Inotuzumab ozogamicin Clinical Data in Pediatric Patients

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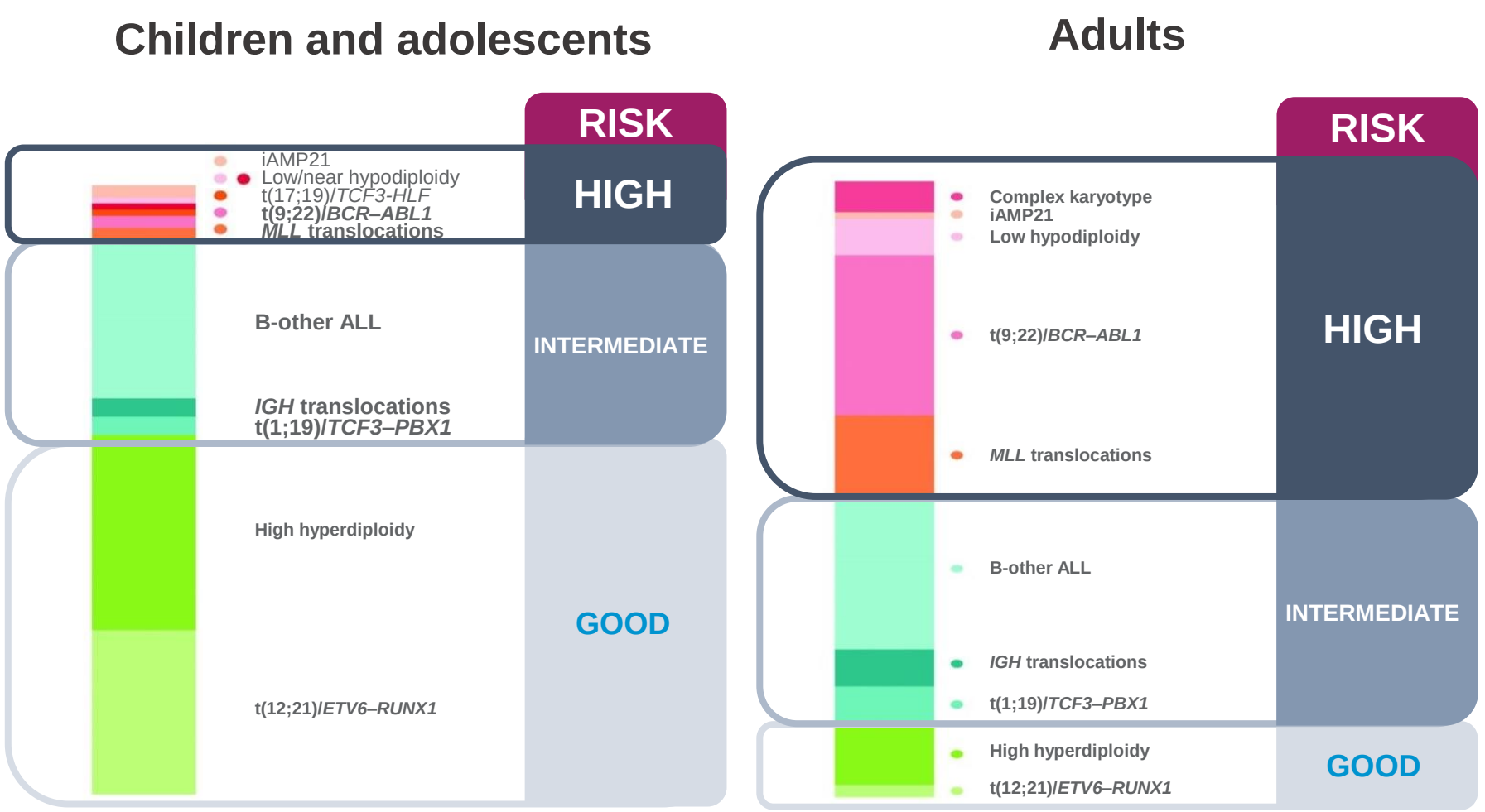
Background

- Approximately 10-15% of pediatric patients with acute lymphoblastic leukemia (ALL) experience disease relapse[1]
- Following relapse, the estimated 10-year overall survival (OS) probability is around 50%, depending on the risk group. [2,3]
- The traditional treatment for relapsed patients is based on intensive chemotherapy. [4] A randomized trial in relapsed and refractory (R/R) pediatric patients comparing the two most used treatment strategies in Europe, the ALL-REZ BFM 2002 and the UKALL-R3, showed no significant differences in the 5-year probability of event-free survival (EFS) or OS. [5]

1. Pui CH, et al. *J Clin Oncol*. 2015;33(27):2938-2948.
2. Oskarsson T, et al. 2016;101(1):68-76.
3. Rheingold SR, et al. J Clin Oncol. 2019;37:(Suppl 15):10008.
4. Parker C, et al. Lancet. 2010;376(9757):2009-2017.
5. Von Stackelberg A, et al. Blood. 2022;140(Suppl 1):3247-3249.

Risk Stratification of Genetic Abnormalities in B-Cell Precursor ALL

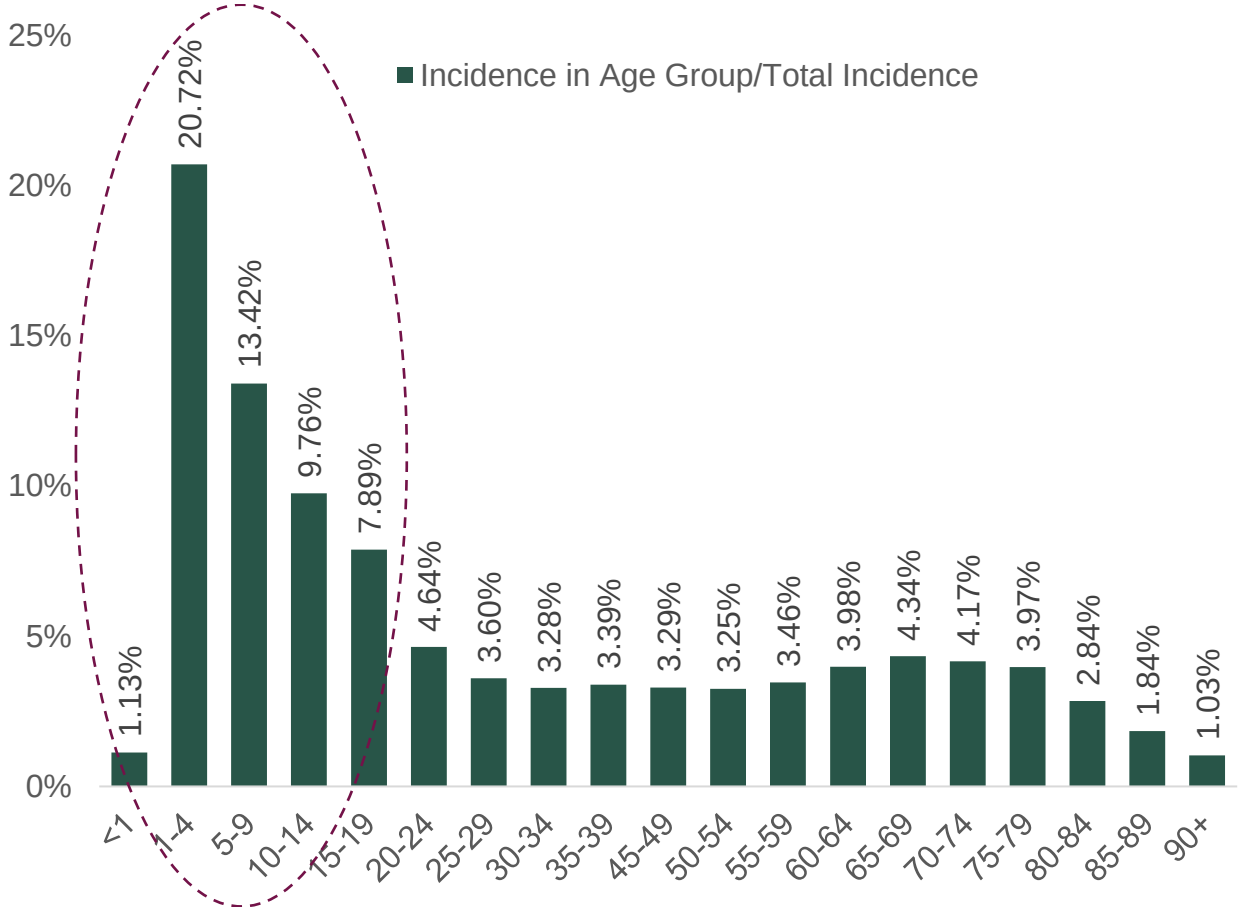


ALL, acute lymphoblastic leukaemia; iAMP21, intrachromosomal amplification of chromosome 21

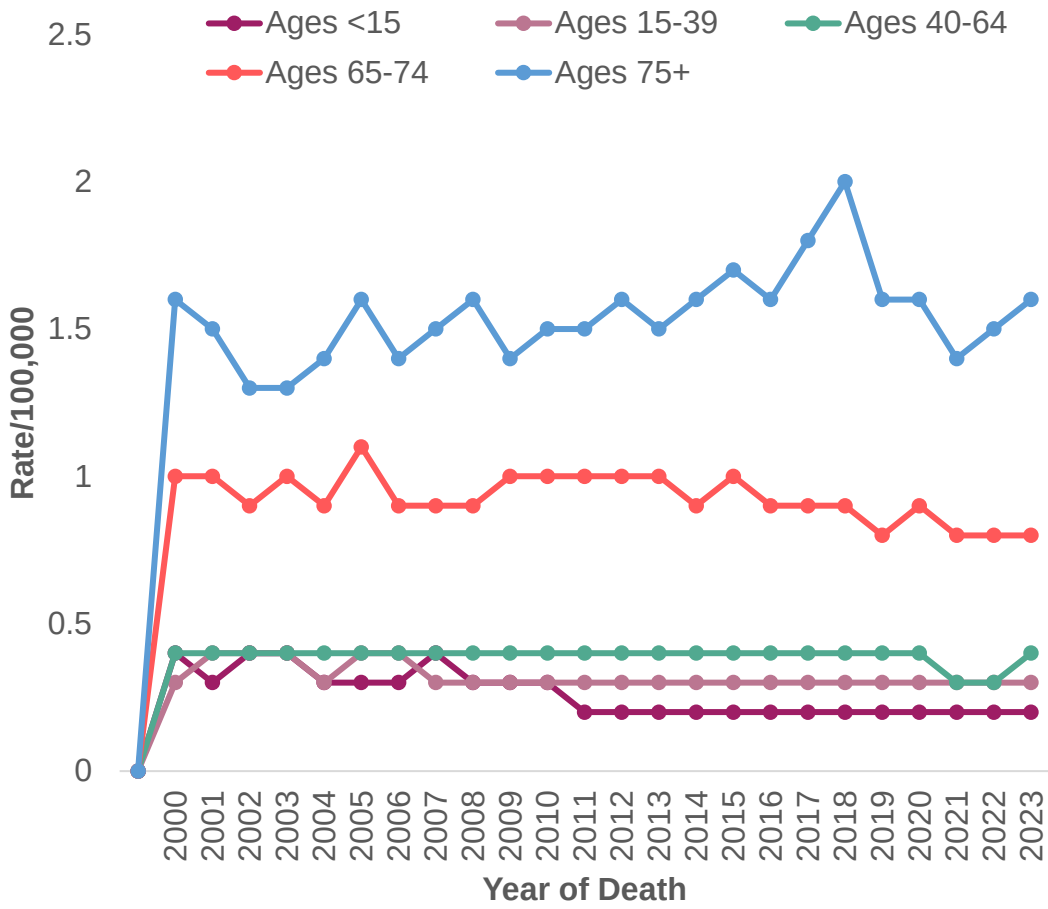
Moorman AV. *Haematologica* 2016;101:407–416

US Epidemiology

Incidence by Age



Mortality Trends

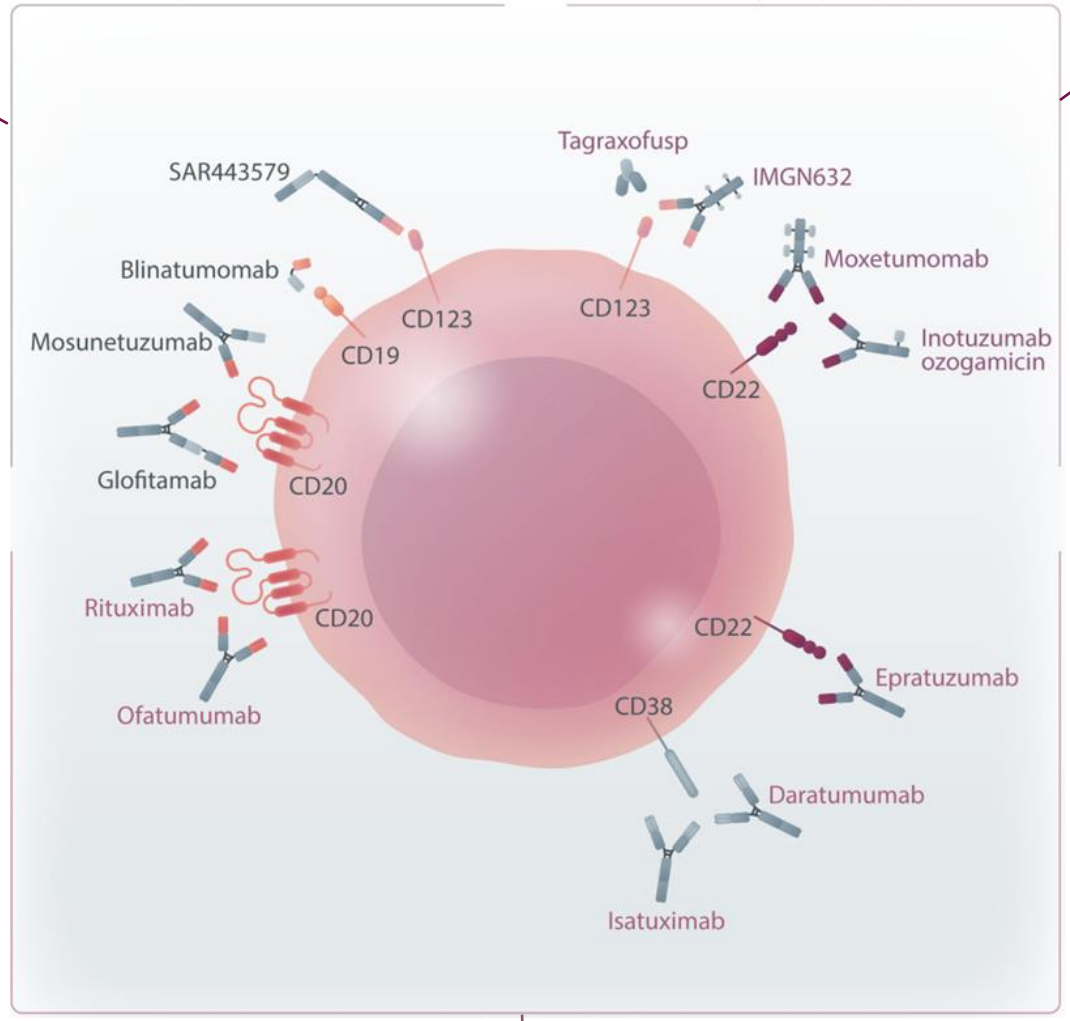


•SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2025 Jul 2. [cited 2025 Dec 15]. Available from: https://seer.cancer.gov/statistics-network/explorer/. Data source(s): U.S. Mortality Data (1969-2023), National Center for Health Statistics, CDC.

