1ST INTERNATIONAL CONFERENCE ON

Ph+ Leukemias

Bologna, Royal Hotel Carlton **September 29-30, 2025**

Antibodies in R/R Ph+ ALL: present and future

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Disclosures Cristina Papayannidis

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Pfizer					x	x	
Amgen						x	
Astellas					x		
Abbvie					x		
Menarini Stemline						x	
Servier					x		
Incyte					x		
Janssen						x	
Syndax						x	
Blueprint					x	x	
GSK						x	
Istituto Gentili					x	x	
Jazz Pharmaceuticals					x	x	

Antibodies in R/R Ph+ ALL: state of the art

Today

- Blinatumomab
- Inotuzumab Ozogamicin

Today in clinical trials

- s.c. Blinatumomab
- Surovatamig
- Tafasitamab (US)

Tomorrow

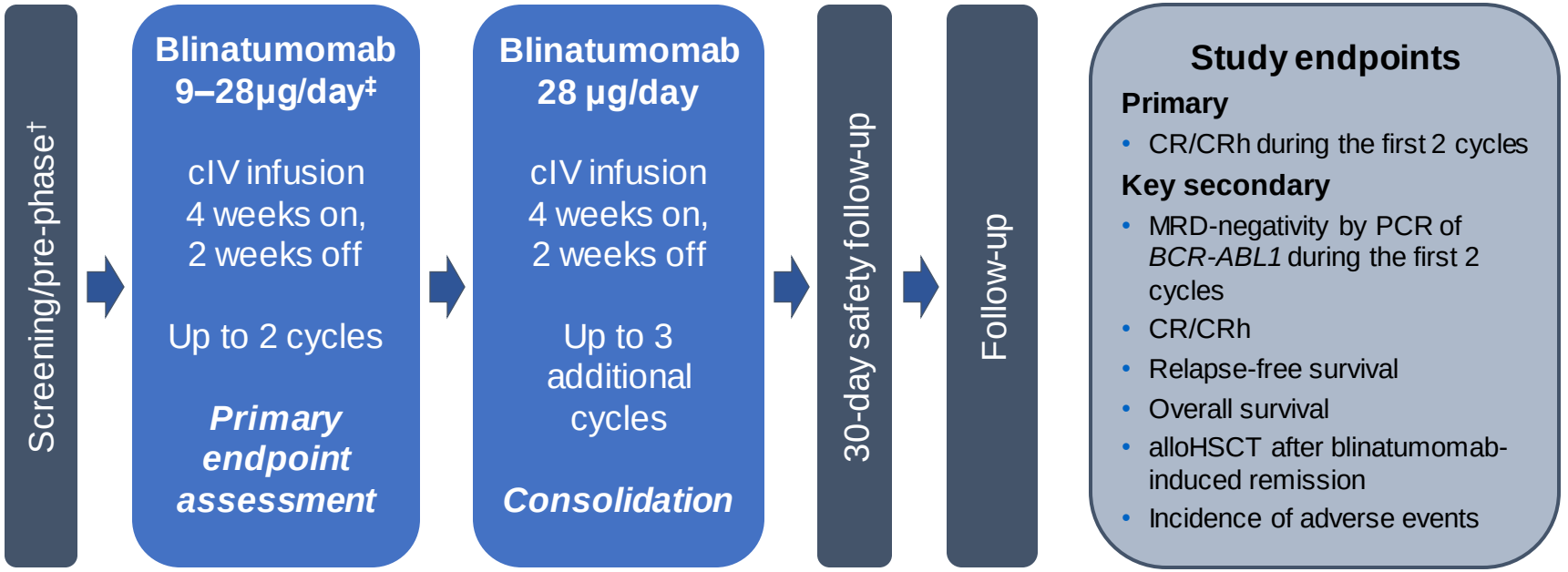
- VpreB1 ADC
- Trispecific TCE
- ???

Blinatumomab: approved for R/R Ph+ALL adult patients

- Blinatumomab approved as monotherapy in adult B-ALL patients with CD19+ R/R Ph neg disease

- Blinatumomab approved as monotherapy in adult Ph+ B-ALL with CD19+ R/R disease, who have failed at least two TKIs

Phase 2 study of Blinatumomab in adult patients with Ph-positive r/r B-precursor ALL (ALCANTARA)



†To reduce tumour burden and CRS, patients with a high baseline blast count received pre-phase treatment with dexamethasone 10 mg/m^2/day (for up to 5 days) up to a maximum of 24 mg/day (absolute);
‡9 µg/day in Week 1 of Cycle 1, followed by 28 µg/day from Weeks 2–4

Martinelli G, et al. JCO 2017

Patients' characteristics

	n/N	%
Male sex	24/45	53
Median age, years (range)	55 (23–78)	-
Age group		
18 to <55 years	22/45	49
≥55 years	23/45	51
Cytogenetics and molecular analyses*		
Ph-positive *and* other cytogenetic abnormalities	22/38	58
ABL kinase domain mutations	17/37	46
T315I mutation	10/37	27
Bone marrow blasts		
<10%	2/45	4
10% to <50%	9/45	20
50% to <75%	6/45	13
≥75%	28/45	62

Martinelli G et al, JCO 2017

Number of prior therapies

	n/N	%
Number of prior TKIs*		
1	7/45	16
2	21/45	47
3	13/45	29
4	4/45	9
Prior allogeneic HSCT	20/45	44
Prior TKIs†	45/45	100
Imatinib	25/45	56
Dasatinib	39/45	87
Nilotinib	16/45	36
Ponatinib	23/45	51

