Treatment of Adults with ALL: Treatment (R)Evolution!

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Is there an optimal approach in 2023?

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Disclosures

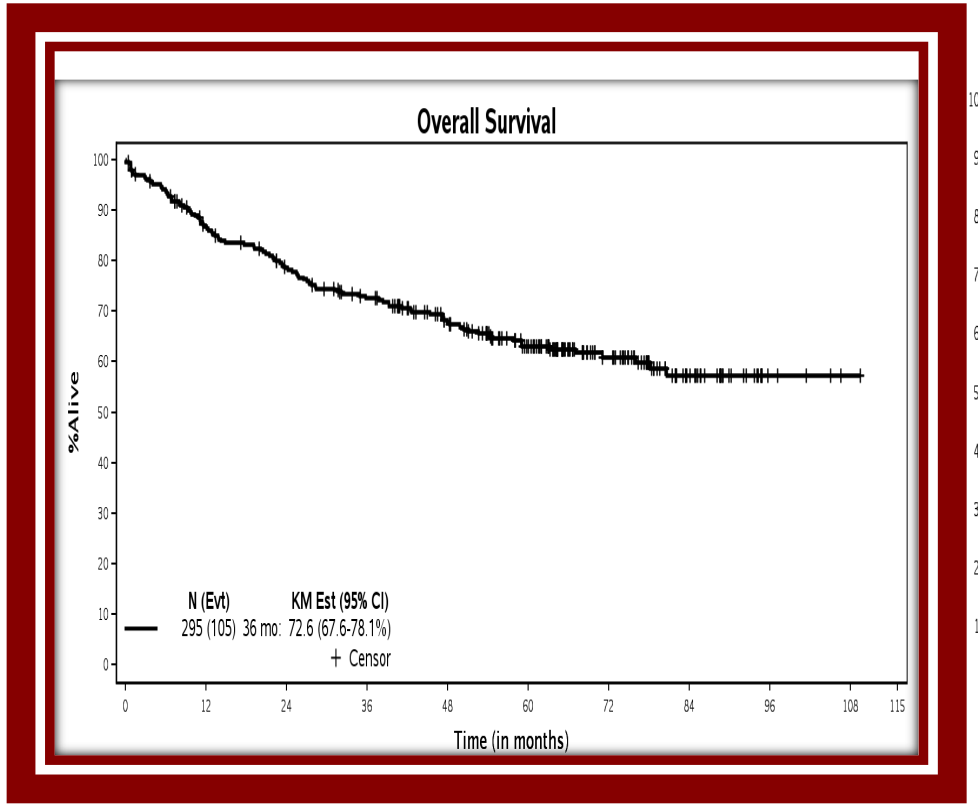
- Advisory Boards: Agios, Amgen, Astra Zeneca, Beam, Glaxo Smith Kline, Jazz, Kite, Kronos, Kura, Morphosys, Newave, Pfizer, Servier, Syndax
- Honoraria: Up to Date, Jazz, Pfizer, Research to Practice
- Service honoraria: American Society of Hematology – *Blood Advances*

Outline: The ALL World has Changed

- Themes: MRD eradication, Blending of New and Old, Less is more!
- Frontline: Younger Adults with B-ALL, T-ALL, T-LBL
  - Pediatric regimens are now standard of care
  - Frontline trials incorporate chemo + targeted agents
- Frontline: Older Adults with B-ALL
- Ph+ ALL: Moving away from alloSCT in CR1
- Relapse: Innovation – where will CAR-T fit in?

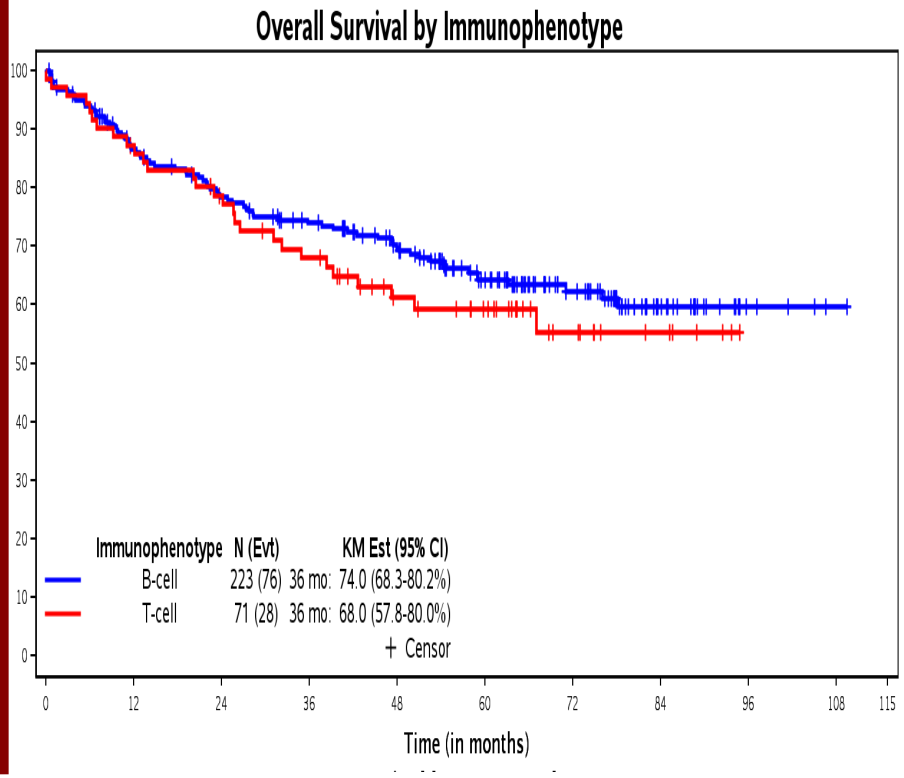
Improved Survival for AYAs: CALGB 10403

- 72% Survival at 3 years



Stock et al, Blood 2019

- Immunophenotype: B vs T



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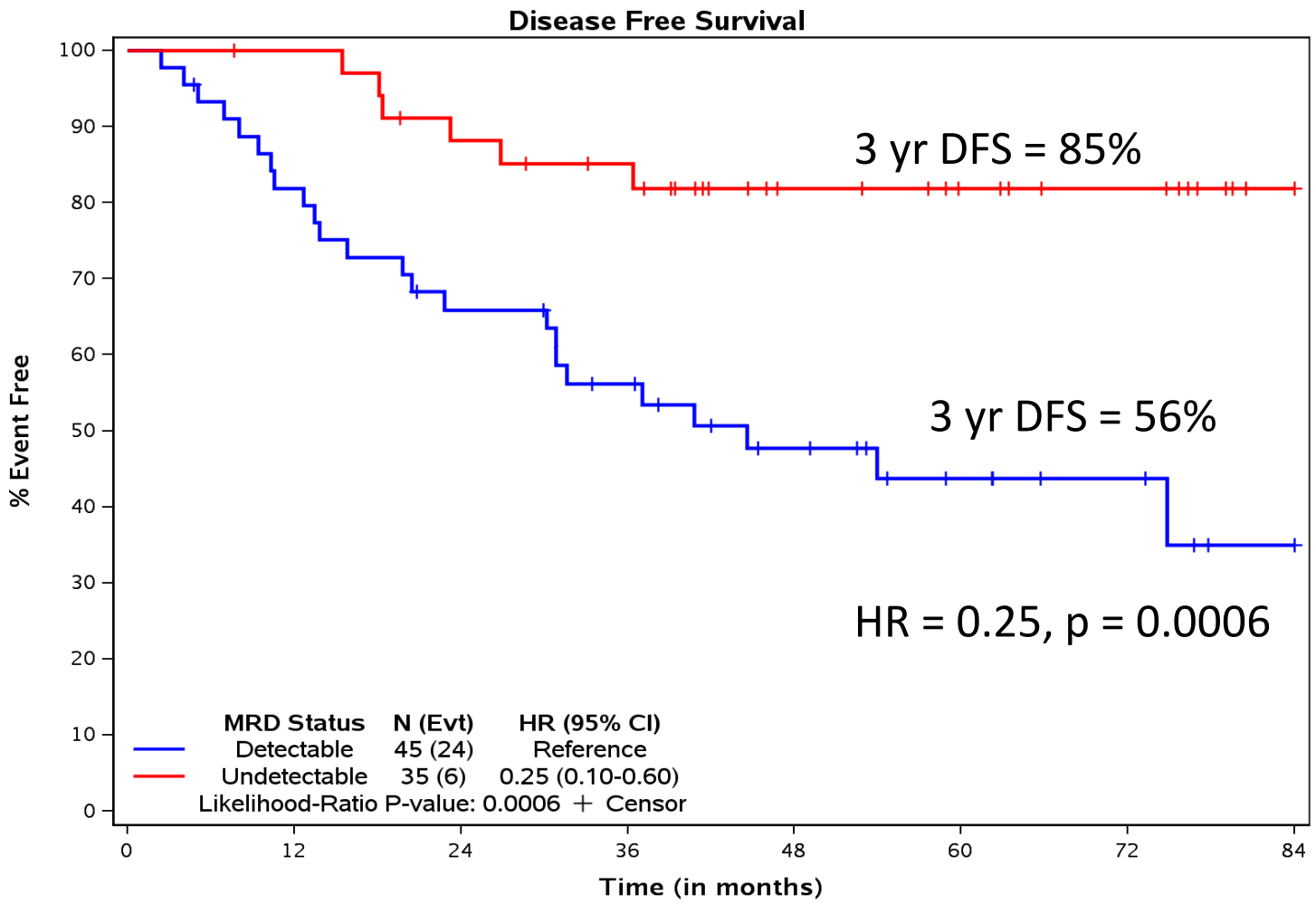
Excellent Outcomes: Achievement of early MRD neg CALGB 10403



Q-PCR following Induction

Blood, 2019; 133, 1548-1559

Only 40% of patients are MRD negative early in treatment

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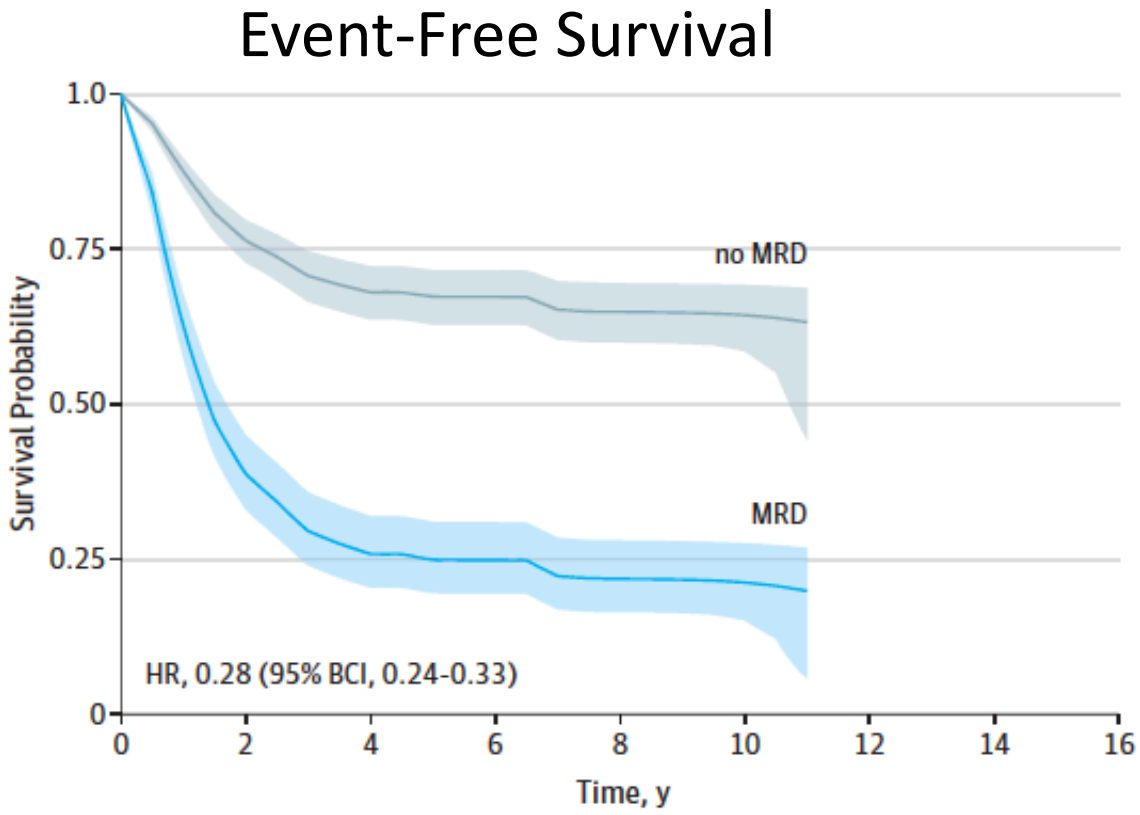
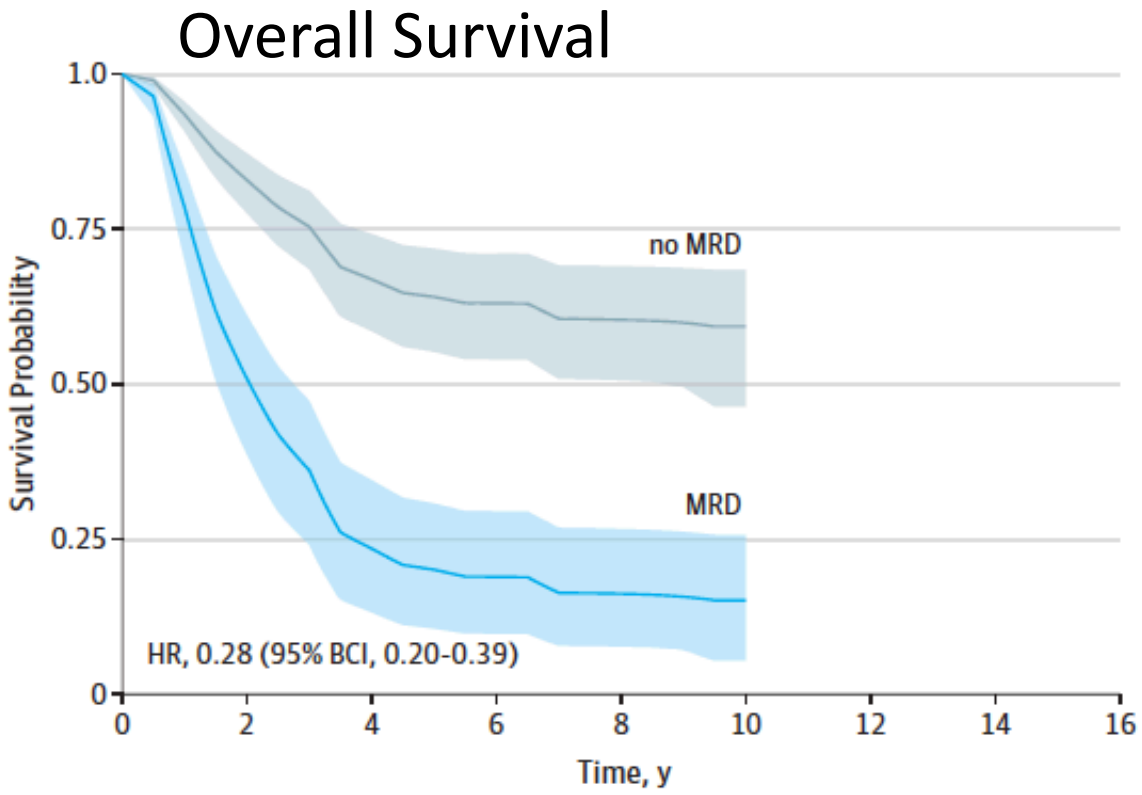
MRD associated with inferior EFS and OS in adult ALL





Berry, et al. JAMA Oncol 2017

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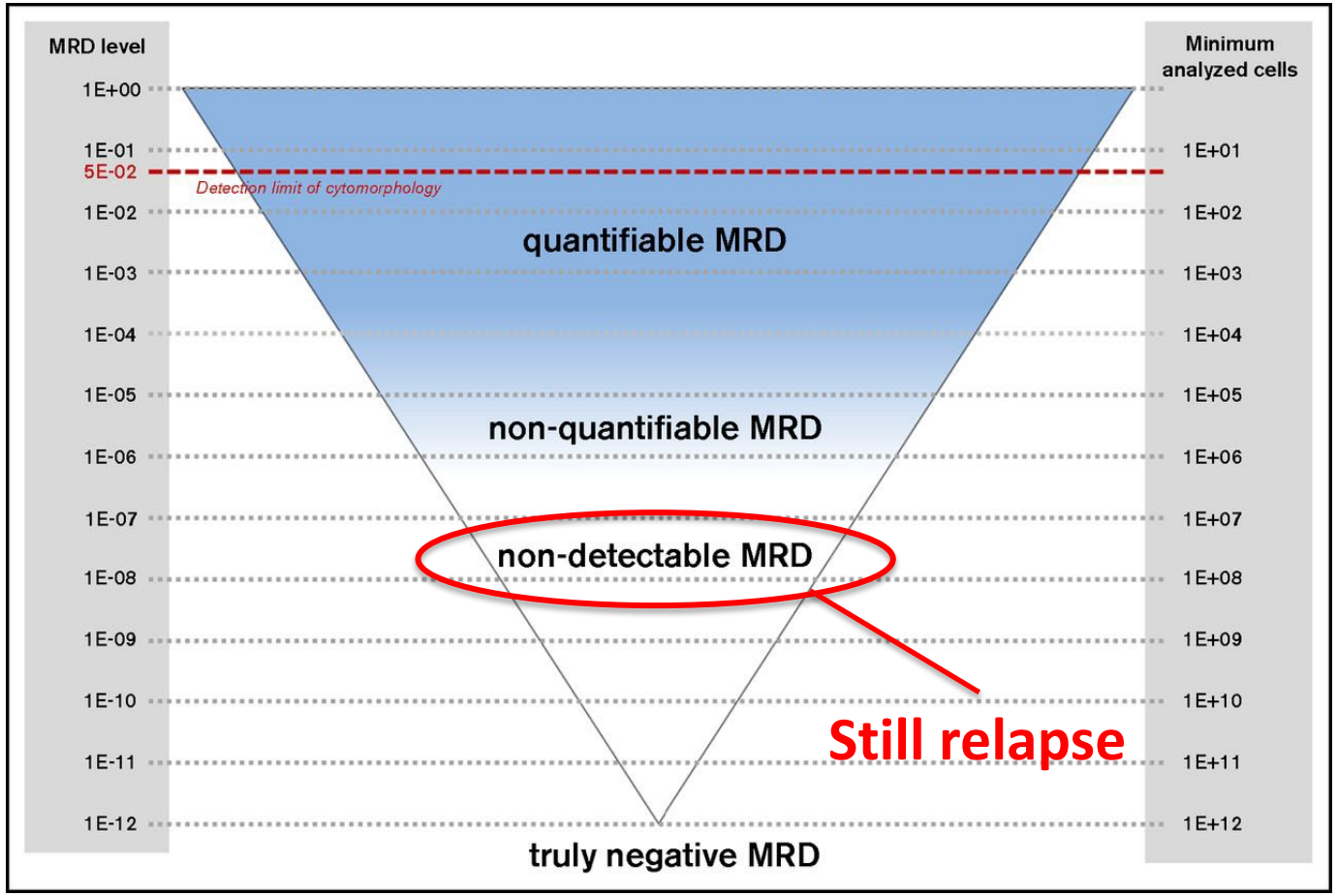
MRD: “Minimal” or “Measurable” Residual Disease



- **Multiparameter Flow Cytometry (MFC)**
  - Sensitivity: 10^{-4}
- **Allele-Specific Oligonucleotide PCR (ASO-PCR)**
  - Sensitivity 10^{-5} to 10^{-6}
- **Next Generation Sequencing (NGS)**
  - Sensitivity: 10^{-6}

Bruggemann & Kotrova Blood Adv 2017

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How can we best ”eradicate” MRD?