Targets and Mechanisms of Action of Antibodies for Pediatric Acute Lymphoblastic Leukemia

Bispecific Antibodies

Antibody-Drug Conjugates



Monoclonal Antibodies

Topics

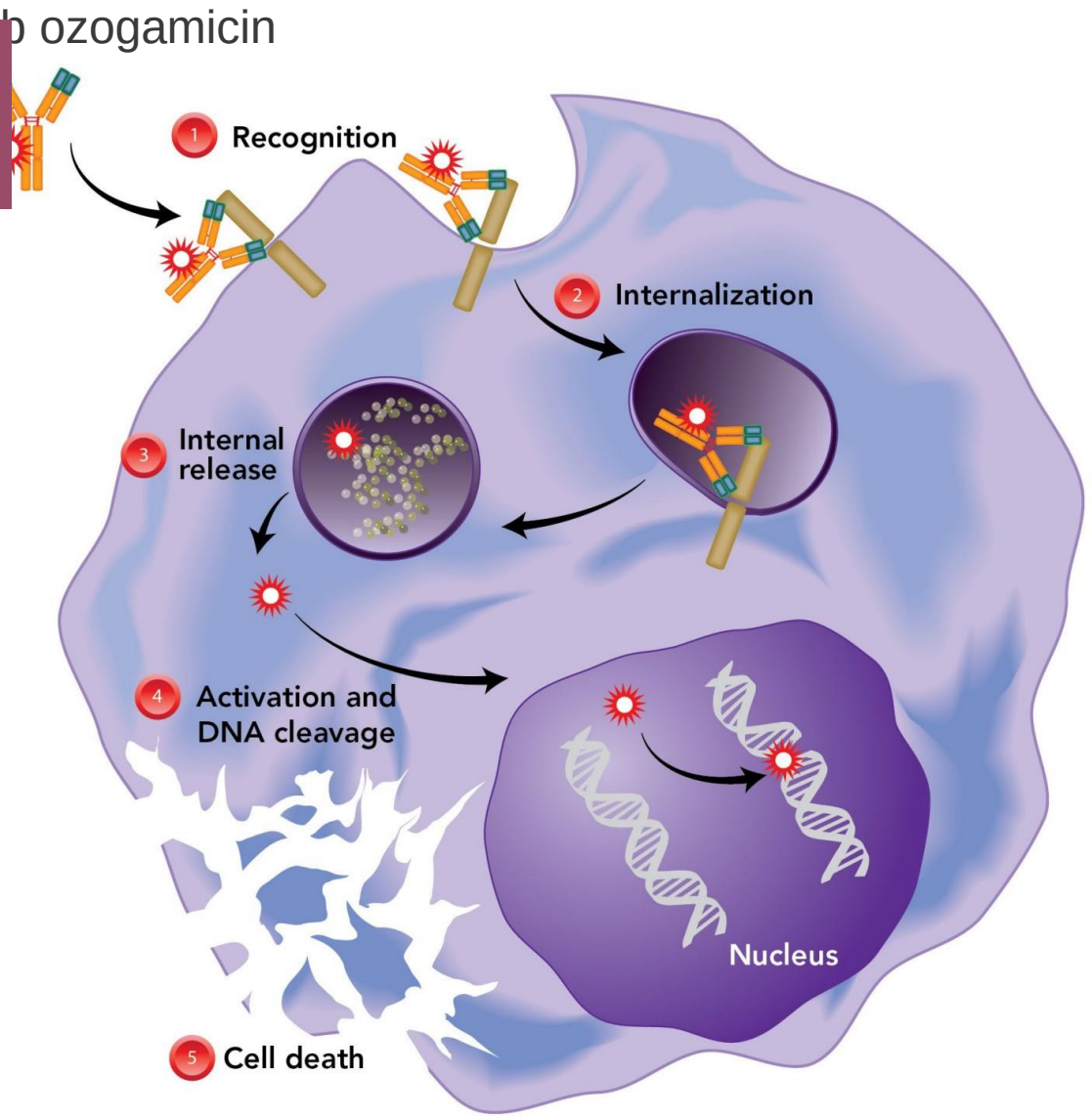
- Mechanism of action
- Dosing
- ITCC-059 trial Design
  - Phase 1 Results
  - Phase 2 Results
  - Phase 1B Results (Combination Regimen)
  - Safety profile
- Children’s Oncology Group Protocol AALL1621
- VOD/SOS
- Summary

Mechanism of Action

CD22 is an antigen on the cell surface of most normal B-cells (60–90%), and is expressed on the leukemic blasts in more than 90% of childhood BCP-ALL

Nonclinical data suggest:

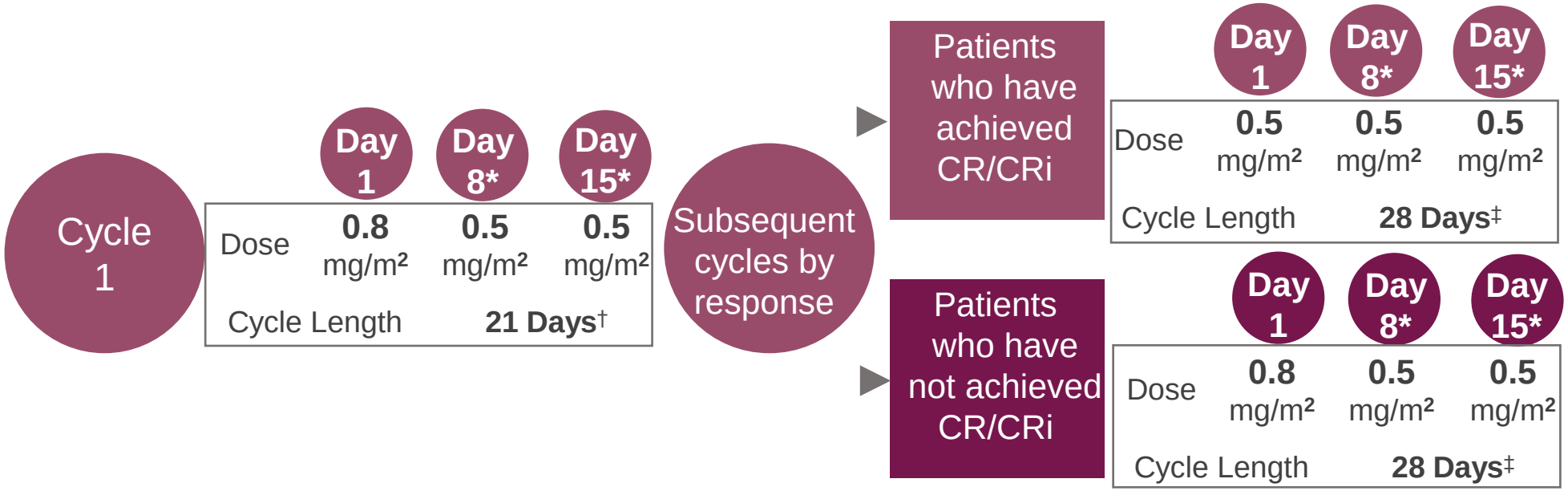
1. Inotuzumab ozogamicin binds preferentially to CD22 on the surface of leukemic blasts
2. Upon binding to CD22, the complex is internalized
3. The linker is cleaved inside the cell, allowing calicheamicin to enter the nucleus
4. Calicheamicin is activated and binds to DNA inside the malignant cell
5. Inside the nucleus, calicheamicin induces double-strand DNA breaks that result in apoptosis



Dosing

Inotuzumab ozogamicin offers convenient 1-hour dosing by IV infusion and can be administered in the outpatient setting. Other dosing regimens might be helpful and safe in different settings.

Dosing for inotuzumab ozogamicin is based on a patient's body surface area (m^2)



* +/– 2 days (maintain a minimum of 6 days between doses)
† The first cycle of BESPONSA is 21 days, while Cycles 2-6 are each 28 days. Cycle 1 may be extended to 28 days for patients achieving CR/CRi or if recovery from toxicity is needed.
‡ 7-day treatment-free interval starting on Day 21.
Maintain a minimum of 6 days between doses.

Reference: BESPONSA Prescribing Information. New York, NY: Pfizer Inc.

IV=intravenous.

Treatment Duration

The recommended number of inotuzumab ozogamicin cycles will vary depending on both response to treatment and plans for further therapeutic intervention with HSCT

Patients who proceed to HSCT	Patients who do not proceed to HSCT
The recommended duration of treatment with inotuzumab ozogamicin is 2 cycles A third cycle may be considered for those who do not achieve CR/ CRi and MRD negativity after 2 cycles	Up to a maximum of 6 cycles may be administered
Patients who do not achieve CR/ CRi and MRD negativity after 3 cycles should discontinue treatment	

Premedication and cytoreduction

- Premedication with a corticosteroid, antipyretic, and antihistamine is recommended prior to each dose
- For patients with circulating lymphoblasts, cytoreduction with a combination of hydroxyurea, steroids, and/or vincristine to a peripheral blast count of ≤10,000/mm^3 is recommended prior to the first dose of Cycle 1

Reference: BESPONSA Prescribing Information. New York, NY: Pfizer Inc.

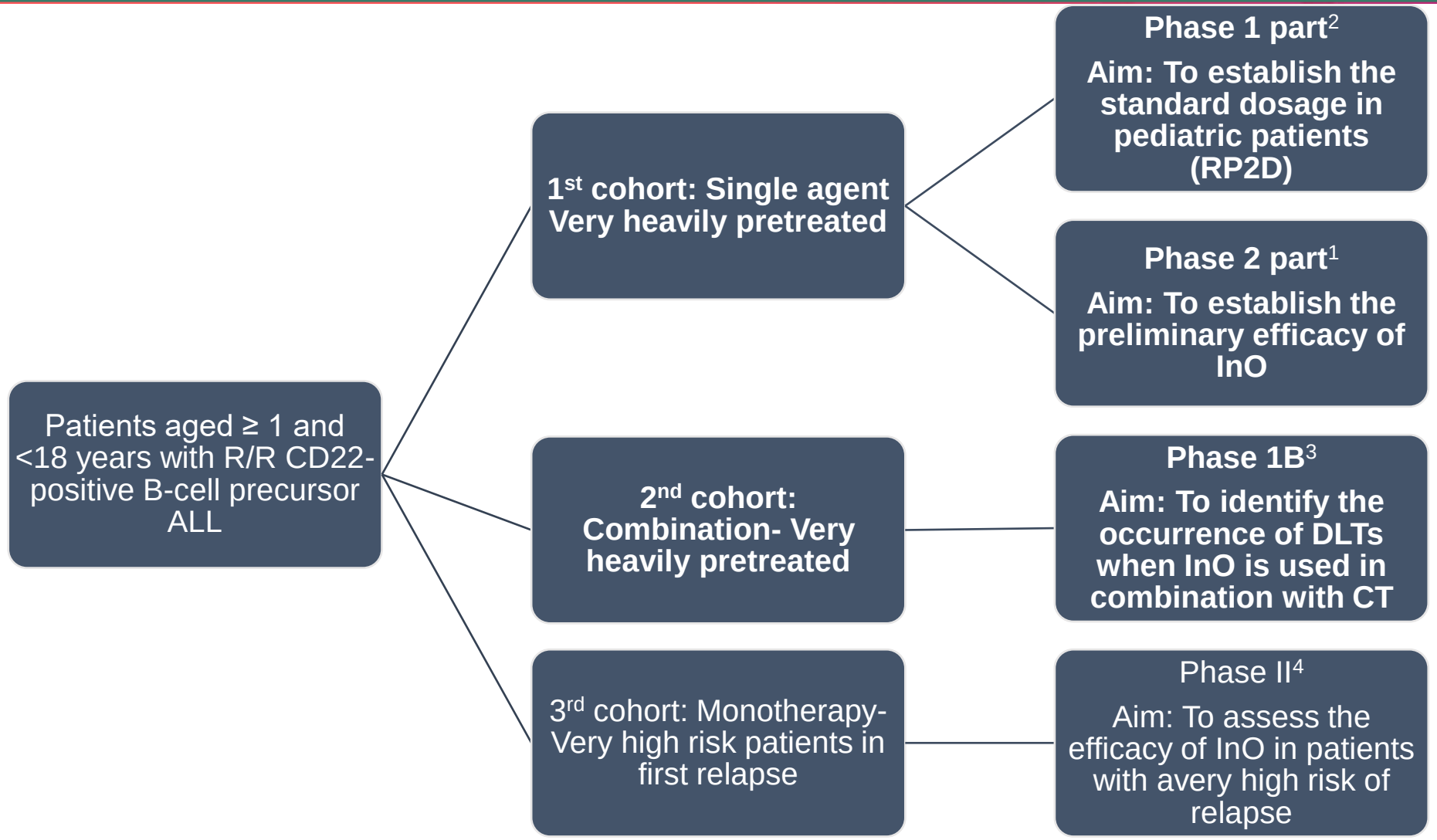
Published Results on Inotuzumab Ozogamicin in Heavily Pre-Treated Pediatric ALL

Study	Disease Status	Number of Subjects	Complete Remission Rate (%)	MRD Negativity (%)	Overall Survival	Event-Free Survival
ITCC-059 Phase I (1st cohort)	R/R BCP-ALL ≥2nd relapse; post-HSCT	27	80	84	1-year: 40%	1-year: 28%
ITCC-059 Phase II (1st cohort)	R/R BCP-ALL ≥2nd relapse; post-HSCT	28	81.5	81.8	1-year: 55%	1-year: 36%
ITCC-059 Phase IB (2nd cohort)	InO + vincristine + dexamethasone R/R BCP-ALL ≥2nd relapse; post-HSCT	30	76.7	65.2	1-year: 65.2%	1-year: 58.1%
ITCC-059 Phase II (3rd cohort)	First relapse very high-risk ALL	45 (31 evaluable at the time of report)	71%	77%	1-year: 57%	1-year: 49%
COG AALL1621	R/R BCP-ALL ≥2nd relapse; post-HSCT	48	58.3%	66.7%	2-year: 36%	2-year: 36%
Ped-ALL-1	R/R BCP-ALL ≥1st relapse; post-HSCT	6	83.3%	60%	-	-

The ITCC-059 trial (Study WI203581): A Phase 1/2 pediatric study of InO, as a single agent or in combination with chemotherapy

1. Pennesi E, Michels N, Brivio E, et al Inotuzumab ozogamicin as single agent in pediatric patients with relapsed and refractory acute lymphoblastic leukemia: results from a phase II trial. Leukemia. 2022;36(6):1516-24.
2. Brivio E, Locatelli F, Lopez-Yurda M, et al. A phase 1 study of inotuzumab ozogamicin in pediatric relapsed/refractory acute lymphoblastic leukemia (ITCC-059 study). Blood. 2021;137(12):1582-90.
3. Pennesi E, Brivio E, Ammerlaan ACJ, et al. Inotuzumab ozogamicin combined with chemotherapy in pediatric B-cell precursor CD22+ acute lymphoblastic leukemia: results of the phase IB ITCC-059 trial. Haematologica [Epub ahead of print]. Published online January 4, 2024

