Global Leukemia Academy

Bridging Science and Practice: From Newest Clinical Approaches to Real-World Clinical Cases

August 23 and 24, 2024 – Asia-Pacific

Meeting sponsors AMGEN rigel

APTITUDE HEALTH

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Welcome to Day 2

Naval Daver

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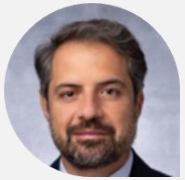
Meet the Faculty

CHAIR



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

CO-CHAIR

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National Cancer Center Hospital East,
Kashiwanoha, Kashiwa, Japan

Shaun Fleming, MBBS(Hons), FRACP, FRCPA
Alfred Hospital, Melbourne, VIC, Australia

Objectives of the program

- Understand current treatment patterns for acute leukemias including incorporation of new technologies
- Uncover when genomic testing is being done for acute leukemias, and how these tests are interpreted and utilized
- Understand the role of stem cell transplantation in acute leukemias as a consolidation in first remission
- Comprehensively discuss the role of MRD in managing and monitoring acute leukemias
- Gain insights into antibodies and bispecifics in ALL: what are they? When and how should they be used? Where is the science going?
- Discuss the evolving role of ADC therapies in acute leukemias
- Review promising novel and emerging therapies in acute leukemias
- Explore regional challenges in the treatment of acute leukemias across JAPAC

Agenda: Day 2

Time (UTC +8)	Title	Speaker
8.00 AM – 8.10 AM	Welcome to Day 2	Naval Daver
8.10 AM – 8.30 AM	Current treatment options for relapsed ALL in adult and elderly patients	Elias Jabbour
8.30 AM – 8.50 AM	Long-term safety considerations for leukemias (focus on ALL)	Jae Park
8.50 AM – 9.10 AM	Current and future role of transplantation in acute leukemias in Asia-Pacific	Shaun Fleming
9.10 AM – 9.20 AM	Break	
9.20 AM – 9.40 AM	Current treatment options for relapsed AML in adult and elderly patients	Junichiro Yuda
9.40 AM – 10.10 AM	AML case-based panel discussion • Case 1 AML: Ane Veu (Fiji) • Case 2 AML: Feng-Ming Tien (Taiwan)	Naval Daver and Patient case presenters And all faculty
10.10 AM – 10.50 AM	Panel discussion: How treatment in first line influences further therapy approaches in ALL and AML • Will CAR T and bispecifics change the treatment landscape? • Role of HSCT – is it still necessary? • What does the future look like? Adoption of therapies and evolving standards of care in Asia-Pacific	Naval Daver and all faculty
10.50 AM – 11.00 AM	Session close	Naval Daver

Question 1

What age group is considered elderly for patients with AML?

A. ≥50 years
B. ≥55 years
C. ≥60 years
D. ≥65 years
E. ≥70 years

Question 2

How do you assess minimal residual disease (MRD) for ALL?

A. Multicolor flow
B. Molecular PCR
C. Next-generation sequencing platform
D. We do not check for MRD

Question 3

Which of the following is NOT true for ALL?

A. Inotuzumab and blinatumomab + chemotherapy is active in both front line and salvage for ALL

B. Kinase inhibitors can be combined with other therapy modalities in Ph-positive ALL

C. MRD is highly prognostic for relapse and survival in Ph-negative ALL

D. There are no effective consolidation treatments for patients who remain MRD positive after induction therapy

Question 4

The prognosis of patients with R/R AML depends on:

A. Age
B. Prior therapy (eg, HSCT)
C. Timing of relapse
D. The mutational and cytogenetic profile of the disease
E. All of the above
F. A and D

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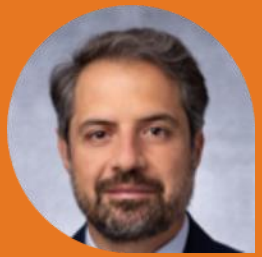
Current treatment options for relapsed ALL in adult and elderly patients

Elias Jabbour



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Adults With R/R Acute Lymphocytic Leukemia in 2024: Immunotherapies and Sequencing of CD19-Targeted Therapies

Elias Jabbour, MD

Department of Leukemia

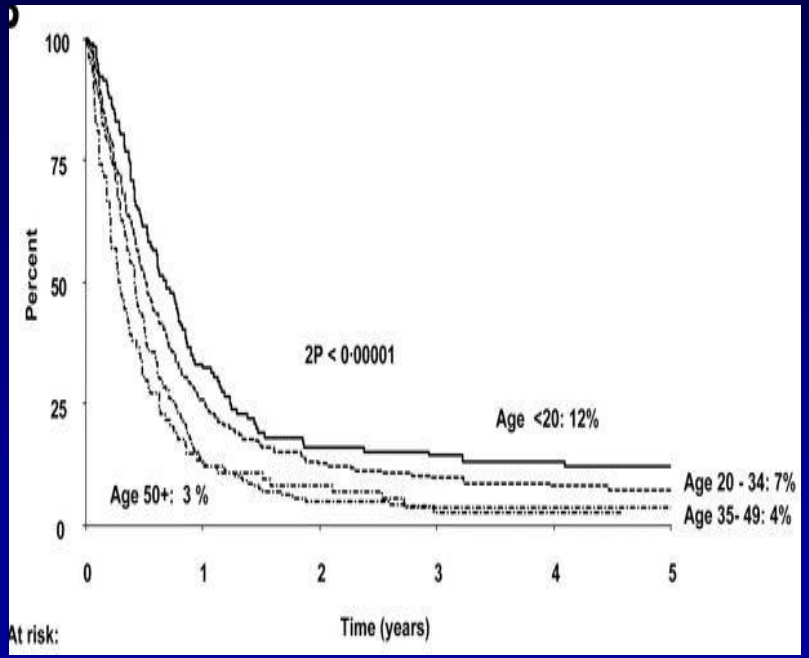
The University of Texas MD Anderson Cancer Center, Houston, USA

Summer 2024

ALL – Historical Survival Rates After First Relapse

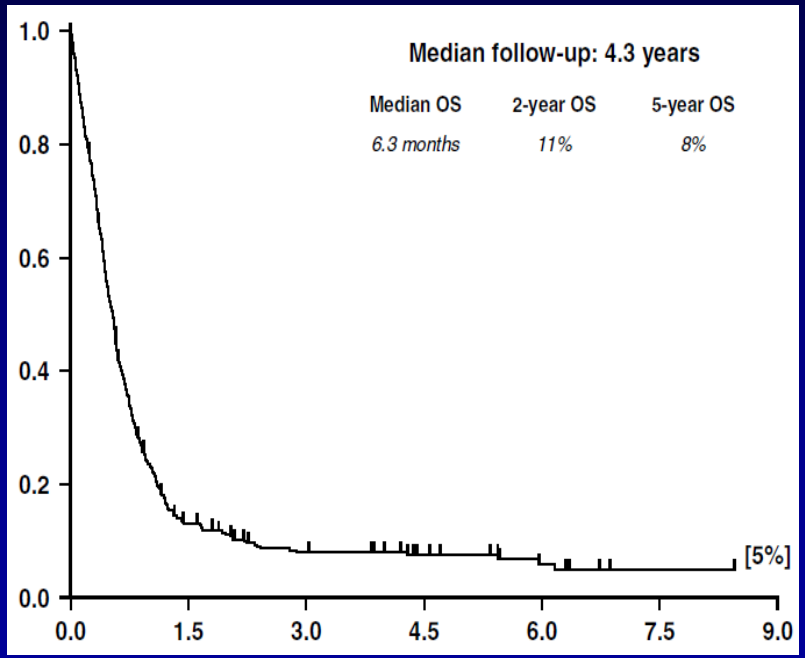
MRC UKALL2/ ECOG2993 Study (n = 609)[1]

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% and 5-yr OS: 8%



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

Historical Results in R/R ALL

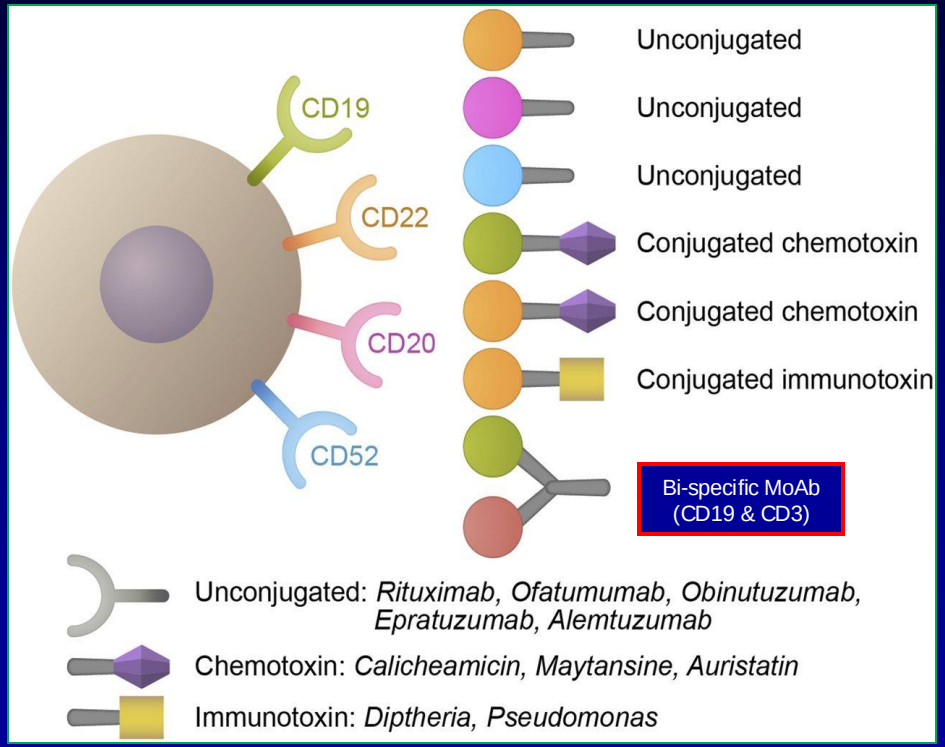
- Poor prognosis in R/R ALL Tx with standard of care (SOC) chemotherapy

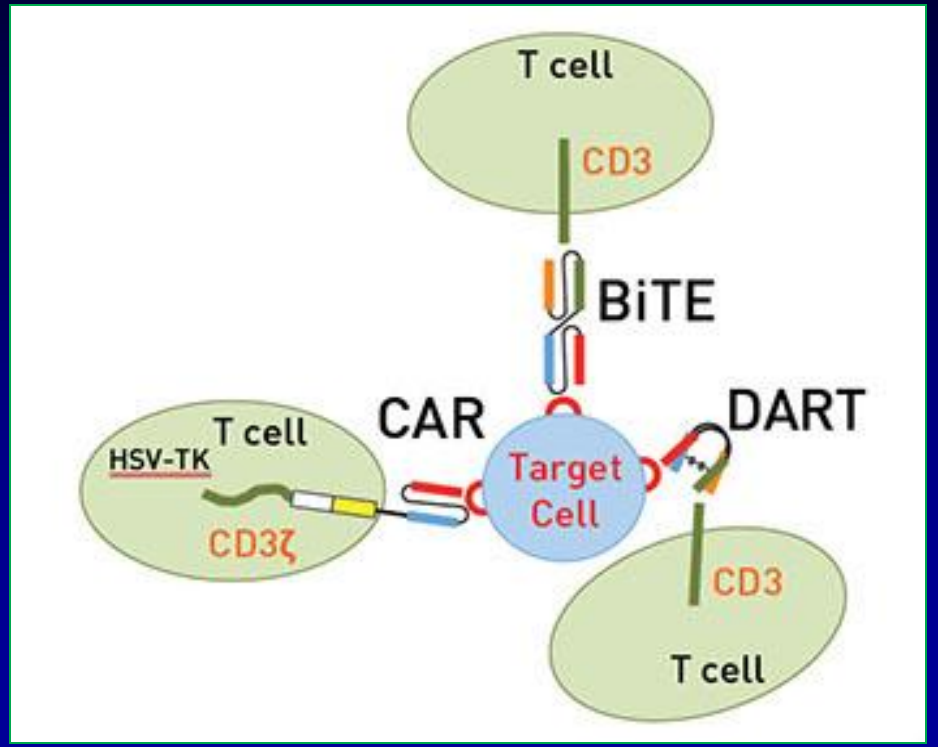
Rate (95% CI)	No Prior Salvage (S1)	One Prior Salvage (S2)	≥2 Prior Salvages (S3)
Rate of CR, %	40	21	11
Median OS, months	5.7	3.4	2.9

Gökbuget N, et al. *Haematologica.* 2016;101:1524-1533.

Immuno-Oncology in ALL

- **Antibodies, ADCs, immunotoxins, BiTEs, DARTs, CAR T cells**



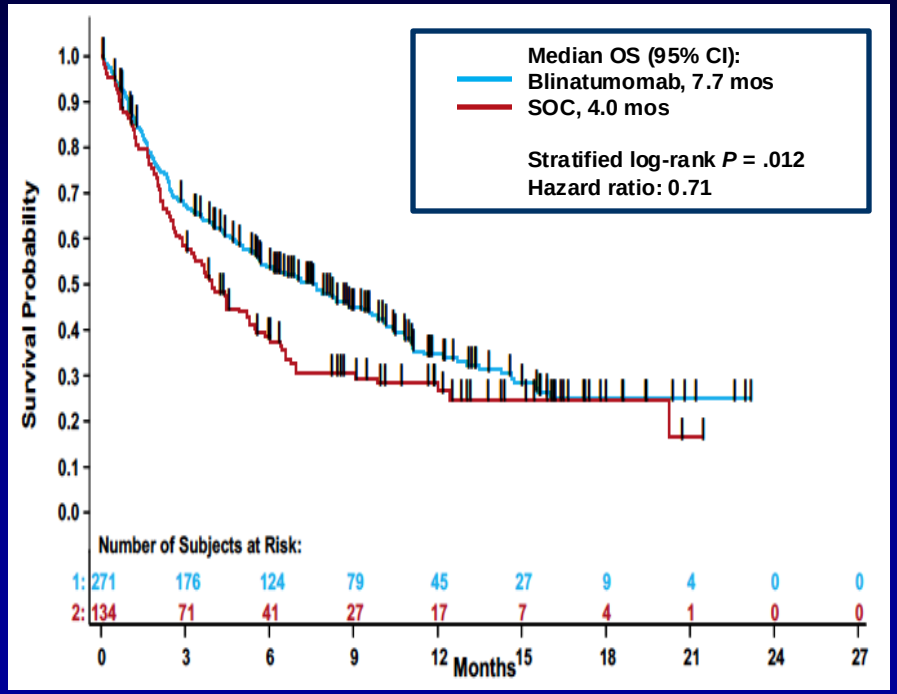


Jabbour E, et al. *Blood.* 2015;125:4010-4016.

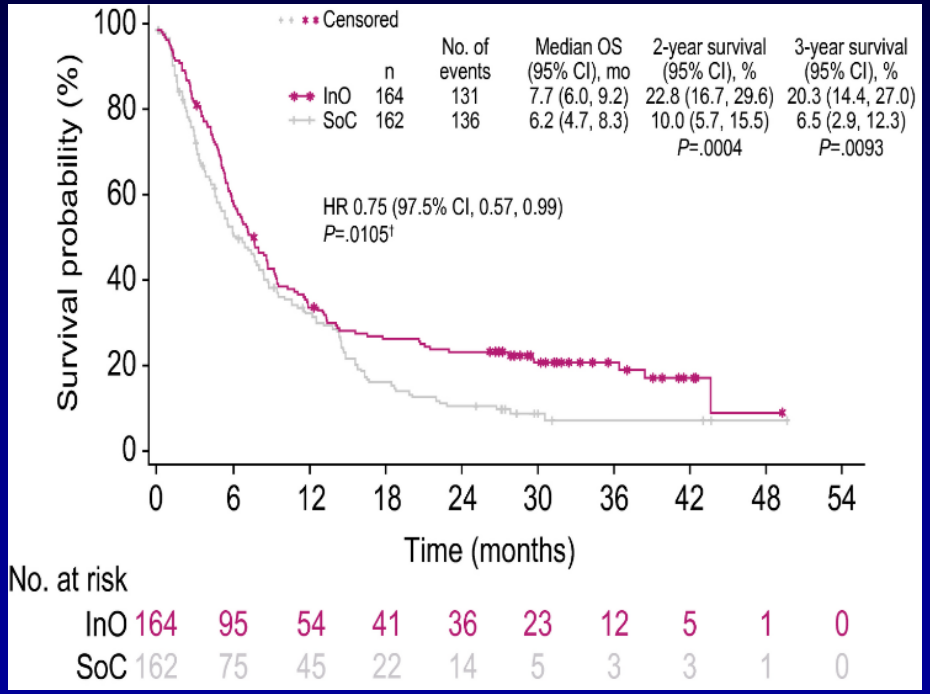
Blinatumomab/Inotuzumab vs ChemoRx in R/R ALL

- **Marrow CR**

Blina vs SOC: 44% vs 25%[1]

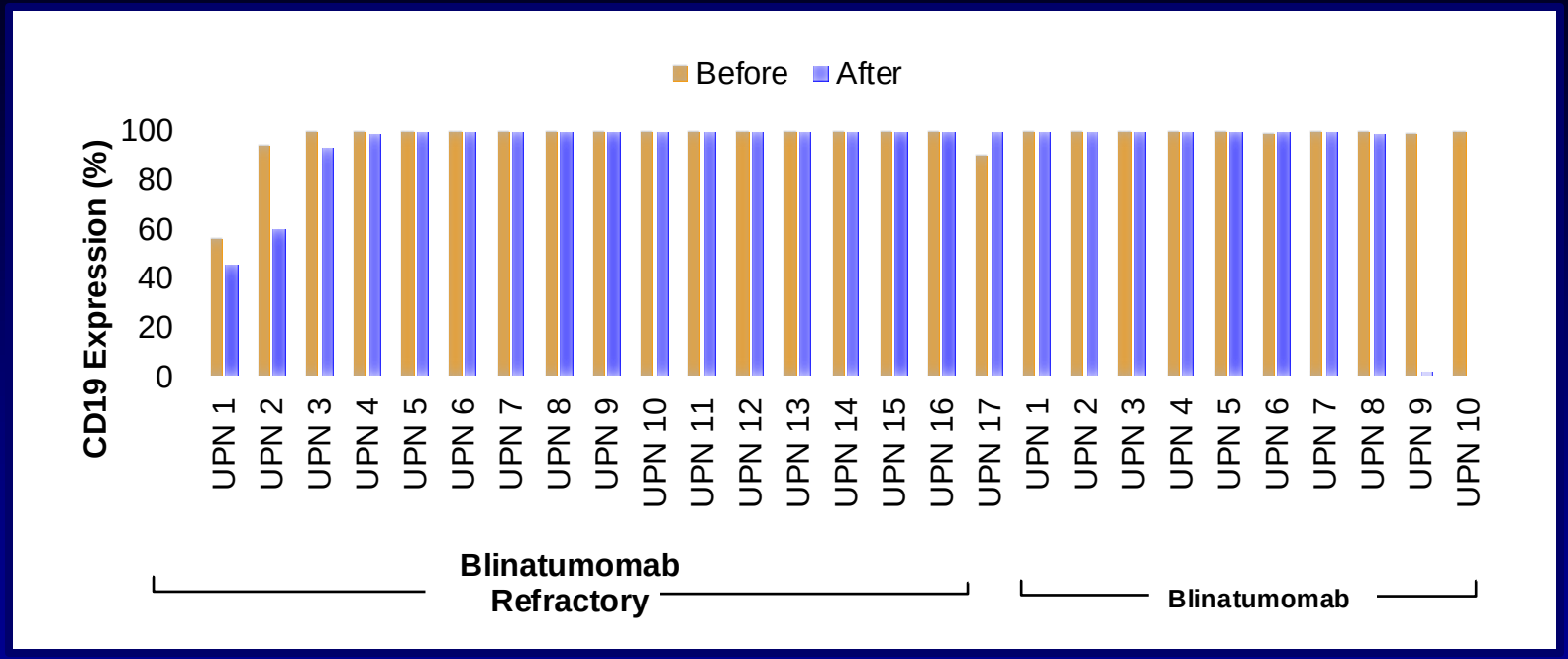


Ino vs SOC: 74% vs 31%[2,3]



1. Kantarjian H, et al. *N Engl J Med*. 2017;376:836-847; 2. Kantarjian H, et al. *N Engl J Med*. 2016;375:740; 3. Kantarjian H, et al. *Cancer*. 2019;125(14):2474-2487.

CD19 (%) Expression Before and After Blinatumomab Therapy

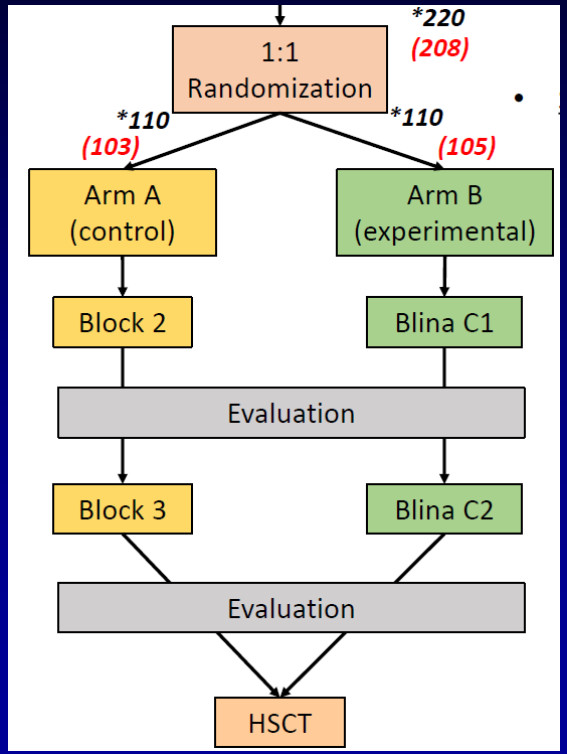


- **61 patients evaluated for immunophenotype; 56 (92%) had CD19-positive disease**
  - 5 (8%) had ALL recurrence with CD19-negative disease
  - 2 patients experienced progression with lower CD19-positive disease

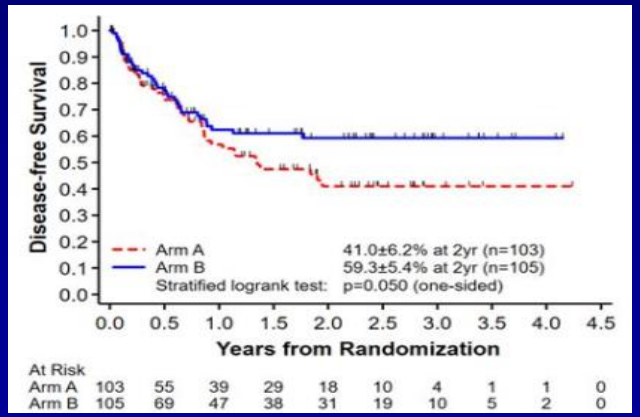
Jabbour E, et al. *Am J Hematol.* 2018;93:371-374.

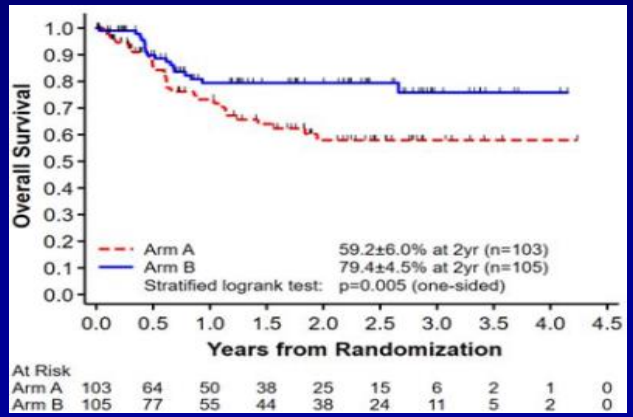
Phase III Study of Blinatumomab vs ChemoRx in Children/AYA in Salvage 1

- 208 pts HR/IR randomized 1:1 to blina (n = 105) vs chemoRx (n = 103) post Block 1 reinduction



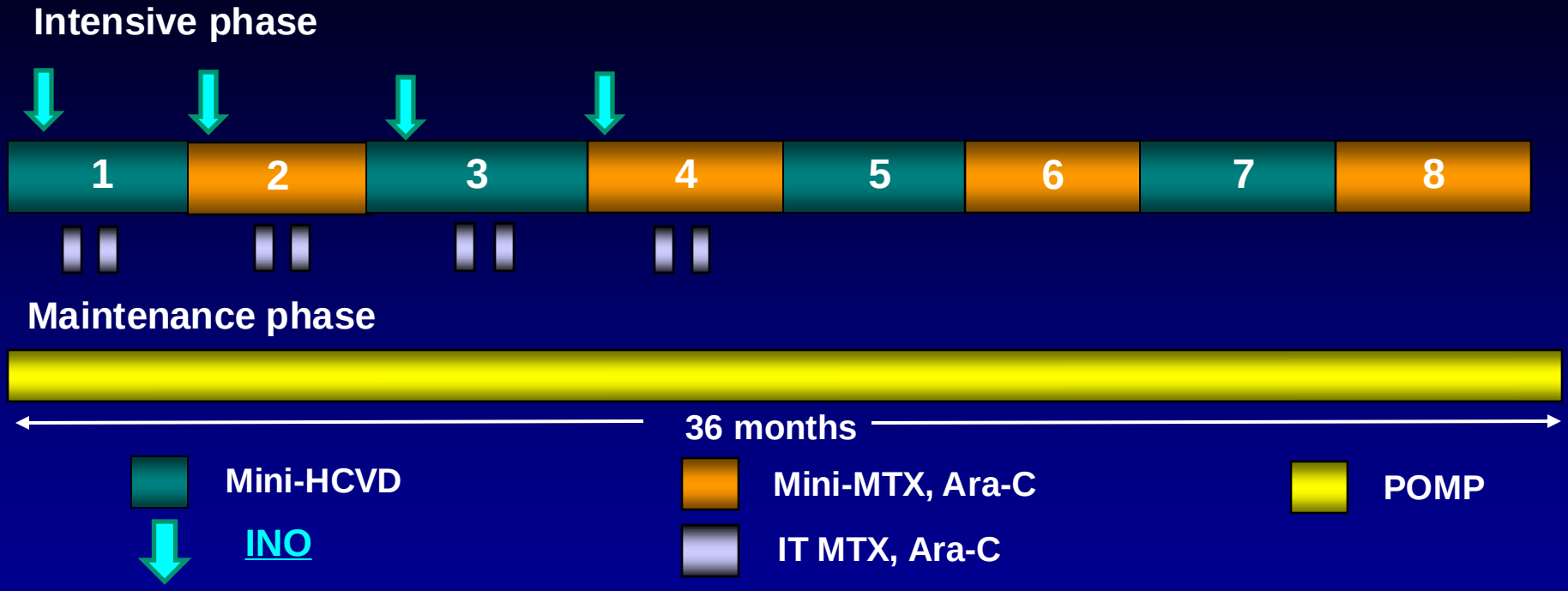
Parameter	Blina	Chemo	*P* Value
2-yr DFS, %	59	41	.05
2-yr OS, %	79	59	.005
SCT, %	70	43	<.001
MRD clearance, %	75	32	<.001





Brown PA, et al. *JAMA.* 2021;325:833-842; Brown PA, et al. ASH 2019. Abstract LBA-1 and oral presentation.

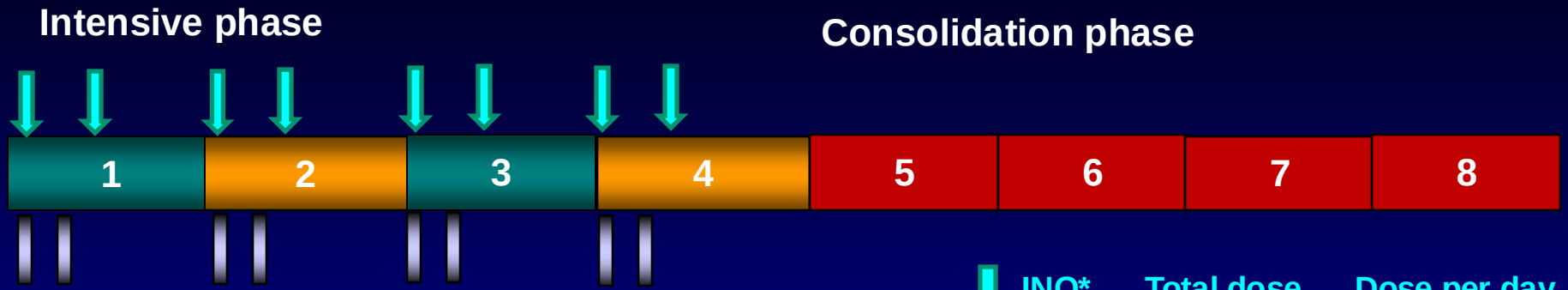
Mini-HCVD + INO ± Blina in R/R B-ALL: Original Design (Pts #1–67)



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

Short N, et al. EHA 2023; Abstract S119 and oral presentation.

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



INO*	Total dose (mg/m²)	Dose per day (mg/m²)
C1	0.9	0.6 D2, 0.3 D8
C2–4	0.6	0.3 D2 and D8

Total INO dose = 2.7 mg/m²

*Ursodiol 300mg tid for VOD prophylaxis

Mini-HCVD

Mini-MTX, Ara-C

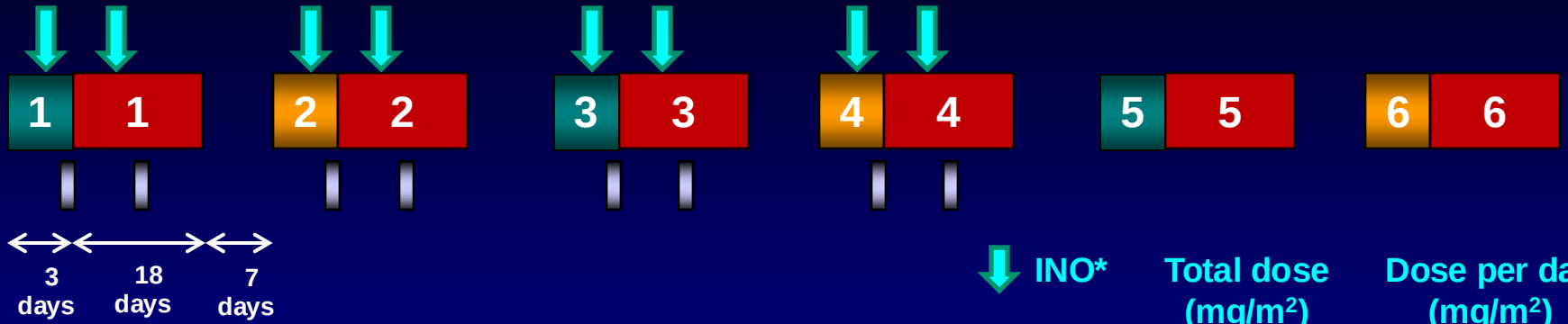
Blinatumomab

IT MTX, Ara-C

POMP

Short N, et al. EHA 2023; Abstract S119 and oral presentation.

Mini-HCVD + INO ± Blina in R/R B-ALL: "Dose-Dense" Design (Pts #111–125+)



Maintenance phase

INO*	Total dose (mg/m²)	Dose per day (mg/m²)
C1	0.9	0.6 D2, 0.3 D8
C2–4	0.6	0.3 D2 and D8

Total INO dose = 2.7 mg/m²

*Ursodiol 300mg tid for VOD prophylaxis

Mini-HCVD
Mini-MTX, Ara-C
Blinatumomab
IT MTX, Ara-C
POMP

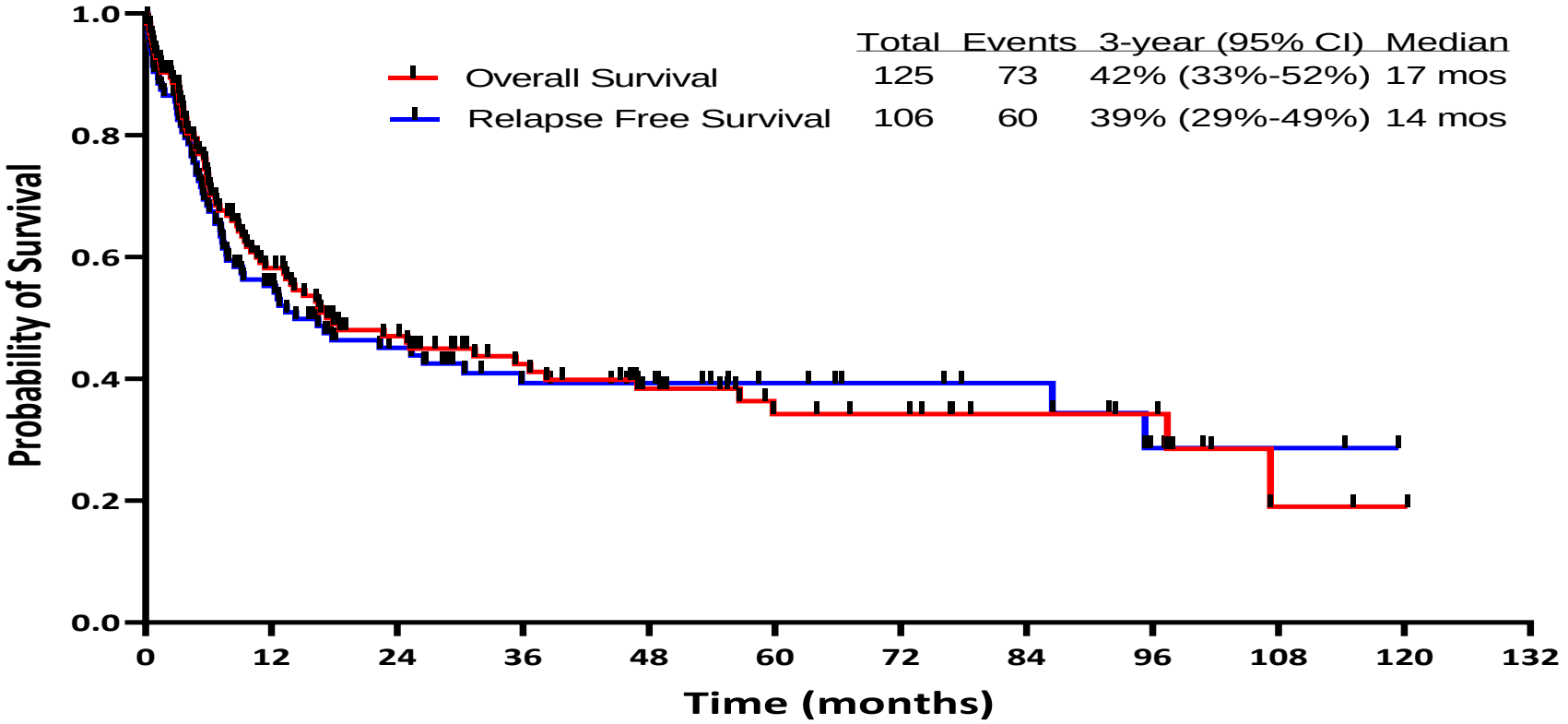
Short N, et al. EHA 2023; Abstract S119 and oral presentation.