- Intro of effective agents for relapse into frontline combinations
  - FDA Approved for Relapsed ALL
    - CD19 target: Blinatumomab* (also approved for treatment of MRD+) CD22 target: E1910
    - CD22: Inotuzumab ozogamycin (A041501 for AYA ALL)
    - T- ALL: Nelarabine
  - Early phase data
    - BH3 mimetics

ASH 2022: Late Breaking Abstract

ECOG-ACRIN-E1910 NCTN Clinical Trial: A Phase III Randomized Trial of Blinatumomab for Newly Diagnosed BCR::ABL-negative B lineage Acute Lymphoblastic Leukemia in Adults

Mark R. Litzow, MD

Zhuoxin Sun, Elisabeth Paietta, Ryan Mattison, Hillard Lazarus, Jacob Rowe, Daniel Arber, Charles Mullighan, Cheryl Willman, Yanming Zhang, Matthew Wieduwilt, Michaela Liedtke, Julie Bergeron, Keith Pratz, Shira Dinner, Noelle Frey, Steven Gore, Bhavana Bhatnagar, Ehab Atallah, Geoffrey Uy, Deepa Jeyakumar, Tara Lin, Daniel DeAngelo, Richard Stone, Harry Erba, Richard Little, Selina Luger, Martin Tallman

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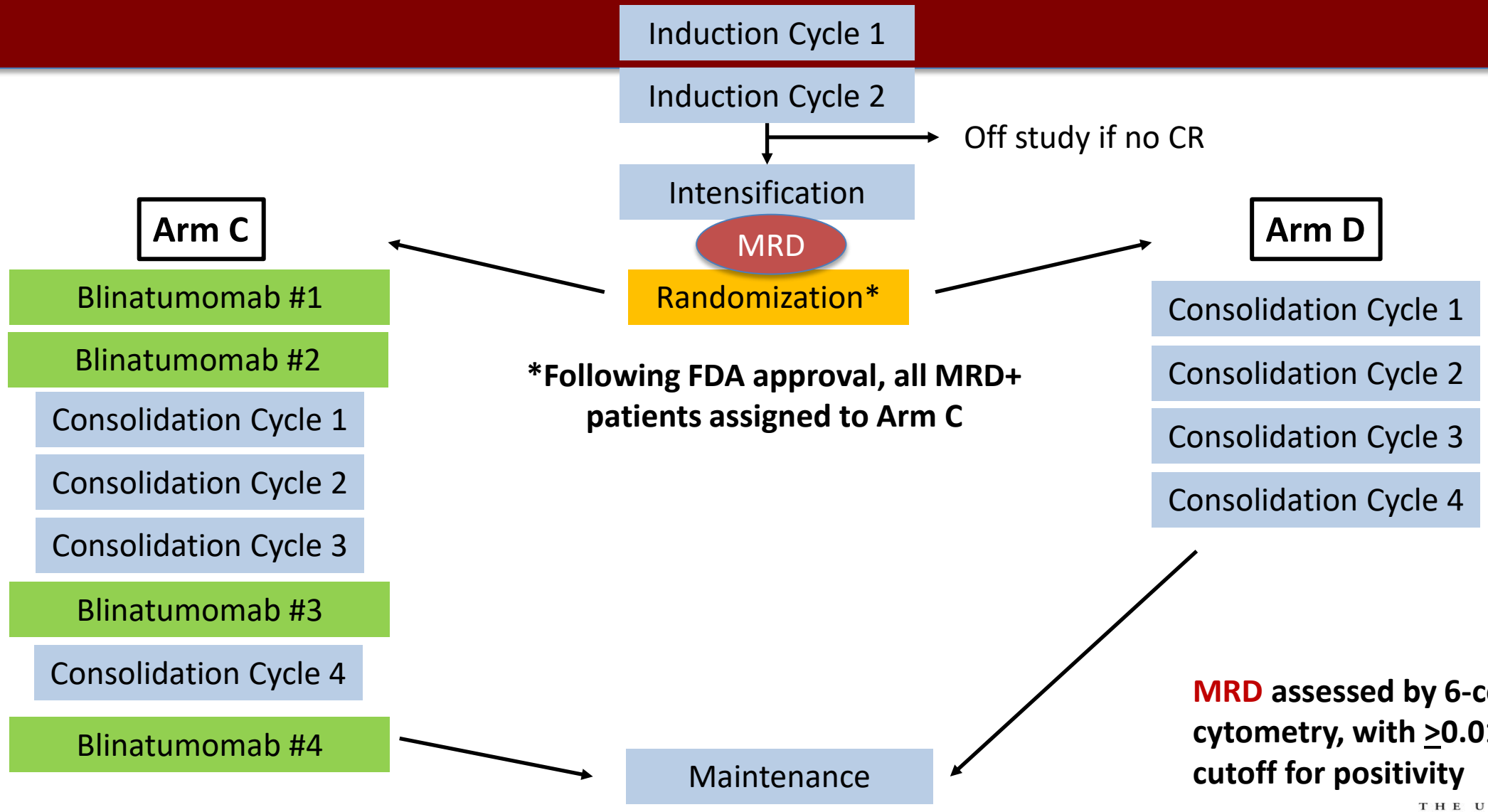
E1910: Randomized CD19+ B- ALL



***Following FDA approval, all MRD+ patients assigned to Arm C**

MRD assessed by 6-color flow cytometry, with ≥0.01% as the cutoff for positivity

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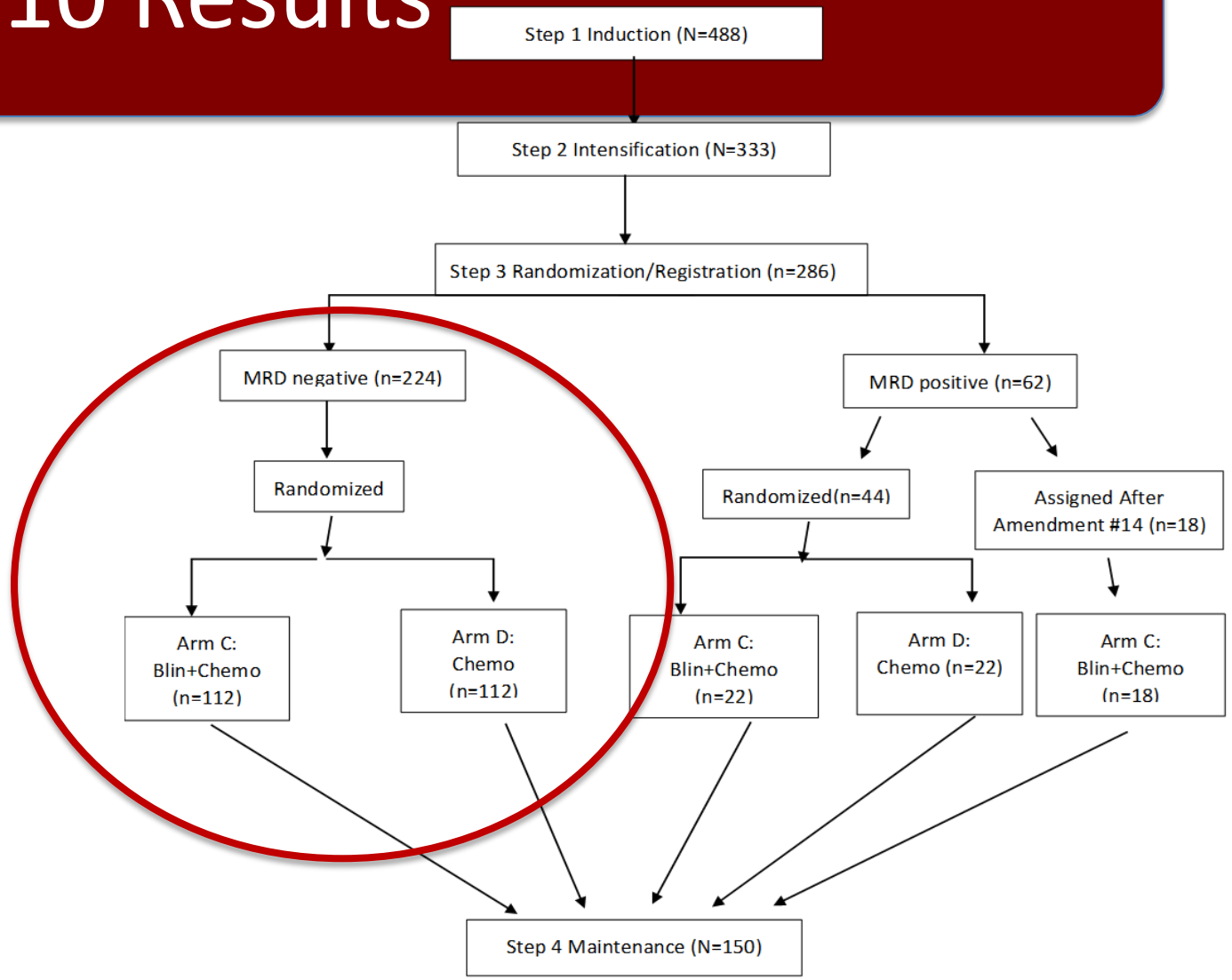
E1910 Results

- 488 pts enrolled
- Median age: 51yrs (range 30-70yrs)
- Median follow-up 3.6 yrs
- CR/CRi rate 81% (395/488 pts)
  - CR 75% (364 pts)
  - CRi 6% (31 pts)
- 224 MRD – patients
  - Among MRD-neg, 22 patients in each arm underwent alloHSCT
  - 80% of pts received ≥2 cycles of blinatumomab



Litzow et al, ASH 2022

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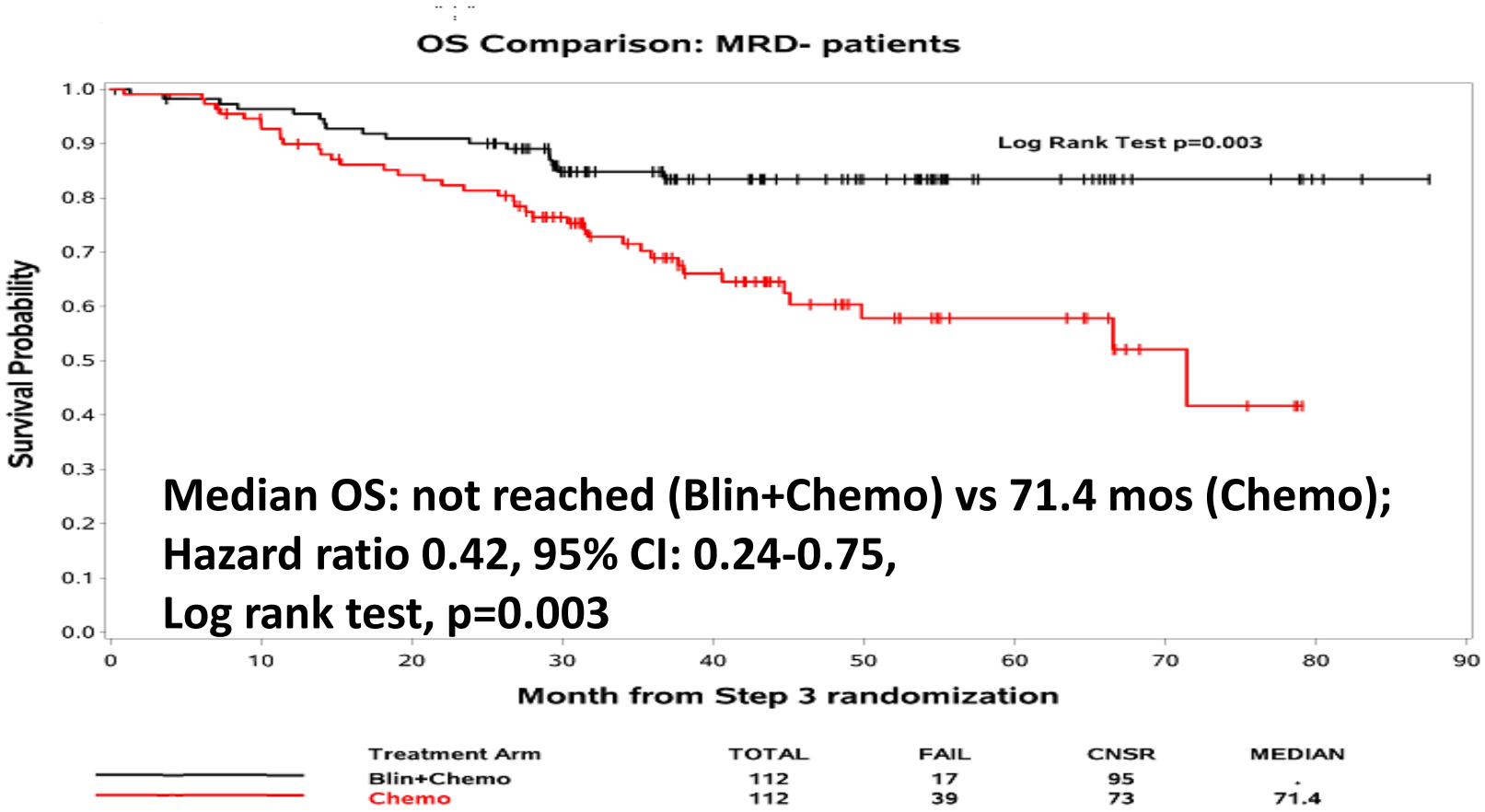
Overall Survival : MRD negative patients



Deaths on Blin+Chemo Arm=17 (2° to ALL=8, NRM=9), Chemo Arm=39 (2° to ALL=20, NRM=17, Unknown=2)

Litzow et al, ASH 2022

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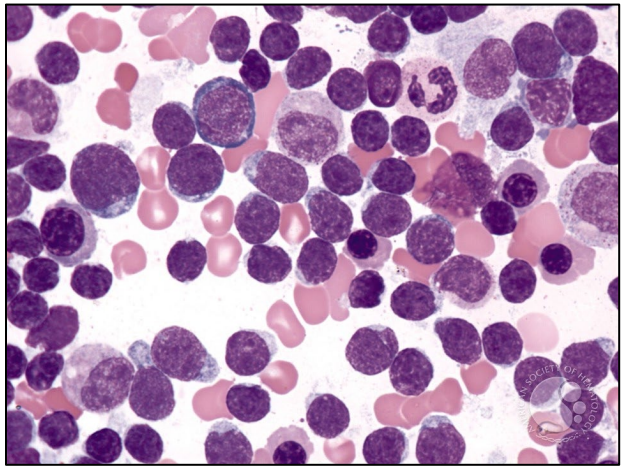
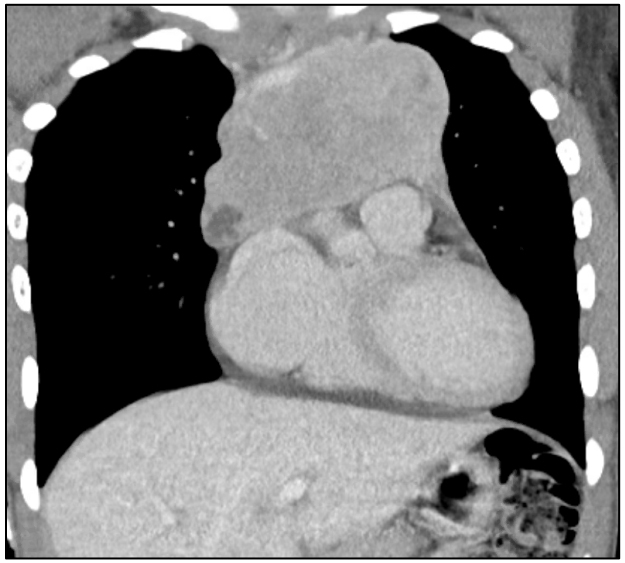
Commentary