Martinelli G et al, JCO 2017

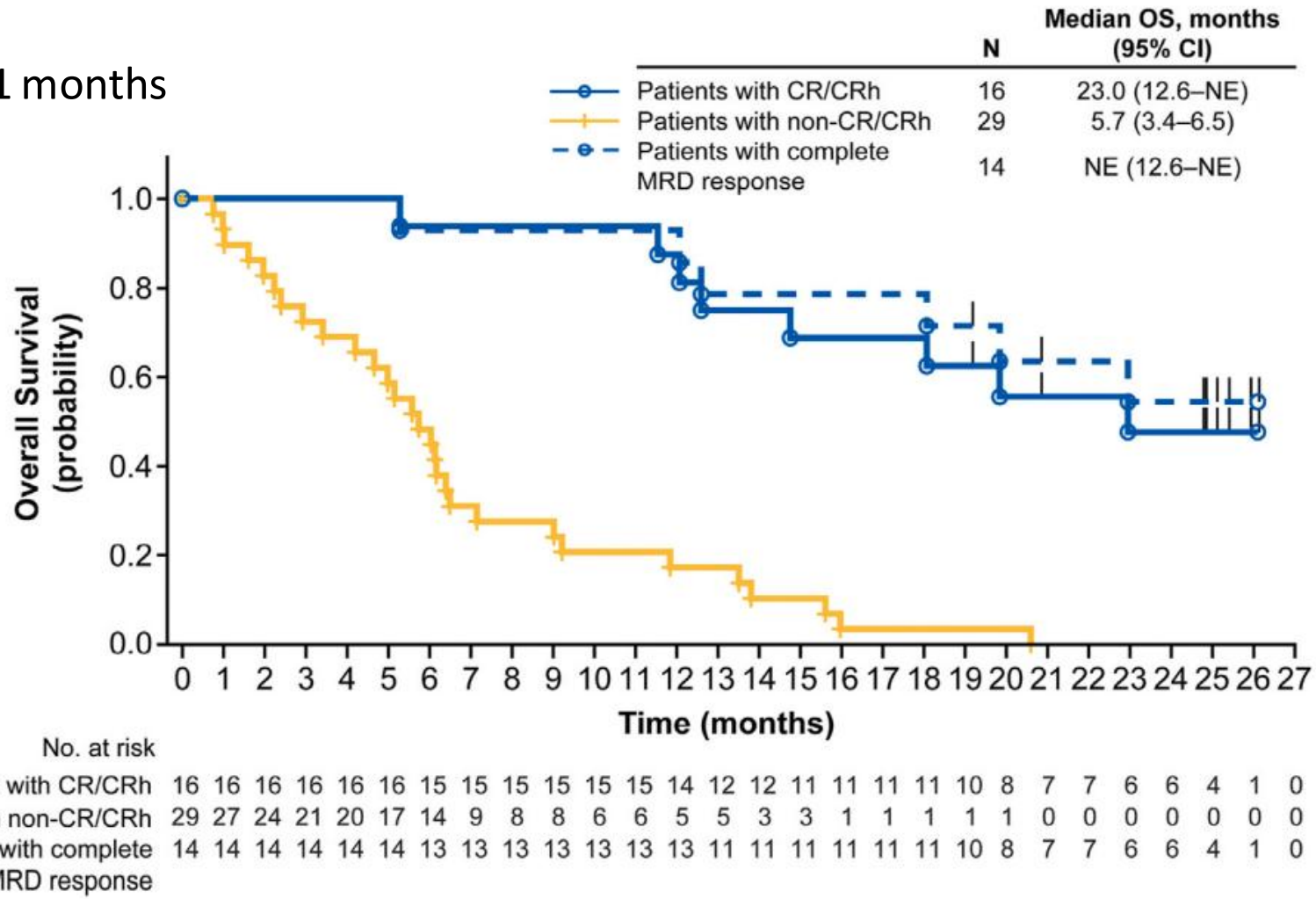
Response after 2 courses

Primary endpoint	n/N	% (95% CI)
CR/CRh during the first two cycles	16/45	36 (22–51)
Secondary endpoints	**n/N**	**% (95% CI)**
Best response during the first two cycles		
CR	14/45	31 (18–47)
CRh	2/45	4 (1–15)
MRD-negativity*	14/16	88 (62–98)
Allogeneic HSCT after blinatumomab-induced remission†	4/16	25 (7–52)
Age 18 to <55 years	2/8	25 (3–65)
Age ≥55 years	2/8	25 (3–65)
100-day post-transplant mortality rate†	1/4	25 (4–87)

Martinelli G et al, JCO 2017

Long term follow-up

Median follow up: 25.1 months



Martinelli G et al, Eur J Cancer 2021

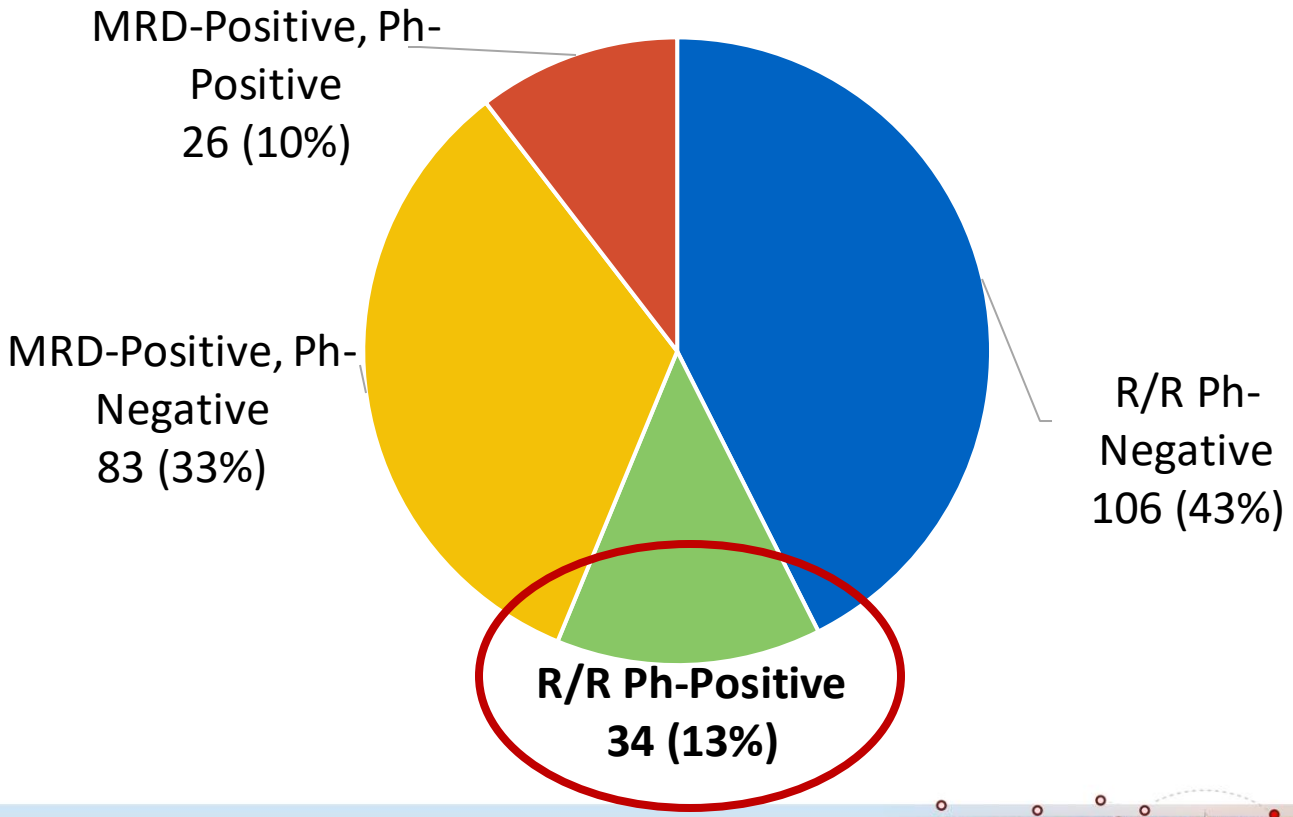
European real-life experience: NEUF study

Objectives:

- A retrospective observational study of **adult and pediatric patients** with diagnoses **of R/R Ph-negative or Ph-positive BCP-ALL, or MRD-positive Ph-negative or Ph-positive** ALL enrolled in the **expanded access program** across European countries

Outcomes:

- **Remission rate**
  - MRD response
  - Hematological response (CR/CRh/CRi)
- **HSCT realization**
- **Survival rates:**
  - Overall survival
  - Disease-free survival
  - Relapse-free survival
- Mortality after allogeneic HSCT



