POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

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Bologna
Palazzo Re Enzo
13-15 Febbraio 2025

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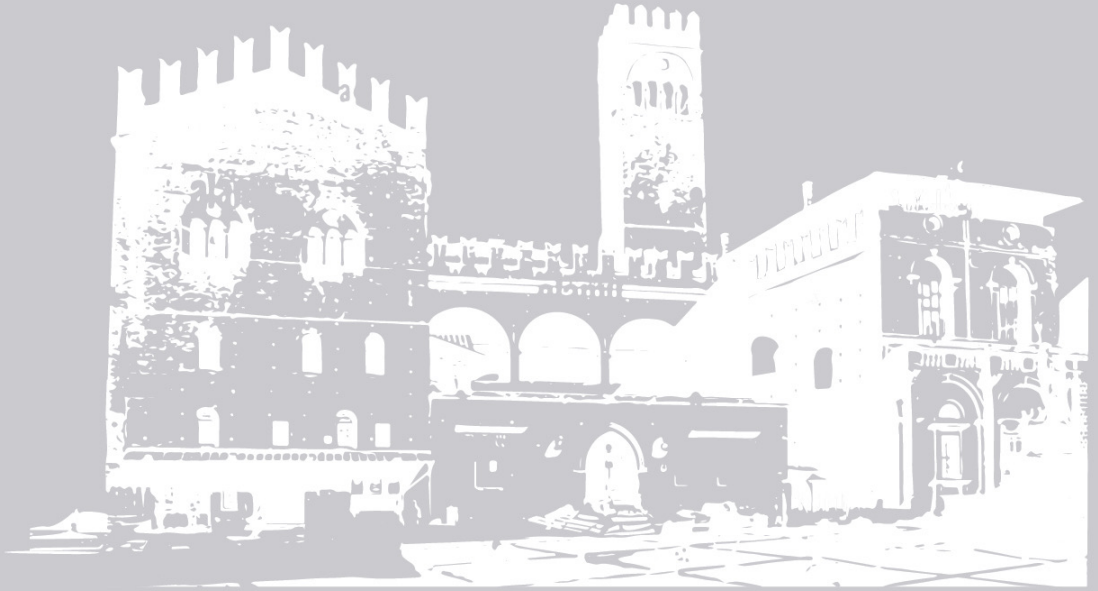


SAPIENZA
UNIVERSITÀ DI ROMA

Anticorpi monoclonali e CAR-T

Sabina Chiaretti

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Gilead						x	
Abbvie					x		
Amgen							
Incyte						x	

Topics

Blinatumomab in Ph+ ALL

Blinatumomab in pediatric Ph-ALL

A bit of biology…

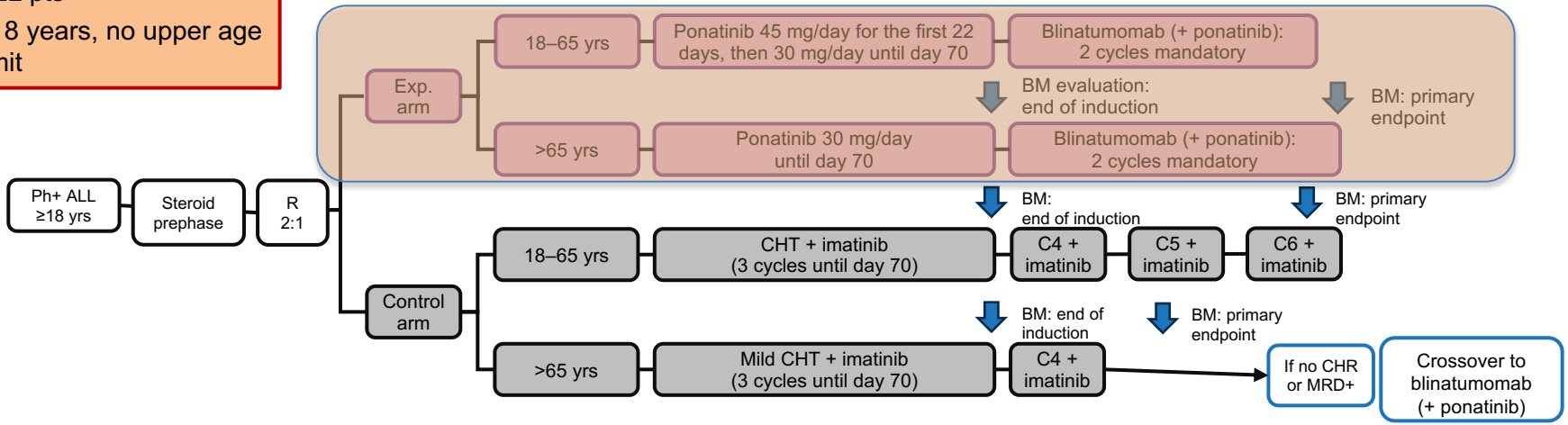
Inotuzumab

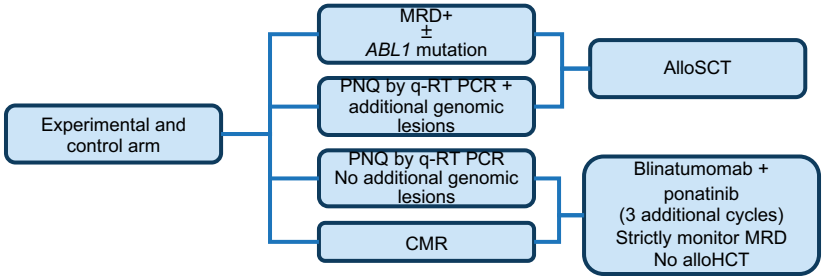
CAR-T

GIMEMA ALL2820 trial

Newly diagnosed Ph+ ALL pts

≥18 years, no upper age limit





- Ponatinib in place of dasatinib
- CNS prophylaxis increased
- Allo-SCT allocation according to molecular features
- Sample size 236. Enrolled 225
- 151 evaluable so far

Chiaretti et al, abs 835, ASH 2024

Experimental arm: patients' features and disposition

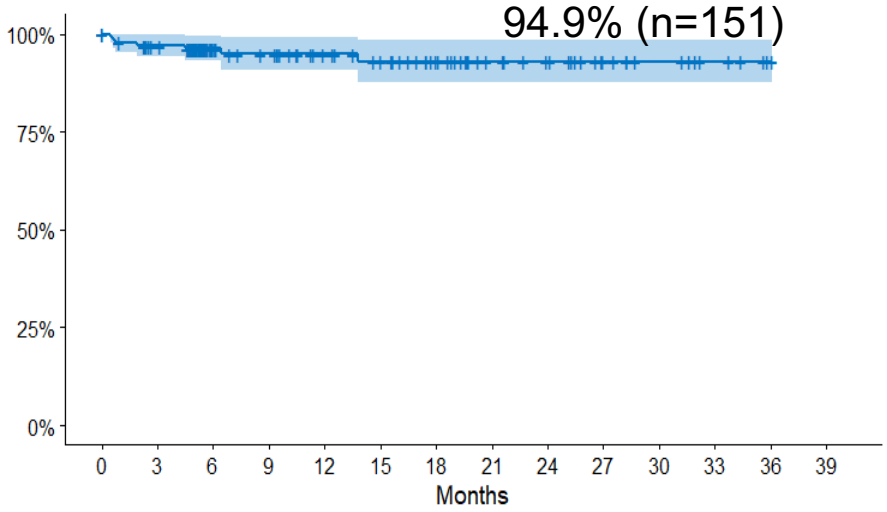
	N=151
Age, median (range)	57 (19-84)
≤65 years	110 (73)
>65 years	41 (27)
Gender: M/F (%)	75/76 (50/50)
WBC, median (range)	11 (1-244)
p190 (%)	105 (70)
p210, p190/210 (%)	40 (26), 6 (4)
IKZF1^{plus} (%)	45 (32)