- First evidence that Blina significantly improves survival for MRD negative patients in CR1: IMPRESSIVE!
- May be new standard for post remission Rx for CD19+ CR1
- Comments:
  - MRD method in E1910 was less sensitive flow cytometry
    - Wonder about impact of blina if MRD neg using more sensitive methods of detection: Can we have even better selection of pts?
  - Many patients were lost prior to blina – relapse, transplant, alternative therapies, toxicity
    - Likely more useful to introduce blina earlier in treatment

T-lineage acute lymphoblastic leukemia/lymphoma (T-ALL/LBL)

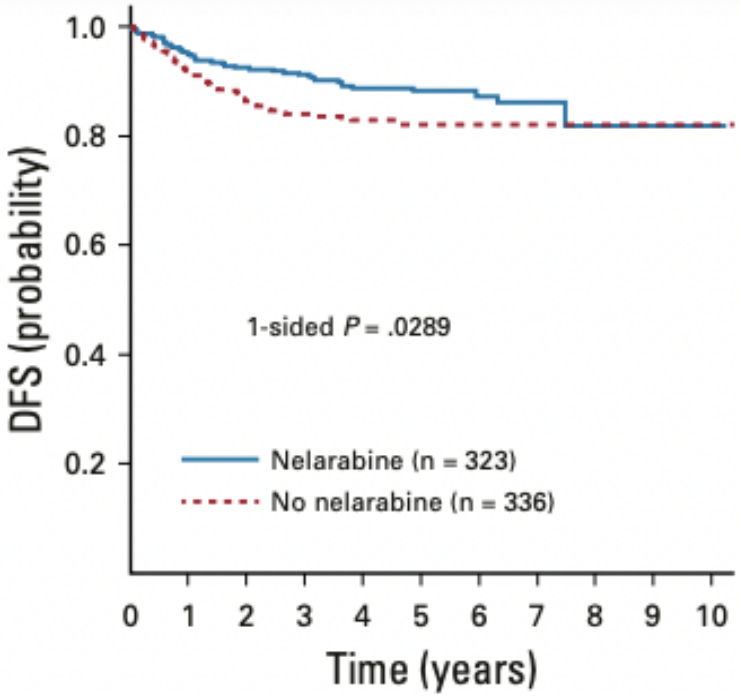




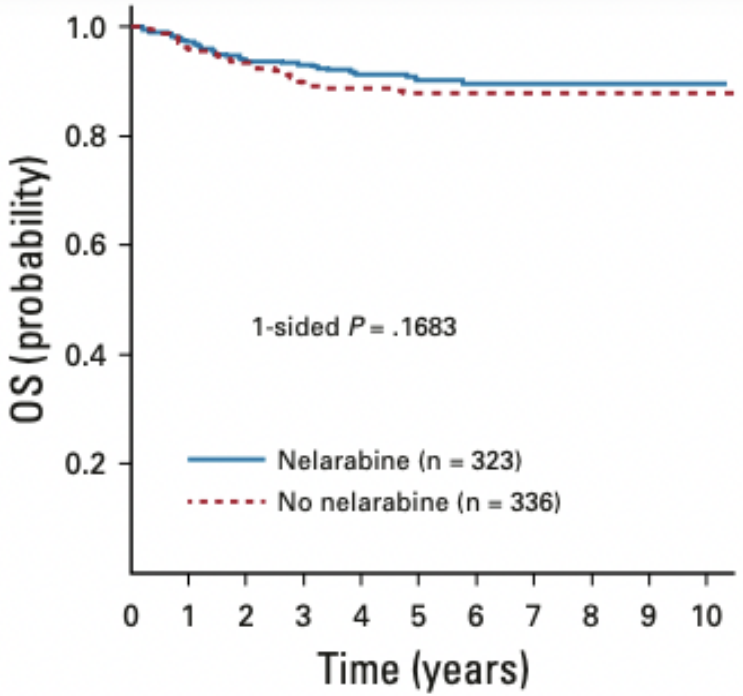
- 10-15% of pediatric and 25-30% of adult ALL cases
- Blood/bone marrow involvement (T-ALL) lymph node involvement common and/or sole extramedullary disease - mediastinal mass (T-LBL)
- **Nelarabine-containing pediatric-inspired regimens improves DFS in children and young adults**

Arber DA, *et al.* Blood 2016 Marks DI, *et al.* Blood 2017 Dunsmore KP, *et al*. J Clin Oncol 2020

Nelarabine improves DFS



No. at risk:											
Nelarabine	323	303	293	285	222	156	91	32	15	6	1
No nelarabine	336	304	284	273	224	167	97	43	17	8	2



No. at risk:											
Nelarabine	323	310	296	291	234	164	100	37	15	6	2
No nelarabine	336	319	306	290	240	177	108	45	20	9	2

- **Nelarabine incorporated into ABFM; six 5-day courses**
- **3% of the 1895 patients were AYAs between 20-30 years old**
- **5 yr DFS was 88.2% with nelarabine vs 82% DFS without (p=.02)**

Dunsmore et al, J Clin Oncol 2020:28, 3282-3293

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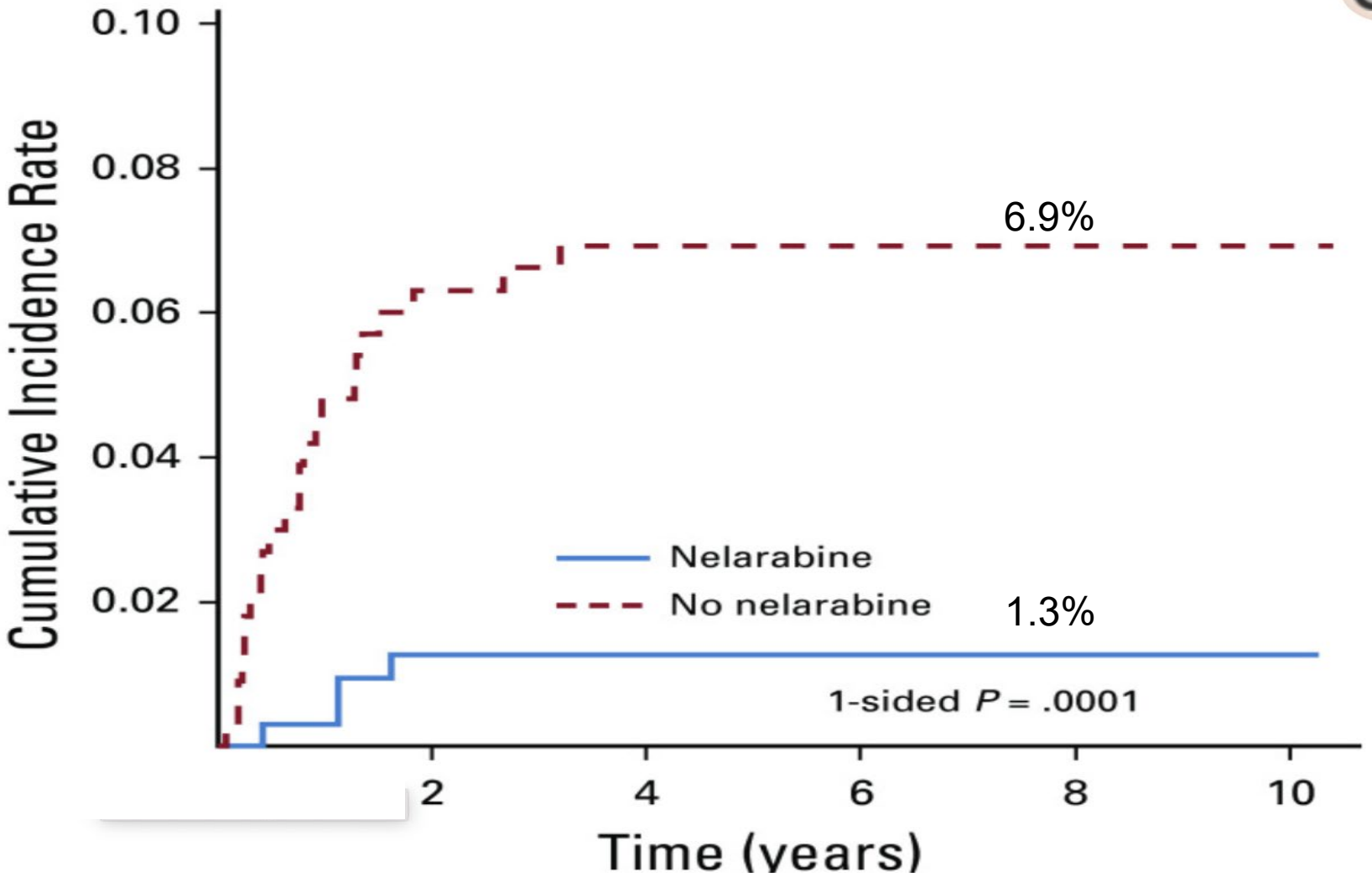
Nelarabine reduces CNS relapse



Dunsmore et al, J Clin Oncol 2020:28, 3282-3293

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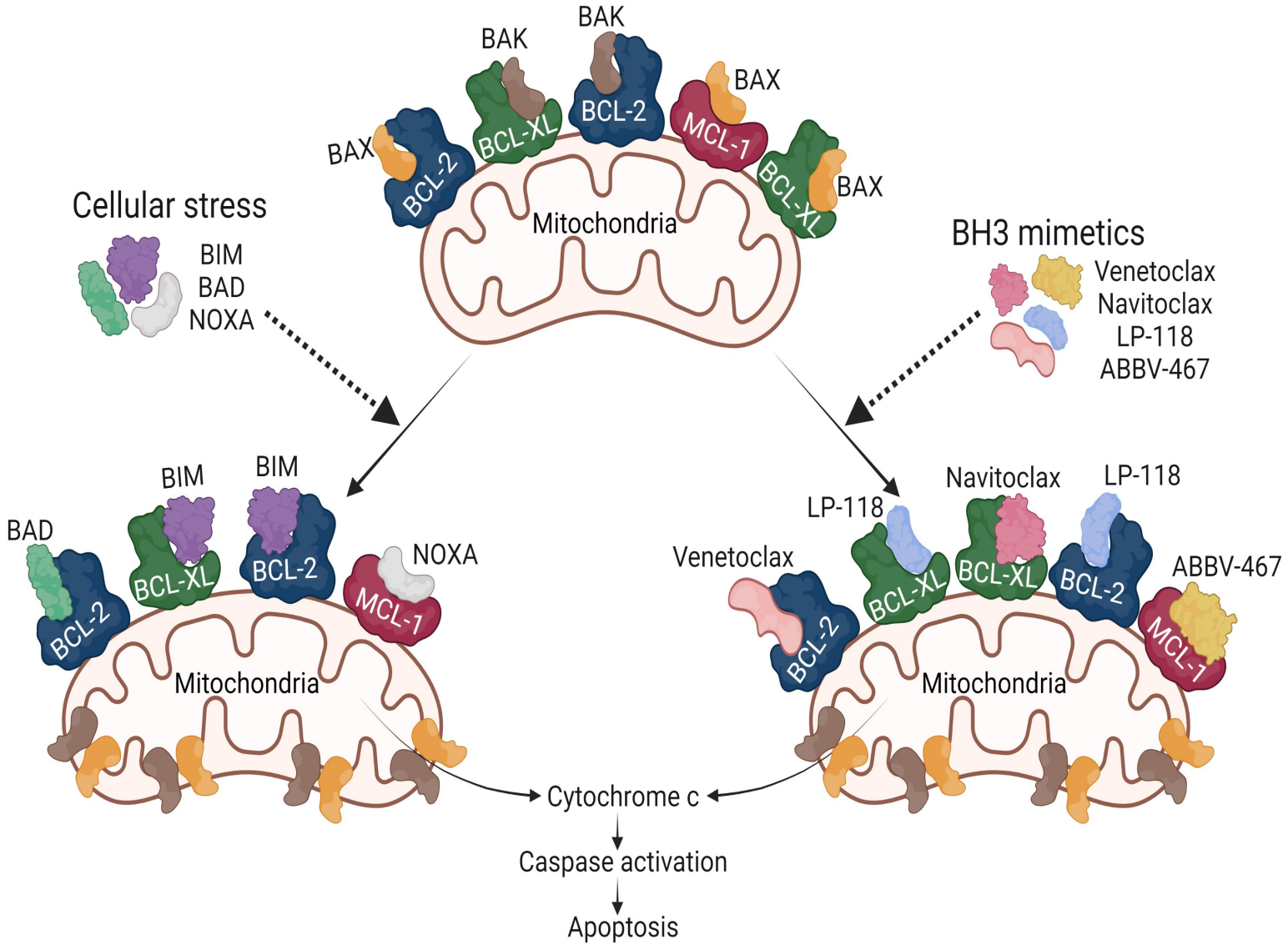
Apoptotic pathways and BH3 mimetics



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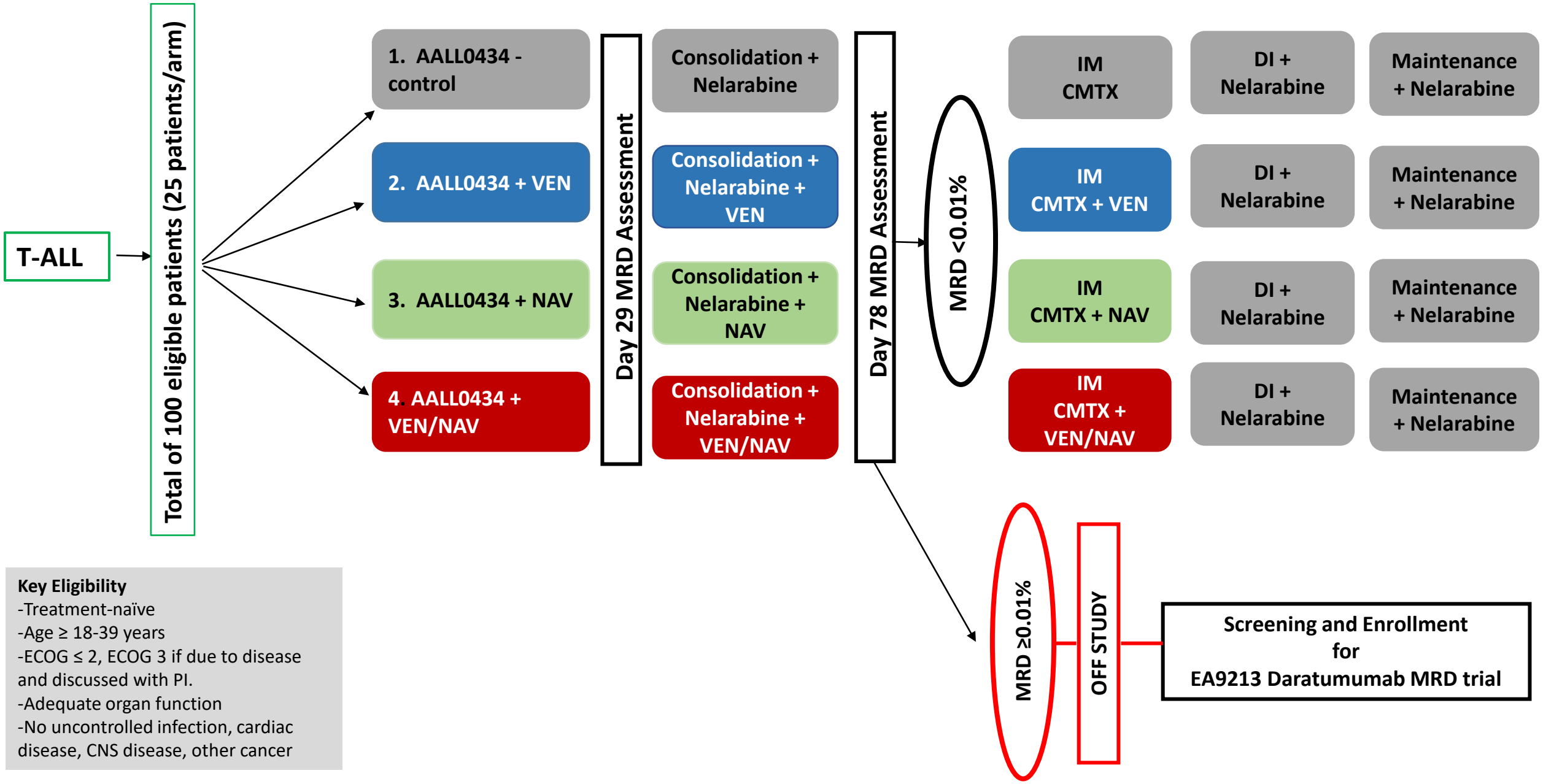
Venetoclax/Navitoclax in combination with chemotherapy has activity in relapsed/refractory T-ALL

Response	B-ALL (n=25)	T-ALL (n=19)	LL (n=3)	All Patients (N=47)
CR/CRi/CRp, n (%)	**16 (64)**	**10 (53)**	**2 (67)**	**28 (60)**
ALL patients with ≥5% BM blasts at baseline, n/N	15/23 (65)	7/14 (50)	NA	22/37 (59)
ALL patients with morphologic CR at baseline, n/N	0/1 (NE)	3/4 (75)	NA	3/4 (75)
PR, n (%)	3 (12)	0 (0)	0 (0)	3 (6)
MRD-negative CR/CRi/CRp in ALL, n/N (%)	9/16 (56)	6/10 (60)	NA	15/26 (58)
Median DOR (95% CI), mo	9.1 (1.4–14.6)	4.2 (0.8–12.3)	NE (NE–NE)	4.2 (2.3–11.5)
Median OS (95% CI), mo	9.7 (4.0–15.7)	6.6 (3.2–12.5)	NR (2.0–NE)	7.8 (4.0–12.5)
Proceeded to SCT or CAR-T, n (%)	8 (32)	3 (16)	2 (67)	13 (28)