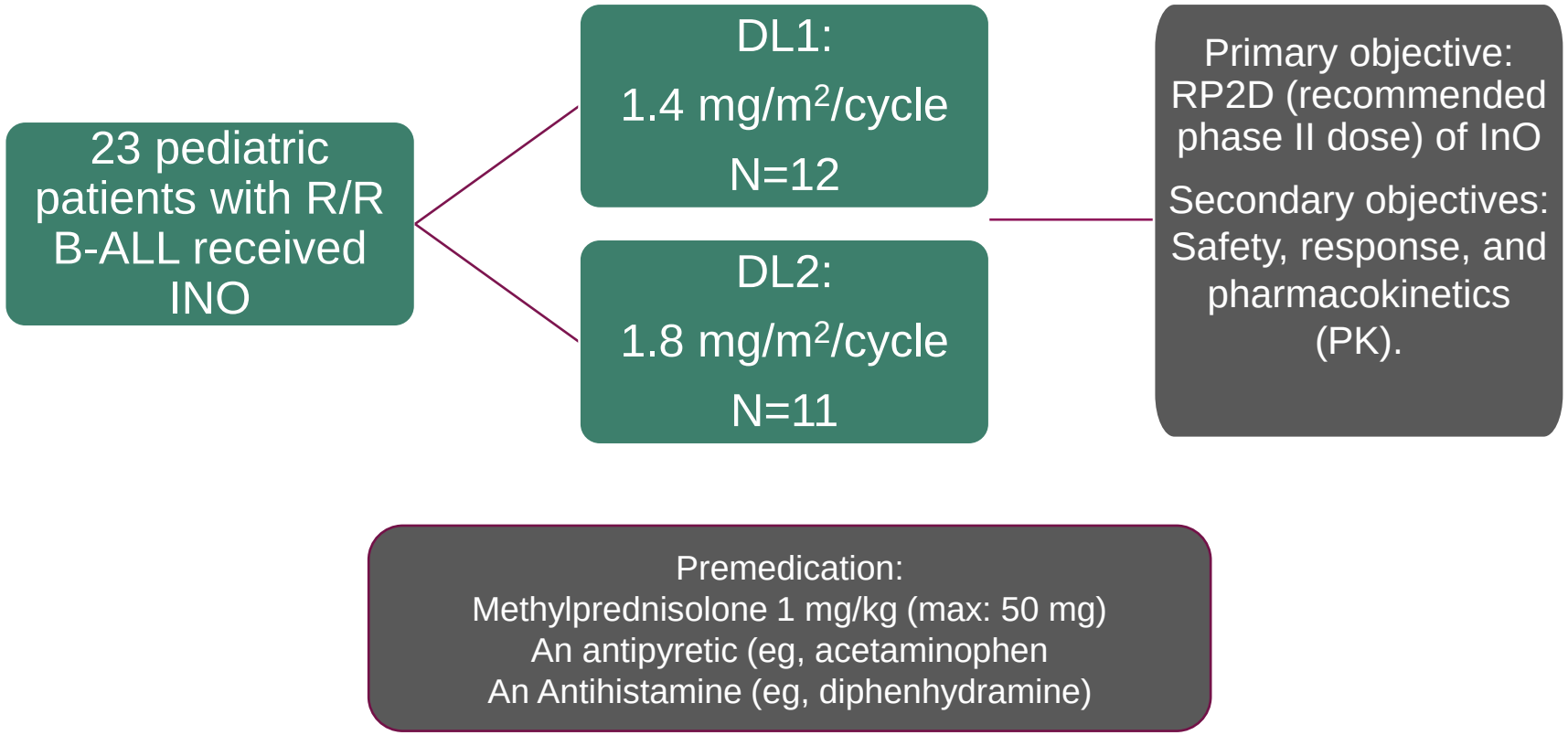
Study Design: ITCC Study (InO in pediatric patients with R/R ALL)



1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.
2. Brivio E. et al. *Blood*. 2021;137(12):1582-90.
3. Pennesi E. et al. *Published online January 4, 2024*
4. Brivio E. et al. *EHA Library.* 06/14/2025; 4160447; PS1371

RP2D: Recommended Phase 2 Dosage
DLT: Dose-Limiting Toxicity
CT: Chemotherapy

First Cohort, Phase 1: Study Design



RP2D: Recommended Phase 2 Dosage; InO: Inotuzumab ozogamicin; DL: Dose Level, PK: Pharmacokinetic

1. Brivio E. et al. *Blood*. 2021;137(12):1582-90.

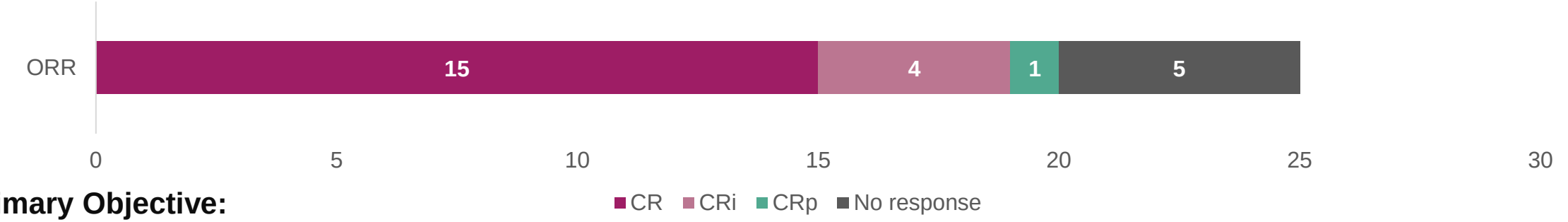
First Cohort, Phase 1: Baseline Characteristics

Characteristics	
Median age	11 years (1.7-16.9)
Refractory/relapsed status	
Refractory disease- n(%)	3 (12%)
≥2nd relapse- n(%)	15 (60%)
1st relapse post HSCT- n(%)	7 (28%)
Median number of prior treatments- n(%)	2 (range 2-7)
Bone marrow status at screening	
M3	22 (88)
M2	3 (12)
Median white blood cell count at screening × 10^9/L (range)	3.5 (0.19-8.59)
Specific elements of previous treatment	
HSCT	14 (56)
Blinatumomab	6 (24)
CAR T-cell therapy	1 (4)

RP2D: Recommended Phase 2 Dosage; InO: Inotuzumab ozogamicin; VOD: Veno-occlusive disease; HSCT: Hematopoietic Stem Cell Transplantation

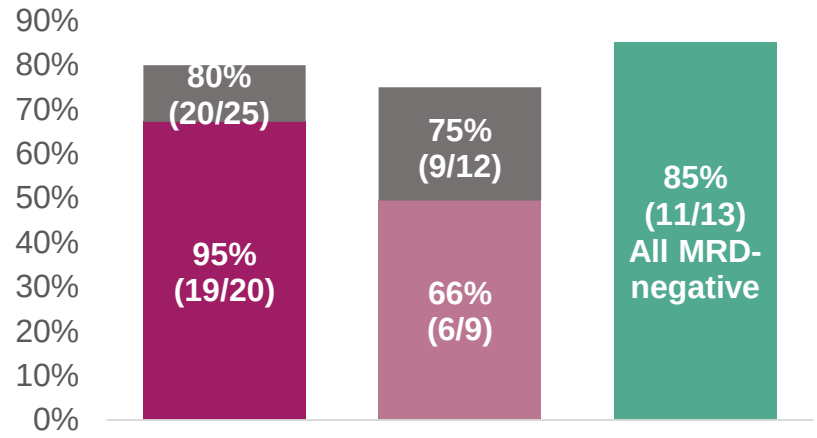
1. Brivio E. et al. *Blood*. 2021;137(12):1582-90

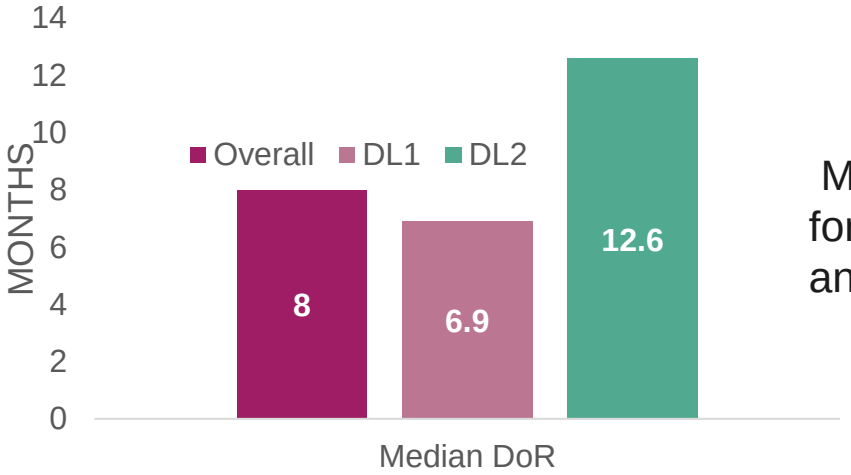
First Cohort, Phase 1: Results



Primary Objective:

After benefit-risk consideration of the first two dose level cohorts, RP2D was established as 1.8 mg/m² per cycle (0.8, 0.5, 0.5 mg/m² on Day 1, 8, 15)





Median survival: 7.2 months for patients treated at DL1 and not reached at DL2)

Safety

All treated patients (n=25) had at least one AE, and 23 patients had ≥1 Grade 3/4 AE). Four patients had Grade 5 AEs, all considered unrelated or unlikely to be related to InO (disease progression, n=2; lung infection, n=1; sepsis after HSCT, n=1). No VOD was reported during InO treatment.

1. Brivio E. et al. *Blood*. 2021;137(12):1582-90.

First Cohort, Phase 2: Baseline Characteristics

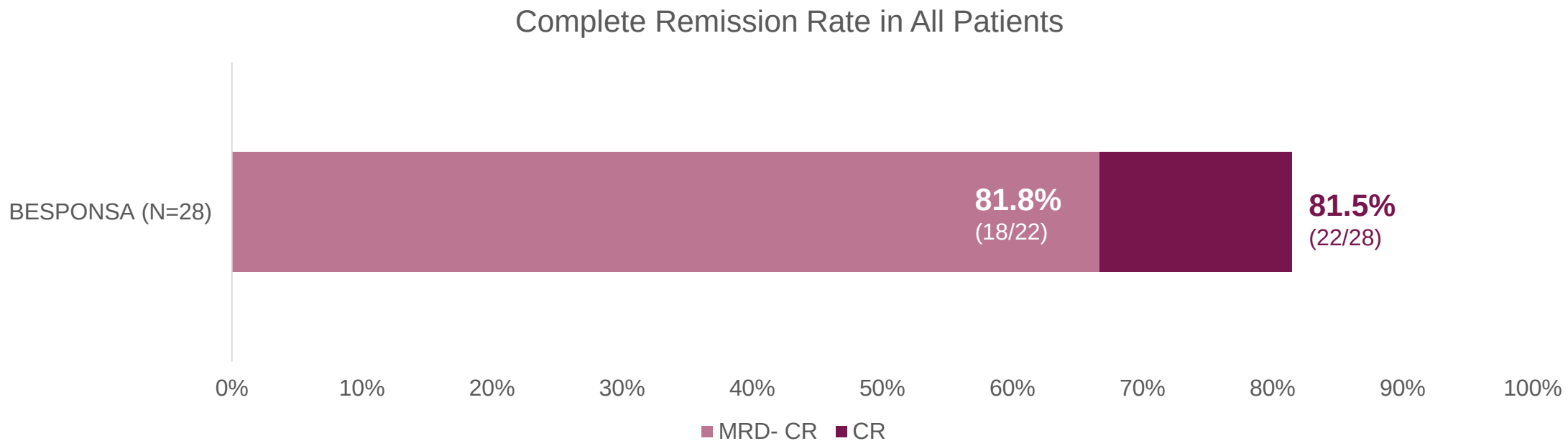
Characteristics	
Median age	7.5 years (4-13)
Gender	
Male/ Female- n(%)	19/9 (67.9%/22.1%)
Refractory/relapsed status	
Refractory disease- n(%)	6 (21.4%)
≥2nd relapse- n(%)	16 (57.1%)
1st relapse post HSCT- n(%)	6 (21.4%)
Median number of prior treatments- n(%)	2 (range 2-7)

The patients received 1-4 courses of InO.

27 out of 28 were evaluable for efficacy

1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.

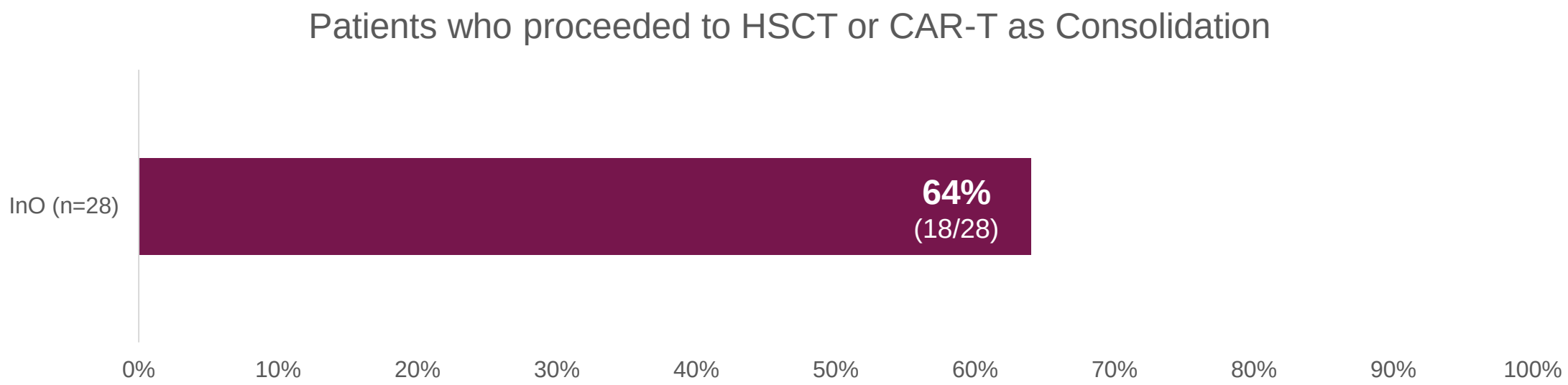
First Cohort, Phase 2: Response to Treatment



Median follow-up of survivors was 16 months (IQR: 14.49–20.07).
Median duration of response: 7.74 mo (95% CI: 5.65-not reached).

1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.

