Lymphoma · Leukemia & Myeloma Congress

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The Outpatient ALL Blueprint: Scaling Low-Toxicity T-Cell Reduction in the Community

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Disclosures

- **Elias Jabbour, MD:** Consultant—AbbVie, Adaptive Biotechnologies, Amgen, BMS, Celgene, GSK, Johnson & Johnson (Janssen), Karyopharm, Oncopeptides, Pfizer, Prothena, Regeneron, Sanofi, Sebia, Takeda
- **Alexandra Gomez-Arteaga, MD:** Speakers Bureau—Amgen, Bristol Meyers Squibb, Celgene, Dermavant, Incyte, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi (terminated, August 15, 2024)

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Learning Objectives

- Differentiate the safety profiles of low-affinity CD3 and fast-off CD19 T-cell redirecting therapies from conventional constructs in R/R ALL
- Apply a risk-stratified management and sequencing framework for delivering outpatient BsAb therapy as a bridge to CAR T-cell therapy in people with R/R ALL, particularly in community settings
- Design an evidence-based post-CAR T management strategy for people with R/R ALL who are transplant-ineligible, including the role of BsAb therapy

R/R = relapsed/refractory; BsAb = bispecific antibody.

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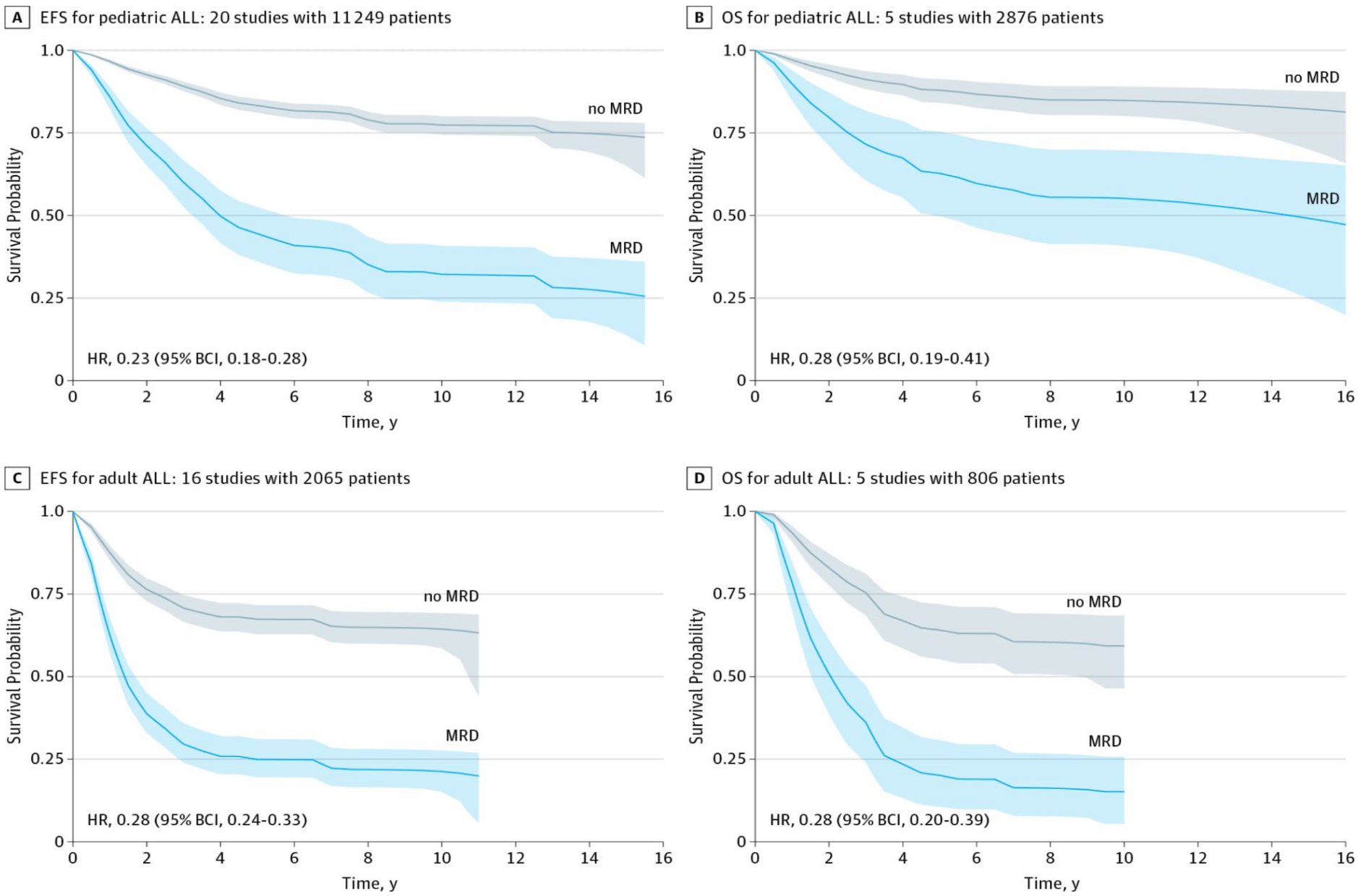
Adults with R/R Acute Lymphocytic Leukemia in 2026: Immunotherapies and Sequencing of CD19-Targeted Therapies—Optimal Use of CAR T Cells

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MRD in ALL

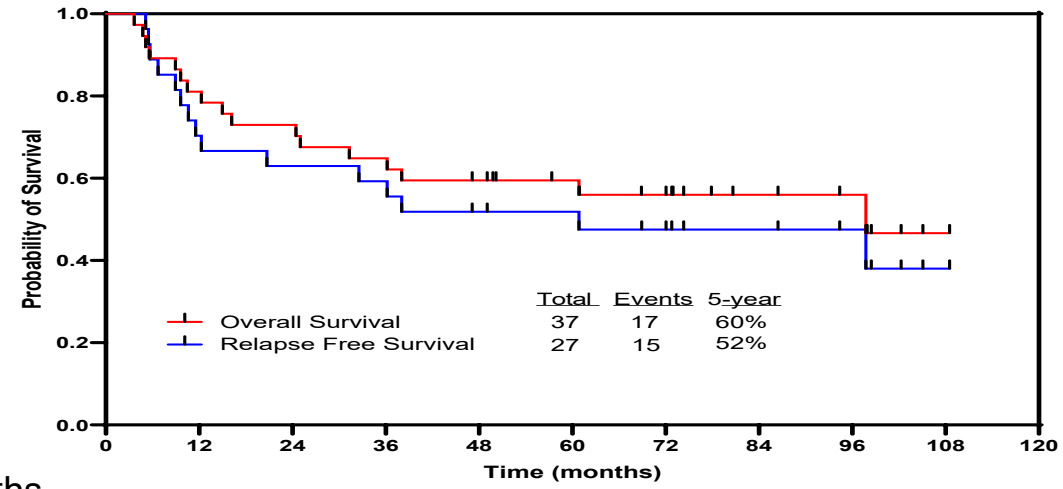


MRD = measurable residual disease; ALL = acute lymphocytic leukemia; EFS = event-free survival; OS = overall survival.
Berry DA, et al. *JAMA Oncol*. 2017;3(7):e170580

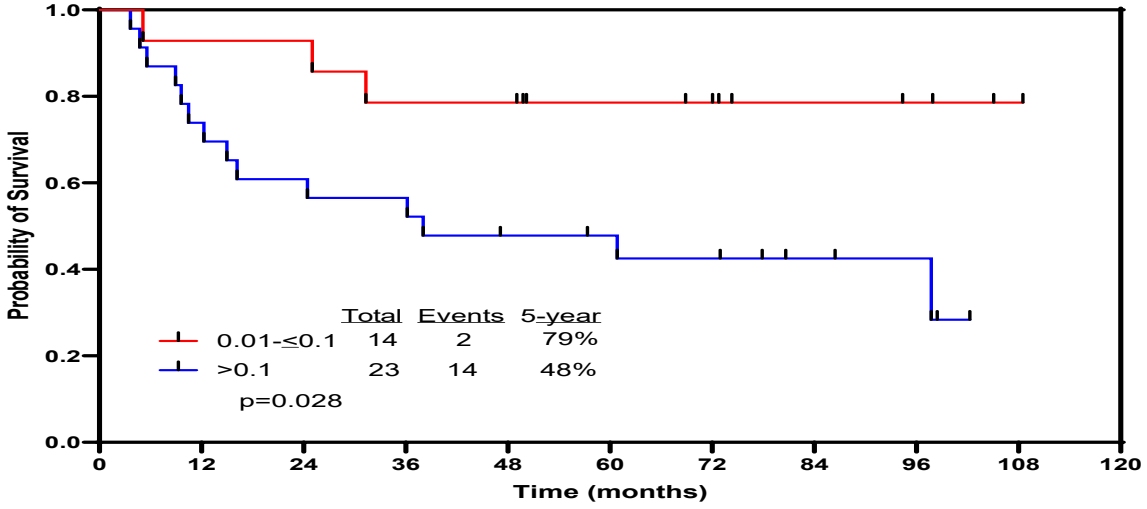
Blinatumomab for MRD-Positive ALL in CR1/CR2+

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

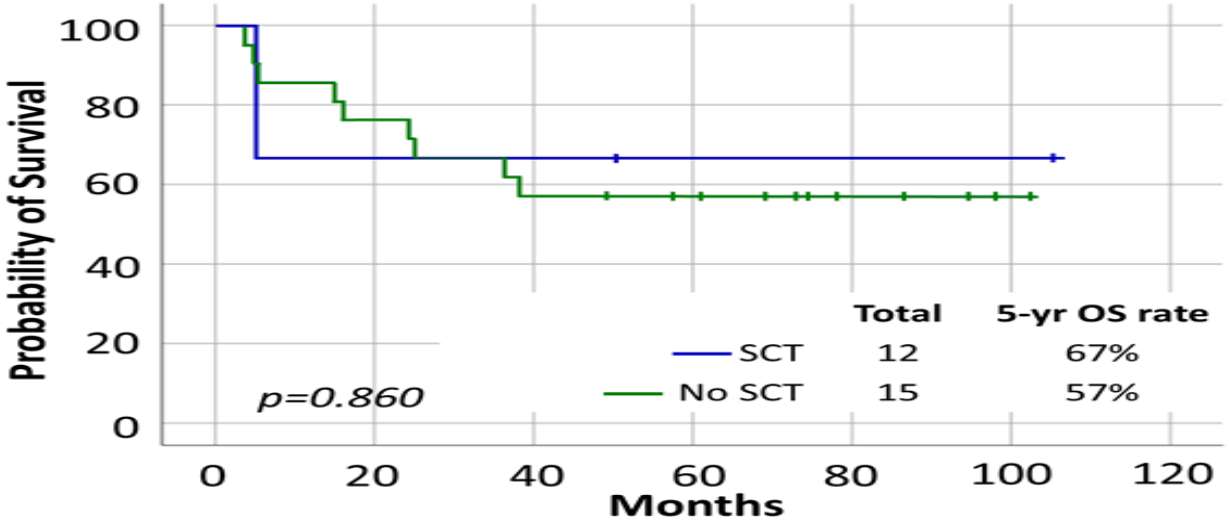
Outcomes



OS by MRD level



OS by ASCT



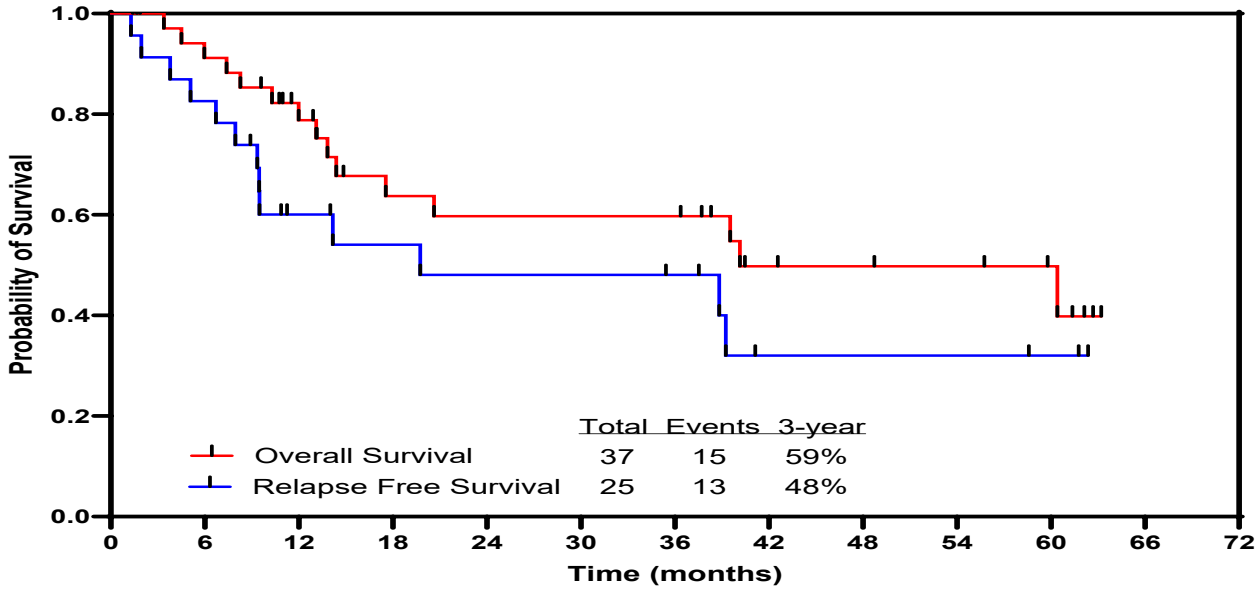
C = cycle; NGS = next-generation sequencing; alloSCT = allogeneic stem cell transplantation; f/u = follow-up; CR = complete response.

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

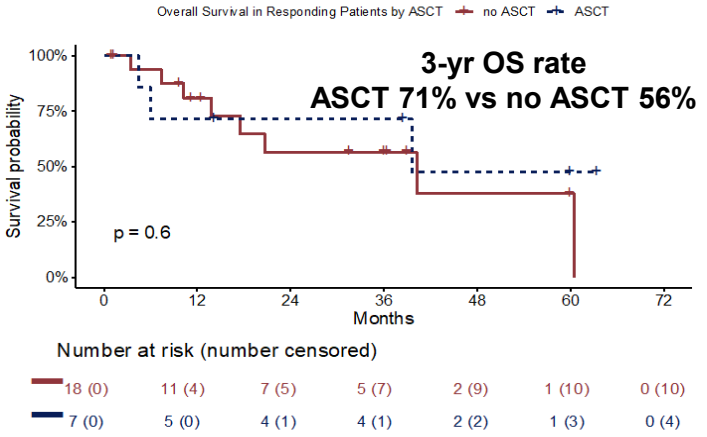
Inotuzumab for MRD-Positive B-ALL Longterm F/U

- 37 pts; median age 49 yrs (19-71)
- 76% CR1, 24% CR2+
- InO 0.9 mg/m2 C1 and 0.6 mg/m2 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 months
- 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)

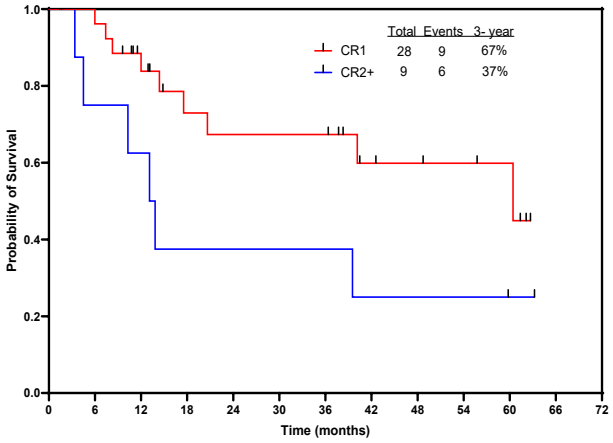
Outcomes



OS by ASCT



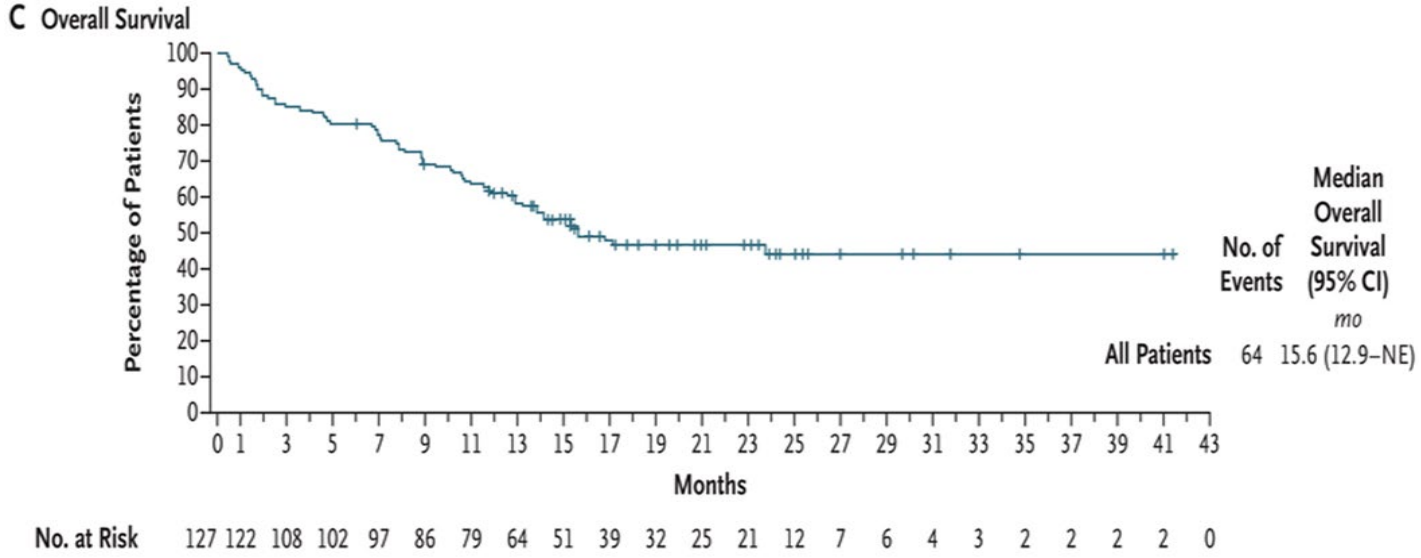
OS by CR1 vs CR2+

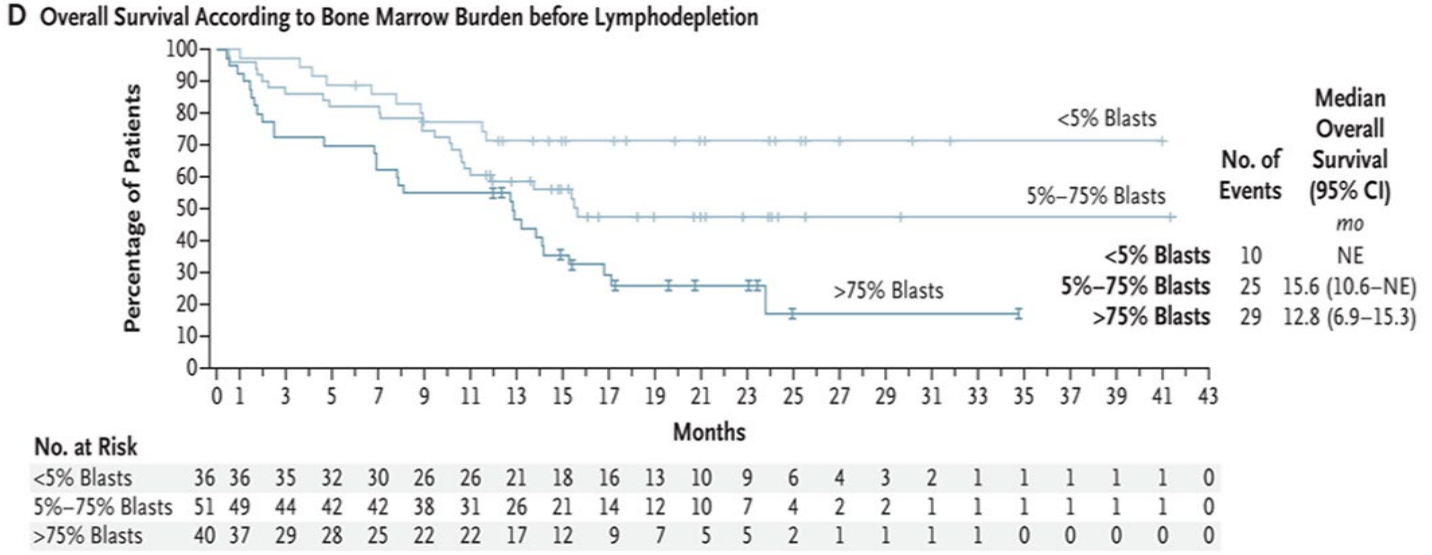


B-ALL = B-cell ALL; ASCT = autologous stem cell transplantation; FCM = flow cytometry; SOS = sinusoidal obstruction syndrome.