End of induction (d +70)	n=137
CHR	131 (96%)
Deaths	4 (3%)
Off treatment	2 (1%)

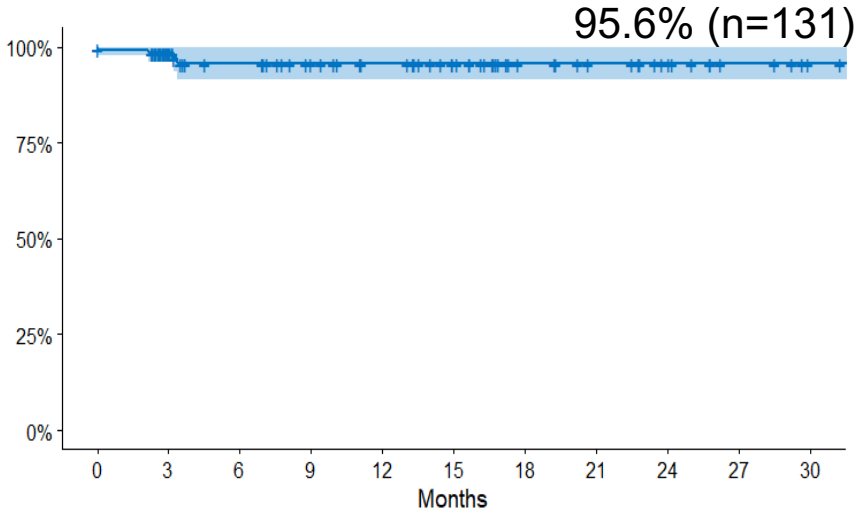
	No molecular responses (%)	CMR	PNQ	Overall molecular responses (%)
End of induction (d +70)	71/131 (54)	40/131	20/131	60/131 **(46)**
After 2 cycles of blinatumomab	30/117 (26)	59/117	27/117	86/117 **(74)**

Estimated 12-months OS and DFS

OS

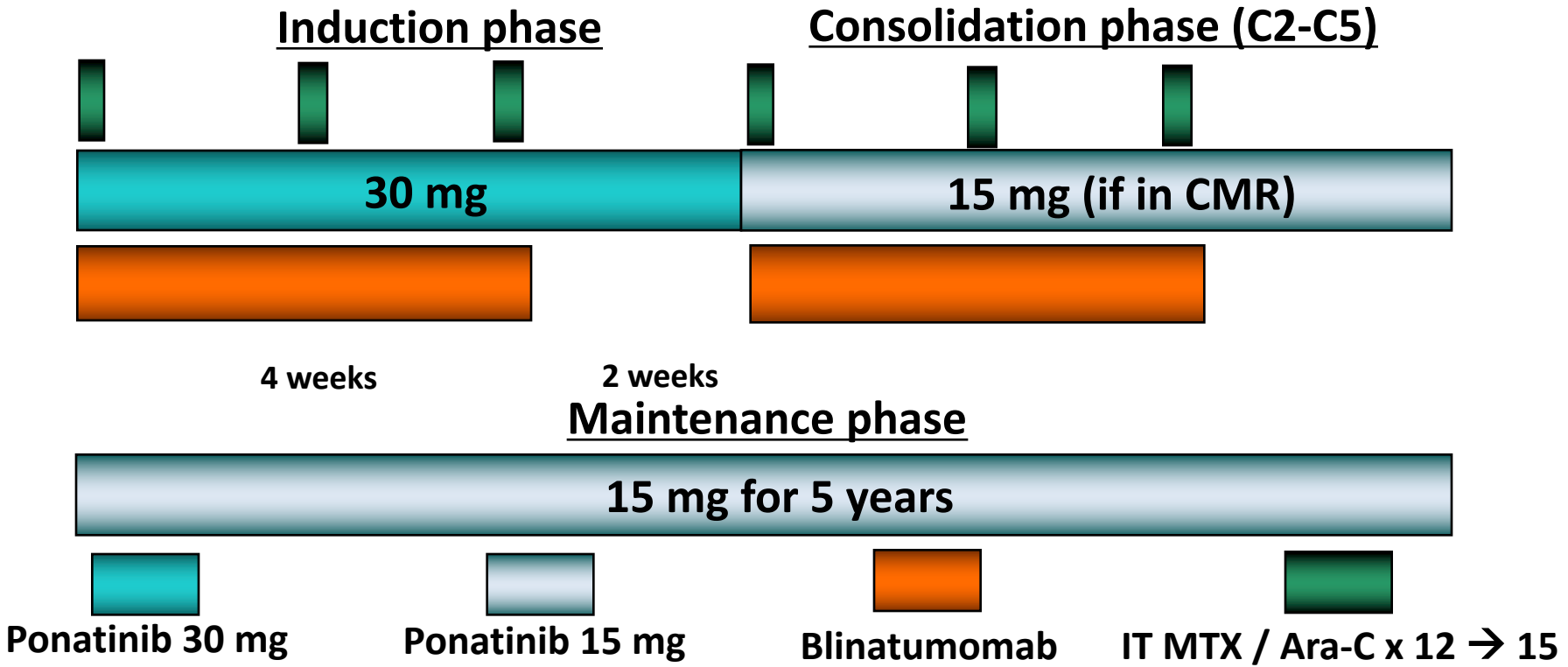


DFS



Median follow-up: 8.5 months (0.1 - 36.1)

Ponatinib + Blinatumomab in Ph+ ALL: Regimen



Short et al, abs 837, ASH 2024

Ponatinib + Blinatumomab in Ph+ ALL: responses

Response, n/N (%)	N = 76
CR/CRi*	52/53 (98)
CR	51/53 (96)
CRi	1/53 (2)
Early death	1/53 (2)
MMR**	64/66 (97)
CMR**	57/69 (83)
After 1 cycle	41/69 (59)
NGS MRD negative	55/57 (96)
After 1 cycle	17/36 (47)