- Of 12 pediatric patients, 9 (75%) achieved CR/CRi/CRp, and of those, 6 achieved MRD-negative CR/CRi/CRp
- 4/32 (13%) patients achieved CR/CRi/CRp on Day 8 with Ven + Nav prior to starting chemotherapy on Day 9
- **CR rates were ≥50% across patient subgroups, including in those who had relapsed or were refractory to:**
  - **Blinatumomab: 8/13 (62%)**
  - **Inotuzumab ozogamicin: 8/14 (57%)**
  - **SCT: 5/8 (63%)**
  - **CAR T-cell therapy: 3/6 (50%)**

Pullarkat et al, Cancer Discovery 2021

S2306: Coming soon! Frontline Trial for T-ALL/T-LBL



Key Eligibility
-Treatment-naïve
-Age ≥ 18-39 years
-ECOG ≤ 2, ECOG 3 if due to disease and discussed with PI.
-Adequate organ function
-No uncontrolled infection, cardiac disease, CNS disease, other cancer

Transplant in CR1? No Survival Benefit

Hypothesis: AYA regimen is superior to alloHCT for post-remission "consolidation" in CR1

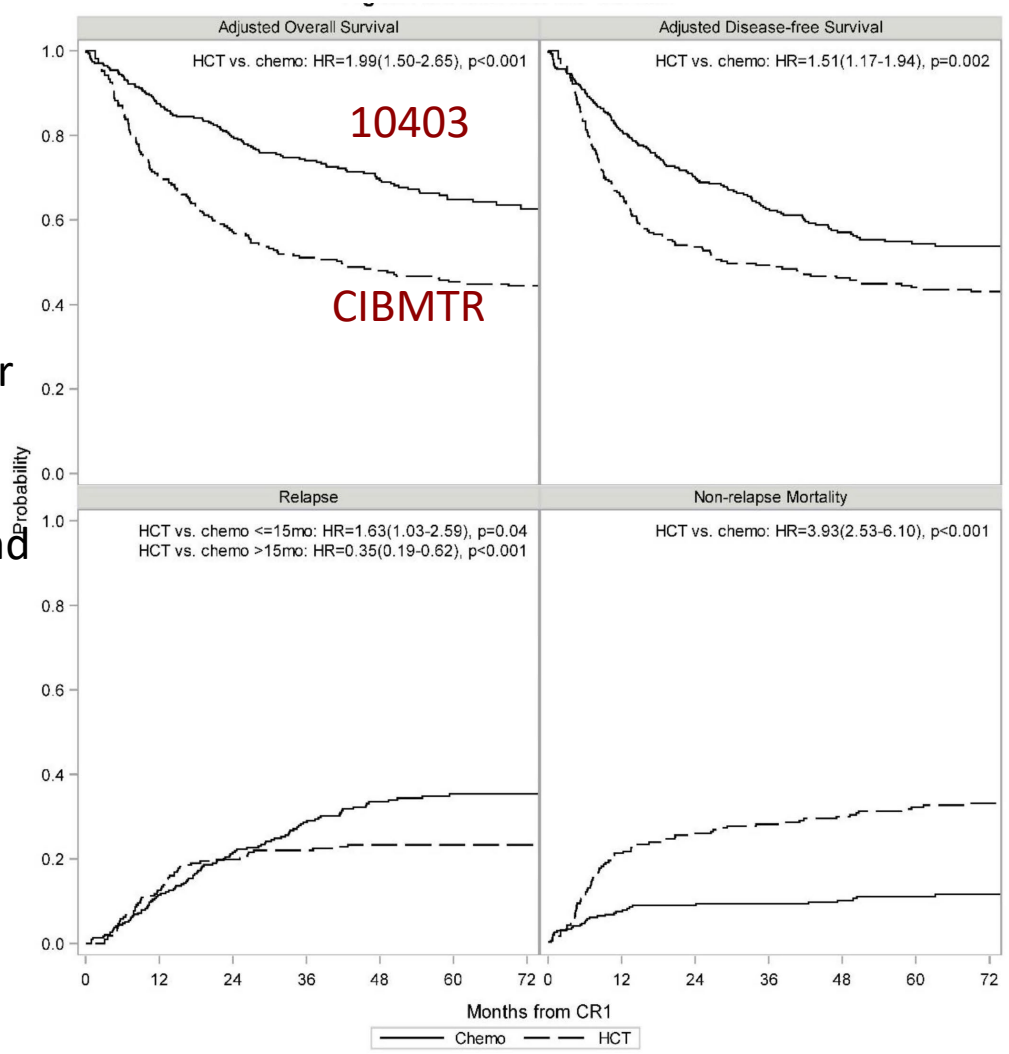
Compared 10403 (n= 295) to contemporary cohort undergoing myeloablative alloHCT in CR1 (n=217)

In multivariate analysis, alloHCT INFERIOR to AYA 10403 for both OS (HR= 1.99) , DFS (HR = 1.51) and non relapse mortality

- alloSCT associated with higher NRM; but beyond 15 mos, 10403 associated with higher relapse rate

Conclusions: CALGB 10403 SUPERIOR to alloHCT in newly diagnosed Ph-neg B cell and T cell ALL

Cautionary note: Further refinements by MRD in CR1, disease genetics needed to evaluate potential benefit of HCT in CR1 in selected subsets



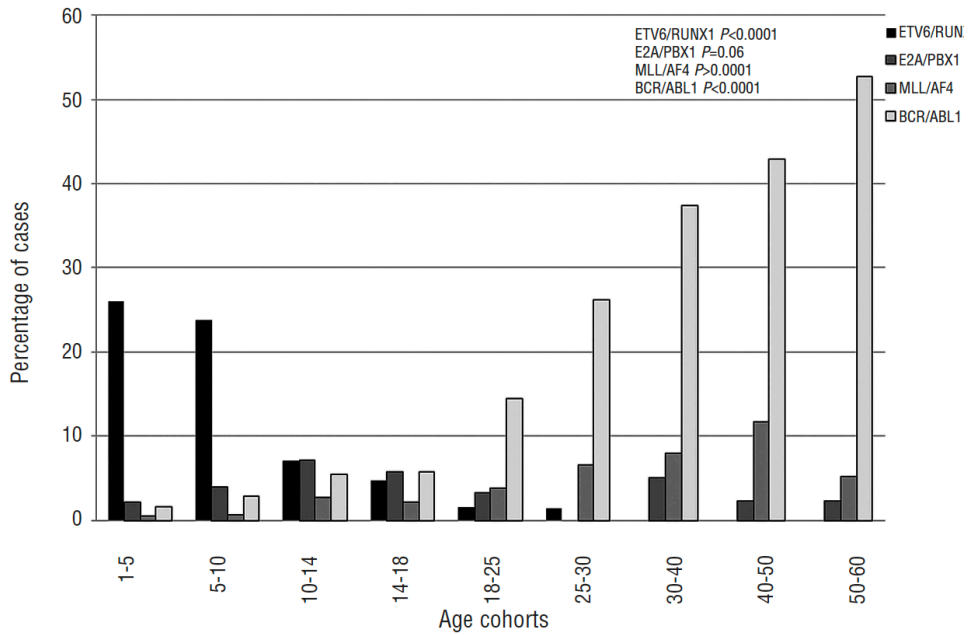
Wieduwilt et al, Leukemia 2021

Summary : Younger Adults

- Pediatric intensive regimens have improved survival
  - B-ALL: ongoing work to enhance EFS/ OS by addition of Antibody based therapies (INO/BLINA) in frontline
  - Paradigm shift E1910 data: Blina improves survival in MRD+ and MRD-
  - T-ALL: Nelarabine improves survival by decreasing CNS relapses
    - Targeting apoptotic pathways shows great promise: Next NCTN trial to test
    - Will daratumomab be useful (like blina) for MRD "erasing"?
- Allogeneic transplant in CR1: Not the "go to" for most pts

Ph+ ALL Treatment (R)EVOLUTION!

- Philadelphia chromosome/BCR-ABL1 fusion present in ~1/3 of ALL cases.
- Prevalence increases with age (>50% in patients >50 years).
- Historically adverse prognosis prior to 2nd and 3rd generation TKIs.



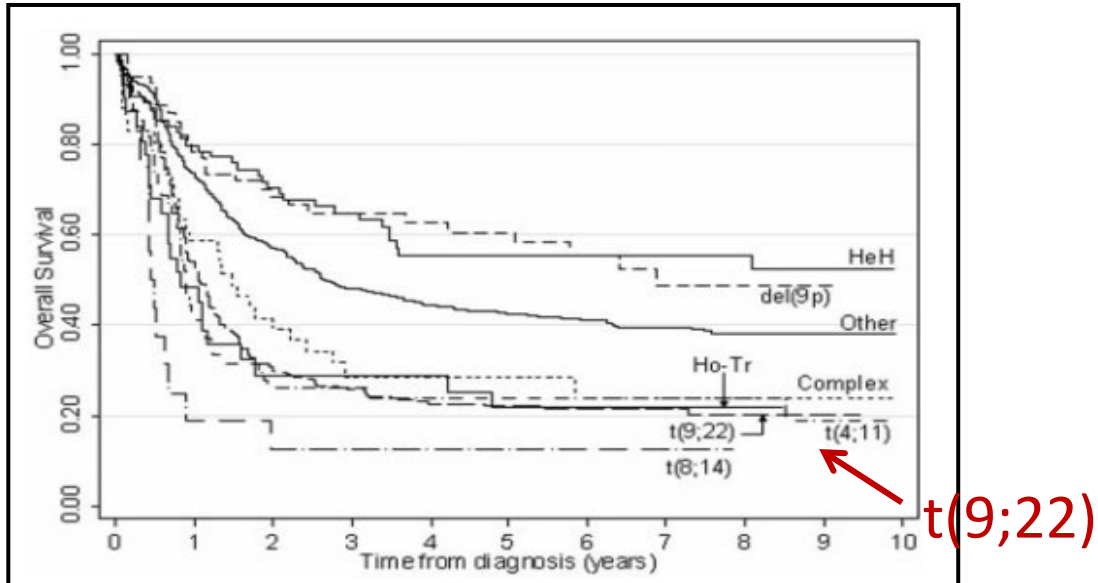


Figure 2. Overall survival by cytogenetic subgroup of patients registered on MRC UKALLXII/ECOG 2993.

Chiaretti S, et al. *Haematologica* 2013;98:1702–10; Burmeister T, et al. *Blood* 2008;112:918–9; Ribera JM, et al. *Br J Haematol* 2012;159:485–8; Moorman AV, et al. *Blood* 2007;109:3189–97; Rowe JM, et al. *Blood* 2005;106:3760–7.

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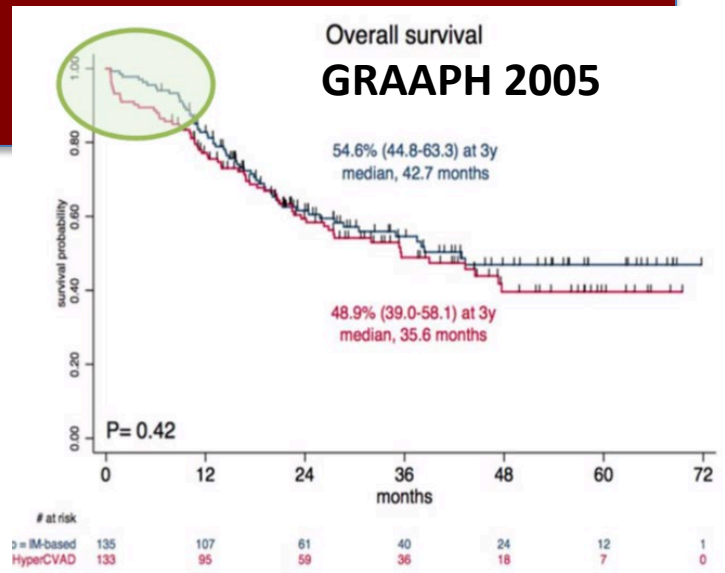
Ph+ ALL, recent context

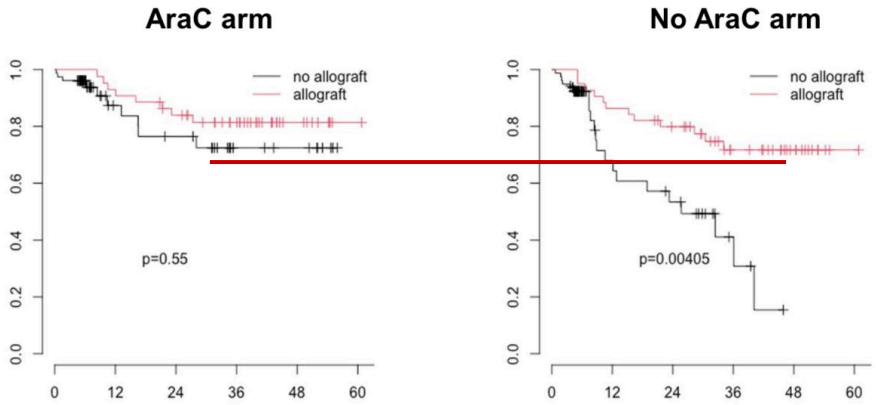
- **GRAAPH 2005 (IMATINIB)** → IM + VCR/Dex: ↑CR rate and ↓mortality compared to IM + hyperCVAD (**lesson**: reduce chemo in induction)

- **GIMEMA** → "chemotherapy-free" induction (imatinib LAL 0201-B; dasatinib LAL 1205, ponatinib LAL 1811).
  - High CR rates (>90%); (**lesson: 2G**/3G TKIs - Deeper and more durable); minimal toxicity

- **GRAAPH-2014 (NILOTINIB)** → Omission of HiDAC consolidation associated with more relapse in non-transplanted patients (**lesson:** still need intensive conventional chemo or BMT *in context of 2G TKI*)



GRAAPH 2014



Chalandon et al. *Blood* 2015;125:3711-9; Rousselot ASH 2021 Abstract 614

Ph+ALLCON Study design

- Adult patients with newly diagnosed Ph+ALL or BCR::ABL1-positive ALL
- ECOG PS 0–2
- Absence of history or current diagnosis of CP-, AP-, or BP-CML
- Absence of clinically significant or uncontrolled CV disease
- Randomized, N=245

Randomization 2:1

Ponatinib + reduced-intensity chemotherapy (n=164)
Ponatinib starting dose 30 mg once daily with dose reduction to 15 mg once daily[a]

Primary endpoint

Induction
Three 28-day cycles
TKI + vincristine + dexamethasone

Consolidation
Six 28-day cycles
TKI + methotrexate + cytarabine

Post-consolidation
Eleven 28-day cycles
TKI + vincristine + prednisone

Single-agent
TKI only until end of study

- Intrathecal therapy was performed twice per month for the first 6 cycles for CNS disease prophylaxis.

Imatinib + reduced-intensity chemotherapy (n=81)
Imatinib starting dose 600 mg once daily

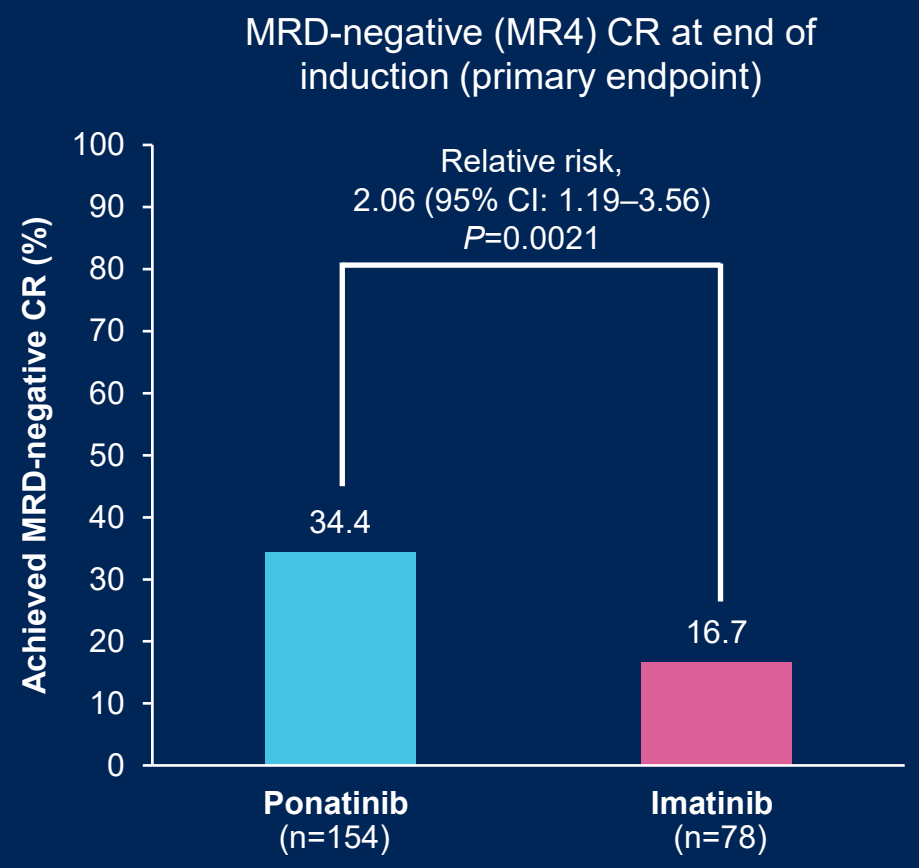
- Primary endpoint: MRD-negative CR, defined as hematologic CR (for ≥4 weeks) in combination with MRD negativity (≤0.01% *BCR::ABL1/ABL1* transcripts [also referred to as MR4])
- Key secondary endpoint: event-free survival
- Other secondary endpoints: molecular response rates, duration of MRD-negative CR, OS, and incidence of TEAEs and AOEs