Goulart H, et al. *Blood*. 2025;146(Suppl 1):3348.

CARTs for MRD-Positive ALL—OBE-CEL Experience





Roddie C, et al. *N Engl J Med*. 2024;391(23):2219-2230.

Tisagenlecleucel for Persistent MRD in Pediatric B-ALL

- 121 pediatric/AYA HR B-ALL pts with persistent MRD after frontline consolidation
- Phase 2 CASSIOPEIA/ COG AALL1721 evaluating tisagenlecleucel after lymphodepletion
- 4-yr OS 85%; 5-yr DFS 64% without censoring and 62% with censoring
- MRD negativity 95% at day 29 and 86% at 3 mos
- CRS 37% (grade ≥3 2%); ICANS 3% (grade ≥3 1%)

Outcome (%)	Tisa-cel
4-yr OS	85
5-yr DFS	64
MRD-neg day 29	95
Grade ≥3 CRS	2

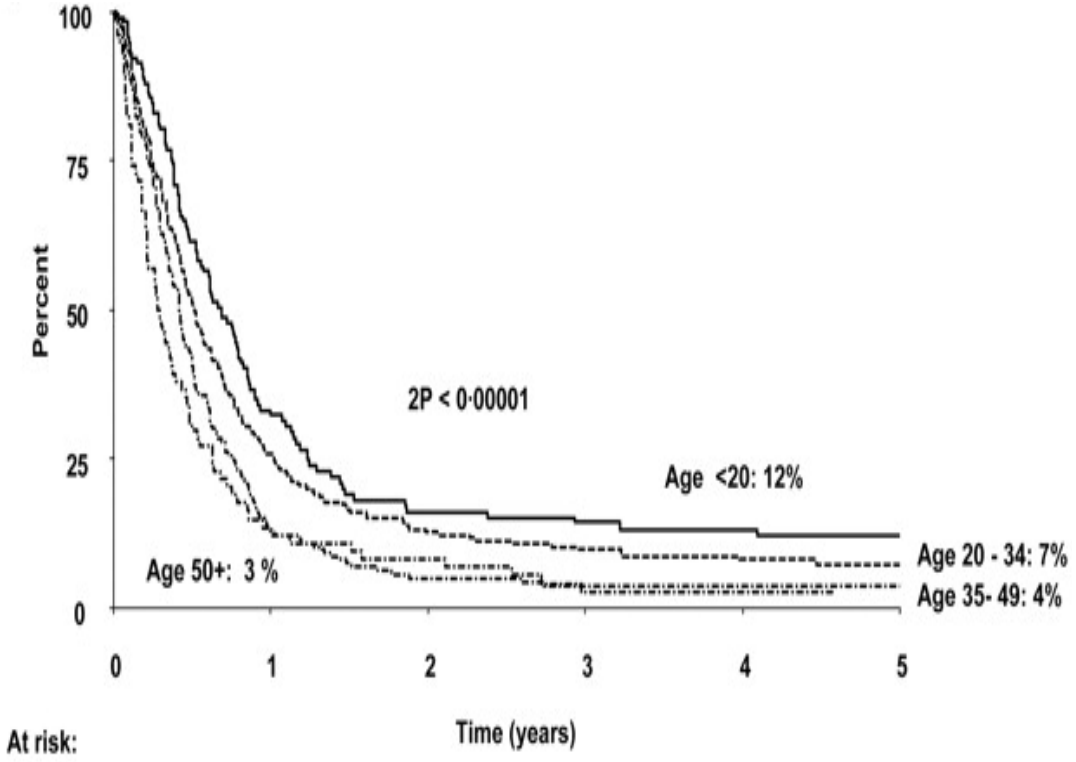
AYA = adolescent and young adult; DFS = disease-free survival; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome.

Maude S, et al. *HemaSphere*. 2026;10(Suppl 1):S135

ALL—Historical Survival Rates after 1st Relapse

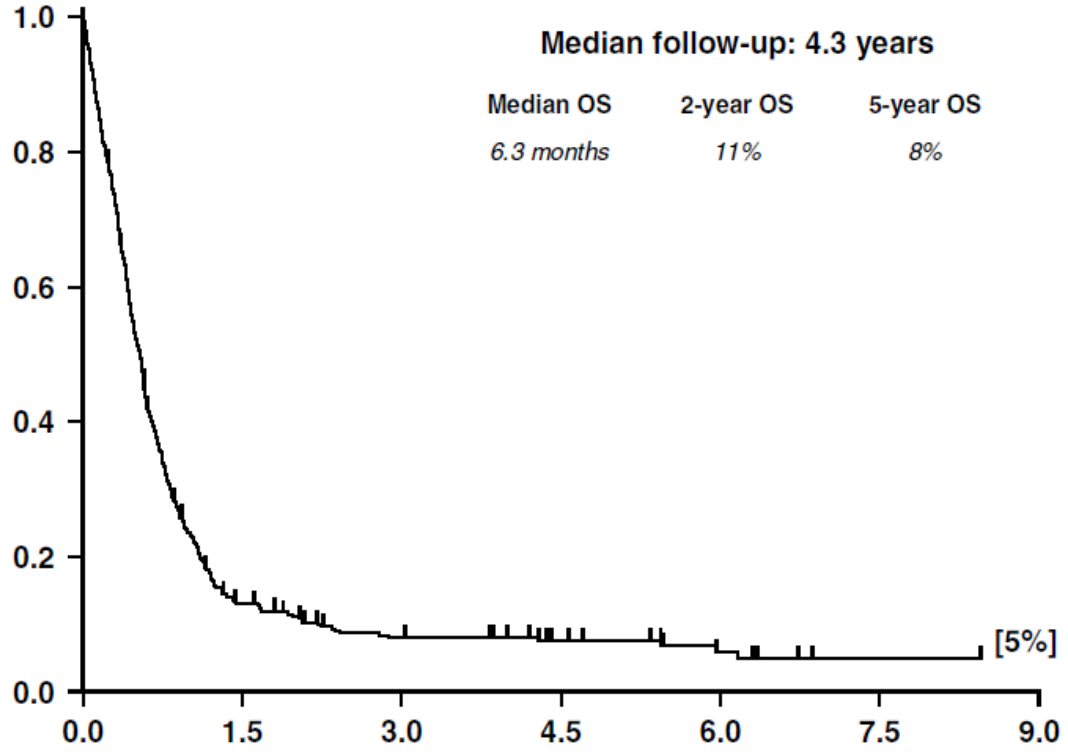
MRC UKALL2/ECOG2993 Study (n=609)[1]

Outcome of patients after 1st relapse
5-yr OS: 7%



LALA-94 Study (n=421)[2]

Outcome of patients after 1st relapse
2-yr OS: 11% & 5-yr OS: 8%



1. Fielding AK, et al. *Blood*. 2007;109(3):944-950. 2. Tavernier E, et al. *Leukemia*. 2007;21(9):1907-1914.

Historical Results in R/R ALL

- Poor prognosis in R/R ALL Tx with standard of care (SOC) chemotherapy

Rate (95% CI)	No prior salvage (S1)	One prior salvage (S2)	≥2 prior salvages (S3)
Rate of CR, %	40	21	11
Median OS, months	5.7	3.4	2.9

R/R = relapsed/refractory.
Gökbuget N, et al. *Haematologica.* 2016;101(12):1524-1533.

ALL Salvage Standards of Care in 2026

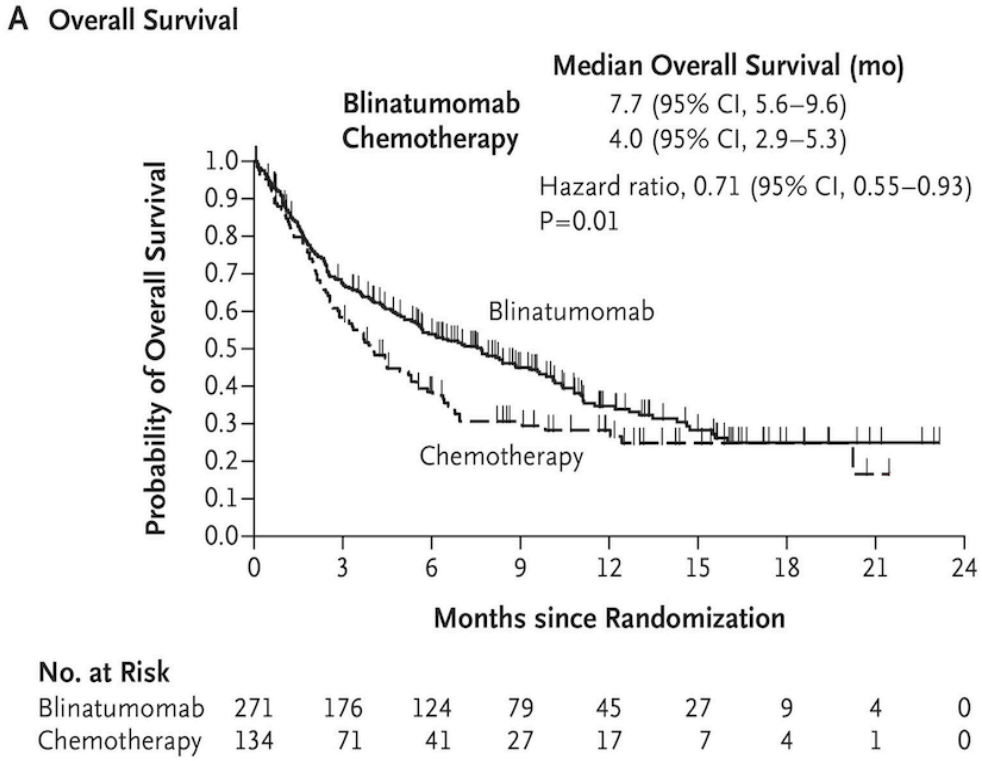
- Pre-B ALL
  - Blinatumomab (FDA approval 12/2014)
  - Inotuzumab (FDA approval 8/2017)
  - 3 CARTs: 1) tisagenlecleucel FDA approvals 2017; age <26 yrs, salvage 2+; 2) brexucabtagene (KTE-X19) FDA approval 2021 for adult R/R ALL; 3) obecaptageneE (OBE-CEL 2024)
- T ALL: nelarabine
- ChemoRx: FLAG IDA, hyper-CVAD, augmented hyper-CVAD, MOAD
- BUT—very promising new therapies with chemoRx + TKIs/ADCs/BiTEs/CARTs
- Ph-positive ALL—potent TKIs (ponatinib preferred) + blinatumomab/chemoRx/alloSCT
- Refer for investigational therapies—dose-dense miniCVD-INO-BLINA/CART

FDA = US Food and Drug Administration; FLAG = fludarabine, cytarabine, idarubicin, granulocyte colony-stimulating factor; hyper-CVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, cytarabine; MOAD = methotrexate, vincristine, asparaginase, dexamethasone; TKI = tyrosine kinase inhibitor; ADC = antibody-drug conjugate; BiTE = bispecific T-cell engager.

Blinatumomab/Inotuzumab vs ChemoRx in R-R ALL

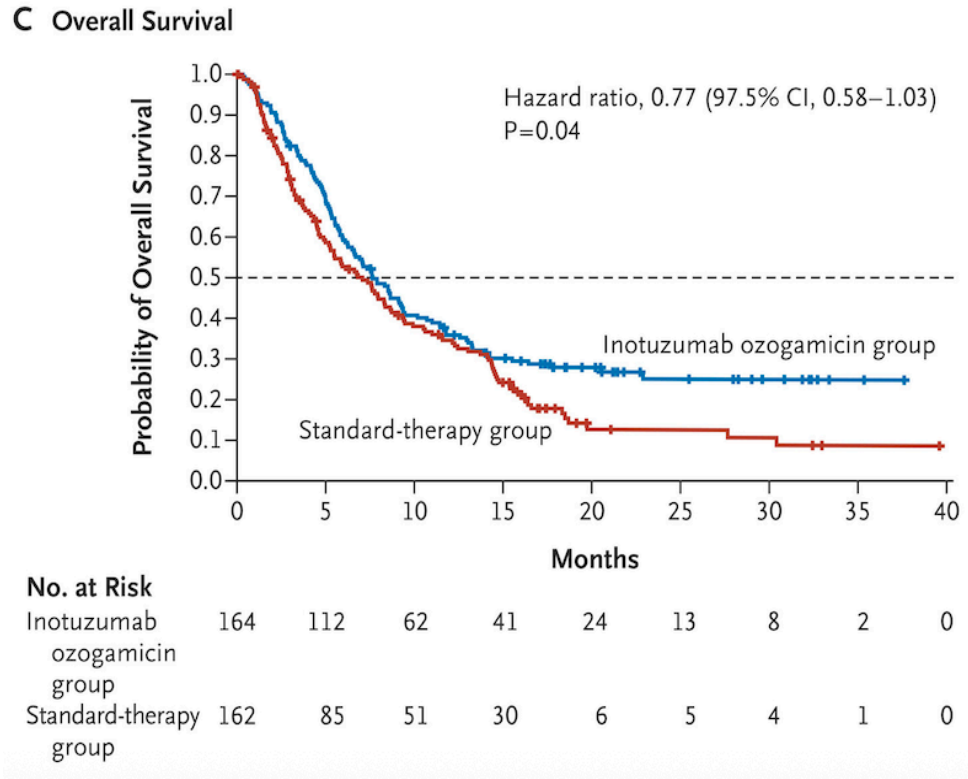
Blinatumomab vs SOC Chemotherapy

Marrow CR 44% vs 25%



Inotuzumab vs SOC Chemotherapy

Marrow CR 74% vs 31%



Kantarjian HM, et al. *N Engl J Med.* 2017;376(9):836-847. Kantarjian HM, et al. *N Engl J Med*. 2016;375(8):740-53.

ALL Salvage Strategies Increasing Survival/Cure

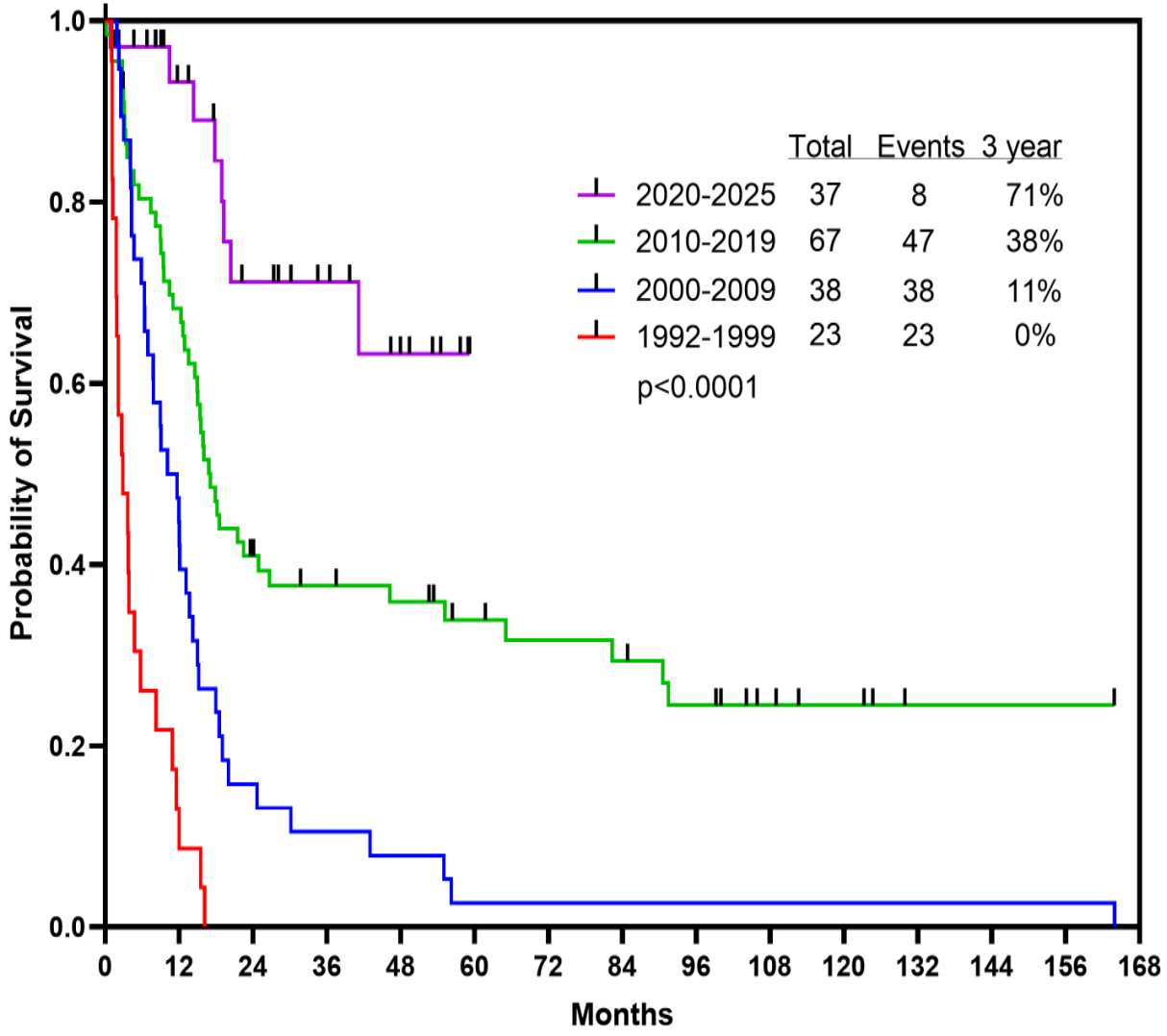
- Blinatumomab IV and SQ
- Inotuzumab
- BRICK regimen = DD miniCVD-ino-blina
- CART
- ChemoRx
- Allogeneic HSCT
- BCR::ABL1 inhibitors in Ph+ALL
- Venetoclax
- Any of above not used optimally, or at all, in frontline Rx

BRICK = blinatumomab, rituximab or other CD20 antibody, inotuzumab, condensed with chemotherapy; DD = dose-dense; HSCT = hematopoietic SCT.

Second-Line Therapy in Ph-Positive ALL

165 pts with Ph-positive ALL treated with second-line Rx

Parameter	% CR	% 3-yr OS
No TKIs (<2000/2000+)	30/58	0/0
IMA combo	92	8
2nd GEN TKI combo	93	38
3rd GEN TKI combo	86	58
2020+ (PONA-BLINA)	84	71



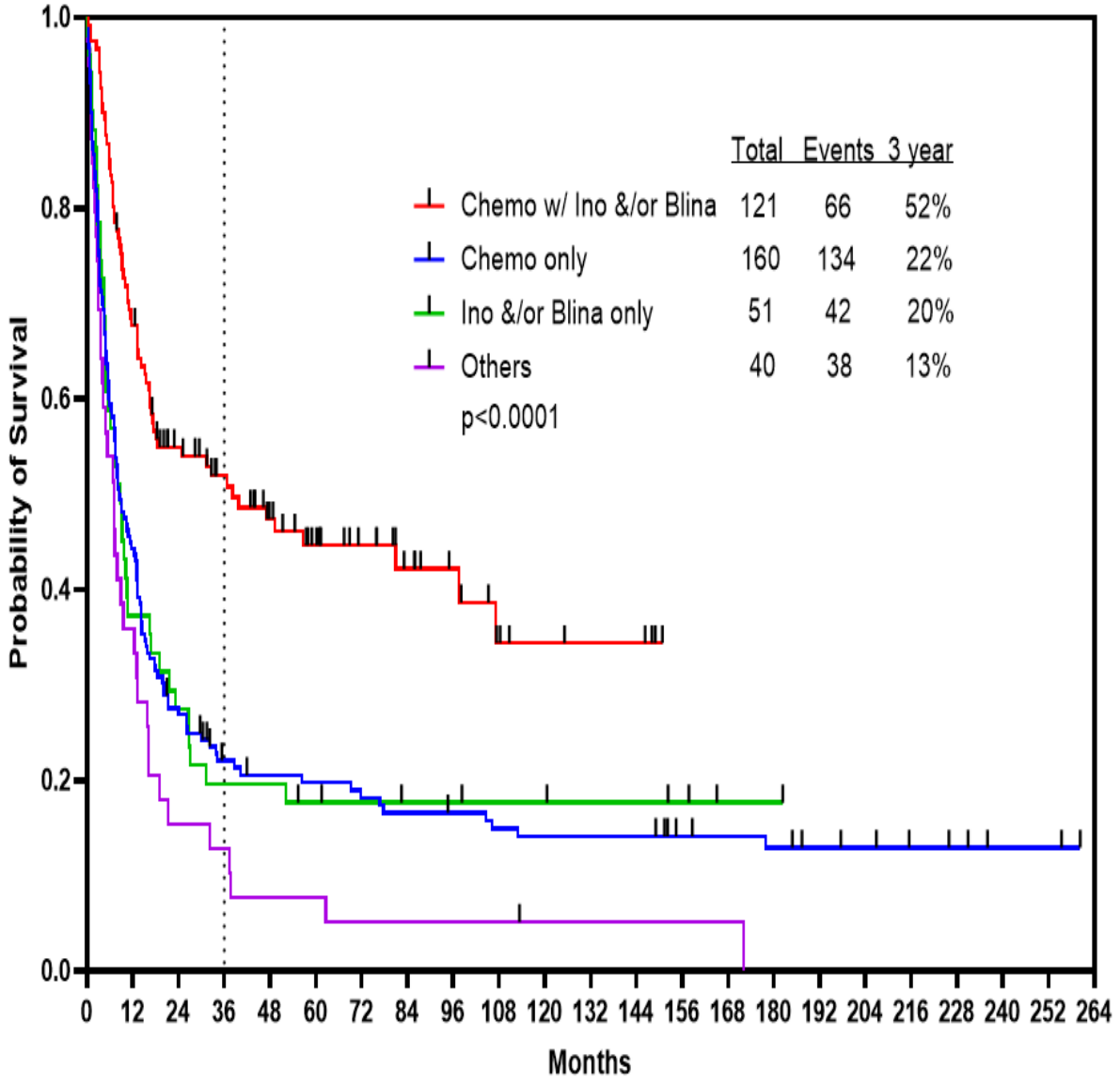
Kantarjian HM, et al. *Cancer*. 2026;132(15):e70533.