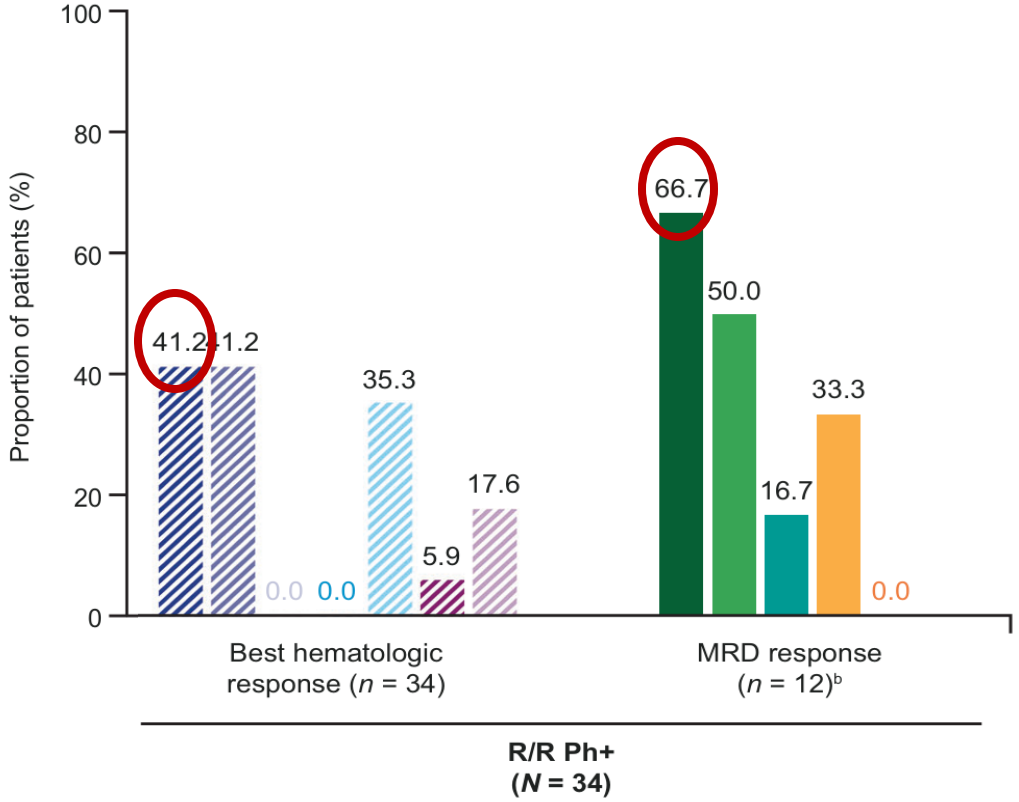
Boissel N et al, Blood Cancer Journal 2023

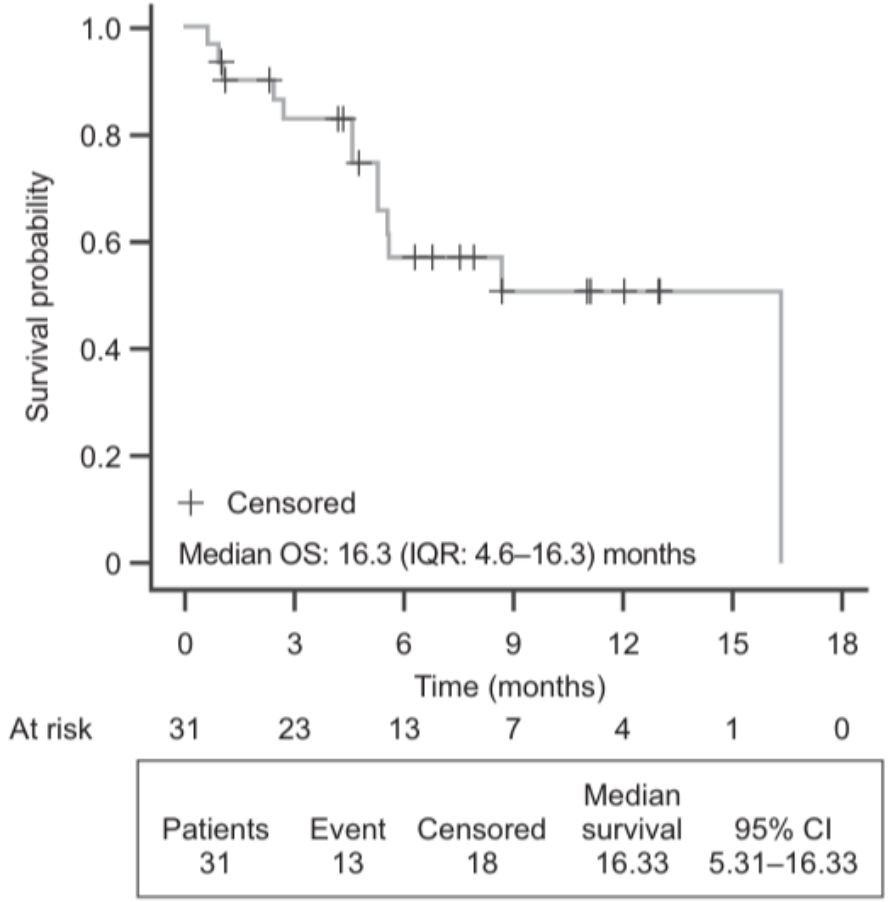
NEUF study: baseline characteristics

	Adult ALL		
	R/R Ph-Negative (n = 106)	**MRD-Positive (n = 109)**	**R/R Ph-Positive (n = 34)**
Female, n (%)	50 (47.2)	45 (41.3)	16 (47.0)
Age, years, median (IQR)	36.5 (24.0–52.0)	43.0 (27.0–55.0)	51 (37.0–64.0)
Number of salvage therapies, median (IQR)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	1.0 (1.0–2.0)
Disease status at initiation, n (%)			
Hematological relapse	64 (60.4)	NA	20 (58.8)
Refractory	42 (39.6)	NA	14 (41.2)
Molecular failure	NA	77 (70.6)	NA
Molecular relapse	NA	32 (29.4)	NA
HSCT prior to blinatumomab, n (%)	43 (40.6)	17 (15.6)	12 (35.3)
Duration between HSCT and initiation, months, median (IQR)	13.0 (7.2–20.0)	10.2 (3.8–24.9)	10.4 (7.1–20.6)
CR/CRh/CRi at frontline therapy, n (%)	84 (79.2)	NA	25 (73.5)
Blast count at blinatumomab initiation, n (%)			
< 50%	52 (54.2)	90 (95.7)	14 (50)
≥ 50%	44 (45.8)	4 (4.3)	14 (50)
Unknown	10 (-)	15 (-)	6 (-)

Boissel N et al, Blood Cancer Journal 2023

NEUF study: results





Boissel N et al, Blood Cancer Journal 2023

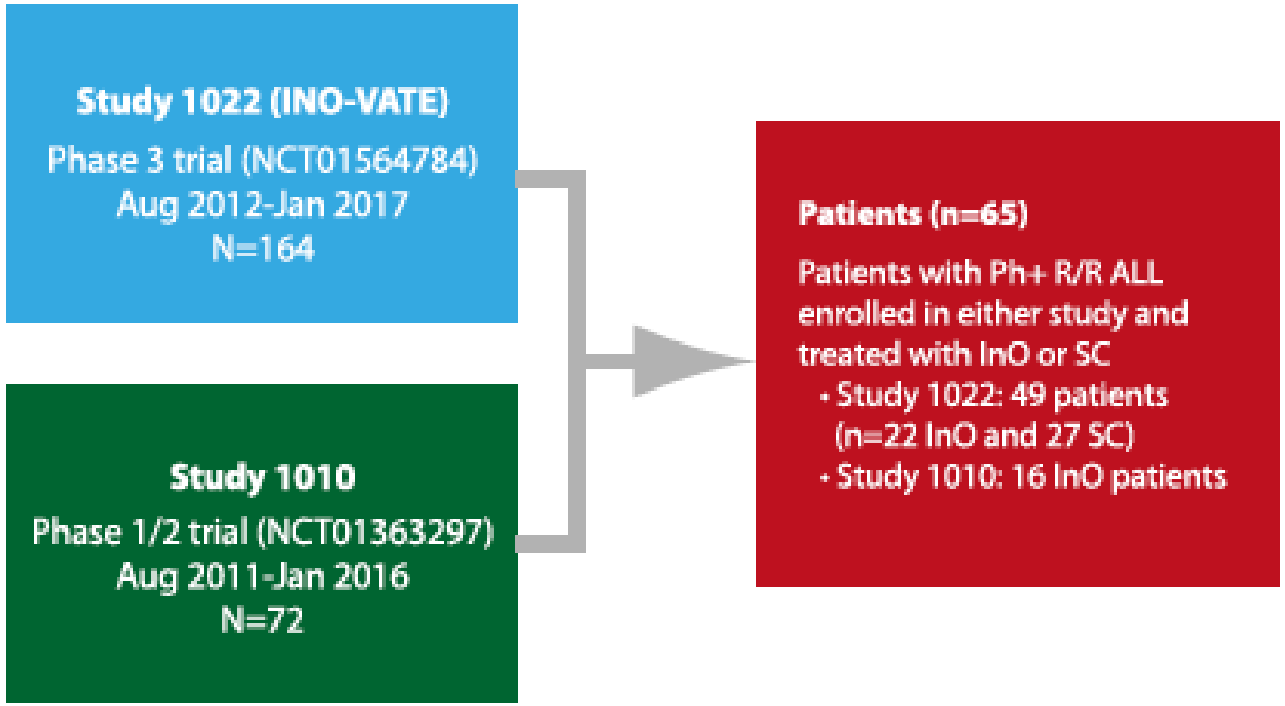
Inotuzumab Ozogamicin: approved for Ph+ALL