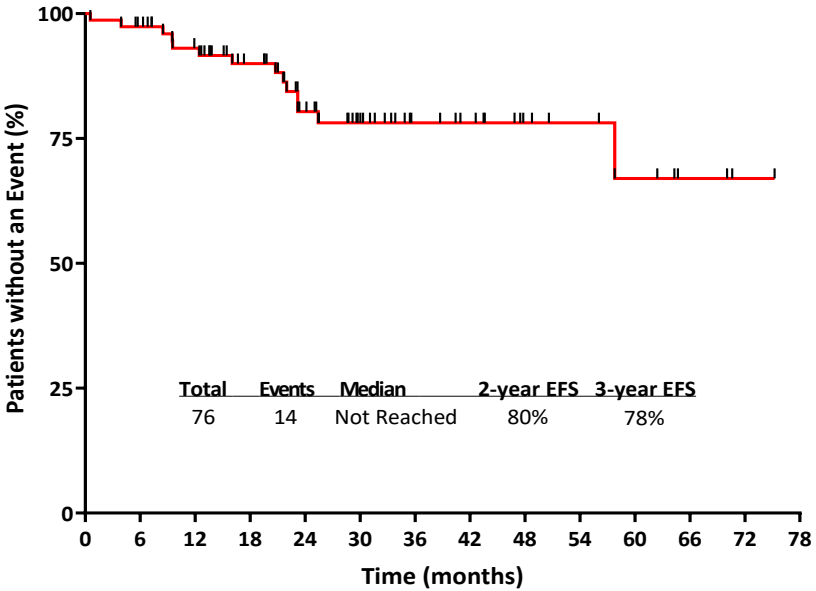
* 23 pts in CR at start

** 10 pts were in MMR, 7 were in CMR, and 2 were NGS MRD negative at start

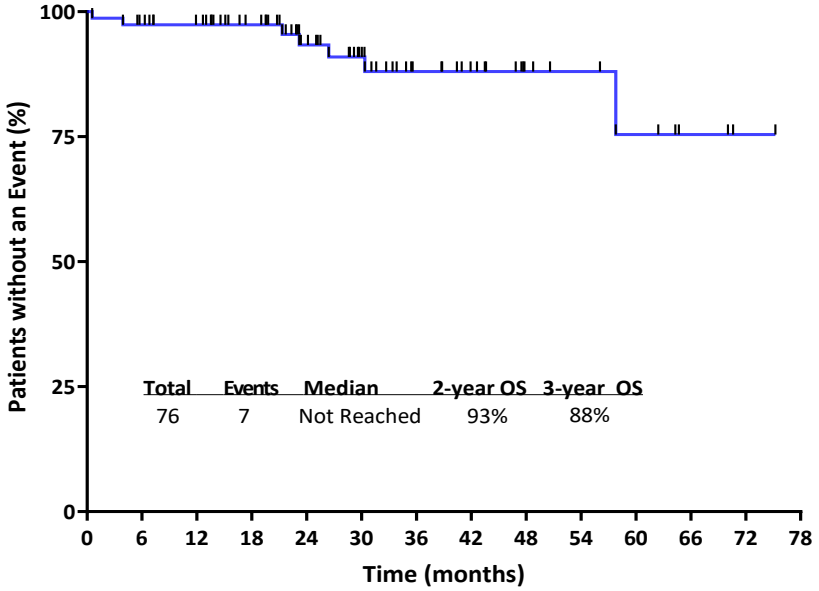
8/8 of tested pts not achieving CMR were NGS MRD negative

Ponatinib + Blinatumomab in Ph+ ALL: survival

Event-Free Survival

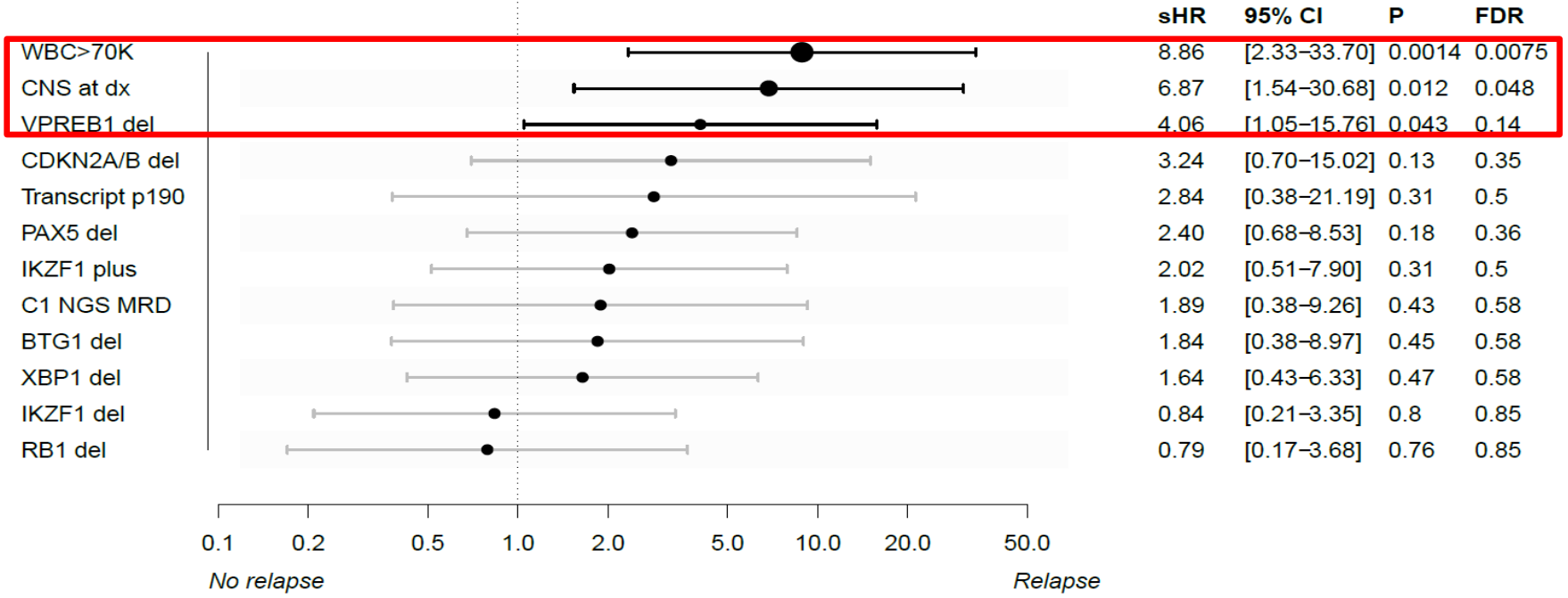


Overall Survival



Median follow-up: 29 months (range, 5-75 months)

Ponatinib + Blinatumomab in Ph+ ALL: UVA for Relapse Risk



Short et al, abs 837, ASH 2024

AALL1731: study design

NCI Standard Risk (SR) B-ALL
At diagnosis:
Age 1-<10 years
WBC <50,000/µL

NCI SR B-ALL

3-drug induction

Excluded:
Central nervous system leukemia (CNS3)
Testicular leukemia
Steroid pre-treatment
BCR::ABL1+ ALL

SR-Favorable

Favorable genetics
and
Day 8 blood MRD <1%
and
End of induction marrow
MRD <0.01%

SR-Average

SR-High

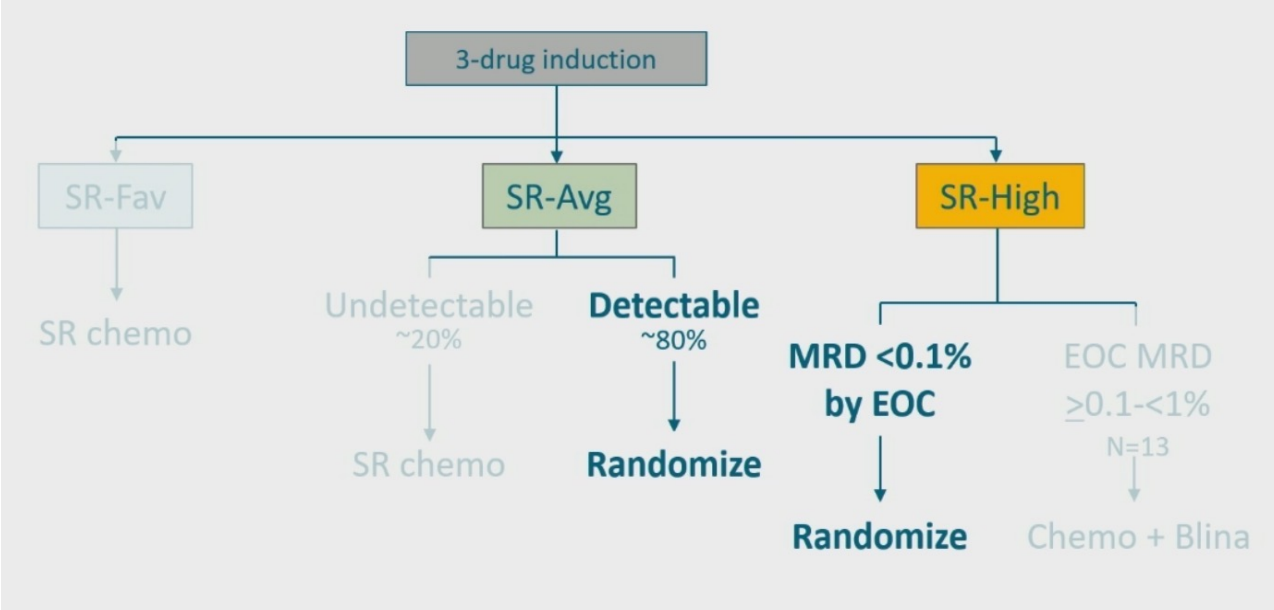
Unfavorable genetics
or
Neutral genetics and CNS2
or
End of induction marrow
MRD ≥0.01% (≥0.1% DT)