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Second-Line Therapy in B-ALL

372 pts with B-cell ALL treated with second-line therapies

Parameter	N	% CR	% 3-yr OS
ChemoRx +/- INO+/- Blina	**121**	**96**	**52**
Chemo only	**160**	**66**	**22**
INO or Blina	**51**	**55**	**20**
Other	**40**	**23**	**13**



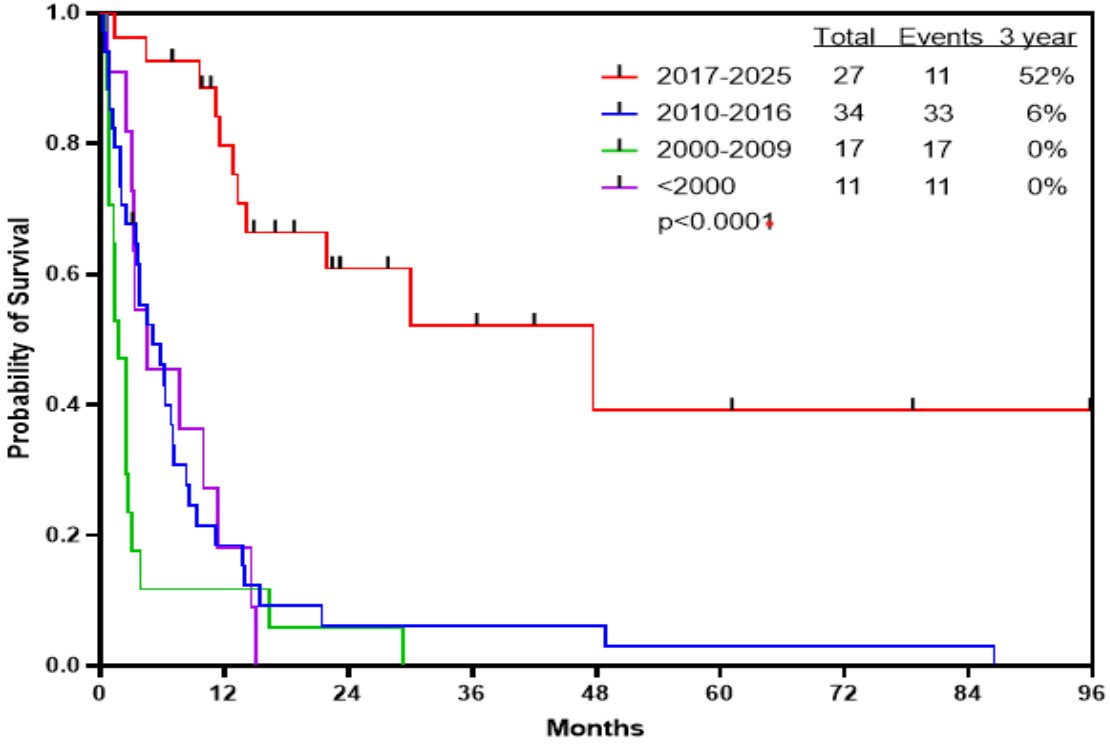
Kantarjian HM, et al. *Cancer*. 2026;132(8):e70401.

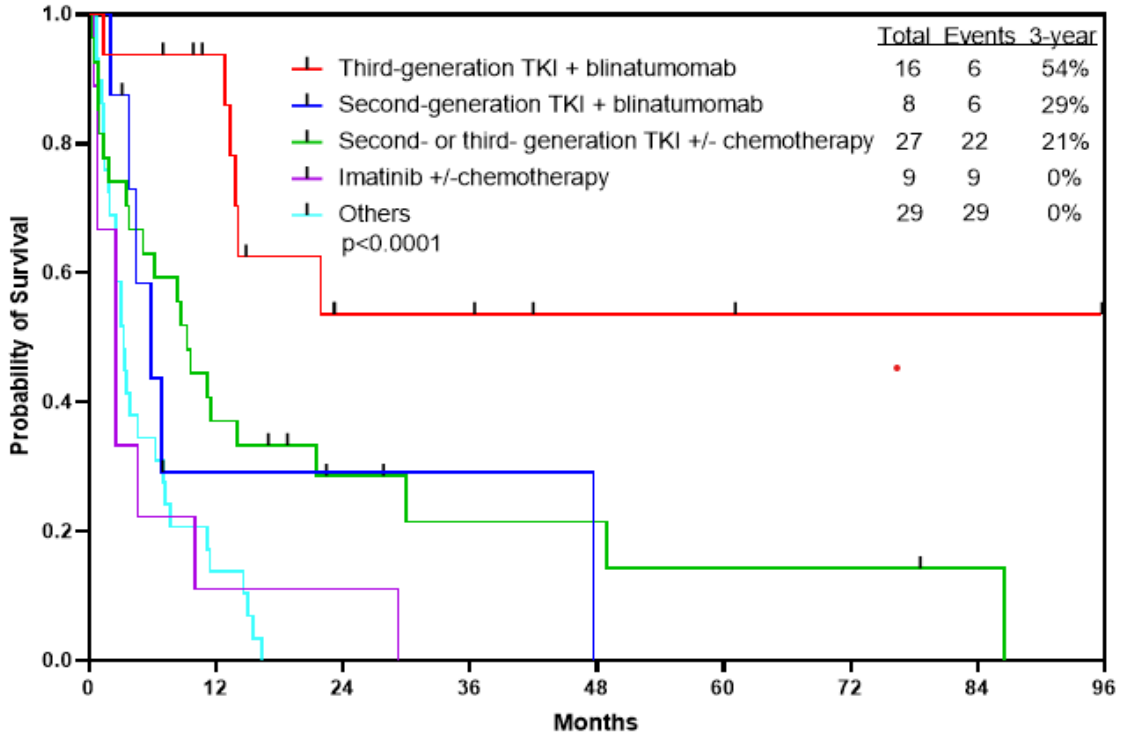
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Third-Line Therapy in Ph-Positive ALL

- 89 pts with Ph-positive ALL treated with third-line Rx
- CR 58%; 3-yr OS 17%; increased to 52% 2017+.

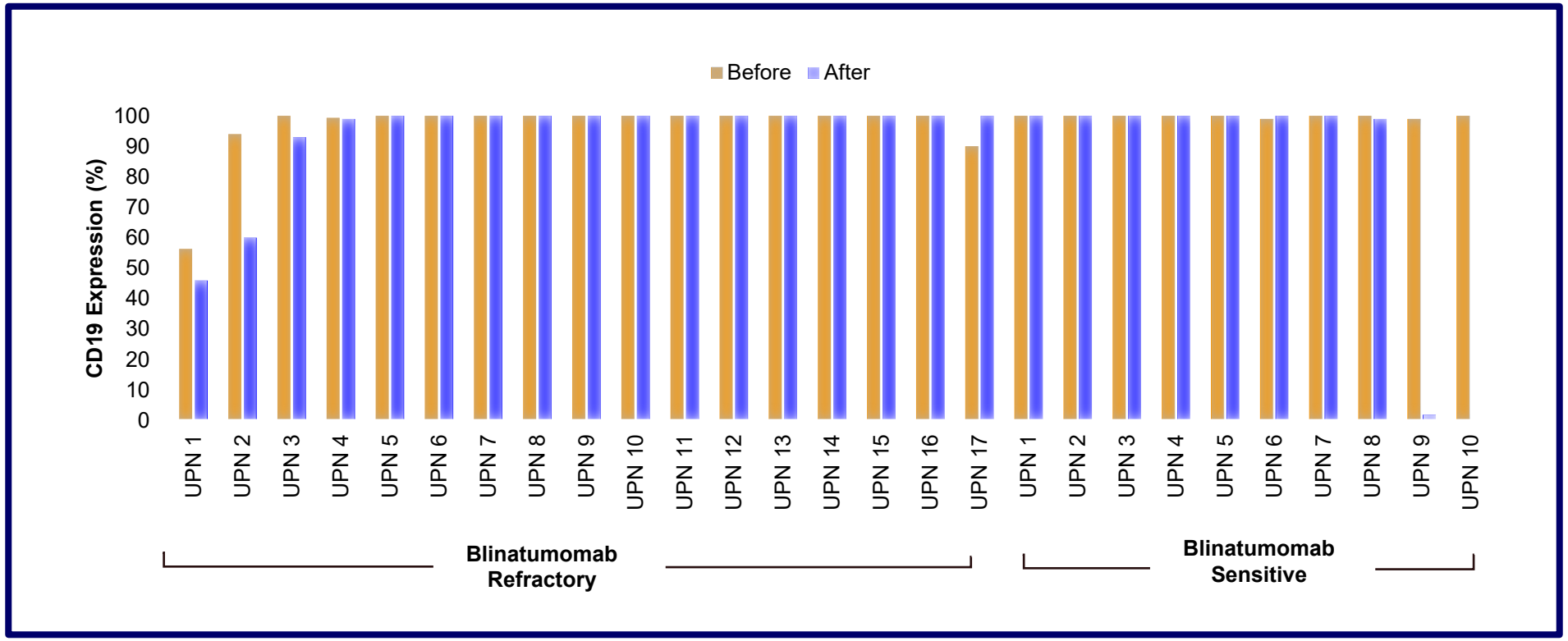
Parameter	% CR	% 3-yr OS
<2000/ 2000-2009	55/18	0/0
2010-2016	56	6
2017-2025	89	52
3rd GEN TK-BLINA combo (n=16)	100	54





Jen WY, et al. *Clin Lymphoma Myeloma Leuk*. 2026;26(8):519-525

CD19 (%) Expression before and after Blinatumomab Therapy



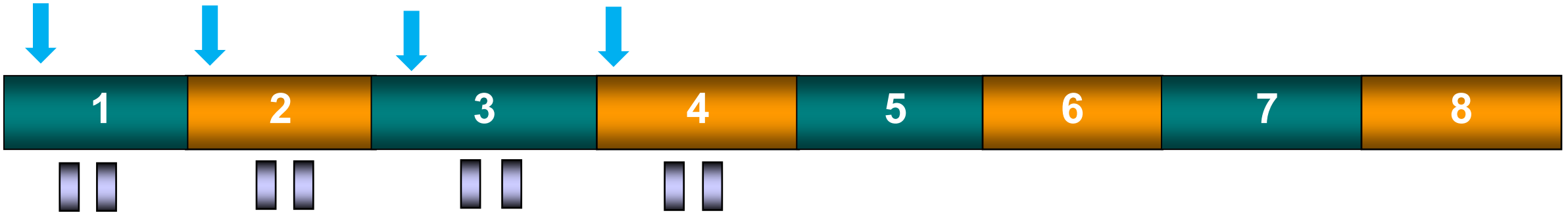
- **61 patients evaluated for immunophenotype; 56 (92%) had CD19-positive disease**
  - 5 (8%) had ALL recurrence with CD19-negative disease
  - 2 patients progressed with lower CD19-positive disease

Jabbour E, et al. *Am J Hematol.* 2018;93:371-374.

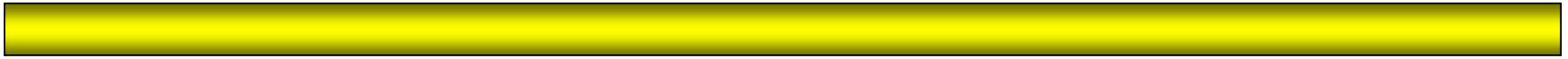
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Mini-HCVD + INO ± Blina in R/R B-ALL: Original Design (Pts #1-67)

Intensive phase



Maintenance phase



36 months

Mini-HCVD

INO

Mini-MTX-cytarabine

IT MTX, Ara-C

POMP

INO	First 6 pts	7 to 34	35+
C1 (mg/m^2)	1.3	1.8	1.3
C2-4 (mg/m^2)	0.8	1.3	1.0

Ara-C = cytarabine; POMP = 6-mercaptopurine, vincristine, methotrexate, prednisone.

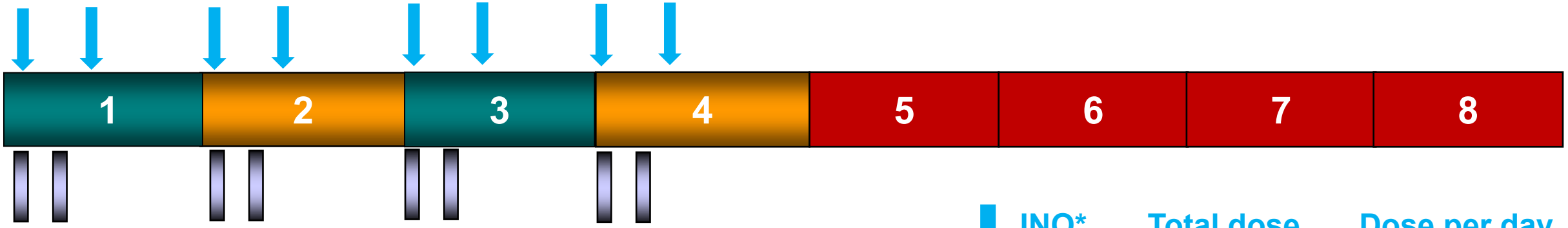
Short N, et al. Presented at: European Hematology Association (EHA) Hybrid Congress; 2023. Abstract S119.

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Mini-HCVD + INO ± Blina in R/R B-ALL: Modified Design (Pts #68-110)

Intensive phase

Consolidation phase



Maintenance phase



18 months

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

Mini-HCVD

Mini-MTX-Ara-C

Blinatumomab

IT MTX, Ara-C

POMP

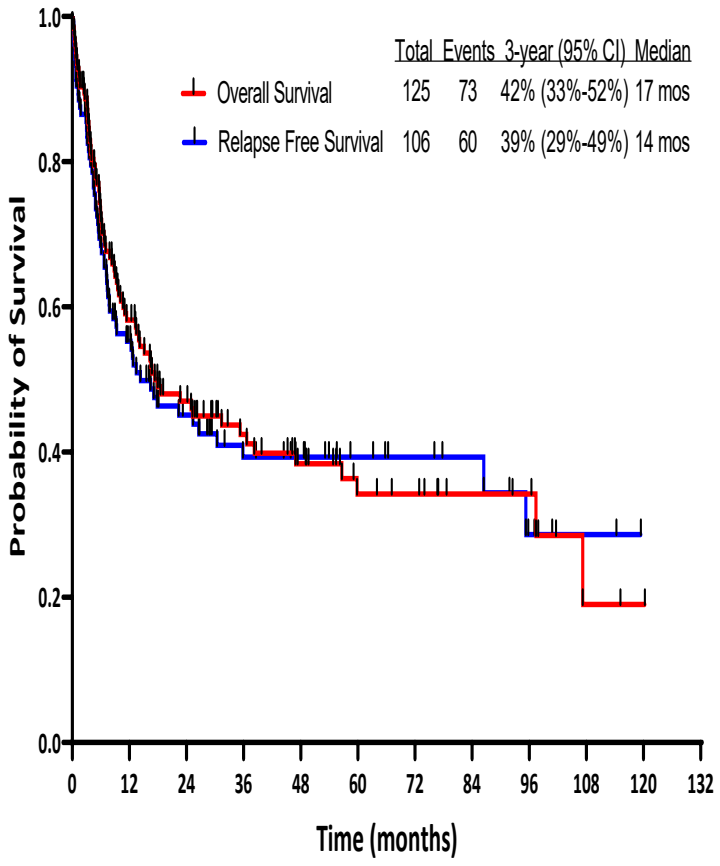
VOD = veno-occlusive disease.

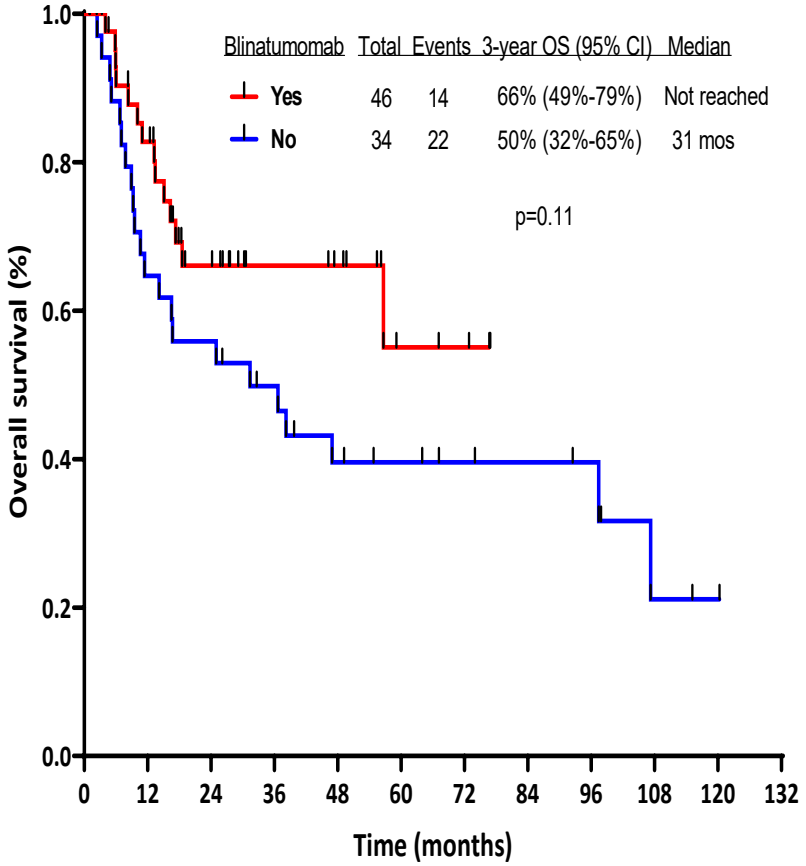
Short N, et al. Presented at: EHA Hybrid Congress; 2023. Abstract S119.