- Inotuzumab Ozogamicin approved as monotherapy in adult B-ALL patients with CD22+ R/R disease

- Inotuzumab Ozogamicin approved as monotherapy in adult Ph+ B-ALL with R/R disease, who have failed at least one TKI

Efficacy of Inotuzumab Ozogamicin in Patients With Philadelphia Chromosome–Positive Relapsed/Refractory Acute Lymphoblastic Leukemia

Wendy Stock, MD[1]; Giovanni Martinelli, MD[2]; Matthias Stelljes, MD[3]; Daniel J. DeAngelo, MD, PhD[4]; Nicola Gökbuget, MD[5]; Anjali S. Advani, MD[6]; Susan O'Brien, MD[7]; Michaela Liedtke, MD[8]; Akil A. Merchant, MD[9]; Ryan D. Cassaday, MD [10]; Tao Wang, PhD[11]; Hui Zhang, PhD[12]; Erik Vandendries, MD, PhD[11]; Elias Jabbour, MD [13]; David I. Marks, MD, PhD[14]; and Hagop M. Kantarjian, MD [13]



Cancer, 2021

Better response with InO vs SC: 72.7% vs 55.6%
Higher MRD neg with InO vs SC: 81.3% vs 33.3%

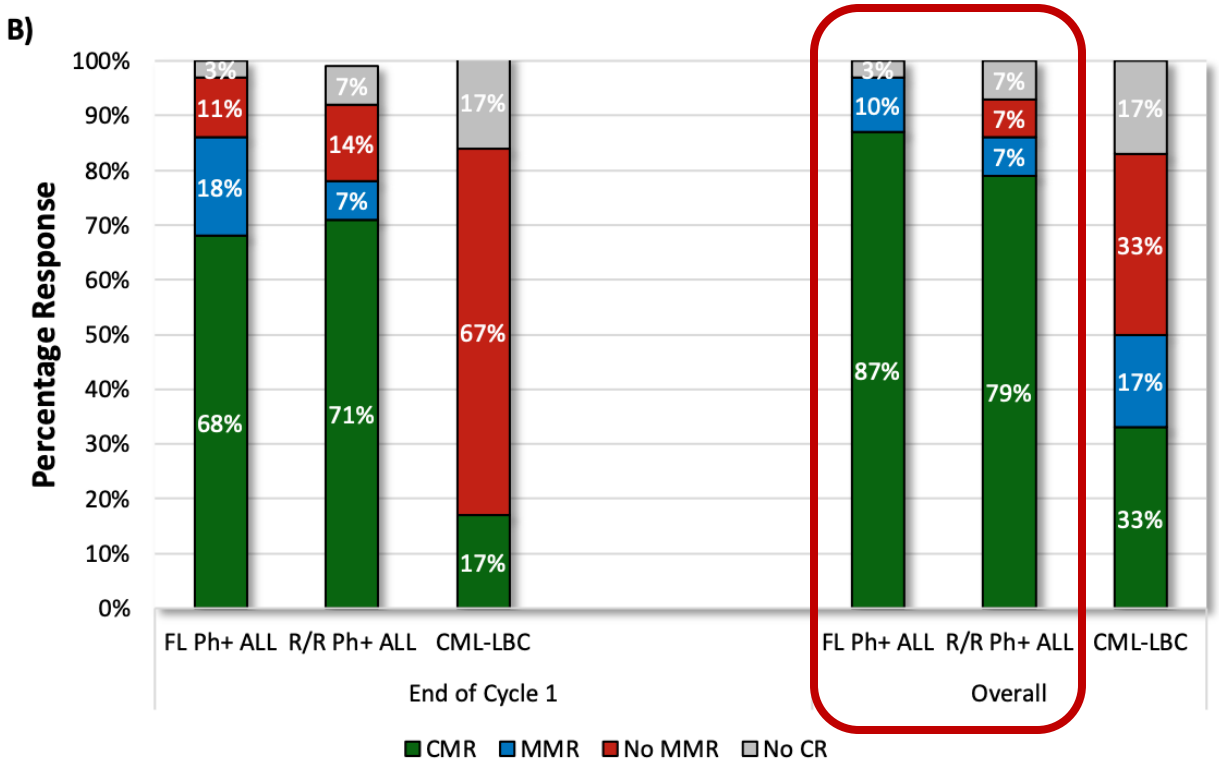
Efficacy Endpoints	Study 1022 InO (n = 22)	Study 1022 SC (n = 27)	P	Study 1010 InO (n = 16)
CR/CRi, n (% [95% CI])	16 (72.7 [49.8-89.3])	15 (55.6 [35.3-74.5])	.1075	9 (56.3 [29.9-80.3])
CR, n (% [95% CI])	10 (45.5 [24.4-67.8])	8 (29.6 [13.8-50.2])	.1265	4 (25.0)
CRi, n (% [95% CI])	6 (27.3 [10.7-50.2])	7 (25.9 [11.1-46.3])	.4577	5 (31.3)
MRD negativity, n (% [95% CI])[a]	13 (81.3 [54.4-96.0])	5 (33.3 [11.8-61.6])	.009	9 (100.0 [66.4-100.0])
OS				
Median, mo (95% CI)	8.7 (3.6-14.1)	8.4 (5.0-14.3)		7.4 (4.3-11.3)
HR (95% CI)	1.17 (0.64-2.14)		.6912	—
PFS				
Median, mo (95% CI)	3.9 (2.1-9.2)	3.1 (1.1-6.2)		4.4 (1.8-5.9)
HR (95% CI)	0.65 (0.34-1.25)		.0963	—

