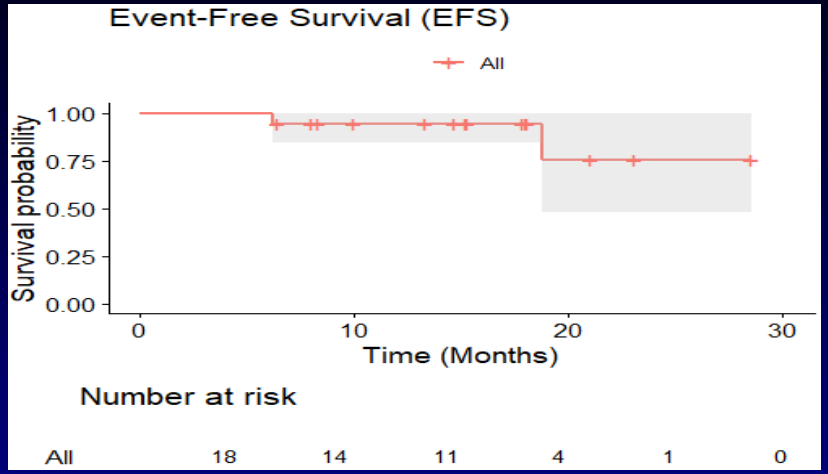
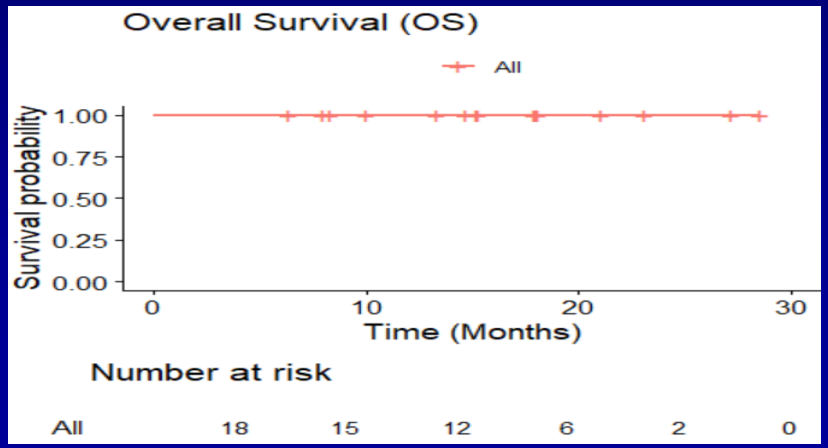


Wieduwilt M, et al. *J Clin Oncol*. 2025;43:3526-3535; Wieduwilt M, et al. *Blood*. 2025;146(suppl 1):444.

CD19 CAR T-Cells Rx in Older ALL in CR1

- 22 pts ≥55 yr; 18 evaluable: (200 million CAR Ts)
- Median age 64 yr (55–79); 6 Ph-pos; 2 hypodiploidy/*TP53* mutations; 2 Ph-like; 1 *KMT2A*r
- 15 (83%) Rx blina and 2 (11%) Rx InO; 18/18 MRD-neg CR at LD
- No ICANS and G≥2 CRS; 72% G1 CRS
- Median F/U 14.5 mo: 1-yr PFS 90%; 1 pt Ph-pos ALL mol relapse (alive in MRD-neg CR post-ASCT >2yr); 1 t-MDS 18 mo post-CAR; 16 in MRD-neg CR; all 6 Ph-pos ALL on TKI maintenance
- No death: 1-yr OS 100%
- CAR T cells expanded (peak 7–14 days; 13%)
- D28 17/17 pts LP CAR T cells expanded in CSF (median 0.4 × 10^3/mL)
- Baseline and D100 walk speed and cognitive function similar





Aldoss I, et al. *Blood*. 2025;146(suppl 1):443.

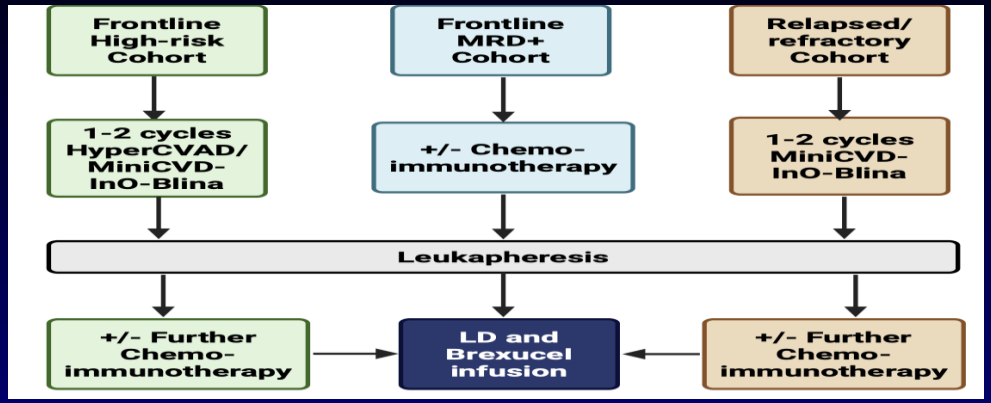
Frontline CD19 CAR T Consolidation in ND Ph-Negative ALL

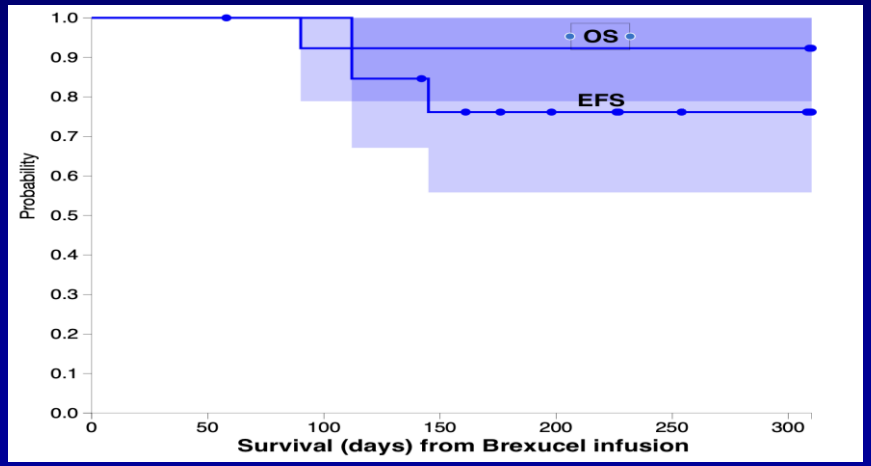
- Pediatric-inspired induction (w/VEN) → 1–2 cycles consolidation → 1 infusion CD19 CAR T → POMP (w/VEN)
- 44 pts Rx; median age: 36 yr (18–70)
  - 18% Ph-like; 9% complex karyotype; 2% EMD
  - 11% *TP53*; 9% *KMT2A*r; 9% *ZNF384*r; 11% *IZKF1*; 14% *PAX5* or *BCOR*
  - 16% MRD-pos (MFC), 12/33 (52%) NGS MRD-pos prior to CAR T
- After CAR T: 100% MRD-neg (MFC), 32/33 (97%) NGS MRD-neg within 3 mo
- All pts exhibited CAR T-cell expansion
- Median F/U: 10.6 mo; 1-yr OS 100%; 1-yr LFS 98%
- 4 pts allo-SCT during CR1; 1 allo-SCT after relapse
- CRS: 59% (G1 only); ICANS: 0; no G3+ non-heme AE

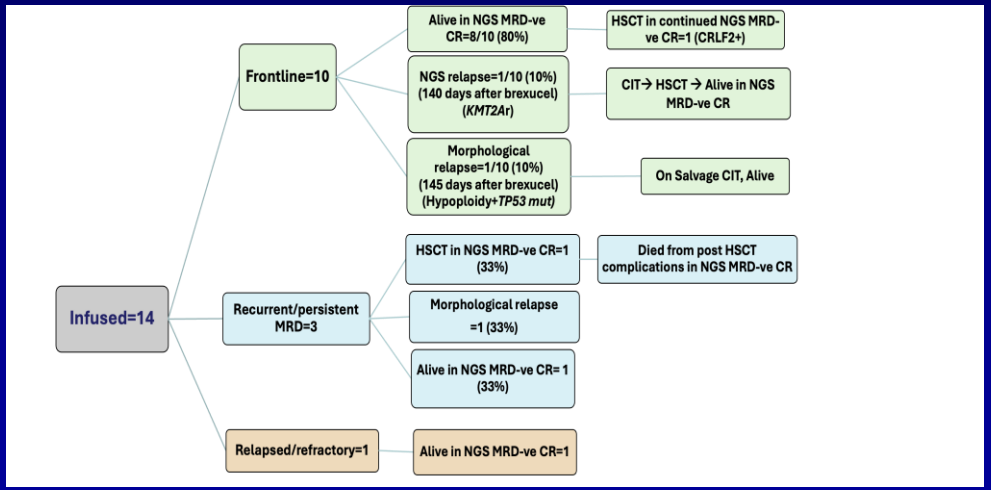
Gu R, et al. *Blood*. 2025;146(suppl 1):1561.

Brexu-Cel Consolidation Post-HCVAD/Mini-HCVD-InO-Blina in ALL

- 14 pts, median age 35 yr (19–77), 10 high-risk FL, 3 MRD, 1 R/R
- At LD, 100% CR, 93% MRD-neg NGS
- Median CAR T expansion 14 cells/µL (0–69)
- 57% G1 CRS only, no ICANS
- Median F/U 7.1 mo; 2 relapses (1 FL, 1 MRD) and 1 molecular relapse; 1 death post-HSCT
  - 6-mo EFS 79%; 6-mo OS 93%







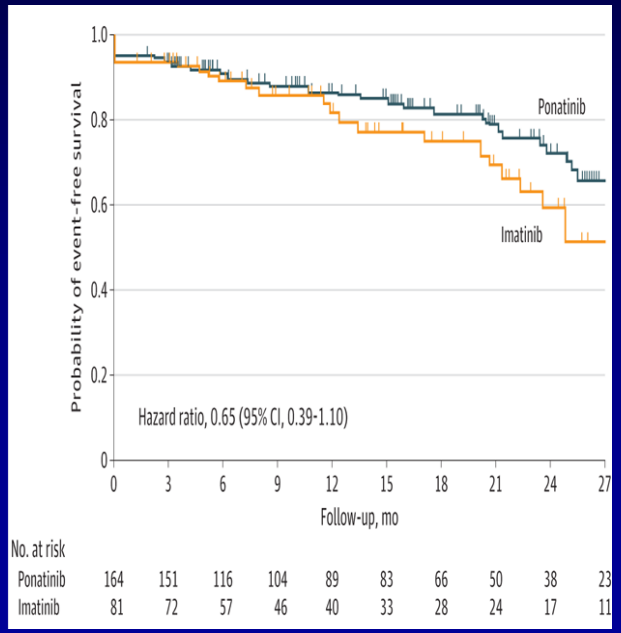
Senapati, et al. *Blood*. 2025;146(suppl 1):1573.