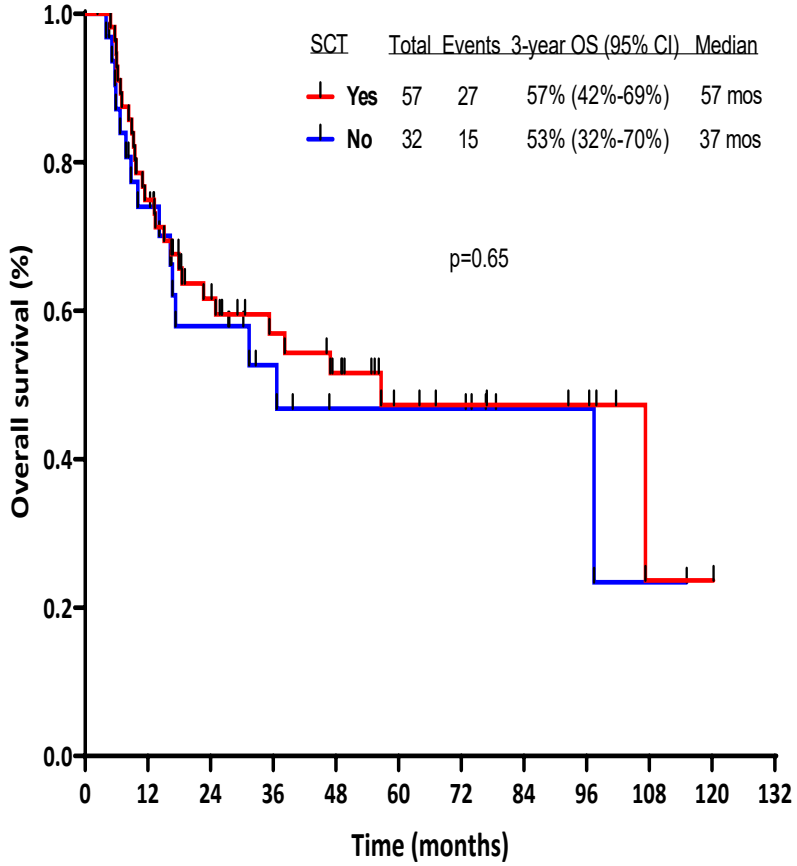
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Mini-Hyper CVD-Inotuzumab-Blinatumomab in R/R ALL

- 125 pts; median age 38 yrs (18-87). 70 S1. Rx with mini-HCVD x 6-8; blinax4→POMP 1 yr with blina Q3 mos; ino 0.6 mg/m^2 D1 and 0.3 mg/m^2 D8 and 0.3 mg/m^2 D1 and D8 C2,4,6,8 (2.7 mg/m^2).
- ORR rate 83% (63% CR); MRD negative 85% (53% at CR); 57 (46%) alloSCT; F/U 36 mos
- VOD 8/125 (8%)—9/67 (13%) before blina; 1/58 (2%) with blina (*P*=0.02)





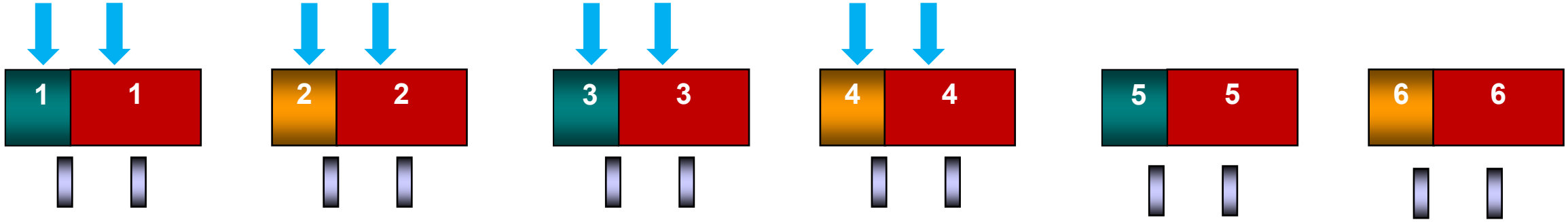


ORR = objective response rate.

Kantarjian. Journal of Hematology & Oncology 16: 44; 2023. Short. HemaSphere 7: abst S119: 2023

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Blinatumomab-Rituximab-Inotuzumab-Condensed with KemoRx (**BRICK** Regimen)

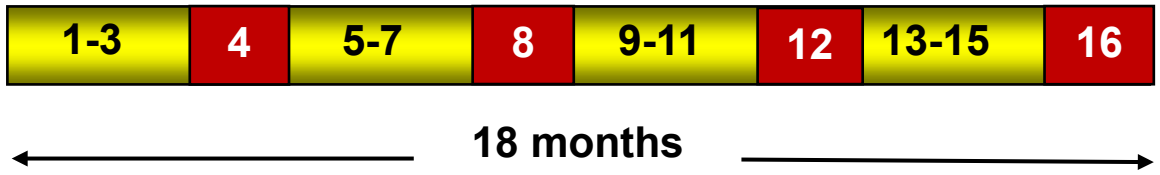


INO*	Total dose (mg/m^2)	Dose per day (mg/m^2)
C1	0.9	0.6 D2, 0.3 D8
C2-4	0.6	0.3 D2 and D8

Total INO dose = 2.7 mg/m^2

*Ursodiol 300 mg tid for VOD prophylaxis

Maintenance phase



Mini-HCVD

Mini-MTX-Ara-C

Blinatumomab

IT MTX, Ara-C

POMP

Mini-HCVD-Ino-Blina in R/R ALL

- 133 pts (median age 37 yrs; 17-87) Rx with mini-HCVD-ino (n=67); same+blina (n=44); and DD-mini HCVD-ino-blina (n=22). AlloSCT 43%

% Parameter	Total (n=133)	CT+Ino (n=67)	CT+ Ino+Blina (n=44)	DD (n=22)
ORR	86	76	93	100
CR	65	60	66	81
MRD-neg	85	82	85	95
3-yr OS	-	34	50	76
3-yr RFS	-	35	44	68
1-yr OS (S1)	-	51 (63)	66 (66%)	90 (94%)

- 3-yr OS 54% in S1, 20% in S2
- 3-yr OS 60% with SCT vs 56% without
- SOS=10 pts—9 (13%) initial vs (2%) later

RFS = relapse-free survival.
Habib D, et al. *Blood*. 2024;144(Suppl 1):2811.

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

- 30 pts; median age 39 yrs (19-63)
- 87% S1, 13% S2+, 53% high cytomolecular risk, 10% prior ASCT, 33% prior blina
- ORR: 97%, 96% MRD-negativity by NGS, 88% by NGS
- Median F/U 36 months—3-yr EFS 68%, 3-yr OS 79%
- 3-yr EFS by consolidation: CAR 82% versus ASCT 60% versus maintenance 83%

EFS: Entire Cohort

OS: Entire Cohort

EFS by Consolidation

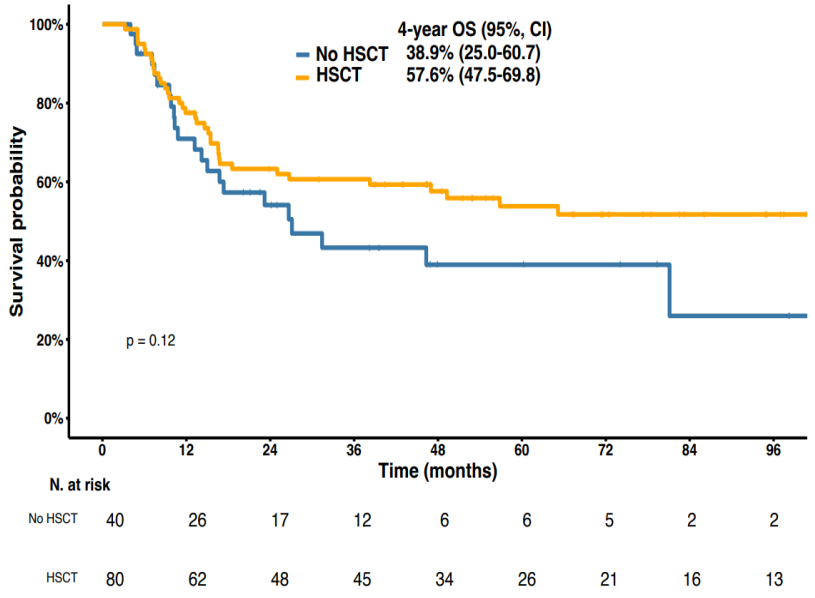
CRi = CR with incomplete count recovery.
Goulart H, et al. *Blood*. 2025;146(Suppl 1):3350.

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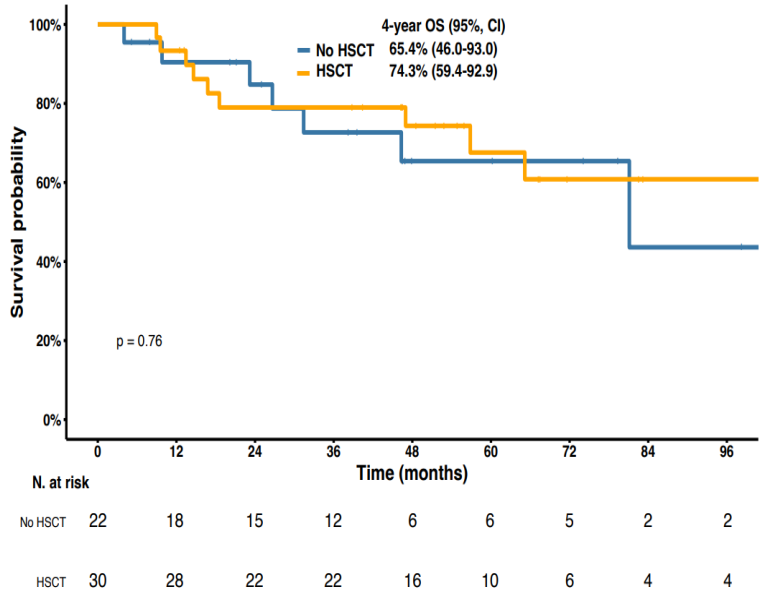
Outcomes after S1 in R-R ALL: Role of AlloSCT Consolidation

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

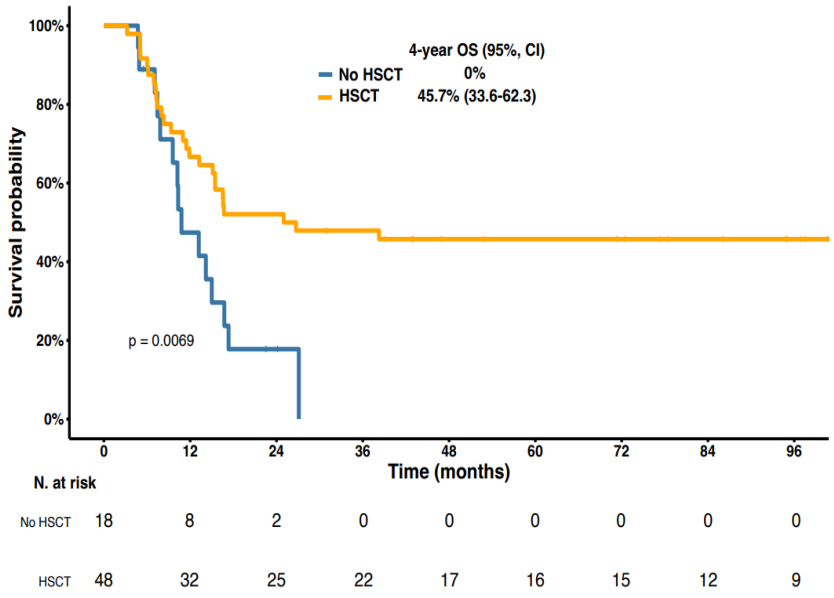
OS: Overall



OS: MRD-neg EOC1 & CR1D≥ 12 mos



OS: MRD-pos EOC1 or CR1D< 12 mos



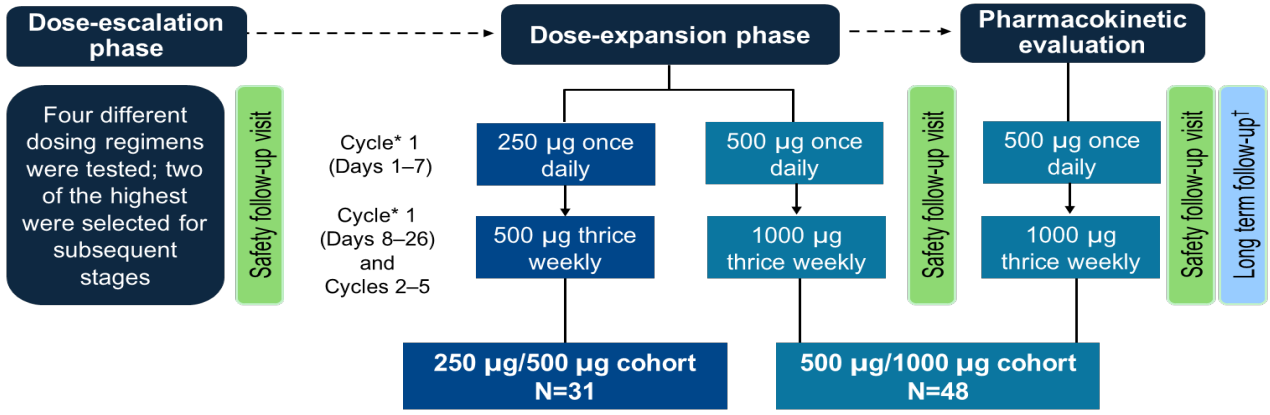
EOC = end of cycle; CIR = cumulative incidence of relapse; MVA = multivariate analysis; CR1D = duration of first CR.

Azevedo RS, et al. *Leukemia*. 2026;40(9):2008-2017

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Subcutaneous Blinatumomab in R-R ALL

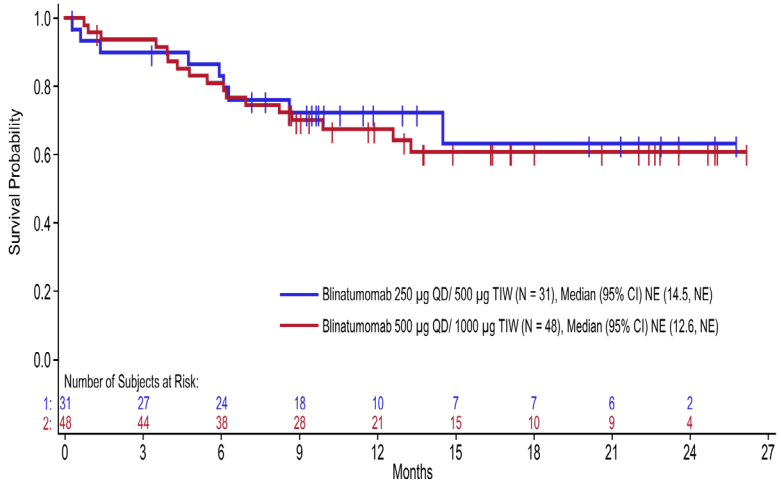
- 88 pts Rx: 36 at 250/500; 52 at 500/1000
- Rx 250 mcg daily x 7 then 500 mcg TIW; or 500/1000
- Median age 49 yrs (19-78). Median prior Rxs 2(1-7). Baseline BM blasts 60%.
- Prior CART 16%, blina 19%, INO 33%, HSCT 28%
- Median F/U 14 mos



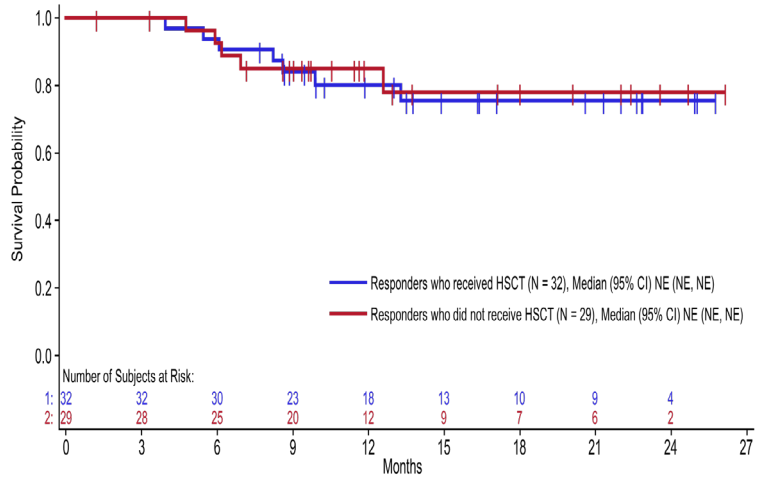
*Patients could receive 1–5 cycles of SC blinatumomab as monotherapy. Each cycle included 4 weeks of treatment followed by 1 week of treatment-free interval. Hospitalization was required for the first 12 days of cycle 1.
†Long-term follow-up lasted two years following the first dose of SC blinatumomab.
Data presented is as of July 3, 2025.

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

Overall Survival



OS of Responders by HSCT Status



CRh = CR with partial hematological recovery; BM = bone marrow.

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

Phase 1B/2 of MK-1045 (CD3-CD19 BiTE) in R/R ALL

- 75 pts Rx in dose-escalation (10 DL), weekly IV; priming→intermediate→target; doses up to 2/20/90 mg
- Median age 46 yrs (18-73); 28% Ph-positive; median prior Rx 2 (1-8); 9% prior blina, 7% prior CAR T, 15% prior ASCT

Parameter	Total	TD ≥60 mg	2/20/90
No Rx	**73**	**20**	**12**
%CR-CRi-CRh	**55**	**83**	**92**
% MRD-neg	**NA**	**90**	**91**
DOR (mos)	**NA**	**11.3**	**NR**

- Among pts with prior blina or CAR T-cell Rx who had received a TD ≥60 mg, 5/5 achieved CR/CRi/CRh and 4/5 MRD negativity

DOR = duration of response; NA = not applicable; NR = not reached.
Wang Y, et al. *Blood*. 2025;146(Suppl 1):647.

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 yrs (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 ICANS 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**

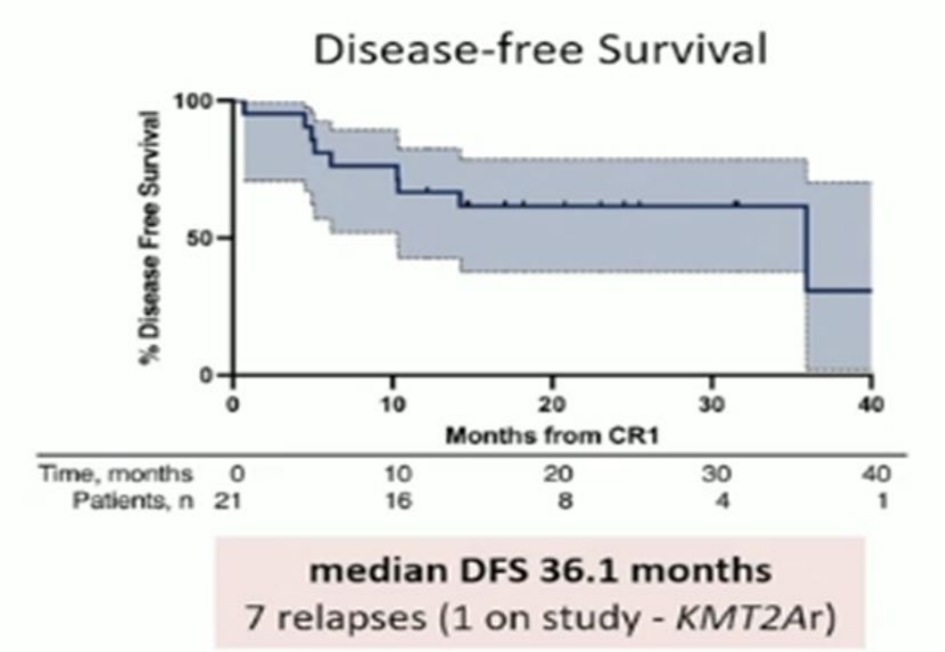
- Among pts Rx at 15 mg, ORR 88% with prior blina, 73% with prior CAR T, 86% in double-exposed, and 86% in triple-exposed pts
- Six of 7 pts with Ph-positive ALL achieved CR

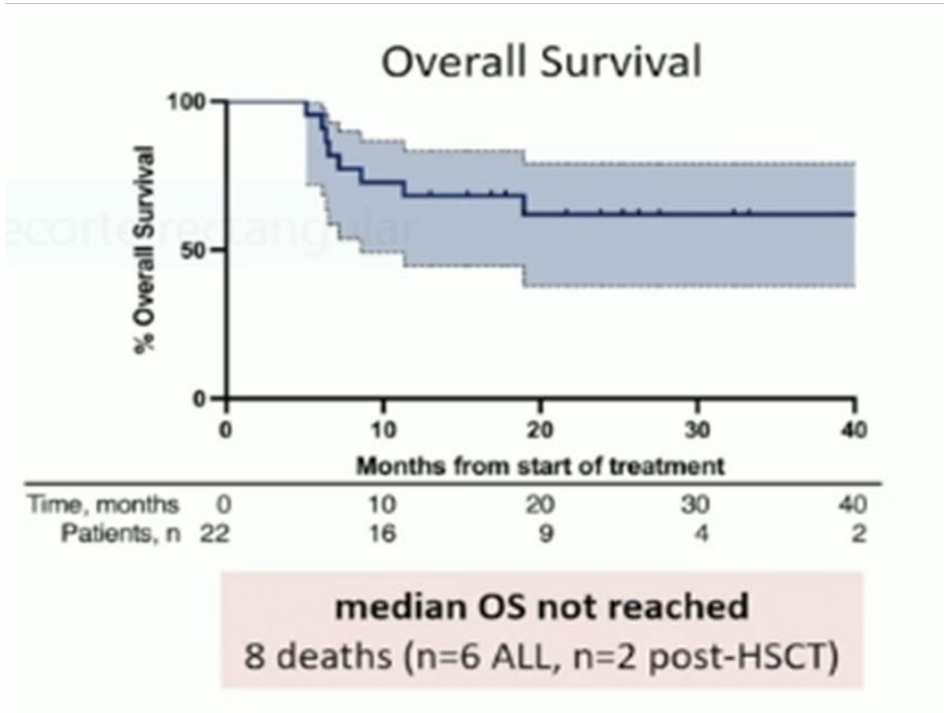
DLT = dose-limiting toxicity.
Aldoss I, et al. *Blood*. 2025;146(Suppl 1):3345.