Mini-HCVD + INO ± Blina in R/R B-ALL: MRD Negativity Rates

MRD Negativity by Flow Cytometry	N (%)			
	Overall (N = 125)	Before Blinatumomab (n = 67)	After Blinatumomab (n = 43)	Dose Dense (n = 15)
All patients				
End of cycle 1	53/100 (53)	25/49 (51)	18/38 (47)	10/13 (77)
Overall	87/102 (85)	41/50 (82)	34/39 (87)	12/13 (92)
Salvage 1				
End of cycle 1	45/82 (55)	22/34 (65)	17/37 (46)	8/11 (73)
Overall	73/83 (88)	31/35 (89)	32/37 (86)	10/11 (91)
Salvage 2+				
End of cycle 1	6/18 (33)	3/15 (20)	1/1 (100)	2/2 (100)
Overall	14/19 (74)	10/15 (67)	2/2 (100)	2/2 (100)

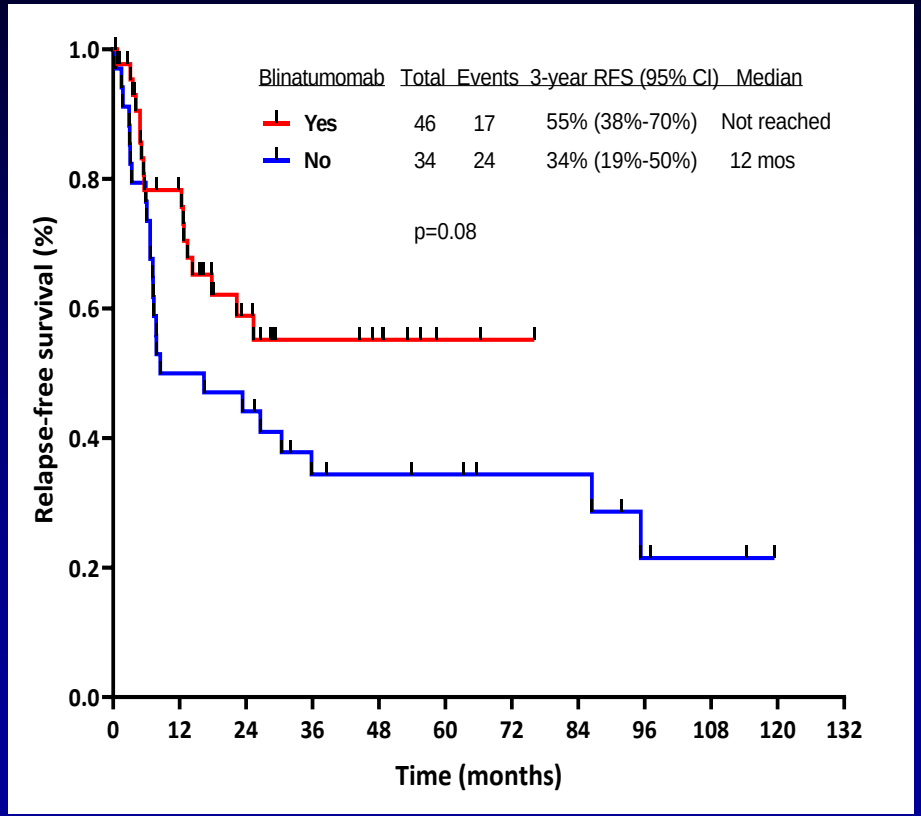
Short N, et al. EHA 2023; Abstract S119 and oral presentation.

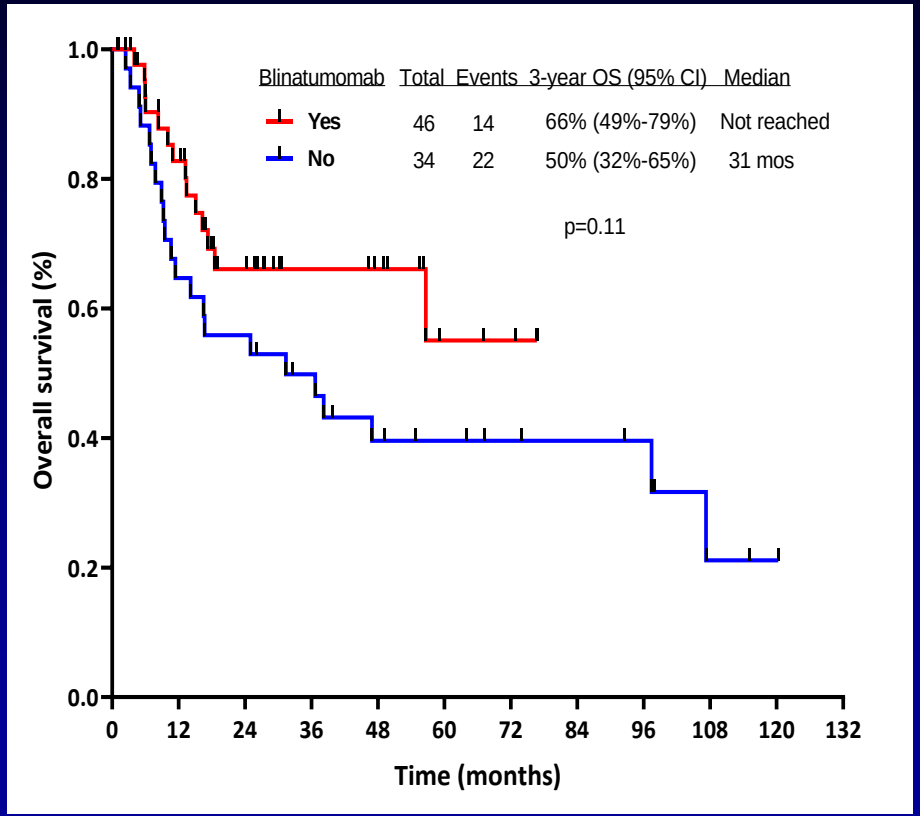
Mini-HCVD + INO ± Blina in R/R B-ALL: RFS and OS (Entire Cohort)



Short N, et al. EHA 2023; Abstract S119 and oral presentation.

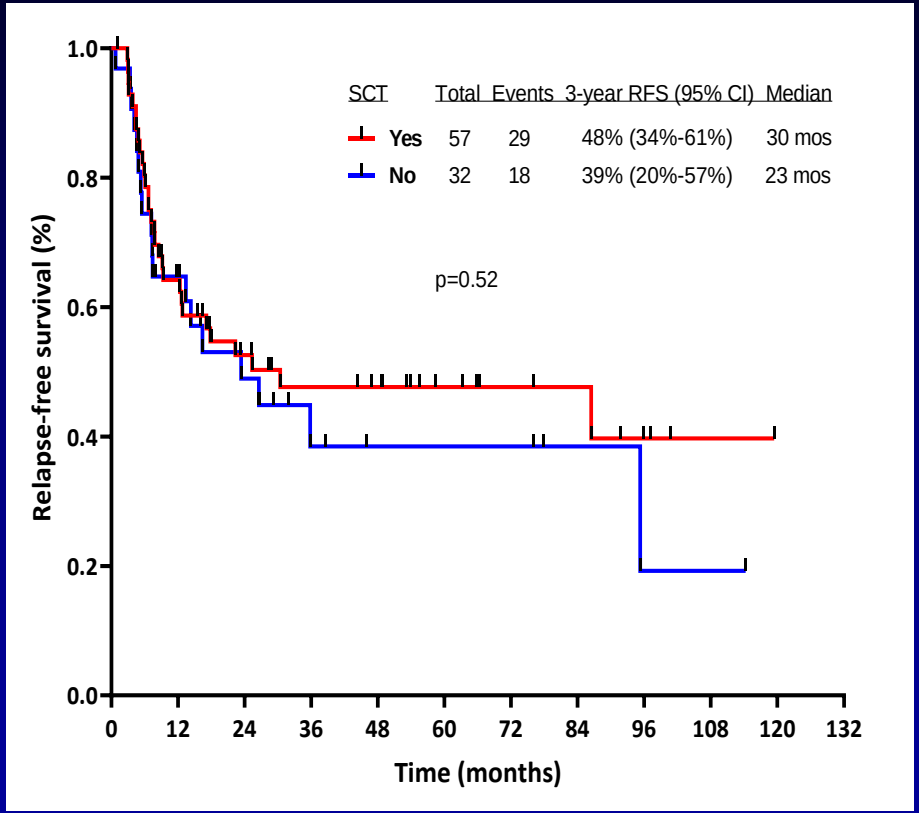
Mini-HCVD + INO ± Blina in R/R B-ALL: OS and RFS by Receipt of Blinatumomab (Salvage 1 Only)

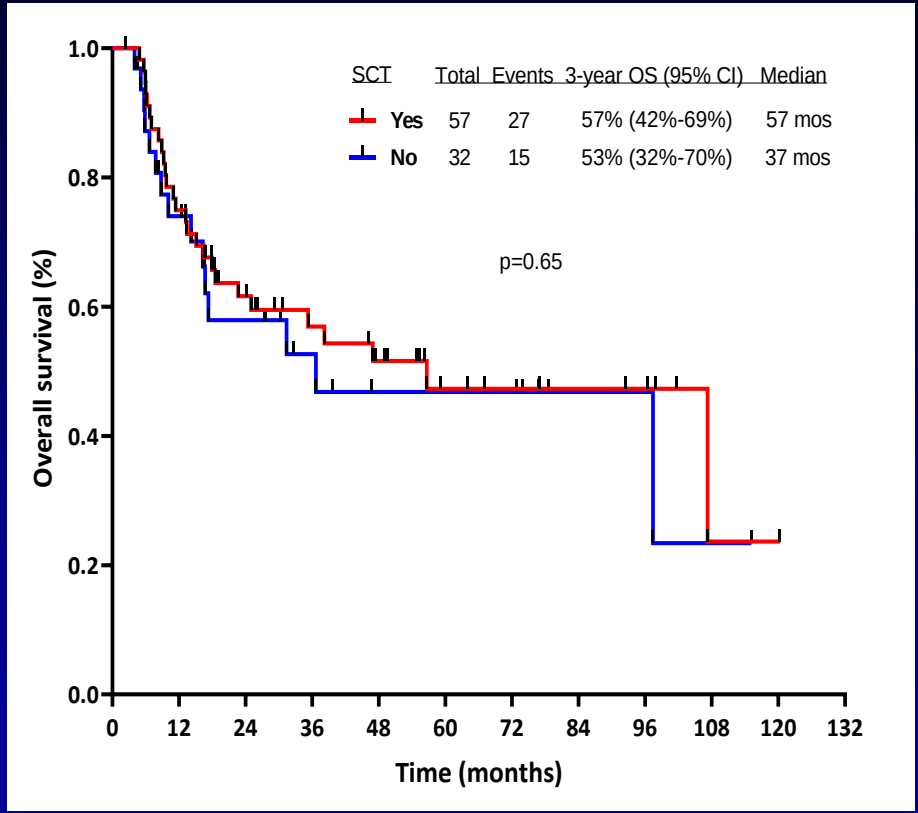




Short N, et al. EHA 2023; Abstract S119 and oral presentation.

Mini-HCVD + INO ± Blina in R/R B-ALL: OS and RFS by HSCT (Landmark Analysis)

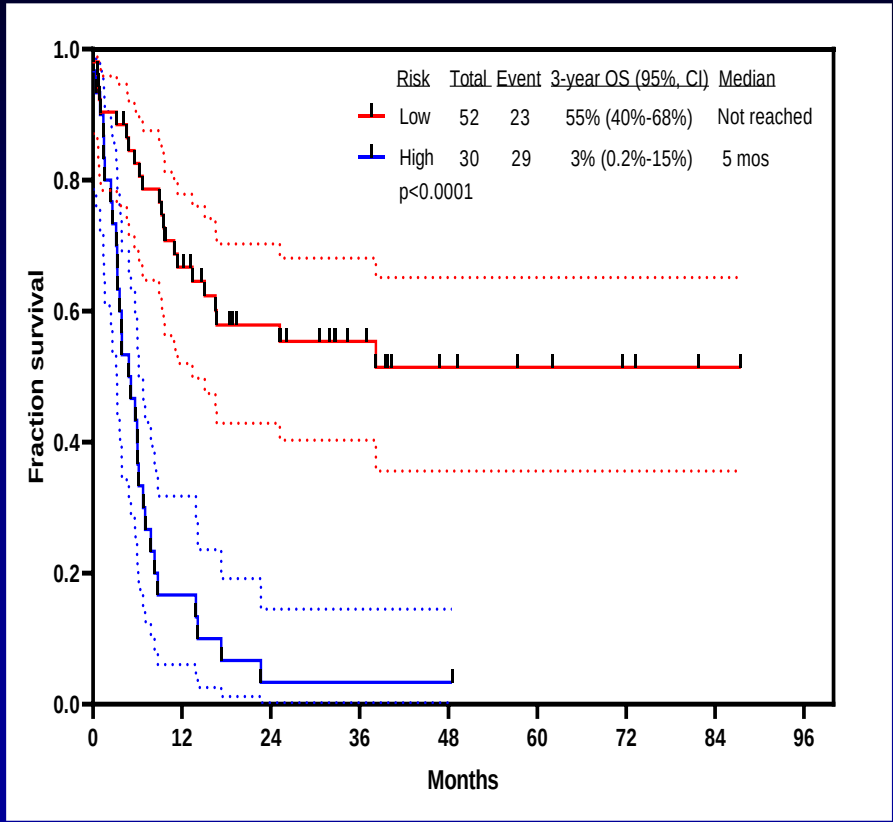




Short N, et al. EHA 2023; Abstract S119 and oral presentation.

Model: mHCVD + INO ± Blina in R/R ALL – a Prognostic Model for Survival

Variable	Risk Classification	
	Low*	High**
% CD22	≥70%	<70%
Cytogenetic	Diploid, complex, others	11q23 rearrangements Ho-Tr



*Low risk required all low-risk criteria.
**High risk required any one of high-risk criteria.

Sasaki Y, et al. *Blood*. 2020;136(suppl 1):abstract 1899.

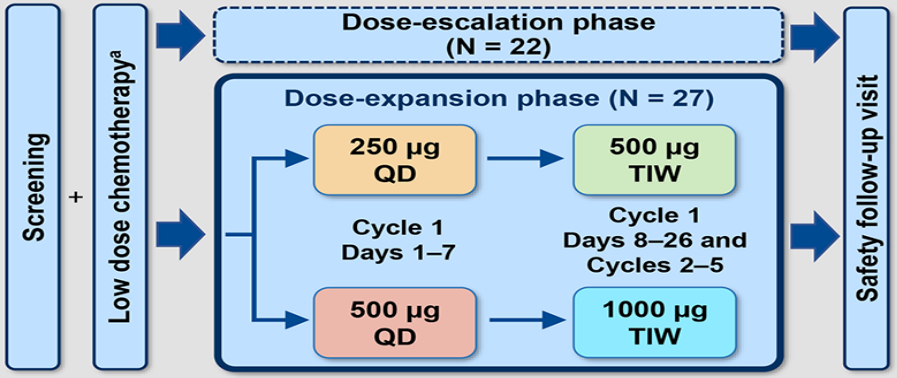
Single Agent Subcutaneous Blinatumomab for Advanced Acute Lymphoblastic Leukemia

Results from the expansion phase of a phase 1b trial

Objective

To assess the efficacy and safety of subcutaneous blinatumomab in heavily pretreated adults with R/R B-ALL at two doses

Study Schema



Results

Efficacy

250 µg QD/500 µg TIW (N = 14)
- CR/CRh: 85.7%
- MRD-neg CR/CRh: 75%

500 µg QD/1000 µg TIW (N = 13)
- CR/CRh: 92.3%
- MRD-neg CR/CRh: 100%

Dosing regimen 500 µg QD/1000 µg TIW demonstrated higher MRD-negative CR/CRh within 2 cycles (100%) compared with dosing regimen 250 µg QD/500 µg TIW (75%)

Safety

250 µg QD/500 µg TIW (N = 14)
- Grade ≥3 CRS[b]: 21.4%
- Grade ≥3 NE[b]: 42.9%

500 µg QD/1000 µg TIW (N = 13)
- Grade ≥3 CRS[b]: 23.1%
- Grade ≥3 NE[b]: 23.1%

- SC injections were well tolerated
- No treatment-related grade 4 CRS or NE

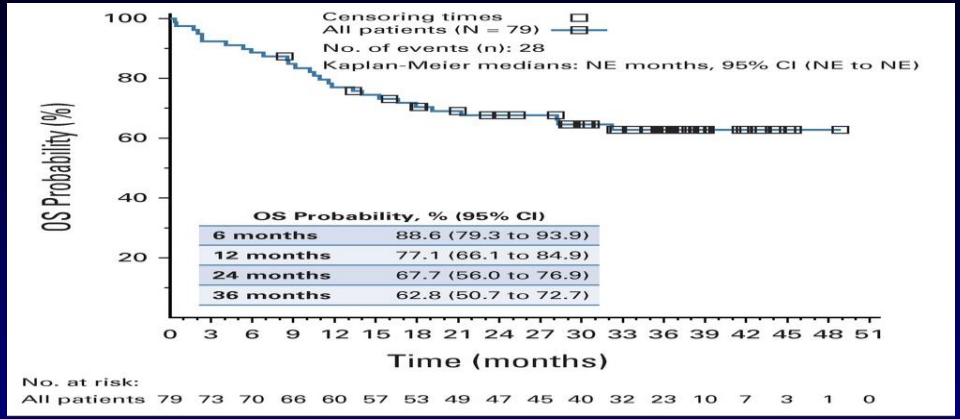
Conclusion

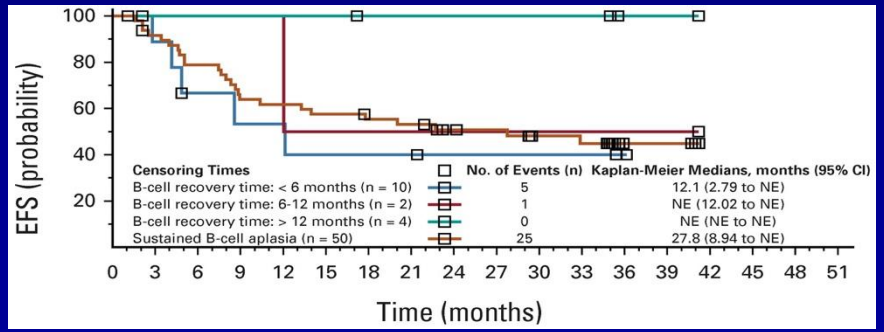
Treatment with single agent SC blinatumomab resulted in a high CR rate, high MRD-negativity rate, and an acceptable safety profile in heavily pretreated adults with R/R B-ALL

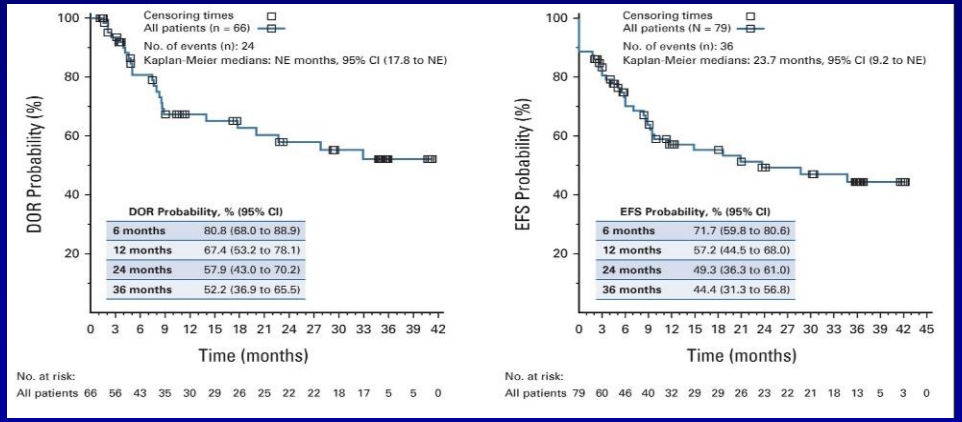
Jabbour E, et al. *Am J Hematol.* 2024;99(4):586-595.

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%







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

Brexucabtagene Autoleucel (CD19 CAR T) in R/R ALL (ZUMA)

- 78 pts Rx with brexu-cel. Median FU 54 mos
- CR/CRi 57/78 = 73%

ALL Subset	No	Median OS (mos)	% 4-yr OS
Total	78	25.6	40
Prior Rx			
1	15	60.4	57
2+	63	25.4	36
Prior blina			
Yes	38	15.9	55
No	40	60.4	24
Later allo SCT			
Yes	14	36.3	-
No	43	60.4	-

Oluwole. *J Clin Oncol.* 2024;24:S6531.

Toxicities of Brexu-Cel in R/R ALL: ROCCA Results

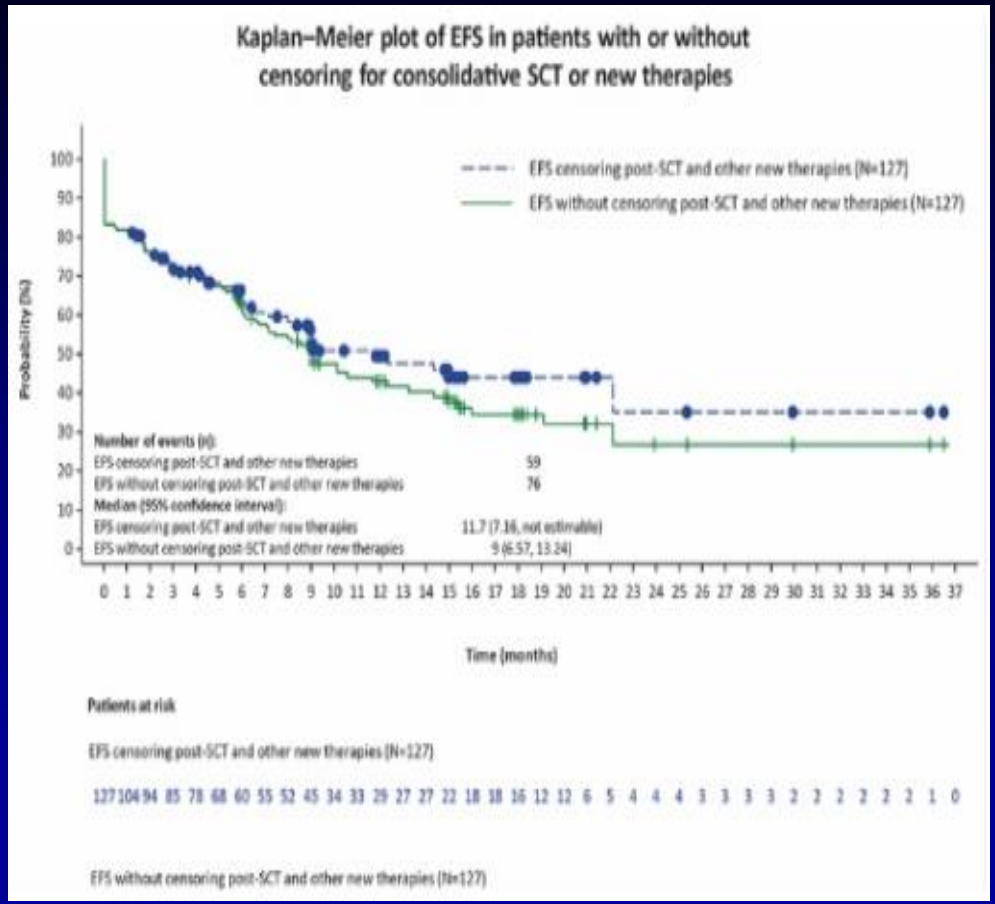
- Retrospective analysis of adults (N = 152) with R/R B-ALL receiving commercial brexu-cel
- Grade 3 CRS higher in ZUMA-3 than seen in the ROCCA dataset, but ICANS rates were comparable
- Grade 3+ CRS showed a numerical increase in patients with active disease at apheresis (>5% marrow blasts and/or EMD); OR: 2.35, 95% CI: 0.69–8.0, *P* = .17
- Grade 3+ ICANS more likely in pts with active disease at apheresis; OR: 2.63, 95% CI: 1.28–5.38, *P* = .008

Factor	ROCCA	ZUMA-3
Patients infused, n	152	55
Any CRS	82%	89%
Grade ≥3 CRS	9%	24%
Time to onset, days	5 (0–14)	–
Any ICANS	56%	60%
Grade ≥3 ICANS	31%	25%
Time to onset, days	7 (0–21)	–
Early death by day 28, n (%)	9 (6)	–

Kopmar NE, et al. ASH 2023. Abstract 522 and oral presentation.

Obecaptagene Autoleucel (OBE-CEL) in Adult R/R ALL (FELIX)

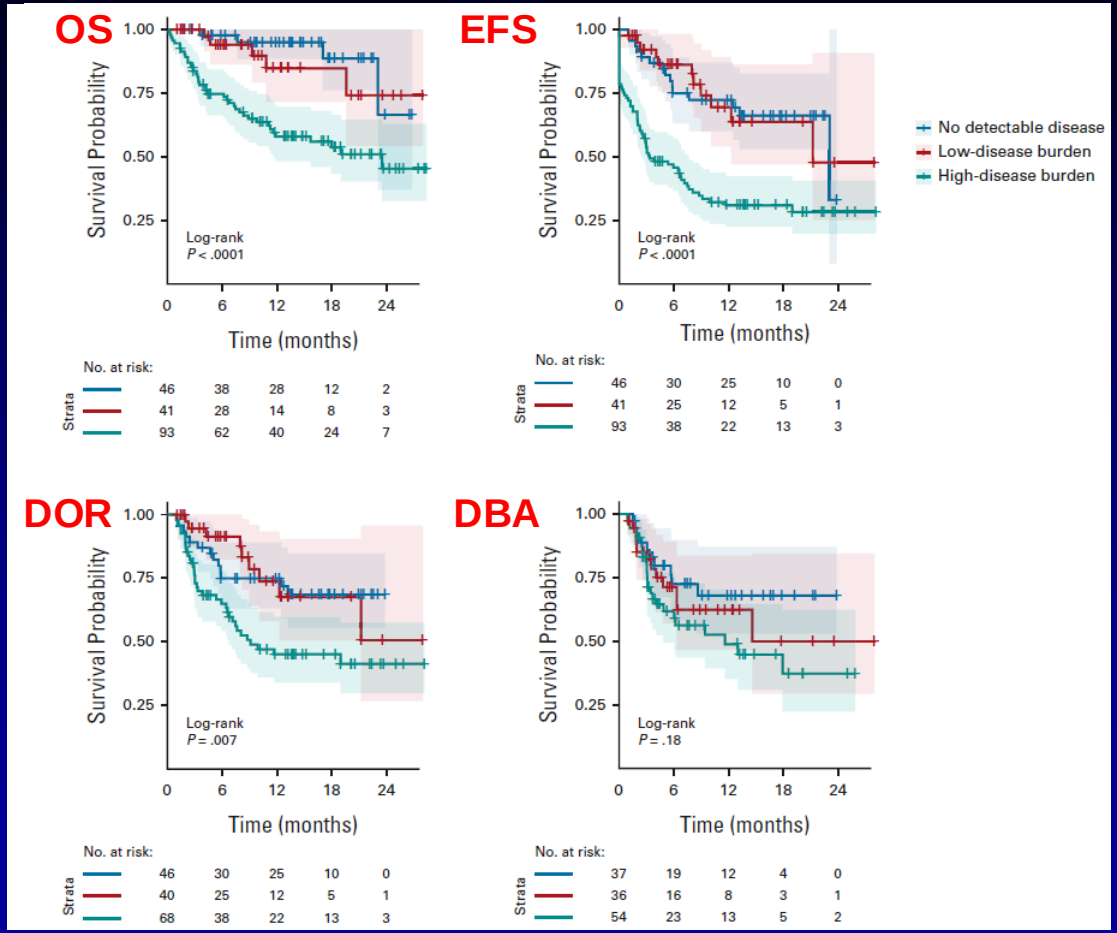
- AUTO 1 fast off-rate CD19 binder CAR T
- 153 enrolled, 127 (83%) infused. Median age 47 yrs
- Prior blina 42%, ino 31%, allo SCT 44%
- cCR-CRi 99/127 = 78% (99/153 = 65%). 19/77 allo SCT
- Loss of CAR T = HR 2.9
- 12-mos EFS 49%, 12-mos OS 61%



Jabbour E, et al. *J Clin Oncol.* 2024;24:S6504; Roddie et al. *HemaSphere*. 2024;8:S114.

Real-World CAR Consortium and Disease Burden

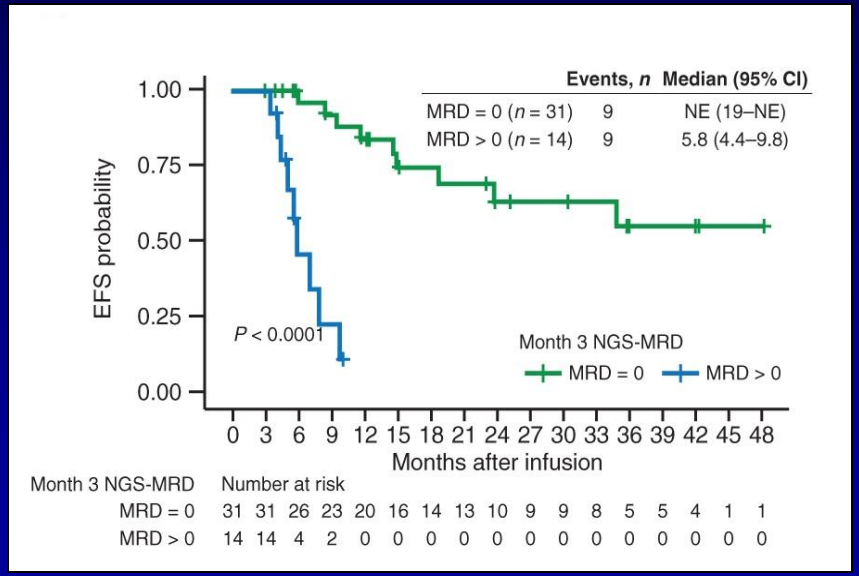
- 200 pts (185 pts infused)
- Median age: 12 yrs (0–26 yrs)
- CR: 85%
- Disease burden
  - HBD: n = 94 (51%)
  - LBD: n = 41 (22%)
  - ND: n = 46 (25%)
- Survival outcomes
  - 12-mo EFS: 50%
  - 12 mo OS: 72%
- Safety
  - G3 CRS: 21% (35% in HBD)
  - G3 NE: 7% (9% in HBD)

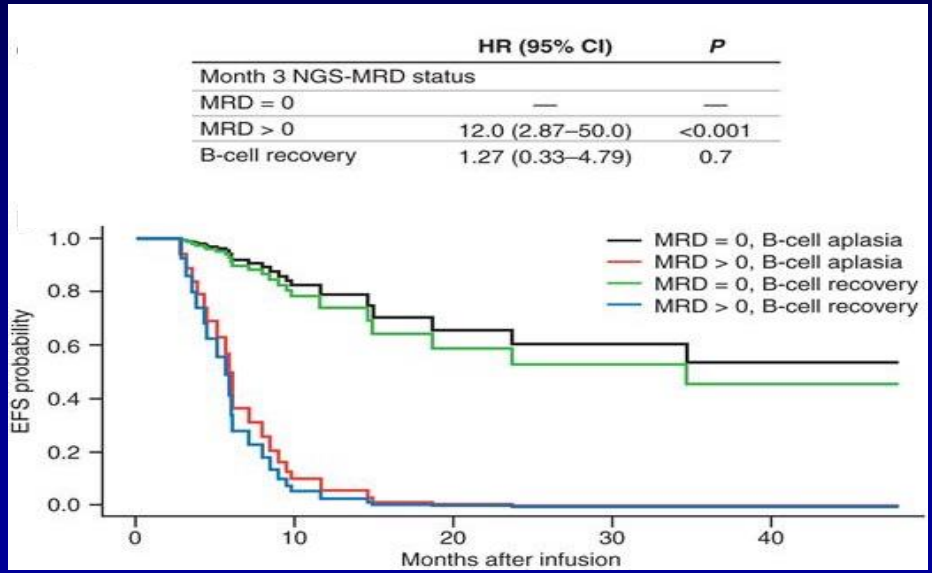


Schultz LM, et al. *J Clin Oncol*. 2022;40(9):945-955.

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

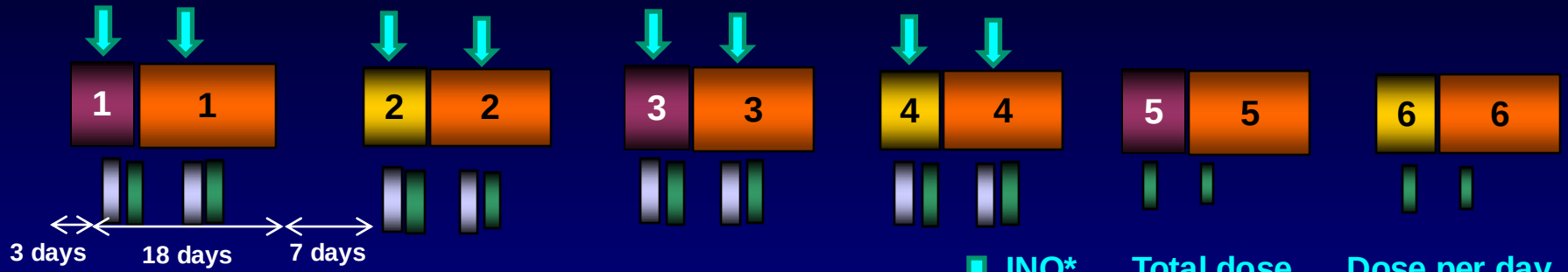




Pulsipher MA, et al. *Blood Cancer Discov.* 2022;3(1):66-81.

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

Induction phase: C1–C6



INO*	Total dose (mg/m²)	Dose per day (mg/m²)
C1	0.9	0.6 D2, 0.3 D8
C2–4	0.6	0.3 D2 and D8

Total INO dose = 2.7 mg/m²

*Ursodiol 300 mg tid for VOD prophylaxis

Consolidation phase

CAR T Consolidation

Mini-HCVD

Mini-MTX, Ara-C

Rituximab

IT MTX, Ara-C

Blinatumomab

ALL 2024: Conclusions

- Significant improvements across all ALL categories
- Incorporation of Blina-InO in FL therapy highly effective and improves survival
- Early eradication of MRD predicts best overall survival
- Antibody-based Txs and CAR Ts both outstanding; not mutually exclusive/competitive (vs); rather, complementary (together)
- Future of ALL Tx
  1) Less chemotherapy and shorter durations
  2) Combinations with ADCs and BiTEs/TriTEs targeting CD19, CD20, CD22
  3) SQ blinatumomab
  4) CAR Ts CD19 and CD19 allo and auto in sequence in CR1 for MRD and replacing ASCT

Thank You

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Q&A

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Long-term safety considerations for leukemias (focus on ALL)

Jae Park

APTITUDE HEALTH

ALL in Adults Is Becoming Highly Curable

Subtype	Treatment	Curability
Mature B (Burkitt)	Specific chemotherapy + **rituximab** DA-R-EPOCH	70%–80%
Ph-pos	**TKI** ± CHT ± **immunotherapy** ± HSCT ± maintenance TKI	>50%, >70%
T-ALL, non-ETP **T-ALL ETP**	Chemotherapy (HDMTX, HDARAC, Asp) ± **nelarabine?** Chemotherapy (HDMTX, HDARAC, Asp) + Allo-HSCT	60% 30%
ALL in AYA	Pediatric-based or -inspired chemotherapy	70%
CD20-pos ALL	Chemotherapy + **rituximab**	50%
Ph-like ALL	Chemotherapy + **TKI? or JAK inhibitors?** + Allo-HSCT	??
Any ALL MRD positivity	Chemotherapy + **immunotherapy** + Allo-HSCT in CR1	~40%

Lack of systematic approach to analyze the health condition of long-term survivors of adult ALL

Consensus Identification of Long-Term Severe Toxicities (n = 21) (Ponte di Legno Working Group)

- Hearing loss
- Blindness
- Heart failure
- Coronary artery disease
- Arrythmia
- Heart valve disease
- Gastrointestinal failure
- Hepatic failure
- Insulin-dependent diabetes
- Renal failure
- Pulmonary failure

- Osteonecrosis
- Amputation and physical deformations
- Cognitive dysfunction
- Seizures
- Psychiatric disease
- Neuropathy, myopathy, and movement disorders
- Vocal cord paralysis
- Cytopenia
- Immunodeficiency
- Solid malignant neoplasms

Andrés-Jensen L, et al. *Lancet Haematol*. 2021;8:e513-e523.

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

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

Andrés-Jensen L, et al. *Lancet Haematol*. 2021;8:e513-e523; Nielsen CG, et al. *Front Pediatr.* 2023;11:1155449.

Limitations for Safety Considerations in Adult ALL

- **Toxicities defined according to pediatric trials**
- **Other toxicities not considered**
  - Infertility
  - Sexual dysfunction
  - Chronic pain
  - Fatigue
  - Work impairment
  - Social function impairment
  - … / …

General Condition and Comorbidity of Long-Term Survivors of Adult ALL

- 1,413 long-term survivors from databases of GMALL trials (1984–2003)
- 584 questionnaires from 538 patients eligible
- Median f/u: 7.5 years (range, 3–24)
- Age at Dx: <25 years (n = 191, 36%), >55 years (n = 26, 5%)
- Median age at f/u: 39 years (range, 19–74)
- Alive >5 years from Dx (416, 78%), >10 years 35%
- HSCT: 168 (31%) (allo/auto 147/21)
- ≥4-year f/u after HSCT: 73%

Gökbuget N, et al. *Haematologica*. 2023;108:1758-1767.