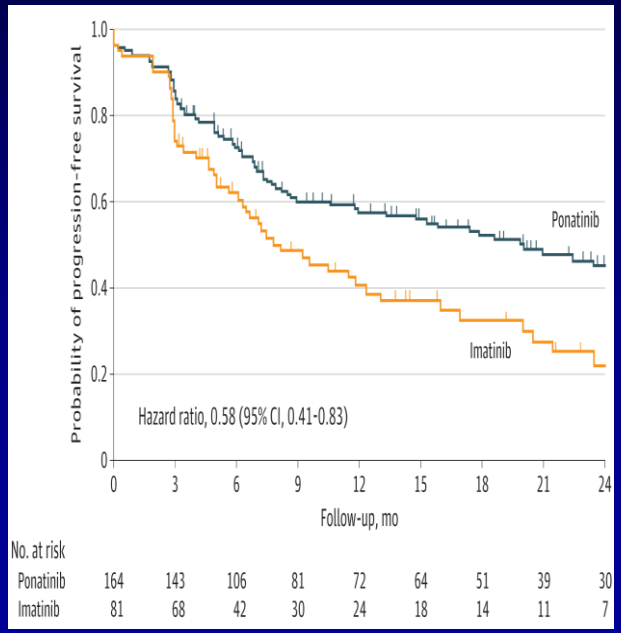
ALL: What Is New in 2026

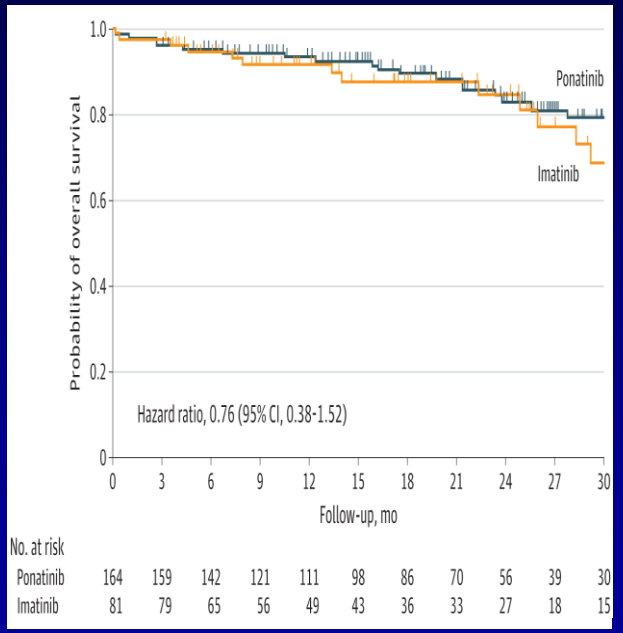
- Philadelphia-negative ALL
- **Philadelphia-positive ALL**
- Measurable residual disease (MRD)
- Relapsed/refractory disease

Ponatinib vs Imatinib in ND Ph-Positive ALL: PhALLCON Phase III Trial

- 245 pts randomized (2:1) to ponatinib 30 mg/D (n = 164) or imatinib (n = 81), both with VCR-Dex for 90 days; then continuation of TKIs and chemoRx
- Primary endpoint MR4 CR at 90 days: 34.4% vs 16.7% (*P* = .002)
- Subsequent ASCT 30% vs 37%







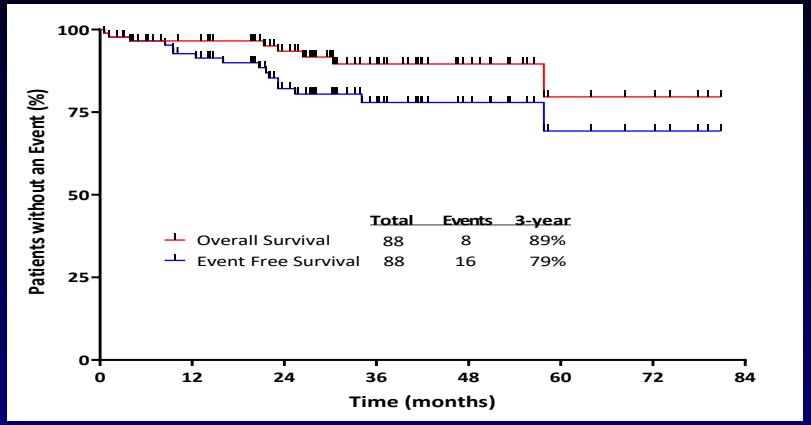
Jabbour E, et al. *JAMA*. 2024;331(21):1814-1823.

Ponatinib + Blina in ND Ph-Positive ALL

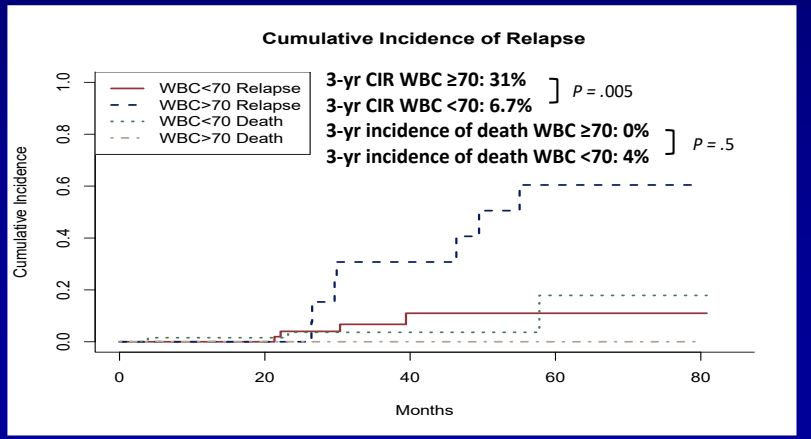
- 88 pts median age 50 (18–83) – 19% >70 yrs Rx with simultaneous ponatinib 30–15 mg/D and blina × 5 courses. 12–15 IT
- p190 78%, p210 20%, *IK7F1*^{plus} 52%
- Median F/U 32 mo, only 2 underwent ASCT
- N = 11 relapses (3-yr CIR 12%), median time: 20 mo (8–33) (5 BM only, 5 CNS only, 1 EMD only; 64% of relapsed pts with WBC ≥70)
- No diff in CIR with *IKZF1*^{plus}

Parameter	N (%) or median [range]
Overall response rate	61/65 (96)
CR rate	60/65 (95)
Molecular Response Rate	
MMR	74/77 (96)
CMR	65/79 (83)
MRD-Negativity Rate by NGS	
Post-C1	19/44 (43)
Overall	64/67 (95)
Time to MRD-neg by NGS	2.8 mo [0.8–51]
MRD Discordance	
NGS neg/PCR pos	13 (16)
NGS pos/PCR neg	3 (4)

Outcome



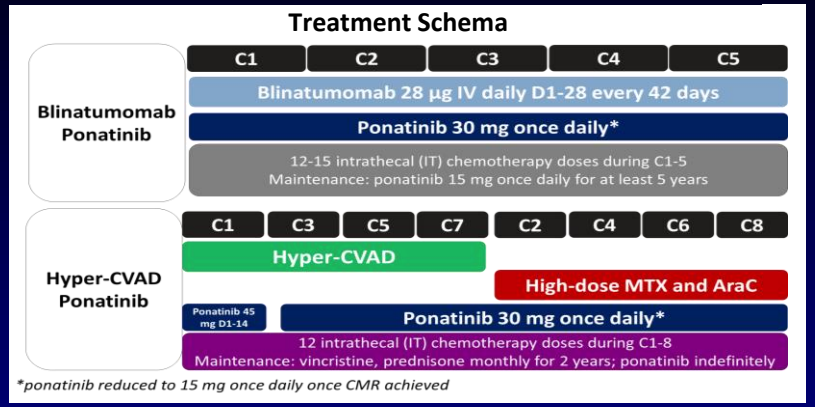
CIR

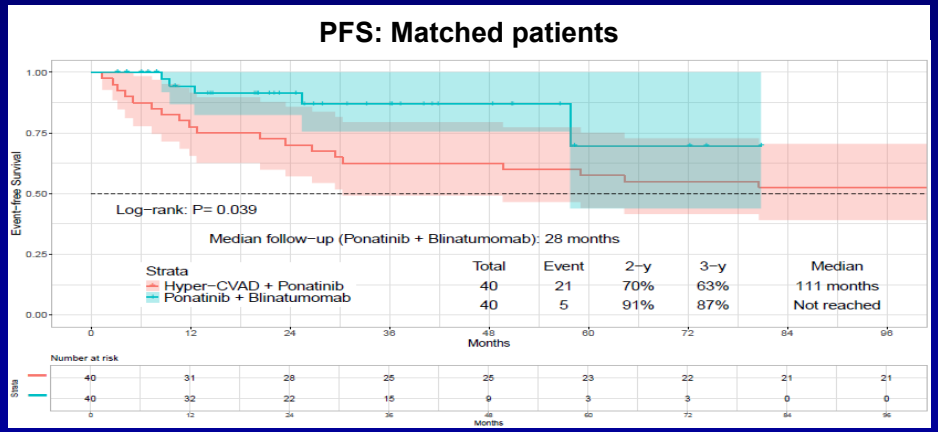


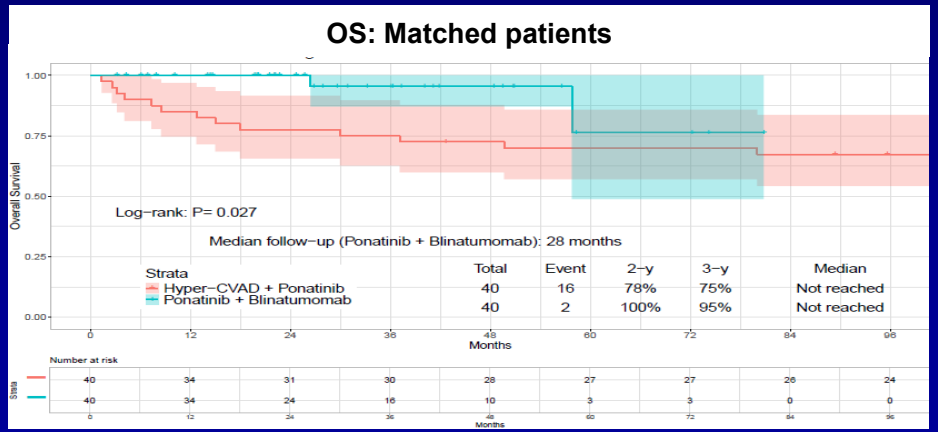
Goulart, et al. *Blood*. 2025;146(suppl 1):1571.