MRD = minimal residual disease

CHILDREN'S ONCOLOGY GROUP

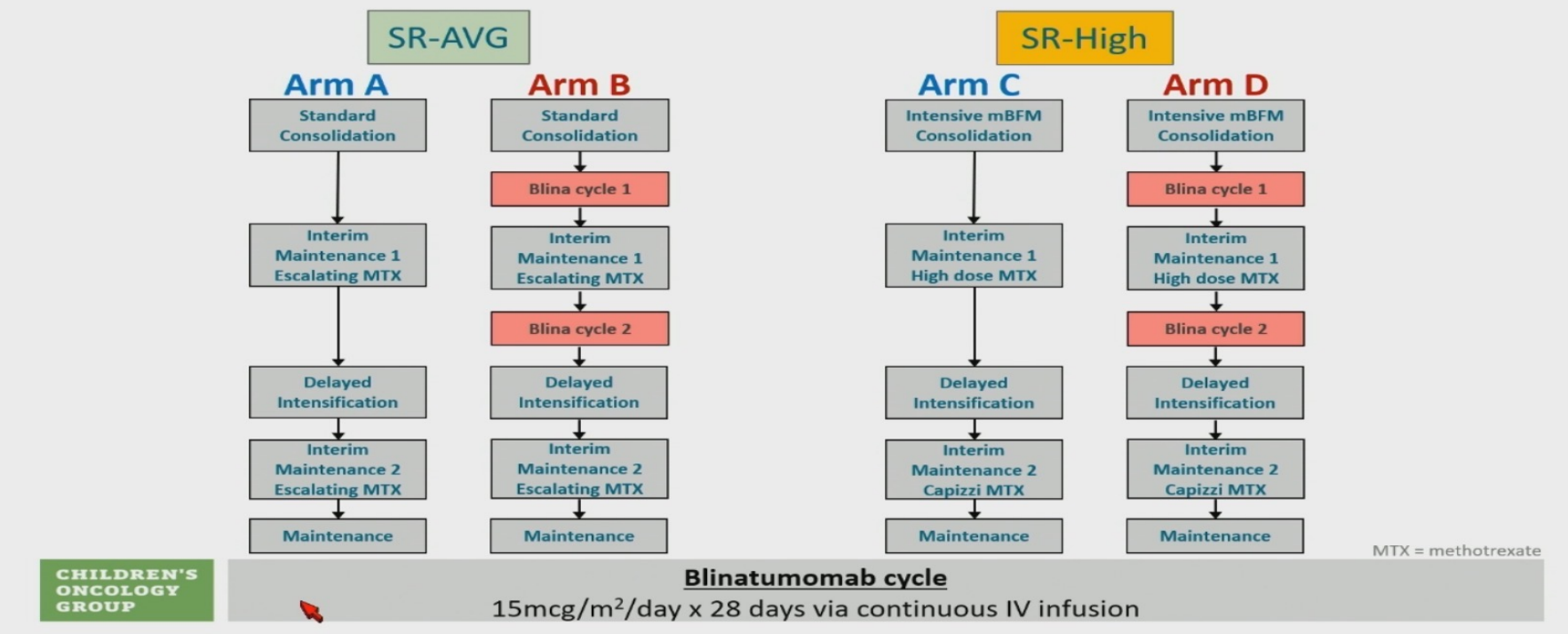
Favorable genetics = ETV6::RUNX1 or double trisomies chr 4 and 10 (DT)
Unfavorable genetics = iAMP21, KMT2Ar, hypodiploidy (<44chr), t(17;19)
Neutral genetics = no favorable or unfavorable lesions present

AALL1731: randomization and patients' features

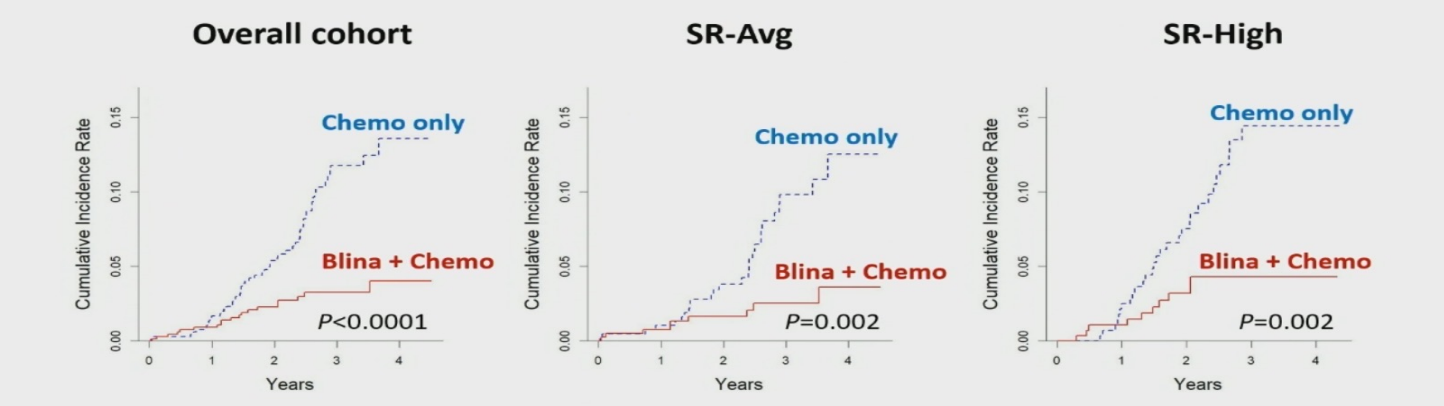


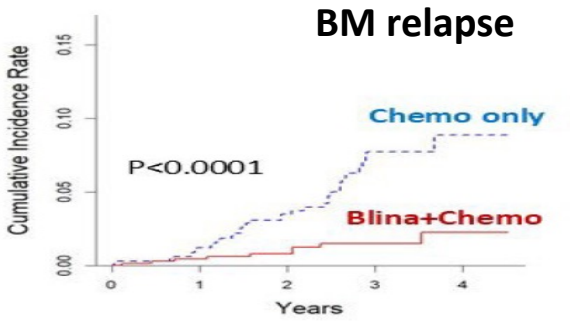
Characteristic	SR-AVG		SR-High	
	Chemo Only (N=418)	Blina + Chemo (N=417)	Chemo Only (N=304)	Blina + Chemo (N=301)
Median age (range) - years	4.3 (1.0-10.0)	4.0 (1.0-9.9)	4.2 (1.1-9.9)	4.6 (1.0-10.0)
Median WBC - x10^9/L	7.5 (0.0-49.7)	7.7 (0.3-49.7)	7.4 (0.6-49.8)	8.8 (0.4-47.8)
Sex – N (%)				
Female	195 (46.7%)	207 (49.6%)	137 (45.1%)	143 (47.5%)
Male	223 (53.3%)	210 (50.4%)	167 (54.9%)	158 (52.5%)
Race/ethnicity – N (%)				
Hispanic	104 (24.9%)	100 (24.0%)	84 (27.6%)	84 (27.9%)
Non-Hispanic Asian	19 (4.5%)	20 (4.8%)	10 (3.3%)	13 (4.3%)
Non-Hispanic Black	20 (4.8%)	26 (6.2%)	18 (5.9%)	16 (5.3%)
Non-Hispanic White	213 (51.0%)	217 (52.0%)	140 (46.1%)	156 (51.8%)
Other/Unknown	62 (14.8%)	54 (12.9%)	52 (17.1%)	32 (10.6%)