Questionnaire

- **Part 1**
  - Comorbidity in 1 of 8 organ systems (skin, lung, neurologic, endocrine, kidney/liver, cardiac, gastrointestinal, eyes)
- **Part 2**
  - Specific syndromes (eg, fatigue, GvHD, secondary malignancies, infections, osteonecrosis, hyperthyroidism/hypothyroidism)
- **Part 3**
  - General health condition (ECOG performance status at last visit)
- Classification of severity according to CTCAE

Gökbuget N, et al. *Haematologica*. 2023;108:1758-1767.

Overall Incidences of Comorbidities and Specific Syndromes

Incidences	Comorbidity		Evaluable per item
	N	%	N
No comorbidity	355	66	538
Comorbidities according to organ classes			
Skin	97	18	538
Lung	41	8	538
Cardiac system	70	13	538
Gastrointestinal system	30	6	537
Neurologic system	147	27	538
Kidney/liver	56	10	538
Eyes	65	12	537
Endocrine system			
Women	50	24	211
Men	55	17	327
Specific syndromes			
Infection (in past 12 months)	64	12	533
Fatigue	71	13	533
GvHD	79	15	538
Osteonecrosis	41	8	538
Secondary malignancy	21	4	538
Hypothyreodism	26	5	537
Hyperthyreodism	7	1	538

GvHD: graft-*versus*-host disease.

Gökbuget N, et al. *Haematologica*. 2023;108:1758-1767.

Predictive Factors for Comorbidities

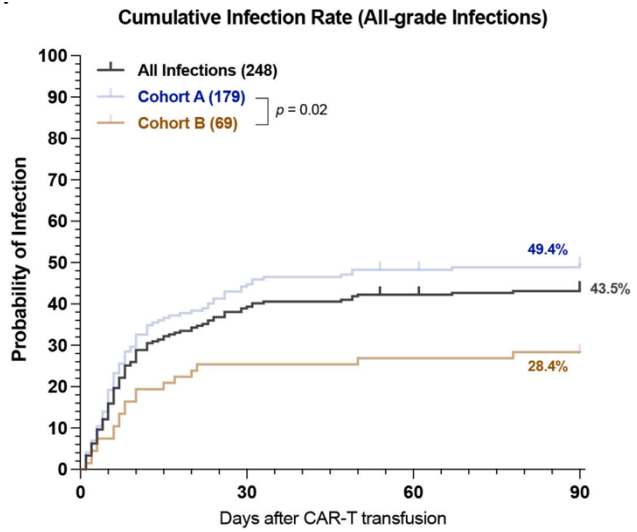
	HSCT vs CHT	Male vs Female	Aged ≤55 Yr vs >55 Yr
ECOG 0–1	<.0001		.02
Skin	<.0001	.02	
Lung	<.0001		
Cardiac	.03		.02
GI system	.02		
Neurologic	.002	.02	
Kidney/liver	<.0001		
Endocrine	.001		
Eye	<.0001		.04
Infection	.0001	.01	
Fatigue	.007		
Sec. malignancies			.03

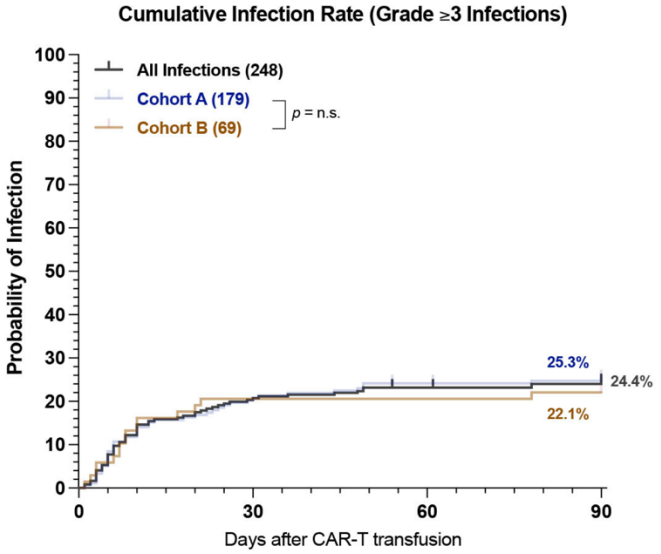
Gökbuget N, et al. *Haematologica*. 2023;108:1758-1767.

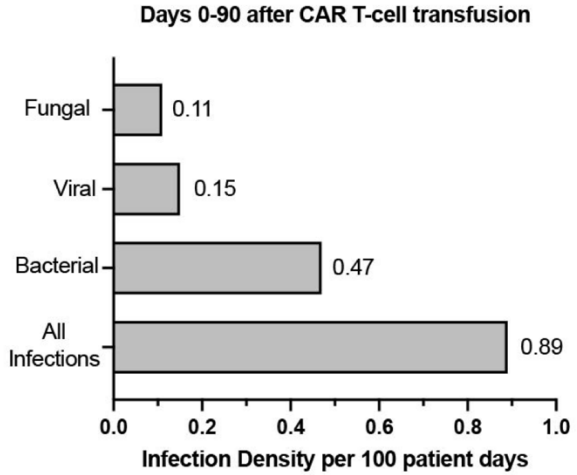
Remarks

- Incorporation of recommendations for long-term follow-up in the design of specific trials in ALL
- Multidisciplinary approach of f/u of long-term survivors
- Need for studies of long-term safety with the incorporation of immunotherapies (MoAb, CAR T) and new targeted therapies (TKI and others)
- Prophylaxis of long-term toxicity during the development of trials

Infections After CAR T-Cell Therapy Are Common and Associated With Increased Mortality

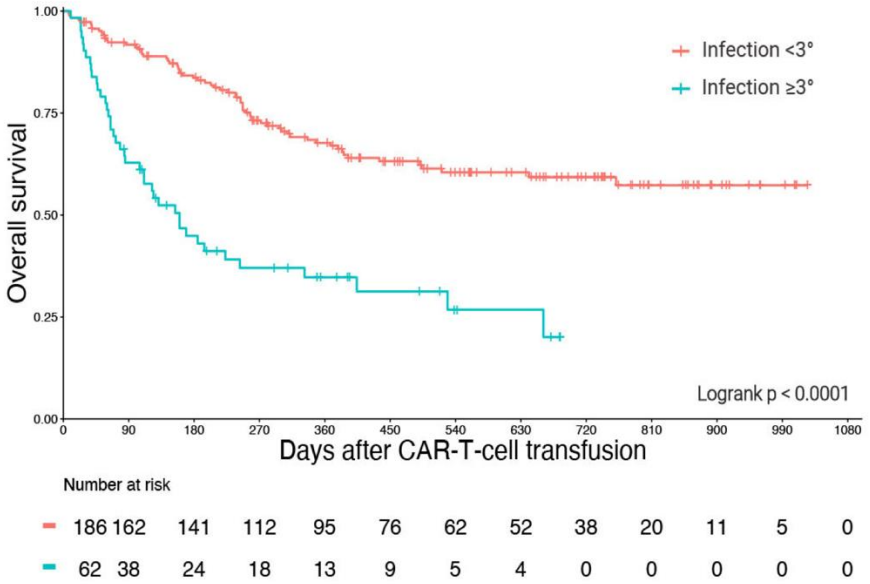






Rajeski K, et al. *J Immunother Cancer*. 2022;10(5):e004475.

Infections After CAR T-Cell Therapy Are Common and Associated With Increased Mortality

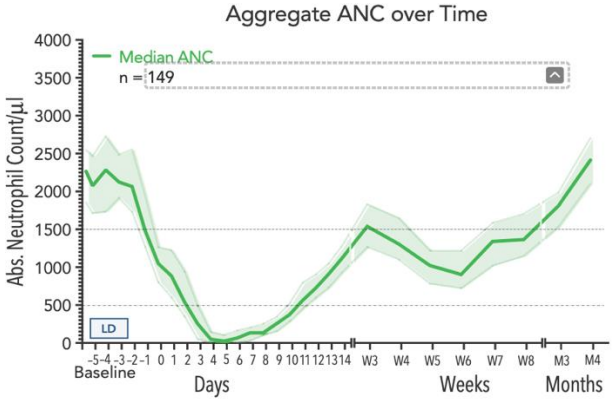


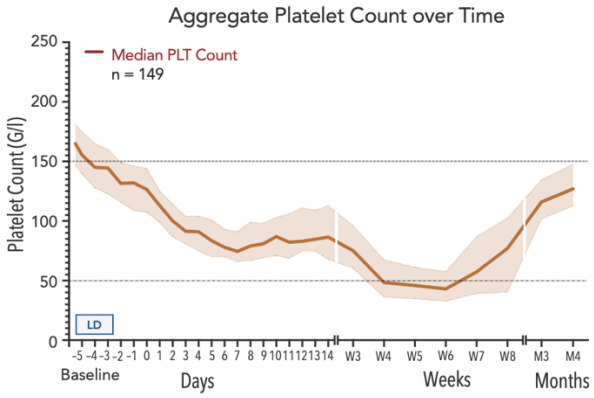
Etiologies of infections are multifactorial

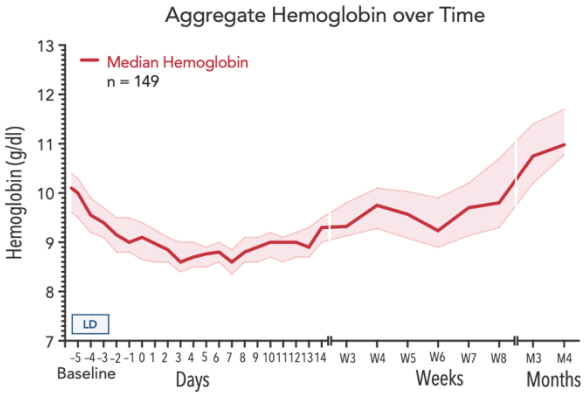
- Lymphodepleting chemotherapy
- Pre-existing disease and prior chemotherapies
- Baseline cytopenia
- Prolonged post-treatment cytopenia
- Persistent disease following CAR T

Rajeski K, et al. *J Immunother Cancer*. 2022;10(5):e004475.

Cytopenia After CAR T-Cell Therapy Can Be Prolonged





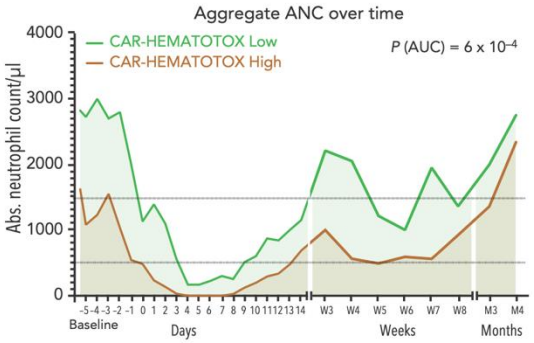


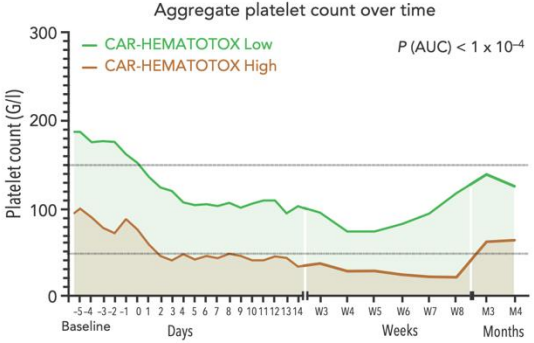
CAR-HEMATOTOX Score

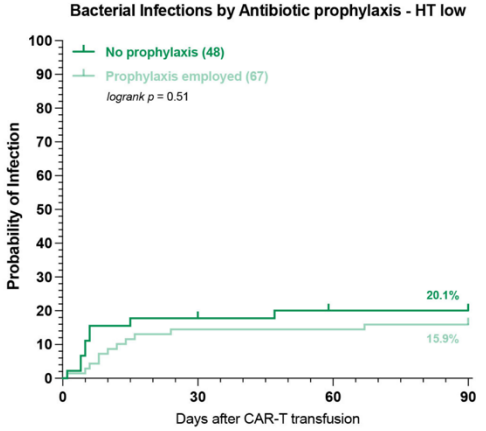
Baseline Features	0 Point	1 Point	2 Points
Platelet Count	> 175,000/µl	75,000 – 175,000/µl	< 75,000/µl
Absolute Neutrophil Count (ANC)	> 1200/µl	< 1200/µl	-
Hemoglobin	> 9.0 g/dl	< 9.0 g/dl	-
C-reactive protein (CRP)	< 3.0 mg/dl	> 3.0 mg/dl	-
Ferritin	< 650 ng/ml	650 – 2000 ng/ml	> 2000 ng/ml
Low: 0-1	**High: ≥ 2**		

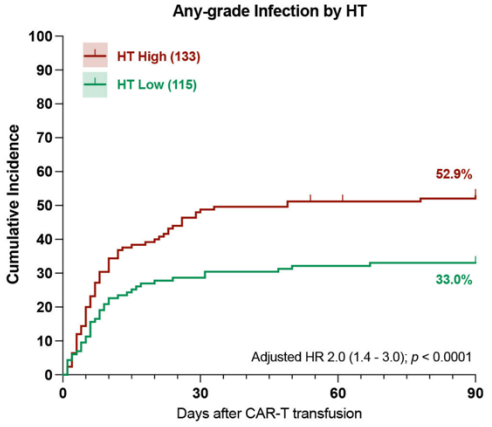
Rajeski K, et al. *Blood.* 2021;138(24):2499-2513.

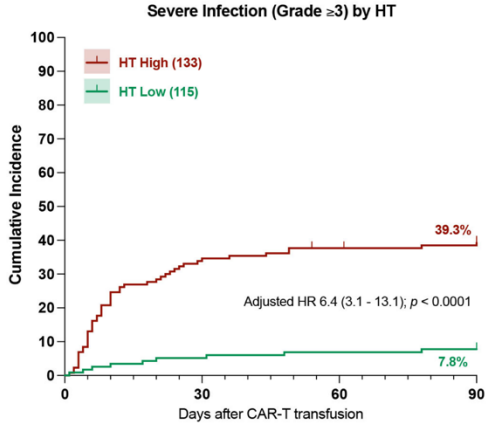
CAR-HEMATOTOX Score Can Predict High-Risk Patients for Cytopenia and Infections

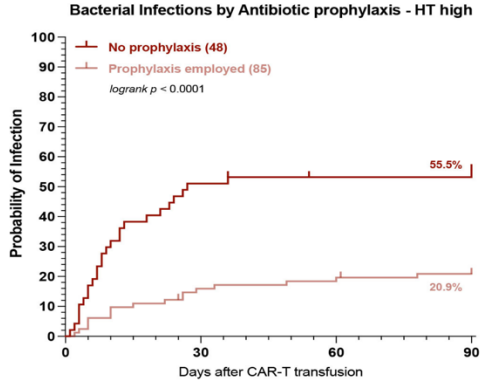












Rajeski K, et al. *J Immunother Cancer.* 2022;10(5):e004475; Rajeski K, et al. *Blood.* 2021;138(24):2499-2513.

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Current and future role of transplantation in acute leukemias in Asia-Pacific

Shaun Fleming

APTITUDE HEALTH®

Current and Future Role of Transplantation in Acute Leukemias

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Disclosures

Consultancy/advisory board participation/honoraria

- Amgen
- Novartis
- Servier
- AbbVie
- Pfizer
- Gilead
- BMS

Research grants

- Amgen


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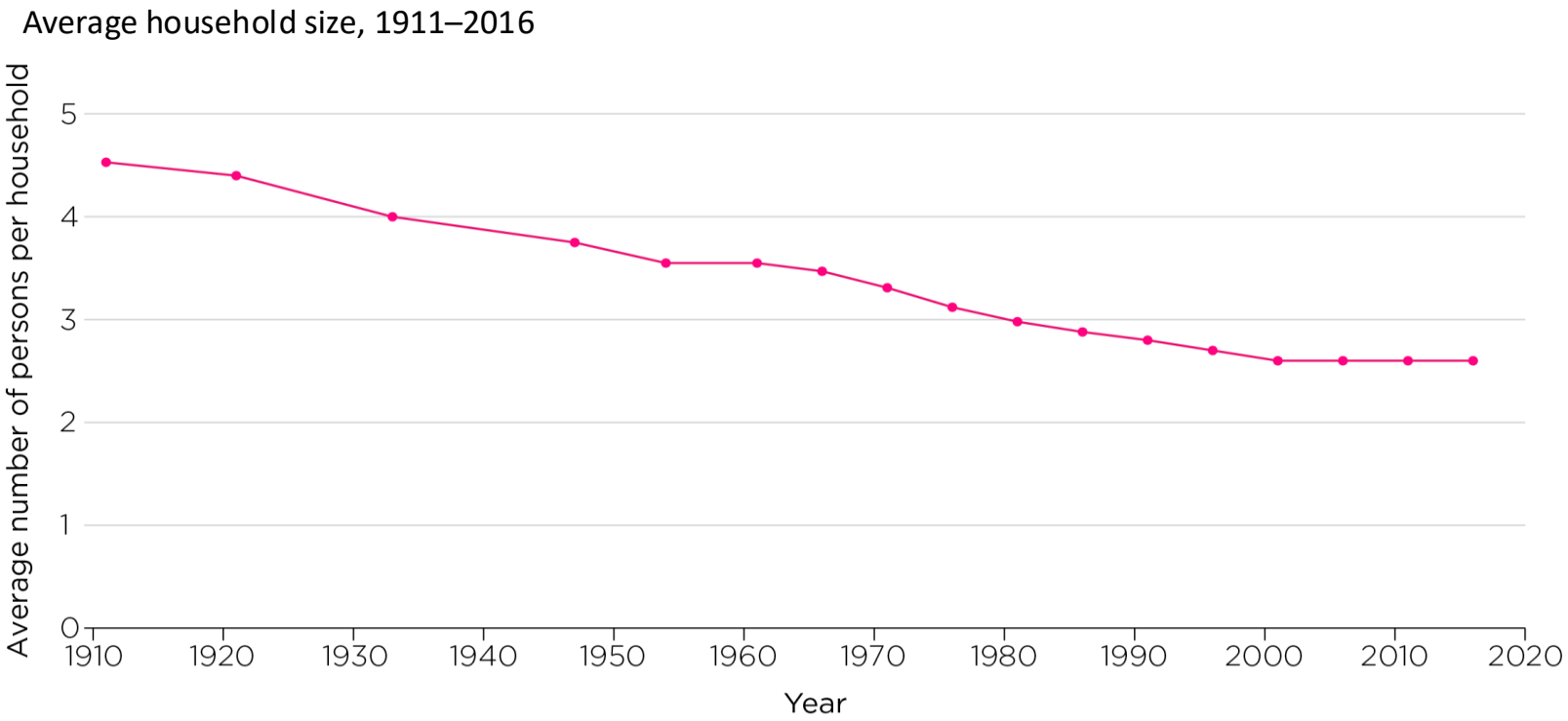
The Balance Is Shifting in Allo-HSCT, but Not Universally

- Ongoing impact of TRM
- Availability of new drugs in frontline and relapsed disease
- CAR T

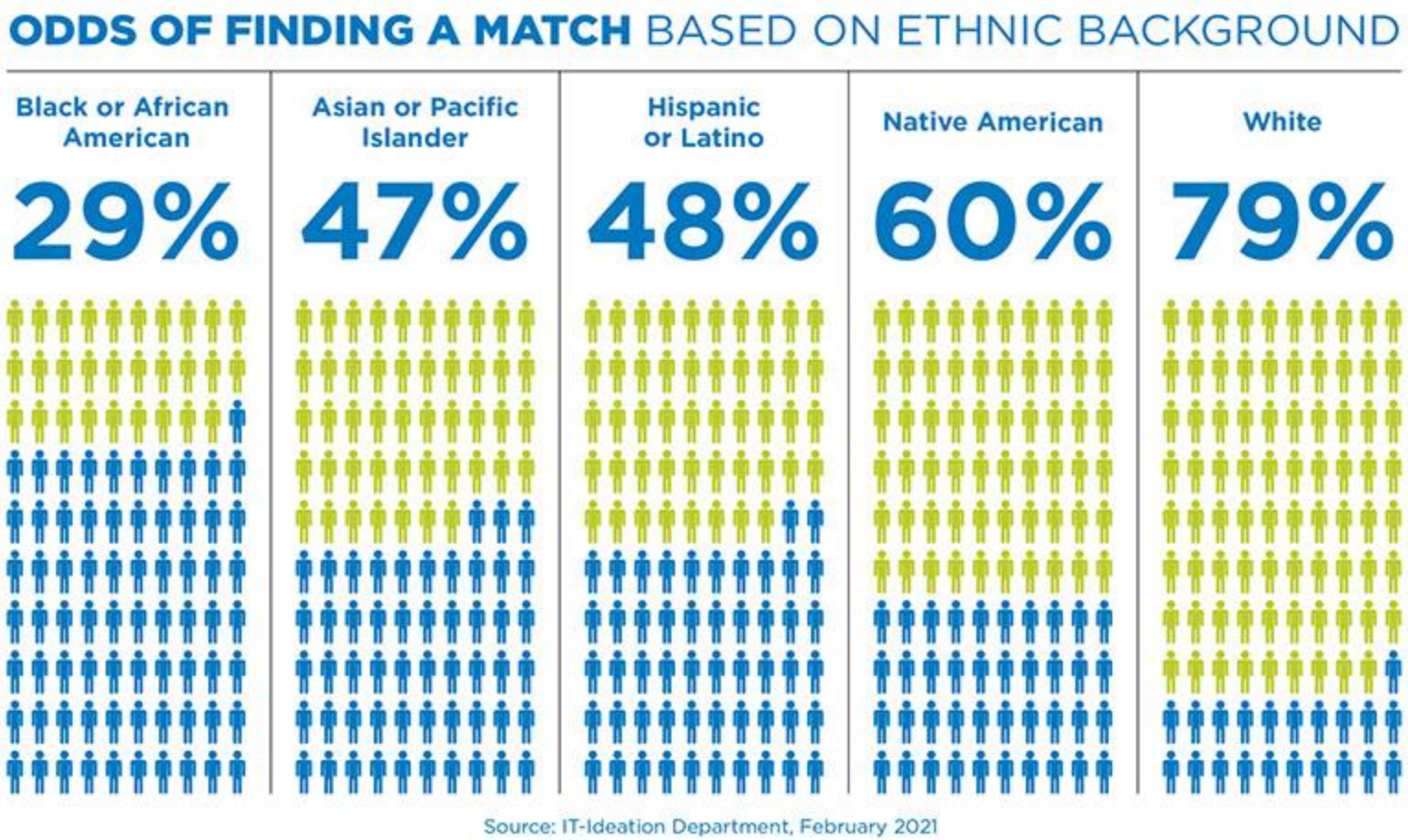
- Remains highly effective at controlling leukemia – can we make that even better?
- More access to donors through haploidentical transplantation
- New approaches to GVHD prophylaxis

Expanding the Donor Pool: Haploidentical Transplantation

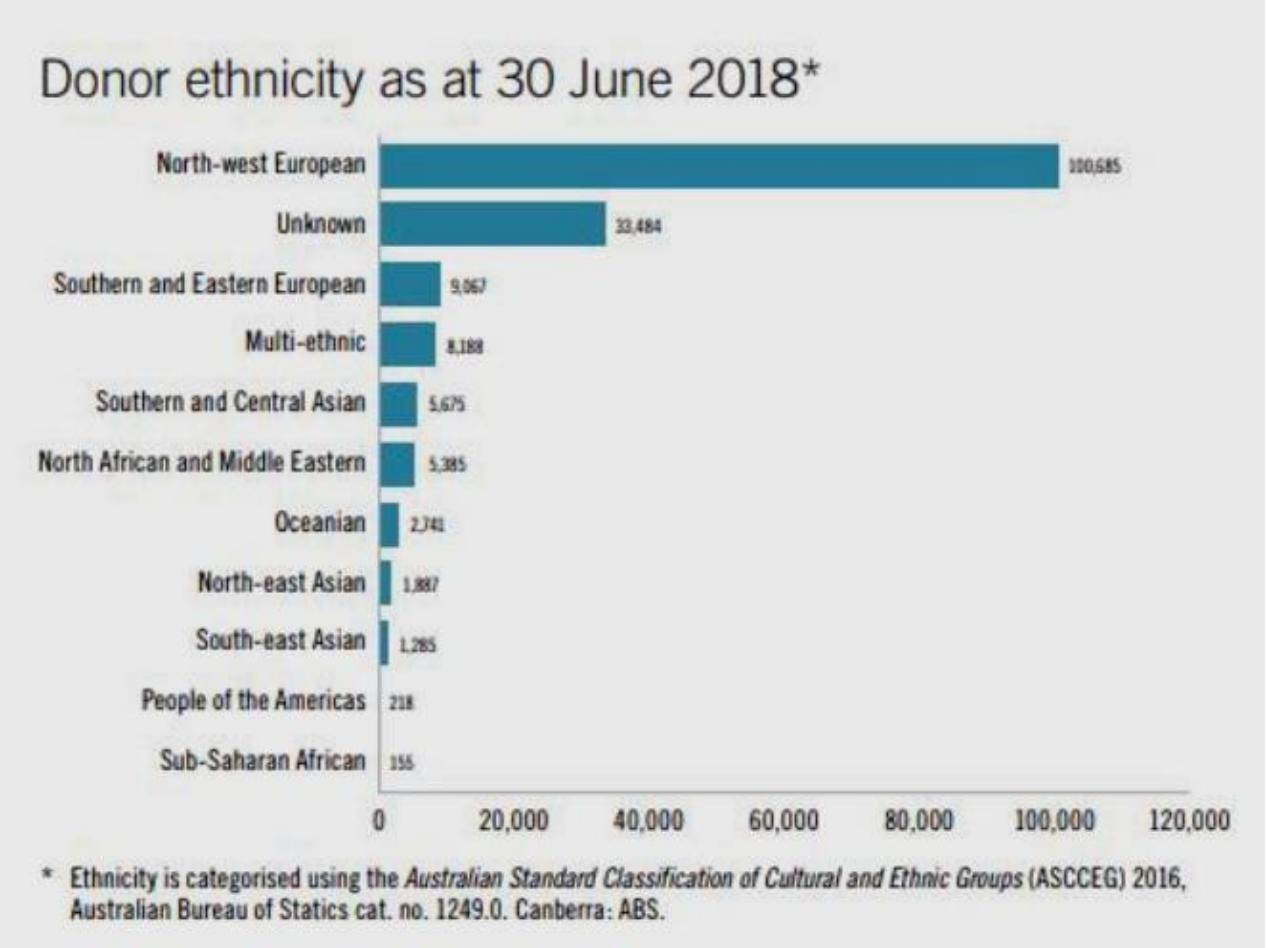
Families Are Getting Smaller – Fewer Sibling Donors



Australian Institute of Family Studies. Population and Households. Accessed Sep 7, 2023.
https://aifs.gov.au/research/facts-and-figures/population-and-households

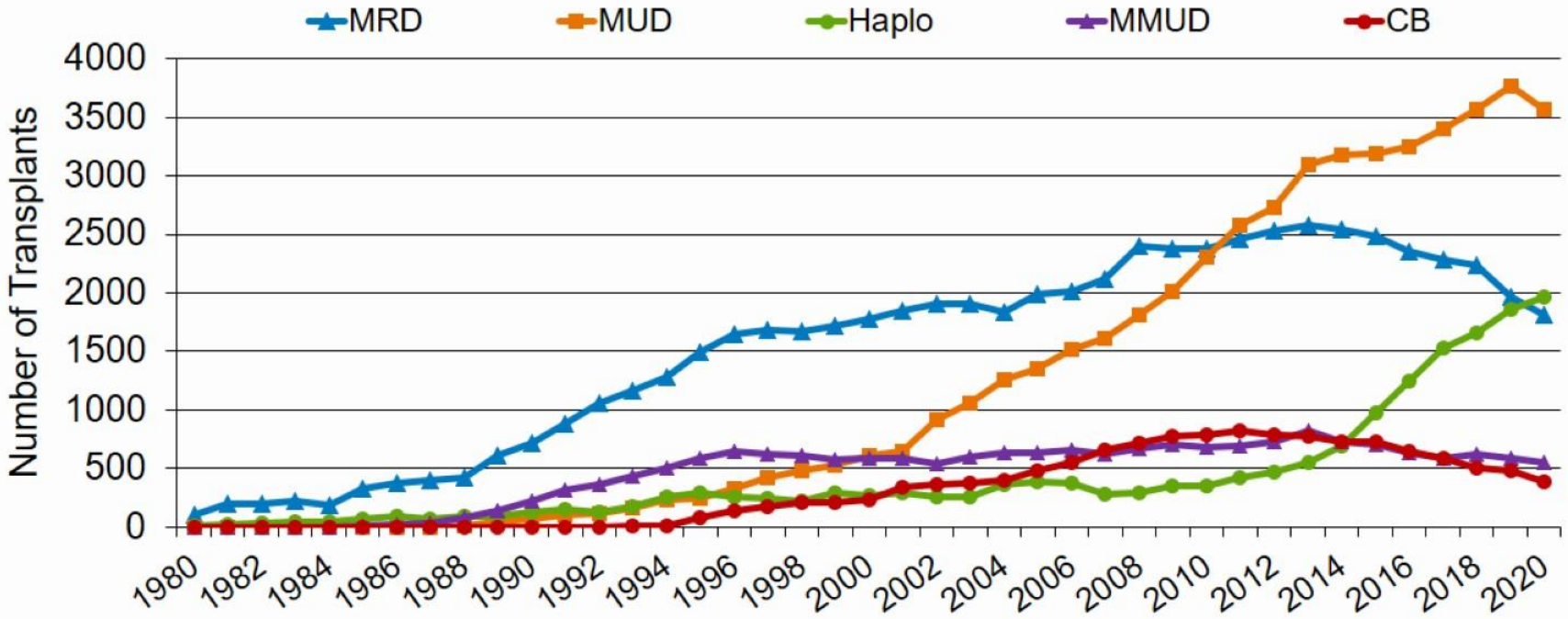


Be the Match. Accessed Sep 7, 2023. https://www.bethematchhosa.org/



Miles D. ABC News. Oct 1, 2019. Accessed Sep 7, 2023.
https://www.abc.net.au/news/2019-10-02/donor-registry-plea-for-ethnic-diversity-to-save-cancer-patients/11563250

Number of Allogeneic HCTs in the US by Donor Type



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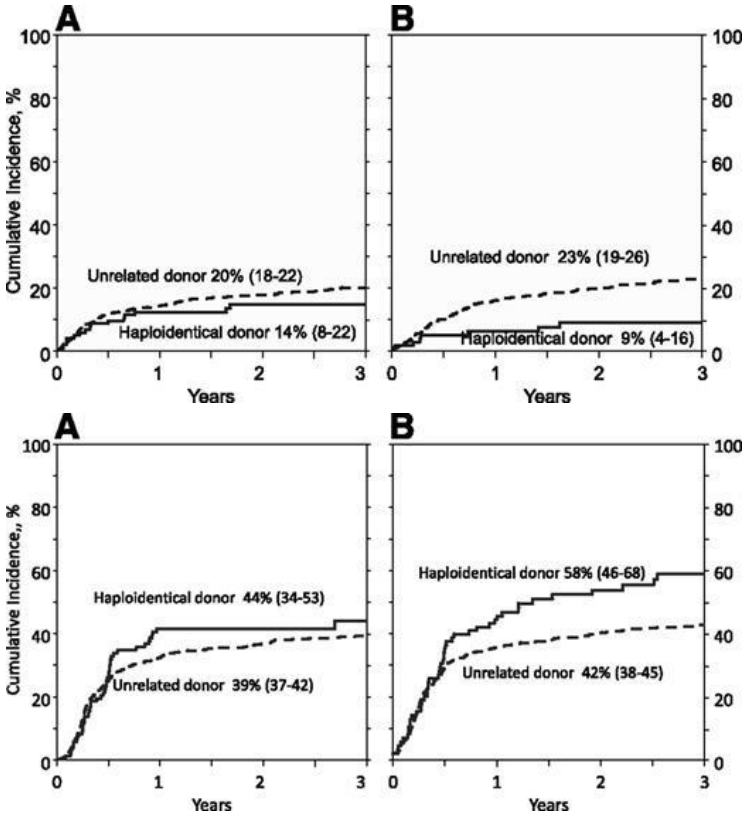
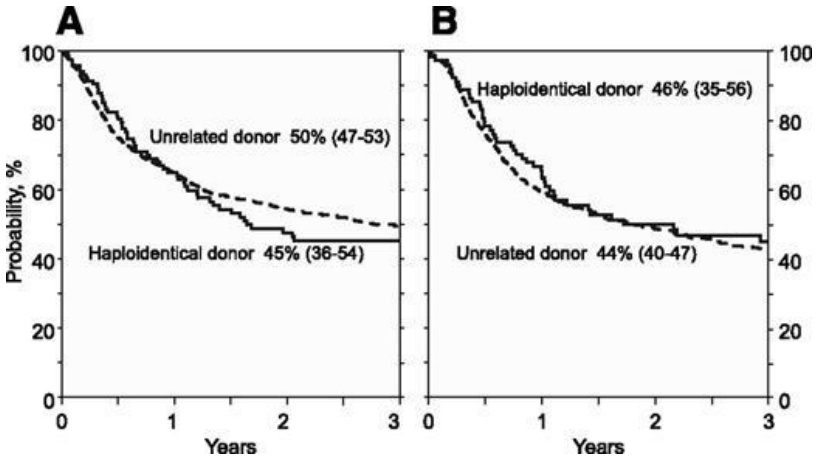
Abbreviations - MRD: Matched related donor; MUD: Matched unrelated donor;
Haplo: Haploidentical donor (includes all mismatched related donors); MMUD: Mismatched unrelated donor; CB: Cord blood

Haplo vs VUD Donors in Acute Leukemia

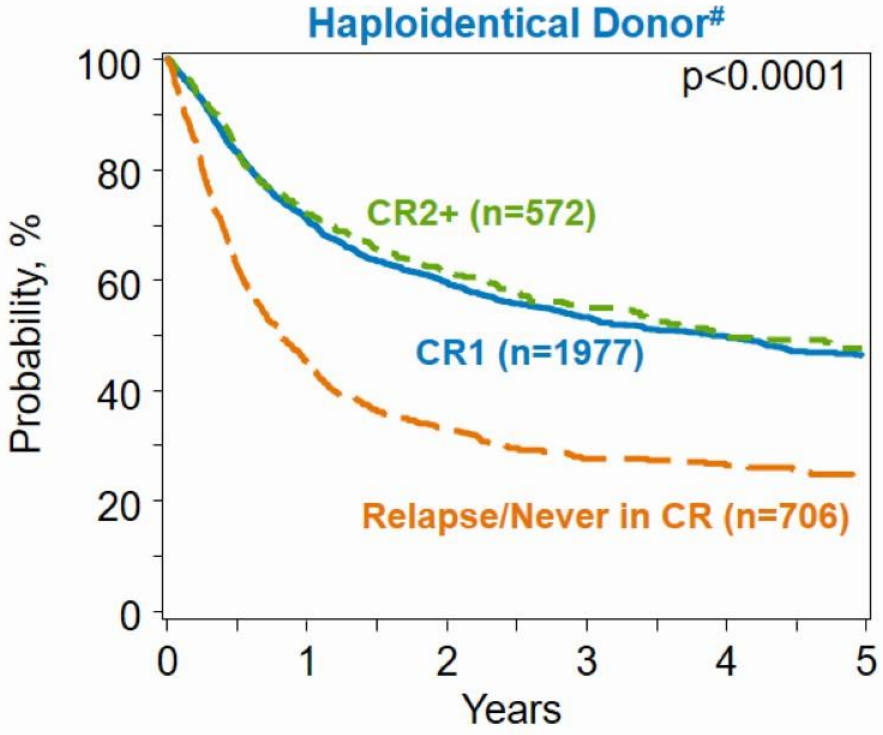


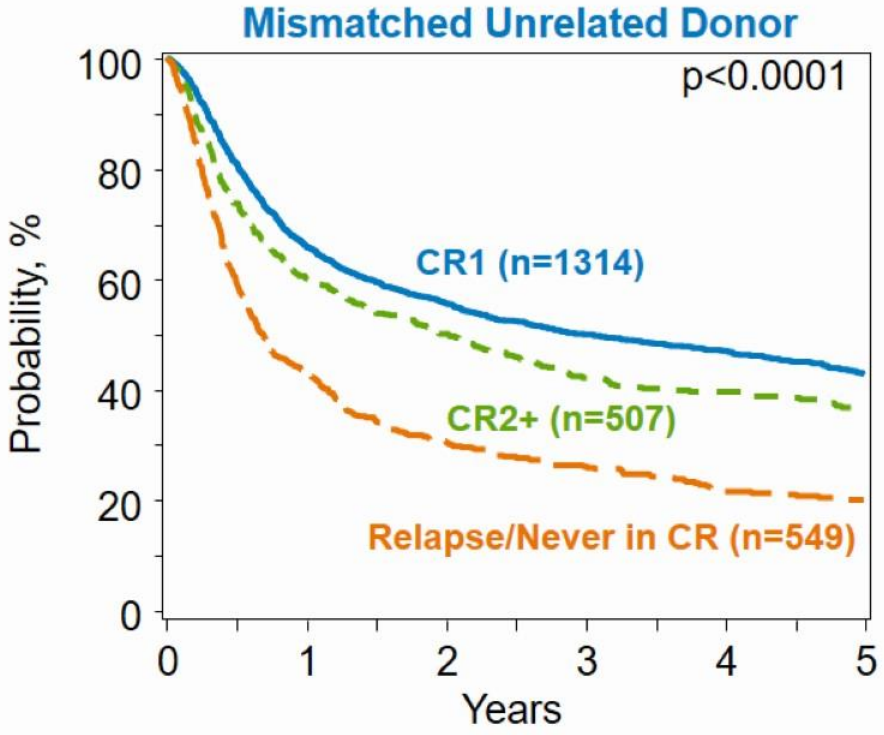
- Ciurea et al compared patients receiving haploidentical transplants with unrelated donor transplants
  - 192 haplos vs 1982 VUDs



Ciurea SO, et al. *Blood*. 2015;126:1033-1040.