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InO-VEN in R-R ALL: Phase I

- VEN (D1-21) DL1 200 mg vs DL2 400 mg (RP2D=400) + ino (D1, D8, and D15)
- Up to 2 IND followed by consolidation (up to 6 cycles total)
- Dex 10 mg/m^2 D1-4 during IND; CNS and ASCT per SOC
- 23 pts; median age 39 yrs (24-74); 35% LBL; 17% Ph+
- CR 95% (21/23—ALL 100%; LBL 86%); MRD- flow 89%; MRD- NGS 74%
- Consolidation: blina (n=9); ASCT (n=14); DLI (n=1); XRT (n=1); POMP (n=1)
- Median F/U 25 mo → median DFS 36 mo; OS NR
- SOS (n=4; 17%—3 post-SCT)
- 7/21 (33%; 1 *KMT2Ar*) relapsed; 8/22 (36%; 6 ALL, 2 post ASCT—1 SOS) died



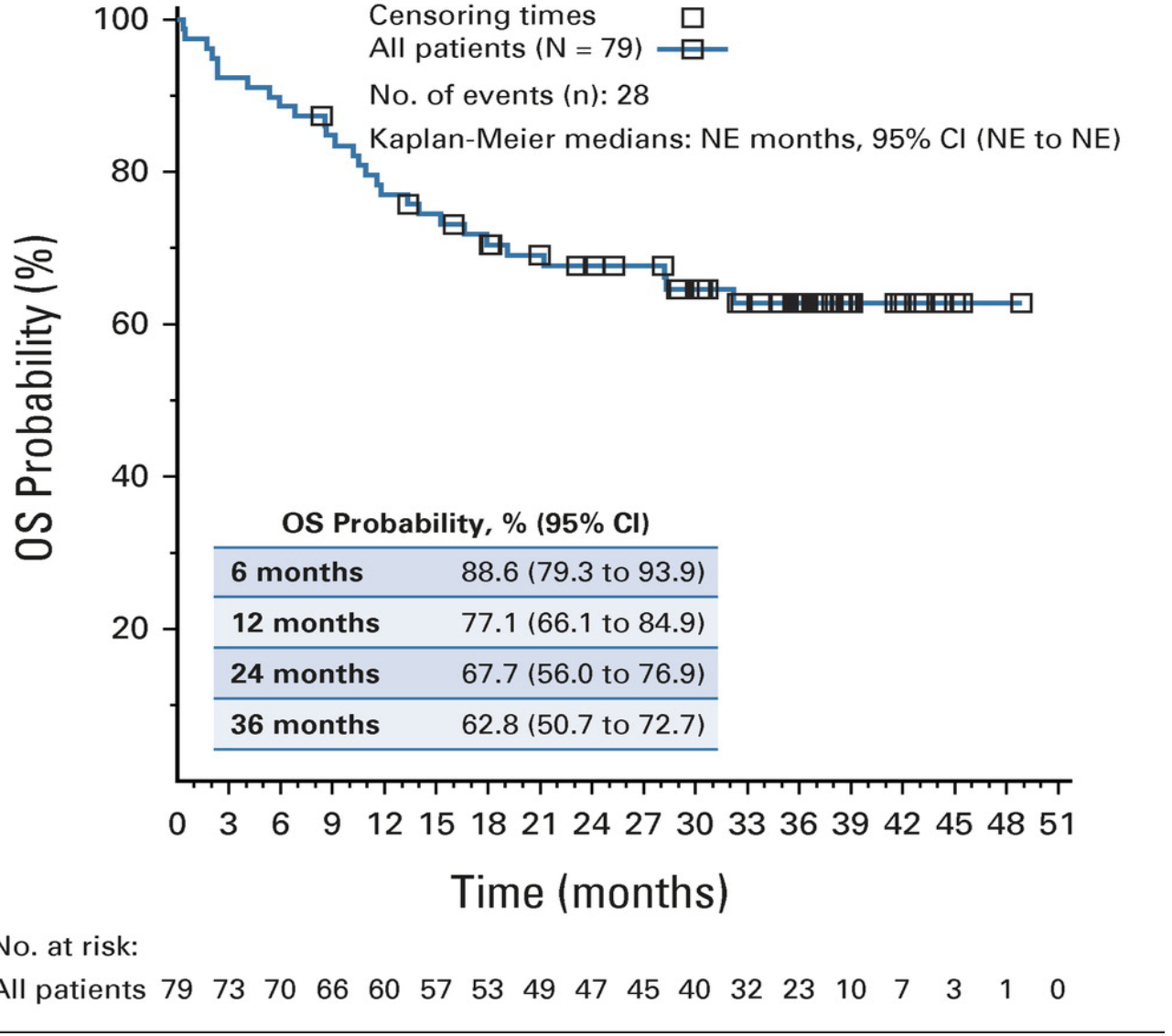


RP2D = recommended phase 2 dose; CNS = central nervous system; LBL = lymphoblastic lymphoma; DLI = donor lymphocyte infusion; XRT = radiation therapy.

Luskin M, et al. *Blood*. 2025;146(Suppl 1):645

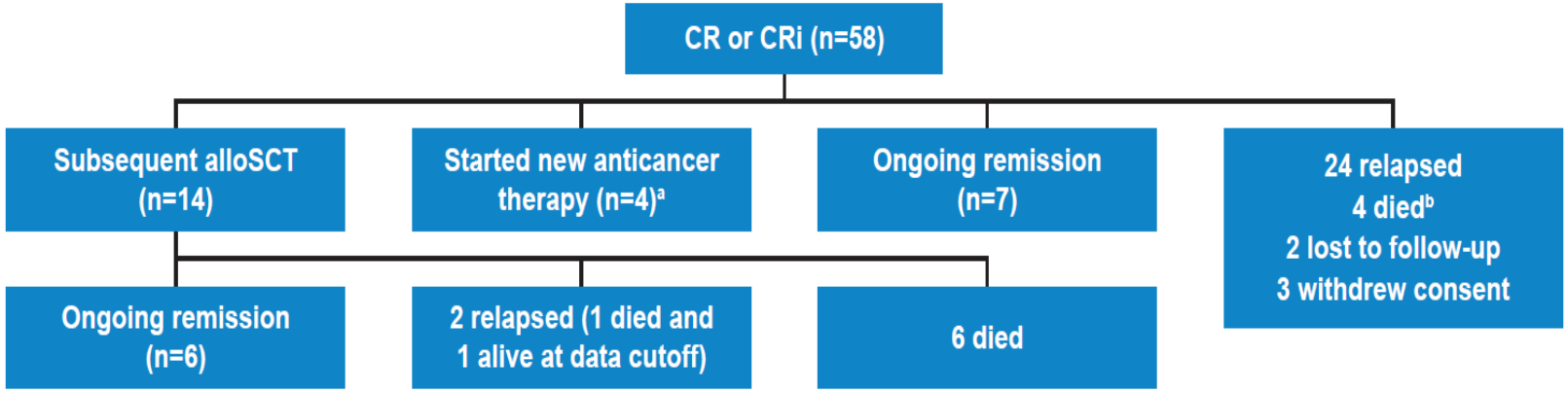
3-Year Update of Tisagenlecleucel in R/R ALL

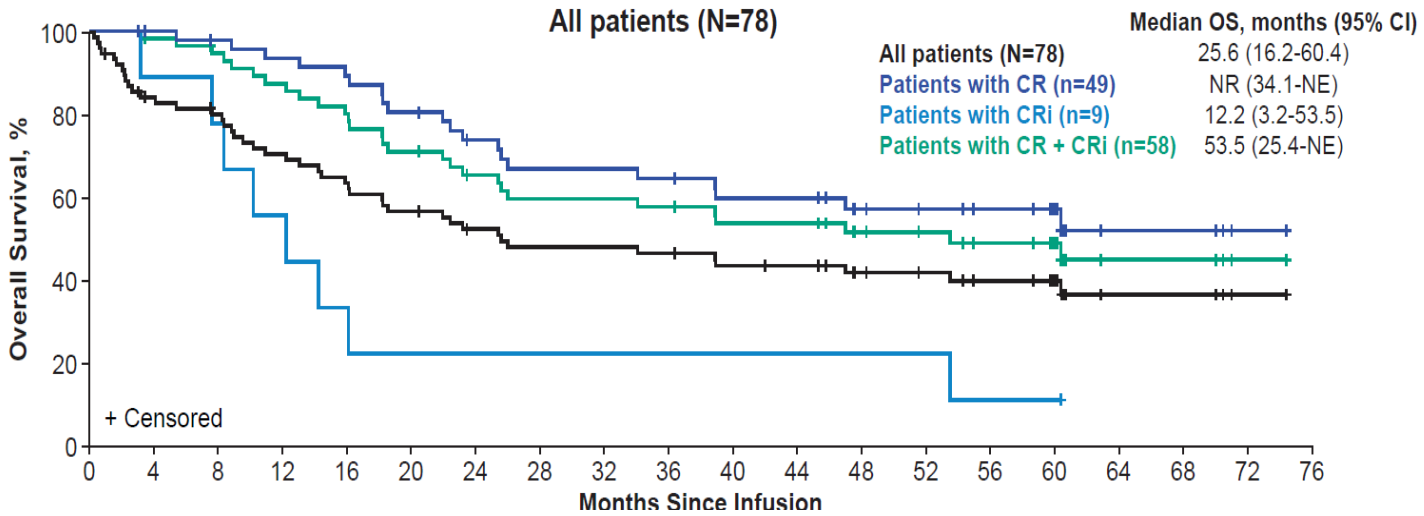
- 97 pts ≤26 yrs old enrolled
  - 79 (81%) received tisa
- Median age 11 yrs (3-24)
- Median prior Tx 3 (1-8)
- Marrow CR 66 = 82%
  - 66% of denominator
- Median F/U 38.8 mos
- 5-yr RFS 49% in pts in CR/CRi
- 3-yr EFS 44%; 3-yr OS 63%
- Grade 3/4 AE 29%



AE = adverse event.
Laetsch TW, et al. *J Clin Oncol*. 2023;41(9):1664-1669.

Zuma-3: 5-Year Follow-Up



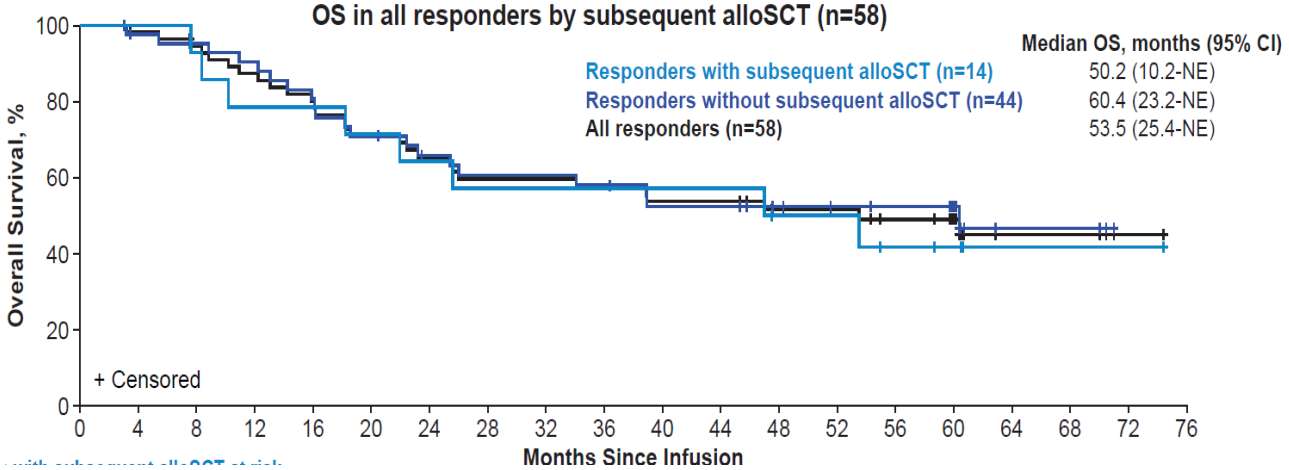


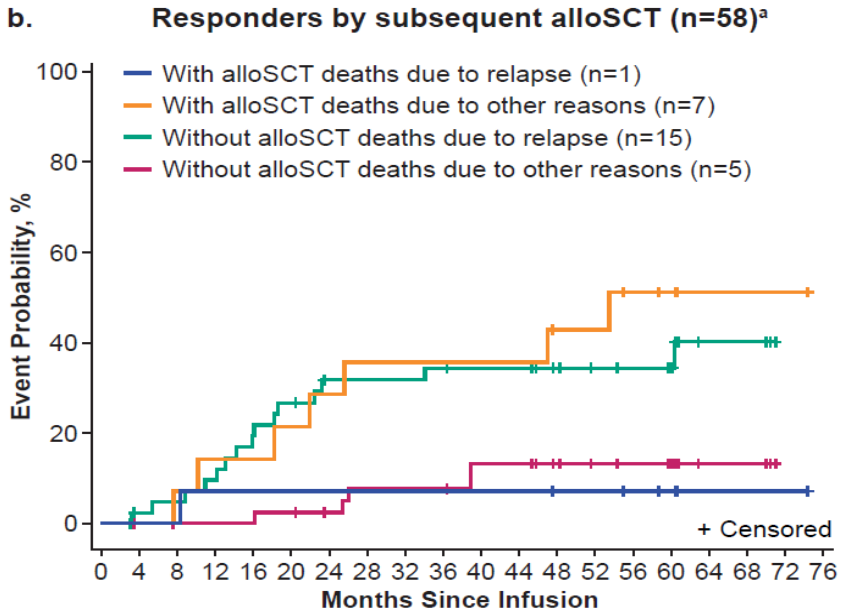
- 7 out of 58 (12%) patients are in ongoing remission at 5 years of follow-up
- No additional relapses noted between years 4 and 5 of extended follow-up
- OS remains unchanged at 40%, at 5 years

Oluwole OO, et al. Presented at: EHA Congress; 2025. Abstract PF374.

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Zuma-3: Role of AlloSCT post-CAR T





- Non-relapse mortality high in patients undergoing subsequent alloSCT, with a 5-year rate of 26%
- Death due to relapse post-alloSCT low compared with patients without alloSCT
- Without alloSCT, the main reason for death was relapse

Oluwole OO, et al. Presented at: EHA Congress; 2025. Abstract PF374.

KMT2Ar = 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-: 79% v 78%; median OS: 22 vs 21 mos

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

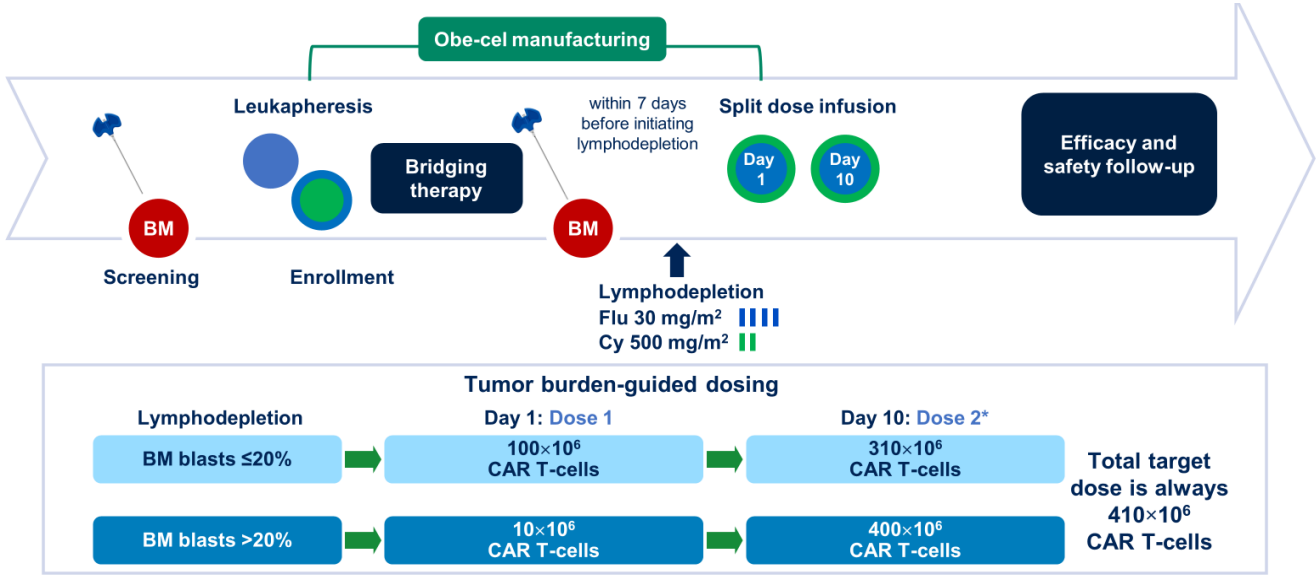
- *KMT2Ar* only subgroup with inferior OS (HR 3.17, 95% CI 1.53-6.58, *P*=0.02)

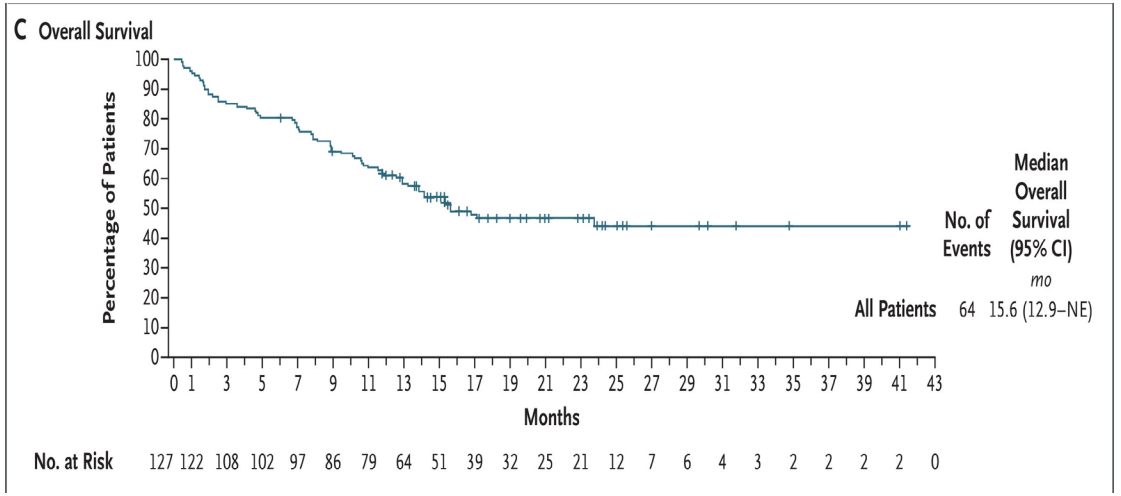
EMD = extramedullary disease.
Leonard J, et al. *Blood*. 2025;146(Suppl 1):3365.

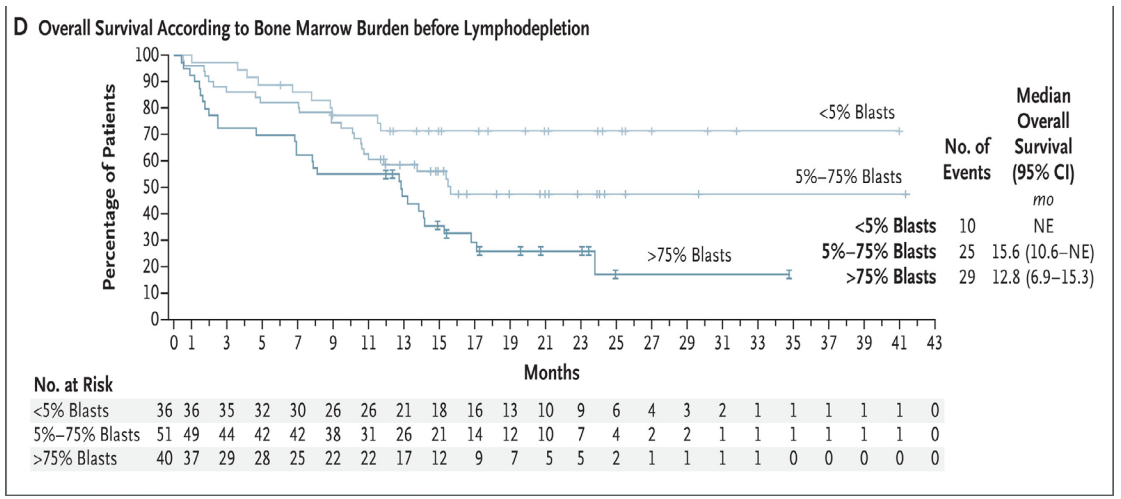
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Obecabtagene Autoleucel (OBE-CEL) in Adult R;R ALL (FELIX)

- AUTO 1 fast off-rate CD19 binder CAR T
- 153 enrolled, 127 (83%) infused. Median age 47 yrs.