Blina-Ponatinib vs HCVAD-Ponatinib Propensity Matched Analysis

Parameter	Blina-Ponat (n = 40)	HCVAD-Ponat (n = 40)	*P* Value
ORR	100%	100%	--
C1 CMR	56%	38%	.115
Overall CMR	80%	90%	.348
Overall NGS MRD-neg	53/55 (96%)	--	--
Relapse rate	10%	28%	.083
Death in CR	3%	25%	.007
Allo-SCT	1 (3%)	8 (20%)	.029







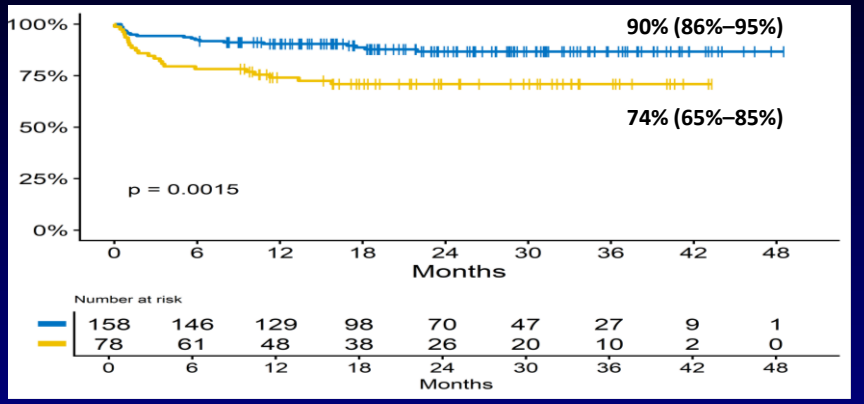
Sasaki, et al. *Blood*. 2025;146(suppl 1):1578.

Phase III GIMEMA ALL2820: Blina-Ponatinib vs Imatinib-ChemoRx in ND Ph-Positive ALL

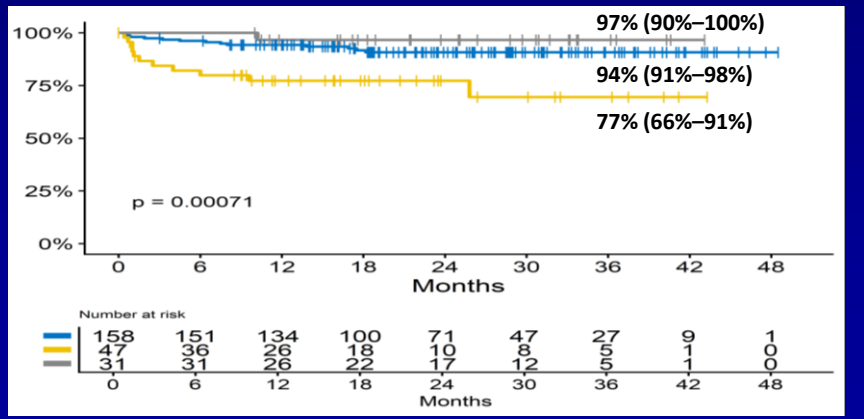
- 236 pts randomized 2:1 Blina-PON (n = 158) or ChemoRx-IM (n = 78). Induction 70 D (2 courses) or 3 ChemoRx
- Median age 57 yr vs 58 yr (28% and 27% >65 yr); *IKZF1*^{plus} 34% vs 26%
- Median F/U 23.4 mo (range 1–48 mo)

%	Blina-PON	ChemoRx-IM	
CHR (D70)	94	79	*P* = .001
Induction death	4	10	
MRD-neg (D70)	47	44	
MRD-neg (D133)	71	59	*P* = .009
MRD-neg post-crossover	NA	62 (18/29)	
Relapses	6 (n = 9; 1 CNS)	8 (n = 5; 0 CNS)	
Death	5	8	
ASCT	19	19	
18-mo EFS	90	77	*P* = .01

EFS



OS



Chiaretti, et al. *Blood*. 2025;146(suppl 1):439.

Ponatinib vs Dasatinib + Blina in Ph-Positive ALL

Parameter	Pona + Blina (n = 88; 5 blina)	Dasa + Blina (n = 63; 2+ blina)	Dasa + Blina (n = 24; 3 blina)	Pona + Blina (n = 158; 2–5 blina)
Median age (yr)	50	54	73	57
PCR neg, % NGS-clonoSEQ neg, %	83 95	93 (+PNQ)	75	71
4-yr OS, %	89	82	63 (5 yr)	18-mo OS 92%
Allo SCT, %	2	39	4	19
Relapses (CNS)	11 (5)	9 (4)	8 [3 T315I] (2)	9 (1)

Goulart, et al. *Blood*. 2025;146(suppl 1):1571; Foà R, et al. *J Clin Oncol*. 2024;42(8):881-885; Advani, et al. *Blood*. 2025;146(suppl 1):3343; Chiaretti, et al. *Blood*. 2025;146(suppl 1):439.

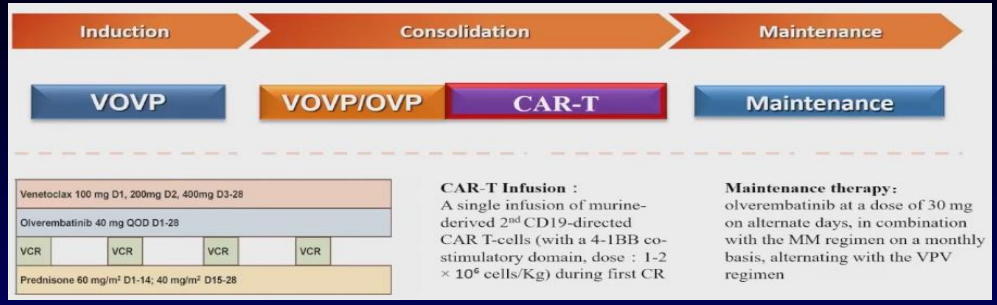
Olverembatinib + LD ChemoRx in FL Ph-Positive ALL: Part A of Phase III POLARIS-1

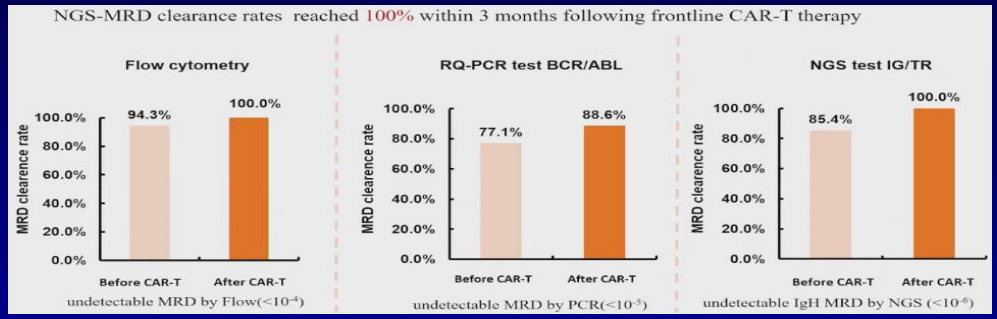
- 55 pts median age 43 yr; p190 65.5%
- Olverembatinib 30–40 mg QOD with 3 cycles of VP-VPD followed by 3 cycles of HD MTX alternating with 3 cycles of HDAC followed by 12 cycles of maintenance of 6-MP-MTX-VP
- Median duration of Rx 9.6 mo
- Primary endpoint MR4 CR at 90 days 52.8% (35.8% EOC1)
- Rx well tolerated, 1 pt G2 CAD
- Subsequent ASCT in 5 pts (9.1%)
- Progression in 4 pts (1 refractory and 3 CNS/BM)
- 9/10 pts with *IKZF1*^{plus} MRD-neg CR
- No difference between olverembatinib 30 and 40 mg QOD
- Randomization 2:1 of olverembatinib vs dealer's choice TKI with LD ChemoRx ongoing

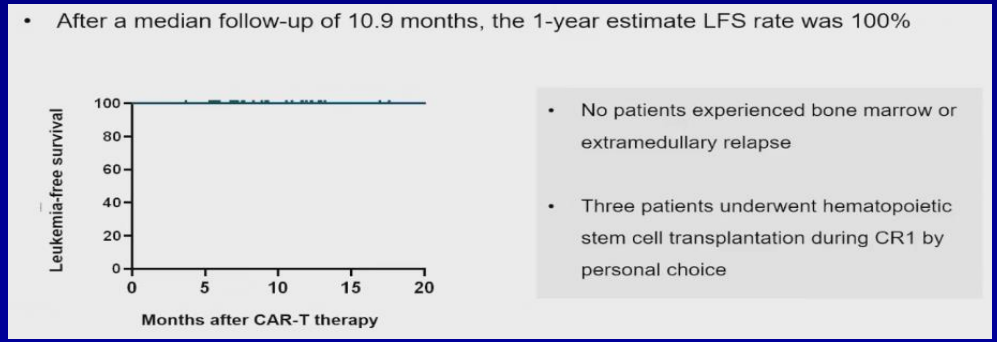
Chen S, et al. *Blood*. 2025;146(suppl 1):1574.