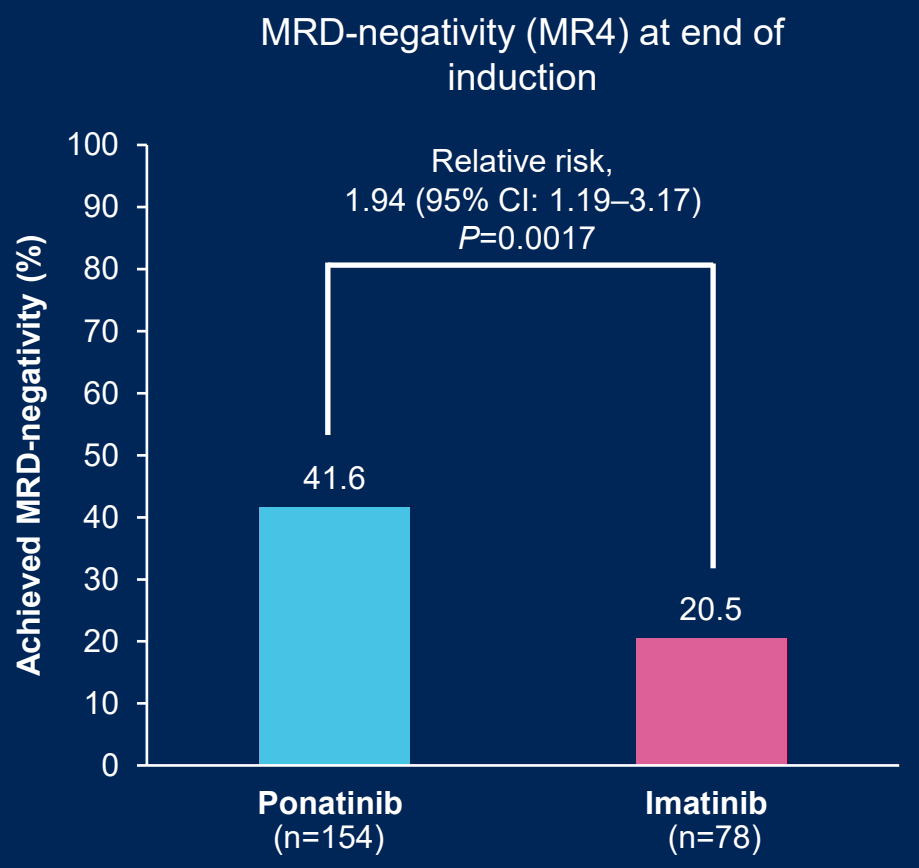
- Data cutoff date: 12 August 2022
- Median follow-up was 20.4 months (range: 18.4–23.9) in the ponatinib arm and 18.1 months (13.9–24.3) in the ponatinib arm

[a]Dose reductions to 15 mg QD were implemented in patients who achieved MRD-negative CR after completion of the induction phase.

Primary endpoint: MRD-negative CR

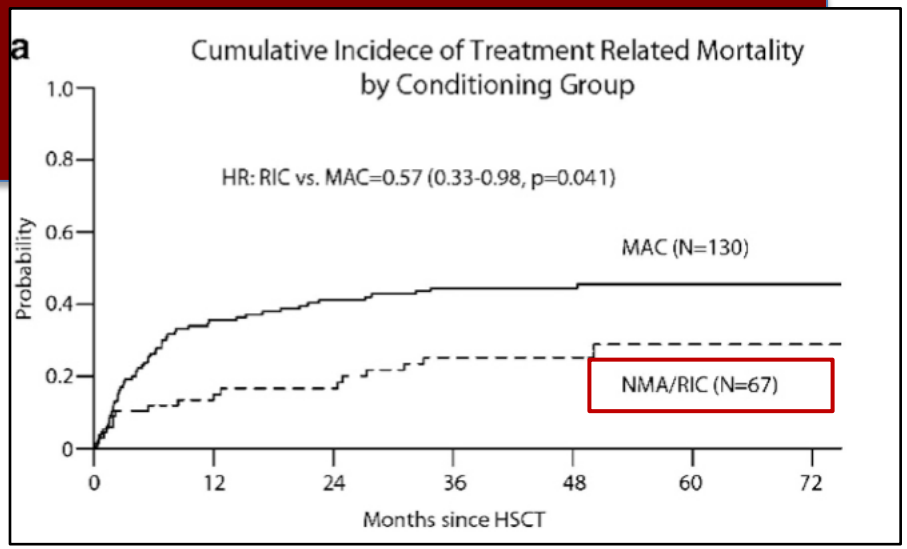
- **MRD-negative CR:** hematologic CR (for ≥4 weeks) + MRD negativity (≤0.01% BCR::ABL1/ABL1 transcripts)

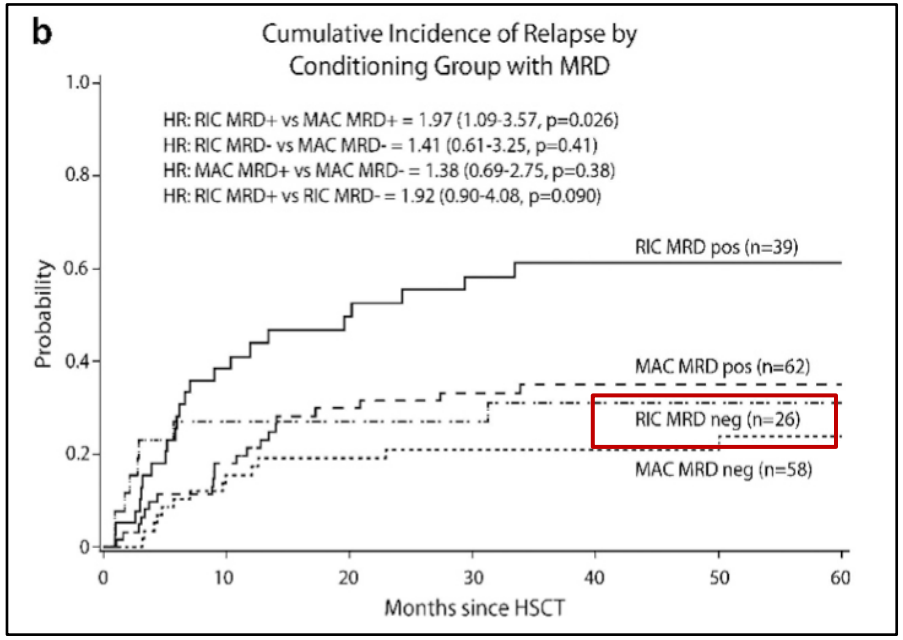




Ph+ ALL: Transplant in Older Adults

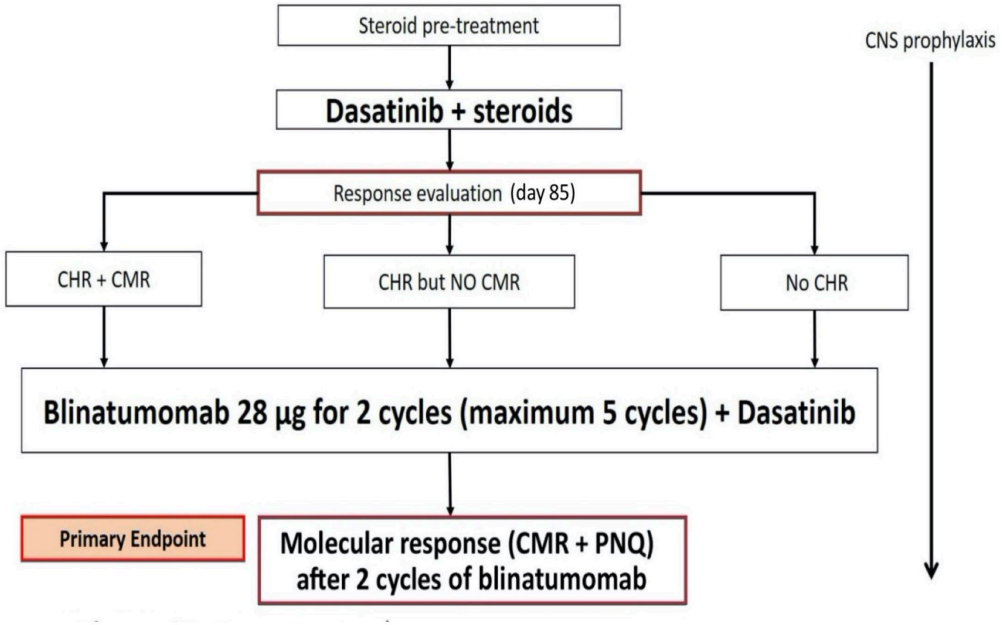
- Potentially curative.
- Compared to non-HCT chemotherapy approaches, ↓relapse but ↑non-relapse mortality, ↑graft-versus-host-disease (↓GRFS).
- **CIBMTR analysis (2014)[1]:** RIC vs MAC HSCT in Ph+ ALL (CR1). Among **RIC vs MAC**:
  - ↓ **1-yr TRM** (13 *vs* 36%, *P*=0.002).
  - ↑ **relapse** (49 *vs* 28% *P*=0.058).
  - = **OS similar** (39 *vs* 35%, *P*=0.62).
  - ***Patients receiving pre-HCT TKI (imatinib) and MRD-neg at time of HCT, <u>3-yr OS of RIC (55%)</u>*** *superior to MAC (33%, P=0.0042).*





Mohty et al. *Blood* 2010;116:4439-43; Marks et al. *Blood* 2010;116:366-74; [1]Bachanova et al. *Leukemia* 2014;28:658-65; Rosko et al. *Am J Hematol* 2016;92:42-49; Roth-Guepin et al. *Oncotarget* 2017;8:112972-79; Leonard et al. *Curr Hematol Malig Rep* 2018;4:329-340

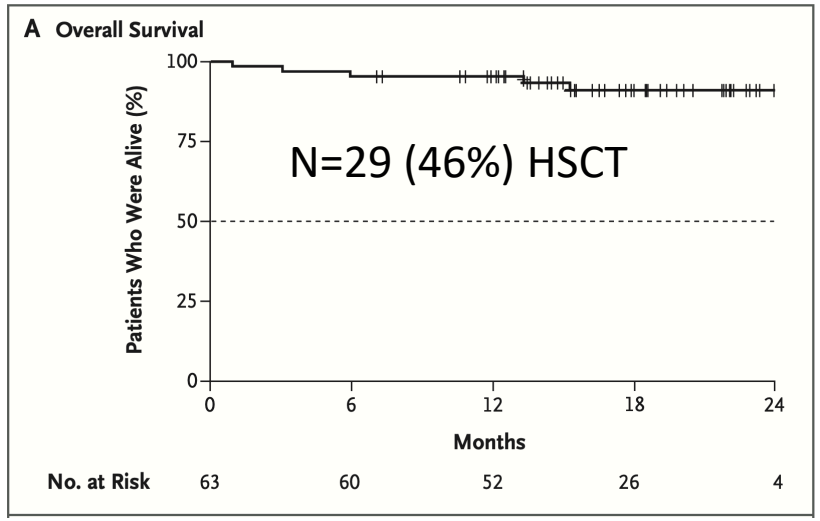
Ph+ ALL: Blinatumomab Consolidation (GIMEMA D-ALBA)



N=63, median age 54 (range 24-82) yrs

Note:
Follow-up still short.
Approximately half → HSCT.

- Day 85 – 29% Molecular Response
- Blina C2 (n=55) – 60% Molecular Response
- Blina C4 – 81% Molecular Response



- 36-mo DFS (71%) and OS (80%), respectively, median follow-up 28.8 mos.
- Worse outcomes in *IKZF1* deletion.

Foa et al. *N Eng J Med* 2020;383:1613-23

T315 drives most relapses after 2nd generation TKIs, role for novel agents and ponatinib?

- *BCR::ABL1* T315I KD mutation common at relapse after dasatinib (~70-75%).
- Ponatinib is a 3rd gen TKI active against T315I.
- Ponatinib associated with serious arterial thrombotic events, hepatotoxicity, and pancreatitis (unrandomized).
- IS THERE A BEST STRATEGY?

Foa et al. *Blood* 2011;118:6521-28; Rousselot et al. *Blood* 2016; 128:774-82; Wieduwilt et al. *Blood Advances* 2021;4691-700; Moslehi et al. *J Clin Oncol* 2015;33:4210-8; Martinelli et al. *Blood Advances* 2022;6:1742-53

ASH 2022: Abstract 213 (Short et al)
Ponatinib/Blinatumomab for Newly-diagnosed Ph+ ALL