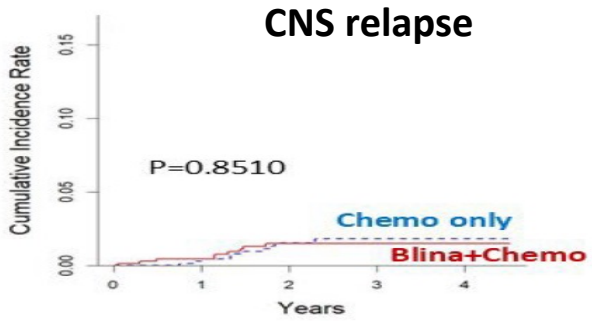
AALL1731: randomization and patients' features



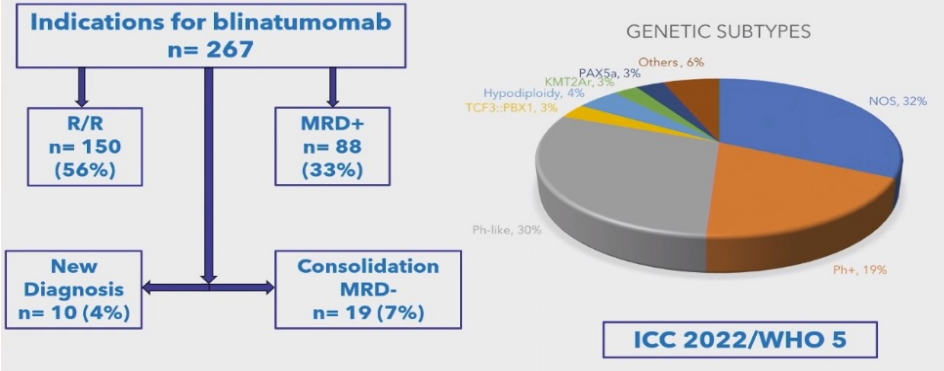
AALL1731: impact of blinatumomab on relapse

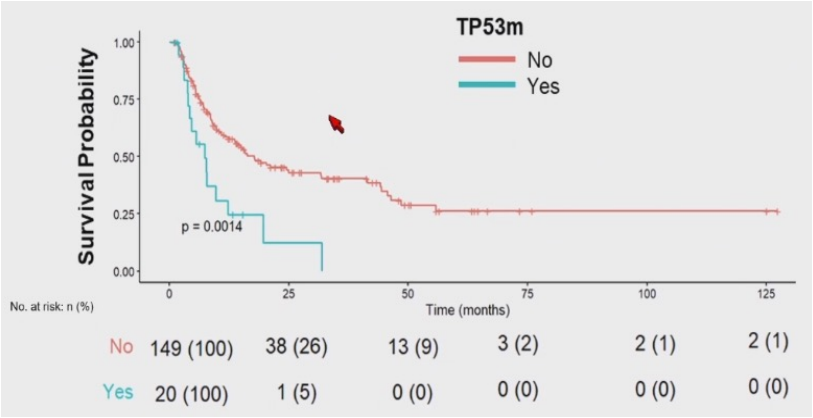


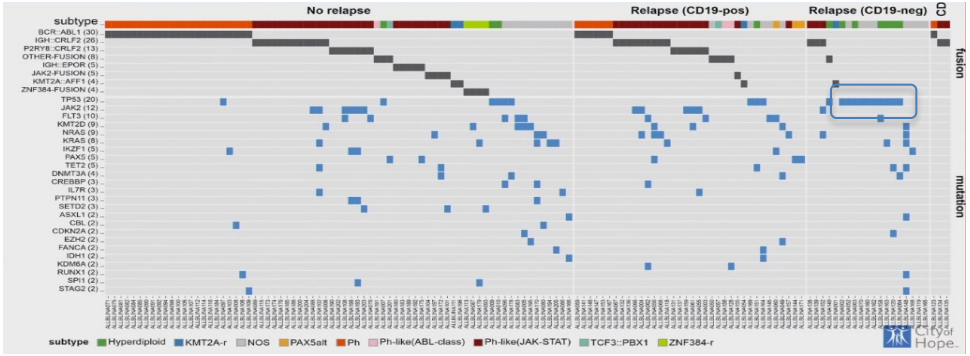


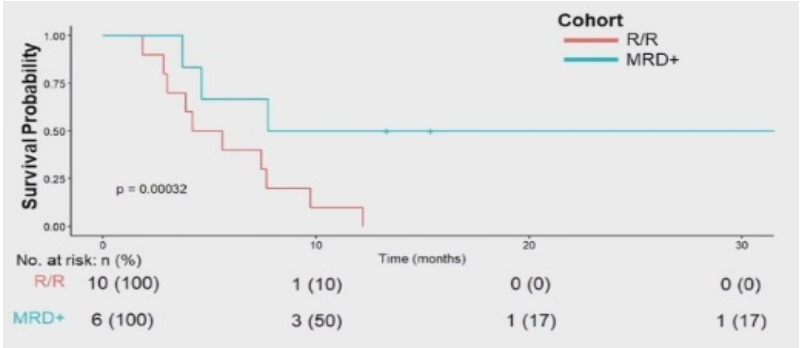


TP53 mutations increased the risk of CD19-relapse following blinatumomab in adults with B-ALL