Survival after Allogeneic HCTs for Acute Myelogenous Leukemia (AML), Using Mismatched Donors, Age ≥18 Years, in the US, 2009-2019





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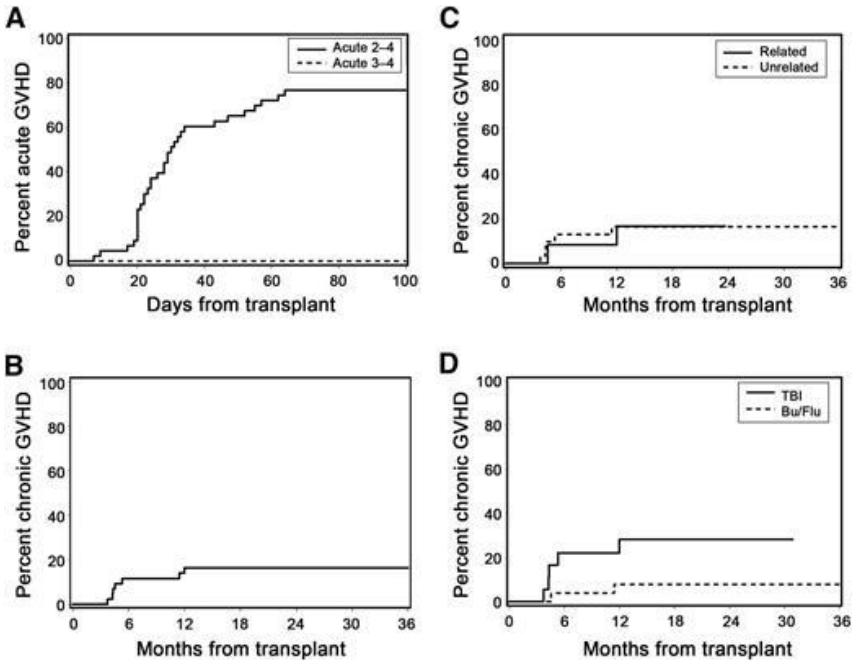
#includes all mismatched related donors; Abbreviation – CR: Complete remission

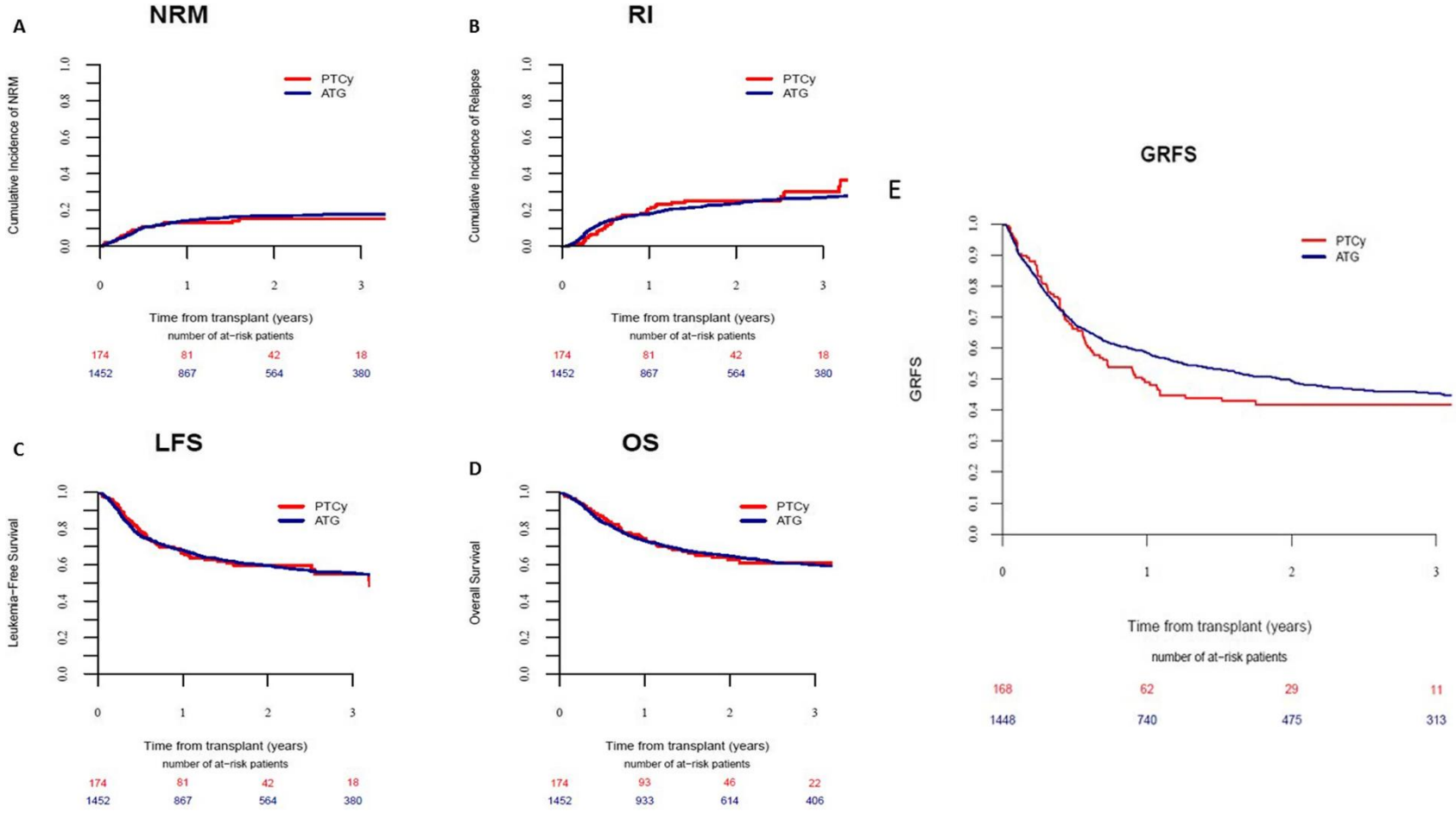
Post-Transplant Cyclophosphamide (PTCy) in Non-Haplo Transplants

Use of PTCy With Matched Grafts

- Mielcarek et al explored the use of PTCy with matched grafts (either sib or 10/10 VUD)
  - Demonstrated deliverability of PTCy with non-haplo transplants
  - Low rates of acute graft-versus-host disease (GVHD) and chronic GVHD
  - Survival outcomes were good, suggesting this is a valid strategy for further evaluation

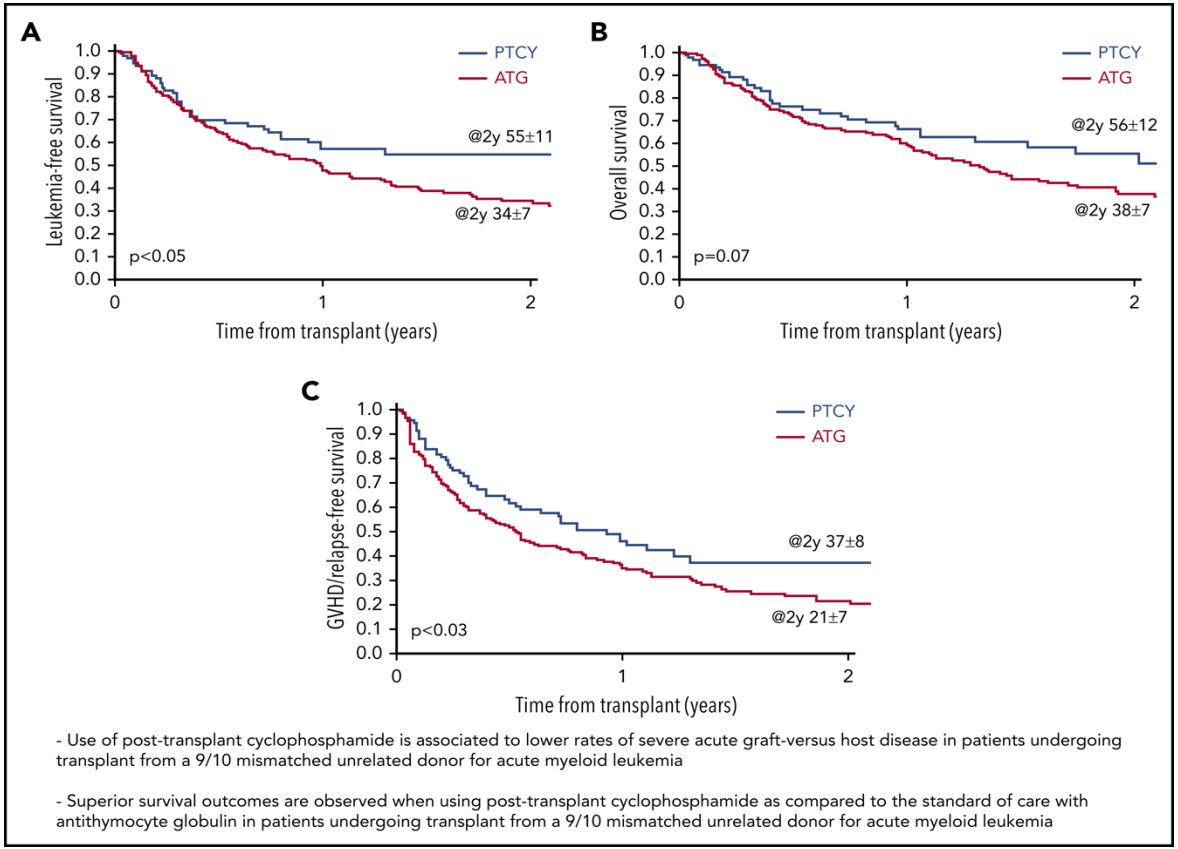


Mielcarek M, et. *Blood*. 2016;127:1502-1508.



Brissot E, et al. *J Hematol Oncol.* 2020;13:87.

If PTCy Allows Overcoming Haplotype Mismatched, What About 9/10 VUDs?

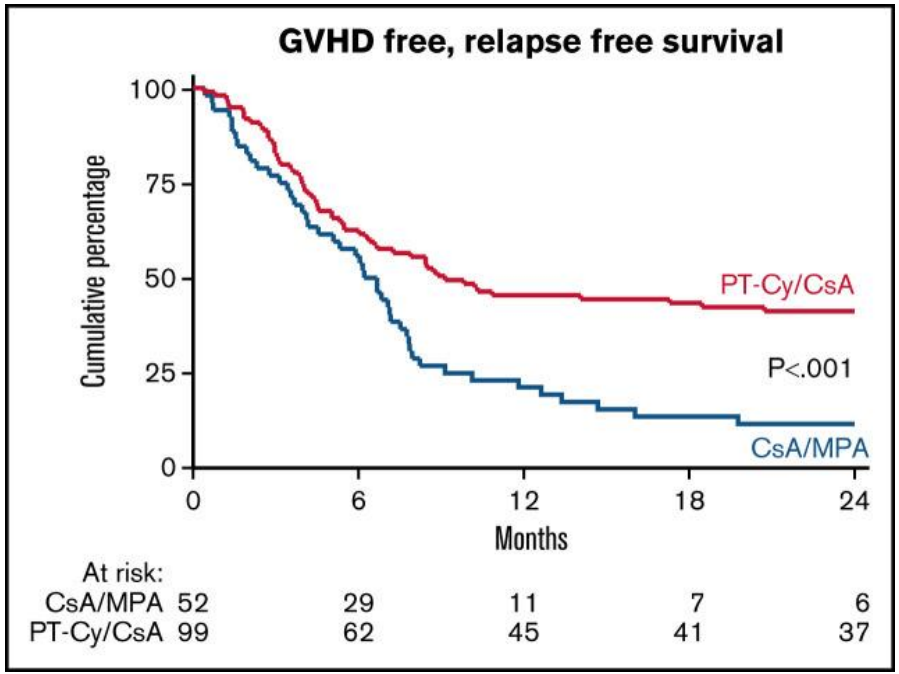


- Use of post-transplant cyclophosphamide is associated to lower rates of severe acute graft-versus host disease in patients undergoing transplant from a 9/10 mismatched unrelated donor for acute myeloid leukemia

- Superior survival outcomes are observed when using post-transplant cyclophosphamide as compared to the standard of care with antithymocyte globulin in patients undergoing transplant from a 9/10 mismatched unrelated donor for acute myeloid leukemia

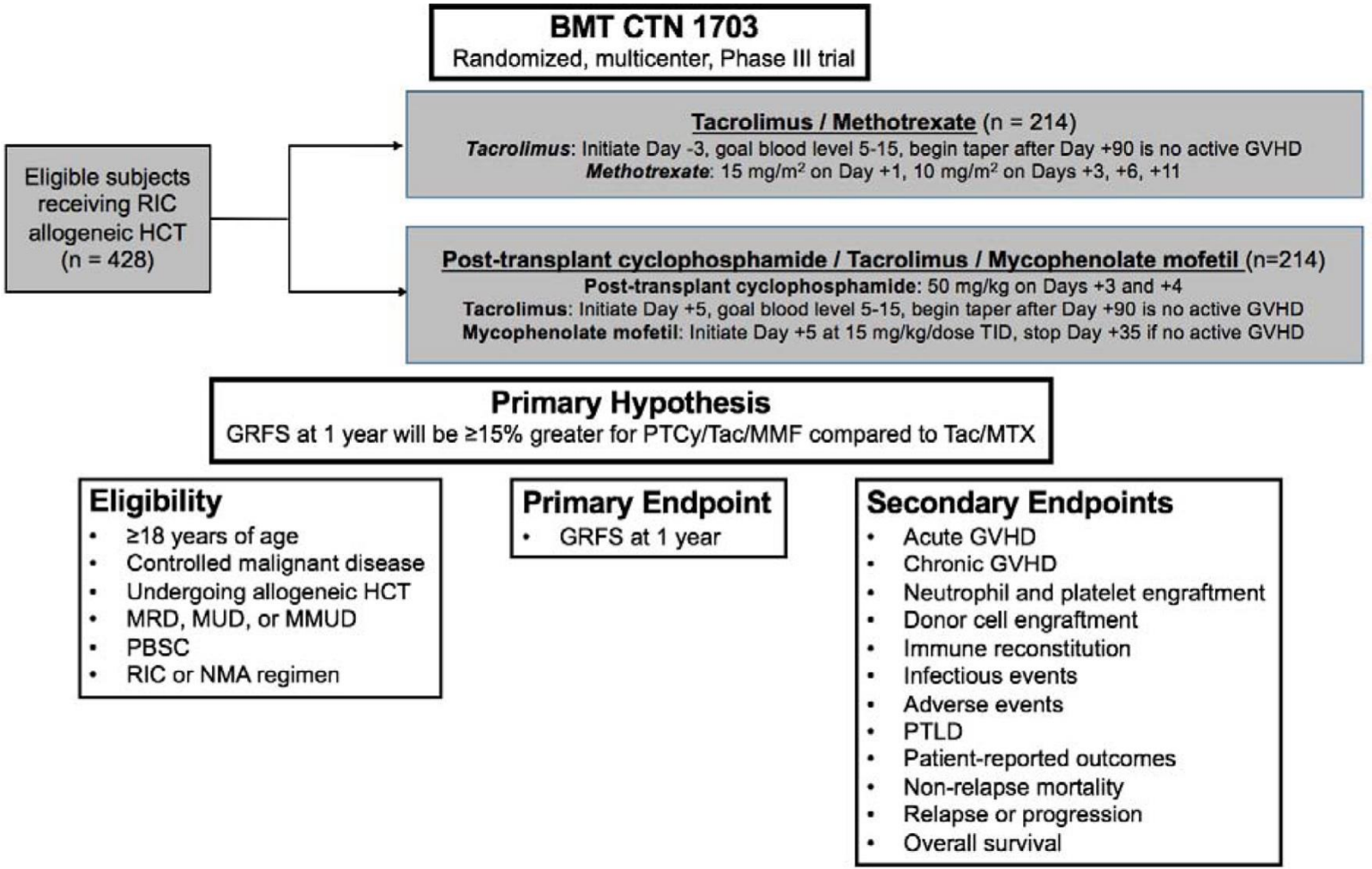
Battipaglia B, et al. *Blood*. 2021;134:892-899.

HOVON-96 Study: PTCy vs SOC



- HOVON-96 study randomized 151 patients to receive PTCy + CsA vs SOC (MTX + CsA) immunosuppression
  - Lower rates of Gr II–IV aGVHD (30% vs 48%, *P* = .007)
  - Lower rates of extensive cGVHD (16% vs 48%, *P* <.001)
  - Similar EFS, OS across both modalities

Broers AEC, et al. *Blood Adv.* 2022;6:3378-3385.



Bolaños-Meade J, et al. *N Engl J Med*. 2023;388:2338-2348.

CAST Study: ALLG BM12

- Randomized study
  - 134 adult patients with AML, ALL, or MDS
  - Available sibling donor
  - Receiving either MAC or RIC transplant with defined regimens
- Currently enrolling in 8 Australian and 2 NZ sites
- 73 patients randomized to January 2022
- Plan to complete accrual by 2023

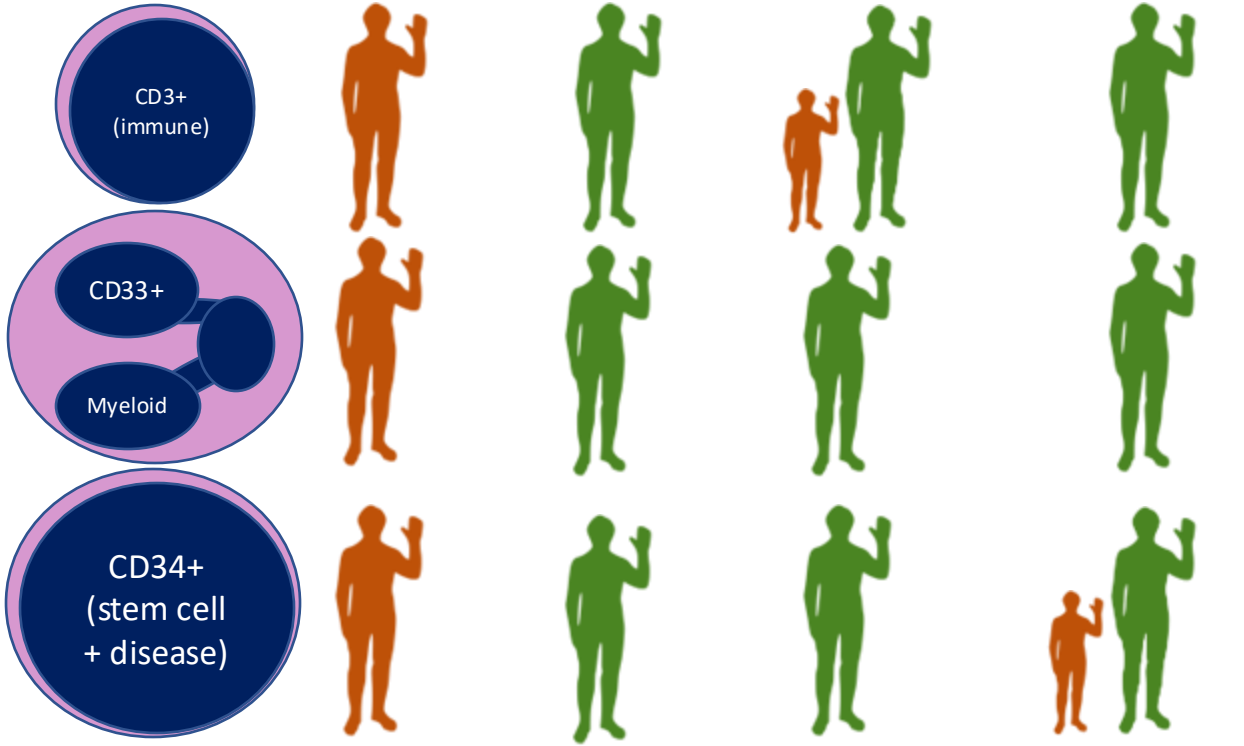
Source: allg.org.au

Conclusion: PTCy

- PTCy reduces rates of severe GVHD when compared with standard immunosuppression in non-haplo transplants
  - Caveat of the possible impact of in vivo T-cell depletion with ATG
  - Outcomes at least equivalent; however, most data here are based on BM as donor source, where GVHD rates are lower
- Current trials overseas and in Australia are exploring the use of PTCy as immunosuppression

CD34+ Chimerism

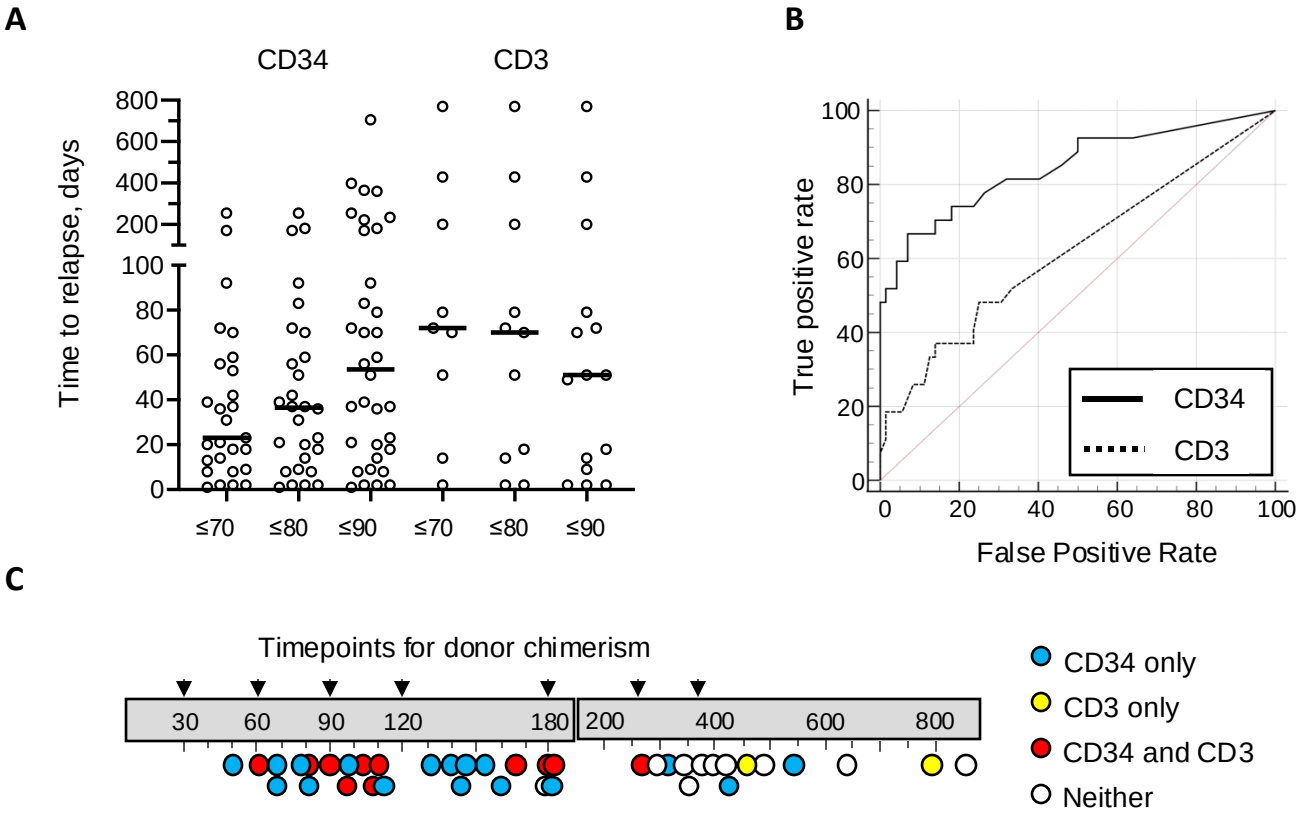
Chimerism Analysis



Chimerism analysis: Tongted Das, PhD, Clinical Haematology, Alfred Health

Total, n	134
Median age, yr (range)	52 (19–70)
Male, n (%)	75 (56)
Indication, n	
AML (Fav, Int, Adv, Unk)	115 (19, 56, 39, 1)
MDS	19
CD34 expression, n (%)	98 (85)
Stage of AML at BMT, n (%)	
CR	98 (85)
Conditioning, n (%)	
MAC	68 (51)
RIC	51 (38)
NMA	15 (11)
Donor, n (%)	
Matched related	56 (42)
Matched unrelated	72 (54)
Cord/mismatch	6 (4)
TCD (%)	76 (57)
ATG/Campath/PTCy, n	40/13/23
Median follow-up, d (range)	508 (41–2973)
Relapse, n	40
Death, n	66
Infection/GVHD, n	34
Disease, n	27
Other, n	5

Unpublished data



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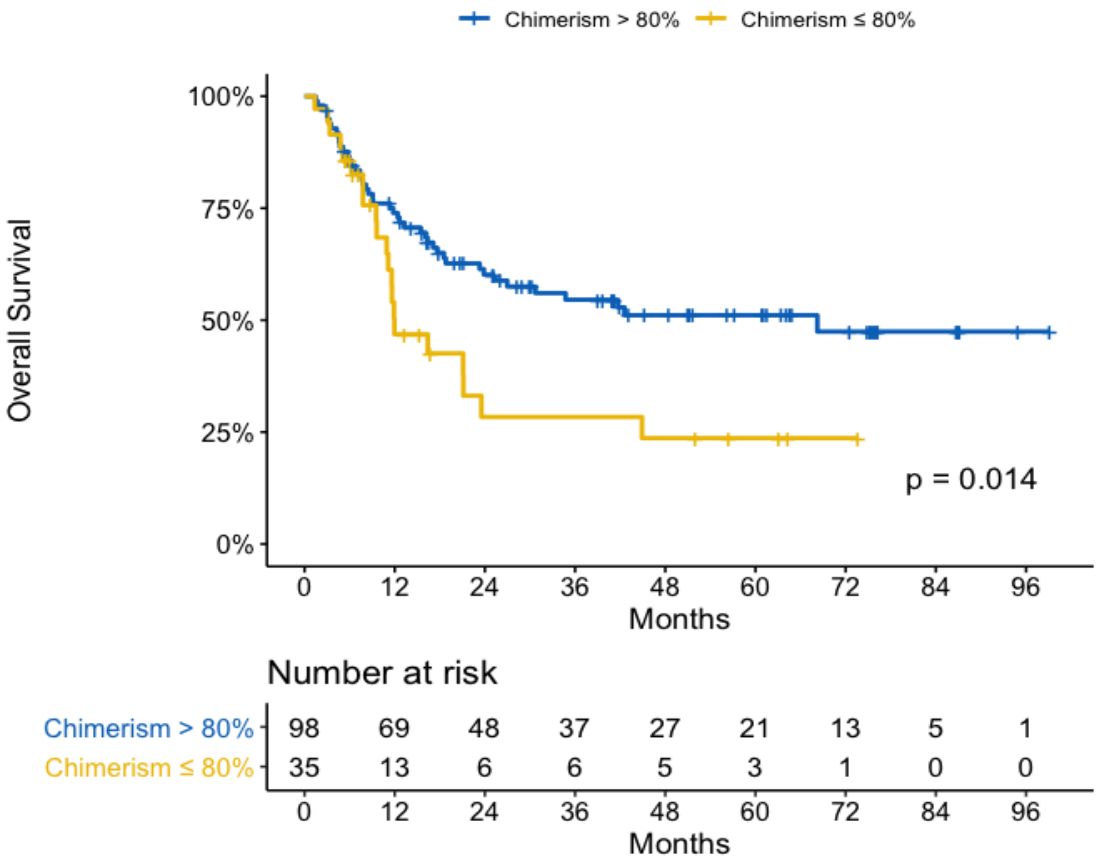

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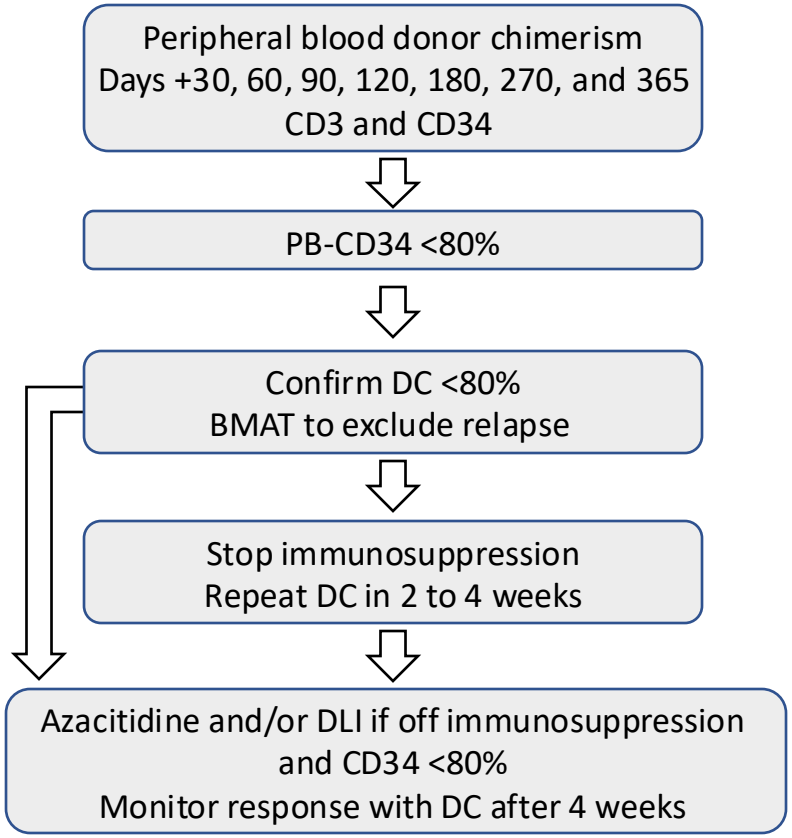
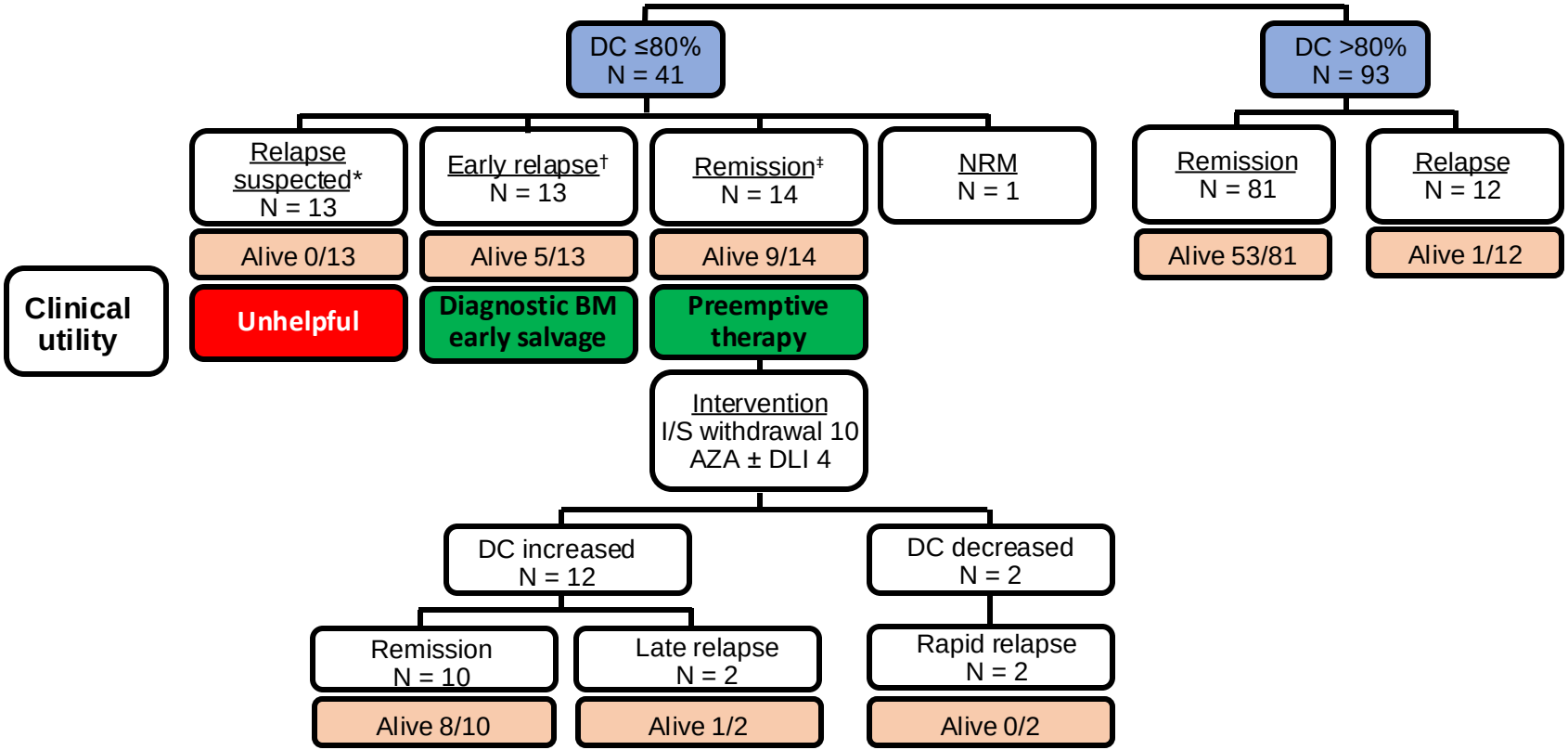

Peripheral blood donor chimerism
Days +30, 60, 90, 120, 180, 270, and 365
CD3 and CD34
PB-CD34 <80%
Confirm DC <80%
BMAT to exclude relapse
Stop immunosuppression
Repeat DC in 2 to 4 weeks
Azacitidine and/or DLI if off immunosuppression
and CD34 <80%
Monitor response with DC after 4 weeks



*Circulating blasts and/or new cytopenias attributable to morphologic relapse;
†Normal peripheral blood counts, but either morphologic relapse or MRD in the bone marrow;
‡Morphologic remission and no MRD where available.