CD19 CAR T Consolidation in ND Ph-Positive ALL: Phase II

- 35 pts; median age 39 yr (20–60)
- IT for CNS as SOC
- At LD: 100% CR; 6% MRD-pos (MFC); 23% MRD-pos (*BCR::ABL1*); 15% MRD-pos (NGS)
- Post-CAR: 100% MRD-neg (MFC); 11% MRD-pos (*BCR::ABL1*); 100% MRD-neg (NGS)
- Median F/U 11 mo: 1-yr OS 100%; 1-yr LFS 100%
- No relapses; 3 elected allo-SCT by preference
- CRS 74% all G1; ICANS 0%



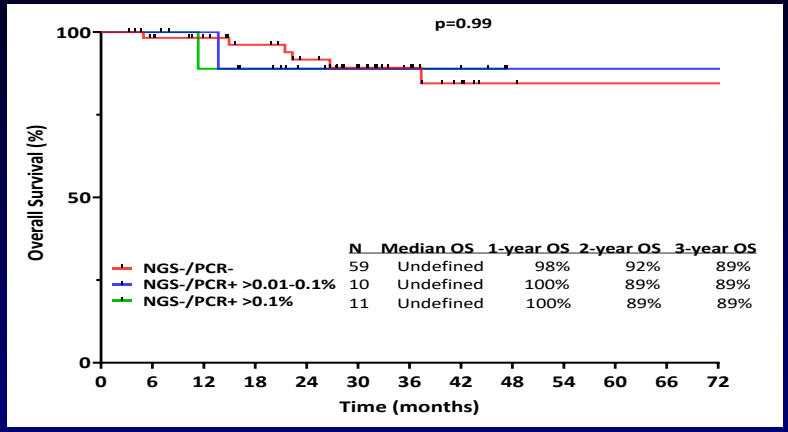


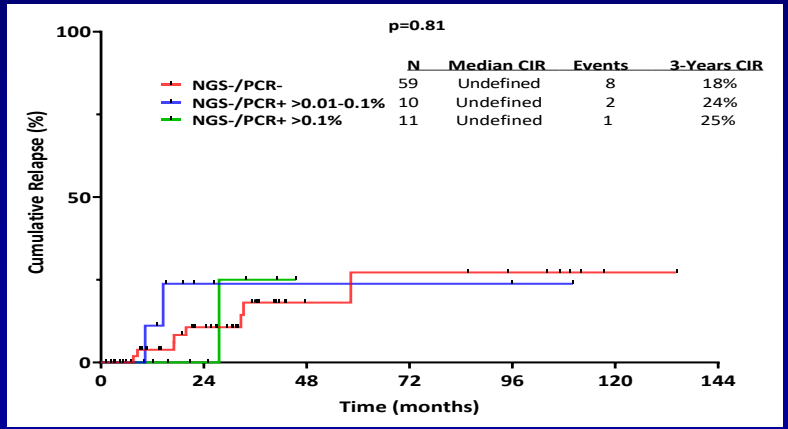


Gu R, et al. *Blood*. 2025;146(suppl 1):442.

PCR for *BCR::ABL1* vs NGS for IG/TR in Ph-Positive ALL

- 187 pts with Ph-pos ALL → NGS MRD-neg + PCR for *BCR::ABL1* pos or neg
- Discordance (NGS neg/PCR pos) in 23%
  - PCR >0.1% in ~50% of discordance cases
  - Similar rates in p190 and p210
  - High WBC → ↓ discordance
  - FISH pos in granulocytes → ↑ discordance
- No impact of discordance or level of *BCR::ABL1* PCR on relapse or OS
- 2 NGS neg/PCR-pos pts discontinued TKI → PCR >10% (but still NGS neg)





Maroun M, et al. *Blood*. 2025;146(suppl 1):551.

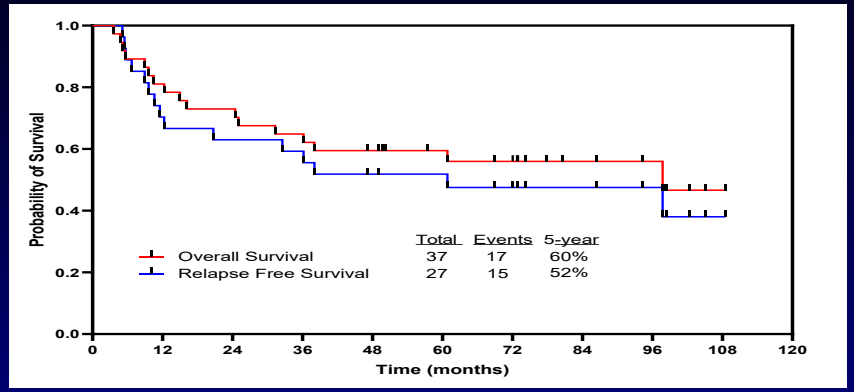
ALL: What Is New in 2026

- Philadelphia-negative ALL
- Philadelphia-positive ALL
- **Measurable residual disease (MRD)**
- Relapsed/refractory disease

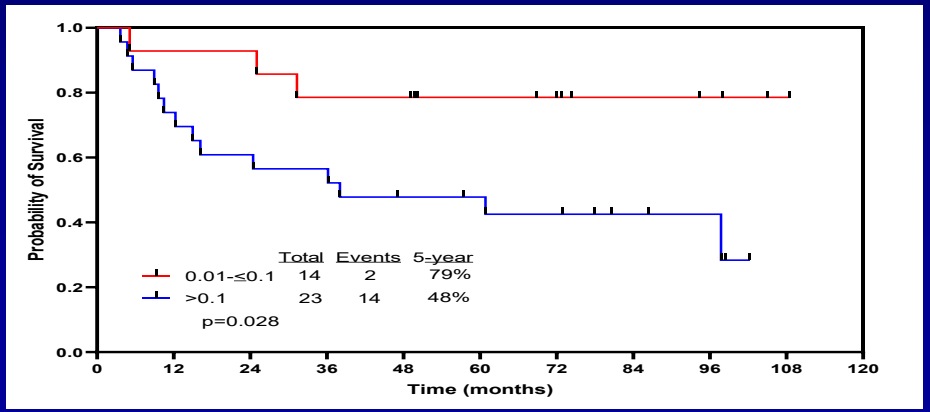
Blina for MRD-Positive ALL in CR1/CR2+

- 37 pts Rx. Post-blina MRD-neg 27/37 = 73%; 84% in Ph-neg ALL
  - 65% after C1
  - 3/5 (60%) NGS MRD-neg → all alive without allo-SCT
- Median number of cycles 3 (1–9); 8% received maintenance blina
- Median f/u 74 mo: 5-yr OS 60%; 5-yr OS if MRD-neg 63%
- 14 pts 0.01 to <0.1%: 5-yr OS 79%; 23 pts ≥0.1%: 5-yr OS 48%
- Allo-SCT (n = 15; CR1: 12 CR2+: 3)
- Median time (CR1 pts): 2 mo (0.6–6.9)
- Post–allo-SCT → 6 (40%) deaths; no allo-SCT→9 (41%) relapses, 11 (50%) deaths

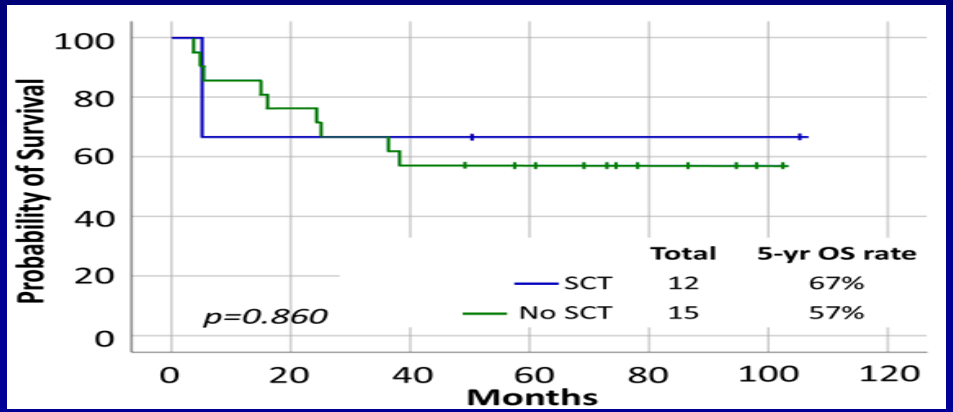
Outcomes



OS by MRD level



OS by ASCT

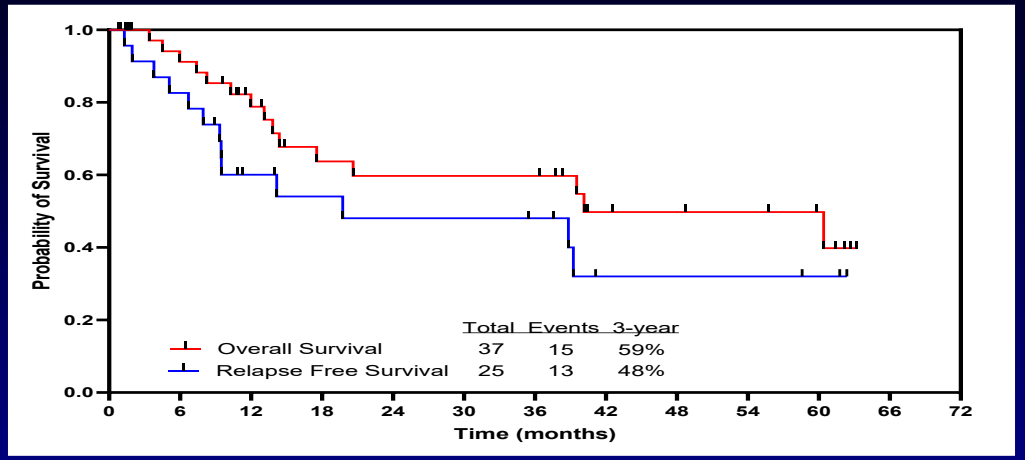


Jabbour E, et al. *Am J Hematol.* 2022;97(9):1135-1141; Rausch, et al. *Blood*. 2025;146(suppl 1):1575.