First Cohort, Phase 2: Bridging, EFS and OS



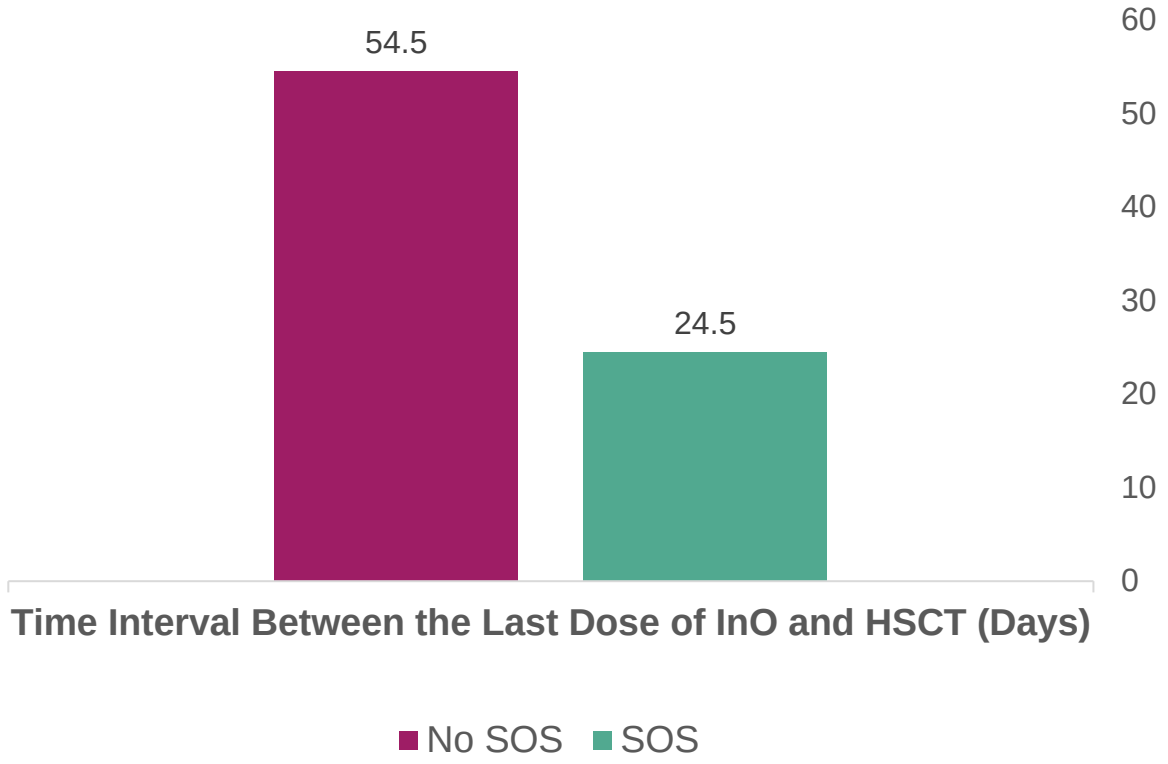
End-point	Result
1-year event-free survival rate	36.7% (95% CI: 22.2–60.4%)
1-year overall survival rate	55.1% (95% CI: 39.1−77.7%)

1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.

First Cohort, Phase 2: Safety

Incidence of Adverse Events	No of Patients n(%)
All-Grades Adverse Events	28 (100%)
Grade 3/4 Adverse Events	20 (71.4%)
All-Grades VOD/SOS	7 (25%)
Grade 3/4 VOD/SOS	6 (21%)
Death Due to Adverse Events	2 (7%)

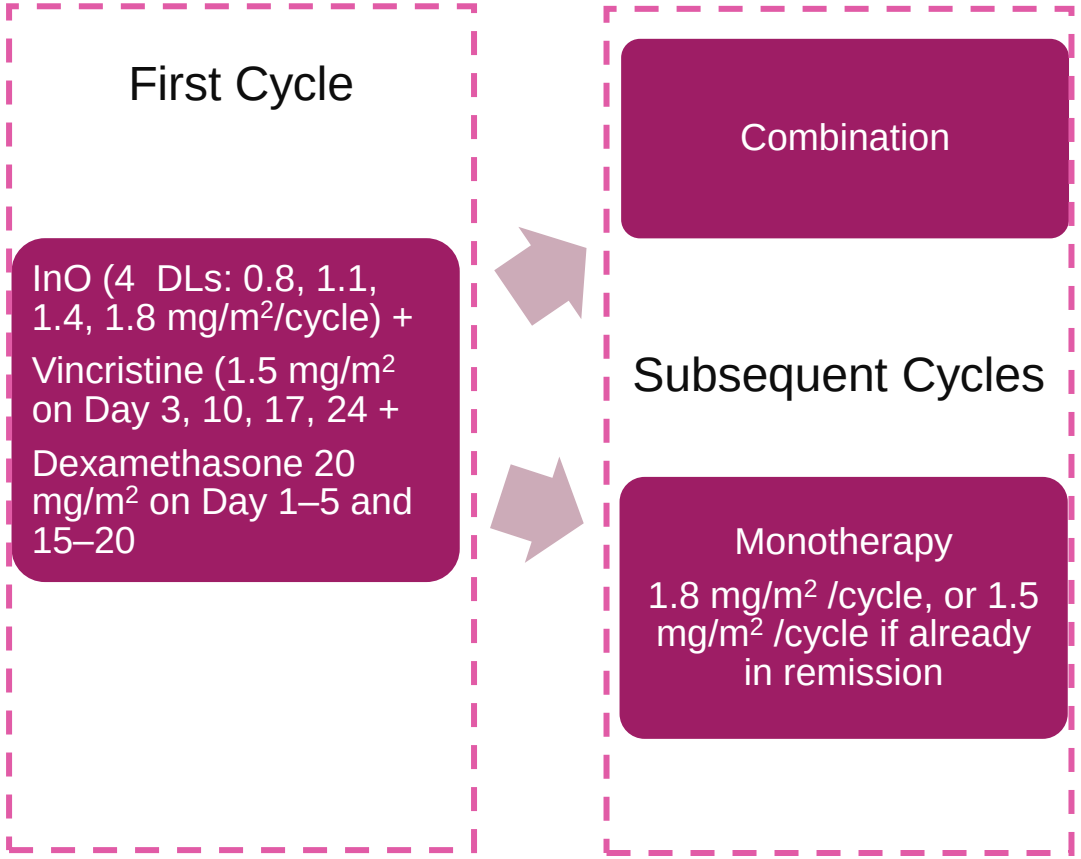
SOS Occurrence	Number of Patients	Time Interval	P-value
No SOS	17	54.5	0.01
SOS	6	24.5	



1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.

Second Cohort, Phase 1B: Study Design

The primary endpoint: Occurrence of DTLs, when used in combination.
Secondary endpoints included frequency and severity of AEs based on the Common Terminology Criteria for Adverse Events version 4.03, and occurrence of toxic death. Preliminary efficacy end-points included ORR and MRD negativity status (as best response after InO treatment and after cycle one), OS, EFS, duration of response (DOR).



Occurrence of DLTs at Different InO Dose Levels[1]			
InO Dose Level	Patients	DLTs	Notes
1.1 mg/m²	4	2 (SOS, ↑AST)	Both events resolved
0.8 mg/m²	7	0	-
Protocol amendment: Dexamethasone reduced to 10 mg/m²/cycle			
1.1 mg/m²	6	1 (↑ AST)	AST normalized after 9 days
1.4 mg/m²	3	0	-
1.8 mg/m²	7	1 (↓ ANC, Day> 42)	ANC recovered on Day 45
1.8 mg/m²	3	N/A	Expansion cohort

DLT: Dose-Limiting Toxicity; Including:
Any grade 5 toxicity
ANC< 50,000/ µL for 42 days in the absence of persisting leukemia
Any grade 3-4 non-hematologic toxicities persisting for > 48 hours (> 7 days for hepatic transaminases or bilirubin abnormalities

1. Pennesi E. et al. *Published online January 4, 2024*

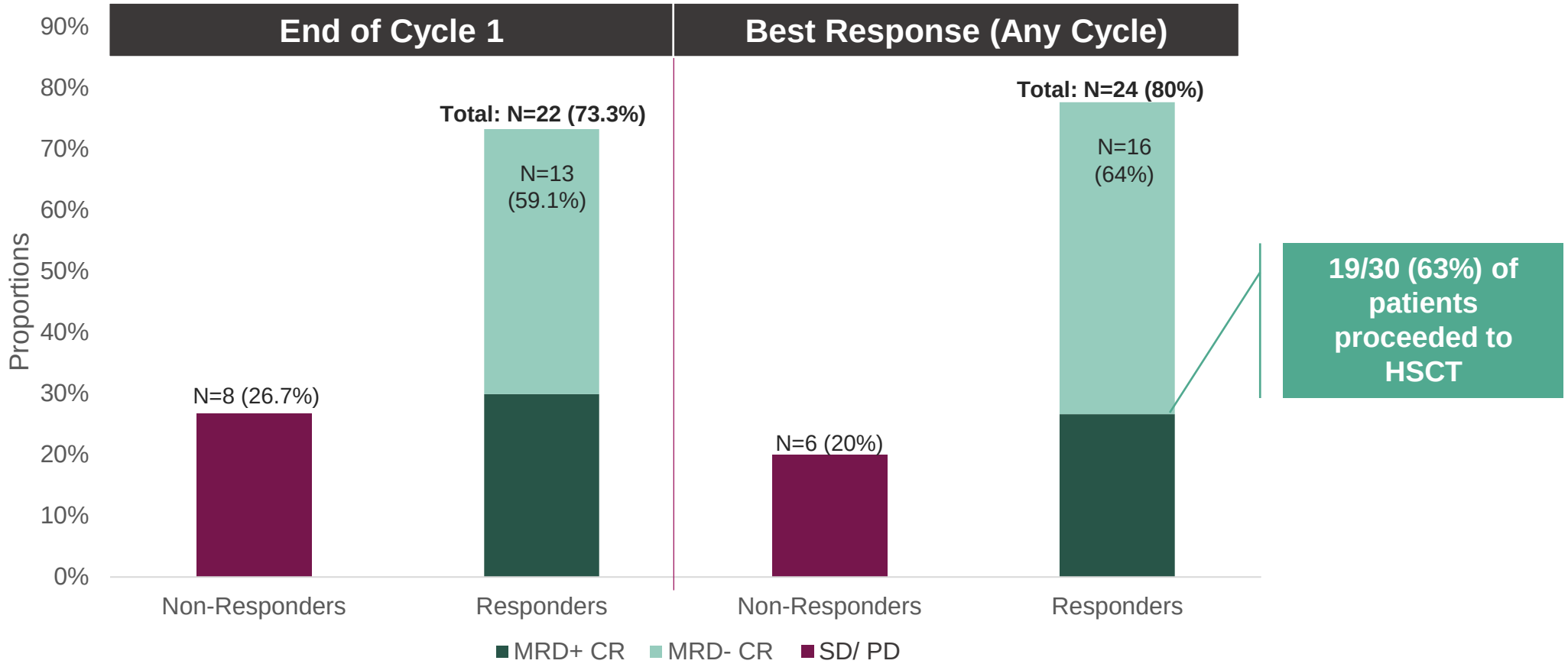
Second Cohort, Phase 1B: Baseline Characteristics

Characteristics	N (%)
Sex	
Male Female	19 (63%) 11 (37%)
Age at Enrollment (years)	
Median (range)	8.5 (1-17)
Status at Enrolment (%)	
First relapse post HSCT ≥ 2nd relapse Refractory disease	2 (7%) 20 (67%) 8 (27%)
Extramedullary Disease (%)	
CNS1 CNS2 CNS3 Testicular involvement Lymph nodes enlarged Other locations	27 (90%) 2 (7%) 1 (3%) 0 (0) 0 (0) 0 (0)

Overall, 30 patients were treated, with all evaluable for response, and 29 evaluable for the assessment of DLTs.

1. Pennesi E. et al. *Published online January 4, 2024*

Second Cohort, Phase 1B: Response to Treatment



- Median DOR was 8.38 months (IQR: 2.3-11.9).
- The cumulative incidence of relapse at 6 months and 12 months was 8.3% (95% CI, 1.0–27.0) and 13.6% (95% CI, 2.9–34.0), respectively
- The cumulative incidence of non-relapse mortality was 6.7% (95% CI, 1.1–19.5) at 6 months, and 10.2% (95% CI, 2.5–24.3) at 12 months.

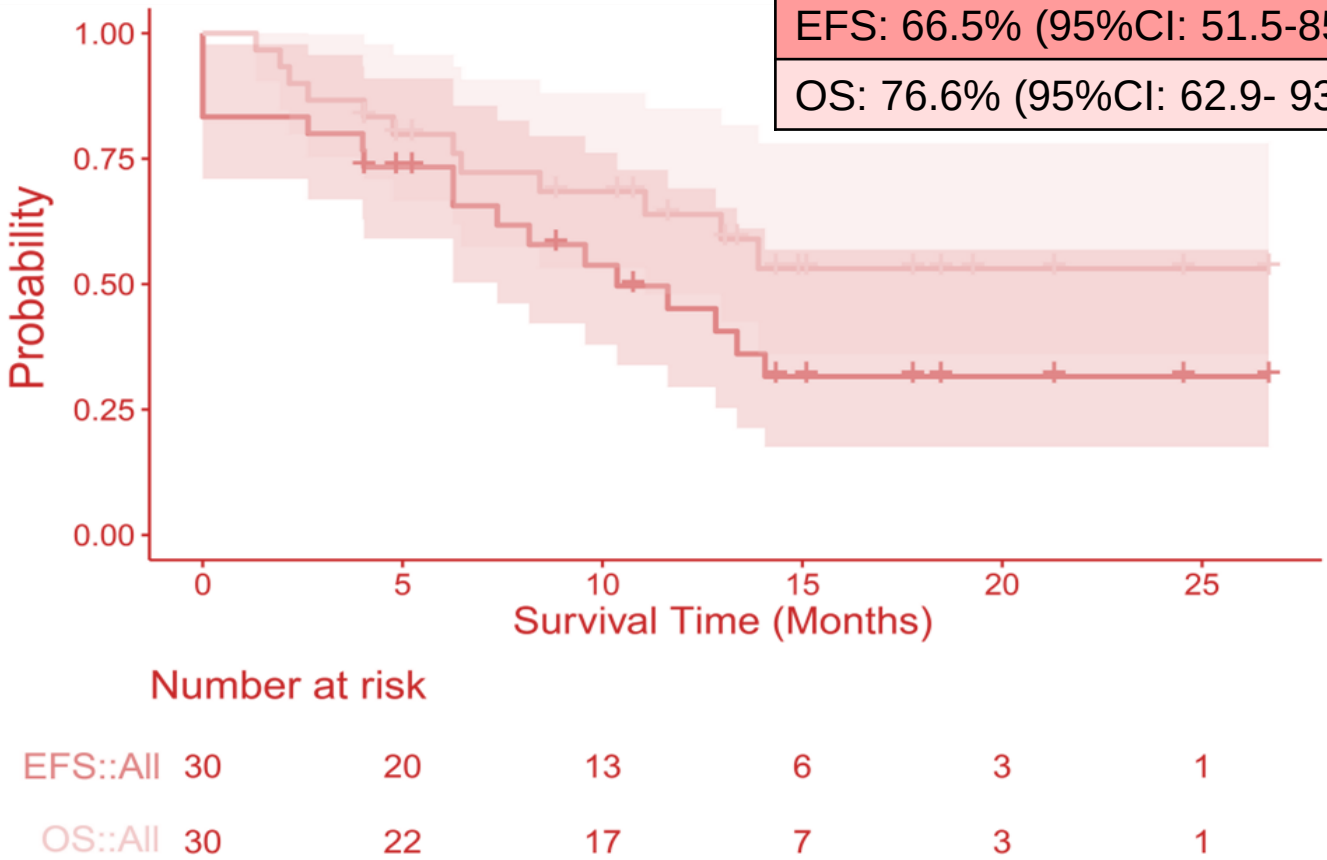
1. Pennesi E. et al. *Published online January 4, 2024*

CR: Complete Remission
MRD: Minimal Residual Disease
SD: Stable Disease
PD: Progressive Disease

Second Cohort, Phase 1B: EFS and OS

With a median follow-up of 15.9 months (Interquartile Range [IQR]: 12.4–18.4):

6- month probabilities	12 month probabilities
EFS: 66.5% (95%CI: 51.5-85.8)	EFS: 41.7% (95%CI: 27.1-64.3)
OS: 76.6% (95%CI: 62.9- 93.4)	EFS: 62.3% (95%CI: 46.9-82.8)