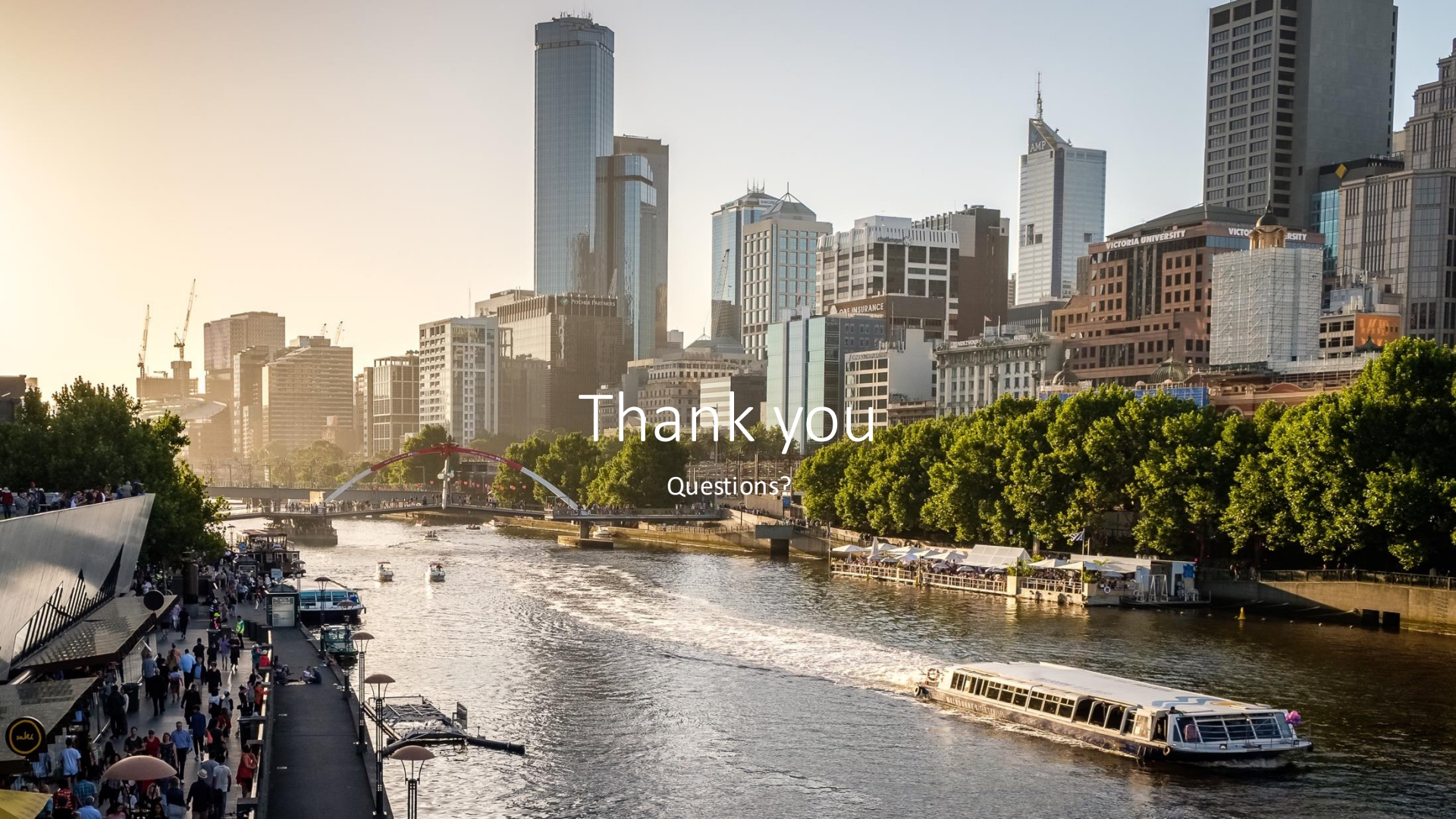
Das et al. *Transplant Cell Ther.* 2023.

Conclusion: CD34+ Chimerism

- CD34+ chimerism provides a reliable and broadly applicable method to detect imminent relapse following allogeneic stem cell transplant
- The 80% cutoff maximizes sensitivity and specificity for detection of disease relapse
- Most relapses are detected by earlier timepoints – calls into question the need for later chimerism monitoring
- Withdrawal of immunosuppression and intervention with azacitidine ± donor lymphocyte infusion may salvage a proportion of patients

Conclusion

- Transplantation numbers continue to increase globally as the access to donors, advancing age of eligibility for transplant, and increased indications for transplant all lead to increasing numbers
- Haploidentical transplantation has expanded the number of patients who are eligible for transplant and is particularly important in our culturally diverse community with smaller family sizes
- PTCy has allowed us to overcome the HLA-mismatch barrier and may be a superior method of immunoprophylaxis in matched transplants
- CD34+ chimerism monitoring allows early detection of imminent relapse, allowing time for interventions to avert relapse



Thank you

Questions?

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Q&A

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Current treatment options for relapsed AML in adult and elderly patients

Junichiro Yuda

APTITUDE HEALTH

Current treatment options for relapsed AML in adult and elderly patients

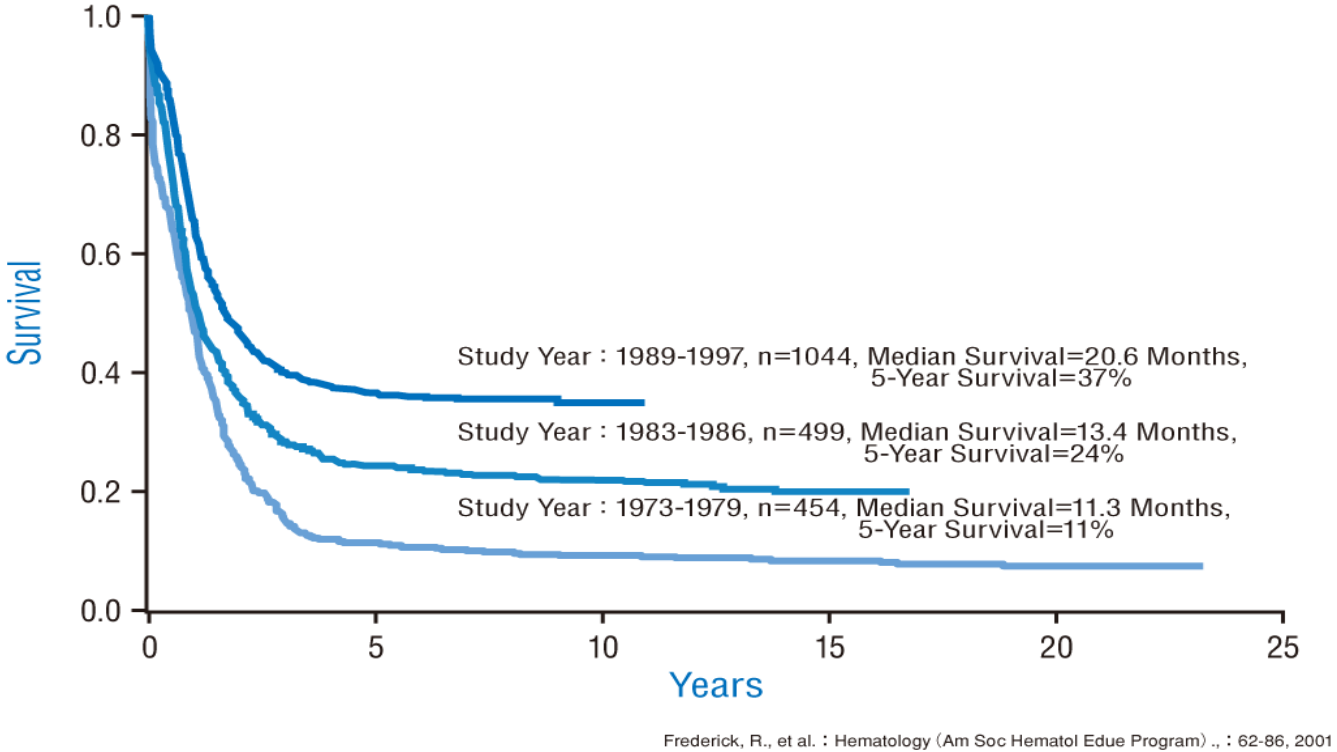
Junichiro Yuda, MD, PhD

National Cancer Center Hospital East
Department of Hematology and Experimental Therapeutics
Hematological Treatment Development Promotion Office,
Department for the Promotion of Drug and Diagnostic Development

2020s

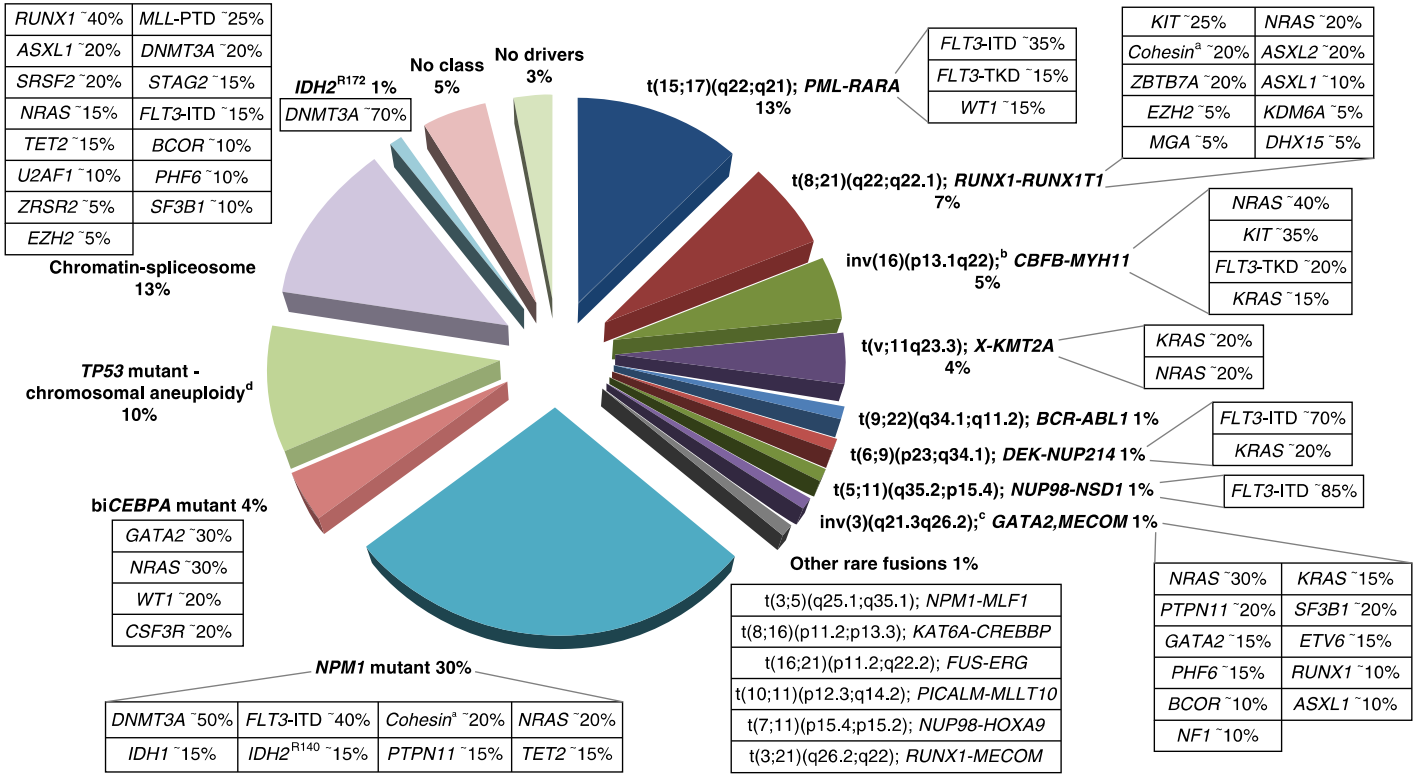
2030s

Changes in treatment outcomes for AML



Frederick, R., et al. : Hematology (Am Soc Hematol Edue Program)., : 62-86, 2001

Genetic mutations in adult patients with AML



Döhner H, et al. *Blood.* 2017;129(4):424-447.

ELN stratification system (2022)

Risk Category[b]	Genetic Abnormality
Favorable	• t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1*[b,c] • inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11*[b,c] • Mutated *NPM1*[b,d] without *FLT3*-ITD • bZIP in-frame mutated *CEBPA*[e]
Intermediate	• Mutated *NPM1*[b,d] with *FLT3*-ITD • Wild-type *NPM1* with *FLT3*-ITD • t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A*[b,f] • Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	• t(6;9)(p23;q34.1)/*DEK*::*NUP214* • t(v;11q23.3)/*KMT2A*-rearranged[g] • t(9;22)(q34.1;q11.2)/*BCR*::*ABL1* • t(8;16)(p11;p13)/*KAT6A*::*CREBBP* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*, *MECOM(EVI1)* • t(3q26.2;v)/*MECOM*(*EVI1*)-rearranged • -5 or del(5q); -7; -17/abn(17p) • Complex karyotype,[h] monosomal karyotype[i] • Mutated *ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, or ZRSR2*[j] • Mutated *TP53*[k]

Döhner H, et al. *Blood*. 2022;140(12):1345-1377.

NCCN Guidelines Version 3.2024
Acute Myeloid Leukemia (Age ≥18 years)

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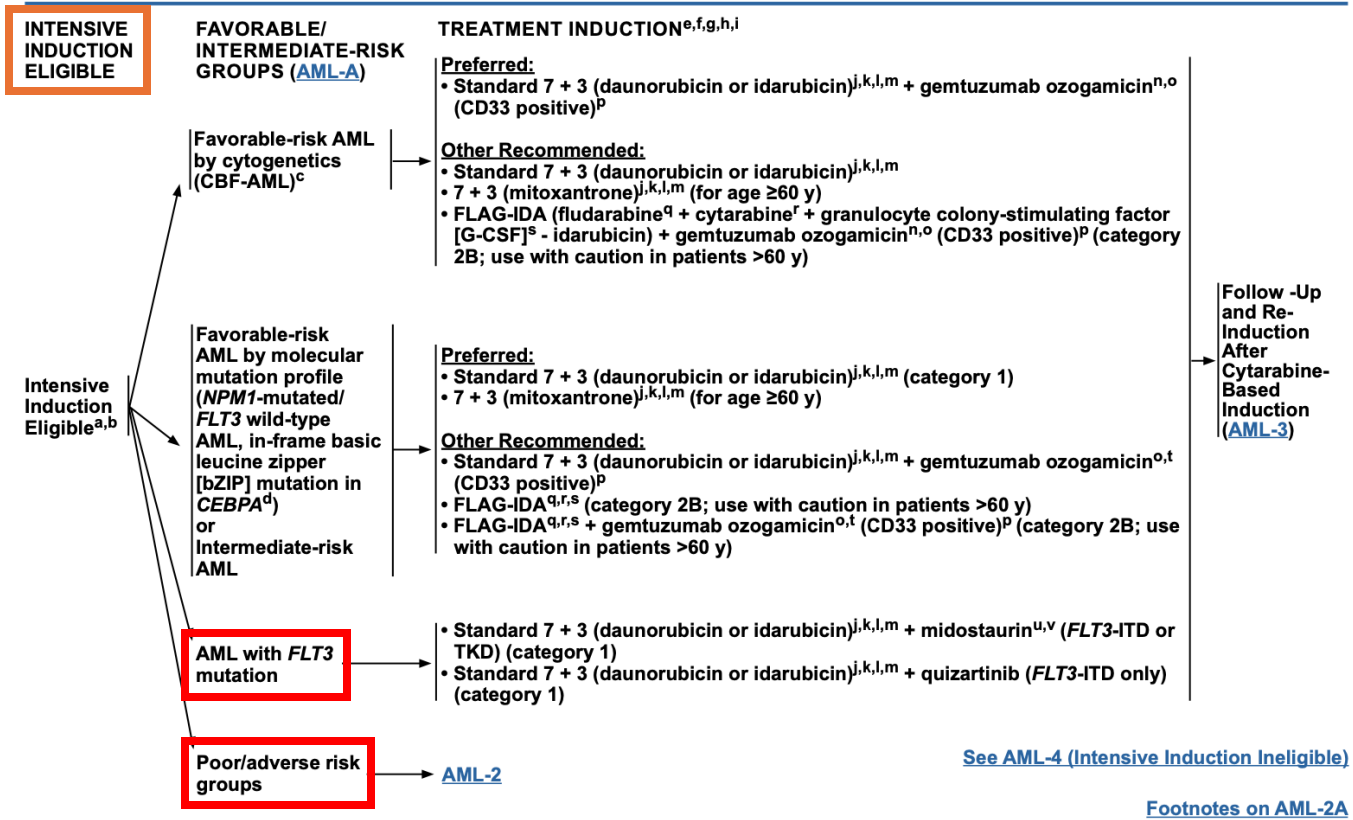
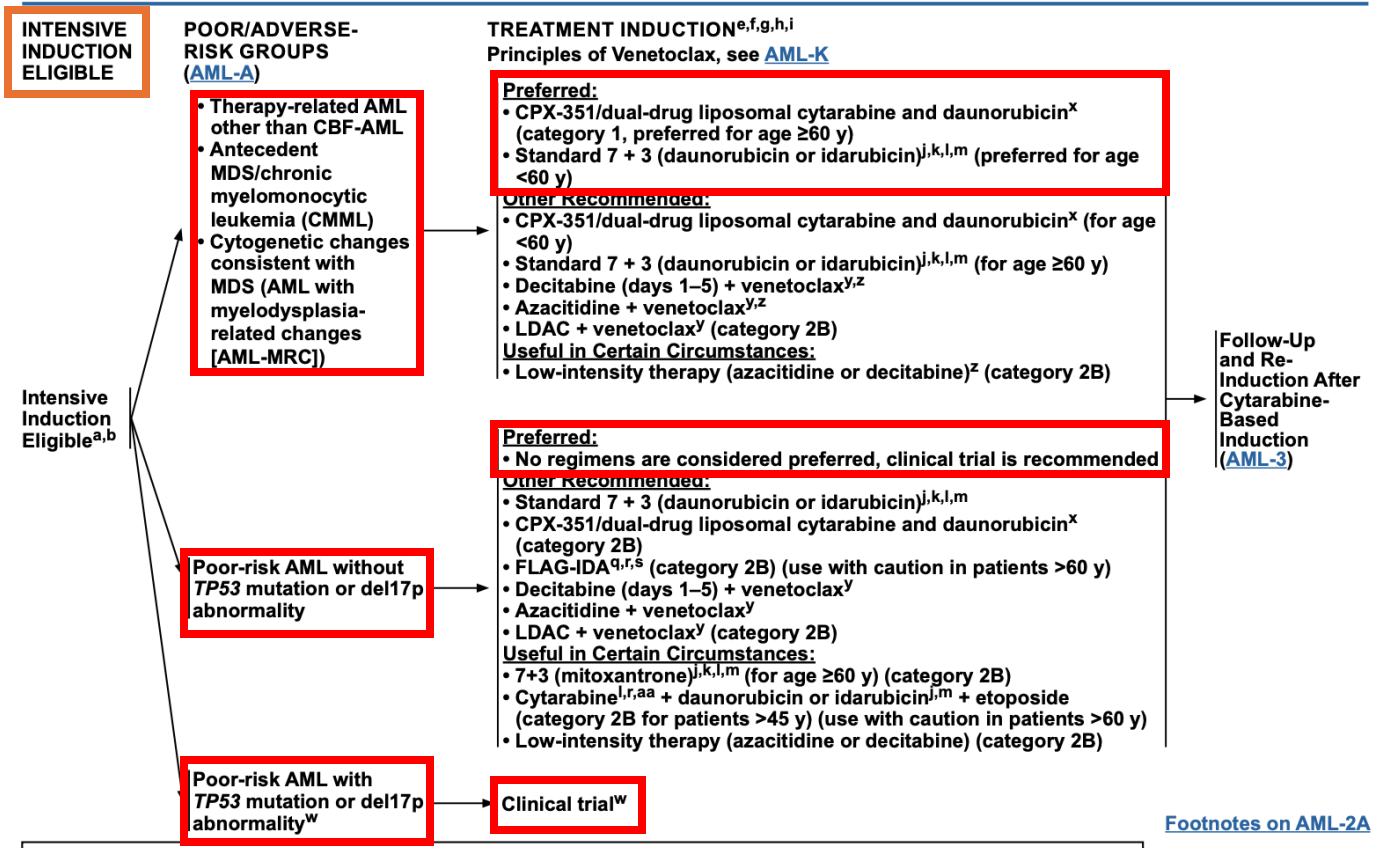


See AML-4 (Intensive Induction Ineligible)

Footnotes on AML-2A

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



Footnotes on AML-2A

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Version 3.2024
Acute Myeloid Leukemia (Age ≥18 years)

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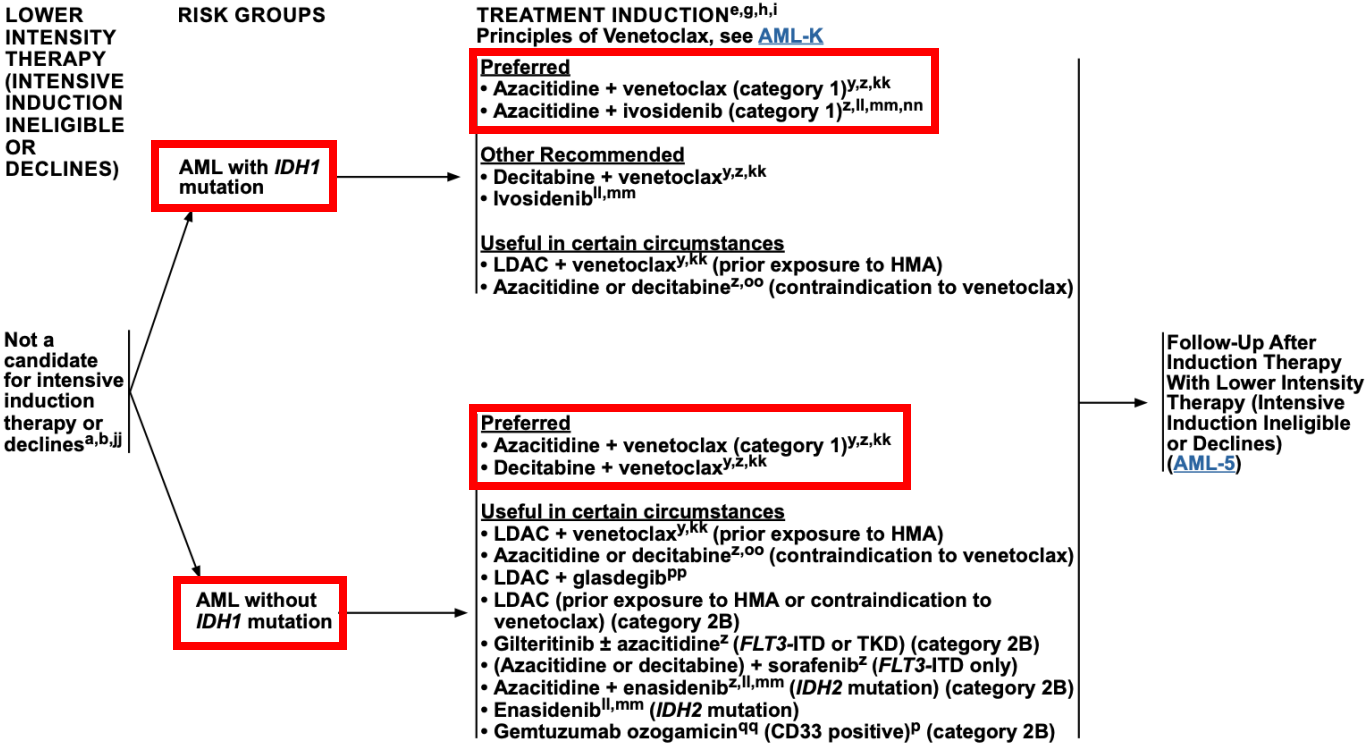
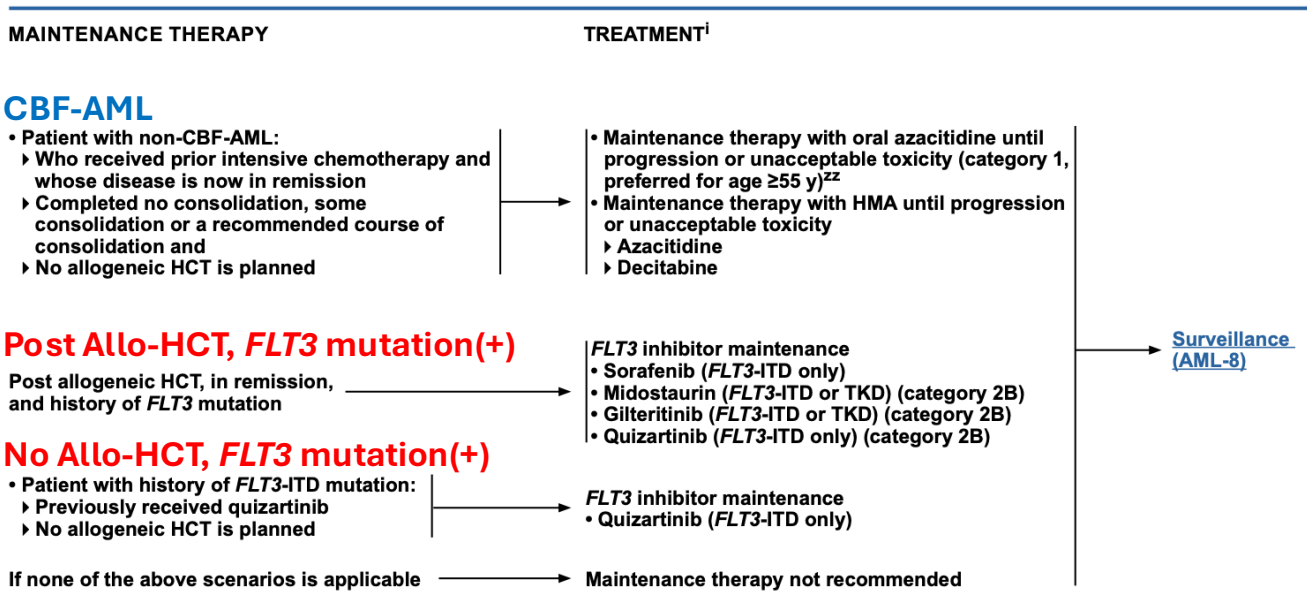


Footnotes on AML-4A

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

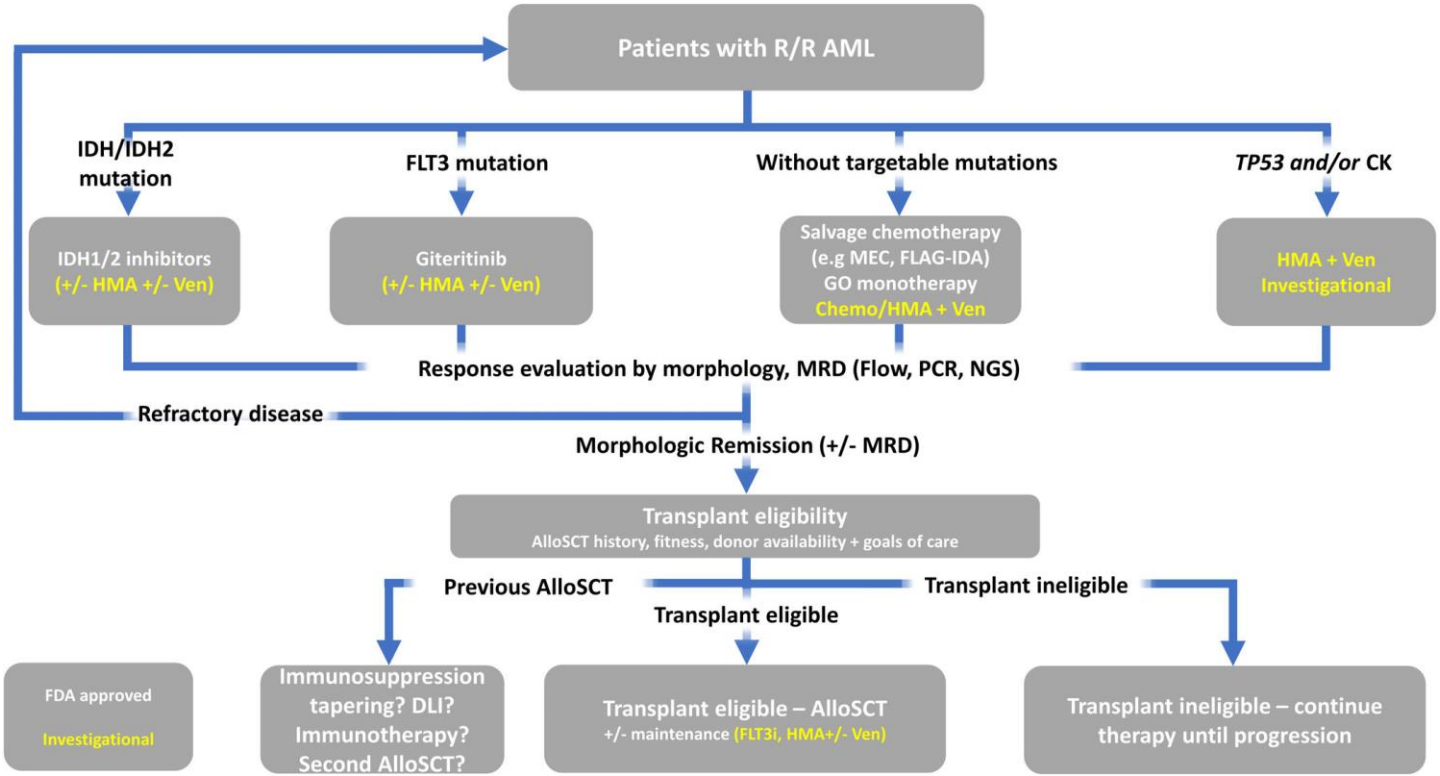


[i] See Principles of Systemic Therapy (AML-E).

[zz] This is not intended to replace consolidation chemotherapy. In addition, patients who are fit may benefit from HCT in first CR, and there are no data to suggest that maintenance therapy with oral azacitidine can replace HCT. The panel also notes that the trial did not include patients <55 years of age or those with *CBF*-AML; it was restricted to patients ≥55 years of age with AML with intermediate or adverse cytogenetics who were not felt to be candidates for HCT. Most patients received at least 1 cycle of consolidation prior to starting oral azacitidine. Wei AH, et al. N Engl J Med 2020;383:2526-2537.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Treatment algorithm for patients with relapsed or refractory AML



Shimony S, et al. *Am J Hematol.* 2023;98(3):502-526.

Selected investigational drugs for AML

Target	Drug	Regimens	Population	Early efficacy outcomes	Ongoing trials
Menin	SNDX-5613 (revumenib)	Monotherapy[183]	R/R *MLL* rearranged or mutated *NPM1* AML	44% composite CR	Phase I-II AUGMENT-101, NCT04065399
	KO-539 (ziftomenib)	Monotherapy[184]		25% CR rates	Phase I-II KOMET-001, NCT04067336
CD 47	Magrolimab	Magrolimab + HMA[185,186]	ND-AML (enriched for *TP53* and high risk)	ORR 69%, 50% CR/CRi	Phase III, *TP53 mutated* AML ENHANCE-2, NCT04778397
			TP53 mutated AML	ORR 49%, CR 33%, median OS 10.8 months	
		Magrolimab + HMA + ven.[187]	ND + R/R AML	CR/CRi 94% in ND CR/CRi 63% in ven naïve; 27% in ven failure	Phase III, ND-AML ENHANCE-3, NCT05079230
TIM-3	Sabatolimab (MBG453)	Sabatolimab+ HMA[188]	ND-AML unfit for intensive chemotherapy	ORR 40%. ORR 54% in *RUNX1/ASXL1/ TP53* mutated AML	Phase Ib, NCT03066648
		Sabatolimab+ HMA + ven[189]	ND-AML unfit for intensive chemotherapy	CR/CRi 67%	Phase II, NCT04150029
E-selectin	Uproleselan[190]	"7 + 3" + Uproleselan	ND-AML ≥60 years fit for intensive therapy	CR/CRi—72%	Phase III ongoing, NCT03701308
		MEC + uproleselan	R/R AML fit for intensive therapy	41% composite CR median OS 8.8 months	Phase III ongoing, NCT03616470
CD123	Tagrasofusp[191]	Tagrasofusp + HMA	ND-AML not fit for intensive therapy, BPDCN, R/R-AML	ND-AML—20% CR/CRi	Phase I, NCT03113643
		Tagrasofusp HMA + Ven		ND-AML—89% CR/CRi.	
	IMGN632	IMGN632 +/− HMA +/− ven[192]	R/R AML	IMGN632 + HMA + Ven 55% ORR, composite CR 31%	Phase Ib/II in both ND and R/R AML, NCT04086264
	Flotetuzumab (DART CD123/CD3)	monotherapy[193]	Refractory or early relapse (<6 mo) AML	CR/CRh/CRi—30%.	2nd generation MGD024 Phase I in R/R AML, NCT05362773

Shimony S, et al. *Am J Hematol.* 2023;98(3):502-526.

Selective MCL-1 inhibitor for AML and myeloma

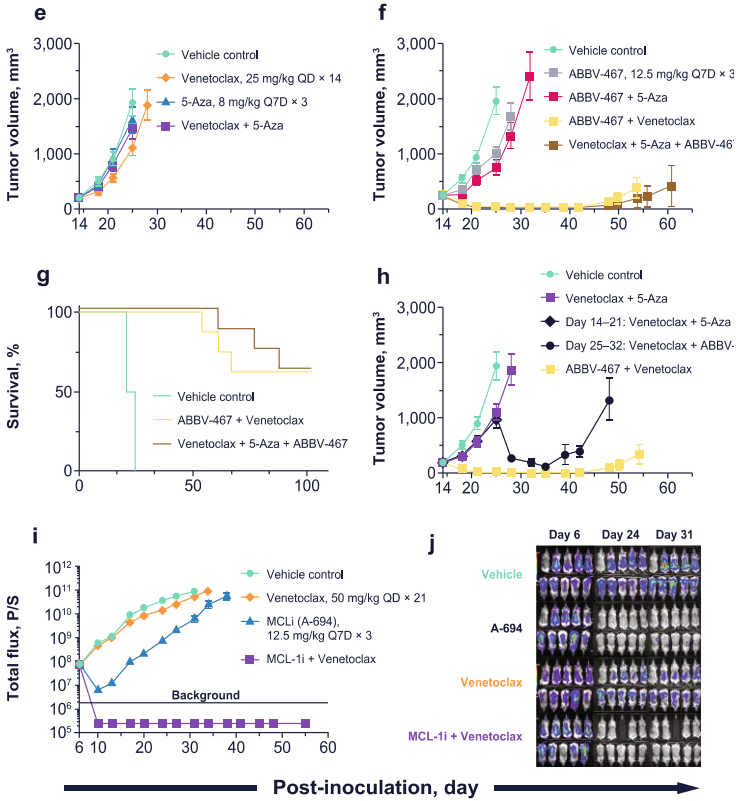


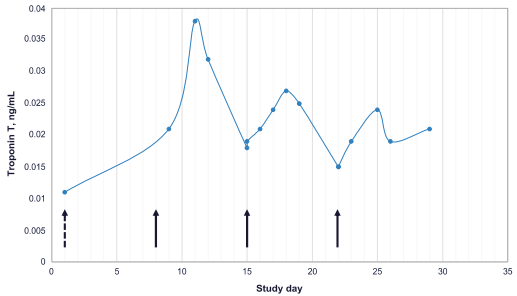
Table 1 Binding affinity of compounds 1, 2, and ABBV-467 to BCL-2 family proteins, and cellular activity of ABBV-467 and other clinical-stage MCL-1 inhibitors in human tumor cell lines.

	TR-FRET, Ki, nM				
	MCL-1	BCL-2	BCL-X_L	BCL-W	BCL2-A1
Binding affinity					
1 (MIK665)	<0.01	599	>660	>468	>468
2	5.54	>1200	>660	NT	NT
ABBV-467	<0.01	>642	>376	>247	>402

	AMO-1 EC_{50} (nM, 10% FBS)	H929 EC_{50} (nM, 10% FBS)	MV4-11 EC_{50} (nM, 10% FBS)	DLD-1 EC_{50} (nM, 10% FBS)
Cellular activity				
ABBV-467	0.16	0.47	3.91	>10,000
MIK665	2.06	4.75	10.87	4750
AMG 176	90.6	195	106	>10,000
AZD5991	22.9	31.7	34.9	>10,000
AMG 397	13.5	13.0	43.6	>10,000

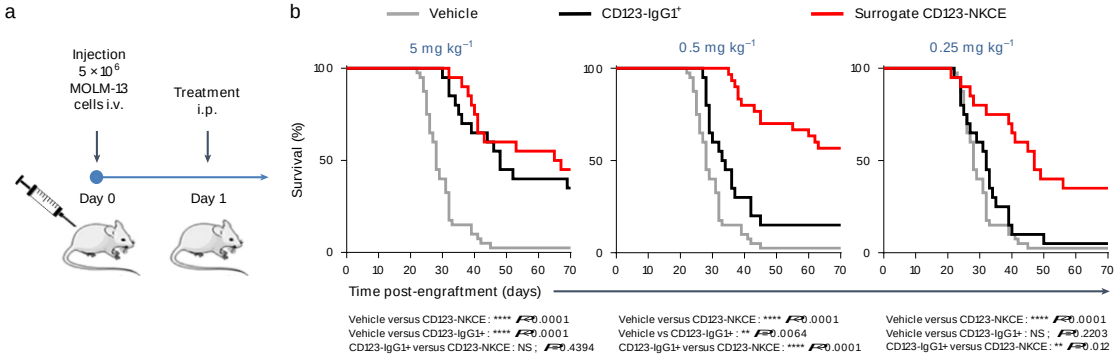
Data are representative of the mean of at least 3 independent experiments. The impact on cell viability was determined by CellTiter-Glo® after 24 h of continuous treatment (see "Methods"). *BCL-2* B-cell lymphoma 2, EC_{50} half maximal effective concentration; *FBS* fetal bovine serum, *Ki* dissociation constant, *NT* not tested, *TR-FRET* time-resolved fluorescence resonance energy transfer.