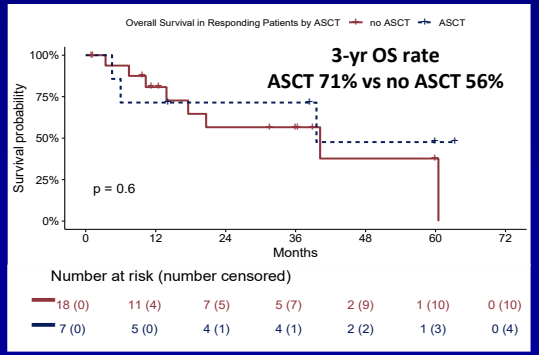
InO for MRD-Positive B-ALL: Long-Term Follow-Up

- 37 pts; median age 49 yr (19–71)
- 76% CR1, 24% CR2+
- InO 0.9 mg/m^2 C1 and 0.6 mg/m^2 C2–6
- 54% Ph-pos, 46% Ph-neg (47% Ph-like)
- Prior Rx: 65% blina, 11% CAR, 14% ASCT
- Median 3 (1–6) cycles of InO received
- Median F/U: 39 mo
- 25/37 (68%) MRD negativity
  - Ph-neg: 10/12 (71%) MRD-neg by FCM; 9/11 (81%) MRD-neg by NGS
  - Ph-pos: 9/9 (100%) MRD-neg by FCM; 4/6 (67%) MRD-neg by NGS; 2/9 (22%) *BCR::ABL1* neg
- SOS in 3 pts (1 after ASCT, 2 while on ponatinib)

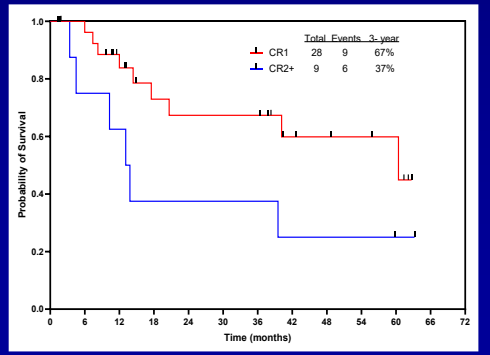
Outcomes



OS by ASCT



OS by CR1 vs CR2+



Goulart N, et al. *Blood*. 2025;146(suppl 1):3348.

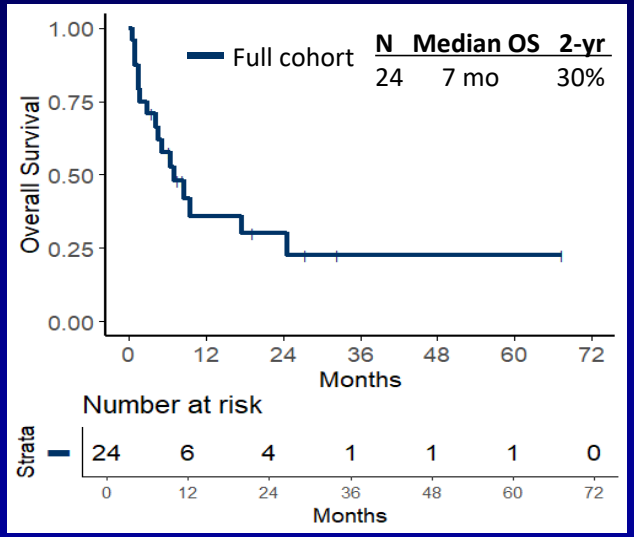
ALL: What Is New in 2026

- Philadelphia-negative ALL
- Philadelphia-positive ALL
- Measurable residual disease (MRD)
- **Relapsed/refractory disease**

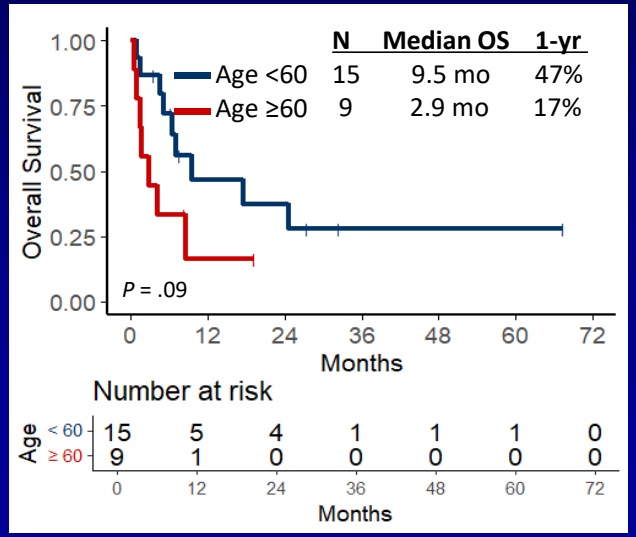
Outcomes Post-FL Blina-Based Regimens Failure

- 213 pts Rx (55% Hyper-CVAD, 45% mini-HCVD); median age 42 (18-88); 28% ≥60 yr
- Median F/U 37 mo: 2-yr CIR 11.4%
- MVA for relapse: BMI >30 (HR 2.98); WBC >50 (HR 3.64); *TP53* mutation (HR 2.71)
- CD19 positivity post-relapse 82%; relapse site: BM (42%), EMD alone (29%), both (29%)
- ORR to S1 = 54%; median OS 7 mo – 2-yr 30%; better OS in pts <60 yr and CR1D ≥12 mo

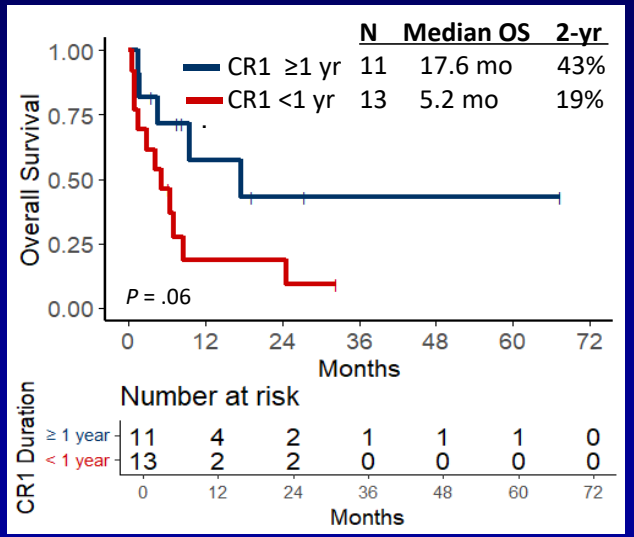
OS



OS by age



OS by CR1D

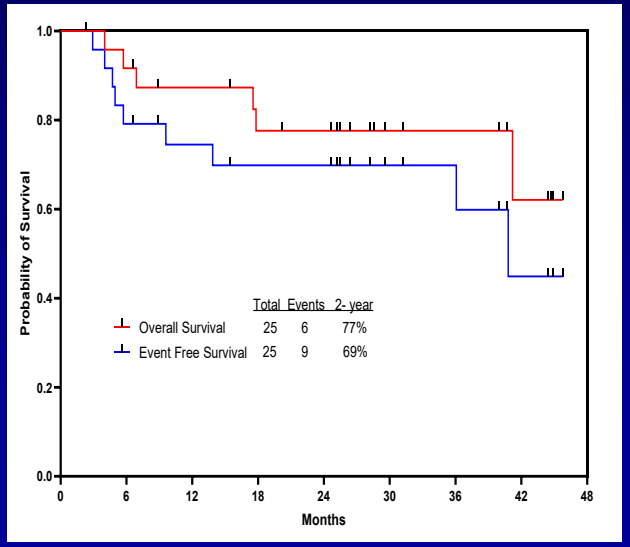


Arora, et al. *Blood*. 2025;146(suppl 1):751.

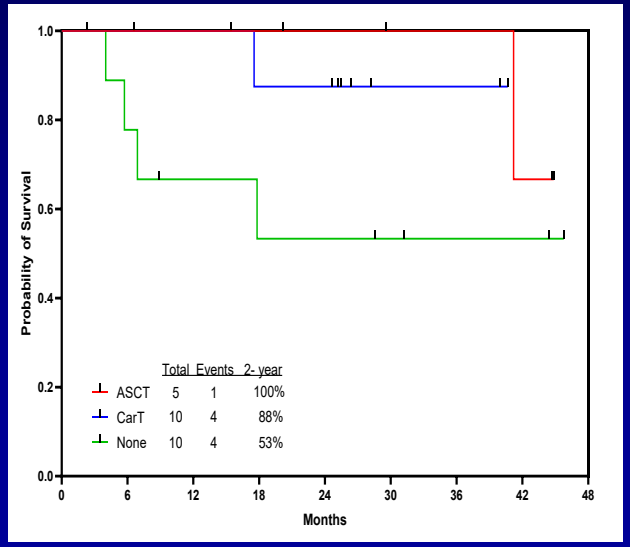
“Dose-Dense” Mini-HCVD + InO + Blina in R/R B-ALL

- 25 pts; median age 39 yr (19–62); 12% ≥60 yr
- 88% S1, 12% S2+, 16% high risk, 24% *TP53*, 12% prior ASCT, 32% prior blina
- ORR: 100%, CR 79%
- Best MRD-FCM 95% (73% post-C1), best MRD NGS 95% (38% post-C1)
- Median F/U 25 mo – 2-yr EFS 69%, 2-yr OS 77%
- 2-yr OS by consolidation: CAR 88%, none 53%, ASCT 100%

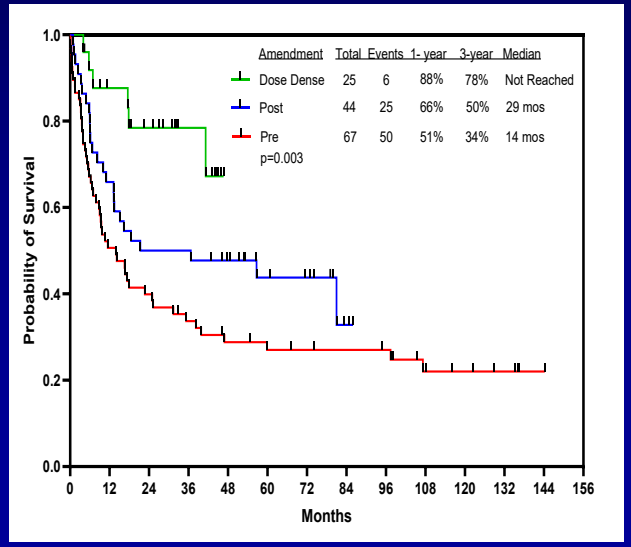
Outcomes



OS by consolidation



OS by regimen

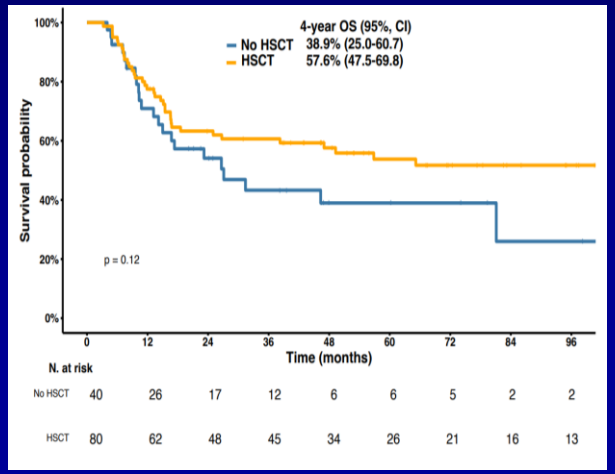


Goulart N, et al. *Blood*. 2025;146(suppl 1):3350.