1. Pennesi E. et al. *Published online January 4, 2024*

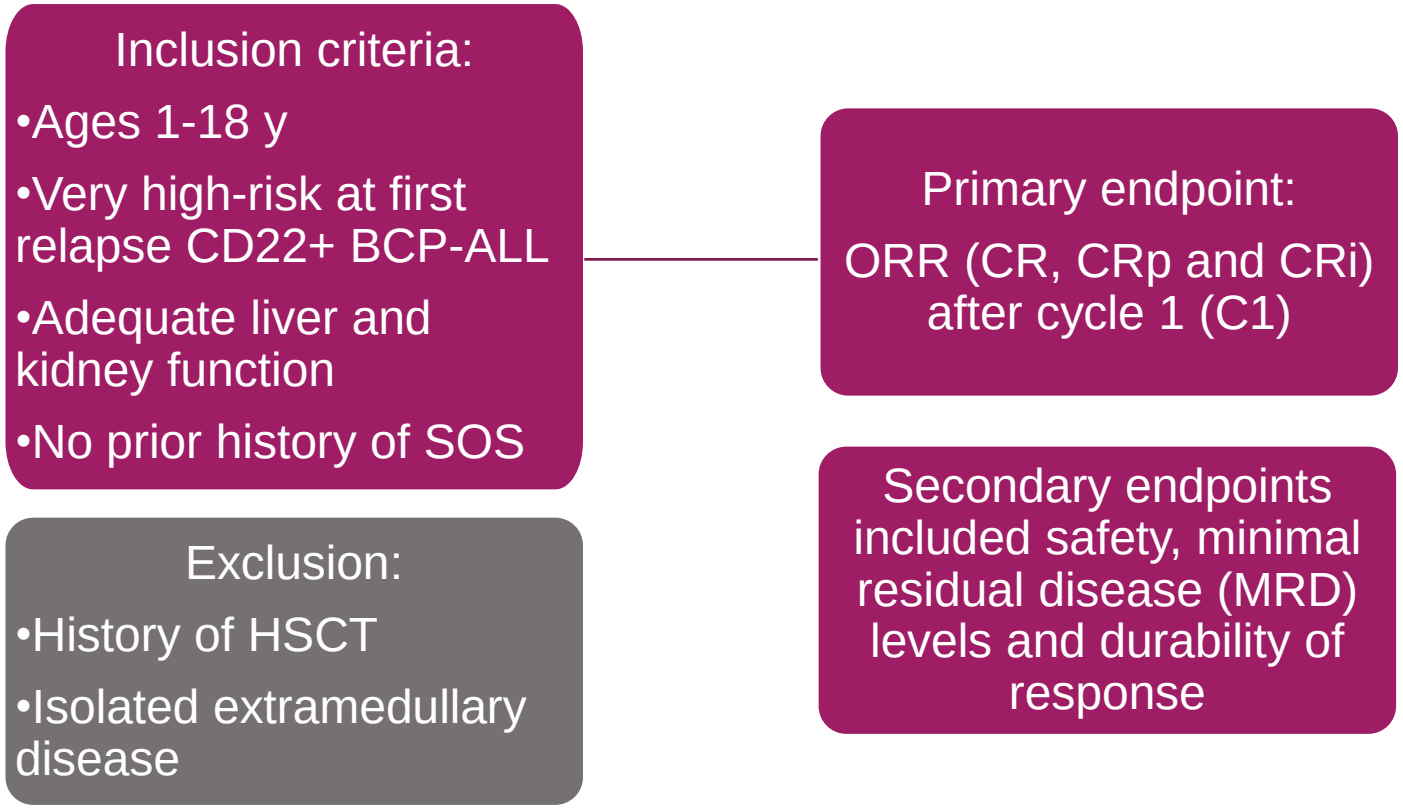
Second Cohort, Phase 1B: Safety

AE Term	Full Dexamethasone dose (20 mg/m2) n= 11		Reduced Dexamethasone dose (10 mg/m2) n= 19		Total
	Grade 1-2	Grade≥ 3	Grade 1-2	Grade≥ 3	
Anemia	2 (18%)	7 (63%)	3 (15%)	12 (63%)	24 (80%)
AST increased	2 (18%)	5 (45%)	6 (32%)	10 (53%)	23 (77%)
ALT increased	3 (27%)	3 (27%)	9 (47%)	7 (37%)	22 (73%)
Platelet count decreased	1 (9%)	8 (72%)	1 (5%)	12 (63%)	22 (73%)
ANC decreased	1 (9%)	6 (54%)	0	12 (63%)	19 (63%)
Constipation	3 (27%)	0	12 (63%)	0	15 (50%)
Fever	6 (54%)	0	7 (37%)	0	13 (43%)
Headache	4 (36%)	1 (9%)	8 (24%)	0	13 (43%)
Febrile neutropenia	0	3 (27%)	0	7 (37%)	10 (33%)
Hypokalemia	0	2 (18%)	0	3 (15%)	9 (30%)
Abdominal pain	3 (27%)	0	5 (17%)	0	8 (27%)
Bilirubin increased	2 (18%)	0	4 (21%)	1 (5%)	7 (23%)
GGT increased	1 (9%)	1 (9%)	2 (11%)	3 (15%)	7 (23%)
SOS	In total, five (17%) patients developed SOS: four following HSCT (one grade 4 and three grade 3) and the fifth during InO treatment (4/5(80%))				

1. Pennesi E. et al. *Published online January 4, 2024*

AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase;
ANC: Absolute Neutrophil Count; GGT: Gamma Glutamyl Transferase

Third Cohort, Phase 2[1]: Study Design



An optimal Simon's 2-stage design was used to test the null hypothesis (H0) ORR≤55% with the alternative hypothesis ORR ≥75%. The design was modified to reduce the sample size due to slow recruitment, maintaining 80% power to reject H0 and increasing the alpha-error to 10%. Recruitment was ongoing until CA approval was obtained, leading to a slight over-enrollment.

1. Brivio E. et al. *EHA Library.* 06/14/2025; 4160447; PS1371

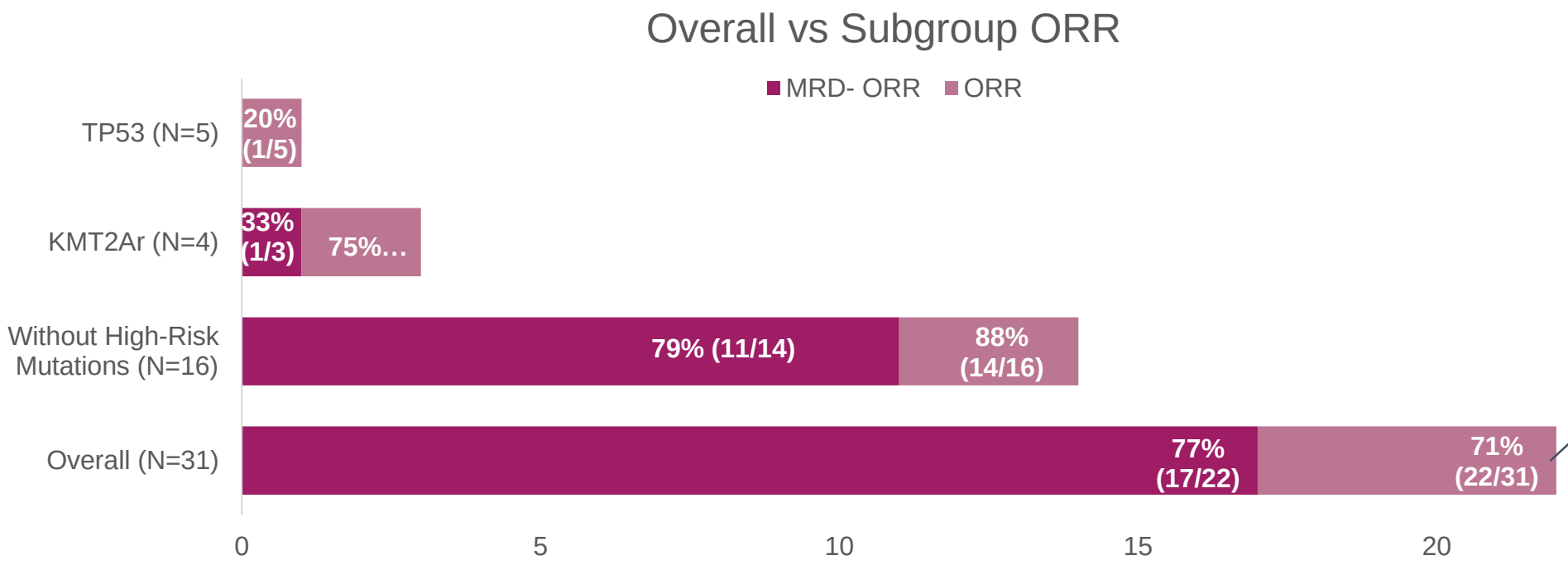
Third Cohort, Phase 2[1]: Baseline Characteristics

Characteristics	N (%)
Sex, n(%)	
Male Female	19 (61%) 12 (39%)
Age at Enrollment (years)	
Median (range)	8 (1-17)
Criteria for being at very high-risk of relapse n(%)	
Very early relapse (<18 months after initial diagnosis) CNS3 High-risk genetics t(1;19) t(1;19)/TP53 mut/del t(1;19, 4 *KTM2A::AF4)* Low hypodiploidy, 2 low hypodiploidy/TP53 mut/del TP53 mut/del only	27 (87%) 3 (10%) 15 (48%) 4 2 2 2 2 1

1. Brivio E. et al. *EHA Library.* 06/14/2025; 4160447; PS1371

Third Cohort, Phase 2[1]: Results

- Median number of administered doses: 3 (range 2-9)

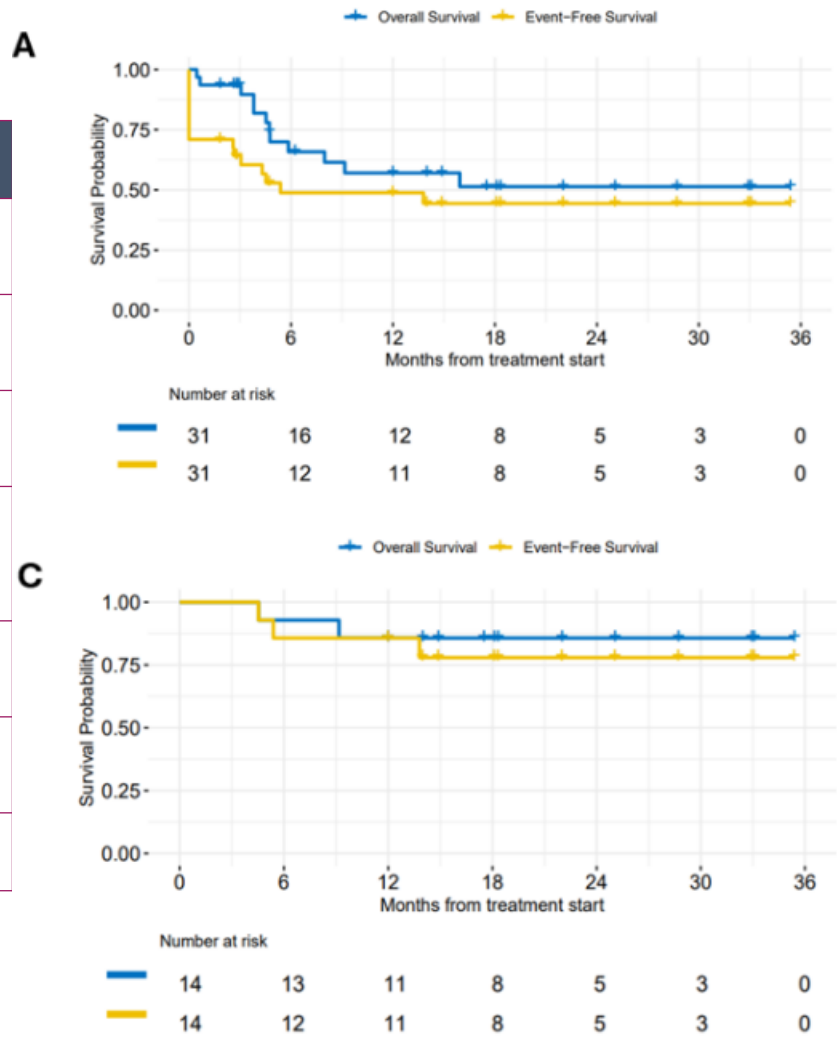


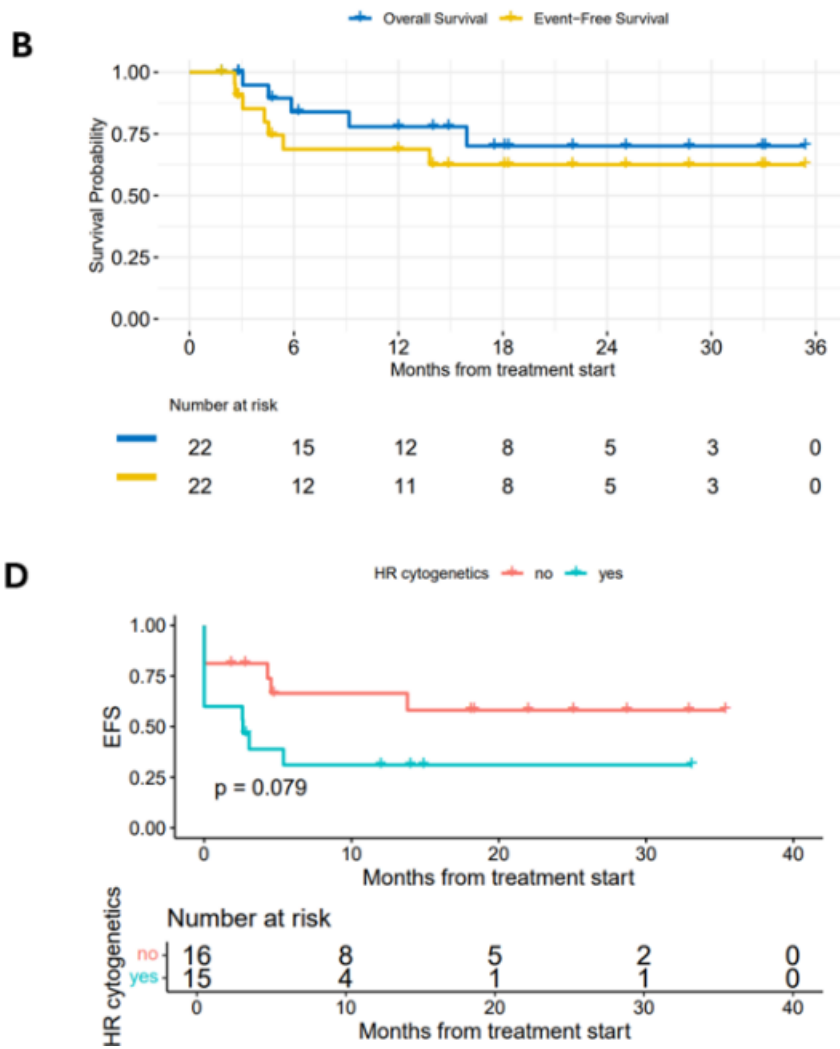
- 14/22 responding pts had proceeded to HSCT consolidation
- 5/22 proceeded to CD19-CART
- 3/22 pts were bridging to consolidation at data snapshot.