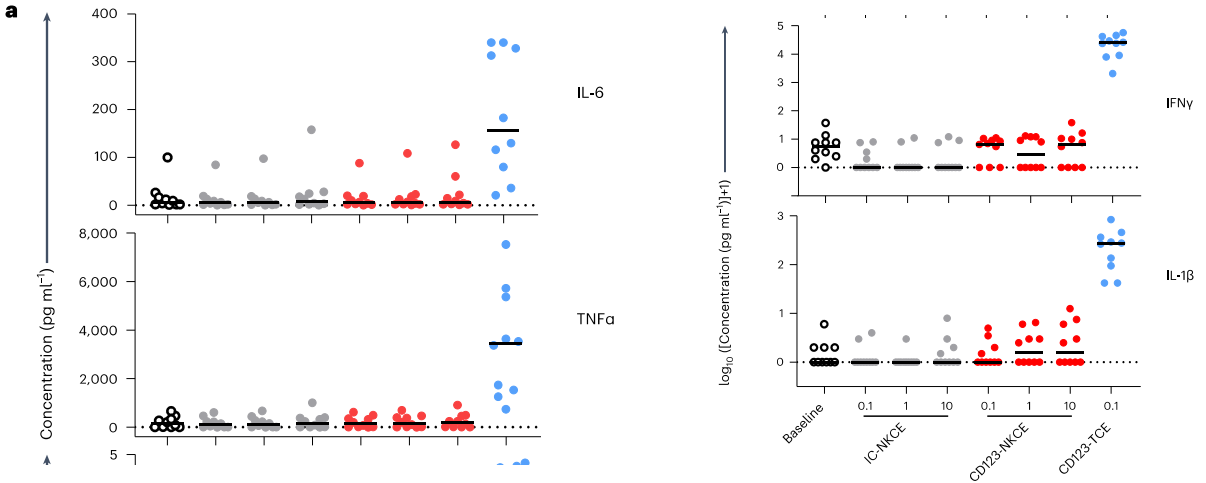
Serum troponin T



Yuda J, et al. *Commun Med.* 2023;3(1):154.

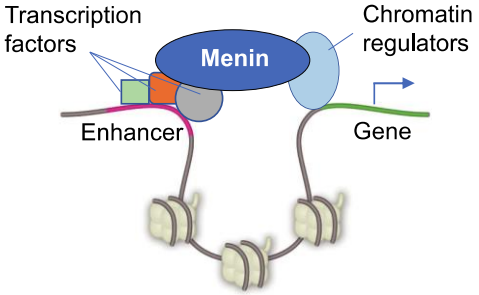
Trifunctional NKp46-CD16a-NK cell engager targeting CD123

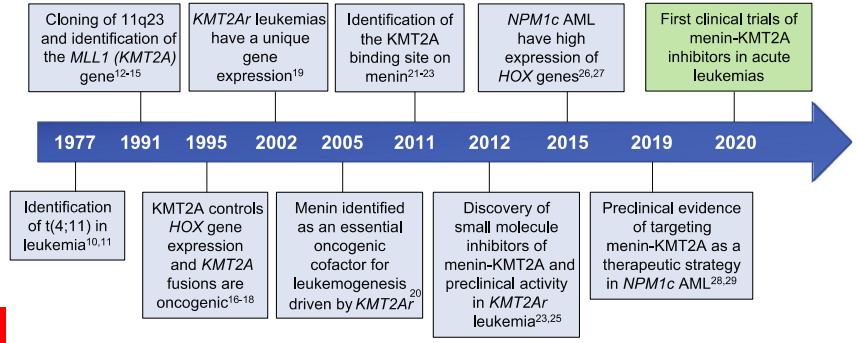


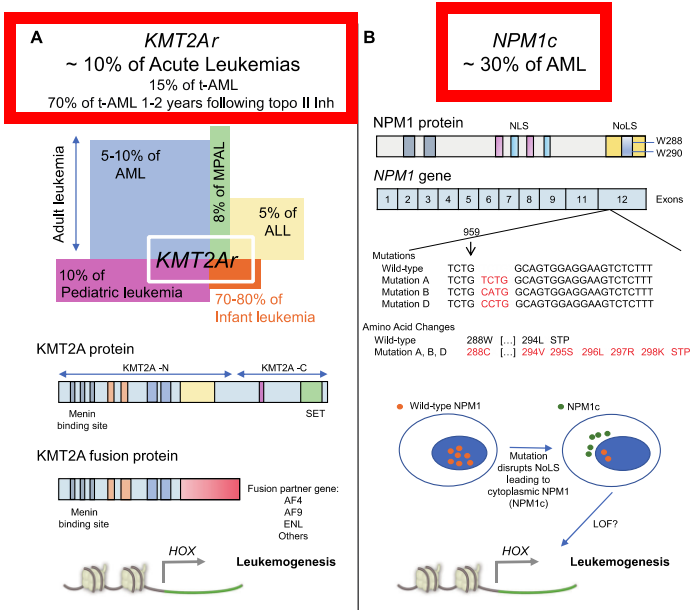


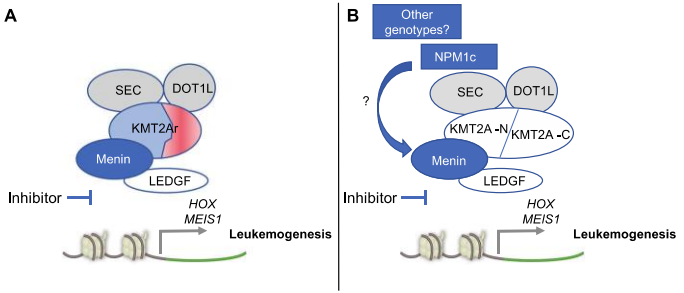
Gauthier L, et al. *Nat Biotechnol.* 2023;41(9):1296-1306.

Menin inhibition: *KMT2Ar*/m or *NPM1*m-positive AML









Differentiation
Antileukemic effect

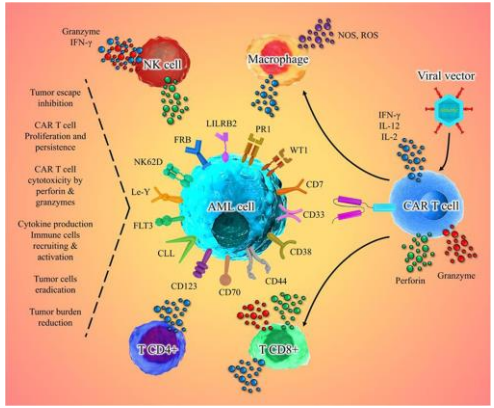
Issa GC, et al. *Leukemia*. 2021;35(9):2482-2495.

Selected menin inhibitors in development

Drug	Company	Lead indication	Status
Revumenib	Syndax	*KMT2A*-rearranged acute leukaemia, *NPM1*-mutated acute leukaemia	Submitted
Ziftomenib	Kura	*NPM1*-mutated acute leukaemia	Phase II
JNJ-75276617	Johnson & Johnson	*KMT2A*-rearranged, *NPM1*-mutated acute leukaemia	Phase I
DSP-5336	Sumitomo	Acute leukaemia	Phase I
BMF-219	Biomea Fusion	Various	Phase I
BN104	Bionova	AML, ALL	Phase I
Balamenib	Eilean	AML	Phase I
D0060-319	Chengdu Easton	*KMT2A*-rearranged acute leukaemia	Preclinical
HG153	HitGen	*KMT2A*-rearranged or *NPM1*-mutated AML and ALL	Preclinical
NA	Ascentage	NA	Preclinical
DS-1594	Daiichi Sankyo	*KMT2A*-rearranged or *NPM1*-mutated AML and ALL	Discontinued

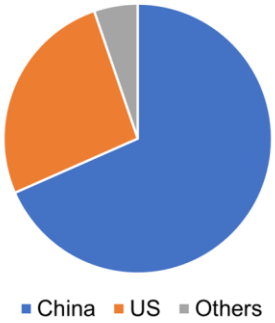
Nat Rev Drug Discov. 2024.

Implications of the association between the CAR T cell and cancer cells in AML

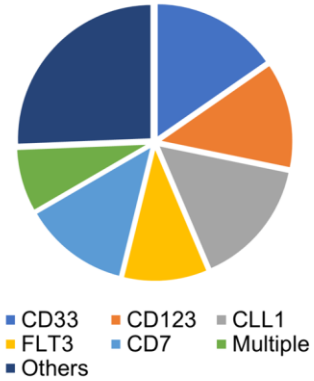


Overview of currently ongoing clinical trials in AML-targeted CAR T therapy

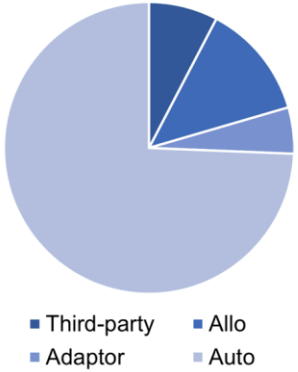
A



B

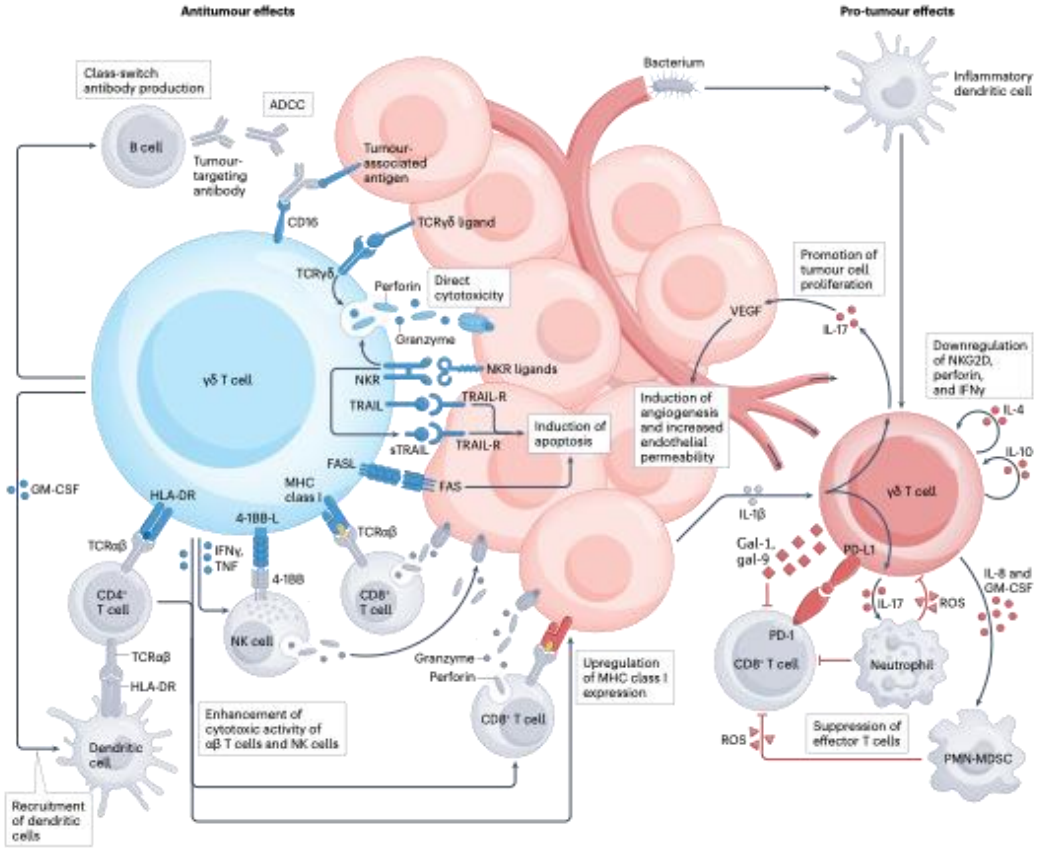


C



Marofi F, et al. *Stem Cell Res Ther.* 2021;12(1):81; Saito S. *Int J Hematol.*

The emerging roles of γδ T cells in cancer immunotherapy



Mensurado S, et al. *Nat Rev Clin Oncol.* 2023;20(3):178-191.

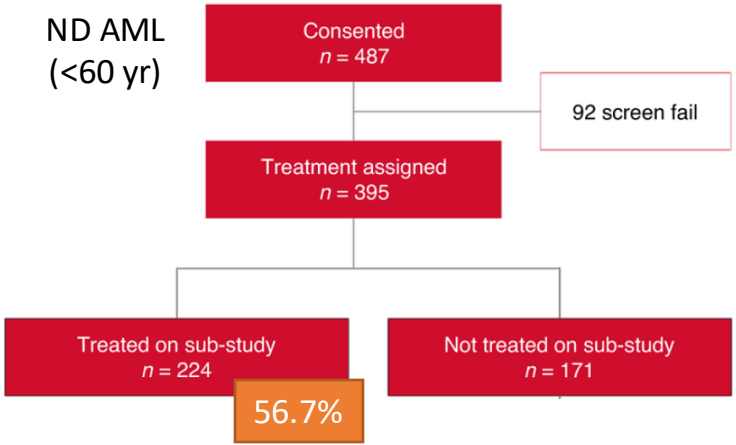
AML Master trial

Genomic testing (within 7days)

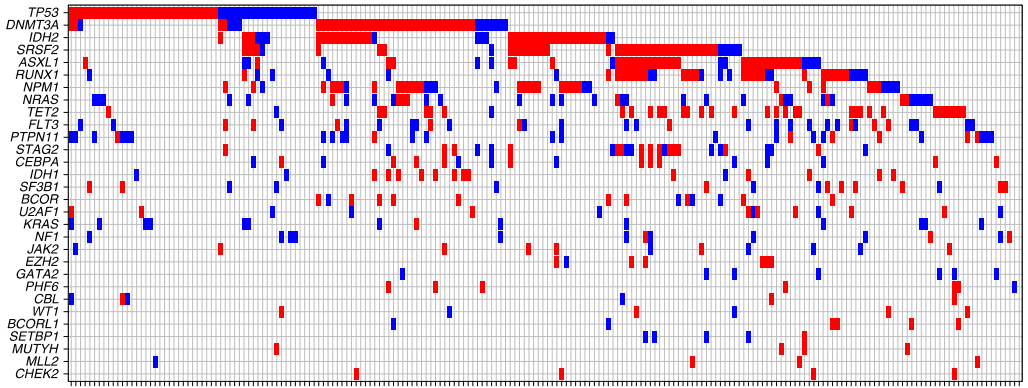
a

- Core binding factor
- *NPM1*$^{+}$ *FLT3*-ITD WT
- MLL-rearranged
- *IDH2*$^{+}$
- *IDH1*$^{+}$
- *TP53*$^{+}$
- *TP53* complex karyotype (>3 abn)
- *FLT3*-ITD^{+} or *FLT3*-TKD^{+}
- Hypermethylation*
- Marker-negative

ND AML (<60 yr)

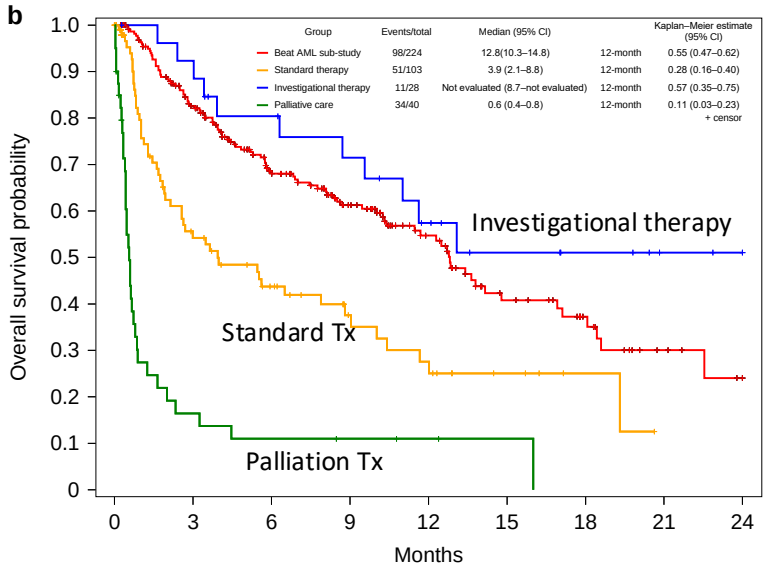


GROUP, n (%)	Prioritized Schema (n = 395)
Core binding factor	9 (2.3)
NPM1+ *FLT3*-ITD WT	46 (11.7)
MLL-rearranged	11 (2 .8)
IDH2+	45 (11.4)
IDH1+	23 (5 .8)
TP53+	76 (19.2)
TP53 complex karyotype (>3 abn)	31 (7.9)
FLT3-ITD+ or *FLT3*-TKD+	27 (6.8)
Hypermethylation	49 (12.4)
Marker-negative	78 (19.8)



Burd A, et al. *Nat Med.* 2020;26(12):1852-1858.

AML Master trial

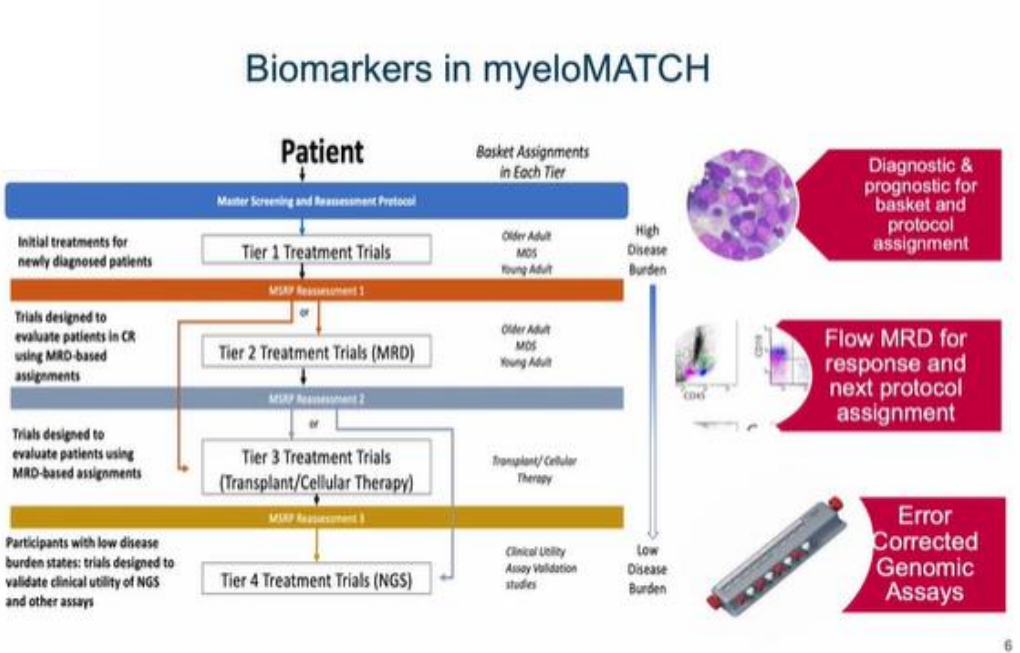


Core binding factor	Samalizumab (CD200Ab) + Induction
NPM1+ *FLT3*-ITD WT	Entospletinib(SYKi) ± Induction
MLL-rearranged	Entospletinib(SYKi) ± AZA
IDH2+	Enasidenib ± AZA
IDH1+	Ivosidenib + AZA
TP53+	Entospletinib(SYKi) + Decitabine, Pevonedistat(Nedd8i) + AZA
TP53 complex karyotype (>3 abn)	Entospletinib(SYKi) + Decitabine
FLT3-ITD+ or *FLT3*-TKD+	Gilteritinib ± Decitabine
TET2/WT1	CD33 Ab + AZA
Marker-negative	CD33 Ab + AZA

- Standard treatment 103, investigational treatment 28, palliative care 40 patients
- 30-day mortality: substudy 3.7%, standard treatment selected 20.4%
- Median overall survival: study treatment 12.8 months, standard treatment 3.9 months, palliative care 0.6 months

Burd A, et al. *Nat Med.* 2020;26(12):1852-1858.

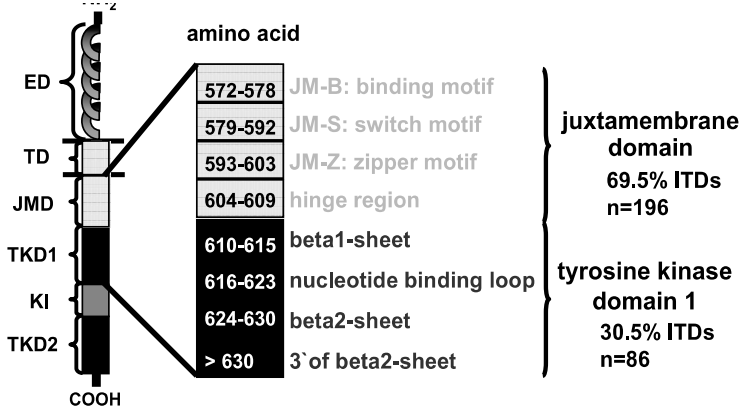
Umbrella trial in myeloid malignancies: The myeloMATCH National Clinical Trials Network Precision Medicine Initiative



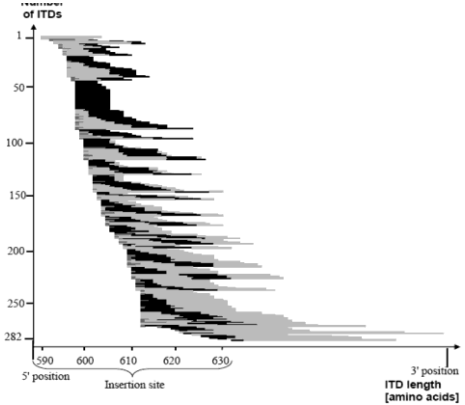
Companies Supporting Biomarker Assessments
Thermo Fisher Scientific
TwinStrand Biosciences
Targets/Drug Classes
TP53 modulation
DNA methyltransferase inhibition
FLT3
NPM1
MLL/KMT2A
KIT
IDH 1 and 2
IRAK4
BCL2
CD-47
Liposomal combination chemotherapy

Little RF, et al. *Blood*. 2022;140(suppl 1):9057-9060.

Schematic structure of the FLT3 receptor

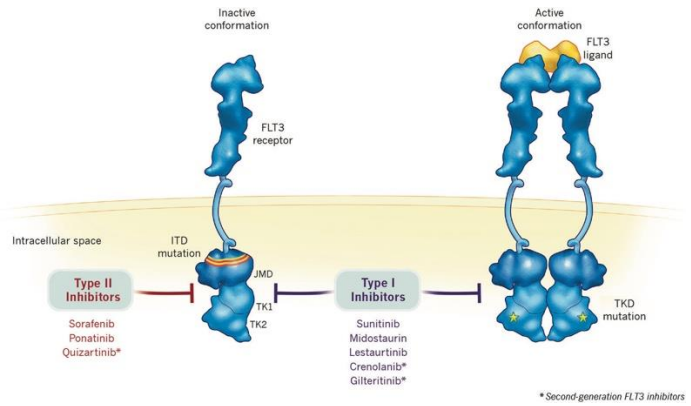


Correlation between ITD insertion site and length

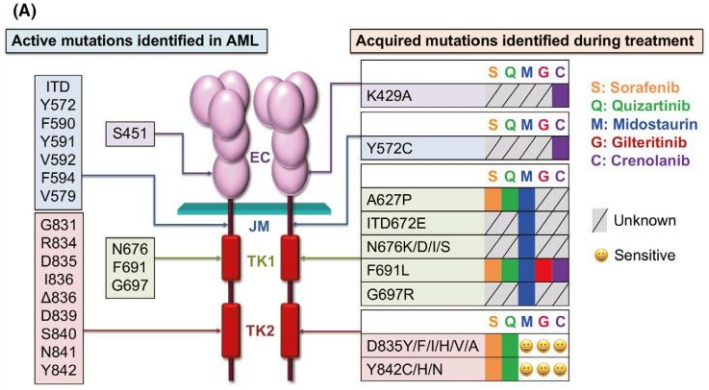


Kayser S, et al. *Blood*. 2009;114(12)2386-2392.

Schematic structure of the FLT3 receptor



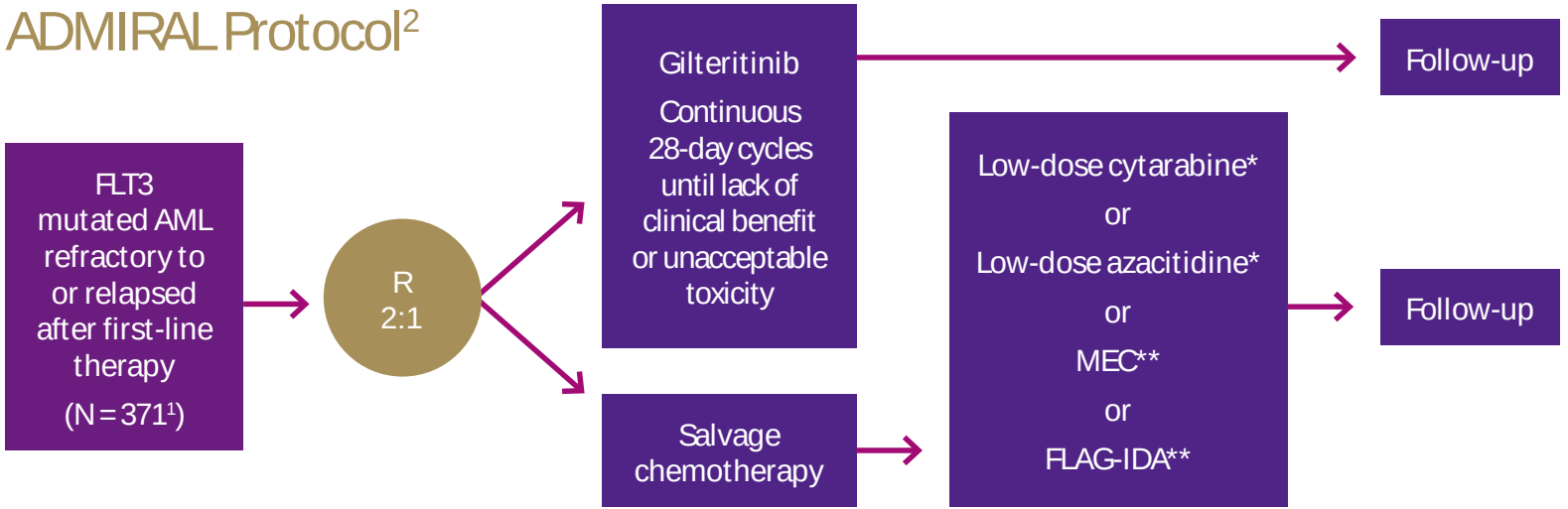
Daver N, et al. *Leukemia*. 2019;33(2):299-312.



Kiyoi H, et al. *Cancer Sci*. 2020;111(2):312-322.

Gilteritinib vs chemotherapy for R/R *FLT3*-mutated AML

ADMIRAL Protocol[2]



AML = Acute Myeloid Leukemia
FLT3 = FMS-like tyrosine kinase 3
FLAG-IDA = fludarabine, cytarabine, granulocyte colony-stimulating factor and idarubicin
MEC = mitoxantrone, etoposide and intermediate-dose cytarabine

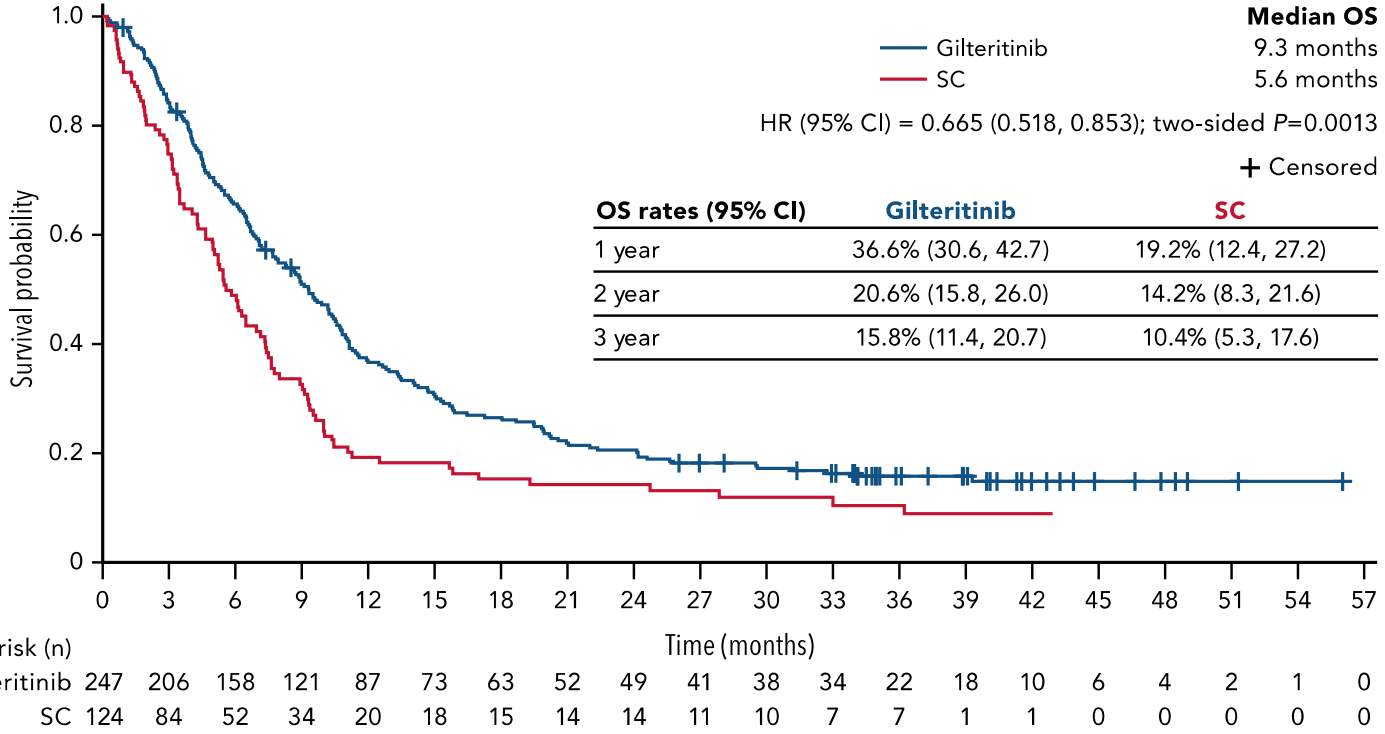
NR = no response
PD = progressive disease
R = randomized

**Continuous 28-day cycles until lack of clinical benefit or unacceptable toxicity.*
***For a maximum of 2 cycles or until NR or PD.*

Perl AE, et al. *N Engl J Med*. 2019;381(180):1728-1740.

ADMIRAL
Phase III

Gilteritinib vs chemotherapy for R/R *FLT3*-mutated AML



OS rates (95% CI)	Gilteritinib	SC
1 year	36.6% (30.6, 42.7)	19.2% (12.4, 27.2)
2 year	20.6% (15.8, 26.0)	14.2% (8.3, 21.6)
3 year	15.8% (11.4, 20.7)	10.4% (5.3, 17.6)

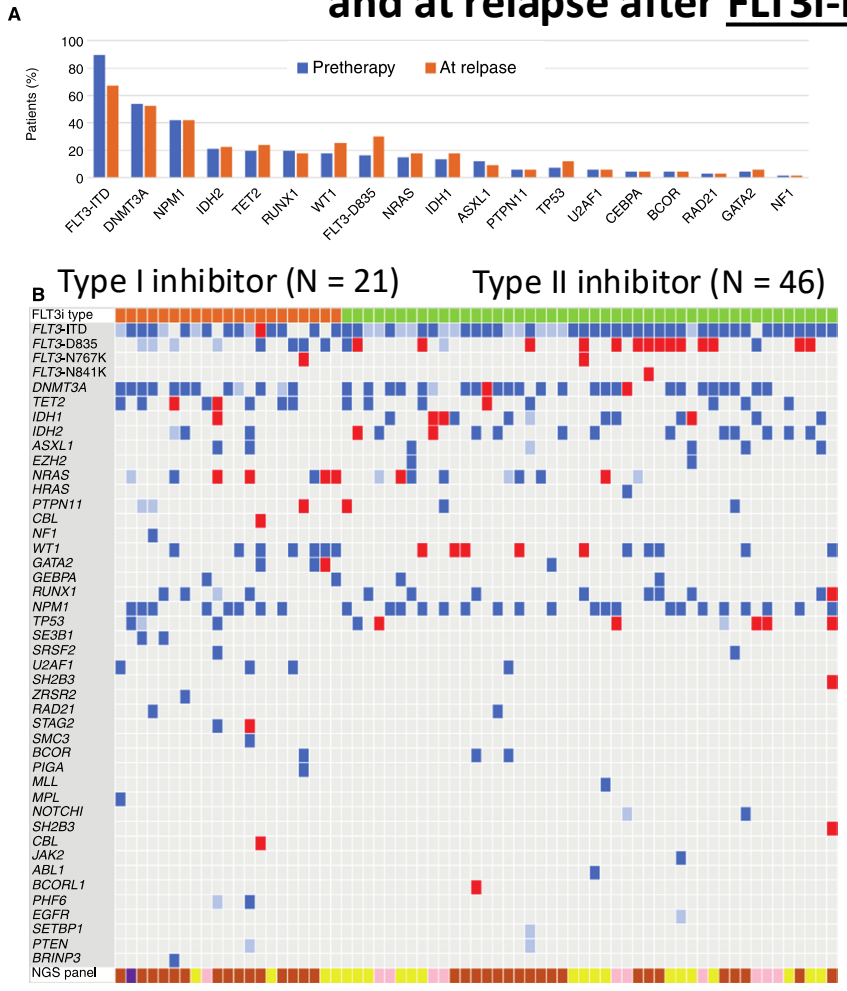
Perl AE, et al. *N Engl J Med*. 2019;381(180):1728-1740.

Second-generation FLT3 inhibitors for R/R *FLT3*-mutated AML

Trial	QuANTUM-R (phase III, n = 367)	ADMIRAL (phase III, n = 371)
Drug	Quizartinib	Gilteritinib
Effective mutation	ITD	ITD and TKD
CR rate	CR 4%, CRc 48%	CR 21%, CRc 54%
Time to CRc Time to best res	1.1 mo 1.9 mo (CRc)	1.8 mo 3.8 mo
Median OS	6.2 mo	9.3 mo
Median DOR	3.0 mo (CRc)	4.6 mo (CRc)
QTc prolongation (Gr ≥3)	4.1%	0.4%
CPK increased (Gr ≥3)	NA	2.4%
Resistance mechanism	TKD、F691L Ras/MAPK	F691 Ras/MAPK
The rate of Allo-HSCT	31.8% (78/245)	35.5% (63/247)

*Unfair comparison as different patient populations.