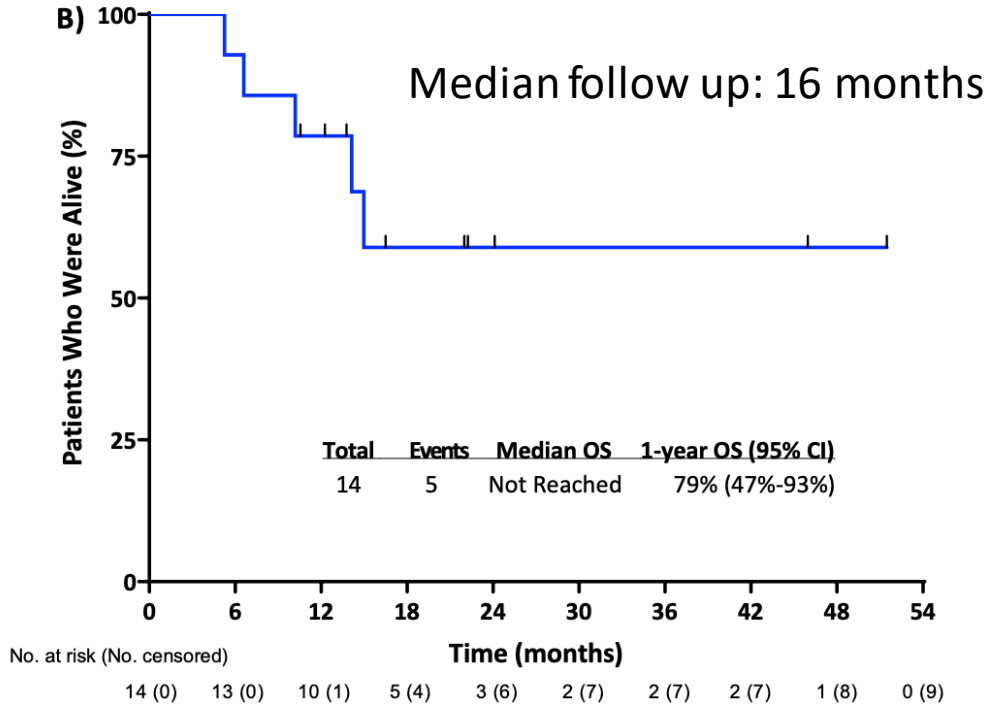
HSCT rate: 41% (InO) vs 19% (SC)

WARNING: VOD RISK

Cancer, 2021

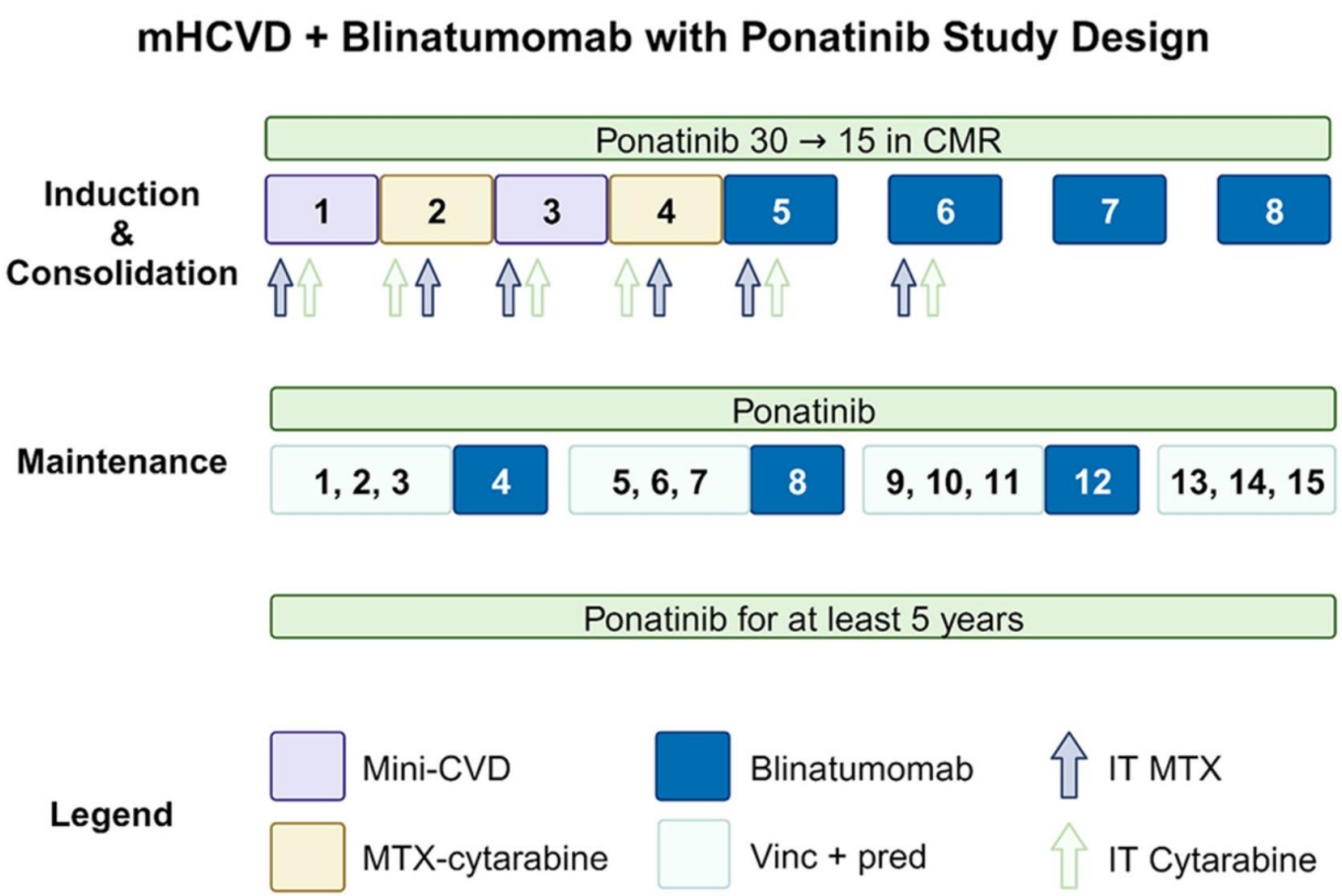
Ponatinib and blinatumomab for Philadelphia chromosome-positive acute lymphoblastic leukaemia: a US, single-centre, single-arm, phase 2 trial





Jabbour E et al, Lancet Haematol 2023

mHCVD+Blinatumomab+Ponatinib



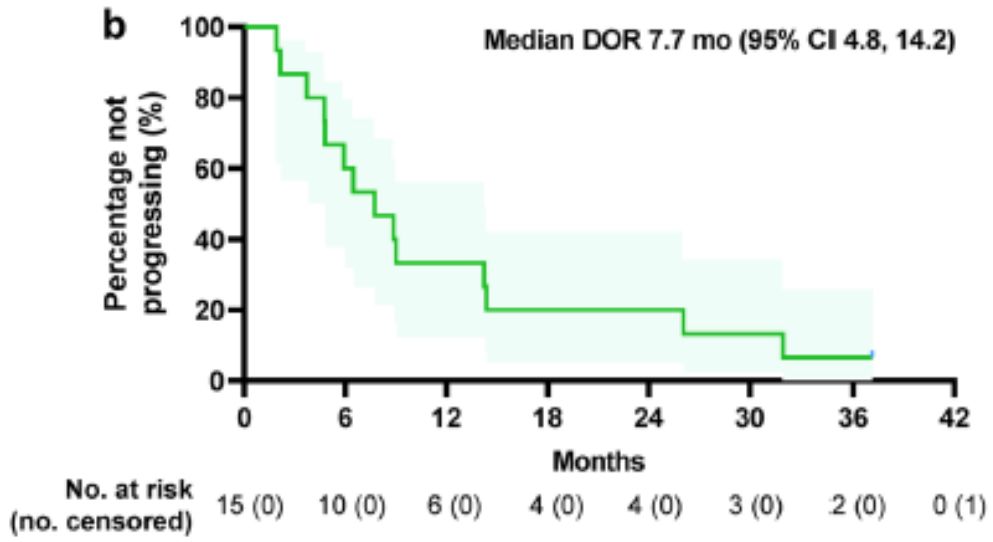
Response N achieved / N evaluable (%)	Total N = 20	ND N = 12	R/R N = 4	CML-LBP N= 4
CR/CRi	10/10 (100)	6/6 (100)	2/2 (100)	2/2 (100)
CMR	12/16 (75)	7/9 (78)	2/3 (67)	3/4 (75)
MMR	12/15 (80)	7/9 (78)	1/2 (50)	4/4 (100)
MRD negative (flow)	14/15 (93)	7/7 (100)	3/4 (75)	4/4 (100)
MRD negative (NGS)	7/8 (88)	5/5 (100)	1/2 (50)	1/1 (100)