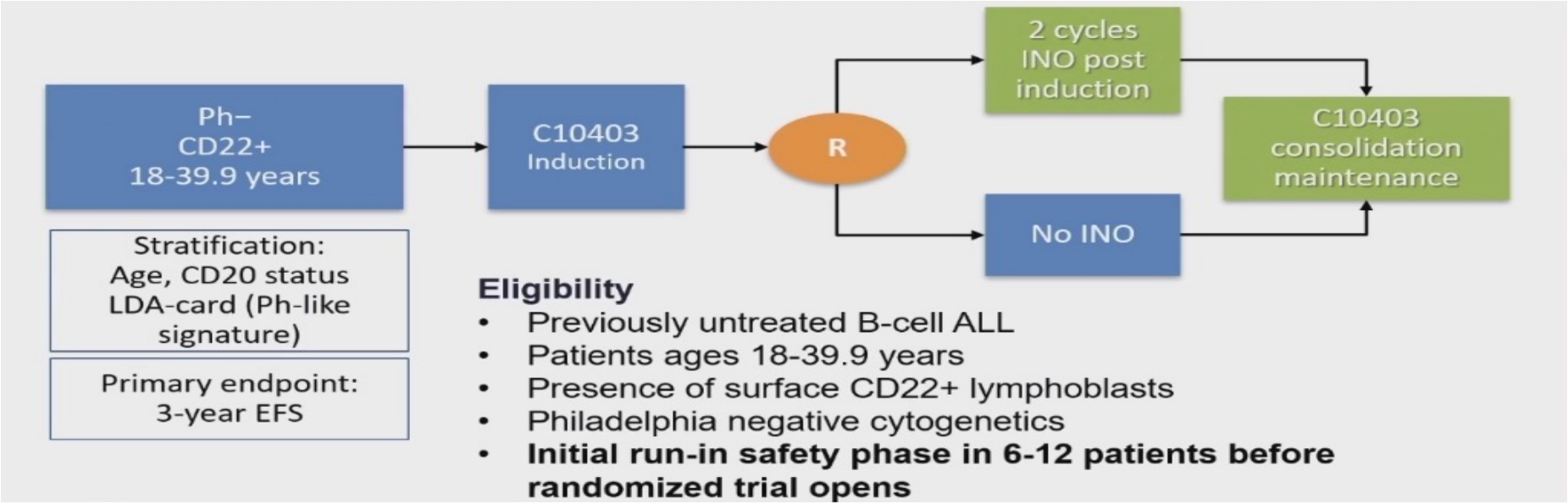




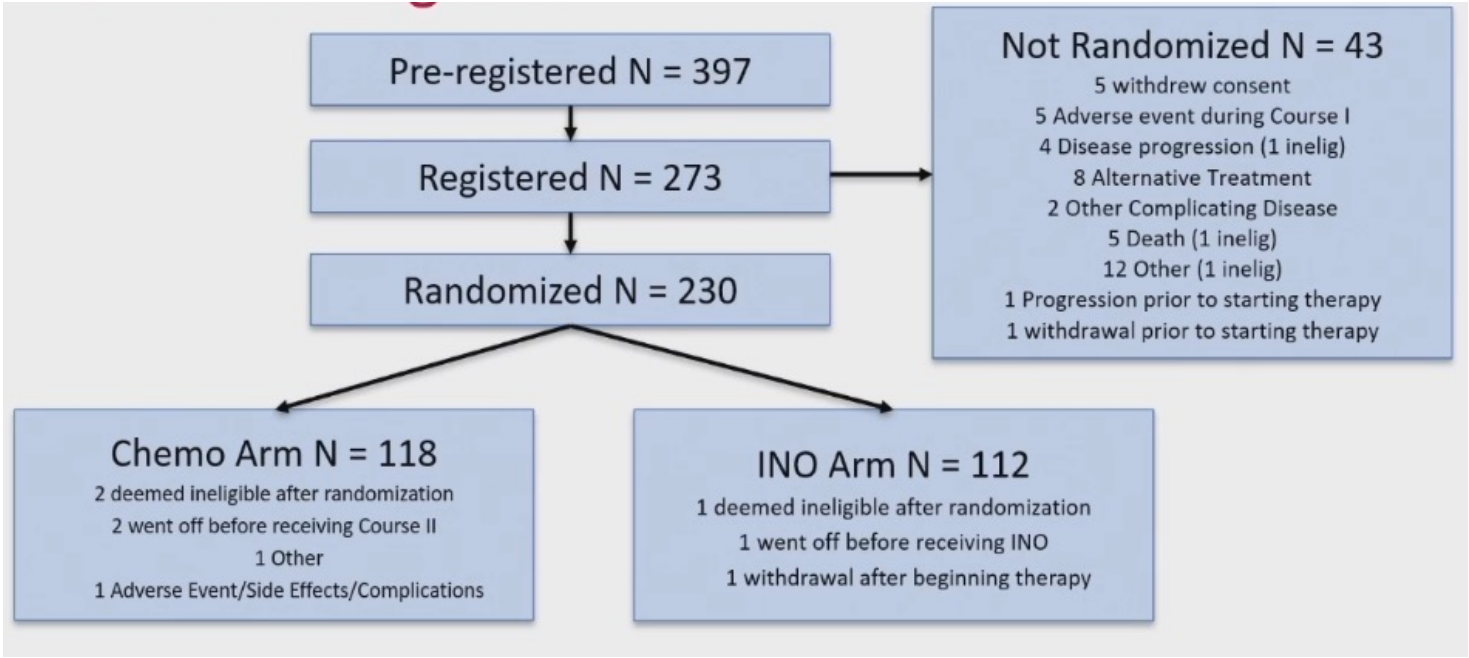




Alliance 041501 phase III trial



Alliance 041501 trial: patients' disposition



Protocol halted to due to late infections

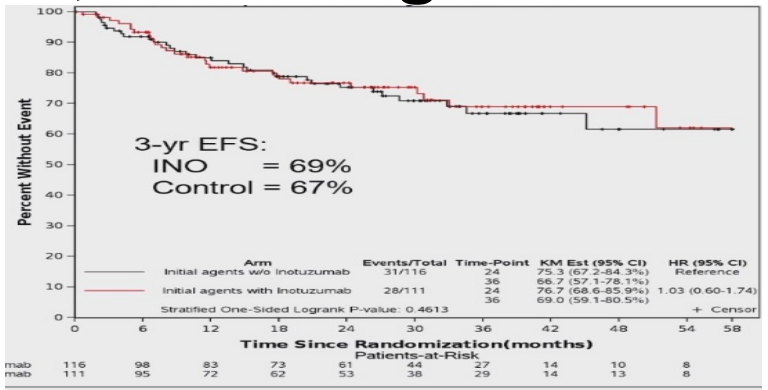
deaths in ino arm

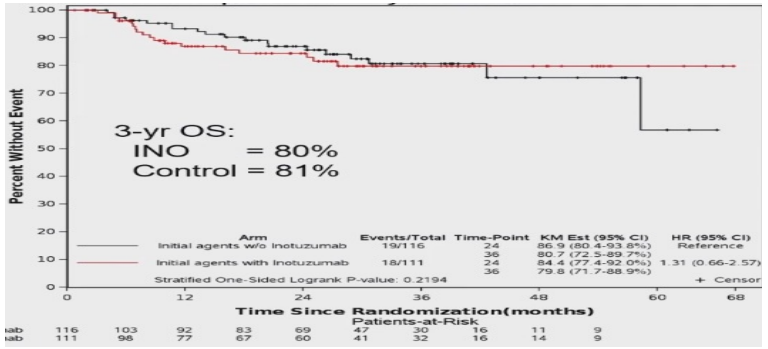
Alliance 041501 trial: EFS, OS and grade 5 events

	Grade 3	Grade 4	Grade 5
Total			
INO	2 (1.8%)	97 (86.6%)	12 (10.7%)
Control	5 (4.2%)	110 (93.2%)	3 (2.5%)
Hematologic			
INO	1 (0.9%)	109 (97.3%)	0 (0%)
Control	3 (2.5%)	111 (94.1%)	0 (0%)
Non-Hematologic			
INO	43 (38.4%)	51 (45.5%)	12 (10.7%)
Control	52 (44.1%)	60 (50.8%)	3 (2.3%)

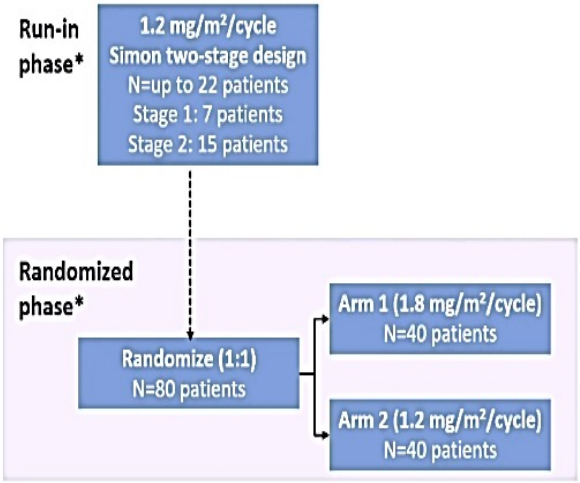
EFS table by arm

	Chemo (N=116)	INO (N=111)	Total (N=227)
Event, n (%)			
Censor	85 (73.3%)	82 (73.9%)	167 (73.6%)
Death	4 (3.4%)	14 (12.6%)	18 (7.9%)
Progression	27 (23.3%)	15 (13.5%)	42 (18.5%)





Optimization of Inotuzumab dose in R/R ALL adults



Population: adults with R/R BCP ALL who were eligible for HSCT and who had higher risk factor(s) for developing post-HSCT VOD after InO treatment

Risk factors for VOD: age (≥55 years), salvage status, prior HSCT, and ongoing/prior hepatic disease