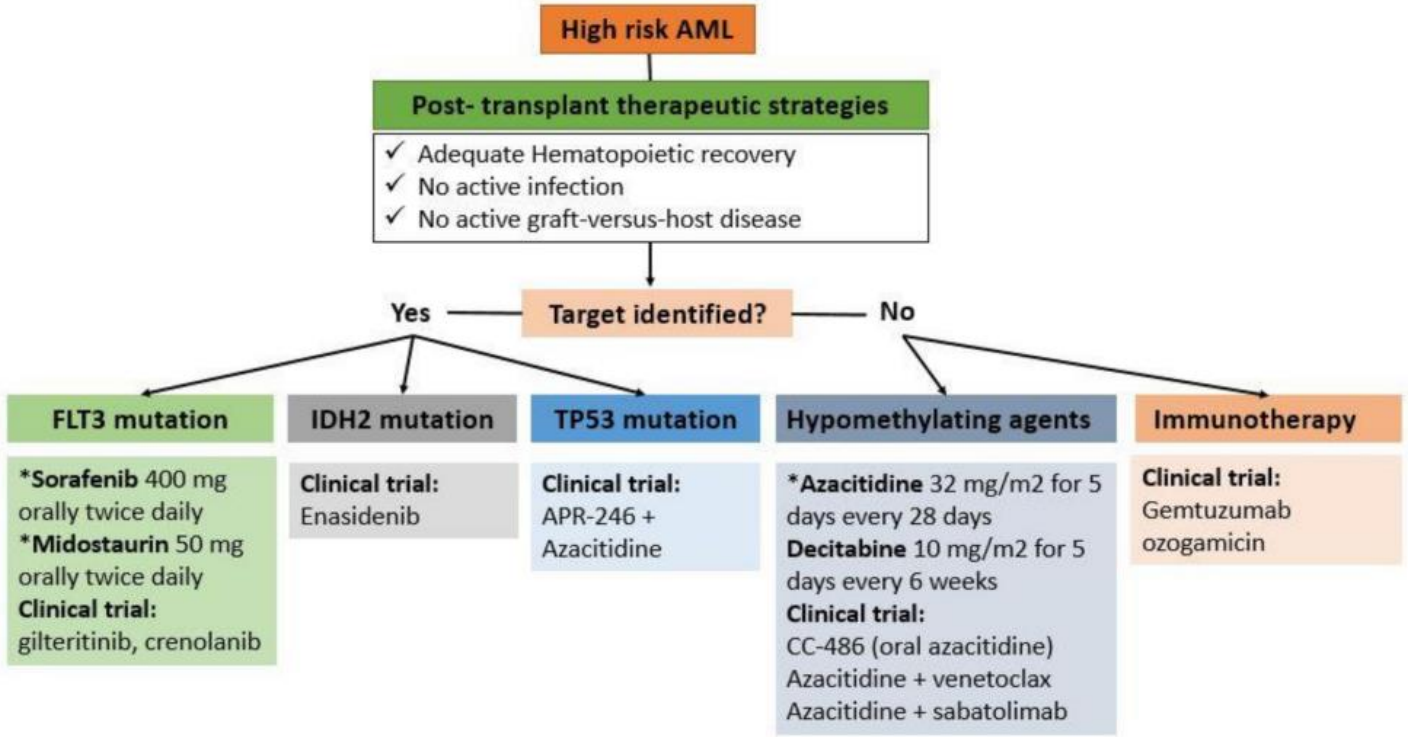
Frequency and landscape of somatic mutations pretherapy and at relapse after FLT3i-based therapies



- Targeted next-generation sequencing (NGS) at relapse identified emergent mutations involving on-target *FLT3*, epigenetic modifiers, *RAS/MAPK* pathway, and less frequently *WT1* and *TP53*
- *RAS/MAPK* and *FLT3*-D835 mutations emerged most commonly following type I and II FLT3i-based therapies, respectively.
- Among pretreatment *RAS*-mutated patients, pretreatment cohort-level variant allelic frequencies for *RAS* were higher in nonresponders, particularly with type I FLT3i-based therapies, suggesting a potential role in primary resistance as well

Alotaibi AS, et al. *Blood Cancer Discov.* 2021;2(2):125-134.

Maintenance therapy after allogeneic transplantation

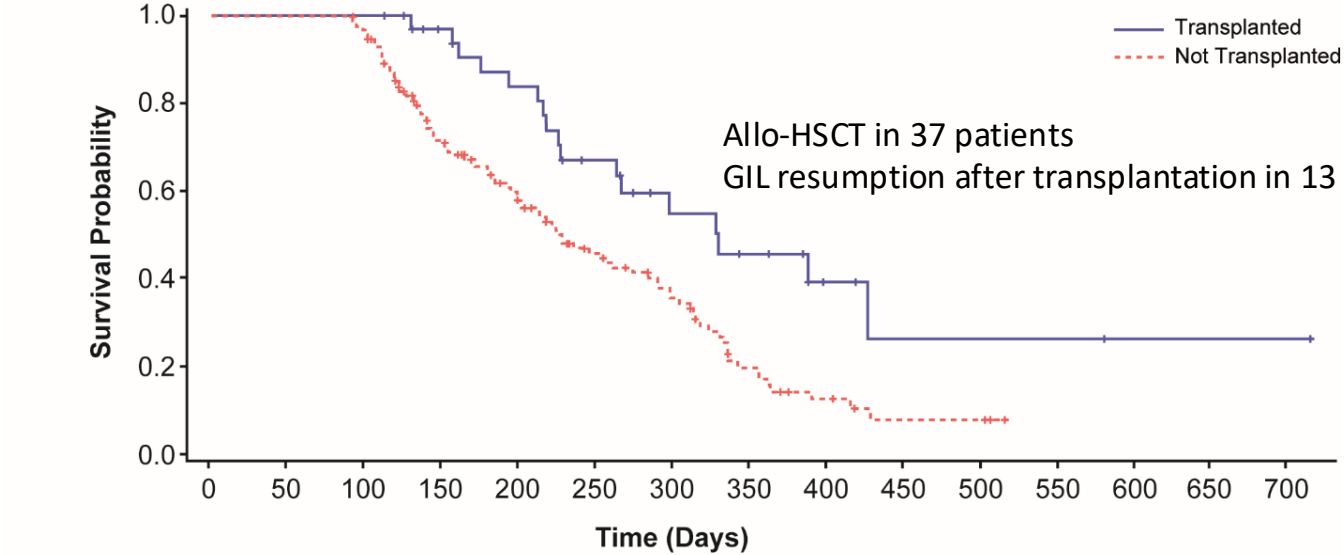


Abou Dalle I, et al. *Cancers (Basel).* 2022;14(6):1490.

CHRYSALIS Study

Selective inhibition of FLT3 by gilteritinib in relapsed or refractory acute myeloid leukaemia: a multicentre, first-in-human, open-label, phase 1–2 study

Alexander E Perl, Jessica K Altman*, Jorge Cortes, Catherine Smith, Mark Litzow, Maria R Baer, David Claxton, Harry P Erba, Stan Gill, Stuart Goldberg, Joseph G Jurcic, Richard A Larson, Chaofeng Liu, Ellen Ritchie, Gary Schiller, Alexander I Spira, Stephen A Strickland, Raoul Tibes, Celalettin Ustun, Eunice S Wang, Robert Stuart, Christoph Röllig, Andreas Neubauer, Giovanni Martinelli, Erkut Bahceci, Mark Levis*

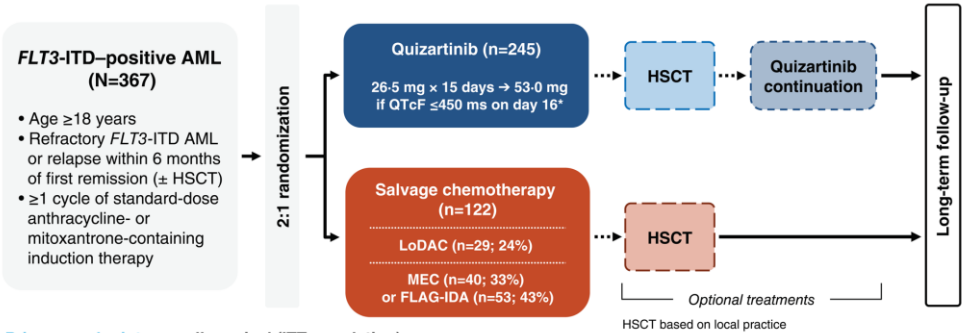


Allo-HSCT in 37 patients
GIL resumption after transplantation in 13 patients

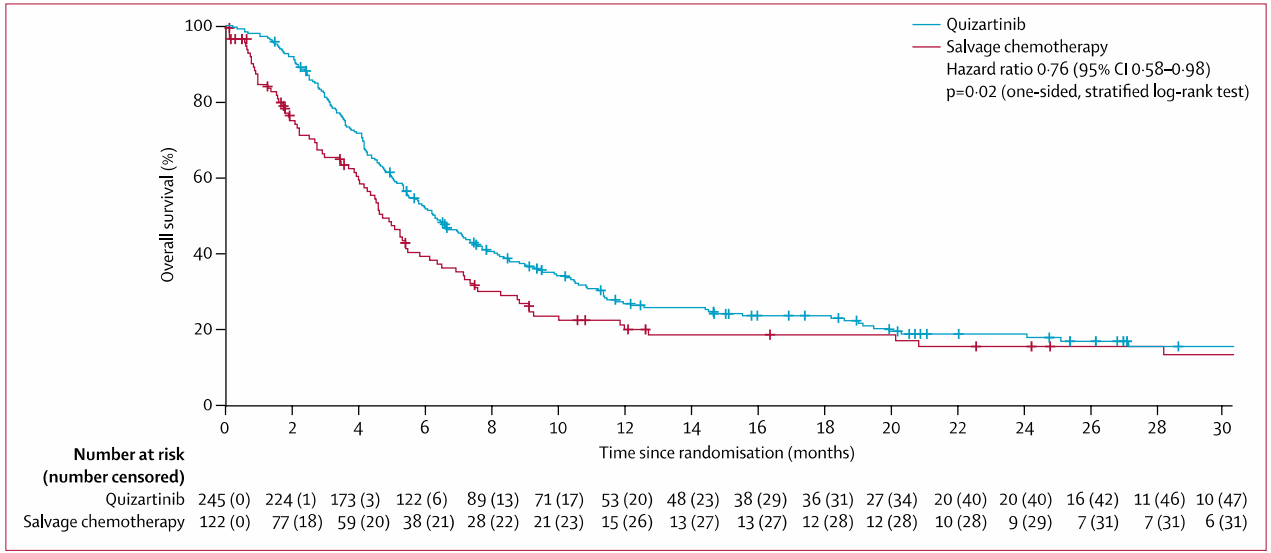
Bridging to allo-HSCT after successful treatment with GIL

Perl AE, et al. *Lancet Oncol.* 2017;18(8):1061-1075.

QuANTUM-R Study



Primary endpoint: overall survival (ITT population)
Secondary endpoint: event-free survival (ITT population)
Select exploratory endpoints: CRc rate, duration of CRc, and transplant rate
Enrollment dates: May 2014 (first patient) to September 2017 (last patient)
Data cutoff: February 2018



Cortes JE, et al. *Lancet Oncol.* 2019;20(7):984-997.

BMT-CTN 1506 (MORPHO): A randomized trial of the FLT3 inhibitor gilteritinib as post-transplant maintenance for *FLT3*-ITD AML

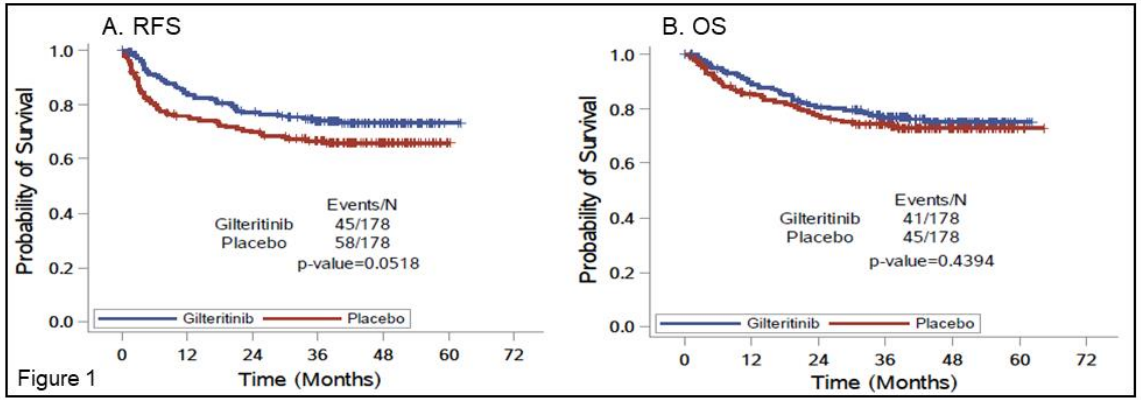


Figure 1

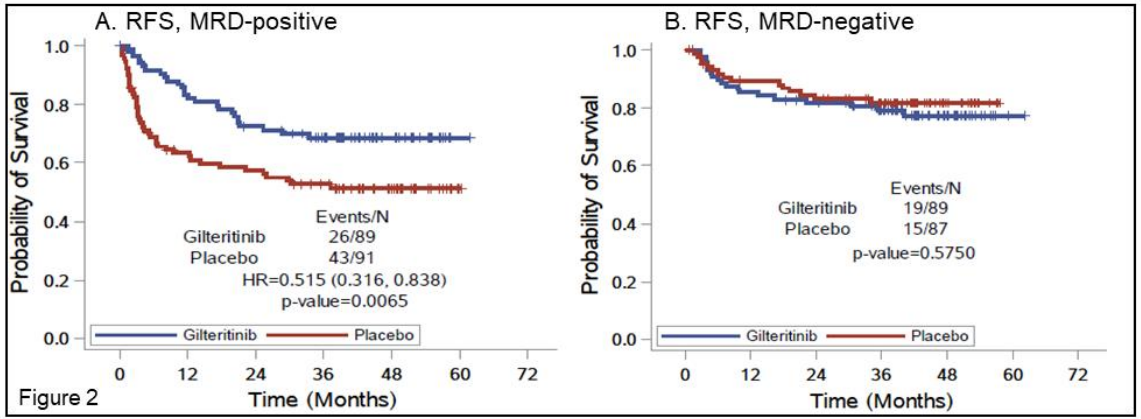


Figure 2

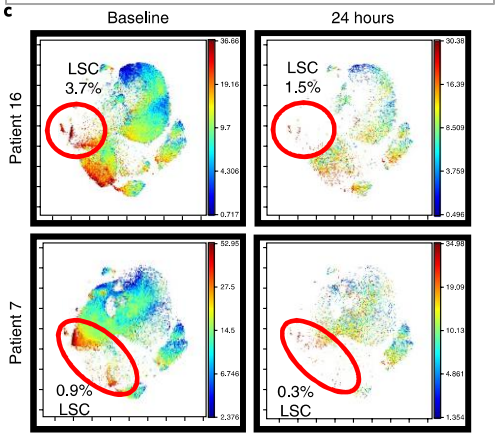
Levis M, et al. EHA 2023. Abstract LB2711.

Efficacy of venetoclax against AML stem cells

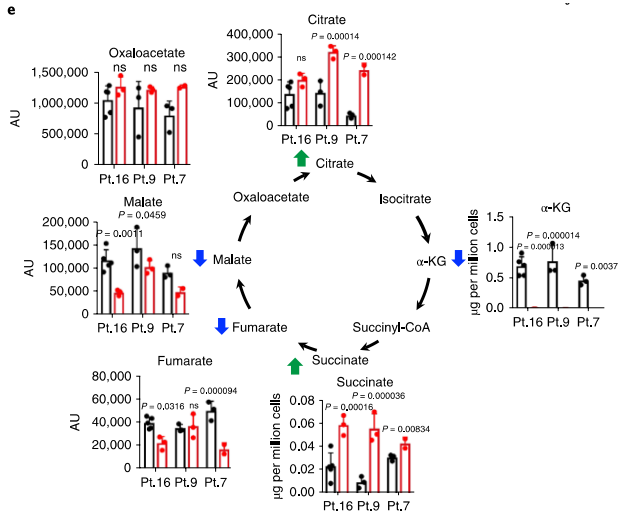
	VEN+DEC	VEN+AZA
Complete remission	8 (35%)	6 (27%)
CRi	6 (26%)	7 (32%)
Partial remission	1 (4%)	0
MLFS*	2 (9%)	5 (23%)
Resistant disease	3 (13%)	2 (9%)
Non-evaluable†	3 (13%)	2 (9%)
Complete remission and CRi	14 (61%)	13 (59%)
Overall response‡	15 (65%)	13 (59%)
Overall outcome§	17 (74%)	18 (82%)

Most common grade 3–4 TEAE:
Thrombocytopenia (9 in group A, 13 in group B), febrile neutropenia (11 in group A, ten in group B,), and neutropenia (12 in group A, eight in group B).

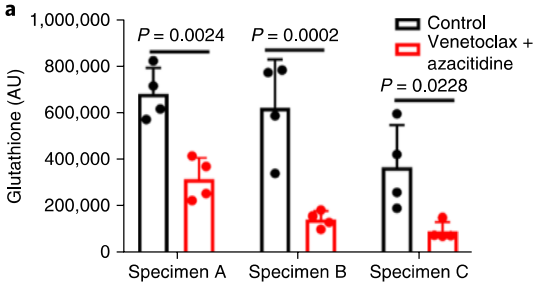
Reduction in LSCs after VEN Tx



Suppression of oxidative phosphorylation by VEN + AZA



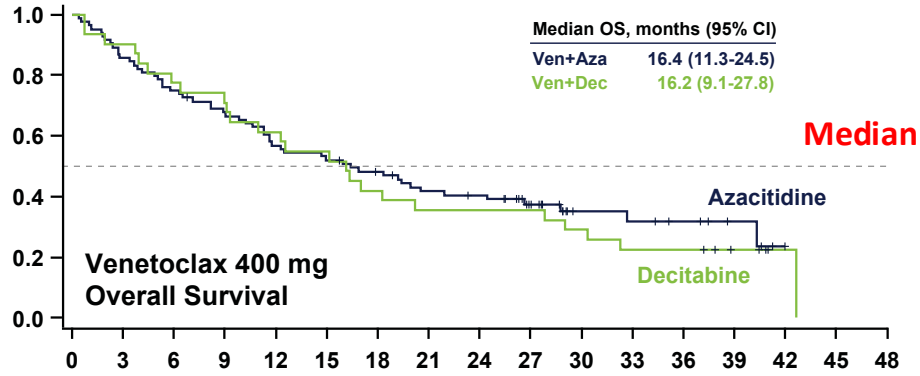
Succinate↓
↓
electron transport system ↓
↓
glutathione ↓
↓
antioxidant effect
↓



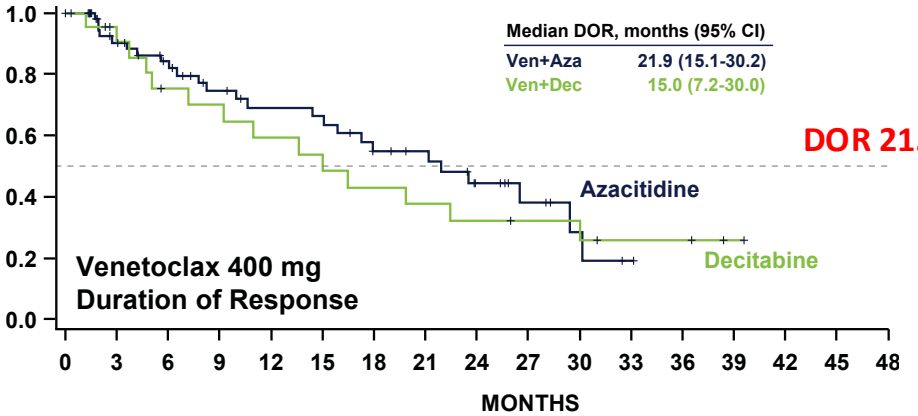
LSC is OXPHOS dependent
↑
(HSCs compensate for glycolysis when OXPHOS is suppressed)

DiNardo CD, et al. *Lancet Oncol.* 2018;19(2):216-228;
Pollyea DA, et al. *Nat Med.* 2018;24(12):1859-1866.

Long-term follow-up data of VEN-based regimen



Median OS 16.4 months



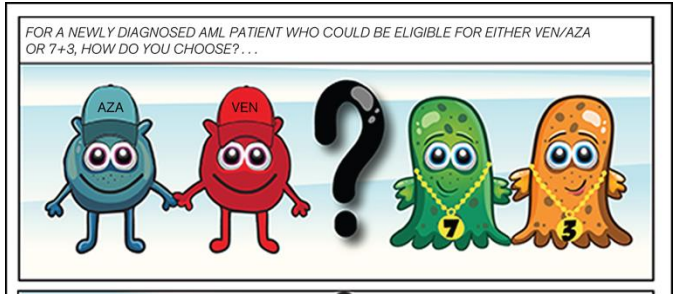
DOR 21.9 months

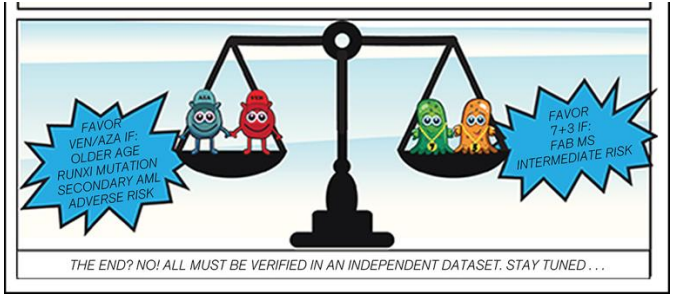
Key grade ≥3 AEs (AZA and DEC)

- Febrile neutropenia (39% and 65%)
- Anemia (30% and 26%)
- Thrombocytopenia (25% and 23%)
- Neutropenia (20% and 10%)

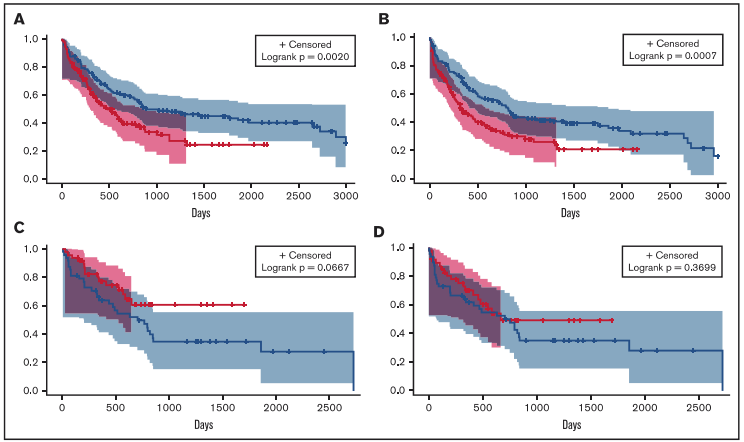
Pollyea DA, et al. *Am J Hematol.* 2021;96(2):208-217.

Newly diagnosed AML: AZA + VEN vs intensive chemotherapy





Retrospective analysis
AZA + VEN: n = 143, IC: n = 149



Propensity-matched cohort

CR/CRi

- AZA + VEN: Elderly, secondary AML, *RUNX1*mut
- IC: AML M5

OS

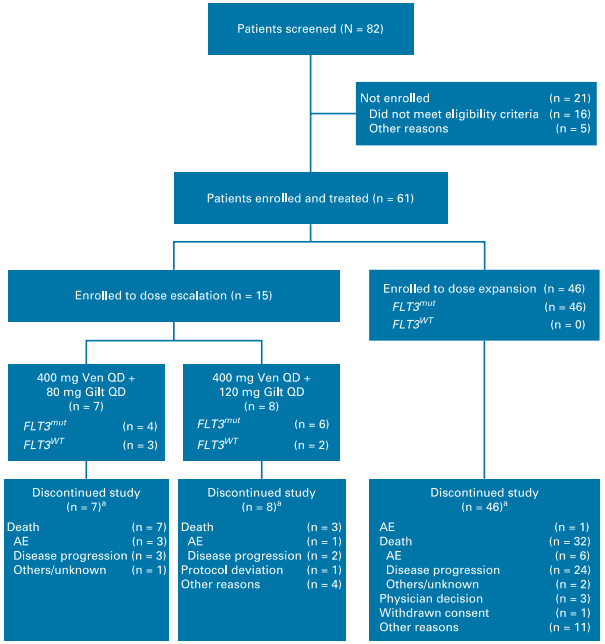
- AZA + VEN: Elderly, secondary AML, *RUNX1*mut
- IC: AML M5

After adjusting for baseline factors, the VEN + AZA group had better OS.

Evan MC. *Blood Advances*. 2021.

Venetoclax + gilteritinib for *FLT3*-mutated R/R AML

Patient enrollment and disposition



- 61 patients enrolled, median age 63 years (range: 21 to ~85 years)
- Prior treatment: 19 patients (31%) received allogeneic transplantation; 10 patients received VEN (no prior gilteritinib)
- 36 of 56 *FLT3* mutation-positive patients had received FLT3 TKIs
- The median duration of exposure was 2.6 months (range: 0.07-16.8) for VEN and 2.6 months (range: 0.1-17.2) for GIL

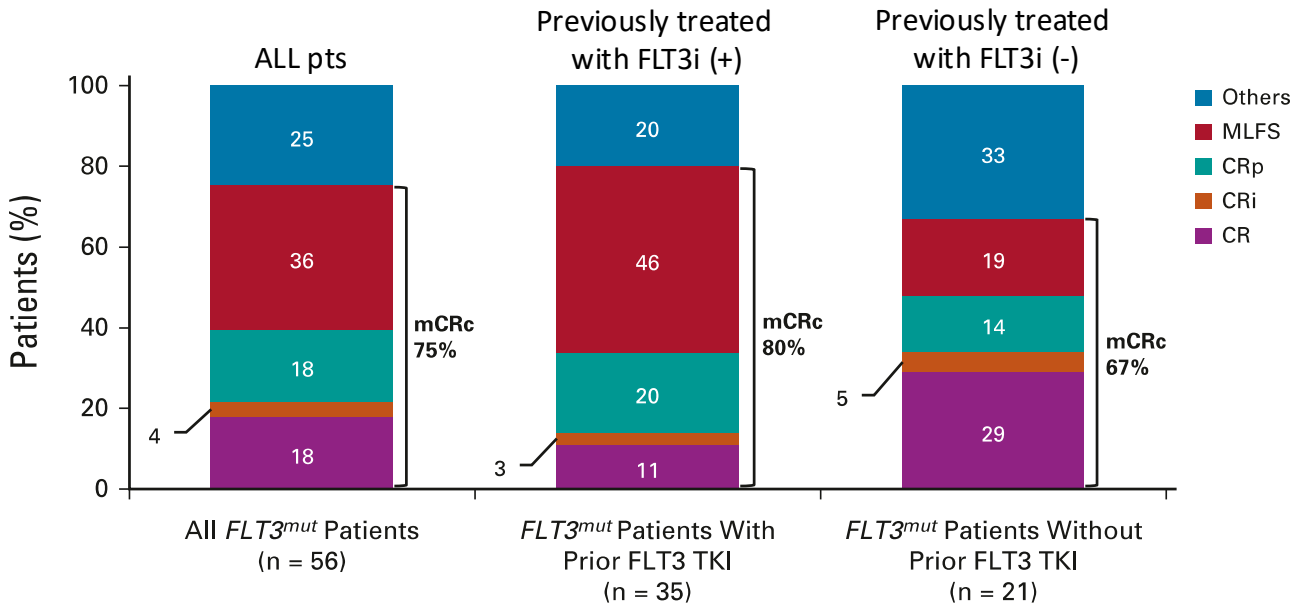
Characteristic	All Patients (N = 61)
Median age, years (range)	63 (21-85)
Sex, No. (%)	
Female	30 (49)
Race, No. (%)	
White	53 (88)
Black or African American	3 (5)
American or Alaska Native	4 (7)
Hawaiian Native or Pacific Islander	0
Missing	1 (2)
ECOG PS, No. (%)	
0	10 (16)
1	42 (69)
2	9 (15)
Cytogenetic risk, No. (%)	
Favorable	2 (3)
Intermediate	33 (56)
Poor	20 (34)
No mitoses or missing	6 (10)
Relapsed disease, No. (%)	42 (69)
Refractory disease, No. (%)	19 (31)
FLT3 mutation, No. (%)	56 (92)
ITD alone	44 (72)
TKD alone	9 (15)
Both	3 (5)
Median prior lines o	
Prior lines of therap	
1	
2	
≥ 3	
Prior venetoclax, No. (%)	10 (16)
Prior alloSCT, No. (%)	19 (31)
Prior FLT3 TKI in *FLT3*^{mut} patients, n/n (%)	36/56 (64)
1 prior FLT3 TKI	22/56 (39)
> 1 prior FLT3 TKI	14/56 (25)

Midostaurin as induction therapy, sorafenib after transplantation

Daver N, et al. *J Clin Oncol.* 2022;40(35):4048-4059.

Venetoclax + gilteritinib for *FLT3*-mutated R/R AML

Response rates in all *FLT3*mut patients treated at any dose (n = 56)

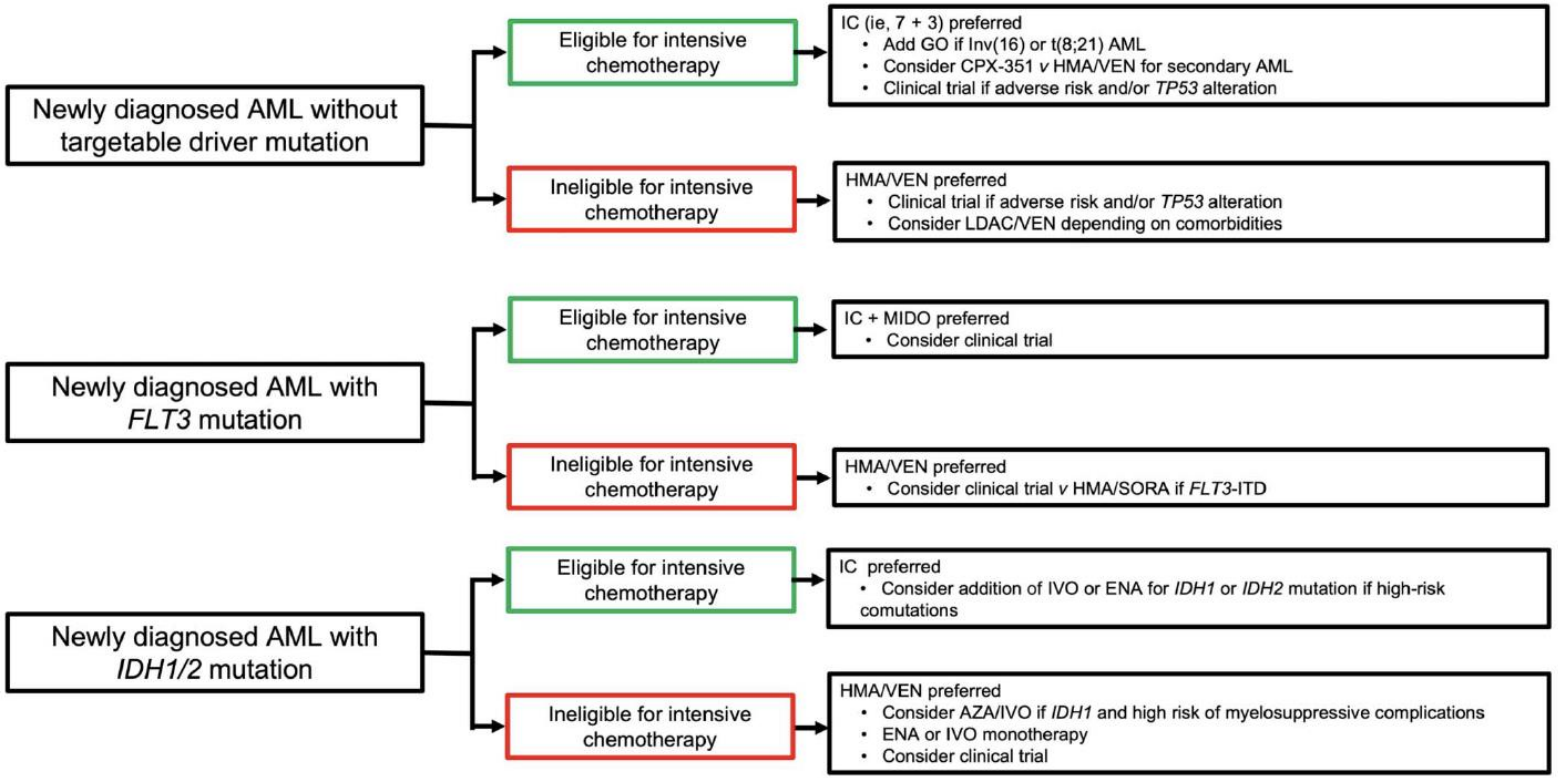


mCRc (modified composite complete response): CR + CRi + CRp (defined in ADMIRAL trial)

- Modified composite complete response was achieved in 75% of patients
- Response rates were 67% and 80% in patients who had not previously received FLT3i

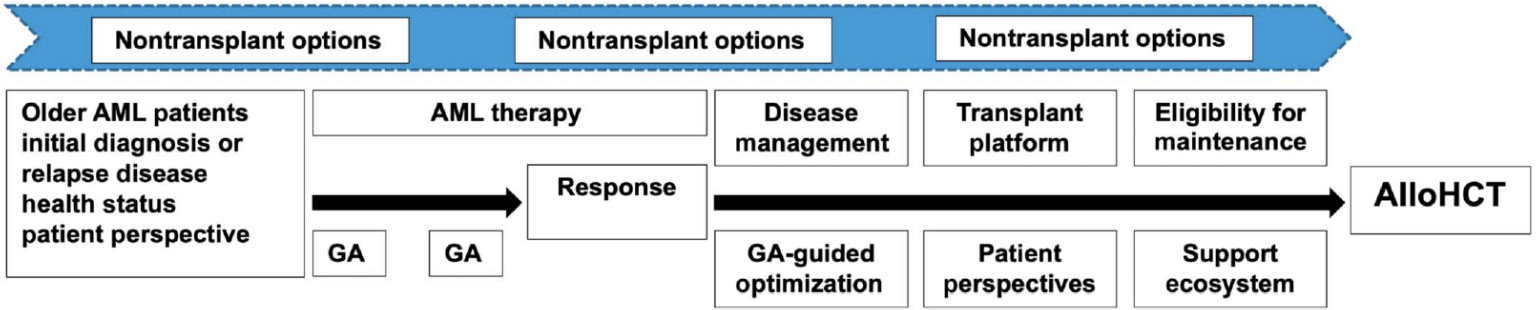
Daver N, et al. *J Clin Oncol.* 2022;40(35):4048-4059.

Older adults with newly diagnosed AML



Lai C, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e390018.

Older adults with newly diagnosed AML



- Treatment of elderly patients with AML may reduce treatment-related mortality by incorporating early diagnosis, long-term geriatric assessment (GA), and GA-guided management
- GA is combined with disease risk assessment for early transplant evaluation to maximize the likelihood of cure in elderly patients

Lai C, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e390018.

Thank you for your kind attention!

Global Leukemia Academy

Q&A

APTITUDE HEALTH®

Global Leukemia Academy

AML case-based panel discussion

Case 1 AML: Ane Veu

(Fiji)

Case 2 AML: Feng-Ming Tien

(Taiwan)

Moderator: Naval Daver

APTITUDE HEALTH®

Global Leukemia Academy

Case 1

Ane Veu (Fiji)

APTITUDE HEALTH

Acute Myeloid Leukemia

Case Study – Fiji

Ane Veu, MD
Consultant Physician
Special Interest: Medical Oncology

Master SS

Biodata

- 18-year-old male
- Keen student and rugby player
- Normal childhood and milestones

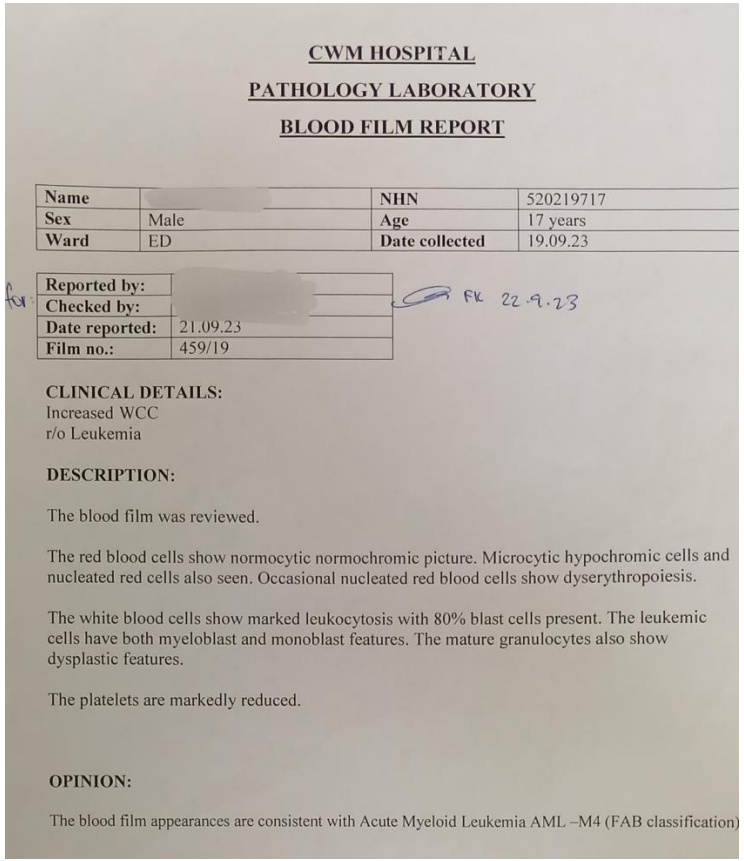
Symptoms

- Noticed progressive fatigue
- Significant bruising with minor bumps
- Slow-healing facial furuncle

Full blood count results

Indices	D1	D8	D10
Hemoglobin (11–16 g/dL)	12.4	11.9	9.9
White cell count (4–11 × 10^3/μL)	66,000	58,700	75,000
Platelet (140–150 × 10^3/μL)	26,000	21,000	19,000

Public hospital opinion – comparison with a private practice facility



CWM HOSPITAL

PATHOLOGY LABORATORY

BLOOD FILM REPORT

Name	[redacted]	**NHN**	520219717
Sex	Male	**Age**	17 years
Ward	ED	**Date collected**	19.09.23

Reported by:	[redacted]
Checked by:	
Date reported:	21.09.23
Film no.:	459/19

FK 22.9.23

CLINICAL DETAILS:
Increased WCC
r/o Leukemia

DESCRIPTION:

The blood film was reviewed.