Jen WY, Jabbour E et al, AJH 2024

Inotuzumab Ozogamicin with Bosutinib for Relapsed or Refractory Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia or Lymphoid Blast Phase of Chronic Myeloid Leukemia

N=18

Outcome	n (%)
Overall response rate	15 (83)
Complete remission (CR)	11 (61)
CR with incomplete hematologic recovery (CRi)	4 (22)
Complete cytogenetic response	13/16 (81) *
Major molecular response	14 (78)
Complete molecular response #	10 (56)
MRD negative by flow cytometry	11 (61)

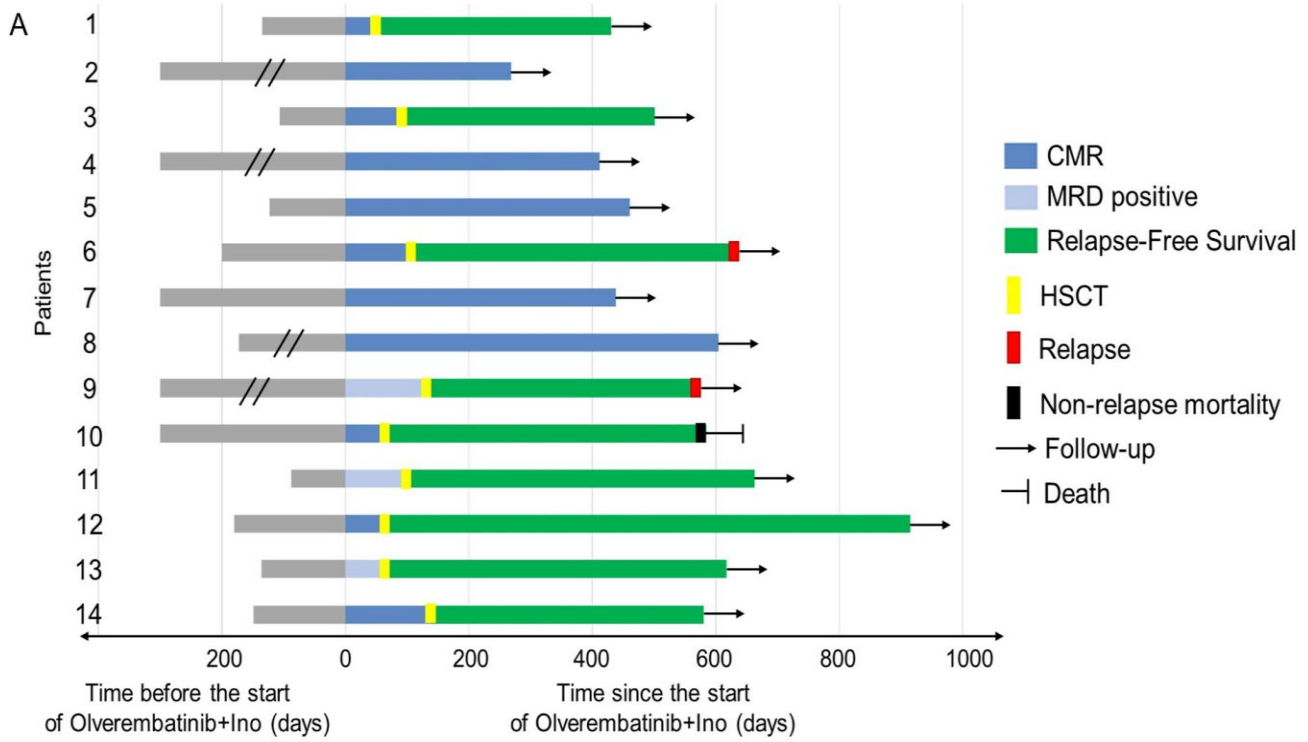


Most frequent grade 3/4 treatment emergent adverse events: thrombocytopenia (60%) and neutropenia (38%).
No VOD

Jain N et al, AJH 2021

Efficacy and Safety of the Third-Generation Tyrosine Kinase Inhibitor Olverembatinib in Combination With Inotuzumab Ozogamicin for the Treatment of Adult Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia Patients With Refractory/Relapsed Disease or Persistent Minimal Residual Disease Bridging to Hematopoietic Stem Cell Transplantation

Characteristic	*N* = 14 (%)
Disease status before olverembatinib+INO	
Hematology relapse	5 (35.7)
MRD persistent positive/relapse	9 (64.3)
Cycles of olverembatinib+ INO	
1	13 (92.9)
2	1 (7.1)
Treatment response	
Complete remission (CR)	14/14 (100)
Complete cytogenetic response	14/14 (100)
Complete molecular response	11/14 (78.6)
MRD negative by flow cytometry	14/14 (100)
Conditioning regimen	
TBI + Cy	6/9
Mel+Cy + Ara-C + Cla	2/9
Mel+Bu + Cy	1/9

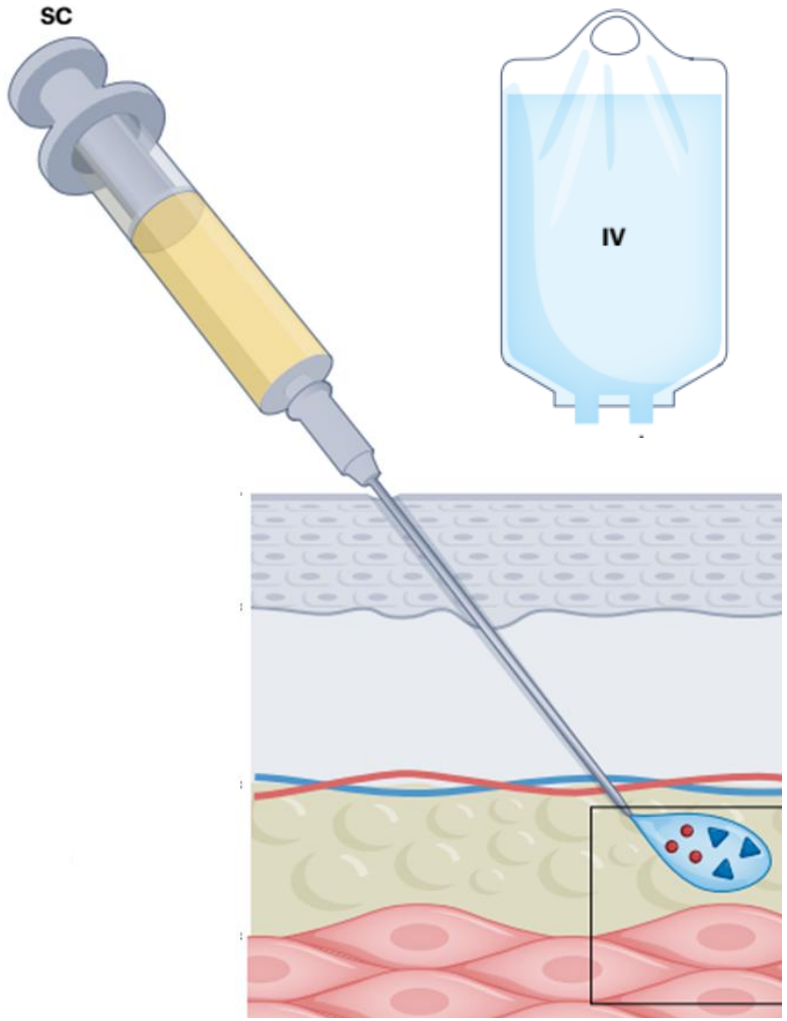


Zhang X et al, AJH 2025

Antibodies in R/R Ph+ ALL: state of the art

Today	Today in clinical trials	Tomorrow
• Blinatumomab • Inotuzumab Ozogamicin	• s.c. Blinatumomab • Surovatamig • Tafasitamab (US)	• VpreB1 ADC • Trispecific TCE • ???