1. Brivio E. et al. *EHA Library.* 06/14/2025; 4160447; PS1371

Third Cohort, Phase 2[1] :Event-Free and Overall Survival

End-point	Result
1-year EFS rate (overall)	49% (95% CI: 33-71)
1-year OS rate (overall)	57% (95% CI: 40-80)
1-year EFS rate (patients who underwent HSCT after InO (n= 14)	86% (95% CI: 69-100)
1-year OS rate (patients who underwent HSCT after InO (n= 14)	86% (95% CI: 69-100)
1-year EFS rate in patients with high-risk cytogenetics (n= 15)	31% (95% CI: 14-68)
1-year OS rate in patients with high-risk cytogenetics (n= 15)	45% (95% CI: 24-84)
median follow-up: 18 months (range 0.5-35)	





Third Cohort, Phase 2[1] : Safety Results

- Twenty-nine patients had at least 1 adverse event (AE) ≥ gr3.
- The most common non-hematological AEs were fever and AST elevation.
- Two cases of grade 3 SOS were reported, both occurred in transplanted pts and resolved after treatment with defibrotide.

1. Brivio E. et al. *EHA Library.* 06/14/2025; 4160447; PS1371

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

O'Brien MM, Ji L, Shah NN, et al. Phase II Trial of Inotuzumab Ozogamicin in Children and Adolescents With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia: Children's Oncology Group Protocol AALL1621. J Clin Oncol. 2022;40(9):956- 67.

Study Sesign

Key inclusion criteria:
Patients aged 1-21 years with R/R CD22-positive B-ALL (n=48)

First cycle:
1.8 mg/m^2/cycle
Day 1: 0.8 mg/m^2
Day 8: 0.5 mg/m^2
Day 15: 0.5 mg/m^2

Primary endpoint analysis on day 28

No CR

Second cycle:
1.8 mg/m^2/cycle
Day 1: 0.8 mg/m^2
Day 8: 0.5 mg/m^2
Day 15: 0.5 mg/m^2
(n=7: 2 PR+ 5 SD after 1st cycle)

CR

Second cycle:
1.5 mg/m^2/cycle
Day 1: 0.5 mg/m^2
Day 8: 0.5 mg/m^2
Day 15: 0.5 mg/m
(n=19, 13 MRD- CR/Cri + 6 MRD+ CR/CRi

Primary Endpoints:
rate of CR or CRi after cycle 1.
Secondary or exploratory efficacy endpoints included event-free survival (EFS) and overall survival (OS), with EFS events including treatment failure, relapse, second malignancy neoplasm, or death because of any cause, whichever occurred first, and OS events being death because of any cause

1. O'brien MM. et al. *J Clin Oncol.* 2022;40(9):956- 67.

Premedications included methylprednisolone 1 mg/kg with a maximum of 50 mg, an antipyretic, and an antihistamine

Patient Characteristics

Characteristics	N (%)
Sex	
Female Male	19 (40%) 29 (60%)
Age at Enrollment (years)	
Median (range)	9 (1-21)
Status at Enrolment (%)	
First relapse/ refractory to at least one prior reinduction attempt First relapse with no prior reinduction attempt ≥ 2nd relapse Primary refractory disease with at least two prior induction attempts Any relapse after HSCT	10 (21%) 1 (2%) 32 (67%) 2 (4%) 3 (6%)
Prior HSCT(%)	
Yes No	37 (77%) 11 (23%)
Prior CAR-T Therapy (%)	
Yes No	37 (77%) 11 (23%)
Prior Blinatumumab	
Yes No	14 (29%) 34 (71%)

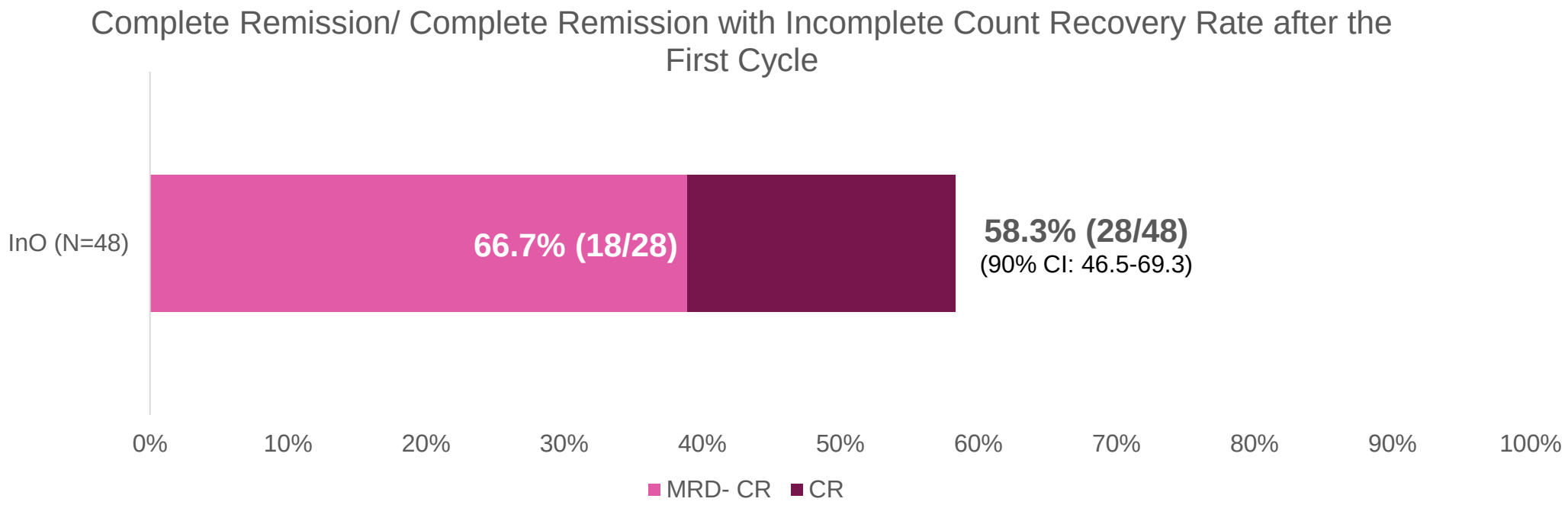
Response to Treatment

Cycle 1 Response to Treatment	CR	CRi	PR	SD	PD
N=48	19	9	3	9	8*
Cycle 2 Response to Treatment	**CR**	**CRi**	**PR**	**SD**	**PD**
Number of patients who received Cycle 2=26	19 (16 CR/CRi of MRD< 0.01% 2 CR/CRi of MRD≥ 0.01% 1 PR)		2 (1 CRi of MRD≥ 0.01% 1 PD)	5 (1 CRi of MRD≥ 0.01% 2 PR, 1 SD 1 PD)	0

CR=complete response; CRi=CR with incomplete count recovery; PR=partial response; SD=stable disease; PD=progressive disease; N=number of patients. *In 2 patients with PD due to CNS progression in cycle 1, bone marrow CR was observed (MRD

1. O'brien MM. et al. *J Clin Oncol.* 2022;40(9):956- 67.

CR/ CRi after the First Cycle



Endpoint	Result
Proceeding to HSCT	21 (43.7%)
2-year EFS Probability Among MRD- Patients	57.7% (95% CI, 31.9 to 76.8
Overall 2-year EFS Probability	28.6% (95% CI, 15.9 to 42.8)
Overall 2-year OS Probability	36.0% (95% CI, 22.3 to 49.9)

1. O'brien MM. et al. *J Clin Oncol.* 2022;40(9):956- 67.

Summary

- CD22 expression confirmed that pre-existing partial CD22-positivity is associated with poor response.
- InO was well tolerated in these heavily pretreated patients.
- The efficacy and safety results in pediatric patients is consistent with adult data
- The standard adult dosage in relapsed/refractory setting is proved to be efficient and tolerable in pediatric population
- Food and Drug Administration approved inotuzumab ozogamicin (Besponsa, Pfizer) for pediatric patients 1 year and older with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukemia (ALL) on March 6, 2024

1. Pennesi E. et al. *Leukemia.* 2022 Jun;36(6):1516-1524.
2. Brivio E. et al. *Blood*. 2021;137(12):1582-90.
3. Pennesi E. et al. *Published online January 4, 2024*
4. O'brien MM. et al. *J Clin Oncol.* 2022;40(9):956- 67.

A real-world multi-institution experience of standard vs alternative dosing of inotuzumab ozogamicin for Relapsed/Refractory pediatric B-cell acute lymphoblastic leukemia

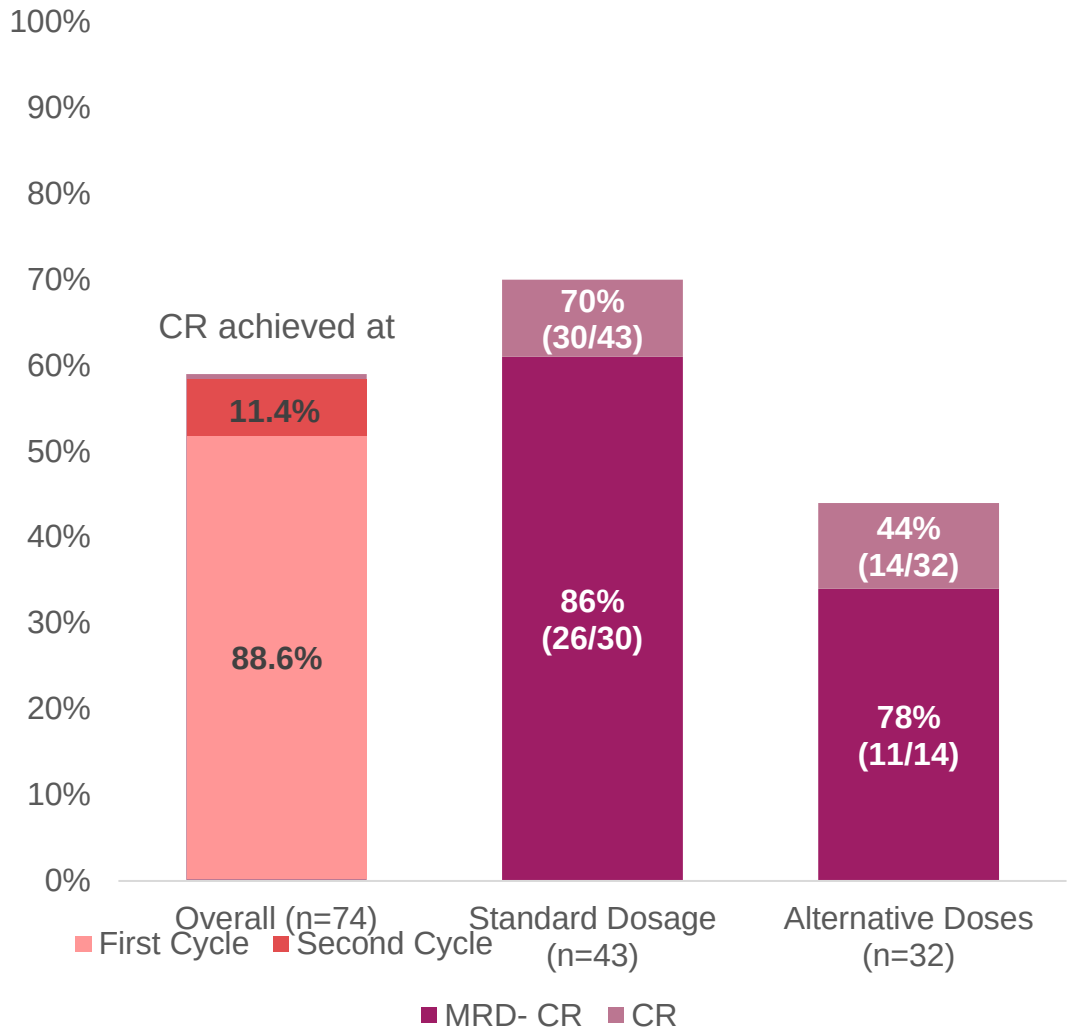
Morgan Drucker, Catherine Aftandilian, Kara Davis, Susan Rheingold, Daisha Ball, Kelly Faulk, Maureen O'Brien, Jamie Stokke, Deepa Bhojwani, Rishi Kotecha, Jeremy Rubinstein
Blood 146 (2025) 1570–1571

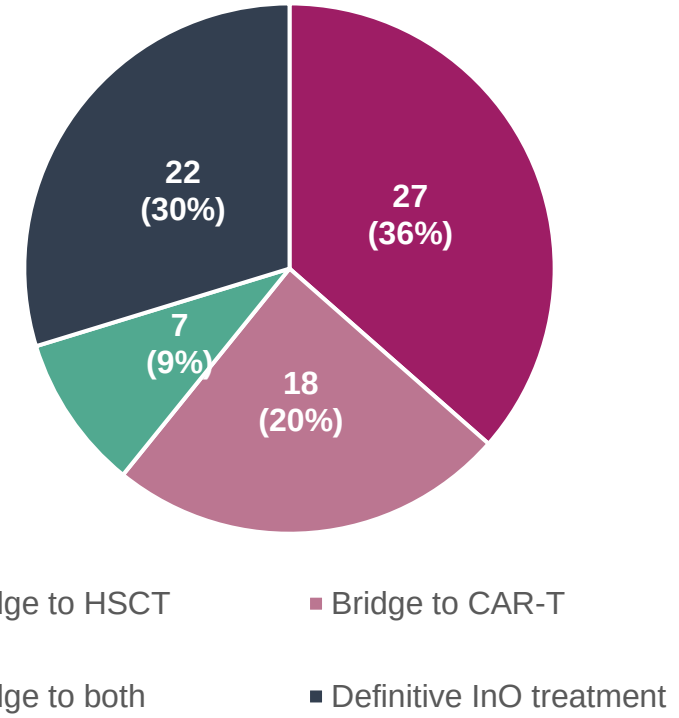
Baseline Characteristics

Characteristics	N (%)
Age at Enrollment (years)	
Median (range)	9 (0-32)
Status at Enrolment, n(%)	
First relapse ≥ 2nd relapse Primary refractory disease	26 (35%) 38 (50%) 11 (15%)
Ethnicity, %	
Non-Hispanic white Asian/Pacific Islander Non-Hispanic black Others	47% 11% 6% 8%
Inotuzumab Ozogamicin dose received, n(%)	
Standard dosage (1.8 mg/m²/cycle) Lower doses (median: 1.5 mg/m²/cycle) Lower number of doses (1 or 2)	43 (57%) 7 (9%) 25 (33%)

Drucker M, et al. *Blood* (2025) 146 (Supplement 1): 1570.