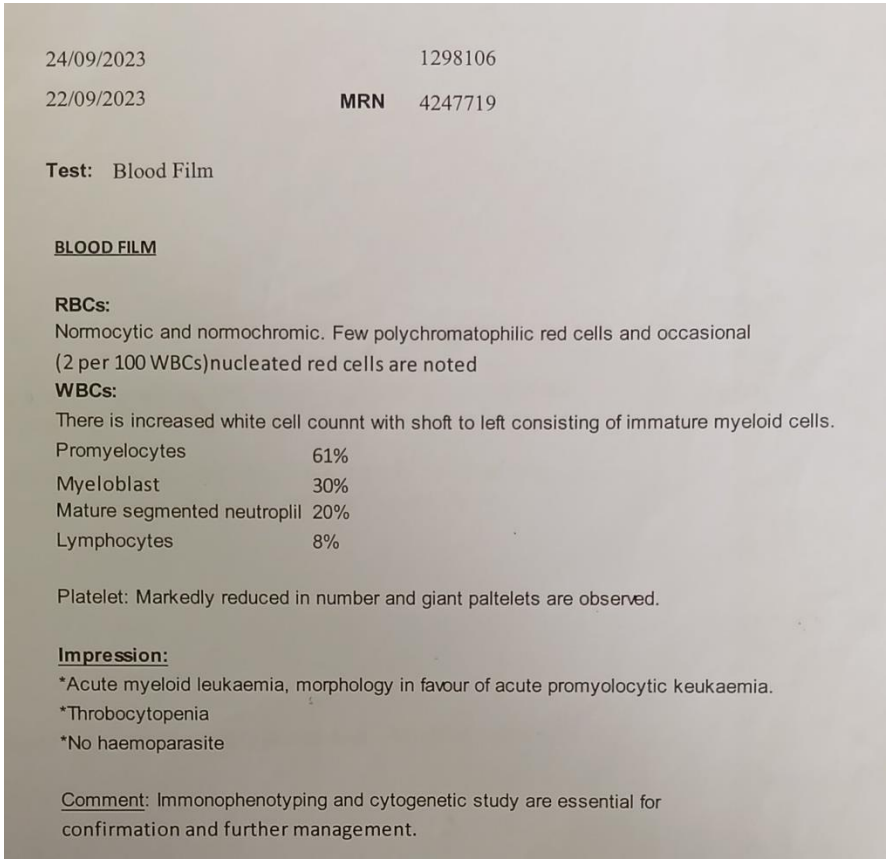
The red blood cells show normocytic normochromic picture. Microcytic hypochromic cells and nucleated red cells also seen. Occasional nucleated red blood cells show dyserythropoiesis.

The white blood cells show marked leukocytosis with 80% blast cells present. The leukemic cells have both myeloblast and monoblast features. The mature granulocytes also show dysplastic features.

The platelets are markedly reduced.

OPINION:

The blood film appearances are consistent with Acute Myeloid Leukemia AML –M4 (FAB classification)



24/09/2023 1298106

22/09/2023 **MRN** 4247719

Test: Blood Film

BLOOD FILM

RBCs:
Normocytic and normochromic. Few polychromatophilic red cells and occasional (2 per 100 WBCs)nucleated red cells are noted

WBCs:
There is increased white cell counnt with shoft to left consisting of immature myeloid cells.

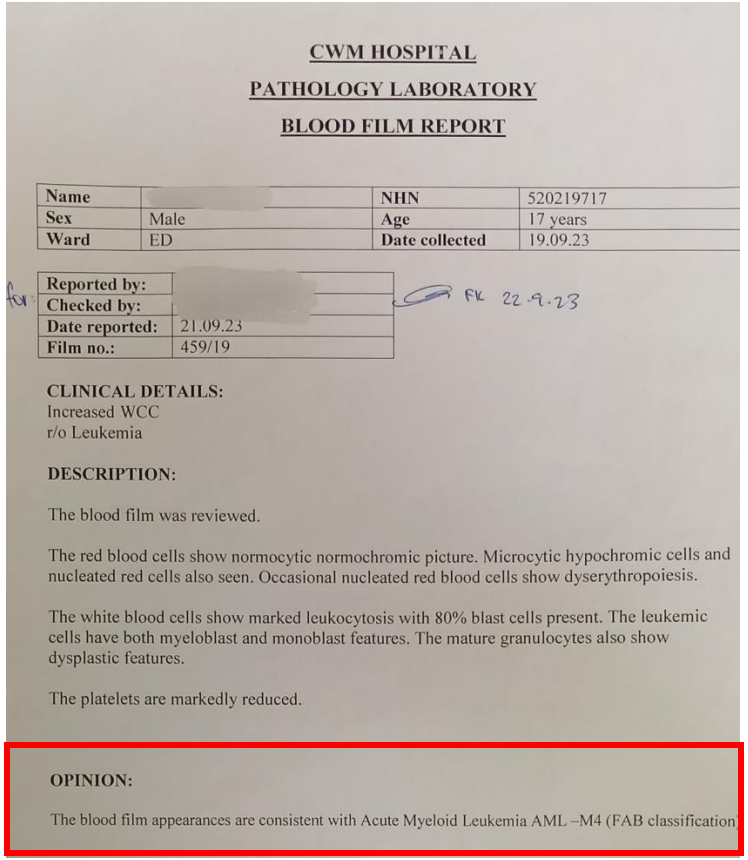
Promyelocytes	61%
Myeloblast	30%
Mature segmented neutroplil	20%
Lymphocytes	8%

Platelet: Markedly reduced in number and giant paltelets are observed.

Impression:
*Acute myeloid leukaemia, morphology in favour of acute promyolocytic keukaemia.
*Throbocytopenia
*No haemoparasite

Comment: Immonophenotyping and cytogenetic study are essential for confirmation and further management.

Diagnosis at a public hospital confirmed by a private practice



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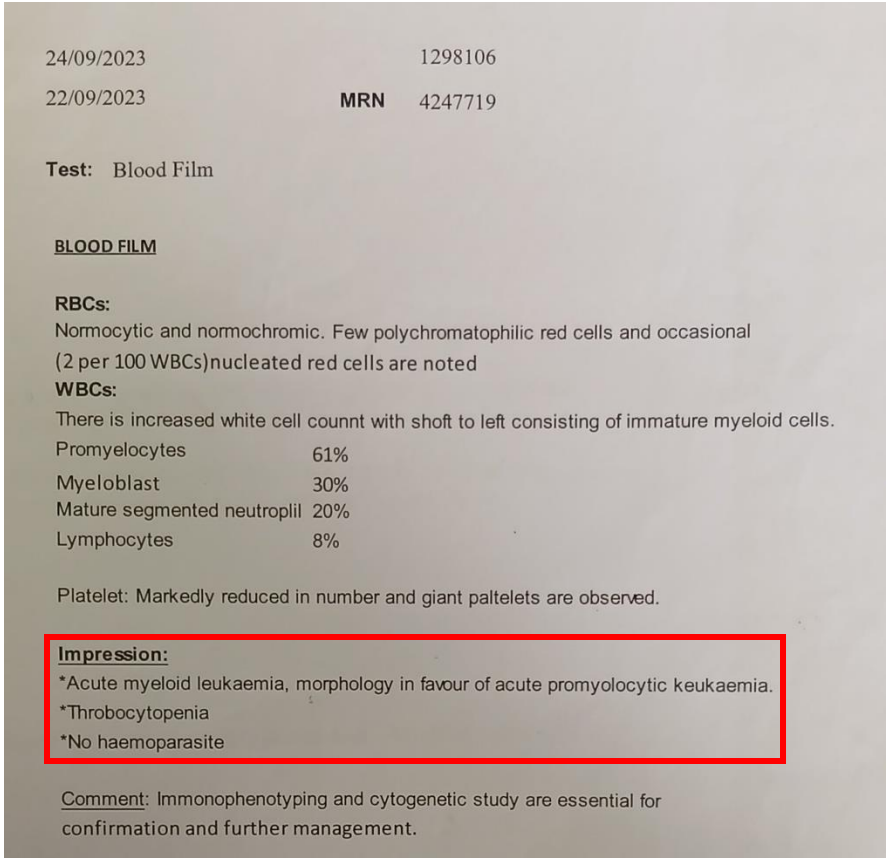

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Sex	Male	**Age**	17 years
Ward	ED	**Date collected**	19.09.23

Reported by:	
Checked by:	
Date reported:	21.09.23
Film no.:	459/19

FK 22.9.23

CLINICAL DETAILS:
Increased WCC
r/o Leukemia

DESCRIPTION:

The blood film was reviewed.

The red blood cells show normocytic normochromic picture. Microcytic hypochromic cells and nucleated red cells also seen. Occasional nucleated red blood cells show dyserythropoiesis.

The white blood cells show marked leukocytosis with 80% blast cells present. The leukemic cells have both myeloblast and monoblast features. The mature granulocytes also show dysplastic features.

The platelets are markedly reduced.

OPINION:

The blood film appearances are consistent with Acute Myeloid Leukemia AML –M4 (FAB classification

24/09/2023 1298106

22/09/2023 **MRN** 4247719

Test: Blood Film

BLOOD FILM

RBCs:
Normocytic and normochromic. Few polychromatophilic red cells and occasional (2 per 100 WBCs)nucleated red cells are noted

WBCs:
There is increased white cell counnt with shoft to left consisting of immature myeloid cells.

Promyelocytes	61%
Myeloblast	30%
Mature segmented neutroplil	20%
Lymphocytes	8%

Platelet: Markedly reduced in number and giant paltelets are observed.

Impression:
*Acute myeloid leukaemia, morphology in favour of acute promyolocytic keukaemia.
*Throbocytopenia
*No haemoparasite

Comment: Immonophenotyping and cytogenetic study are essential for confirmation and further management.

Acute leukemia research – Fiji

A Descriptive Study of

Adult Acute Myeloid Leukemia Patients

at CWMH from

1st Jan 2010 to 31st Dec 2015

By

MARICA MATAIKA
Post Graduate Masters

Internal Medicine

Fiji School of Medicine

Suva, Fiji.

2017

RESULTS: 76 cases

- Demographics

  Male > Female

- Median age

  47 years

- Median time from diagnosis to death

  2 weeks

- Cause of mortality

  Infection

Fiji AML treatment protocol

Peds

- ATRA therapy
- Refer abroad

Adults

- Supportive only

Referral to an international cancer center

Diagnosis	Flow Cytometry	Bone Marrow Analysis
• Refractory AML • MRD negative • ECOG PS0	• CD34 double pos • HLADR double pos • CD 117 pos • MPO pos • CD56/CD 19 pos	AML: 35% blasts FISH pos: *RUNX1/RUNX1T1* FISH neg: *PML/RARA KMT2A* NGS myeloid panel: pos; *ASXL1, ETV6, RUNX1/ RUNX1T1* mutations

Question 1

How would you treat this patient if no stem cell transplant facilities available?

A. 7+3

B. CPX-351

C. FLAG-IDA

D. HMA + venetoclax

E. Palliative care

Treatment in overseas facility

Treatment	Details	Particulars	Other
Induction chemotherapy (10/7/23 – 10/13/23)	3 +7 DA		
Post-induction status (10/30/23)	*Bone marrow asp* *Bone marrow biopsy*	*Morphologic remission* *Suspicious large cells*	*Residual disease*

Treatment	Details	Particulars	Other
Induction chemotherapy (10/7/23 – 10/13/23)	3+7 DA		
Post-induction status (10/30/23)	*Bone marrow asp* *Bone marrow biopsy*	*Morphologic remission* *Suspicious large cells*	*Residual disease*
FLAG therapy (07/11/23 – 12/11/23)	FLAG therapy		
Post-FLAG status (12/4/23)	*Bone marrow asp and biopsy*	*Morphologic remission*	*MRD by MFC:* *AML MRD = <0.1%*

Treatment	Details	Particulars	Other
Induction chemotherapy (10/7/23 – 10/13/23)	3+7 DA		
Post-induction status (10/30/23)	*Bone marrow asp* *Bone marrow biopsy*	*Morphologic remission* *Suspicious large cells*	*Residual disease*
FLAG therapy (07/11/23 – 12/11/23)	FLAG therapy		
Post-FLAG status (12/4/23)	*Bone marrow asp and biopsy*	*Morphologic remission*	*MRD by MFC:* *AML MRD = <0.1%*
Transplant period (Dec–Jan 2024)	Myeloablative conditioning (MAC) regimen	Fludarabine inj (Dec 17–21) Treosulfan inj (Dec 18–20) Cyclophos inj (Dec 28–29) TBI total 6 Gy over 3 days (Dec 21–23)	
	(12/25/23)	Allogeneic haploidentical peripheral blood stem cell transplant	CD34 cell dose infused 5.5×10^6/kg bw

Treatment	Details	Particulars	Other
Induction chemotherapy (10/7/23 – 10/13/23)	3+7 DA		
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	(12/25/23)	Allogeneic haploidentical peripheral blood stem cell transplant	CD34 cell dose infused 5.5 × 10^6/kg bw
Post-transplant test (Mar 2024)	Bone marrow asp and biopsy	Morphologic remission hypocellular marrow (20%–30%)	Negative for residual disease

GVHD prophylaxis (12/30/23)	Tacrolimus Mycophenolate mofetil
Anti-infective prophylaxis	Acyclovir Posaconazole G-CSF Inj (D5 – neutrophil engraftment)
Engraftment	Neutrophil – D14 Platelet – D11
Irradiated blood products	Red cell C: 4 Units (1/1/24) Platelets: 7 units (4/1/24)
Adverse events (WHO CTCAE v5)	Fever: Grade 2–3 Cytokine release syndrome: Grade 2–3 Oral/GI Toxicity: Grade 2–3 Cystitis: Grade 1 Hematuria: Grade 1 Dizziness: Grade 1

Current status: ECOG 1

- April–July weekly blood tests: FBC/Na/K/Mg/Tac level (Aug onwards: 2 weekly)
- April–September weekly Tac levels: Aim 5–20 ng/mL (Oct onwards: 2 weekly)

Date	Norm 5–15 ng/mL	4/24	5/09	6/05	6/12	6/26	7/03	7/10	7/17	7/24	7/31	8/07	8/14
Result		8.8	8.5	11.5	10.5	5.0	2.0	8.6	5.5	1.7	3.5	1.3	2.4

- Vaccination preparation
  - DPT × 3 (Aug/Sep/Oct)
  - H.Inf
  - Pneumococcal
  - HBV
  - HPV

Global Leukemia Academy

Case 1 – Discussion

Ane Veu (Fiji)

APTITUDE HEALTH®

Discussion

- **What management changes would you advise regarding tacrolimus levels?**
- **How would you recommend vaccination schedule planning?**

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Case 2

Feng-Ming Tien (Taiwan)

APTITUDE HEALTH®

Global Leukemia Academy

AML case-based panel discussion

Case AML: young high risk

Feng-Ming Tien, MD, MSc

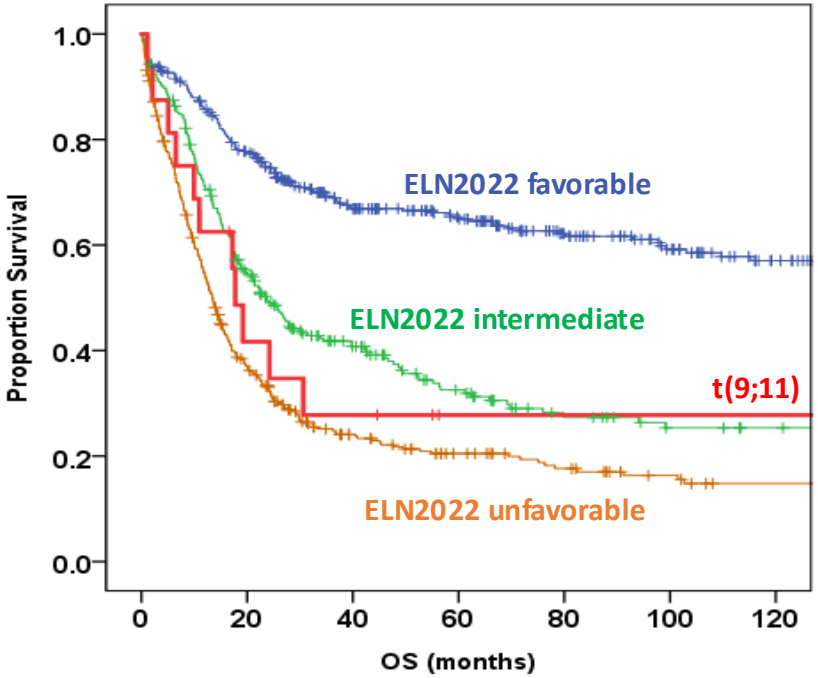
8.24.2024

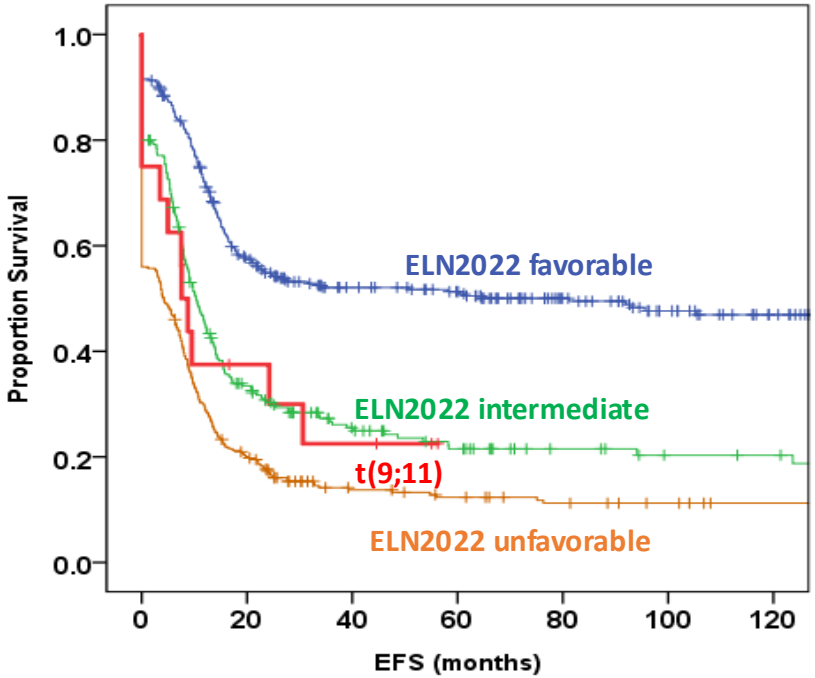
Division of Hematology, Department of Medicine
National Taiwan University Hospital, Taipei, Taiwan

23-year-old woman with *KMT2A*-rearranged AML

	Event/Examination	Evaluation/Management
11/2022	• Pale lips and exertional dyspnea • NTUH: CBC: WBC 14.43 K/μL, blasts 20.0% , PLT 40 K/μL	
12/7/2022	• BM study: AML, M4, t(9;11)(p22;q23)[19]/46,XX[1], *FLT3*-TKD (-), *FLT3*-ITD (-), *NPM1* (-), *CEBPA*(-), *RUNX1*(-), NGS: *WT1* mutation • (ICC) AML with t(9;11)(p21.3;q23.3)/*MLLT3::KMT2A* • (2022 WHO) AML with *KMT2A* rearrangement • (2022 ELN) intermediate risk	

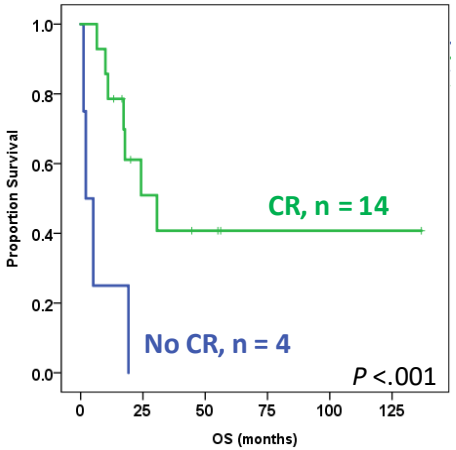
NTUH data: survival for AML with t(9;11)(p21.3;q23.3)

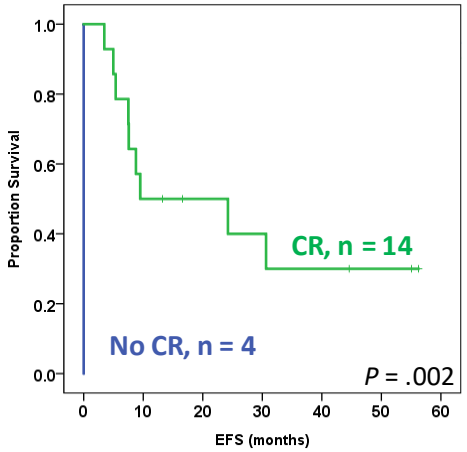




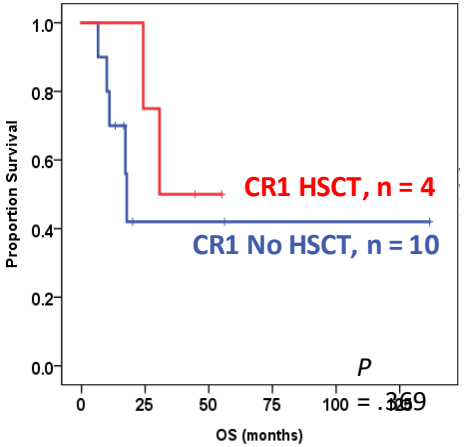
NTUH data: survival for AML with t(9;11)(p21.3;q23.3)

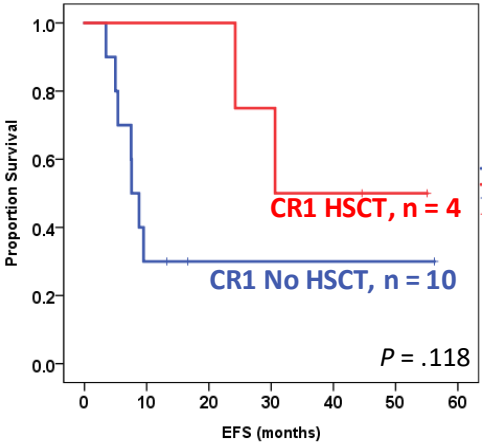
Survival stratified by CR or not





Survival stratified by CR1 HSCT or not





Persistent positive flow MRD

	Event/Examination	Evaluation/Management
12/8/2022	I3A7	BM: CR1, flow MRD positive 0.39%
1/28/2023	HDAC	• Septic shock, typhlitis or pubis soft tissue infection • Port-A infection *(C. arthrosphaerae/S. maltophilia)*, Port-A removal on 2/24 • 3/22 BM: CR1, flow MRD positive 0.9%, *MLLT3::KMT2A* PCR 0.176

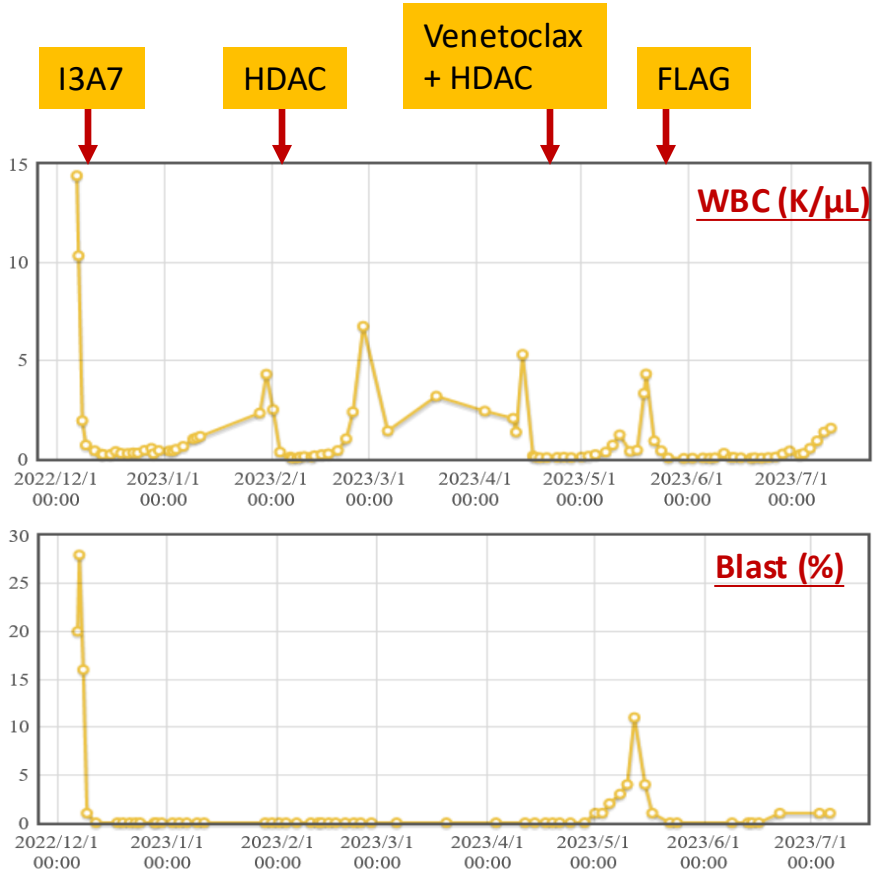
Persistent positive flow MRD

	Event/Examination	Evaluation/Management
12/8/2022	I3A7	BM: CR1, flow MRD positive 0.39%
1/28/2023	HDAC	• Septic shock, typhlitis or pubis soft tissue infection • Port-A infection *(C. arthrosphaerae/S. maltophilia)*, Port-A removal on 2/24 • 3/22 BM: CR1, flow MRD positive 0.9%, *MLLT3::KMT2A* PCR 0.176
4/12/2023	Venetoclax 100 mg qd* 7 days (with posaconazole) + HDAC	Relapse
5/19/2023	FLAG	7/11 BM: smear blast 1.4%, flow MRD 2.18%, MLFS

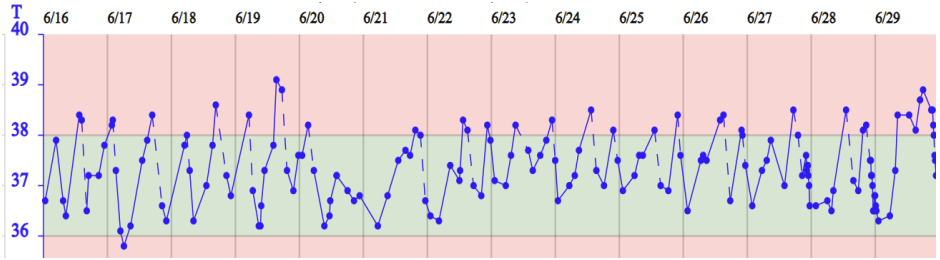
What's the next step for this patient with refractory t(9;11) AML?

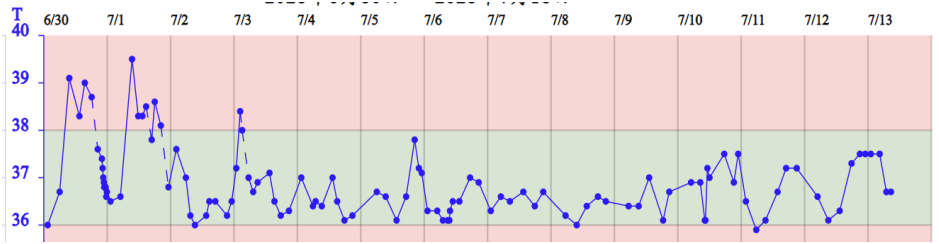
A. Salvage chemotherapy (eg, NEC)
B. Decitabine and venetoclax
C. Menin inhibitor (DSP-5336) trial
D. Anti-CD123 (AZD9829) trial
E. Proceed directly to allo-HSCT

Hemogram and PB blasts before allo-HSCT



- Intermittent fever for several weeks after FLAG
- 7/6 inflammation scan: diffuse bone marrow uptake; no other notable infection





9/10 MMUD allo-HSCT on 2023/7/25

	Event/Examination	Evaluation/Management
7/25/2023	Bu3Cy2 + HLA 9/10 MMUD-PBSCT, CD34+: 4.56 × 10^6/KgBw, 23M to 23F	• CR-KP bacteremia • 8/16 BM: CR2, flow MRD–, full donor chimerism by STR, FISH: XX below cut-off, *KMT2A* PCR -2.292 • Stop all immunosuppressants on 10/16 • No acute GvHD
10/3/2023	Maintenance decitabine 20 mg/m^2 × 3 days, C1D1 10/3, C2D1 11/11	Smooth

Maintenance decitabine after allo-HSCT

	Event/Examination	Evaluation/Management
2/5/2024	Maintenance decitabine 20 mg/m^2 × 3 days, C3D1 2/5	• Prolonged neutropenic fever and diarrhea, despite GCSF and antibiotics • 3/18 BM: CR2, flow MRD–, *KMT2A* PCR–

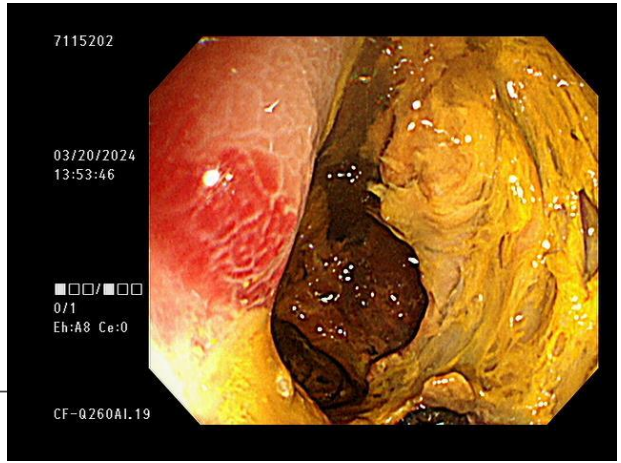
CBC+PLT(1/2)	WBC(k/μL)	RBC(M/μL)	HB(g/dL)	HCT(%)	MCV(fL)	MCH(pg)	MCHC(g/dL)	PLT(k/μL)
2024/03/20 06:51	0.56	1.89	5.7	17.4	92.1	30.2	32.8	145 (Manual checked)
2024/03/25 08:35	0.71	3.31	8.8	26.6	80.4	26.6	33.1	63

WBC D/C(1/2)	Blast(%)	Promyl.(%)	Myelo.(%)	Meta(%)	Band(%)	Seg(%)	Eos.(%)	Baso.(%)
2024/03/20 06:51	0.0	0.0	0.0	0.0	0.0	6.0	0.0	0.0
2024/03/25 08:35	0.0	0.0	0.0	0.0	3.0	13.0	0.0	0.0

WBC D/C(2/2)	Mono.(%)	Lym.(%)	Aty.Lym.(%)	PlasmaCell(%)	Normobl.()	PS()
2024/03/20 06:51	3.0	40.0	1.0	0.0	0.0 /50 WBC	WBC 50X2
2024/03/25 08:35	3.0	31.0	0.0	0.0	0.0 /50 WBC	WBC 50X2

Diagnostic workup for persistent diarrhea

- 3/20/2024 Colonoscopy: Several large deep ulcers, hyperemic mucosa with loss of vasculature and mucus/stool-coatings were noted at the cecum and ascending colon, status post-biopsies



Intestine, large, colon, ascending, colonoscopic biopsy, c/w graft-versus-host disease
Intestine, large, colon, descending, colonoscopic biopsy, c/w graft-versus-host disease
Intestine, large, colon, sigmoid, colonoscopic biopsy, c/w graft-versus-host disease

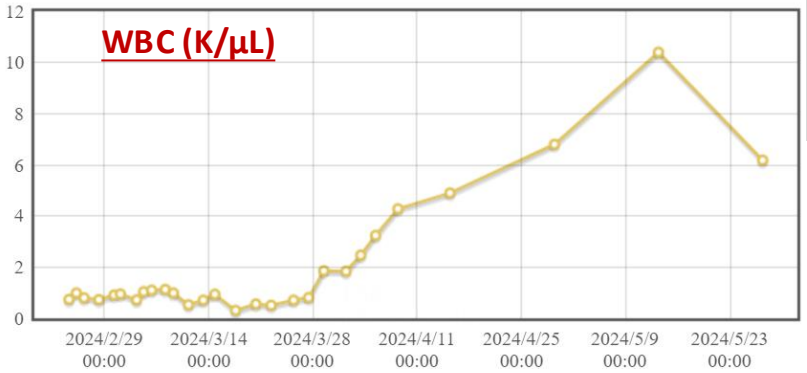
MACROSCOPIC:
A: 4 tissue fragments, up to 0.4 x 0.2 x 0.1 cm in size.
B: 2 tissue fragments, up to 0.5 x 0.3 x 0.1 cm in size.
C: 2 tissue fragments, up to 0.4 x 0.3 x 0.1 cm in size.

All for sections and labeled as: Jar 0
A1: ascending colon
B1: descending colon
C1: sigmoid colon

MICROSCOPIC:
All sections show crypt apoptoses which is most prominent in section A1 accompanied by contiguous crypt loss. Mild inflammation is also noted. CMV immunostain is negative in all sections. Overall, the picture is compatible with graft-versus-host disease, grade 3.

Late acute GvHD around 8 months after allo-HSCT

	Event/Examination	Evaluation/Management
7/25/2023	Decitabine C3D1 2/5	• Prolonged neutropenic fever and diarrhea, despite GCSF, romiplostim, and antibiotics • 3/18 BM: CR2, flow MRD– • Start methylprednisolone 40 mg BID • Diarrhea improved under steroid and tacrolimus
3/20/2024	Grade 3 GI aGvHD was diagnosed	• 6/13 BM: CR2, flow MRD 0.11% • 7/22 Frank relapsed



What's the next step for this patient with relapsed t(9;11) AML after allo-HSCT?

A. Salvage chemotherapy followed by donor lymphocyte infusion
B. Decitabine and venetoclax followed by donor lymphocyte infusion
C. Menin inhibitor (DSP-5336) trial
D. Anti-CD123 (AZD9829) trial
E. Second allo-HSCT with another donor

Global Leukemia Academy

Case 2 – Discussion

Feng-Ming Tien (Taiwan)

APTITUDE HEALTH®

Global Leukemia Academy

Panel discussion: How treatment in first line influences further therapy approaches in ALL and AML

Naval Daver and all faculty

APTITUDE HEALTH®

Panel Discussion

> Will CAR Ts and bispecifics change the treatment landscape?

> What is the evolving role of HSCT – will it still be necessary?

> What does the future in Asia-Pacific look like in terms of

- Adoption of new therapies?
- Evolving standards of care?

Global Leukemia Academy

Panel Discussion

APTITUDE HEALTH®

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ARS questions

Naval Daver

APTITUDE HEALTH

Question 3 [REPEATED]

Which of the following is NOT true for ALL?

A. Inotuzumab and blinatumomab + chemotherapy is active in both front line and salvage for ALL

B. Kinase inhibitors can be combined with other therapy modalities in Ph-positive ALL

C. MRD is highly prognostic for relapse and survival in Ph-negative ALL

D. There are no effective consolidation treatments for patients who remain MRD positive after induction therapy

Question 4 [REPEATED]

The prognosis of patients with R/R AML depends on:

A. Age
B. Prior therapy (eg, HSCT)
C. Timing of relapse
D. The mutational and cytogenetic profile of the disease
E. All of the above
F. A and D

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THANK YOU FOR ATTENDING!

Meeting sponsors AMGEN rigel

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