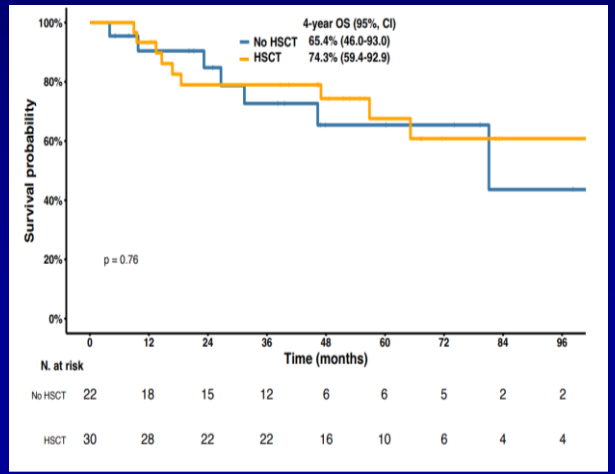
Outcomes After S1 in R/R ALL: Role of Allo-SCT Consolidation

- N = 172/203 pts (85%; 137 Ph-neg, 35 Ph-pos) in CR2; median age 48 (18-88); 10% ≥70 yr
- 9% Rx prior blina and/or InO, 11% prior allo-SCT; 54% CR1D ≥12 mo
- S1: 38% both blina and InO, 41% InO, 21% blina
  - MRD-neg EOC1 60%
- Consolidation 47% allo-SCT, 9% CAR T Rx, 44% none
- Median F/U 56 mo: 4-yr OS 46%, 4-yr RFS 38%, 4-yr CIR 42%
- MVA for worse OS: older age, MRD-pos EOC1, CR1D <12 mo

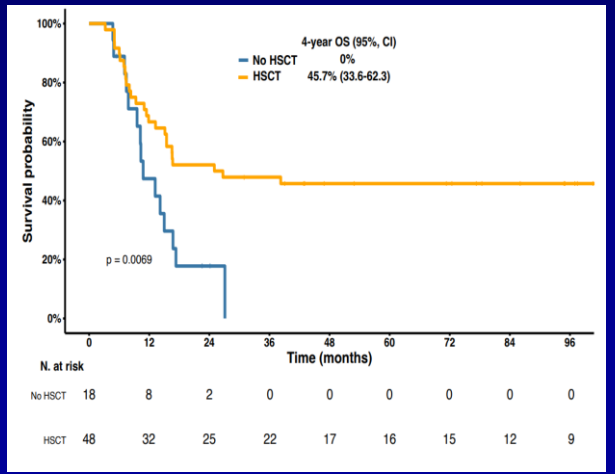
OS: Overall



OS: MRD-neg EOC1 and CR1D ≥12 mo



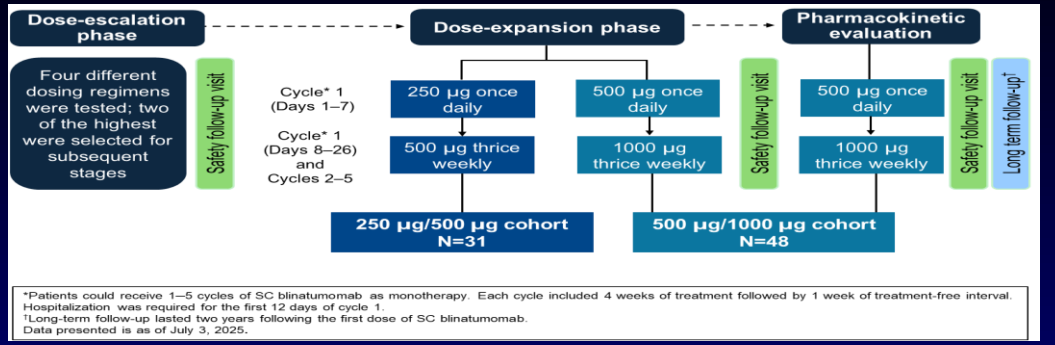
OS: MRD-pos EOC1 or CR1D <12 mo



Azevedo, et al. *Blood*. 2025;146(suppl 1):549.

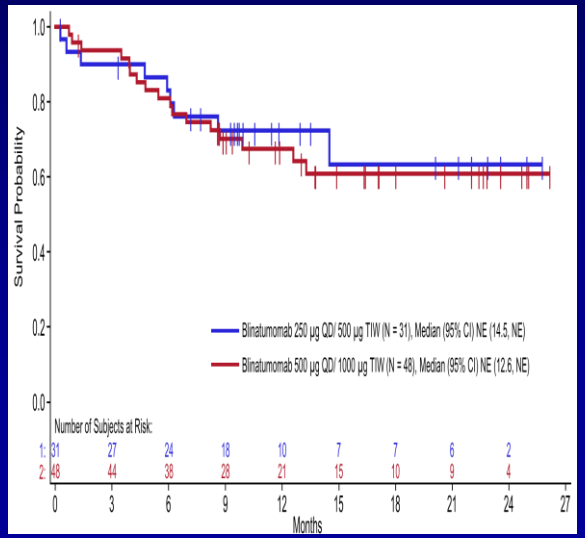
Subcutaneous Blina in R/R ALL

- 88 pts Rx: 36 at 250/500; 52 at 500/1000
- Rx 250 mcg daily × 7 then 500 mcg TIW; or 500/1000
- Median age 49 yr (19–78). Median prior Rxs 2 (1–7). Baseline BM blasts 60%
- Prior CAR T 16%, blina 19%, InO 33%, HSCT 28%
- Median F/U 14 mo

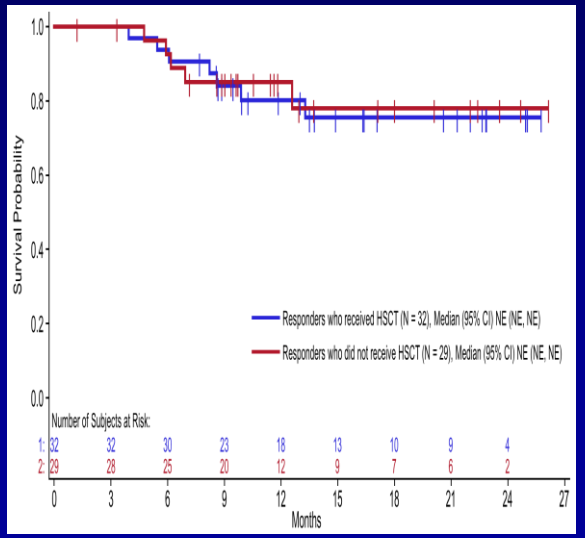


Parameter	250/500	500/1000
CR-CRh, %	75	79
CR-CRh-CRi, %	89	92
MRD-neg, %	89	93
No relapses, %	0	3
12-mo OS, %	72	67
G3 CRS, %	17	23
G3 ICAN, %	28	27

OS



OS of responders by HSCT status



Jabbour E, et al. *Lancet Haematol.* 2025;12(7):e529-e541; Jabbour E, et al. *Blood*. 2025;146(suppl 1):5117.

Surovatamig (AZD0486; CD3-CD19 BiTE) in R/R ALL

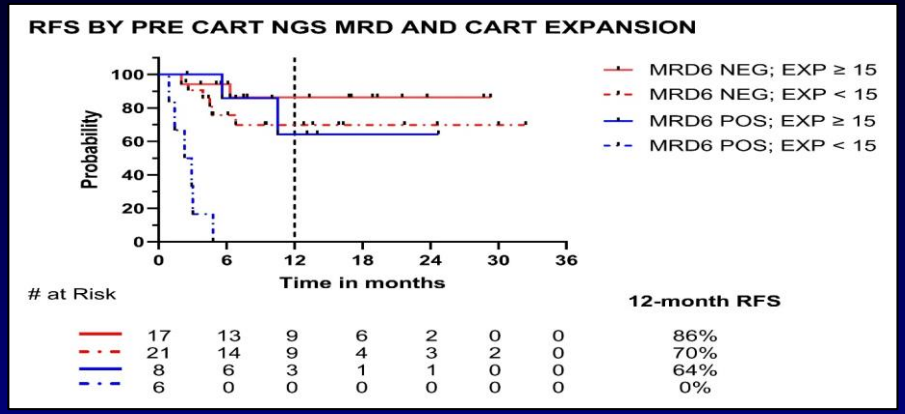
- 42 pts Rx in dose-escalation. Target dose 2.4, 7.2, or 15 mg
- Median age 50 yr (17–77); median prior Rx 3 (2–9); 60% >50% BM blasts; 62% prior CD19 Rx – 43% blina and 40% and/or CAR T Rx
- Median F/U 6.2; median DOR NR; DLTs in 2 pts (both resolved)
- G2+ CRS 9%, G3 ICAN in 1 pt

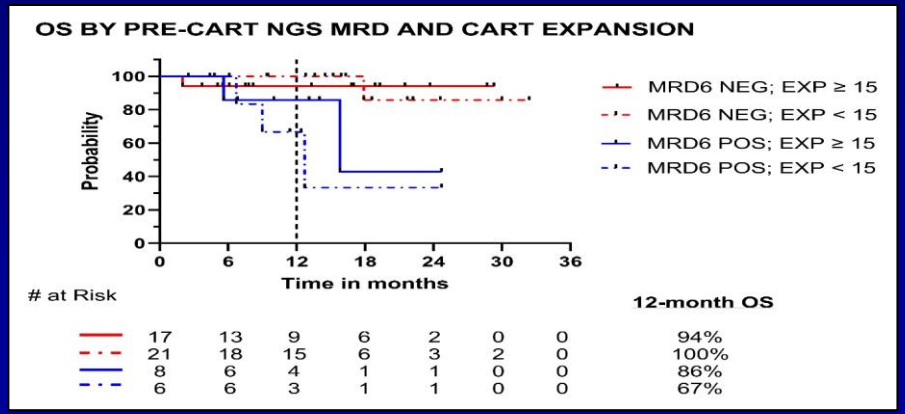
Parameter	Total	2.4 mg	7.2 mg	15 mg
No Rx	42	13	12	17
CR-CRi-CRh, %	67	46	58	82
CR, %	50	38	42	65
MRD-neg, %		83	100	100

- Among pts Rx at 15 mg, ORR 88% with prior blina, 73% with prior CAR T, 86% in double-exposed, and 86% in triple-exposed pts
- 6 of 7 pts with Ph-pos ALL demonstrated CR

Aldoss I, et al. *Blood*. 2025;146(suppl 1):3345.