Complete Remission Rates and





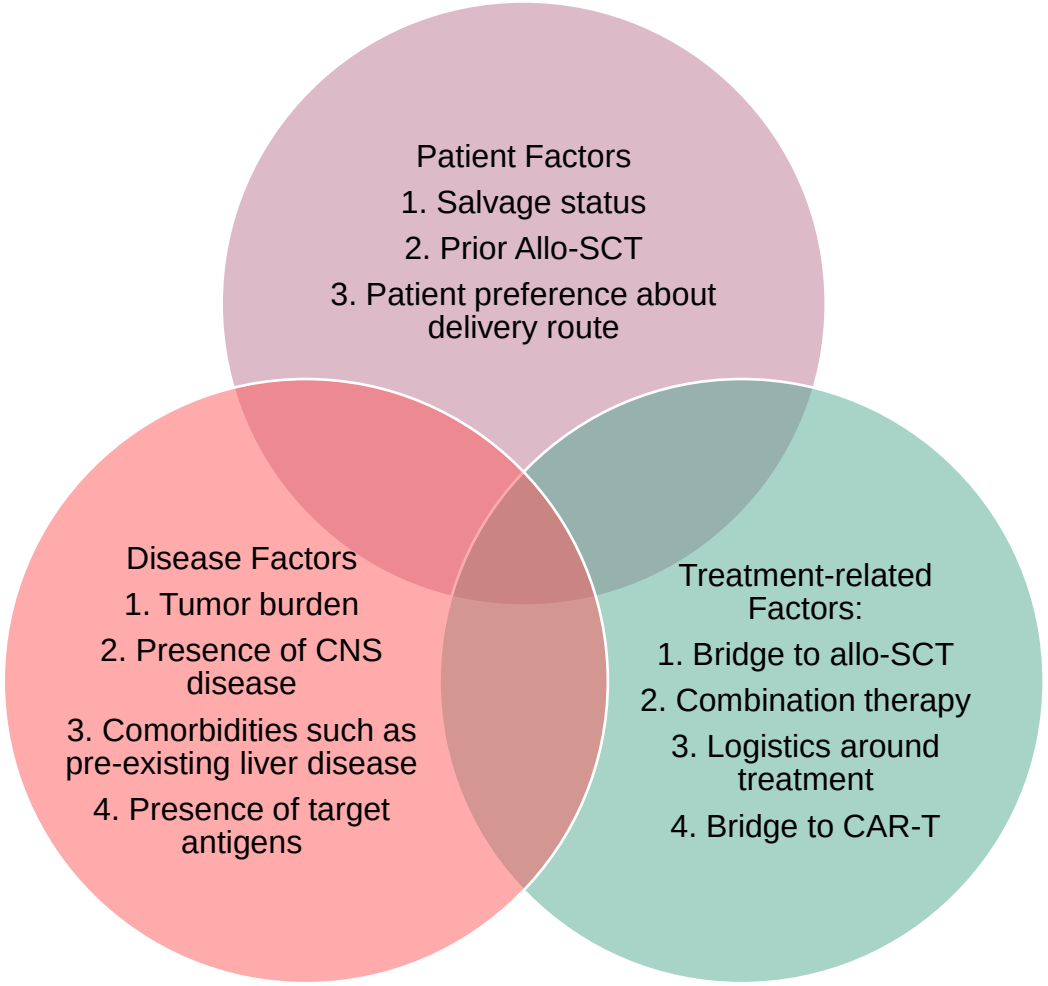
30/43 patients (70%) who received standard dosing and 22/32 (69%) who received alternative dosing of InO proceeded to HSCT and/or CAR-T.
2-year OS rate was significantly better for bridging group: 2-year OS (bridging therapy=85.8% vs. definitive therapy=59.1%; p<0.001). 2-year OS rate for the entire cohort was 77.9%.

Drucker M, et al. *Blood* (2025) 146 (Supplement 1): 1570.

Safety Results

- Patients tolerated InO well with the most common adverse event being febrile neutropenia in 24%.
- No patient experienced SOS during InO therapy; however, 9% (n=7) developed SOS post-InO, during the course of HSCT (grade ≥3, n=6).
- SOS occurred at a mean of 58 days after the last InO administration (range 33-108 days).
- Six of the 7 patients who experienced SOS had received standard InO dosing.

Factors Affecting Patient Selection



Expert Opinion

Factors Affecting CR/CRi Rates

Salvage status

Patients in earlier lines benefit more from InO treatment

- CR/CRi of 78.4% with InO vs 28.4% with SOC in S1, and 64.7% with InO vs 35.6% with SOC in S2) and HSCT rates(52.3% with InO vs 26.5% with SOC in S1, and 39.2% with InO vs 15.3% with SOC in S2

Disease burden

Defined by bone marrow blast (BMB) percentage does not affect InO efficacy (CR and HSCT rates).

- CR/CRi rates in the low (BMB<50%), moderate (BMB 50–90%), and high disease burden (BMB> 90%) groups were 73.6%, 74.7%, and 70.0% compared with 45.8%, 26.5%, and 16.7% in the SOC group, respectively. The probability of 24-month OS was higher in patients treated with InO versus SOC across all categories of disease burden, moreover, a trend toward improved outcomes with lower disease burden was observed in the InO group

Peripheral blast counts

CR/CRi rates decreased as peripheral blast counts increased

- Among patients in the InO and SOC arms, the CR/CRi rates were 87.3% versus 45.9% in those with peripheral blast counts 0/μL, 59.5% and 18.2% in those with counts > 0/μL and 1000/μL, and 65.5% and 19.5% in those with counts >1000 μ

Age

CR/CRi rates are not affected by age

- In INO-VATE, the CR/CRi rates with InO were similar in patients aged ≥55 years and <55 years (80.3% [95% CI, 68.7%, 89.1%]and 81.4% [95% CI, 66.6%, 91.6%], respectively). Among the older adults, a higher proportion of patients achieved CRi versus CR [19]**. In pediatric patients with R/R ALL who received InO, no baseline patient or disease characteristics (age, sex, cytogenetic subtype) were identified as a considerable prognostic indicator for response.**

Cytogenetics

Higher CD22-positivity correlates with better outcomes. KMT2A is related to worse outcomes in adults and pediatrics

- The CR/CRi and MRD negativity rates in the InO group of INO-VATE were generally similar among the diploid group with ≥ 20metaphases, complex karyotype, and Ph+.
- InO resulted in betteroutcomes versus SOC regardless of the patient's CD22 positivity, but outcomes were further improved in patients with ≥ 90%leukemic blast CD22 positivity versus those with < 90% blastCD22 positivity

Marks DI, et al. Expert Rev Hematol. 2025 Jan;18(1):91-103

Factors Affecting Survival Outcomes

Salvage status

Patients in earlier lines benefit more from InO treatment

An updated analysis of INO-VATE showed improved PFS and OS in InO versus SOC in S1 and S2. The patients in the InO arm in S1 showed more pronounced improvements in long-term survival and PFS. Median OS: 8.6 vs 6.9 months in S1, and 7.0 vs 5.2 months. mPFS: 5.4 vs 1.8 months with SOC in S1, and 3.9 vs 1.4 months with SOC in S2

Disease burden

Patients in the InO versus SOC arm had considerably improved PFS and OS irrespective of disease burden (significantly higher in all subgroups).

The probability of 24-month PFS in the InO arm appeared to decline with greater disease burden (19.6% with BMB < 50%, 10.6% with BMB 50–90%, and 6.5% with BMB > 90%) and was either zero or not estimable in all subgroups in the SOC arm. The probability of 24-month OS was higher in patients treated with InO versus SOC (30.0 vs 2.4 months with BMB < 50%, 21.1 vs 15.0 months with BMB 50–90%, and 13.3 vs 8.1 months with BMB > 90%). Moreover, a trend toward improved outcomes with lower disease burden was observed in the InO group.

MRD-negativity

Patients who achieve MRD-negativity have a higher probability of survival

A greater probability of PFS and OS was also seen in patients treated with InO who achieved MRD− versus MRD+: unstratified HR for PFS = 0.423 (97.5% CI, 0.256, 0.699), $p < 0.0001$, unstratified HR for OS = 0.512 (97.5% CI, 0.313, 0.835), $p = 0.0009$

Age

Younger adults have a greater possibility of survival. Pediatric data shows comparable possibility of survival.

- OS was significantly longer for younger versus older adults (8.6 months [95% CI, 7.0, 11.1] in the < 55-year-old subgroup vs 5.6 [95% CI, 4.8, 8.0] in the ≥ 55-year-old subgroup, $p = 0.0032$). Patients who received InO and achieved CR/CRi with follow-up HSCT had longer OS than patients without follow-up HSCT (median OS 12.6 months [95% CI, 9.3, 27.7] vs 7.1 [95% CI, 5.6, 10.8])
- The possibility of survival for pediatric patients reported from several phase I & II trials is between 40% to 65% (1-year) and 36% (2-year OS).

Cytogenetics

Higher CD22-positivity correlates with better outcomes in terms of overall survival

- Patients in INO-VATE treated with InO in the diploid group with ≥ 20 metaphases had a higher mPFS (6.0 months) when compared with the complex karyotype group (4.6 months), Ph+ (3.9 months), and other abnormalities subgroups (5.3 months). There was no significant difference in median OS between the Ph+ subgroup (8.7 months) compared with diploid with ≥ 20 metaphases, complex subgroups, and other cytogenetic abnormality groups ($p \geq 0.1629$).

Marks DI, et al. Expert Rev Hematol. 2025 Jan;18(1):91-103

Post-HSCT VOD/SOS: Risk Factors- Multivariate Analysis*: Factors affecting risk of VOD/SOS in adult patients

Multivariate analysis (n=62)	P-value	OR (95% CI)
Dual alkylator conditioning (dual [n=11] vs single [n=51])	0.015	8.606 (1.516–48.861)
Pre-HSCT bilirubin level (≥ULN vs <ULN)	0.009	15.308 (1.950–120.206)
Pre-HSCT AST or ALT level (>1.5 × ULN vs ≤1.5 × ULN)	0.039	0.027 (<0.001–0.833)
Prior history of liver disease (yes vs no)	0.064	5.133 (0.907–29.060)

In a Phase II trial in pediatric patients (slide 19), thee was a corelation between the timing of HSCT and the last dose of InO and the probability of SOS/VOD (the shorter the interval, the higher the risk.

*Data cut off: 8 March 2016

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; HSCT, haematopoietic stem cell transplantation; OR, odds ratio; ULN, upper limit of normal; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome

Kantarjian HM *et al. Lancet Haematol* 2017;4:e387–e398

VOD/SOS Monitoring and Considerations

- Monitor closely for signs and symptoms of VOD; these may include elevations in total bilirubin, hepatomegaly (which may be painful), rapid weight gain, and ascites
- Monitor liver tests, including ALT, AST, total bilirubin, and ALP, prior to and following each dose of inotuzumab ozogamicin
- Permanently discontinue treatment if VOD (any grade) occurs

Treatment considerations for patients proceeding to HSCT	
Avoid dual alkylating agents	Avoid the use of HSCT conditioning regimens containing dual alkylating agents.
Monitor total bilirubin	Total bilirubin ≥ULN prior to HSCT was significantly associated with an increased risk of VOD. During the first month post HSCT, monitor liver tests closely, then less frequently thereafter according to standard medical practice
Limit number of cycles	Limit treatment with inotuzumab ozogamicin to 2 cycles. A third cycle may be considered for those patients who do not achieve CR or Cri and MRD negativity after 2 cycles

Reference: BESPONSA Prescribing Information. New York, NY: Pfizer Inc.

Discussion: Other Important Factors

- In recent years, the repertoire of novel therapeutic agents for the treatment of patients with R/R ALL has expanded rapidly. However, treatment decisions in the R/R setting can be affected by multiple factors, including prior treatment, disease characteristics (e.g. age, CD19/CD22 positivity, disease burden, genetic subgroup), patient characteristics (i.e. comorbidities, preference), toxicity, and eligibility for allogenic HSCT or CAR T-cell therapy.

- Combination therapy: Another area of interest, and for which limited data exist, is the utility of combining InO with chemotherapy. Research groups are assessing the combination of InO with chemotherapy and immunotherapy, and trials are ongoing. Currently, blinatumomab is being evaluated for first-line treatment of ALL in the ECOG-ACRIN E1910 study

- Hospitalization: The experts also considered that the intermittent intravenous delivery route of InO may be more suitable for patients who preferred outpatient treatment, including those who want less time-consuming therapy and those who do not want pump change or continuous infusion therapy, which may include elderly patients. Beyond a period of inpatient observation for immediate complications of treatment that can be seen with any intervention for acute leukemia (e.g. tumor lysis syndrome), there is nothing inherent about the administration of InO that requires hospitalization.

- **Pediatric population: There have been fewer clinical trials investigating the efficacy and safety of InO in R/R ALL pediatric populations than in adult populations. The outcomes from most adult trials cannot automatically be transferred to the pediatric population because of differences in disease biology and prognosis.**

Marks DI, et al. Expert Rev Hematol. 2025 Jan;18(1):91-103

Before administration of InO

- When considering the use of InO as a treatment for R/R ALL, baseline CD22-positivity of >0% using a validated and sensitive assay is required prior to initiating treatment
- For patients with circulating lymphoblasts, cytoreduction to a peripheral blast count ≤10,000/mm^3 is recommended prior to the first dose
- Pre-medication with a corticosteroid, antipyretic and antihistamine is recommended prior to dosing to minimise the risk of infusion reactions
  - For patients with a high tumour burden, hydration and pre-medication to reduce uric acid levels are recommended prior to dosing
- Patients should be observed during and for at least 1 hour after the end of the infusion for symptoms of infusion-related reactions

ALL, acute lymphoblastic leukaemia; InO, inotuzumab ozogamicin; R/R, relapsed/refractory

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2018

Adverse Event Management

Myelosuppression/ cytopenias

Characterization

- In patients receiving InO, neutropenia, thrombocytopenia, anaemia, leukopenia, febrile neutropenia, lymphopenia and pancytopenia (some of which were life-threatening) have been reported
- Complications associated with neutropenia and thrombocytopenia (including infections and bleeding/haemorrhagic events, respectively) were reported in some patients

Management

- Complete blood counts should be monitored prior to each dose of InO and signs and symptoms of infection during treatment and after HSCT; bleeding/haemorrhage and other effects of myelosuppression should be monitored during treatment[1]
- As appropriate, prophylactic anti-infectives should be administered and surveillance testing should be employed during and after treatment[1]
    - Consider using GCSF as a management technique for myelosuppression/cytopenias[2]
- Management of severe infection, bleeding/haemorrhage and other effects of myelosuppression, including severe neutropenia or thrombocytopenia, may require dosing interruption, dose reduction or discontinuation of InO[1]
- Platelet transfusion remains a common intervention in the management of thrombocytopenia in patients with leukaemia[3]

Pancytopenia includes the following reported preferred terms: Bone marrow failure, Febrile bone marrow aplasia, and Pancytopenia
GCSF, granulocyte-colony stimulating factor; HSCT, haematopoietic stem cell transplantation; InO, inotuzumab ozogamicin.
InO, inotuzumab ozogamicin
BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2018
2. Kebriaei P *et al. Bone Marrow Transplant* 2018;53:449-456; 3. Castaman G and Pieri L. *Thromb Res* 2018;164 Suppl 1:S89-S93

Infection

Management

- Complete blood counts should be monitored prior to each dose of InO, and signs and symptoms of infection should be monitored during treatment
- As appropriate, prophylactic anti-infectives should be administered and surveillance testing should be employed during and after treatment
- Management of severe infection may require a dosing interruption, dose reduction or discontinuation of InO

*Fatal infections included pneumonia, neutropenic sepsis, sepsis, septic shock and *Pseudomonas* sepsis
InO, inotuzumab ozogamicin
BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2018

Bleeding events

Management

- Complete blood counts should be monitored prior to each dose of InO, and signs and symptoms of bleeding/haemorrhage should be monitoring during treatment
- Management of bleeding/haemorrhage may require a dose reduction or discontinuation of InO

*The most common bleeding event was epistaxis, which was reported in 15% of patients
InO, inotuzumab ozogamicin
BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2018

Hepatotoxicity

Monitoring

- In all patients, liver tests, including ALT, AST, total bilirubin and ALP, should be monitored prior to and after each dose of InO
- For patients who develop abnormal liver tests, liver test and clinical signs and symptoms of hepatotoxicity should be monitored more frequently
- For patients who proceed to HSCT, liver tests should be monitored closely during the first month post-HSCT, then less frequently thereafter, according to standard medical practice