- G3 CRS 2.5%; G3 ICANS 7.5%
- Prior blina 42%, ino 31%, alloSCT 44%
- cCR-CRi 99/127 = 78% (99/153 = 65%); 19/77 alloSCT
- Loss of CAR T = HR 2.9
- 12-mos EFS 49%, 12-mos OS 61%

cCR = clinical CR.

Jabbour E, et al. *J Clin Oncol*. 2024;42(16 Suppl):6504. Roddie C, et al. *N Engl J Med.* 2024;391(23):2219-2230.

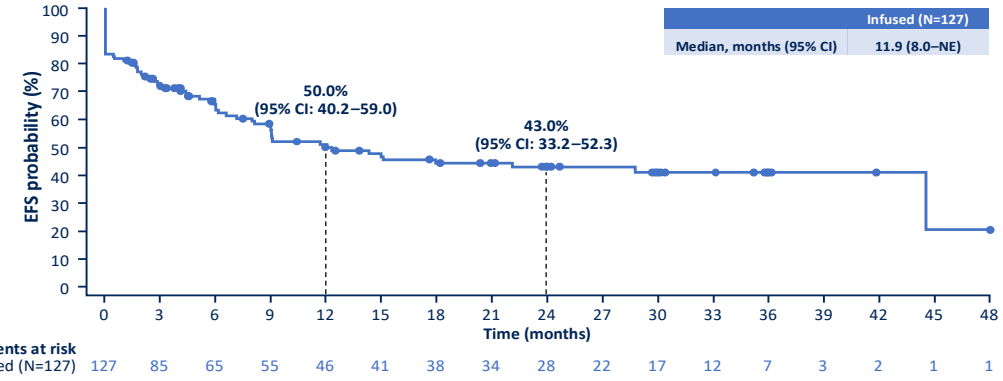
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OBE-CEL in Adult R/R ALL—(FELIX): Long-Term Follow-Up

- Median F/U 32.8 months
  - 2-yr DOR 54%; 2-yr EFS 43%; 2-yr OS 46%
- No CRS, no ICANS
- MVA for better remission rates
  - Ph+ disease
  - Earlier obe-cel use
  - Less refractory disease
- MVA for better survival
  - Lower disease burden at LD
  - Ongoing CAR T-cell persistence

Event-free survival, censoring for consolidative SCT

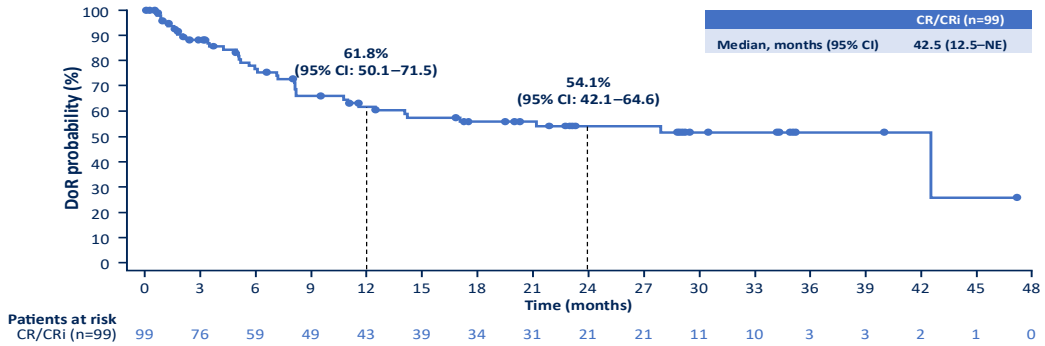
At 24 months, event-free survival probability was 43.0%



Current data cut: 18 Jan 2025; median follow up: 32.8 months (range: 19.952.8).
EFS censoring for non-protocol anti-cancer therapies including consolidative SCT with disease assessment by independent response review committee.
CI, confidence interval; EFS, event-free survival; M, months; NE, not estimable; SCT, stem cell transplant.

Duration of remission, censoring for consolidative SCT

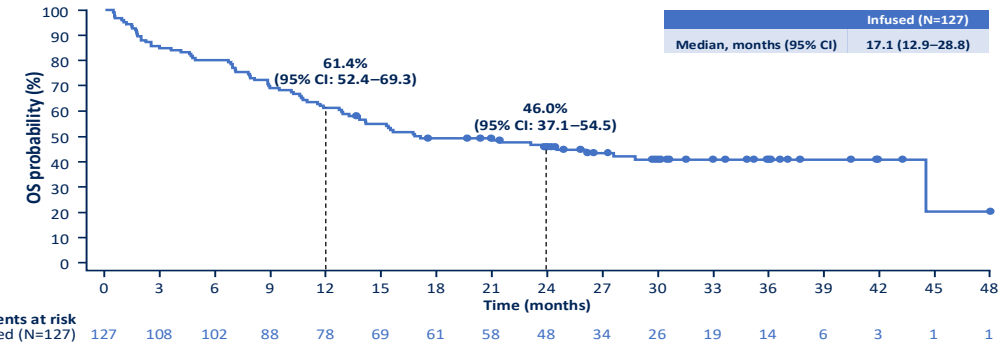
Probability of remaining in remission 24 months after onset was 54.1%



Current data cut: 18 Jan 2025; median follow up: 32.8 months (range: 19.952.8).
DoR censoring for non-protocol anti-cancer therapies including consolidative SCT with disease assessment by independent response review committee.
CI, confidence interval; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; DoR, duration of remission; NE, not estimable; SCT, stem cell transplant.

Overall survival, without censoring for consolidative SCT

At 24 months, overall survival probability was 46.0%



Current data cut: 18 Jan 2025; median follow up: 32.8 months (range: 19.952.8).
OS without censoring for consolidative SCT.
CI, confidence interval; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; OS, overall survival; SCT, stem cell transplant

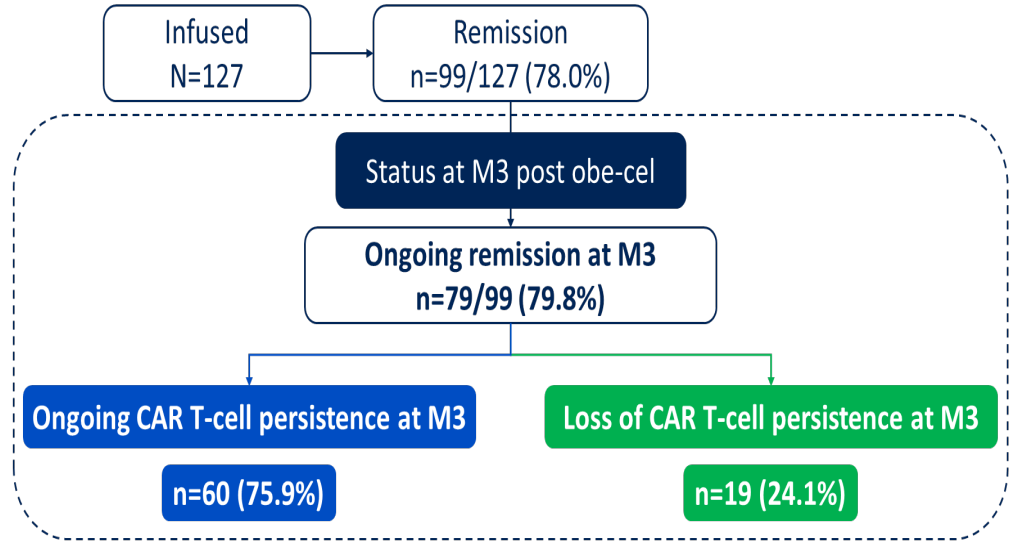
LD = lymphodepletion.

Jabbour E, et al. Presented at: 2026 Society of Hematologic Oncology (SOHO) Annual Meeting; 2026. Abstract ALL-706.

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OBE-CEL in Adults with R-R ALL: T-Cell Persistence at Month 3

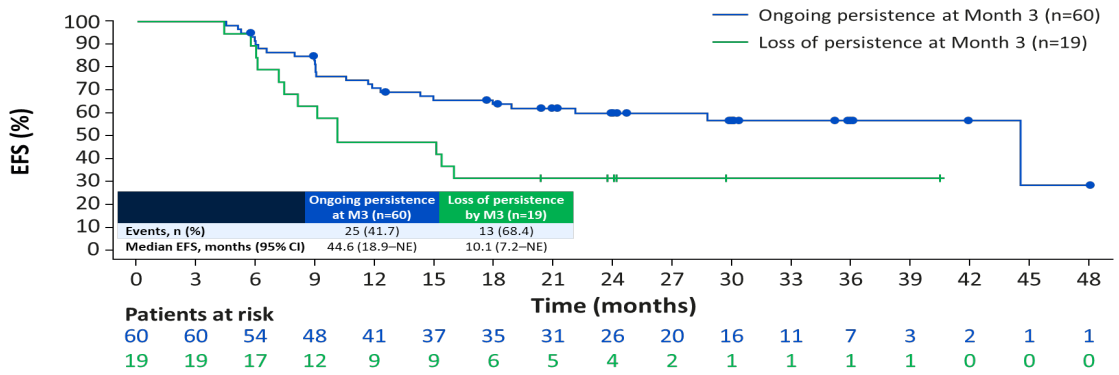
- 127 pts Rx; CR/CRi 78% (99/127)
- Median F/U 33 months; 2-yr OS 46% 2-yr EFS 43%
- M3: 80% (79/99) pts in ongoing CR/CRi; 76% (60/79) CAR T cell persistence
- T-cell persistence: median age 54 (20-81), 40% ≥3 prior Rx; 37% prior blina; 60% prior allo; median BM blast at LD 30%
- Median OS (T-cell persistence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

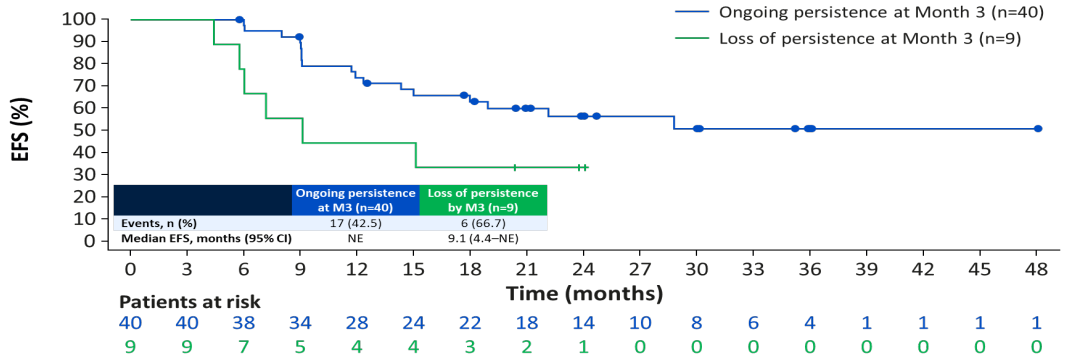
EFS by M3 persistence

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.

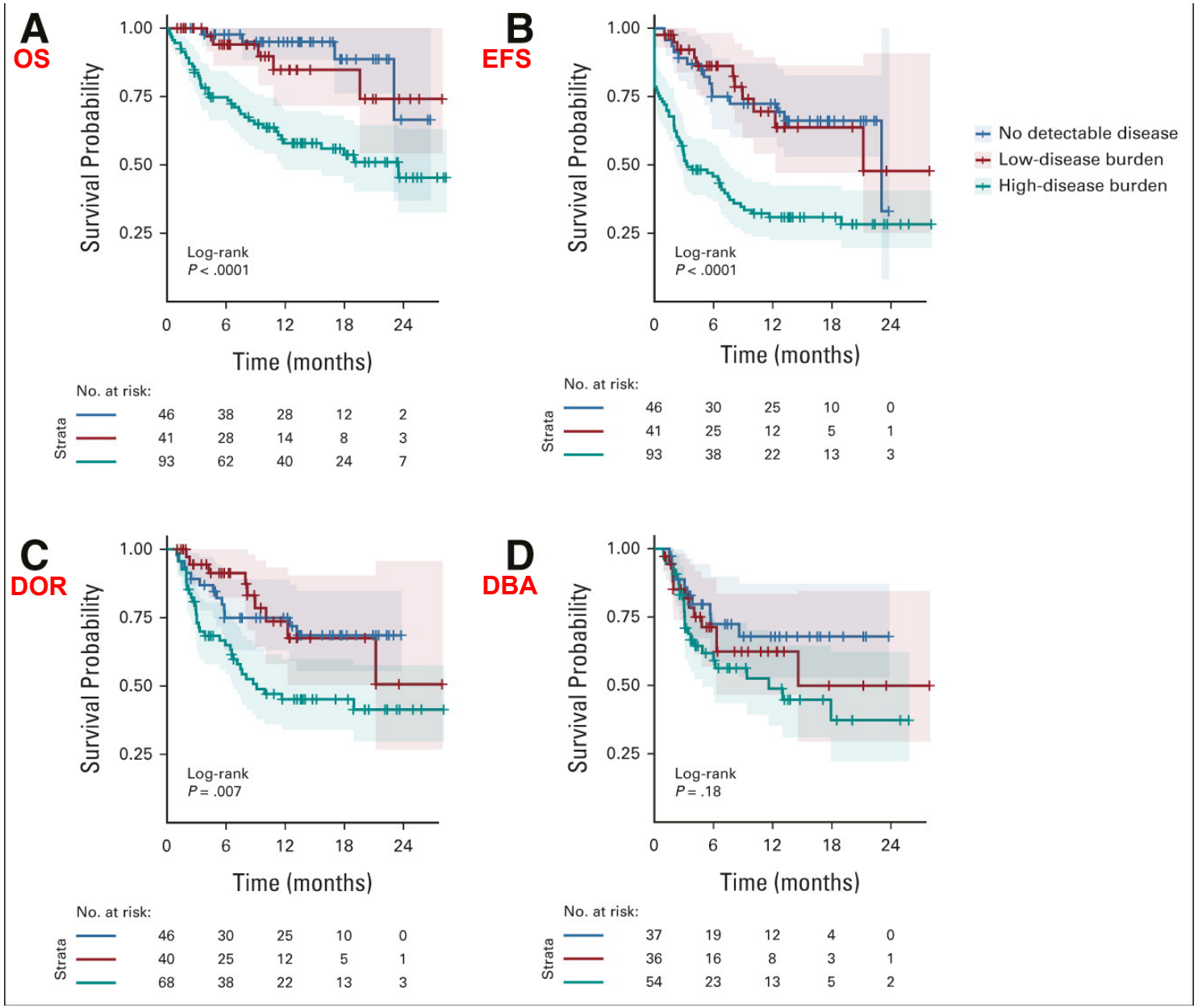


Roddie C, et al. *Blood*. 2025;146(Suppl 1):5118.

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Real-World CAR Consortium and Disease Burden

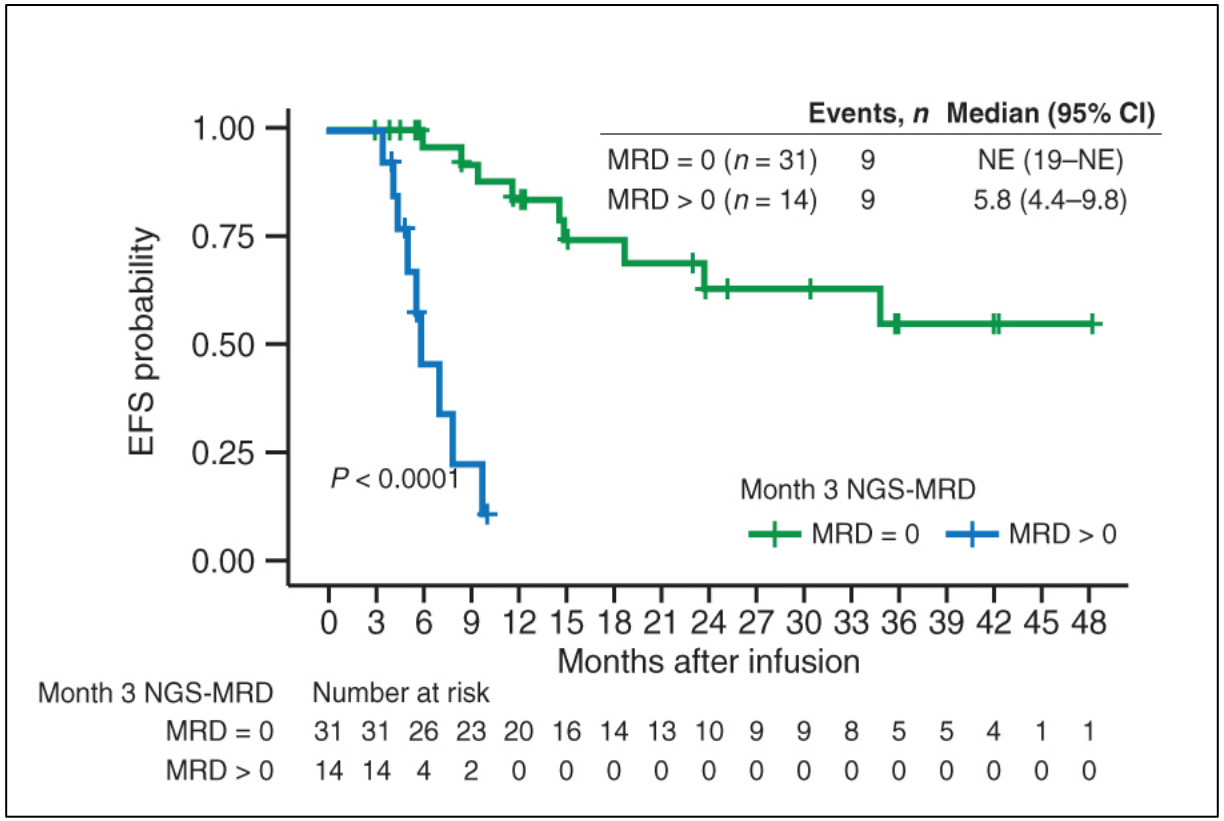
- 200 pts (185 pts infused); median age 12 yrs (0-26 yrs); CR = 85%
- HBD n=94 (47%); LBD n=60 (30%); ND n=46 (23%)
- 12-mos EFS = 50%, 12-mos OS = 72%
- G3 CRS = 21% (35% in HBD); G3 NE = 7% (9% in HBD)



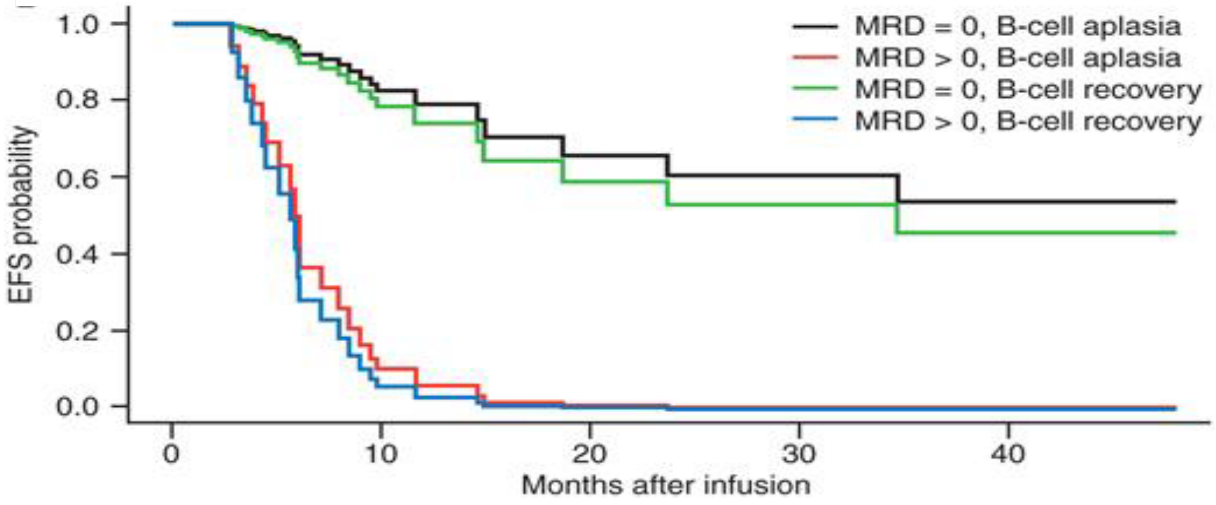
HBD = high-burden disease; LBD = low-burden disease; ND = no disease.
Schultz LM, et al. J Clin Oncol. 2022;40(9):945-955.

NGS MRD Negativity after CAR T-Cell Therapy for ALL

- Detectable MRD after tisagenlecleucel by NGS independently predicted for EFS and OS on multivariate analysis
- NGS MRD status at 3 months was superior to B-cell aplasia/recovery at predicting relapse/survival



	HR (95% CI)	P
Month 3 NGS-MRD status		
MRD = 0	—	—
MRD > 0	12.0 (2.87–50.0)	<0.001
B-cell recovery	1.27 (0.33–4.79)	0.7



Pulsipher MA, et al. *Blood Cancer Discov*. 2022;3(1):66-81.