Brexu-Cel as Consolidation Rx in B-ALL: Peak CAR T Expansion ≥15 Cells/µL and MRD Status





- 52 pts; 10 FL, 25 S1, 17 S2+

Pre-CAR T BM MRD6 NEG n = 38
- Peak CAR T expansion ≥15 (n = 17) → Relapse 1/17 (6%)
- Peak CAR T expansion <15 (n = 21) → Relapse 6/21 (29%)

Pre-CAR T BM MRD6 POS n = 14
- Peak CAR T expansion ≥15 (n = 8) → Relapse 1/8 (13%)
- Peak CAR T expansion <15 (n = 6) → Relapse 6/6 (100%)

Jain N, et al. *Blood*. 2025;146(suppl 1):6543.

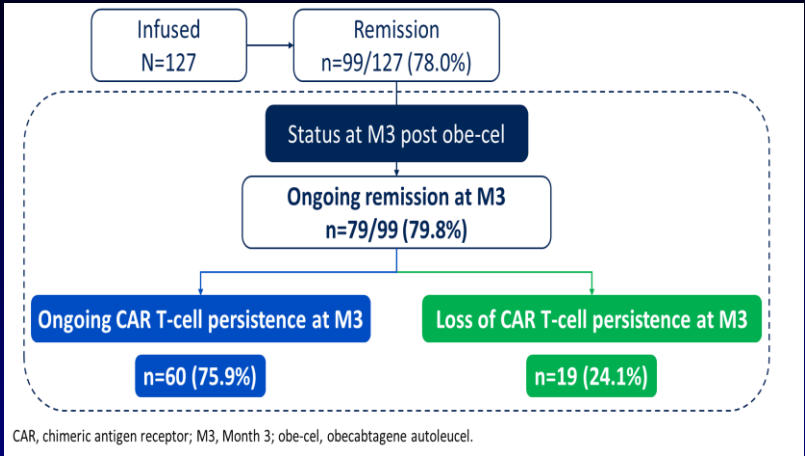
CD19 CAR T-Cell (Tisa-Cel) Rx for CNS Relapse

- 43 pts Rx; median age 8 yr (1–26); 91% first CNS relapse; 84% isolated CNS
- No cranial XRT for this relapse; Flu/Cy LD; dose 5 × 10^6 CART19 cells/kg
- At infusion: 14% BM disease, 19% CNS2, 5% CNS by imaging, no CNS3
- Day 28 CNS remission 98%; best overall response 100%; all MRD-neg
- Median F/U 12 mo: 1-yr and 2-yr EFS 90%; 1-yr and 2-yr OS 100% and 90%, respectively
- Among pts with F/U >4-yr (n = 14): 4-yr EFS 65%, 4-yr OS 93%
- CART19 detectable in CSF at day 28 in 98%
- CRS 77% (mostly G1; 1 G2 and 1 G4); ICANs in 4 pts (9%; no G4+). Fully recovered

DiNofia A, et al. *Blood*. 2025;146(suppl 1):648.

Obe-Cel in Adults With R/R ALL: T-Cell Persistence at Month 3

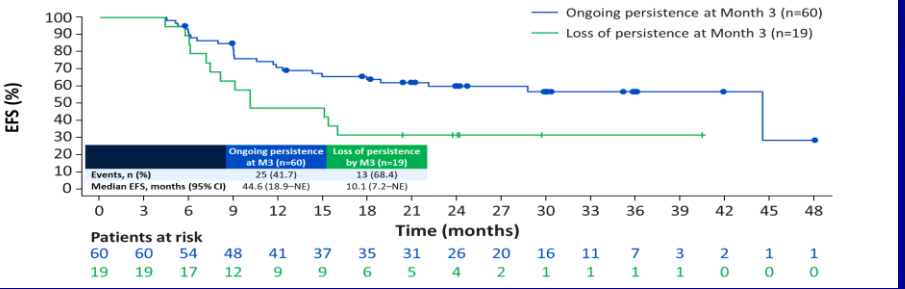
- 127 pts Rx; CR/CRi 78% (99/127)
- Median F/U 33 mo; 2-yr OS 46% 2-yr EFS 43%
- M3: 80% (79/99) pts in ongoing CR/CRi; 76% (60/79) CAR T-cell persistence
- T-cell persistence: median age 54 (20–81), 40% ≥3 prior Rx; 37% prior blina; 60% prior allo; median BM blast at LD 30%
- Median OS (T-cell persistence vs loss): 44.6 mo vs NR
  - 2-yr OS 69% vs 53%; 2-yr EFS 60% vs 32%
- 70/79 in CR/CRi at M3 did not receive allo-SCT
  - 49/54 (91%) pts in NGS MRD-neg CR at M3
  - 2-yr EFS 56% vs 33% (T-cell persistence vs loss)
  - 2-yr OS 68% vs 56% (T-cell persistence vs loss)



CAR, chimeric antigen receptor; M3, Month 3; obe-cel, obecabtagene autoleucel.

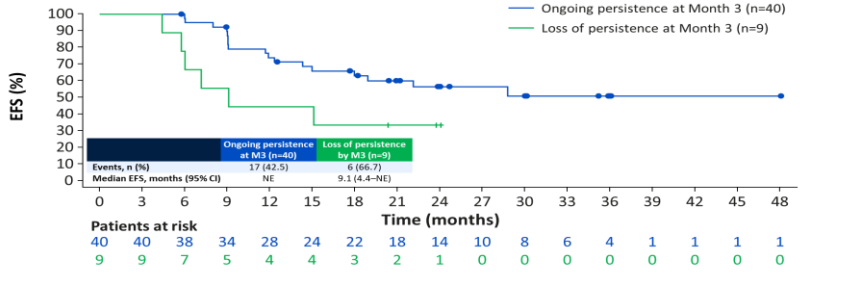
EFS by M3 persistence

Figure 2. Kaplan-Meier plot of EFS in patients with ongoing remission at M3, stratified by persistence status at M3.



EFS by M3 persistence and MRD-neg without HSCT

Figure 4. Kaplan-Meier plot of EFS in patients with ongoing remission at M3, no post-obe-cel SCT, and deep MRD-negative remission, stratified by persistence status at M3.



Roddie C, et al. *Blood*. 2025;146(suppl 1):5118.

*KMT2A*r = Adverse in R/R ALL Rx With Brexu-Cel (ROCCA database)

- 286 pts: 169 high-risk (HR), 117 standard-risk (SR)
  - HR: *TP53* (14%), *KMT2Ar* (9%), *CRLF2r* (29%), other (38%)
- HR more often Hispanic (50% vs 28%), similar disease burden, hx blina/InO/allo, CNS dx, EMD at time of apheresis compared to SR pts
- CR/CRi: 91% (HR) vs 90% (SR); MRD-neg: 79% vs 78%; median OS: 22 vs 21 mo

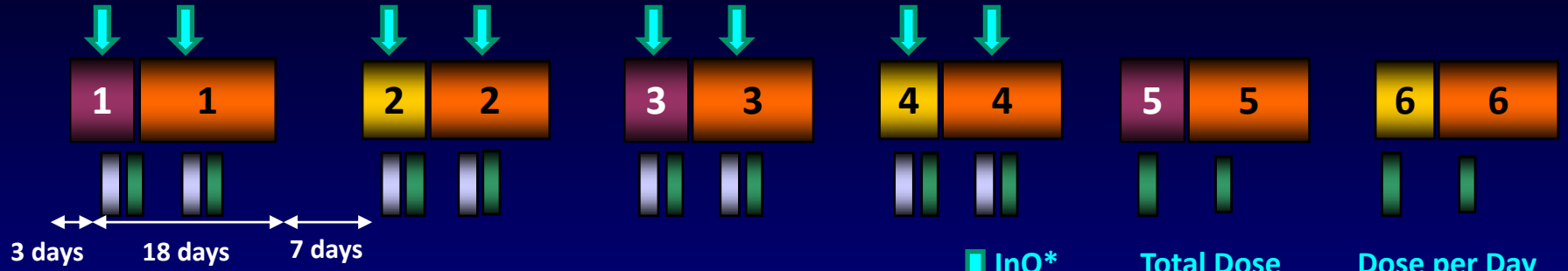
Parameter	*KMT2A*	*TP53*	*CRLF2*	Other
CR-CRi, %	71	95	95	89
Median EFS, mo	4	7	12	11
Median OS, mo	7	22	NR	NR

- *KMT2A*r-only subgroup with inferior OS (HR 3.17, 95% CI 1.53–6.58, *P* = .02)

Leonard, et al. *Blood*. 2025;146(suppl 1):3365.

Dose-Dense Mini-HCVD + InO + Blina + CAR T Cells in ALL: The CURE

Induction phase: C1–C6



InO*	Total Dose (mg/m^2)	Dose per Day (mg/m^2)
C1	0.9	0.6 D2, 0.3 D8
C2–4	0.6	0.3 D2 and D8

Total InO dose = 2.7 mg/m^2

*Ursodiol 300 mg TID for VOD prophylaxis.