Subcutaneous Blinatumomab



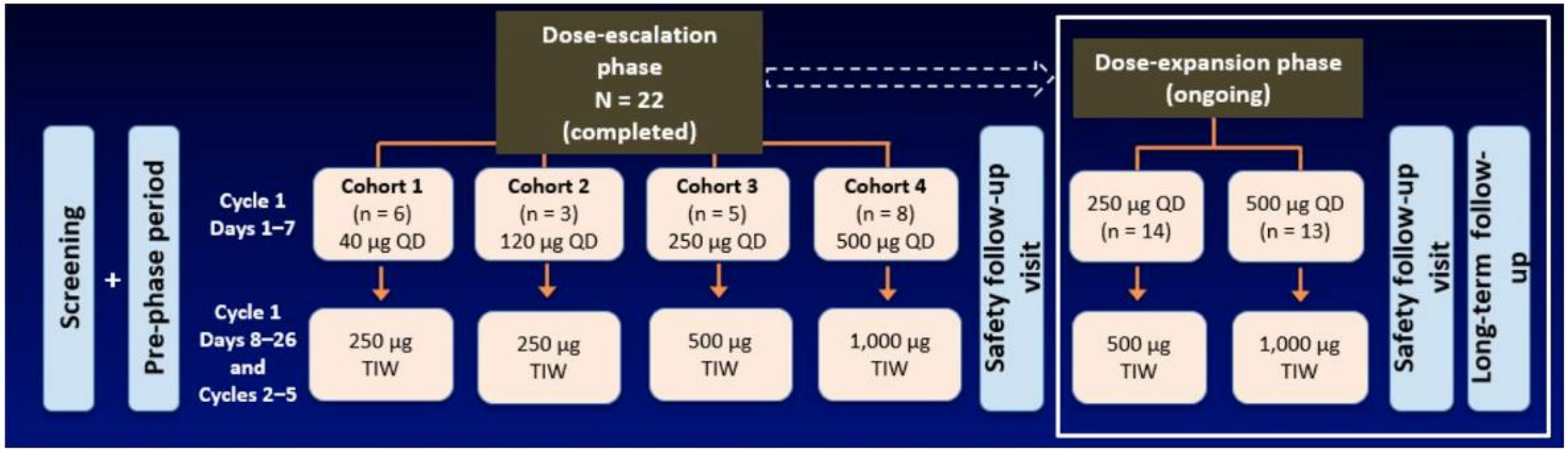
Blinatumomab as a continuous IV infusion is a standard treatment regimen utilized in patients with R/R B-ALL

SC delivery of blinatumomab was developed to evaluate higher doses with an aim to further improve efficacy and simplify administration to enhance convenience for patients

Can simplify administration, improve convenience, reduce treatment burden, and decrease cost for patients	Eliminate the need for a central line or continuous venous access and an infusion device (pump)	Abrogate the risk of device-related complications such as overdose caused by incorrect pump settings and dose interruptions from intravenous line occlusion	Deliver the target dose earlier (cycle 1, day 1) and over all a higher dose of blinatumomab to patients	Improve overall health health-related quality of life of the patients

Martinez Sanchez, P et al. Presented at: 64th Annual Meeting of the American Society of Hematology. December 10-13, 2022; New Orleans, LA. Poster 2727. B-ALL, B-cell precursor acute lymphoblastic leukemia; BiTE, bispecific T-cell engager; CD, cluster of differentiation; IV, intravenous; PD, pharmacodynamics; PK, pharmacokinetics; R/R, relapsed/refractory; SC, subcutaneous.1. Jabbour E, et al. Am J Hematol. 2024;99:586–595

Subcutaneous Blinatumomab: clinical experience



Jabbour E et al. Lancet Hematol 2025

Patients' characteristics

	250 µg/500 µg group (n=36)	500 µg/1000 µg group (n=52)
Sex*		
Male	22 (61%)	33 (63%)
Female	14 (39%)	19 (37%)
Age, years	46 (19–78)	50 (19–76)
Race†		
American Indian or Alaska Native	0	2 (4%)
Asian	0	6 (12%)
Black or African American	2 (6%)	1 (2%)
White	25 (69%)	31 (60%)
Other	9 (25%)	11 (21%)
Missing	0	1 (2%)
Hispanic or Latino ethnic group	15 (42%)	18 (35%)
B-ALL Philadelphia chromosome positive	7 (19%)	8 (15%)
Extramedullary disease		
Yes	1 (3%)	3 (6%)
Yes—CNS	0	2 (4%)
Yes—testis	0	0
Yes—other	1 (3%)	1 (2%)
No	35 (97%)	49 (94%)

	250 µg/500 µg group (n=36)	500 µg/1000 µg group (n=52)
Received previous anticancer therapy		
Blinatumomab	8 (22%)	9 (17%)
CAR T-cell therapy	7 (19%)	7 (13%)
HSCT	11 (31%)	14 (27%)
Inotuzumab ozogamicin	11 (31%)	18 (35%)
Criteria for entry to study		
Refractory to frontline therapy	17 (47%)	15 (29%)
Refractory to salvage therapy	4 (11%)	8 (15%)
First relapse with remission duration of <12 months	16 (44%)	24 (46%)
Untreated second or greater relapse	10 (28%)	12 (23%)
Relapse any time after allogeneic HSCT	11 (31%)	15 (29%)
Primary refractory at enrolment‡	5 (14%)	7 (13%)