Eligibility

Adults: Median age = 57

Newly-diagnosed Ph+ ALL

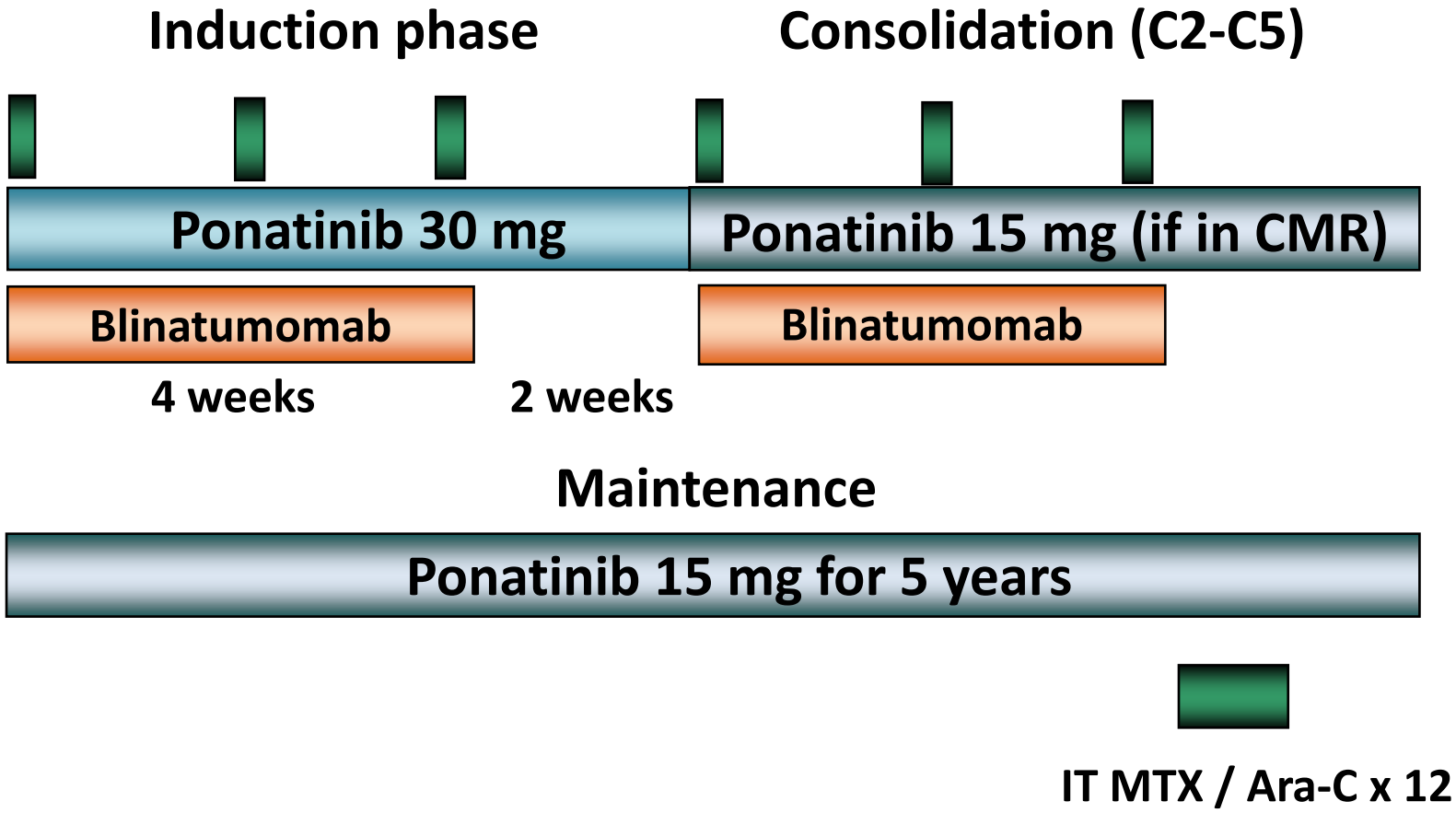
ECOG PS 0-2

No active CV disease

No CNS pathology

Primary endpoint

CMR rate



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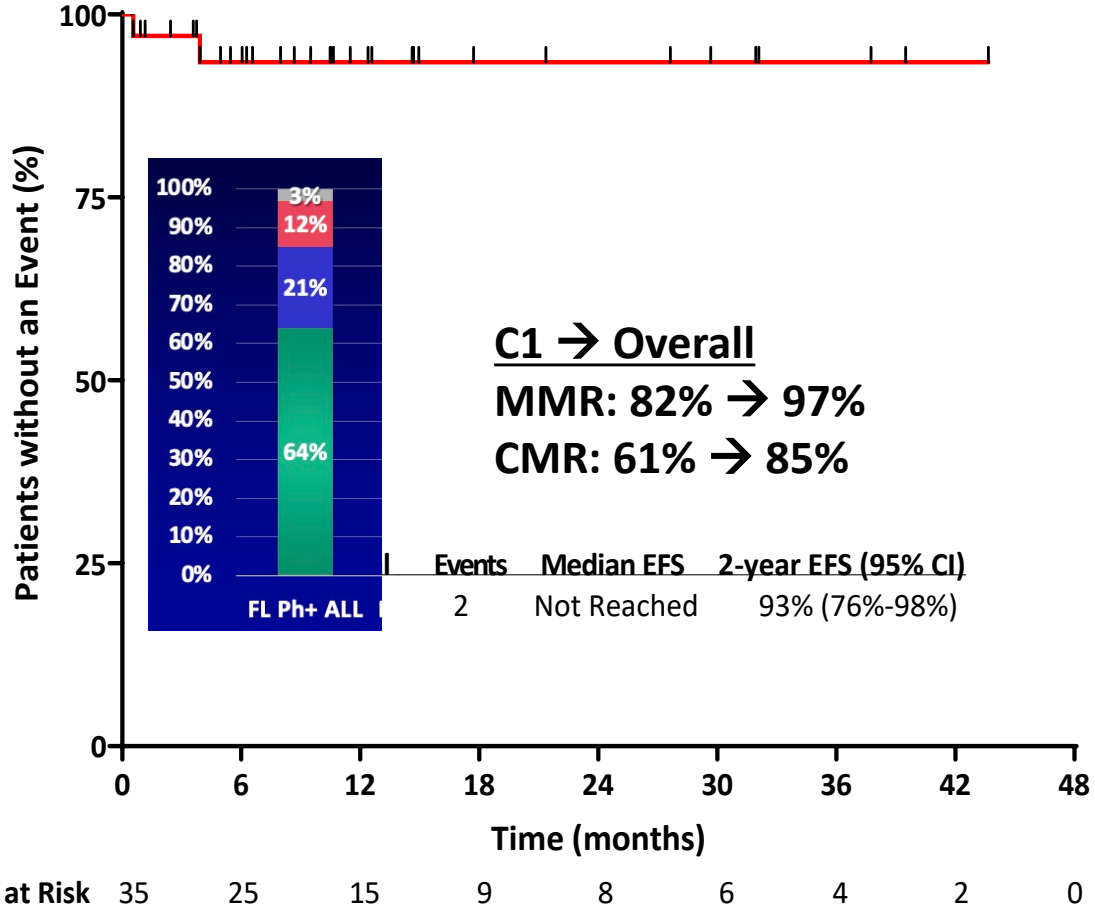
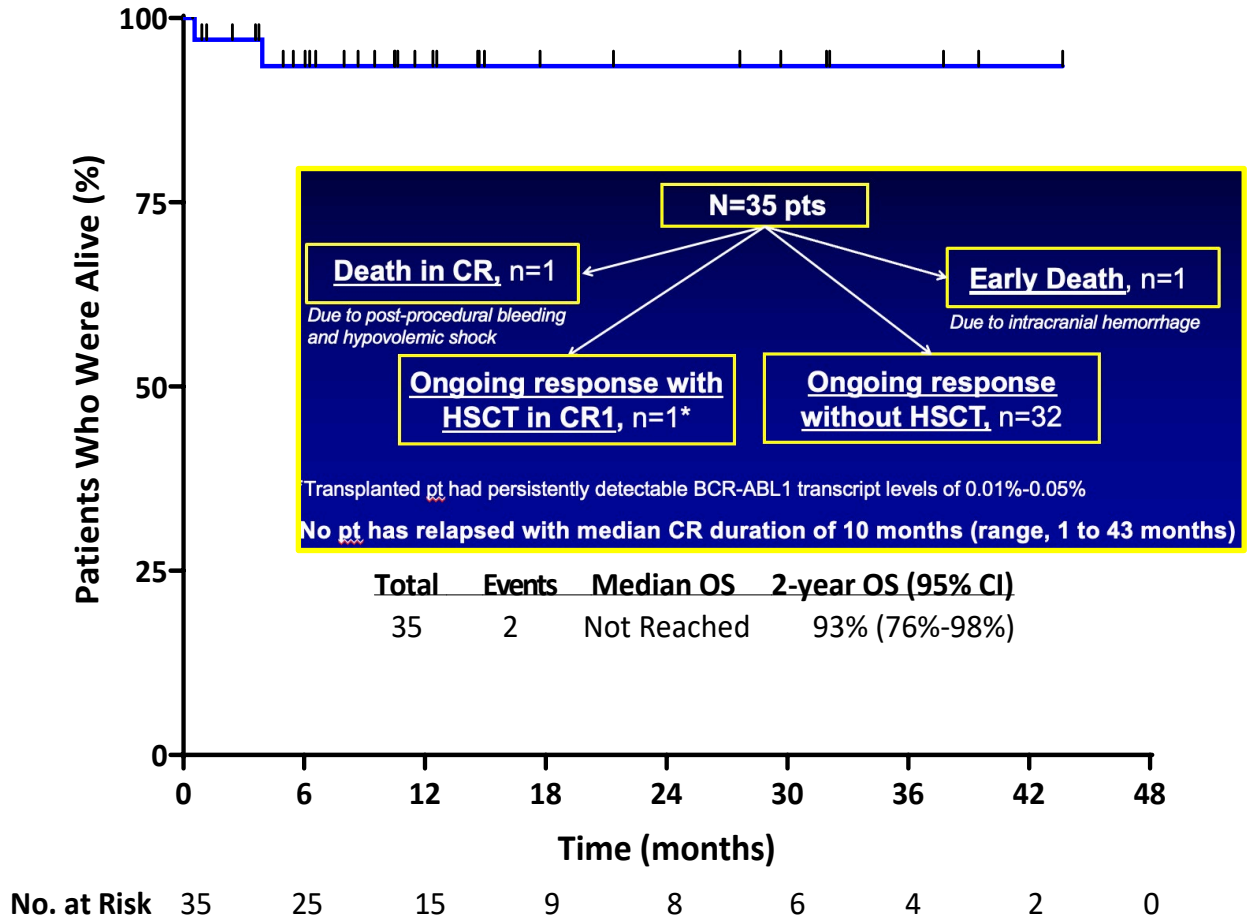
Ponatinib + Blinatumomab in Ph+ ALL: Survival Outcomes for Frontline Cohort



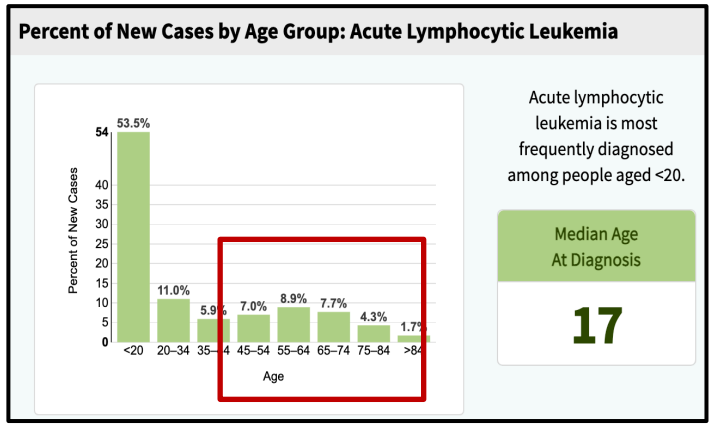


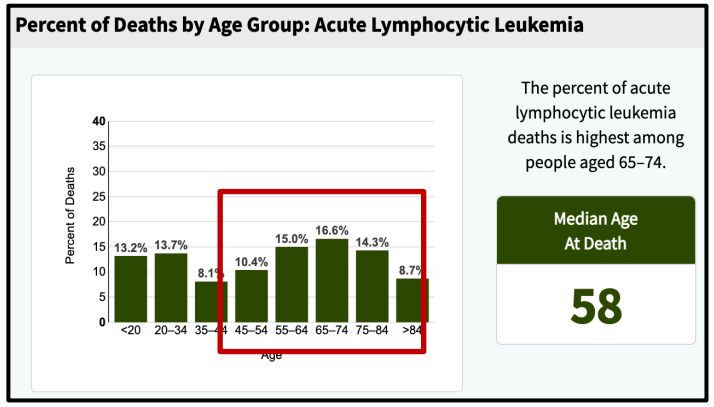
Short et al, MDACC data, courtesy Nicholas Short; and ASH 2022

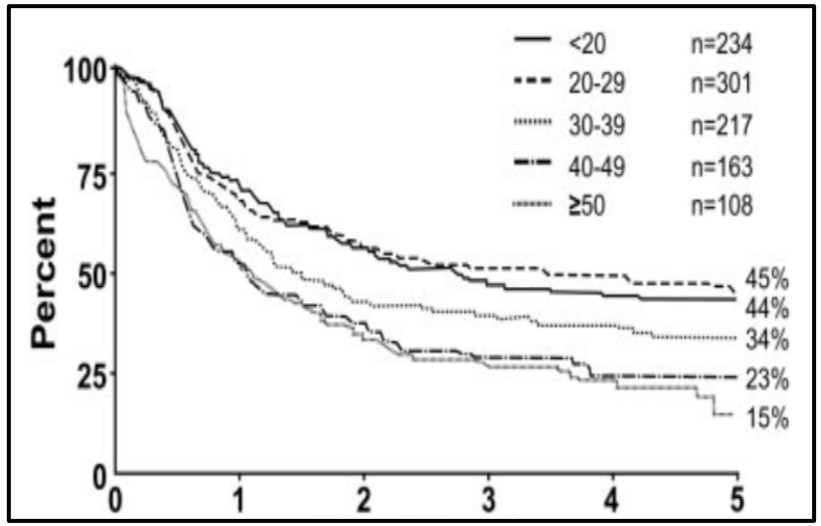
Summary: Ph+ ALL

- TKIs have dramatically changed remission rates, survival
  - Further refinements: Ponatinib may be most effective TKI given ability to overcome emergent T315I resistance mutations
- Aggressive CNS prophylaxis still essential
- Low intensity treatments with minimal or NO traditional chemotherapy becoming standard of care
  - TKI + BLINA
- Evolving role of Allogeneic transplant
  - If no transplant can TKI ever be discontinued?

Older Adults: Poor Outcomes with Traditional Regimens

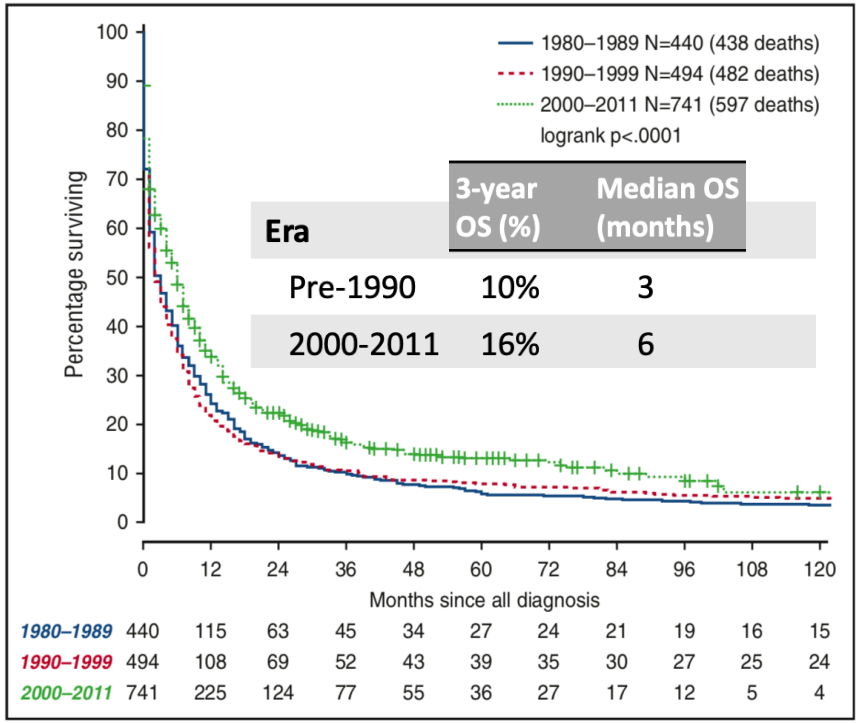






ECOG 2993[1]

Fit for intensive trial



Era	3-year OS (%)	Median OS (months)
Pre-1990	10%	3
2000-2011	16%	6

- Outcomes worsen with increasing age.
- Most ALL-related deaths occur in older adults.
- Little improvement in 3 decades (1980-2011).[3]

https://seer.cancer.gov/statfacts/html/alyl.html; [1]Rowe et al. *Blood* 2005;106:3760-67; Gokbuget N *Hematology Am Soc Hematol Educ Program* 2016;573-79; Luskin MR *Hematology Am Soc Hematol Educ Program* 2021; 1:7-14; [2]Sasaki et al. *Am J Hematol* 2021;96:650-58; [3]Kim et al. *Leuk Lymphoma* 2019;60:1462-68

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Moving Away from Chemotherapy: Inotuzumab plus mini-Hyper-CVD

- Enrolled 52 patients
  - Median age: 68 years (IQR 64-72)
- Efficacy
  - 98% CR/CRp/CRi
  - 96% MRD-neg (flow) CR within 3 cycles
    - (78% at morphologic remission)
  - PFS 59% (95% CI, 32-54%) at 2 years.
  - Median PFS 35 months (95 CI, 15.3-NR).
- Toxicity
  - Thrombocytopenia (81%) beyond 6 weeks.
  - Hepatic adverse events
    - 17 (33%) grade 3 + (induction or later cycles)
    - 4 (8%) with VOD

Kantarjian et al. *Lancet Oncol.* 2018; 24-48.

Inotuzumab ozogamicin in combination with low-intensity chemotherapy for older patients with Philadelphia chromosome-negative acute lymphoblastic leukaemia: a single-arm, phase 2 study

Hagop Kantarjian, Farhad Ravandi, Nicholas J Short, Xuelin Huang, Nitin Jain, Koji Sasaki, Naval Daver, Naveen Pemmaraju, Joseph D Khoury, Jeffrey Jorgensen, Yesid Alvarado, Marina Konopleva, Guillermo Garcia-Manero, Tapan Kadia, Musa Yilmaz, Gautam Bortakhur, Jan Burger, Steven Kornblau, William Wierda, Courtney DiNardo, Alessandra Ferrajoli, Jovitta Jacob, Rebecca Garris, Susan O'Brien, Elias Jabbour

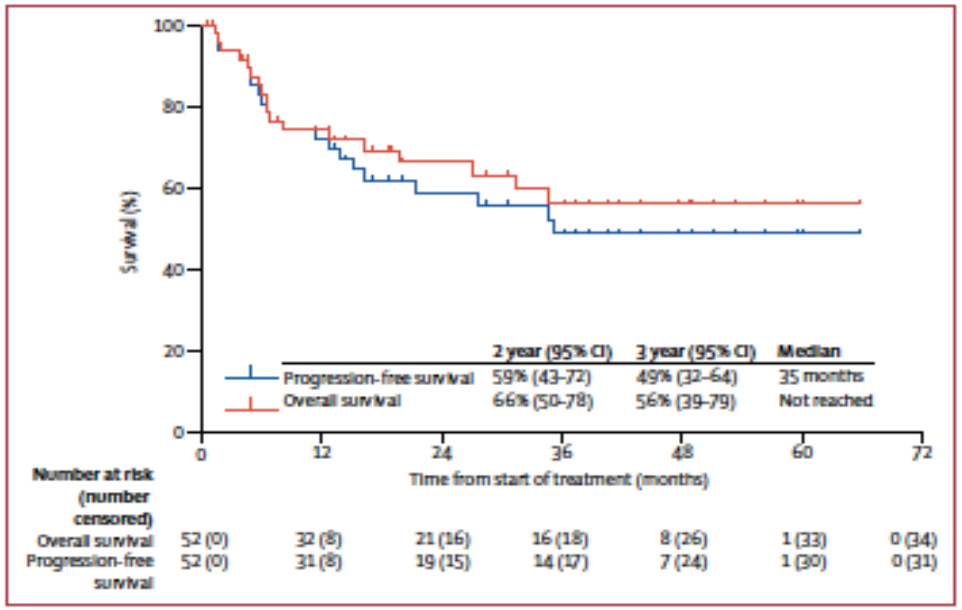
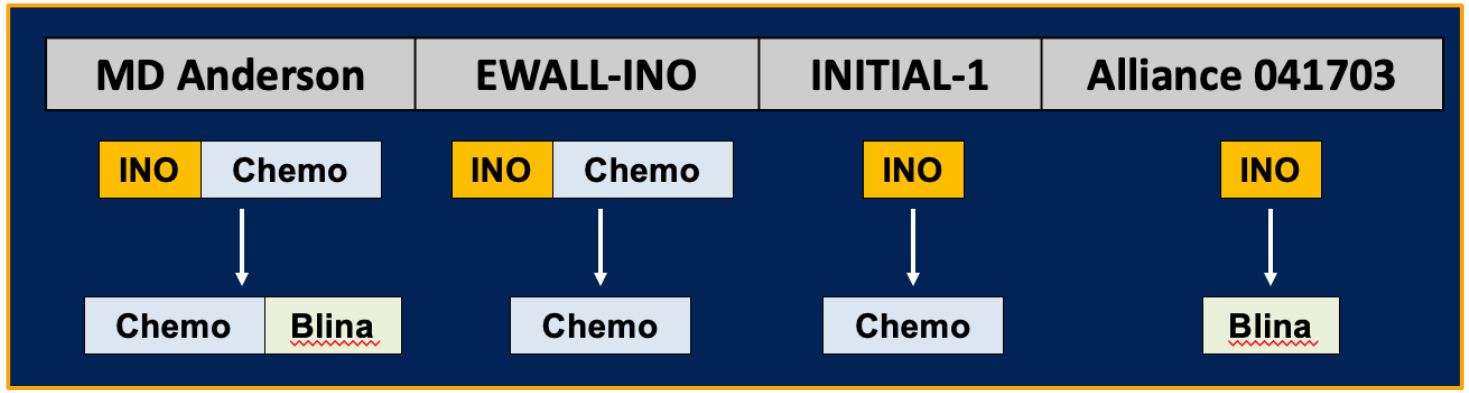


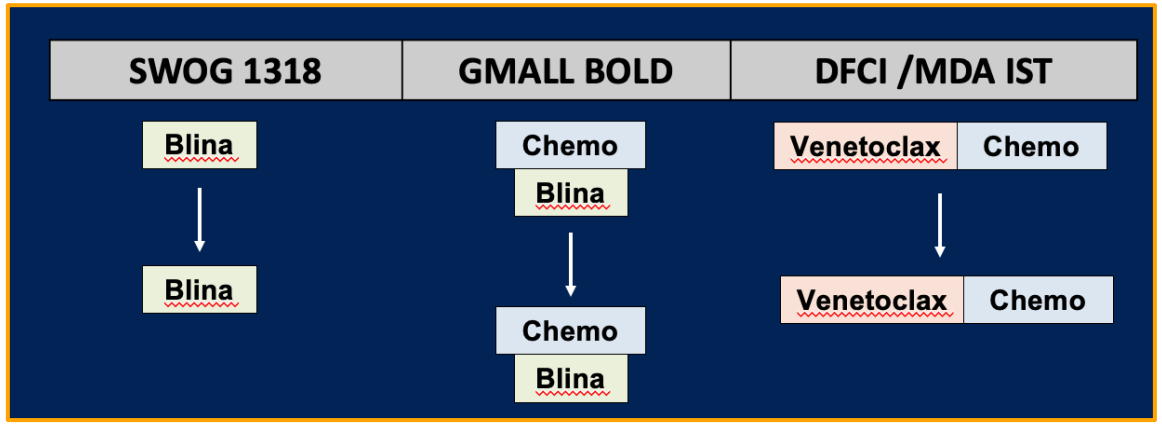
Figure 2: Progression-free and overall survival

Ino + mini-CVD (no anthracycline) : Ino given day 3 of first four cycles

Older Adults: Less is Very Likely MORE!