Consolidation phase

CAR T consolidation

Mini-HCVD

Mini-MTX-Ara-C

Rituximab

IT MTX, Ara-C

Blinatumomab

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ALL Patient Case Discussion

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Disclosures

- Honoraria / advisory board: Abbvie, AMGEN, Asofarma, Novartis, Pfizer, Servier

October 2025

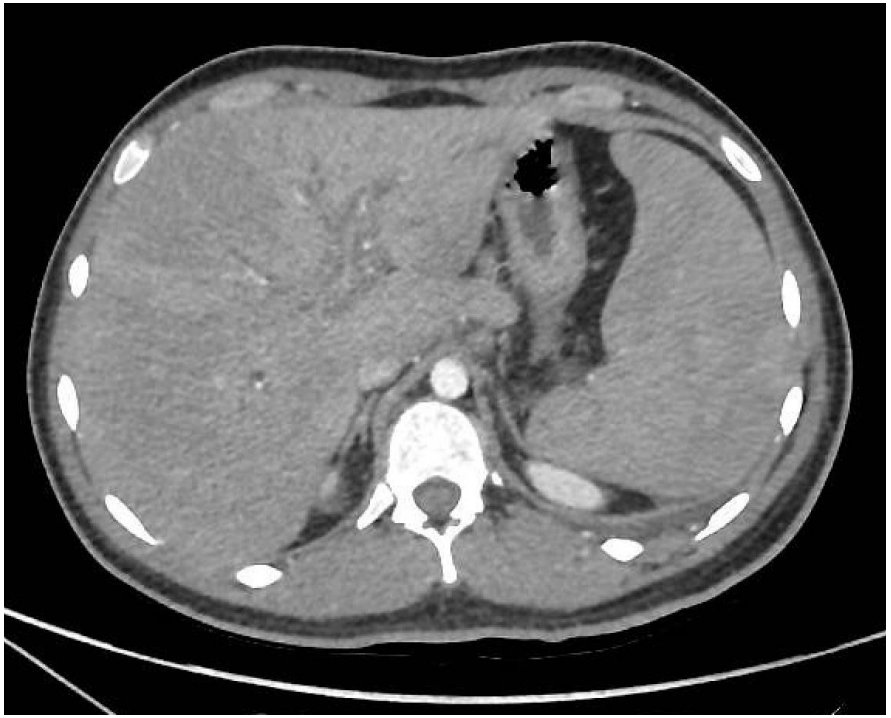
- 21-year-old male
- No previous medical history
- One month of weight loss and progressive jaundice

Parameter	Value
Hb	7.6 g/dL
WBC	222 x 10^9/L
Blast	86 %
Platelets	62 x 10^9/L

Parameter	Value
Total bilirrubin	8.9 mg/dL
Direct bilirrubin	6,6 mg/dL
AST	136 U/L
ALT	186 U/L
GGT	286 U/L

94% blasts: CD10+, CD19+, CD20+ (20%), CD22+, CD13+d, CD33+, CD7+d, CD79a+

- Supra- and infradiaphragmatic **lymphadenopathy** and **hepatosplenomegaly**
- **Hepatic inflammation**
- **Intrahepatic biliary ductal dilatation**, likely secondary to compression/obstruction by periportal lymphadenopathy



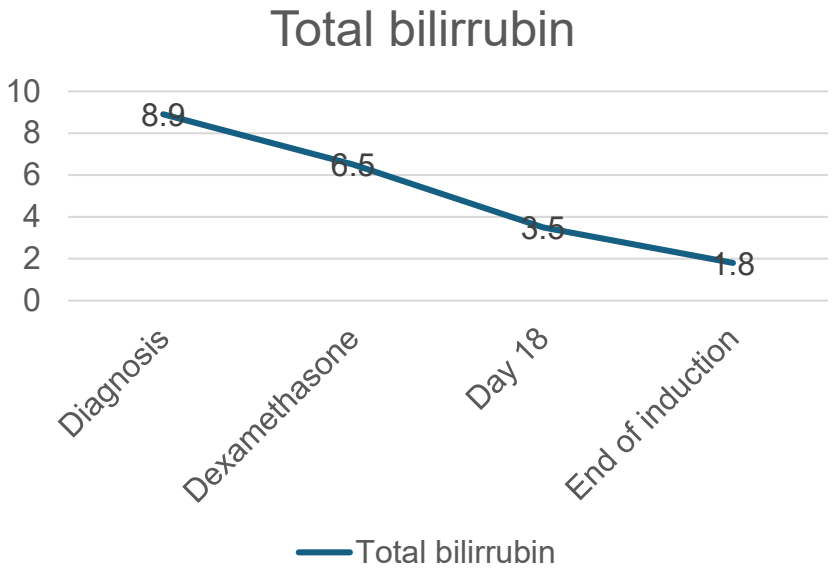
Dose adjustments?
Pediatric inspired regimen?

AYA B-Cell ALL, high WBC

Cytorreduction
- Dexamethasone

CALGB 10403
- + Rituximab

Delayed pegaspargase
- Day 18



Full-dose chemotherapy
Ursodiol

AYA B-Cell ALL, high WBC

Cytorreduction
- Dexamethasone

CALGB 10403
- + Rituximab

Delayed pegaspargase
- Day 18

NGS fusion panel: *RCSD1::ABL2*

Karyotype: no metaphases

End of induction: refractory

AYA B-Cell ALL, high WBC, Ph-like (ABL-type)

CALGB10403 consolidation 1

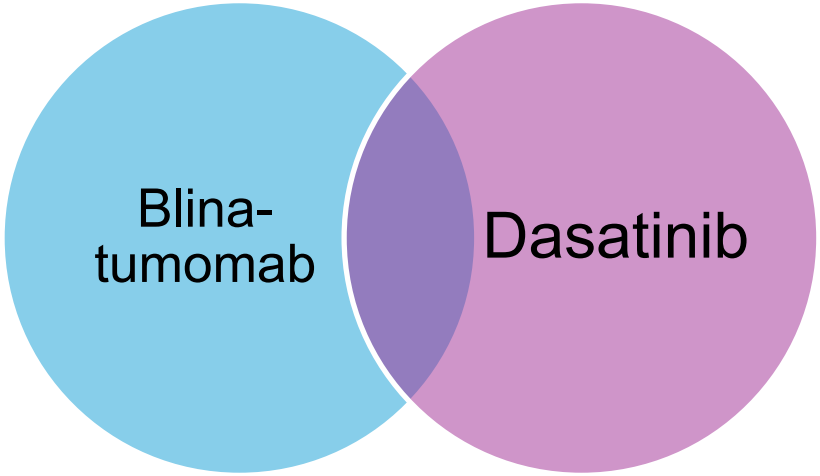
→

4.4% blasts

Immunotherapy?
TKI?

- Hepatotoxicity
- Perianal abscess

AYA B-Cell ALL, high WBC, Ph-like (ABL-type)



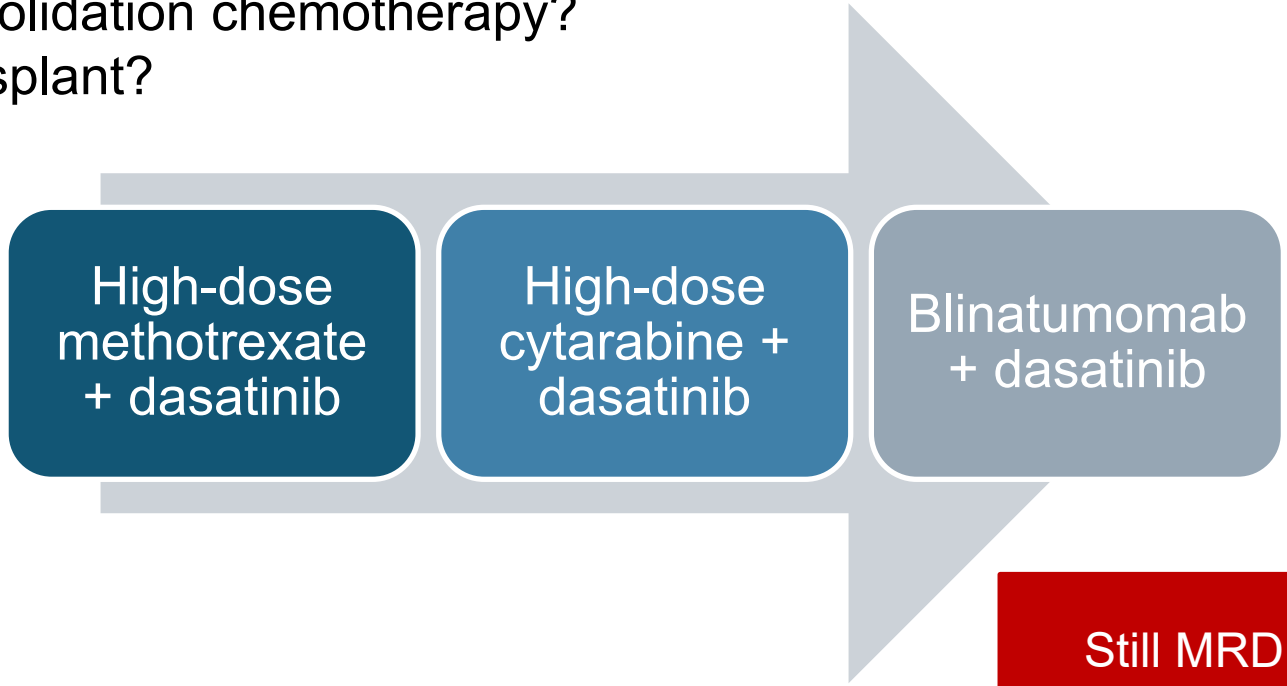
- **Grade 3 cytokine release syndrome**

Dose interruptions and reductions to 9mcg/day
Ended with 28 mcg/day
Dexamethasone and tocilizumab

- **MRD < 0.01%**

Open questions

- Consolidation chemotherapy?
- Transplant?



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Opportunities and Challenges in Everyday Practice (Q&A session)

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Challenges at diagnosis / evaluation

- Genomic stratification at diagnosis: the ideal and the minimum required
- CSF Analysis: flow cytometry for all patients? What to do with a positive result?
- MRD assessment: the minimum and the Ideal (methodology and timing)

Current challenges in frontline ALL management

- Can frontline immunotherapy reduce the need for chemotherapy and its associated toxicities in Ph-negative ALL?
- Does frontline immunotherapy require specific antimicrobial prophylaxis (or IVIG)?
- How many blinatumomab cycles are needed in frontline?
- In 2026, with frontline immunotherapy, who should still undergo transplantation as consolidation in first remission?

Transplantation, cellular therapies, and special populations

- What are the peri-transplant considerations with inotuzumab?
- Where does CAR-T cell therapy fit best in the treatment of ALL?
- Key considerations in the management of T-ALL

Thank you

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Conclusions and Wrap-Up

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