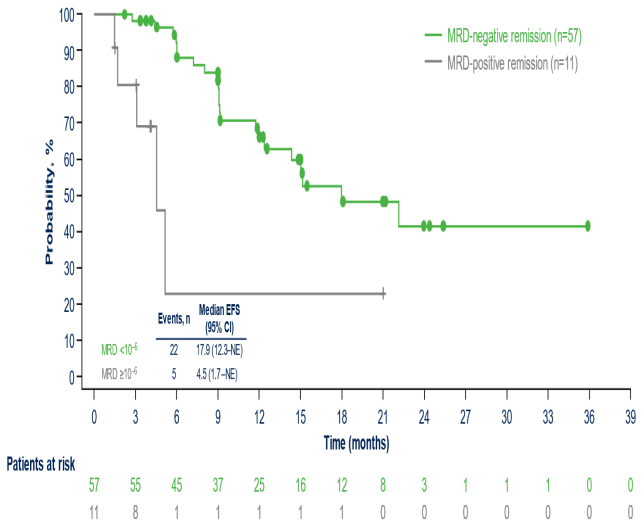
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Obecaptagene Autoleucel (OBE-CEL) in Adult R-R ALL (FELIX): Impact of MRD

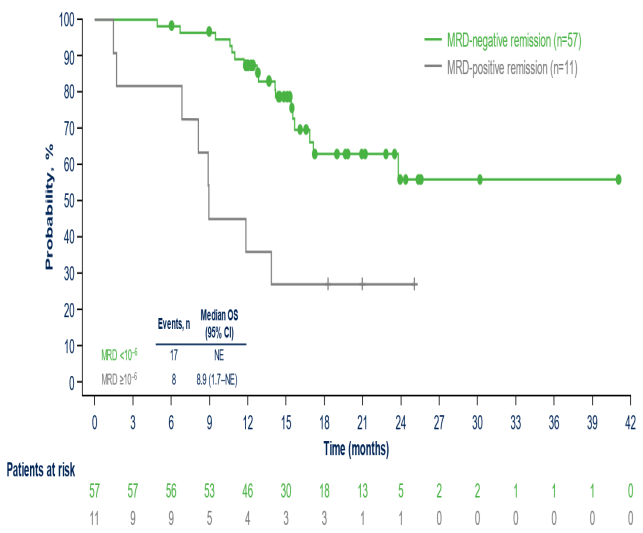
- 96/127 (76%) NGS calibration by NGS; 73/96 (76%) CR/CRi; 68/73 (93%) MRD assessment
- MRD-negative 68/73 (84%); median to MRD-negative 1 mo
- F/U 21.5 mos—70% MRD-neg CR alive

Parameter	% MRD-pos	% MRD-neg	% MRD-neg If <5% BL@ LD	% MRD-neg If ≥5%-≤75% BL@ LD	% MRD-neg If >75% BL@ LD
	16	84	90	87	72
Median EFS (mos)	4.5	18	NR	18	12
Median OS (mos)	9	NR	NR	NR	17

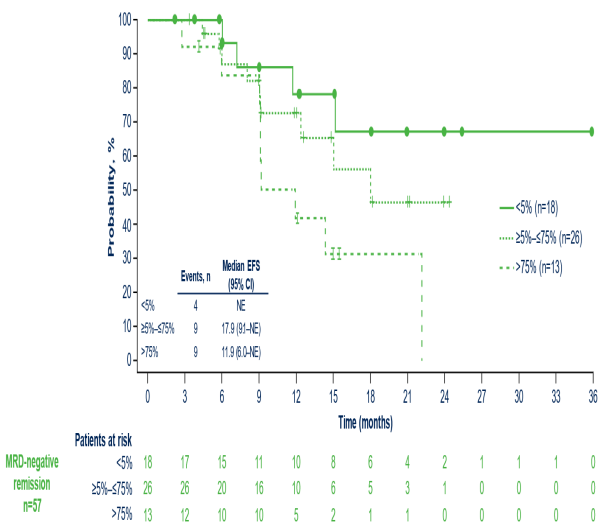
EFS by MRD status



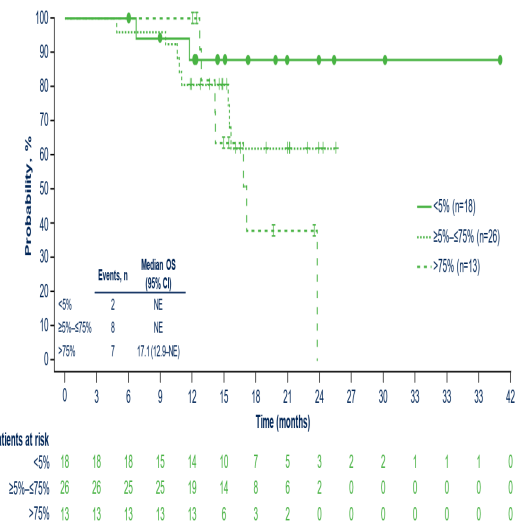
OS by MRD status



EFS in MRD- by Tumor Burden



OS in MRD- by Tumor Burden



Jabbour E, et al. *Blood*. 2024;144(Suppl 1):963.

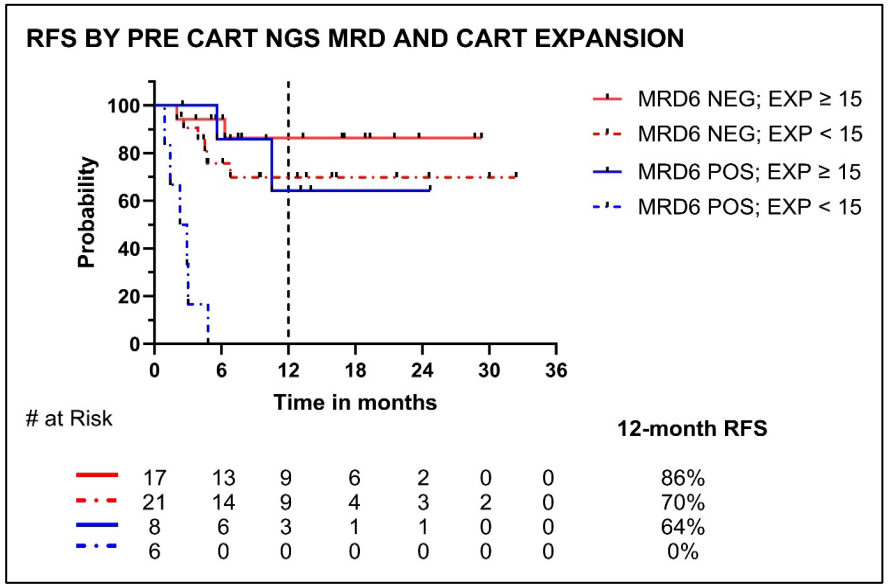
CD19 CAR T-Cell (Tisa-cel) Rx for CNS Relapse

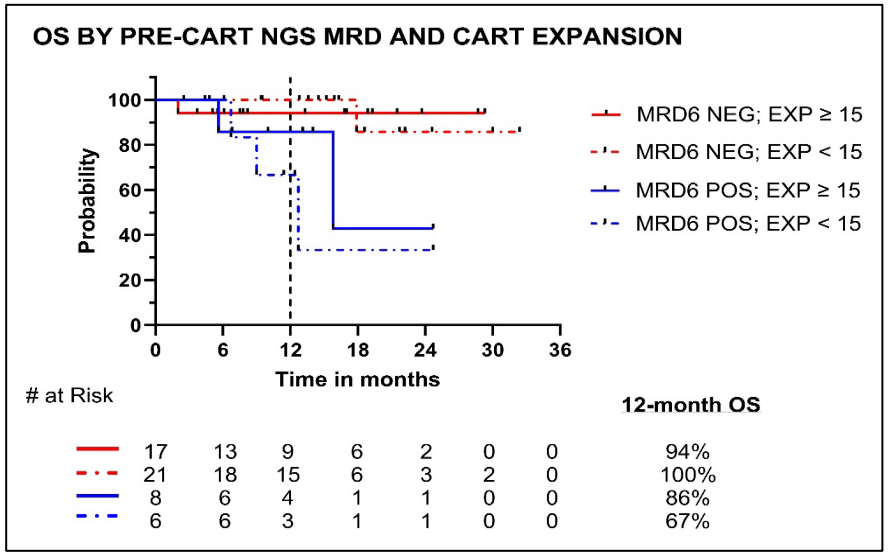
- 43 pts Rx; median age 8 yrs (1-26); 91% first CNS relapse; 84% isolated CNS
- No cranial XRT for this relapse; flu/cy LD; dose 5×10^6 CART19 cells/kg
- @ infusion: 14% BM disease, 19% CNS2, 5% CNS by imaging, no CNS3
- Day 28 CNS remission 98%; best overall response 100%; all MRD-negative
- Median F/U 12 mos: 1-yr and 2-yr EFS 90%; 1-yr and 2-yr OS 100% and 90%
- 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.

LD = low-dose; CSF = cerebrospinal fluid.
DiNofia A, et al. *Blood*. 2025;146(Suppl 1):648.

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Brexu-cel as Consolidation Rx in B-ALL: Peak CART Expansion ≥15 Cells/µL and MRD Status





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

Pre CAR T BM MRD6 NEG n=38

- Peak CART expansion ≥15 (n=17) → Relapse 1/17 (6%)
- Peak CART expansion <15 (n=21) → Relapse 6/21 (29%)

Pre CAR T BM MRD6 POS n=14

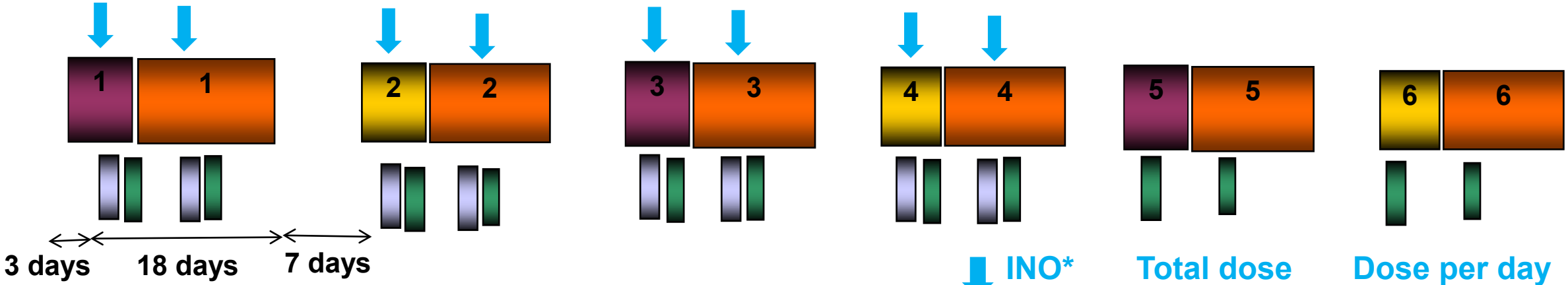
- Peak CART expansion ≥15 (n=8) → Relapse 1/8 (13%)
- Peak CART expansion <15 (n=6) → Relapse 6/6 (100%)

Khaire N, et al. *J Clin Oncol*. 2025;43(16 Suppl):6543.

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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-Hyper-CVD
- Mini-MTX-Ara-C
- Rituximab
- IT MTX, Ara-C
- Blinatumomab

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Thank You

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The University of Texas MD Anderson Cancer Center Houston, TX
Email: ejabbour@mdanderson.org
Cell: 001.713.498.2929

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Four Cases, Four Decisions, from the Data to the Bedside

Alexandra Gomez-Arteaga, MD

Director, Allogeneic BMT Service
Weill Cornell Medicine/NewYork-Presbyterian
New York City, New York

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From the Data to the Bedside: Four Cases, Four Pillars to Improve Outcomes for ALL

1

Access to curative-intent therapy

How do we bring curative-intent therapy closer to home, with academic/subspecialized-center partnership?

2

Safety by design

How are new therapies lowering toxicity?

3

Ready-to-treat pathway

How do we time the CAR T collection and treat on time?

4

Sequencing after CAR T

After CAR T: transplant, or hold and monitor?

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Pillar 1 · How can we promote access to curative-intent therapy?

A Curable Relapse, Three Hours from the Nearest CAR T/BMT Center

AT PRESENTATION

- 34 years old, works full time, primary caregiver at home
- Ph-negative B-ALL, first relapse 14 months after frontline
- Received 2 prior cycles of blinatumomab, then on maintenance
- Fit and motivated; an excellent candidate for curative-intent therapy
- Lives about 3 hours from the nearest CAR T or transplant program
- CD19 expression is preserved
- Salvage options include: chemotherapy backbone+/-venetoclax, inotuzumab/blinatumomab,
  CAR T ----------> alloHCT?

THE ACCESS BARRIER

- Curative options have meant transfer and inpatient admission
- Weeks away from home, work, and caregiving
- Requires a caregiver to travel and stay
- Expertise is needed for toxicity monitoring and complication management
- Any delay risks losing the window in a fast-moving relapse

BMT = bone marrow transplant.

Gökbuget N, et al. *Haematologica*. 2016;101(12):1524-1533. Fielding AK, et al. *Blood*. 2007;109(3):944-50. Arora S, et al. *Blood* 2025;146(Suppl 1):759.

The Access Gap Is Real, and 2025 Began to Close It

Two forces converge: a documented distance barrier, and a regulatory change that improves access to deliver CAR T.

Goal: minimize the burden on healthcare delivery system

~40% lower

CAR T use for patients 2 to 4 hours from a center vs within 30 minutes

June 2025

FDA removed the REMS for all approved CD19 and BCMA CAR T

Changed

The 2-hour-proximity (4 weeks) and no-driving (8 weeks) requirements

What changed: labeling update included revision to language to monitor patients for at least two weeks including daily monitoring for at least one week; to instruct patients to remain within proximity of a healthcare facility for at least two weeks; and to advise patients to avoid driving for two weeks following product administration

Ahmed N, et al. *Transplant Cell Ther*. 2024;30(7):714-725. US Food and Drug Administration (FDA) [www.fda.gov]. Last updated June 26, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor.

Setting the Stage: The Outpatient T-Cell-Engager Landscape

Platform	Status	Delivery	Community angle
Blinatumomab (IV)	Approved, including frontline	28-day continuous IV (pump); front-loaded inpatient	Established outpatient after the early monitoring window
Blinatumomab (SC)	Investigational/emerging	Subcutaneous injection, no pump	Simpler outpatient logistics
Surovatamig (AZD0486)	Investigational	2-hour IV, step-up then every 2 weeks	Off-the-shelf; active after prior CD19 therapy
MK-1045 / CN201	Investigational	Weekly IV, step-up dosing (no pump)	Off-the-shelf; another half-life-extended CD19×CD3 engager

Note: CAR-T products (tisagenlecleucel, brexucabtagene, obecabtagene) are addressed in Pillars 3 and 4.

The frontline consequence: blinatumomab is now used up front, even in MRD-negative disease. Most patients are therefore CD19-exposed before relapse, so relapse therapy increasingly must work after prior CD19 exposure.

Frontline blinatumomab: Litzow MR, et al. *N Engl J Med*. 2024;391(4):320-333. SC blinatumomab: Jabbour E, et al. *Lancet Haematol.* 2025;12(7):e529-e541. MK-1045/CN201: Wang Y, et al. *Blood*. 2025;146(Suppl 1):647.

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Pillar 2 · Safety by design

Choosing a Low-Toxicity Platform for a Patient Who Cannot Be Inpatient or Cannot Tolerate High-Grade CRS/ICANS

AT PRESENTATION

- 65 years old, R/R B-ALL after frontline
- Mild chronic kidney disease and prior cardiac disease
- A poor candidate for high-grade CRS or ICANS
- Limited caregiver support, wants to limit the need for extended care outside the community

THE DESIGN QUESTION

- Can we redirect T cells with toxicity low enough for an infusion center?
  - Available: IV or subcutaneous blinatumomab, inotuzumab
  - Investigational: a low-affinity CD3 × CD19 engager (surovatamig)
  - Investigational: MK-1045/CN201
  - Can he tolerate CAR T therapy?

Options span approved (blinatumomab) and investigational (surovatamig) engagers.

How Three Designs Lower Toxicity: Low-Affinity CD3, Fast-Off CD19, Step-Up Dosing

Toxicity is engineered down in three different ways.

- **Low-affinity CD3 binding (surovatamig).** Engages T cells while limiting excessive cytokine release, which lowers CRS.
- **Fast-off CD19 CAR (obe-cel).** The binding arm (an intermediate-affinity scFv) releases CD19 quickly. The T cell engages the target briefly, then lets go. Less sustained signaling means it is activated less intensely (lower CRS and ICANS) and exhausted less (better expansion and persistence).
- **Step-up dosing plus steroid premedication or chemotherapy.** Blunts the first-exposure cytokine surge.
- The common thread: lower the toxicity ceiling by construction.

- ***Same engager class:*** *surovatamig and MK-1045/CN201 are both half-life-extended CD19×CD3 engagers (weekly-to-biweekly IV, no pump); surovatamig adds the low-affinity CD3 design above.*

scFv = single-chain variable fragment.

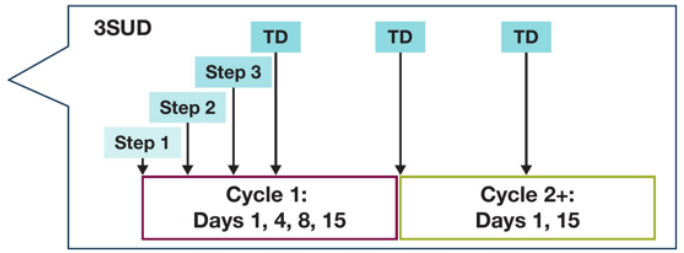
Fast-off design: Ghorashian S, et al. *Nat Med*. 2019;25(9):1408-1414. Roddie C, et al. *N Engl J Med*. 2024;391(23):2219-2230. Low-affinity CD3: Aldoss I, et al. *Blood*. 2025;145(Suppl 1):3345. CD19×CD3 engager class: Wang M, et al. *Blood.* 2025;146(Suppl 1):647.

Surovatamig Is Engineered for Intermittent, Pump-Free Dosing

A fully human IgG4 CD19 × CD3 engager with **low-affinity CD3** and a silenced Fc (half-life about 12 to 15 days); triple step-up on cycle 1 (D1, D4, D8), target dose at D15, then IV every 2 weeks.

Treatment Schedule – 28-day Cycles

- **Triple step-up dosing (3SUD): Surovatamig (2h IV infusion) on first cycle: C1D1, C1D4, and C1D8**
  - SUD-Low (SUD-L): 0.09 mg, 0.27 mg, and 1.0 mg – DL1 & DL3a
  - SUD-High (SUD-H): 0.27 mg, 1.0 mg, and 2.4 mg – DL2 & DL3
- **Target doses (C1D15): DL1: 2.4 mg; DL2: 7.2 mg; DL3/DL3a: 15 mg**
  - Cycles 2+: administered every 2 weeks (D1 and D15)
- Patients with high tumor burden (>50% BM blasts or >15,000/mL PB) received dexamethasone (10–24 mg/d) 4–7 days ± 1 dose of vincristine 2 mg prior to D1

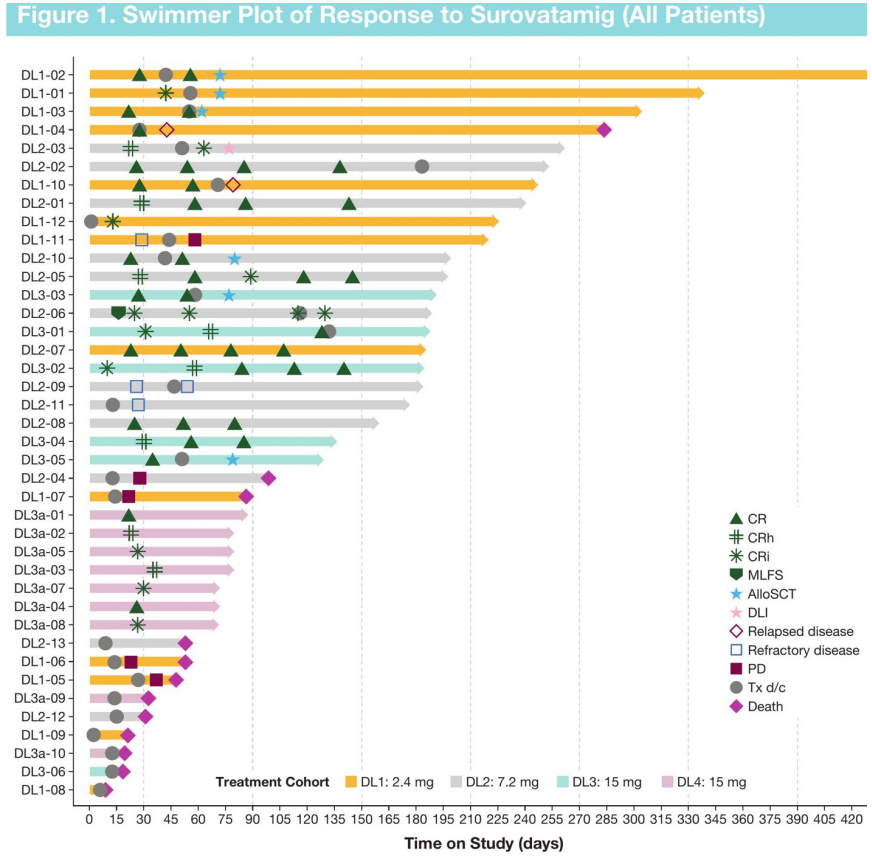


[a]Dose escalation followed mTPI-2 criteria and were based on efficacy and predefined rule-based criteria including incidence of grade 2+ CRS or ICANS and/or grade 2+ AEs.
[b]Backfill slots into the SRC-declared safe dose levels may open at SRC approval.