- High CR rates (80-90%).
- Most MRD negative (80-90%).
- Low induction mortality <5%.
- Late toxicity may still be a problem.
- *Long-term outcomes awaited!*





Kantarjian et al. *Lancet Oncol* 2018;19:240-9; Chevallier et al. *Blood* 2021;138:Abstract 511; Stelljes et al. *Blood* 2021;138:Abstract 2300; Advani et al. *J Clin Oncol* 2022;40:1574-82; Goekbuget et al. *Blood* 2021;139: Abstract 3399; Jain et al. *Blood* 2019;134:Abstract 3867

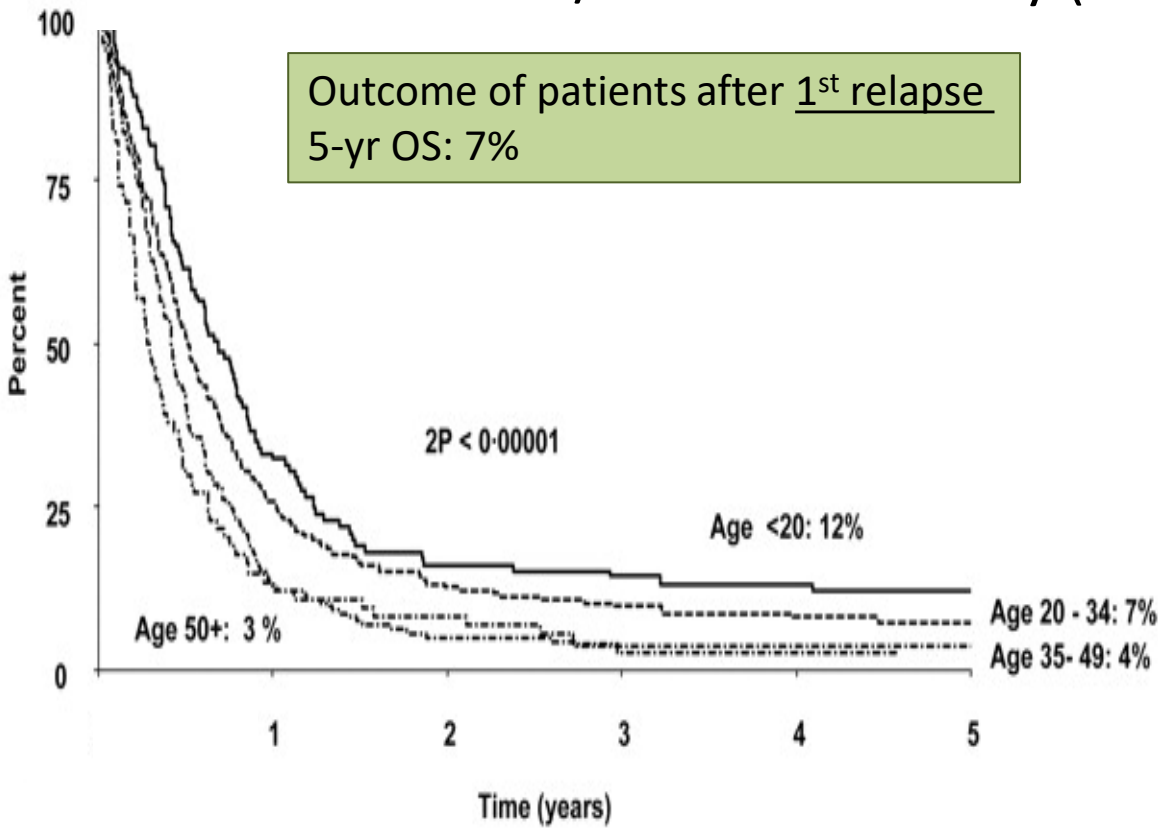
Ph- ALL in Older Adults– How I Treat in 2023

- *Assess comorbidities, fitness, goals.*
- **CNS prophylaxis:** IT chemo- Don't neglect!
- **Induction and Consolidation:**
  - Role of novel agents being established, be wary of adopting novel approaches outside of a clinical trial
- **Clinical trial whenever possible! Alliance 042001 NCT05303792 now open**
  - **Will establish new platform for treatment of adults with ALL > 50 years**
- **Monitor MRD,** blinatumomab for patients with persistent MRD….and now probably for those without MRD (E1910).

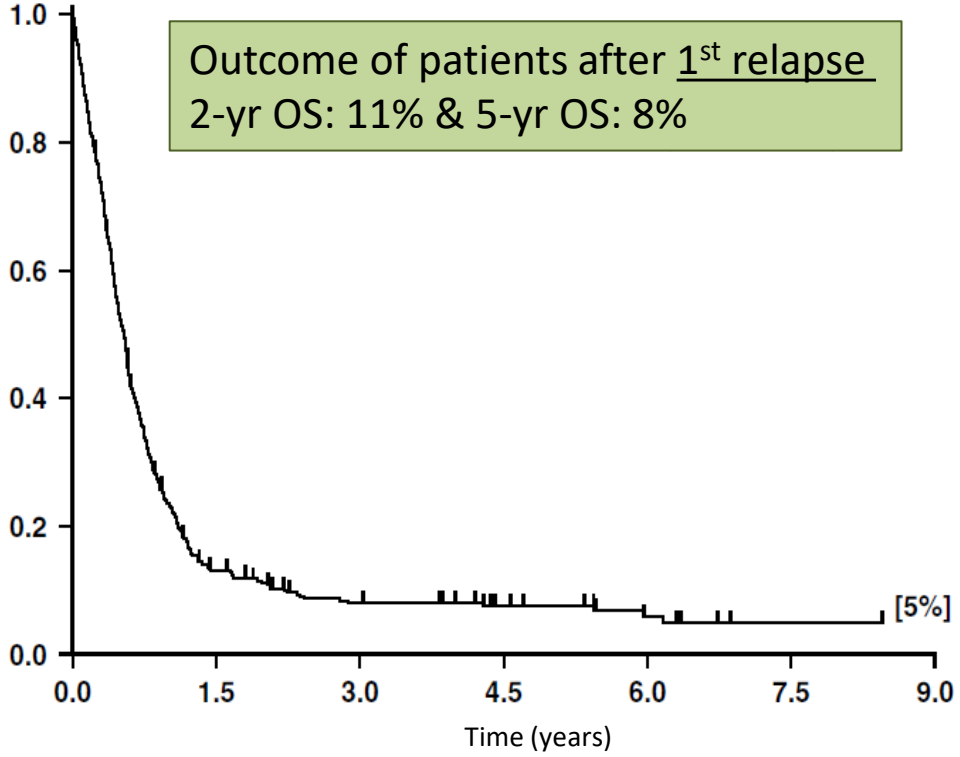
Huguet et al. *J Clin Oncol* 2018;36:2514-2523; Derman et al. *Leuk Lymphoma* 2020;614-622; Patel et al. *eJHaem* 2021;2:413-420

The Problem …..Until Recently:
VERY Poor Prognosis of Relapsed ALL in Adults

MRC UKALL2/ ECOG2993 Study (n=609)



LALA-94 Study (n=421)

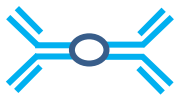


Fielding A, et al. *Blood* 2007;109(3):944-950.

Tavernier E, et al. *Leukemia* 2007;21:1907-1914.

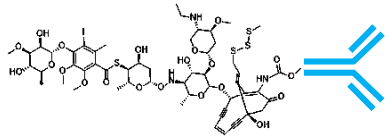
Relapsed/refractory B-ALL in Adults

Blinatumomab



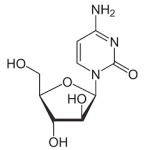
- **CD19 - CD3 BiTE[1]**
- **CR:** 34%
- **ORR:** 44%
- **MRD-neg:** 76% of ORR
- **SCT:** 24%
- **Median OS:** 7.7 mos

Inotuzumab ozogamicin



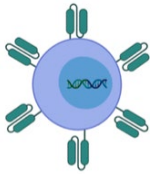
- **CD22 Ab drug conjugate[2]**
- **CR:** 36%
- **ORR:** 81%
- **MRD-neg:** 78% of ORR
- **SCT:** 41%
- **Median OS:** 7.7 mos

Salvage chemo



- **Standard Salvage[1,2]**
- **CR:** 16-18%
- **ORR:** 25-29%
- **MRD-neg:** 8-12%
- **SCT:** 11-24%
- **Median OS:** 4-6.7 mos

CAR T-cell Therapy



- **Anti-CD19 Zuma-3[3]**
- **CR:** 56%
- **MRD-neg:** 97% of CR
- **SCT:** 18%
- **Median PFS:** 12.8 months (95% CI 8·7-not estimable
- **Median OS:** 18.2 months (15·9-not estimable)

1: Kantarjian et al, N Engl J Med 2017; 376:836-847
2: Kantarjian et al, N Engl J Med 2016; 375:740-53
3: Shah et al, Lancet. 2021 Jun 3:S0140-6736

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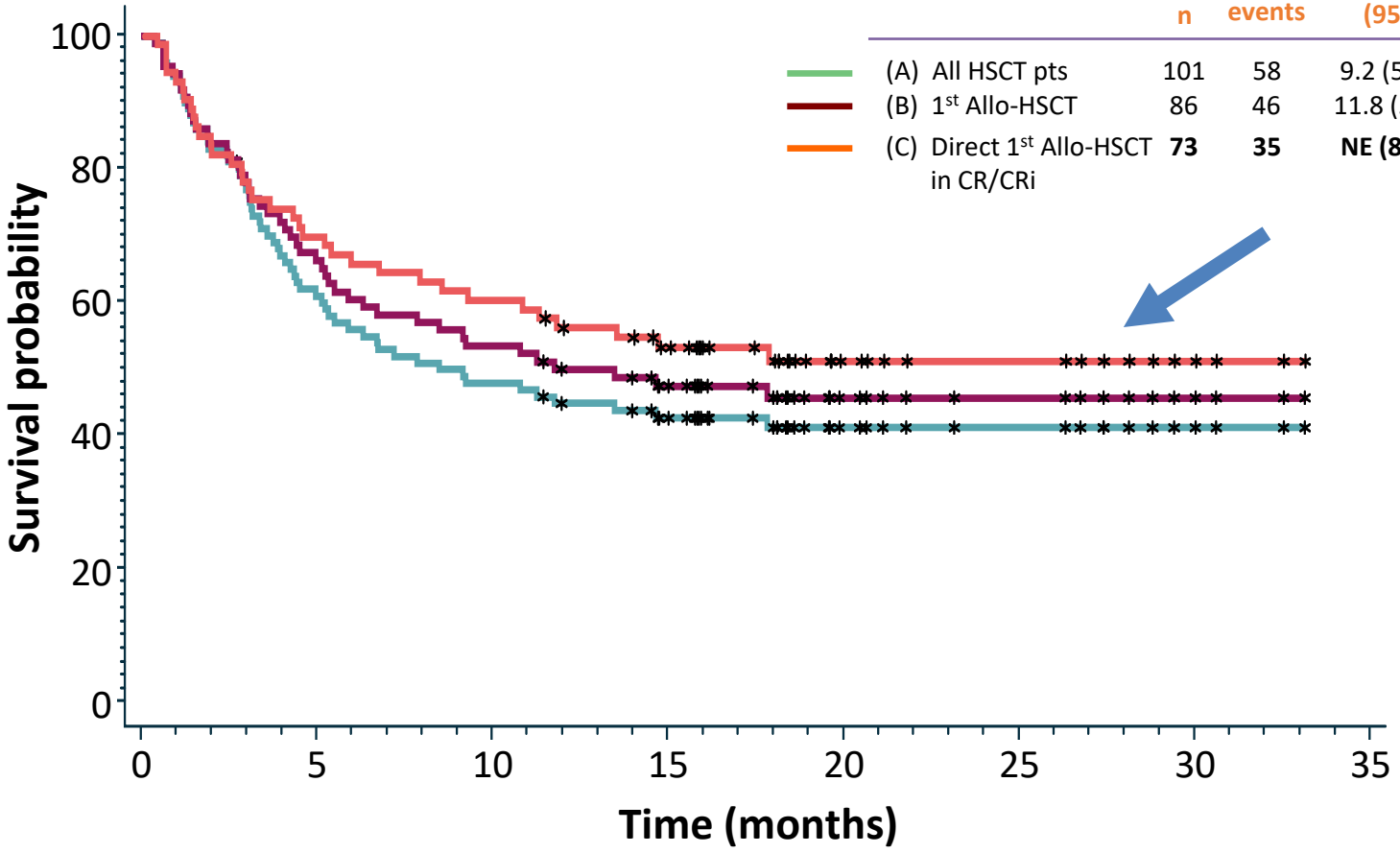
Post-transplant survival for patients who received inotuzumab and proceeded to allo-HSCT



	n	No. events	Median OS, mo (95% CI)	24-month survival, % (95% CI)
(A) All HSCT pts	101	58	9.2 (5.1–NE)	41.4 (31.5–51.0)
(B) 1st Allo-HSCT	86	46	11.8 (5.9–NE)	45.7 (34.7–56.0)
(C) Direct 1st Allo-HSCT in CR/CRi	**73**	**35**	**NE (8.5–NE)**	**51.1 (38.9–62.1)**

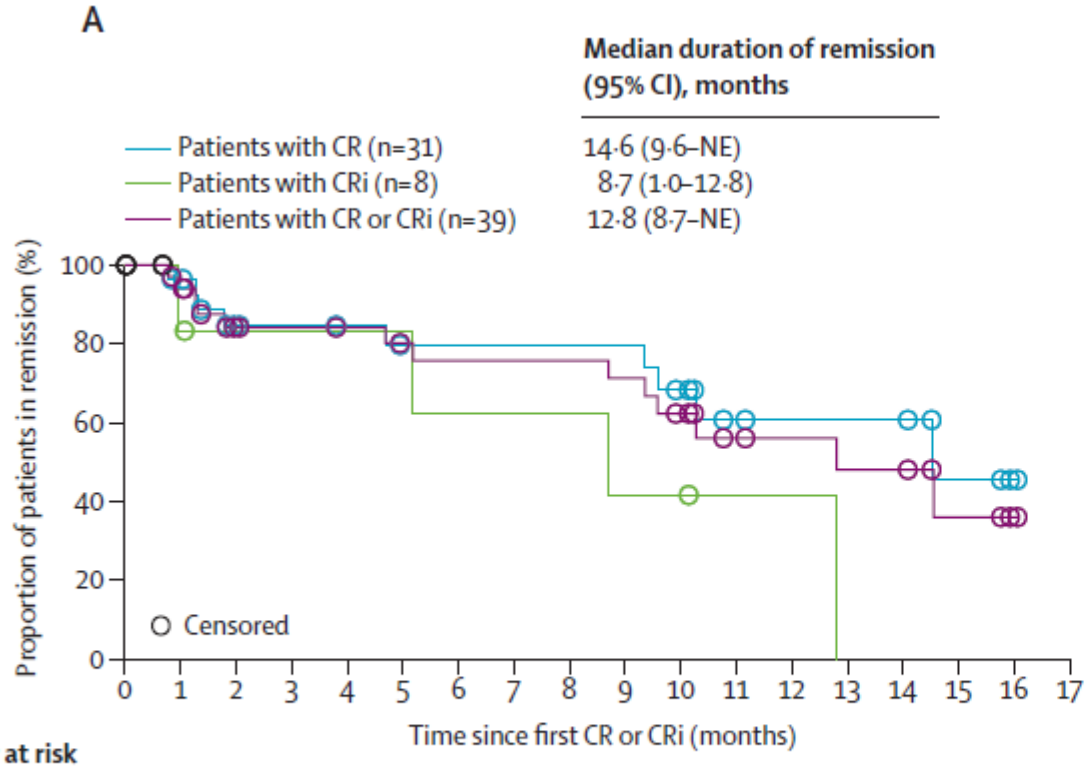
Marks et al., Biol of Blood Marrow Transplant 2019, https://doi.org/10.1016/j.bbmt.2019.04.020