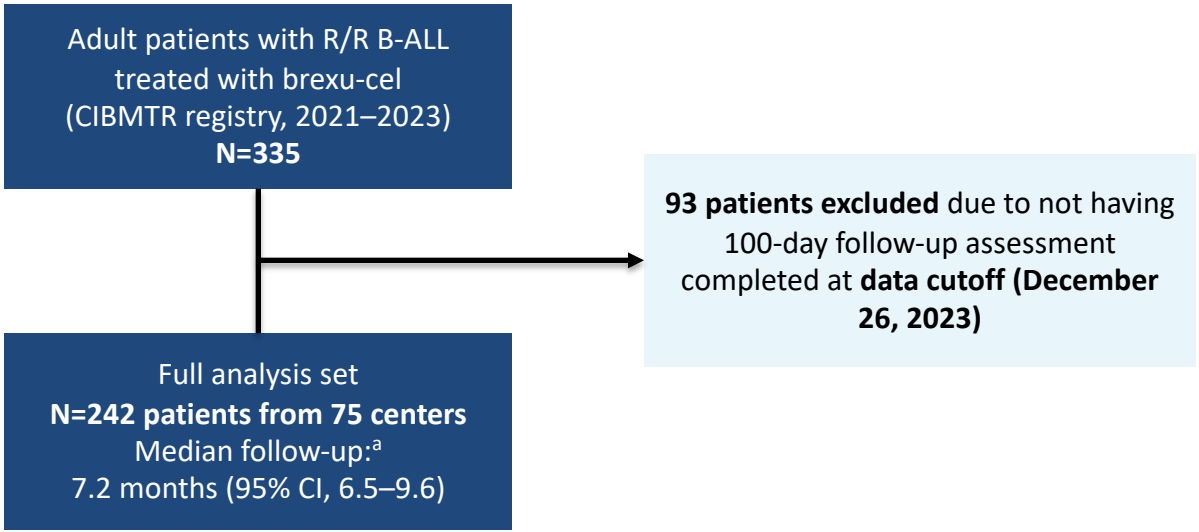
Primary endpoints:

- CR/CRi rate
- VOD rate

Efficacy endpoint	Average InO dose per cycle[a]	INO-VATE study response rate, n/N (%)	Phase 1/2 study response rate, n/N (%)	INO-VATE + Phase 1/2 studies response rate, n/N (%)
CR/CRi	<1.35 mg/m²	11/24 (46%)	5/11 (45%)	**16/35 (46%)**
	≥1.35 and <1.65 mg/m²	7/17 (41%)	7/10 (70%)	**14/27 (52%)**
	≥1.65 mg/m²	102/121 (84%)	37/51 (73%)	**139/172 (81%)**
MRD-negativity	<1.35 mg/m²	8/22 (36%)	4/11 (36%)	**12/33 (36%)**
	≥1.35 and <1.65 mg/m²	8/17 (47%)	6/10 (60%)	**14/27 (52%)**
	≥1.65 mg/m²	81/117 (69%)	31/51 (61%)	**112/168 (67%)**

Safety endpoint	Average InO dose per cycle[a]	Rate of VOD in patients with HSCT, n/N (%)	Rate of VOD in patients with no HSCT, n/N (%)	Total VOD rate, n/N (%)
VOD / SOS (any severity)	<1.35 mg/m²	3/7 (43%)	0/19 (0%)	**3/26 (12%)**
	≥1.35 and <1.65 mg/m²	12/43 (28%)	1/46 (2%)	**13/89 (15%)**
	≥1.65 mg/m²	4/27 (15%)	2/20 (10%)	**6/47 (13%)**

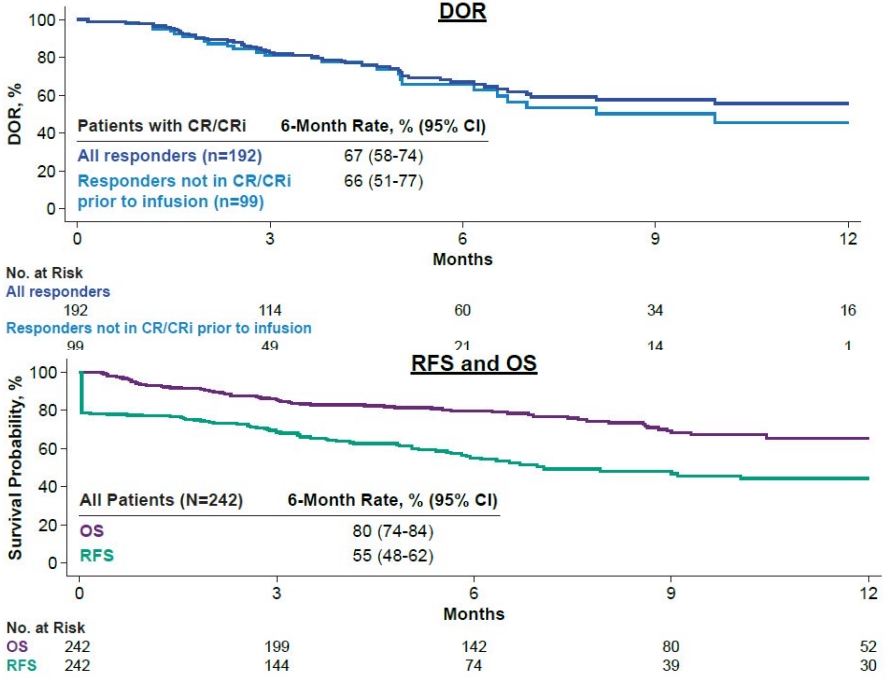
Real-World Outcomes for Brexucabtagene Autoleucel Treatment in Patients With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia by High-Risk Features and Prior Treatments: Updated Evidence From the CIBMTR Registry



- **Effectiveness:** CR/CRi rate, DOR, RFS, and OS
- **Safety:** CRS and ICANS (per ASTCT consensus),[6] prolonged cytopenias,[a] clinically significant infections requiring treatment, and NRM

Characteristic	All Patients (N=242)
Median age at infusion, years (range)	46.8 (18.5-84.3)
<26 years	20 (8)
≥26 to <55 years	138 (57)
≥55 years	84 (35)
Treatment history	
Median number of lines (IQR)	3.0 (2.0-4.0)
Prior blinatumomab, n (%)	144 (62)
Prior inotuzumab ozogamicin, n (%)	103 (44)
Prior alloSCT, n (%), months from prior alloSCT to infusion (IQR)	76 (32); 25.0 (11.4-42.3)
High-risk features, n (%)	
ECOG PS prior to infusion ≥2	17 (8)
Primary refractory	34 (14)
Extramedullary disease prior to infusion	45 (21)
BM blasts prior to LD chemotherapy, n/N of evaluable pts)	162/242
≤5%, n (%)[b]	113 (70)
>5% to ≤50%, n (%)[b]	31 (19)
>50%, n (%)[b]	18 (11)
MRD status prior to LD chemotherapy (among patients in CR/Cri pts)	94 (39)
CR / CRi, MRD negative	59 (24)
CR / CRi, MRD positive	16 (7)
CR / CRi, MRD not reported	19 (8)
Median months from initial diagnosis to infusion (IQR) and from leukapheresis to infusion (IQR)	18.7 (9.5-37.2), 32.0 (27.0-42.0)
Any bridging therapy, n (%)	110 (50)
LD chemotherapy, n (%)	
Cyclophosphamide + fludarabine	228 (94)
Bendamustine	7 (3)

CR/CRi: 80% overall and 68% in pts not in CR prior to infusion



For pts ≥26 years, 6-month rates of DOR, RFS, and OS were 67%, 55%, and 79%, respectively

"Real world" outcome of hematopoietic stem cell transplantation after CAR19 T cell therapy in children and adults with B-ALL: a GoCART coalition study on behalf of the PDWP, ALWP, and CTIWP of the EBMT

Retrospective registry-based study

Adults and children receiving autologous (academic or commercial) CAR19 T cell therapy for B-ALL

Study Period: 2016-2023

40 centres across 17 countries

345 patients enrolled (173 adults & 172 children)