High-tumor-burden patients receive dexamethasone (with vincristine) before the first dose to blunt early cytokine release.

Surovatamig is investigational and not FDA-approved.
Aldoss I, et al. Presented at: 67th American Society of Hematology (ASH) Annual Meeting & Exposition; 2025. Abstract 3345.

Surovatamig Efficacy Concentrates at the 15 mg Dose

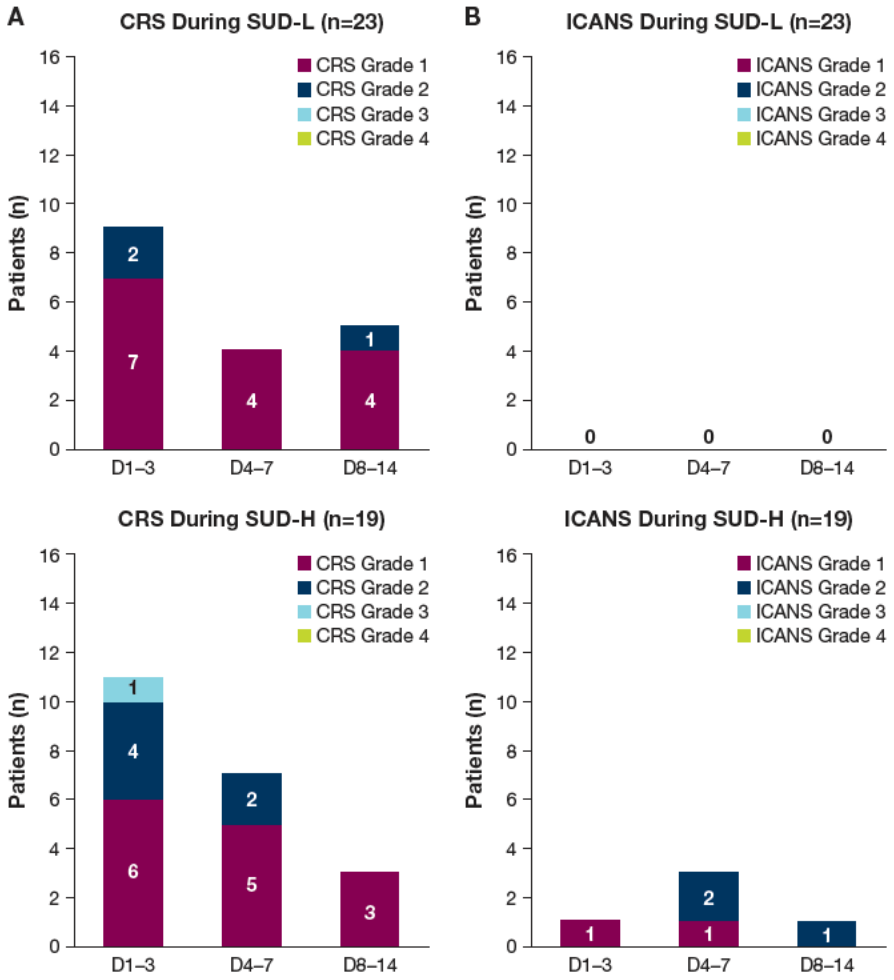


Response rate by target dose

- 2.4 mg 54%, 7.2 mg 58%, 15 mg 82%
- MRD-negative among responders (NGS): 92% at 10^{-4}, 60% at 10^{-6}
- Median duration of response not reached; no relapses so far in the 12 MRD-negative patients
- Activity retained after prior CD19 therapy (15 mg)
  - Prior blina 7/9 (ORR 78%), prior CAR T 8/11 (ORR 73%)

Figure 1 (swimmer plot) reproduced from the SYRUS ASH 2025 poster.
MLFS = morphologic leukemia-free state; PD = progressive disease; d/c = discontinued.
Aldoss I, et al. Presented at: 67th ASH Annual Meeting & Exposition; 2025. Abstract 3345.

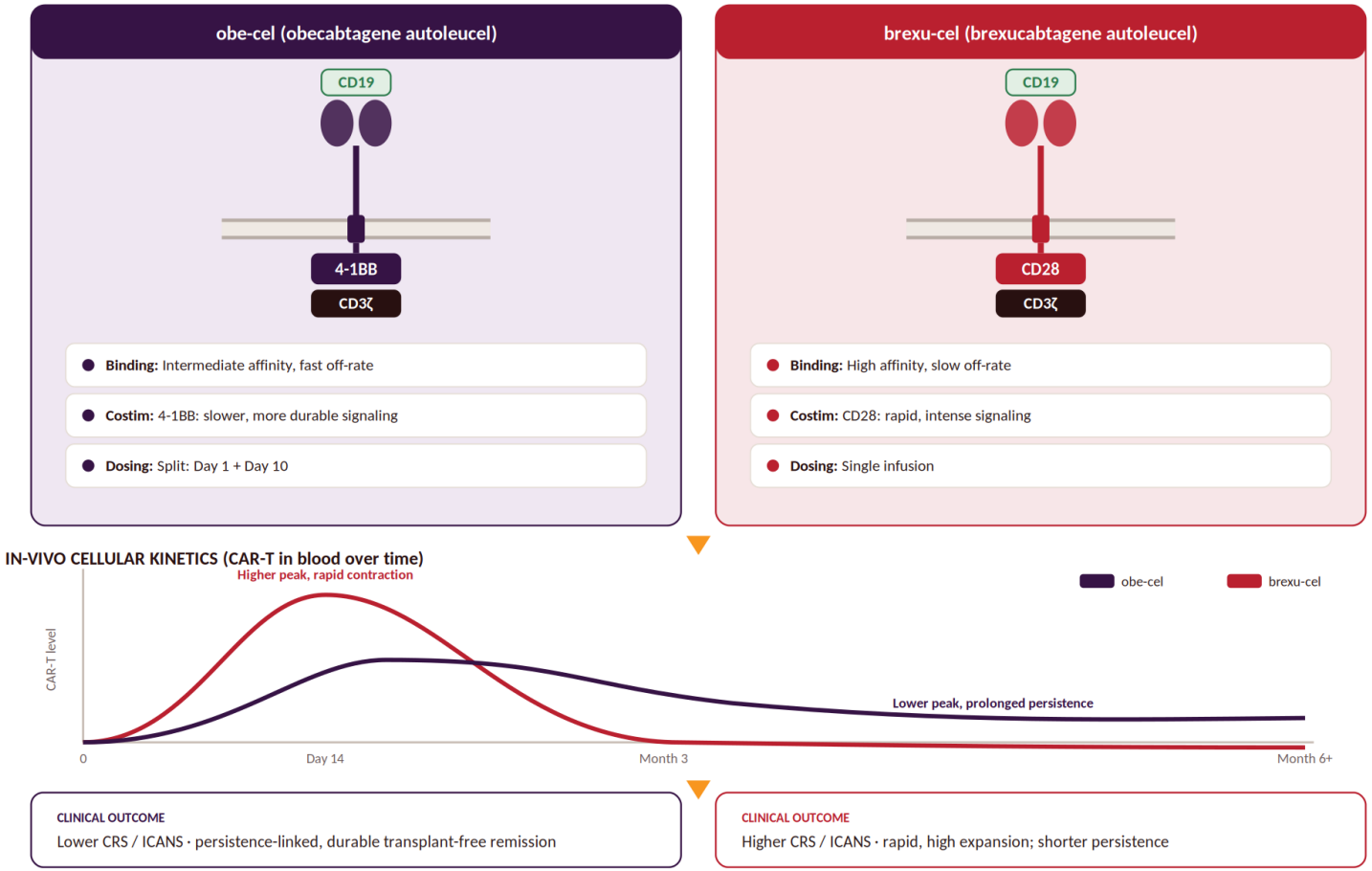
Surovatamig Safety: CRS and ICANS Cluster at Step-Up, then Settle



- CRS any grade 71%, grade ≥3 only 2% (1 patient)
- ICANS any grade 17%, mostly grade 1
- Events cluster during the step-up doses and then resolve
- **Low step-up regimen:** no grade ≥2 CRS observed
- After the target dose: no grade ≥3 CRS, and a single grade ≥3 ICANS
- Practical read: monitor intensively through step-up, then the every-2-week maintenance is low-acuity

Figure 3 (CRS/ICANS during step-up) reproduced from the poster.
Aldoss I, et al. Presented at: 67th ASH Annual Meeting & Exposition; 2025. Abstract 3345.

From Bispecifics to CAR T: Why Obe-Cel and Brexu-Cel Differ: Design, Kinetics, and Outcomes



Kinetics schematic is illustrative (created using Claude large language models).

Ghorashian S, et al. *Nat Med*. 2019;25(9):1408-1414. Roddie C, et al. *N Engl J Med*. 2024;391(23):2219-2230.

From Bispecifics to CAR T: Real-World Toxicity Favors the Fast-Off Design

Independent registry data show construct design translates into far less toxicity, at equal efficacy.

	Obe-cel 36 infused patients	Brexu-cel 53 infused
Any-grade CRS	**56%**	94%
Grade ≥3 CRS	**0%**	6%
Any-grade ICANS	**17%**	51%
Grade ≥3 ICANS	**6%**	32%
MRD-negative CR at day 28	**81%**	80%

Same efficacy, a fraction of the toxicity

- Brexu-cel real-world burden is high (CRS 83%, ICANS 61%), a largely inpatient profile
- Obe-cel's lower toxicity profile is what makes outpatient delivery realistic. More and more centers are implementing a hybrid model, and some have started to offer fully outpatient.

Valtis Y, et al. *Blood*. 2025;146(Suppl 1):2715. Roloff G, et al. *J Clin Oncol*. 2023;41(16 Suppl):7001. Leonard J, et al. *Blood*. 2025;146(Suppl 1):3365.

Toward Faster Community Monitoring, with Expertise Still Leading up Front

Move care closer to home once the risk window has passed, not before.

- Specialized care leads up front: the step-up window (engagers) or the first 2 weeks (CAR T) need experienced monitoring
- The goal is a faster, safe transition to community monitoring after that window, not skipping it
- Maintenance (every-2-week engager) or steady-state CAR T follow-up is low-acuity and outpatient-deliverable
- This will evolve as outpatient experience and real-world data grow; more of the pathway can shift closer to home

Applies across approved and investigational low-toxicity platforms.

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Pillar 3 · Ready-to-treat pathway

Bridging a High-Burden Relapse to CAR T

AT PRESENTATION

- 46 years old, R/R B-ALL, about 60% marrow blasts at relapse
- Rapidly proliferative disease, symptomatic, needs control now
- Planned for obe-cel—how do we coordinate?

THE BRIDGING PROBLEM

- A relapse this explosive cannot simply wait for manufacturing
- Cytotoxic bridging can compromise the very T cells we need to collect
- Goals: Efforts should be made to reduce peripheral blast count while preserving circulating lymphocytes before apheresis to optimize successful CAR T-cell manufacturing
- Goals: control disease and drive toward MRD-negativity before lymphodepletion
- Lower disease burden at lymphodepletion predicts better CAR T outcomes

Roddie C, et al. *N Engl J Med*. 2024;391(23):2219-2230. Schultz LM, et al. *J Clin Oncol*. 2022;40(9):945-955. Muffly L, et al. *Blood*. 2026;148(6):657-668.

Timing the Lymphocyte Collection Is Hard, Even at an Academic Center

Apheresis to collect T cells (leukapheresis) for manufacturing is the step that quietly decides whether CAR T is feasible.

- Explosive disease rarely lets you collect first; patients need something before apheresis
- Collection needs authorization, a scheduled apheresis slot (not a weekend), and adequate T-cell fitness
- The usual sequence: quick control (steroids plus active therapy), then collect, then bridge, then lymphodeplete, then infuse
- In ALL, protect T-cell fitness: hold immunosuppression and limit lymphotoxic agents

In the community, this work is only possible with an early academic center partnership to start and coordinate the process.

Washout and product logistics on the next two slides.

Getting Collection-Ready: What to Hold before Leukapheresis

Agent	Hold before apheresis
Systemic corticosteroids	About 7 days (over 10 mg prednisone or equivalent)
Blinatumomab	1 to 2 weeks
TKIs (Ph+)	Nilotinib about 5 days; imatinib, dasatinib, ponatinib about 14 days
Venetoclax	About 1 week (general 2-week or 5-half-life rule)
Immunosuppression (prior transplant)	Tacrolimus at least 2 weeks (anti-T cell effect)
General rule	2 weeks or 5 half-lives, whichever is shorter

Muffly L, et al. *Blood*. 2026;148(6):657-668. Clinicians' guide to obecabtagene autoleucel CAR T-cell therapy process. Tisagenlecleucel clinical guideline.

Per-Product Logistics: Manufacturing Time and Time to Infusion

	Tisa-cel (peds/AYA ≤ 25)	Brexu-cel (adult)	Obe-cel (adult)
Manufacturing turnaround	About 3 to 4 weeks	Median 16 days (92% success)	Median 3-3.5 weeks (96% at target dose)
Lymphodepletion	Flu 30 ×4 + cy 500 ×2	Flu 25 ×3 (d-4 to -2) + cy 900 ×1 (d-2)	Flu 30 ×4 + cy 500 ×2
Lymphodepletion to infusion	2 to 14 days after LD	Rest d-1, infuse d0	3 days (±1) after LD; at least 48-hour washout
Dosing	Single infusion	Single infusion	Split: day 1 + day 10, tumor-burden-guided

×N means days.

Obecabtagene autoleucel prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated February 2026. https://www.fda.gov/media/183463/download. Brexucabtagene autoleucel prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated April 2026. https://www.fda.gov/media/140409/download. Tisagenlecleucel prescribing information. Drugs@FDA: FDA-Approved Drugs. Last updated June 2025. https://www.fda.gov/media/107296/download. Merges M, et al. *Blood*. 2023;142(Suppl 1):4892. Shah BD, et al. *Leukemia*. 2025;39(5):1058-1068.

Delivering CAR T Outpatient: The ASTCT Framework

An expert panel has already mapped how to run CAR T safely outside the inpatient ward.

- Patient selection: performance status, disease burden, comorbidity, and social support up front
- A committed caregiver and lodging within a defined radius for the monitoring window
- Structured daily assessment with clear CRS and ICANS escalation and admission triggers
- 24/7 access to an experienced cell-therapy team; the community and academic co-management model

Fast-off and low-toxicity constructs make more patients eligible for this pathway.

Oluwole OO, et al. *Transplant Cell Ther*. 2024;30(2):131-142.

A Curative Pathway to CAR T, Co-Managed with the Community

1. **Refer early**
   Partner before you need to collect
2. **Collect**
   Authorize, schedule, protect T-cell fitness
3. **Bridge**
   Towards MRD-
4. **Lymphodeplete**
   Product-specific regimen and timing
5. **Monitor near the center**
   Initial monitoring close to the treatment center, in partnership with community practice
6. **Consolidate if needed**
   Further therapy, alloHCT if indicated

Berry DA, et al. *JAMA Oncol*. 2017;3(7):e170580.

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After CAR T: transplant, or hold and monitor?

Pillar 4 · Sequencing after CAR T

After CAR T: Should We Consolidate with Allogeneic Transplant?

AT PRESENTATION

- 60 years old, good performance status, transplant-eligible
- Received obe-cel for R/R B-ALL
- Month 3: NGS-MRD-negative complete remission
- CAR T cells still detectable (ongoing persistence)

THE DECISION

- Consolidate now with allogeneic transplant, or hold and monitor?
- FELIX 3-year predictors favor durable, transplant-free remission here
- The decision depends on prior transplant status and CAR T persistence
- Monitoring strategy depends on which construct the patient received

Roddie C, et al. *Blood*. 2025;146(Suppl 1):5118. Shah BD, et al. *Leukemia*. 2025;39(5):1058-1068. Faramand RG, et al. *Transplant Cell Ther*. 2026 Jun 27:S2666-6367(26)00516-6 [Epub ahead of print].

Consolidative Allogeneic Transplant after CAR T: For Whom?

The evidence comes from different products and study types, and it is evolving.

OBE-CEL · FELIX (trial)

Supports holding transplant in good responders

- 70 of 79 month-3 responders (89%) did NOT receive
- Ongoing CAR T persistence at month 3 predicts better outcome
  - **2-yr OS 69% vs 53%; 2-yr EFS 60% vs 32% (persistence vs loss)**

BREXU-CEL

Trial (ZUMA-3): no OS benefit from consolidative alloSCT

Responder median OS 60.4 mo (no alloSCT) vs 36.3 mo (alloSCT)

Real world (ROCCA): benefit depends on prior transplant status

- Transplant-naïve (n=37): consolidation → 1-yr EFS 63%, OS 74%; low GVHD/NRM
- Prior allo (n=7): second transplant → all deaths were non-relapse mortality, not relapse

Individualize the decision: a persisting, MRD-negative responder can reasonably hold; a transplant-naïve responder may gain relapse-free survival from consolidative allo-HCT; with a prior transplant, a second one mainly adds non-relapse mortality.

Roddie C, et al. *Blood*. 2025;146(Suppl 1):5118. Shah BD, et al. *Leukemia*. 2025;39(5):1058-1068. Faramand RG, et al. *Transplant Cell Ther.* 2026 Jun 27:S2666-6367(26)00516-6 [Epub ahead of print]. Logan A, et al. *Blood*. 2025;146(Suppl 1):516.

Persistence, B-Cell Aplasia, and Time to Relapse

TISA-CEL: LONG PERSISTENCE

B-cell aplasia is a usable surrogate

- Aplasia persists 71% at 12 months, 59% at 24 months (median 35.3 months)
- Early B-cell recovery predicts CD19-positive relapse: 75 to 88% if recovery within 63 days

BREXU-CEL/OBE-CEL: FAST-OFF

B-cell recovery does not mean imminent relapse

- ZUMA-3: early B-cell recovery (7 of 8 by 6 months) with remission maintained. Persistence not required.
- Obe-cel: month-3 persistence still tracks with better outcome, but aplasia alone is a weaker readout

Bottom line: NGS-MRD at day 28 and month 3 outperforms B-cell aplasia (HR 12 vs 4.5). Combine both and tailor monitoring to the construct.

Pulsipher MA, et al. *Blood Cancer Discov*. 2022;3(1):66-81. Laetsch T, et al. *J Clin Oncol*. 2023;41(9):1664-1669. Shah BD, et al. *Leukemia*. 2025;39(5):1058-1068.

If It Comes Back CD19-Positive: Options and the Horizon

Prior CD19 exposure is not the same as CD19 resistance.

- Confirm the antigen first: a CD19-positive post-CAR T relapse can still respond to another CD19 platform
- Approved options: chemotherapy backbone ± venetoclax, inotuzumab, blinatumomab (IV/SC)
- Investigational: surovatamig after prior CD19 therapy (15 mg), prior blina 78%, prior CAR T 73%, triple-exposed 86% (small numbers), other clinical trials
- CD19-negative relapse is a different problem

Horizon: dual-antigen (CD19/CD22) targeting, CD19-negative strategies

Aldoss I, et al. Presented at: 67th ASH Annual Meeting & Exposition; 2025. Abstract 3345.

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The Outpatient ALL Blueprint

1

Access

Bring curative-intent therapy closer to home

2

Safety by design

New therapies, lower toxicity

3

Ready-to-treat

Bridge to MRD and time the collection

4

Sequencing

Who can safely hold, and how we monitor

Take-home: The goal is getting patients to curative-intent therapy. We need to keep building our community and academic center partnership to improve access.

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Key Learning Points



- Step-up (priming) dosing is a core strategy for limiting CRS severity with T-cell–engaging bispecifics in ALL; in the SYRUS study of surovatamig, CRS was predominantly low grade with optimized step-up dosing.
- Current evidence-based bridging principles point to individualized bridging according to disease burden, prior therapy, antigen profile, and response
- After disease relapse post-CD19-directed CAR T-cell therapy, reassess disease immunophenotype and molecular features at relapse before selecting the next treatment

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Q&A Session