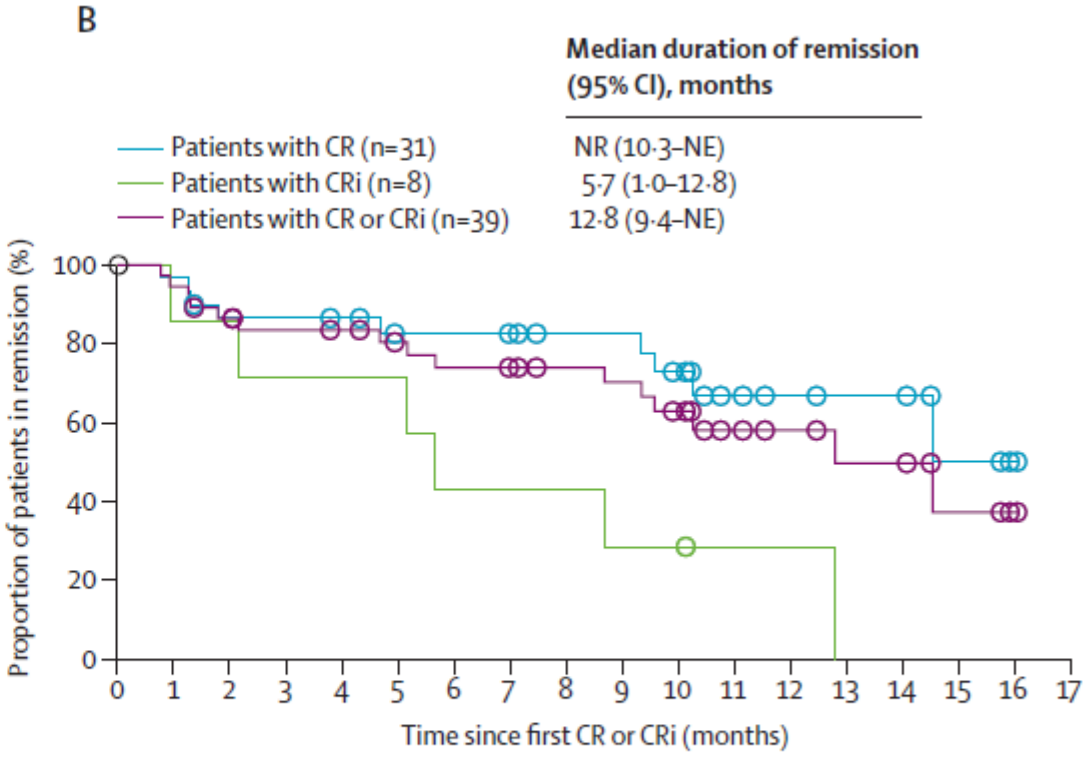
Key Anti-CD19 CAR T-Cell Therapy Trials: B-ALL

	ELIANA[1] (N = 75)	MSKCC[2] (N = 53)	ZUMA-3[3] (N = 45)
CAR T-cell agent	**Tisagenleucel**	**JCAR015**	**Brexucabtagene**
Study phase	II	I	II
Study population	Pediatric/young adults with R/R B-ALL	Adults with R/R B-ALL	Adults with R/R B-ALL
CR, %	MRD negative: 81	Overall: 83	Overall: 71
Median OS, mos	19.1	12.9	18.2
Median EFS, mos	NR	6.1	11.6
Median follow-up, mos	13.1	29	16
	FDA approved	**Halted**	**FDA approved**

1. Maude et al., NEJM. 2018;378:439. 2. Park et al., NEJM. 2018;378:449. 3. Shah et al., Lancet 2021

Zuma -3 CD19 CAR-T Trial: Durable Responses?





Number at risk

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
CR	31	26	19	18	17	14	14	14	14	14	11	7	6	6	6	3	1	0
CRi	8	5	4	4	4	4	3	3	3	2	2	1	1	0	0	0	0	0
CR or CRi	39	31	23	22	21	18	17	17	17	16	13	8	7	6	6	3	1	0

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
CR	31	29	25	24	23	20	20	19	17	17	14	9	7	6	6	3	1	0
CRi	8	6	6	5	5	5	3	3	3	2	2	1	1	0	0	0	0	0
CR or CRi	39	35	31	29	28	25	23	22	20	19	16	10	8	6	6	3	1	0

Shah et al., Lancet 2021

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In 2023, Allogeneic Transplant Remains "Destination" Beyond CR1

- CR rates with new immune targeting approaches significantly better
  - High rates of undetectable MRD with the immune targeting strategies can result in durable remissions
    - RIC conditioning may be good approach for older, frail, MRD-

- However, with possible exception of CAR-T therapy (in children) , none of these approaches are curative in the relapsed setting

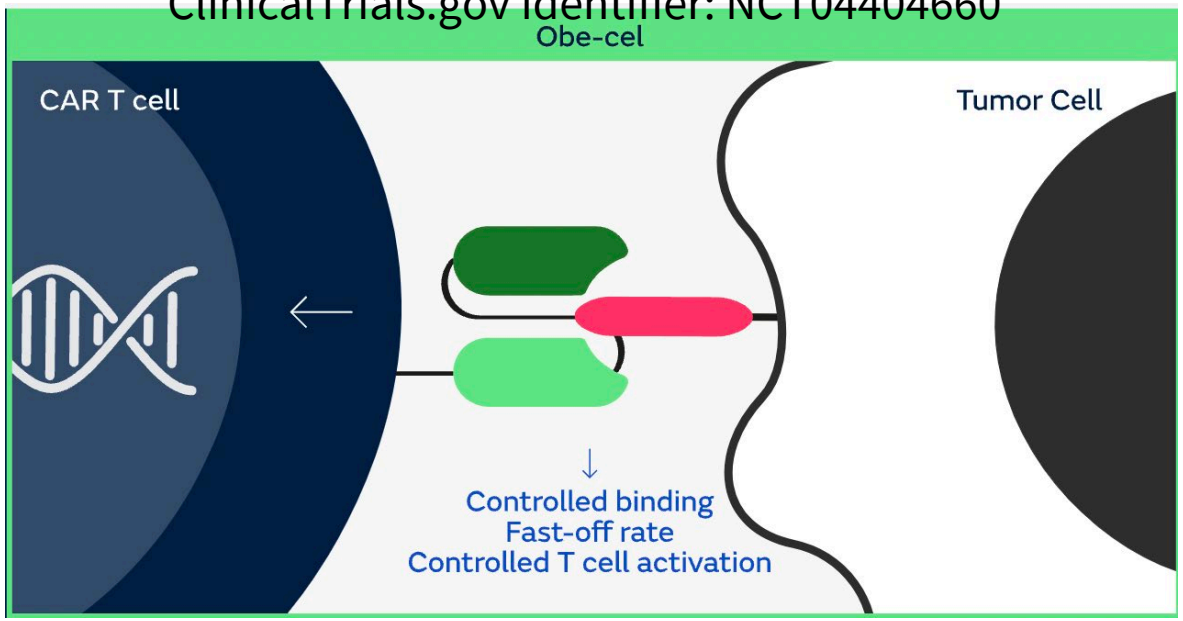
- These therapies can/? should be used as a bridge to allogeneic transplant

Cassaday et al, Leuk Lymphoma 57:2019, 2016
Marks et al, Biol Blood Marrow Transp, 25:1720, 2019

CAR-T: Will “next gen” be less toxic, more durable?

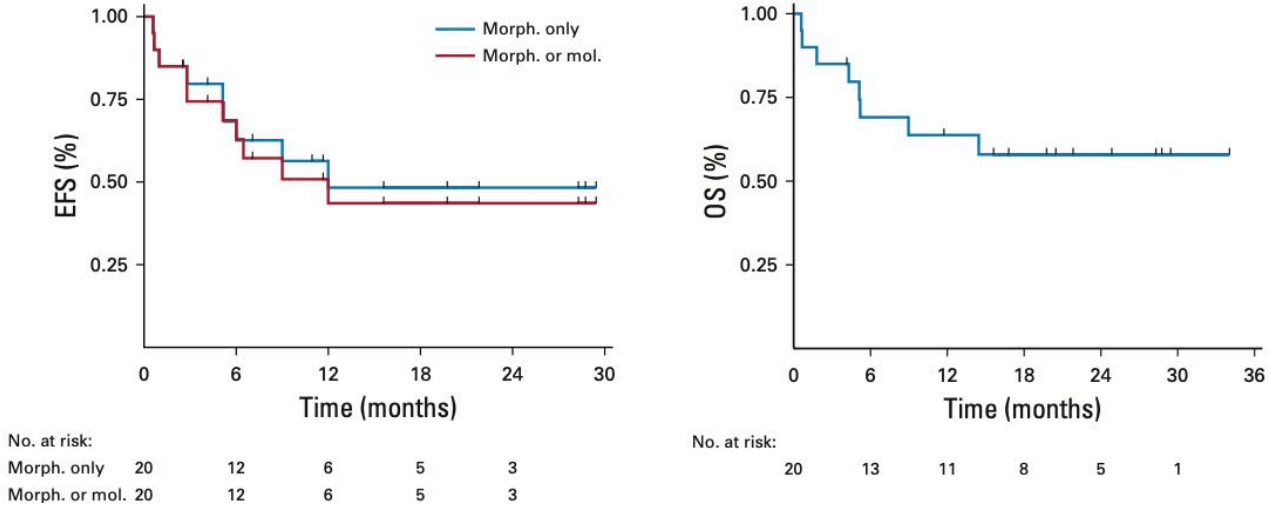
Will we have additional commercial CAR-T options?

ClinicalTrials.gov Identifier: NCT04404660



Durable Responses and Low Toxicity After Fast Off-Rate CD19 Chimeric Antigen Receptor-T Therapy in Adults With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia

J Clin Oncol 39:3352-3363.



Can CAR-T be used as an effective consolidation in the front-line setting?

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Current Treatment Algorithm for R/R B-ALL

SCT naive

- MRD and CR19+ = Blina
- Low disease burden and CD19+ = Blina
- Bulk disease or extramedullary disease and CD22+ = INO → +/- Blina
- CD19- and CD22 - = Venetoclax based chemo/ Menin inhbitor for KMT2a

- Remission = SCT
- If Not fit for allo, consider maintenance (POMP) with ongoing IT chemo ? + Venetoclax

Relapse post SCT

- CD19+ = CAR T-cell
- CD19-/CD22+ = INO
- CD19- and CD22- = Venetoclax based regimen? Menin inhibitor for KMT2a

- If CAR T-cell would watch
- If INO or chemo = Consider 2nd SCT

ASH 2022
Arrival of CAR-T for T-ALL: Early Promise

Analysis of 60 Patients with Relapsed or Refractory (R/R) T-cell Acute Lymphoblastic Leukemia (T-ALL) and T-cell Lymphoblastic Lymphoma (T-LBL) Treated with CD7-targeted CAR-T Cell Therapy

Xian Zhang[1, 2], Junfang Yang[1, 2], Jingjing Li[1, 2], Liyuan Qiu[1], Jianqiang Li[3], Peihua Lu[1, 2]

[1]Beijing Lu Daopei Institute of Hematology, Beijing, China;
[2]Hebei Yanda Lu Daopei Hospital, Langfang, China;
[3]Hebei Senlang Biotechnology Co., Ltd., Shijiazhuang, China;

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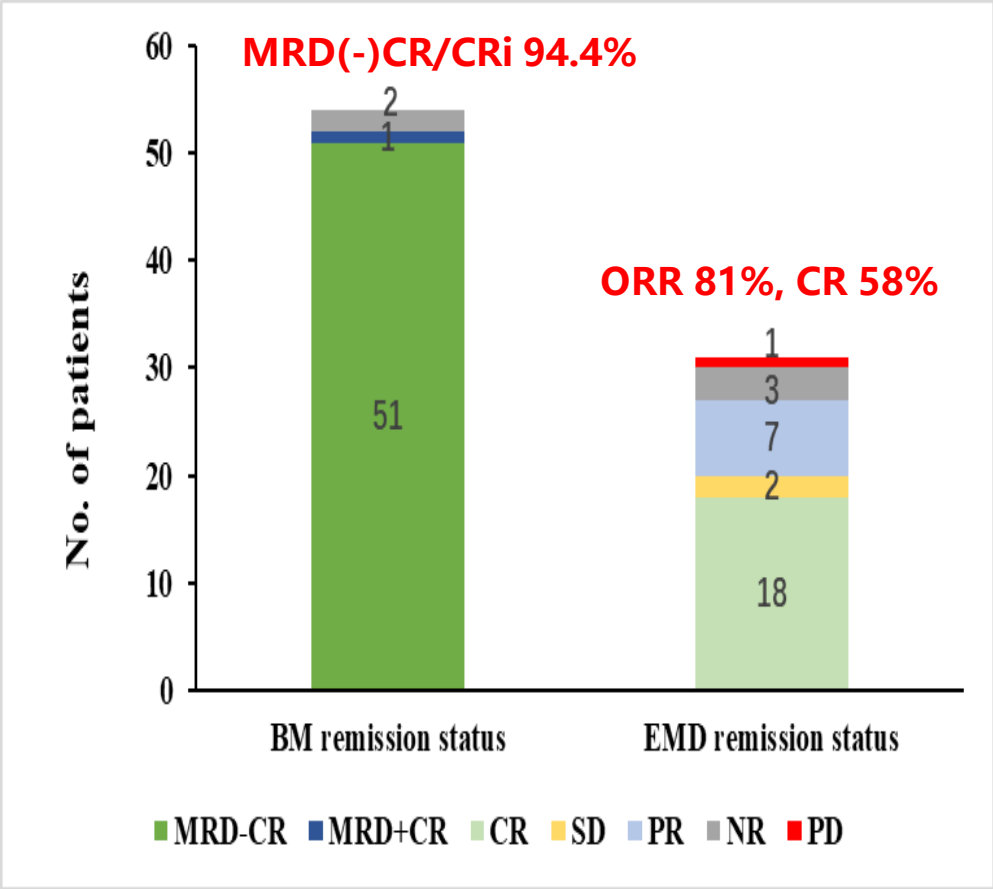
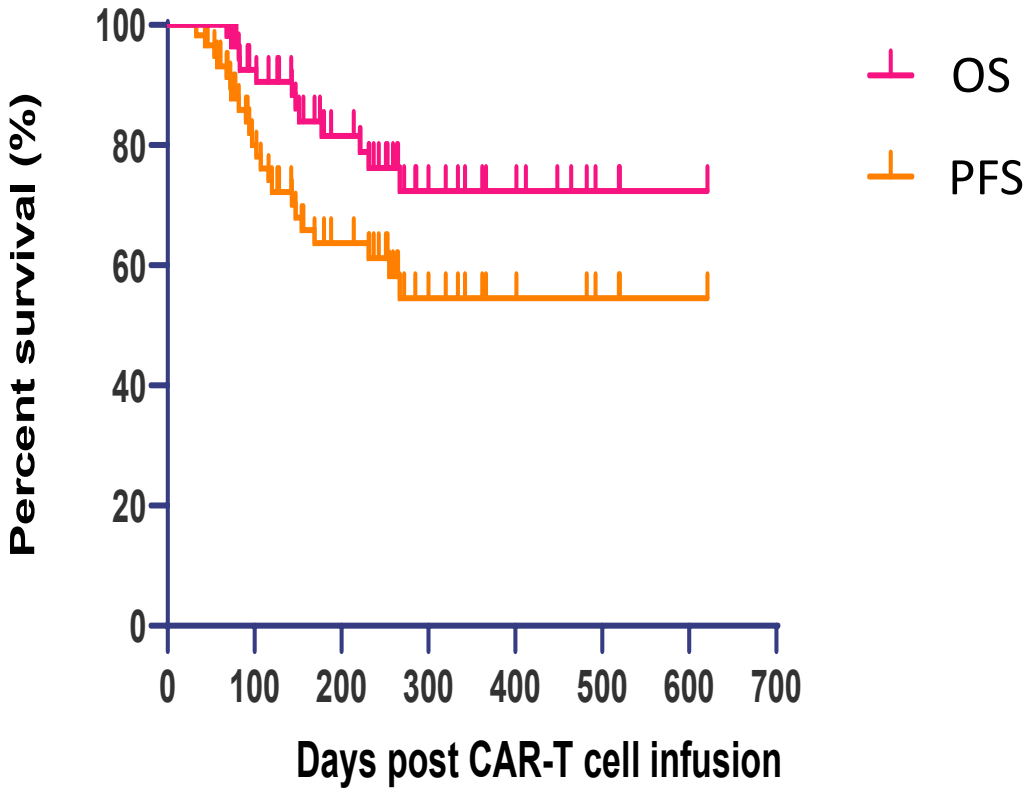
Abstract 980 (Zhang et al.) – Anti-CD7 CART

N=60; 35 T-ALL, 25 T-LL





18-mo PFS improved with alloHCT (61% vs 30%, P=0.0003).

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A041501, Randomized Phase 3 Trial for AYAs: Impact of Inotuzumab Ozogamycin on EFS, MRD

I		C**	IM	DI	M
DEX DNR VCR PEG-Asp IT MTX IT Ara-C	↓ ↓ *Inotuzumab* *× 2 cycles*	Cyclo VCR DEX PEG-Asp Ara-C 6-MP IT MTX Rituximab	MTX VCR PEG-ASP IT MTX Rituximab	DOX Cyclo DEX PEG-Asp Ara-C 6-TG IT MTX Rituximab	DEX VCR 6-MP MTX IT MTX

ClinicalTrials.gov; NCT03150693.

**Patients who remain MRD+ after "C" should receive Blinatumomab
CD20^{+} patients receive rituximab (8 doses) with C, IM, DI.
Maintenance therapy continues for 2 (F) to 3 (M) years.

A041501: Goal to increase EFS to 80%

- Status 3/23: Accrual on temporary hold
- Excessive deaths on experimental arm
  - Sepsis as late event,
    - due to increased risk of myelosuppression during later treatment modules - particularly during DI
- Amendment to be submitted to FDA:
  - Inotuzumab dose modification
  - Mandate antimicrobial prophylaxis
  - Growth factor to avoid prolonged myelosuppression