113 patients

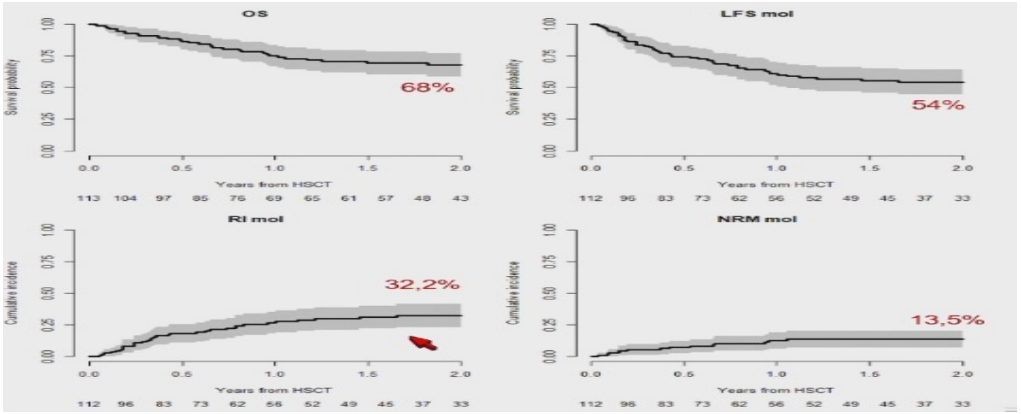
Median follow-up : 2.1 yrs

First CART	Tisa-cel (Kymriah®)	80 (70.8)
	ARI-0001	21 (18.6)
	Brexu-cel (Tecartus®)	4 (3.5)
	Liso-cel (Breyanzi®)	3 (2.7)
	Sheba CART	4 (3.5)
	Tuebingen CART	1 (0.9)
Response after CART	CR MRD neg	99 (88.4)
	CR MRD pos	8 (7.1)
	CR (missing MRD)	2 (1.8)
	No CR	3 (2.7)
	missing	1

Age at HSCT	median [IQR]	14.1 [8.2-22.4]
Months between CART and HSCT	median [IQR]	6.2 [3.7-11.8]
Allo-HSCT naive	No	67(59,3)
	Yes	46 (40,7)

N=113 (100%)

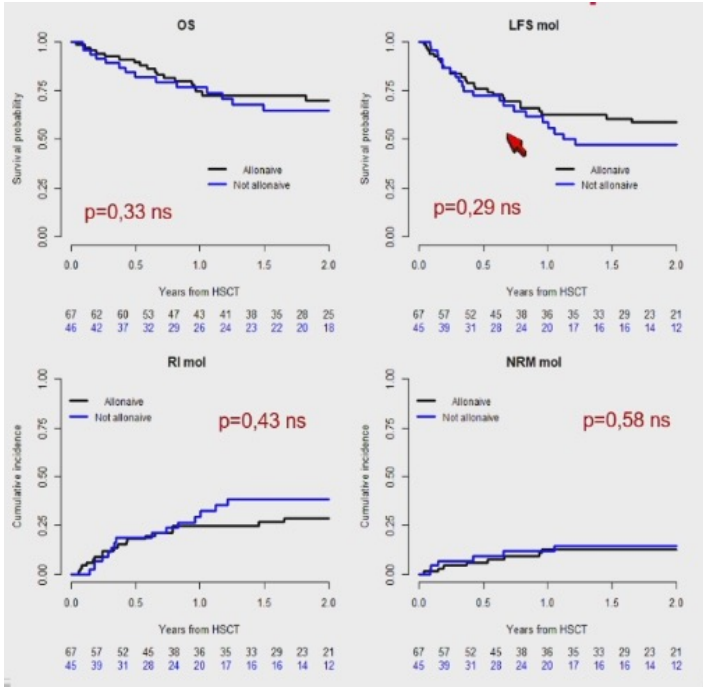
Disease status at HSCT	CR MRD neg	74 (65.5)
	CR MRD pos	28 (24.8)
	EMD only	7 (6.2)
	Relapse	3 (2.7)
	CR (MDS)	1 (0.9)



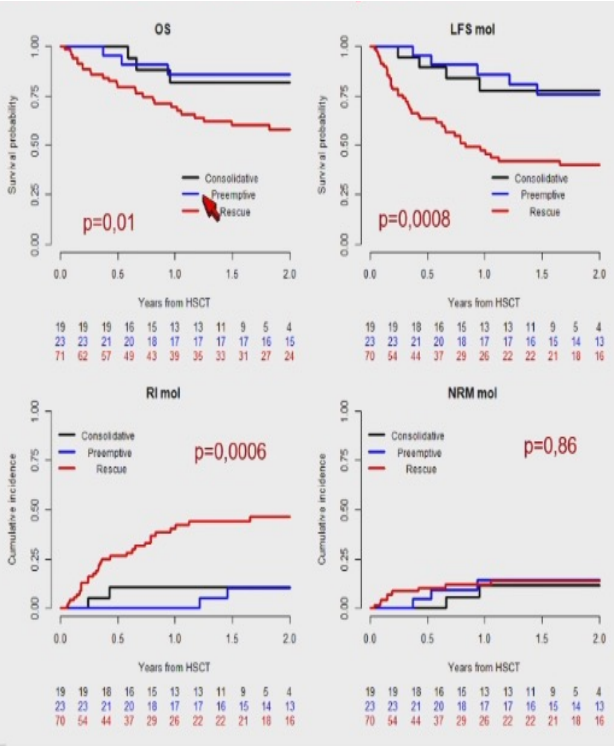
Ottaviano G, et al. Abs 112. ASH 2024

Role of prior and subsequent transplant

Prior transplant



		Consolidative (N=19)	Preemptive (N=23)	Rescue (N=71)
Age at this HSCT	median [IQR]	13 [8.3-23.3]	13.6 [8.4-17]	15.9 [8.4-23.2]
Age at this HSCT	Adult	7 (36.8)	5 (21.7)	26 (36.6)
	Child	12 (63.2)	18 (78.3)	45 (63.4)
Allo HSCT before CART	No	17 (89.5)	17 (73.9)	33 (46.5)
	Yes	2 (10.5)	6 (26.1)	38 (53.5)
CART1	Kymriah	15 (78.9)	15 (65.2)	50 (70.4)
	ARI-0001	0 (0)	6 (26.1)	15 (21.1)
	BREYANZI	0 (0)	1 (4.3)	2 (2.8)
	Sheba CART	2 (10.5)	0 (0)	2 (2.8)
	Tecartus	2 (10.5)	1 (4.3)	1 (1.4)
	Tuebingen CART	0 (0)	0 (0)	1 (1.4)
Months first CART to HSCT	median [IQR]	3.5 [2.7-4.2]	4.4 [3.3-5.7]	9.7 [5.8-17.5]
Response after CART1	CR MRD neg	19 (100)	23 (100)	59 (84.3)
	CR MRD pos	0 (0)	0 (0)	8 (11.4)
	No CR	0 (0)	0 (0)	3 (4.3)
	missing	0	0	1
Myeloablative regimen	No	1 (5.3)	4 (18.2)	17 (25)
	Yes	18 (94.7)	18 (81.8)	51 (75)
	missing	0	1	3
TBI in conditioning regimen	No	1 (5.3)	9 (40.9)	32 (46.4)
	Yes	18 (94.7)	13 (59.1)	37 (53.6)
	missing	0	1	2



Obecabtagene autoleucel (obe-cel) for Adult Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL): Deep Molecular Remission May Predict Better Outcomes

Jabbour E, *et al.* ASH 2024 (Abstract 963; oral presentation)

NGS MRD Negativity on Day 28 after Brexu-cel in Adults with R/R ALL Is Associated with Favorable Progression Free Survival

Valtis YK, et al. ASH 2024 (Abstract 4200; poster presentation)

Conclusions

Blinatumomab has proven to be effective and superior to chemotherapy in Ph+ ALL as well in pediatric Ph- ALL ➡ new standard of treatment

Inotuzumab treatment in AYA and adults is effective in reducing disease progression but is associated with fatal infectious events

Inotuzumab dose reductions are associated with inferior outcomes

CAR-T RW data confirm the efficacy of the strategy; allo SCT strategy as consolidation porbably lead to better outcomes