Dose Modification

- No adjustment to the starting dose is required in patients with hepatic impairment defined by total bilirubin ≤1.5 × ULN and AST/ALT ≤2.5 × ULN
- Interrupt dosing until recovery of total bilirubin to ≤1.5 x ULN and AST/ALT to ≤2.5 × ULN prior to each dose unless due to Gilbert's syndrome or haemolysis
- Permanently discontinue treatment if total bilirubin does not recover to ≤1.5 × ULN or AST/ALT does not recover to ≤2.5 × ULN

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HSCT, haematopoietic stem cell transplantation; InO, inotuzumab ozogamicin; ULN, upper limit of normal

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2018

Prevention and management of VOD/SOS with InO (1)

In all patients

- Monitor liver tests, including ALT, ALP, AST and total bilirubin, prior to and after each dose of InO
  - For patients who develop abnormal liver tests, more frequent monitoring of LFTs and clinical signs and symptoms of hepatotoxicity is recommended
  - Elevation of liver tests may require dosing interruption, dose reduction or permanent discontinuation of InO
  - Daily monitoring of patient's weight

Patients proceeding to HSCT

Monitor LFTs closely during the first month post-HSCT, then less frequently thereafter, according to standard medical practice

Permanently discontinue treatment if VOD/SOS occurs.
If severe VOD/SOS occurs, treat according to standard medical practice

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; HSCT, haematopoietic stem cell transplantation; InO, inotuzumab ozogamicin; LFT, liver function test; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

Prevention and management of VOD/SOS with InO (2)

Alkylating agents

↓

Avoid the use of HSCT conditioning regimens containing two alkylating agents

↓

Carefully consider the benefit–risk before administering InO to patients in whom the future use of HSCT conditioning regimens containing two alkylating agents is likely unavoidable

Serum bilirubin ≥ULN prior to HSCT

↓

Only proceed to HSCT post InO treatment after careful consideration of the benefit–risk

↓

If these patients do proceed to HSCT, monitor closely for signs and symptoms of VOD/SOS

HSCT, haematopoietic stem cell transplantation; InO, inotuzumab ozogamicin; ULN, upper limit of normal; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

Prevention and management of VOD/SOS with InO (5)

Pharmacological prophylaxis of VOD/SOS[1,2]

- Regarding VOD-preventative drug regimens, the BCSH/BSBMT guidelines suggest defibrotide as a potential preventative option in adults and children undergoing allogeneic stem cell transplant, which has a stronger grade of evidence in children. Defibrotide is not currently FDA-approved for prophylaxis of VOD in adults or children.
- The guidelines also suggest ursodeoxycholic acid as an option for VOD prevention, albeit with a weak recommendation due to a low quality of evidence to support this.
- The guidelines recommended against use of prostaglandin E1, pentoxifylline, heparin (unfractionated and low molecular weight), and anti-thrombin for VOD prophylaxis due to lack of efficacy and increased toxicity
- **Treatment of VOD/SOS[3]**
- Defibrotide is indicated for the treatment of severe hepatic VOD, also known as SOS, in HSCT therapy[4]
- Fluid and sodium balance and careful use of diuretics should be introduced at the first suspicion, when VOD/SOS is still only probable
- Several symptomatic measures can be used to reduce the discomfort produced by massive ascites or pleural effusions
- When fluid accumulation and renal failure cannot be controlled, haemodialysis/haemofiltration can be required
- Severe VOD/SOS treatment may require transfer into an intensive care unit
- In extreme cases, a transjugular intrahepatic portosystemic shunt can be discussed for patients with less advanced VOD/SOS

BCSH, British Committee for Standards in Haematology; BSBMT, British Society of Blood and Marrow Transplantation; FDA, Food and Drug Administration; HSCT, haematopoietic stem cell transplantation; InO, inotuzumab ozogamicin; SOS, sinusoidal obstruction syndrome; VOD, veno-occlusive disease

1. Cheuk DK. *World J Transplant* 2012;2:27–34; 2. Fan CQ, Crawford JM. *J Clin Exp Hep* 2014;4:332–346; 3. Mohty M *et al. Bone Marrow Transplant* 2015;781–789; 4. Defitelio (defibrotide sodium) Prescribing Information, 2016

Infusion-related reactions

Characterisation with InO

- Infusion-related reactions were reported in 17/164 (10%) of patients
  - All events were Grade ≤2 in severity
  - They generally occurred in Cycle 1 and shortly after the end of the InO infusion
  - They resolved spontaneously or with medical management

Before Treatment

- InO is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients (sucrose, polysorbate 80, sodium chloride, tromethamine)
- Pre-medication with a corticosteroid, antipyretic and antihistamine is recommended prior to dosing

During Treatment

- Patients should be monitored closely during and for at least 1 hour after the end of the infusion for the potential onset of infusion-related reactions, including symptoms such as hypotension, hot flush or breathing problems
- If an infusion-related reaction occurs, the infusion should be interrupted and appropriate medical management should be instituted
- Depending on the severity of the infusion-related reaction, discontinuation of the infusion or administration of steroids and antihistamines should be considered
- For severe or life-threatening infusion-related reactions, treatment should be permanently discontinued

InO, inotuzumab ozogamicin

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

Increased amylase and lipase

Management

- Patients should be monitored for increases in amylase and lipase
- Potential hepatobiliary disease should be evaluated and treated according to standard medical practice

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

Tumour lysis syndrome (1)

Characterisation

- Tumour lysis syndrome, which may be life-threatening or fatal, was reported in 4/164 (2%) of adult patients
  - Grade 3–4 tumour lysis syndrome was reported in 3/164 (2%) patients
  - Tumour lysis syndrome occurred shortly after the end of the InO infusion and resolved with medical management

Management

- Hydration and pre-medication to reduce uric acid levels is recommended prior to InO dosing for patients with a high tumour burden
- Patients should be monitored for signs and symptoms of tumour lysis syndrome and treated according to standard medical practice

InO, inotuzumab ozogamicin

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

QT interval prolongation

Management

- InO should be administered with caution in patients who have a history of or predisposition to QT interval prolongation, who are taking medicinal products that are known to prolong QT interval and in patients with electrolyte disturbances
- ECG and electrolytes should be obtained prior to the start of treatment and periodically monitored during treatment

ECG, electrocardiogram; InO, inotuzumab ozogamicin

BESPONSA (inotuzumab ozogamicin) summary of product characteristics, 2024

Dosage Modifications for Hematologic Toxicities

Criteria	Dosage Modification
If prior to BESPONSA treatment ANC was greater than or equal to 1 × 109/L	If ANC decreases, then interrupt the next cycle of treatment until recovery of ANC to greater than or equal to 1 × 109/L. Discontinue BESPONSA if low ANC persists for greater than 28 days and is suspected to be related to BESPONSA.
If prior to BESPONSA treatment platelet count was greater than or equal to 50 × 109/L*	If platelet count decreases, then interrupt the next cycle of treatment until platelet count recovers to greater than or equal to 50 × 109/L*. Discontinue BESPONSA if low platelet count persists for greater than 28 days and is suspected to be related to BESPONSA.
If prior to BESPONSA treatment ANC was less than 1 × 109/L and/or platelet count was less than 50 × 109/L*	If ANC or platelet count decreases, then interrupt the next cycle of treatment until at least one of the following occurs: ANC and platelet counts recover to at least baseline levels for the prior cycle, or - ANC recovers to greater than or equal to 1 × 109/L and platelet count recovers to greater than or equal to 50 × 109/L*, or - Stable or improved disease (based on most recent bone marrow assessment) and the ANC and platelet count decrease is considered to be due to the underlying disease (not considered to be BESPONSA-related toxicity).

Abbreviation: ANC=absolute neutrophil count
Platelet count used for dosing should be independent of blood transfusion.
Reference: BESPONSA prescribing information. Revised: 3/2024.

Dosage Modifications for Non-hematologic Toxicitie

Non-hematologic Toxicity	Dosage Modification(s)
VOD or other severe liver toxicity	Permanently discontinue treatment
Total bilirubin greater than 1.5 × ULN and AST/ALT greater than 2.5 × ULN	Interrupt dosing until recovery of total bilirubin to less than or equal to 1.5 × ULN and AST/ALT to less than or equal to 2.5 × ULN prior to each dose unless due to Gilbert's syndrome or hemolysis. Permanently discontinue treatment if total bilirubin does not recover to less than or equal to 1.5 × ULN or AST/ALT does not recover to less than or equal to 2.5 × ULN
Infusion related reaction	Interrupt the infusion and institute appropriate medical management. Depending on the severity of the infusion related reaction, consider discontinuation of the infusion or administration of steroids and antihistamines. For severe or life-threatening infusion reactions, permanently discontinue treatment
Non-hematologic toxicity greater than or equal to Grade 2*	Interrupt treatment until recovery to Grade 1 or pre-treatment grade levels prior to each dose.

Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal; VOD=veno-occlusive disease.
*Severity grade according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 3.0.
Reference: BESPONSA prescribing information. Revised: 3/2024.

Dosage Modifications Depending on Duration of Dosing Interruption Due to Non-Hematologic Toxicities

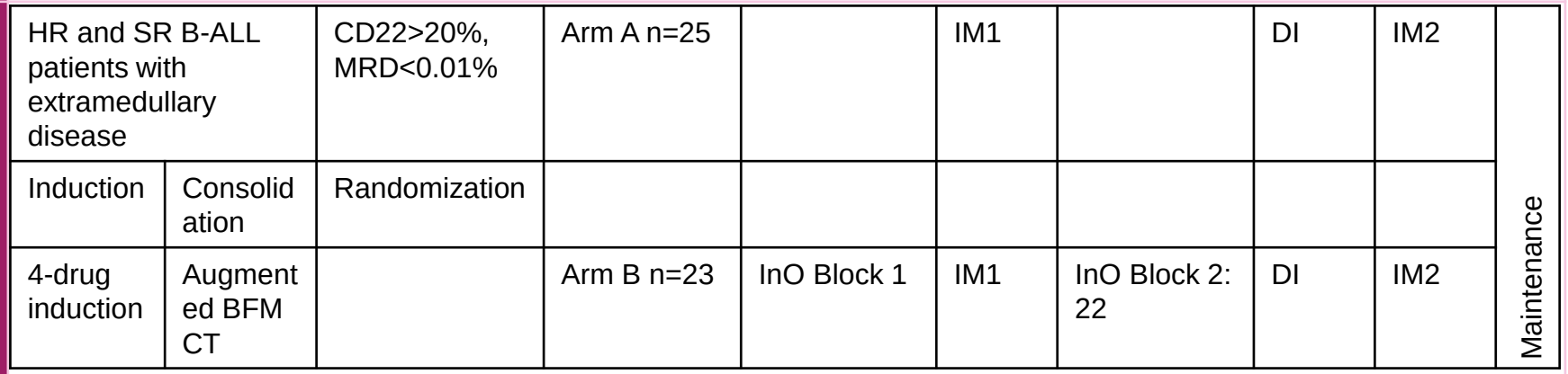
Interruption Due to Toxicity	Dosage Modification(s)
Less than 7 days (within a cycle)	Interrupt the next dose (maintain a minimum of 6 days between doses).
Greater than or equal to 7 days	Omit the next dose within the cycle.
Greater than or equal to 14 days	Once adequate recovery is achieved, decrease the total dose by 25% for the subsequent cycle. If further dose modification is required, then reduce the number of doses to 2 per cycle for subsequent cycles. If a 25% decrease in the total dose followed by a decrease to 2 doses per cycle is not tolerated, then permanently discontinue treatment.
Greater than 28 days	Consider permanent discontinuation of treatment.

Reference: BESPONSA prescribing information. Revised: 3/2024.

InO in Ongoing Clinical Trials in Pediatric Acute Lymphoblastic Leukemia

Monotherapy/Combination	Line of treatment	Phase	Age at enrollment	Trial number
Monotherapy	1st relapse HR ALL	II with randomization	≥1 year <18 years	NCT05748171
InO + chemotherapy (after consolidation and before maintenance)	Front-line ALL, MRD <0.01% by the end of consolidation	III	≥1 year ≤24 years	COG AALL1732 NCT03959085
Monotherapy	Front-line ALL	III	≤45 years	ALL Together NCT04307576
Monotherapy	Post-HSCT (prophylactic)	I/II	≥16 years	NCT03104491
Monotherapy	Post-HSCT (MRD positivity)	II	≥15 years	NCT05940961
Monotherapy	R/R MRD positive	II	≤21 years	St. Jude NCT03913559
InO + blinatumomab+ rituximab	R/R ALL	II	≥1 year ≤25 years	MD Anderson NCT05645718
InO + blinatumomab+ hyper-CVAD + rituximab or ofatumumab	Front-line ALL	II	≥14 years	MD Anderson NCT02877303

Ongoing Phase 3 Trial

Trial Name	Children's Oncology Group AALL1732 trial
Setting	High Risk Newly Diagnosed B-ALL
Age Groups	Children & Young Adults (1-24 years)
Schematic Presentation (Safety Phase Results Are Reported): The primary objective of the safety phases was to assess the first 50 randomized patients for chemotherapy delays, and for hepatic and infectious toxicity. The first safety phase reported SOS in 3 of 23 patients in the InO arm versus in 1 of 25 patients in the no-InO arm, while the second safety phase reported SOS in 4 of 25 InO patients. This led to 1 20% decrease in InO dose.	 B-ALL=B-Acute Lymphoblastic Leukemia; BFM=Berlin-Frankfurt-Munster; DI=delayed intensification; HR=high risk; IM=interim maintenance; InO=inotuzumab ozogamicin; MRD=minimal residual disease; SR=standard risk.
Primary Objective (Efficacy Phase is Ongoing)	5-year disease-free survival (DFS)

McNeer JL, et al. *Blood* 2021;138(Suppl 1):3398.

Preparation and Administration

- Protect the reconstituted and diluted BESPONSA solutions from light. Do not freeze the reconstituted or diluted solution.
- The maximum time from reconstitution through the end of administration should be less than or equal to 8 hours, with less than or equal to 4 hours between reconstitution and dilution.

Reconstitution:

- BESPONSA is a hazardous drug. Follow applicable special handling and disposal procedures.
- Calculate the dose (mg) and number of vial(s) of BESPONSA required.
- Reconstitute each vial with 4 mL of Sterile Water for Injection, USP, to obtain a concentration of 0.25 mg/mL of BESPONSA that delivers 3.6 mL (0.9 mg).
- Gently swirl the vial to aid dissolution. DO NOT SHAKE.
- Inspect the reconstituted solution for particulates and discoloration. The reconstituted solution should be clear to opalescent, colorless to slightly yellow, and essentially free of visible foreign matter.

Dilution:

- Withdraw the required volume of the reconstituted solution from the vial(s) needed to obtain the appropriate dose according to the patient's body surface area. Discard any unused reconstituted BESPONSA solution left in the vial.

Dilute the reconstituted BESPONSA solution in 0.9% Sodium Chloride Injection, USP, in the appropriate infusion container.

Reference: BESPONSA prescribing information. Revised: 3/2024.

Administering Inotuzumab Ozogamicin

Administration Requirenment	
Mode of administration	IV infusion
Infusion time	1 hour
Flow rate	50 mL/h
Temperature	Room temperature (20-25°C)
Special instructions	• Protect from light • Do not mix or administer InO as an infusion with other medicinal products Monitor patients closely during and for at least 1 hour after the end of the infusion for the potential onset of infusion-related reactions, including symptoms such as fever, chills, rash, or breathing problems.1 1 HR Administering Inotuzumab Ozogamicin InO is administered by IV infusion over 1 hour

Reference: BESPONSA prescribing information. Revised: 3/2024.

THANK YOU