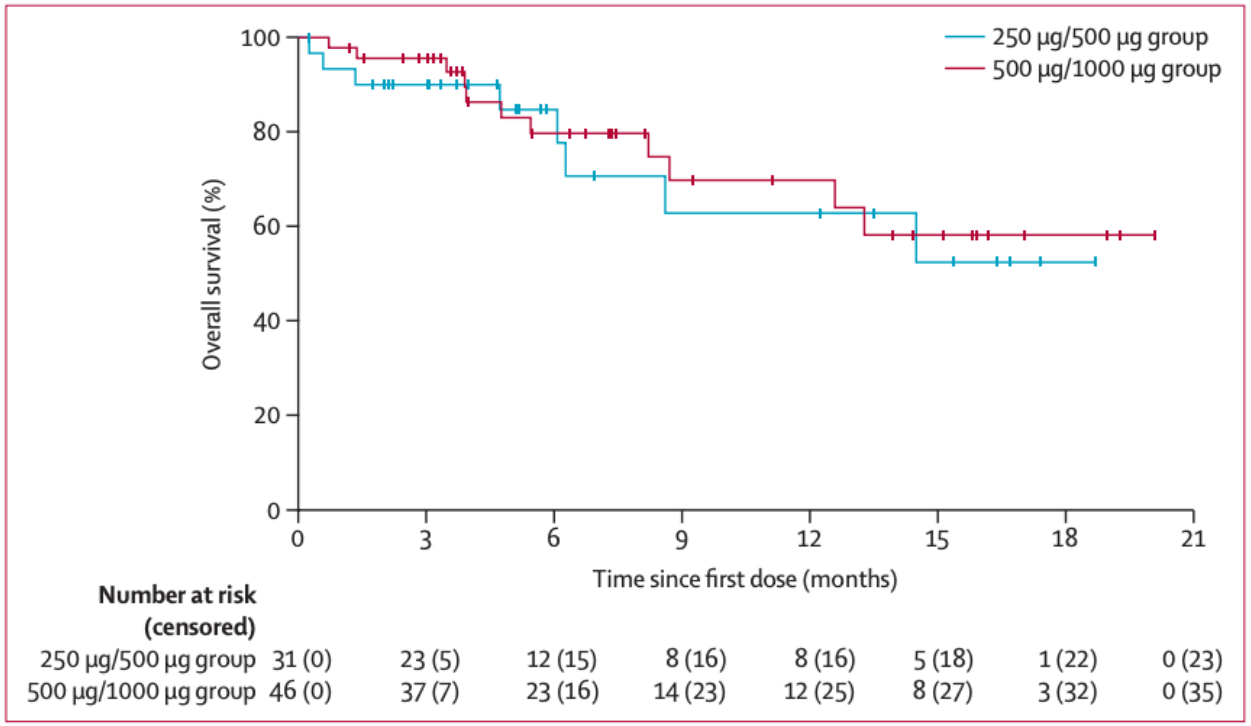
Jabbour E et al. Lancet Hematol 2025

Response rates

	250 µg/500 µg group (n=36)	500 µg/1000 µg group (n=52)
Overall survival*	31	46
Alive	22 (71%)	34 (74%)
Overall survival estimates, % (95% CI)		
3-month survival	90% (72–97)	96% (84–99)
6-month survival	85% (63–94)	80% (62–90)
9-month survival	63% (35–81)	70% (48–84)
12-month survival	63% (35–81)	70% (48–84)
18-month survival	52% (23–75)	58% (35–76)
Patients with at least one post-baseline disease assessment	33 (92%)	50 (96%)
Complete remission	25 (69%)	31 (60%)
Complete remission with partial haematological recovery	2 (6%)	10 (19%)
Complete remission with incomplete haematological recovery	5 (14%)	7 (13%)
No response	1 (3%)	1 (2%)
Unevaluable	0	1 (2%)
Complete remission or complete remission with partial haematological recovery,† n (% [80% CI])‡	27 (75% [63–84])	41 (79% [70–86])
Central or local MRD response ($<10^{-4}$) for complete remission or complete remission with partial haematological recovery§	24 (67%)	38 (73%)
Complete remission or complete remission with partial or incomplete haematological recovery, n (% [80% CI])‡	32 (89% [79–95])	48 (92% [85–97])
Central or local MRD response ($<10^{-4}$) for complete remission or complete remission with partial or incomplete haematological recovery§	29 (81%)	43 (83%)

Jabbour E et al. Lancet Hematol 2025

OS and safety profile



Number at risk (censored)								
250 µg/500 µg group	31 (0)	23 (5)	12 (15)	8 (16)	8 (16)	5 (18)	1 (22)	0 (23)
500 µg/1000 µg group	46 (0)	37 (7)	23 (16)	14 (23)	12 (25)	8 (27)	3 (32)	0 (35)

Median follow up: 5 months

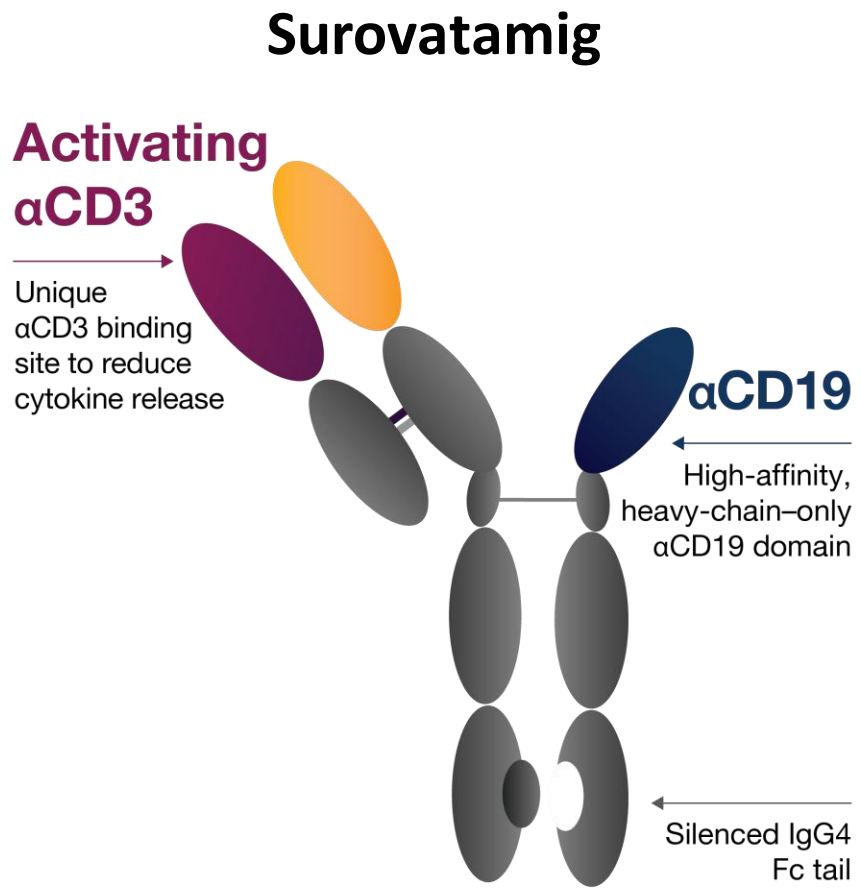
Most common grade 3-4 AEs: neutropenia (22%)
CRS (20%)
ICANS (17%)

No treatment-related deaths reported

Jabbour E et al. Lancet Hematol 2025

Surovatamig

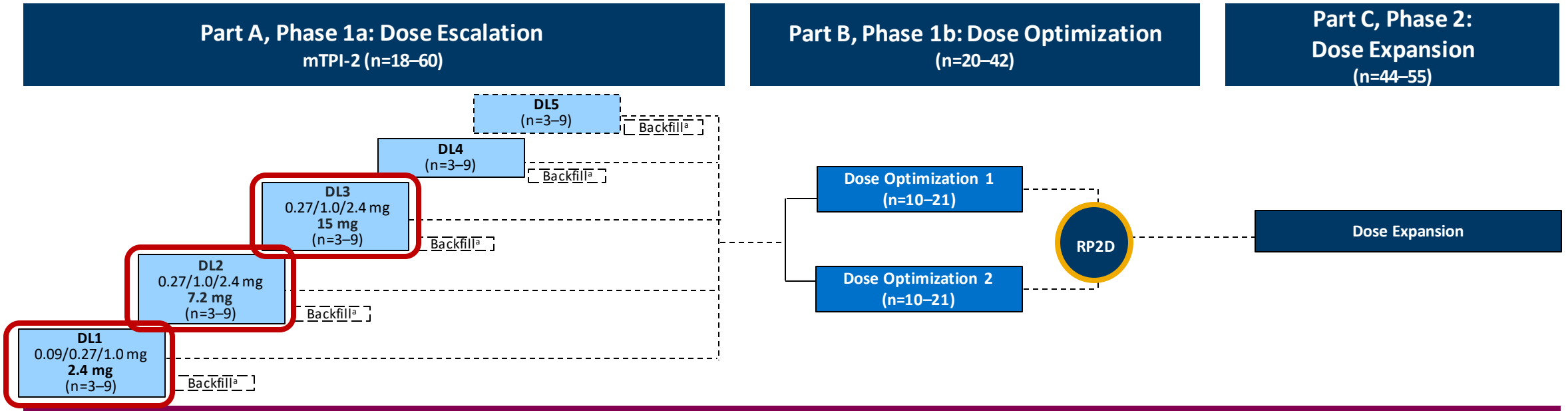
- Surovatamig, previously known as AZD0486, is a novel IgG4 fully human CD19×CD3 bispecific T-cell engager[1] designed for low-affinity CD3 binding to reduce cytokine release from T-cell activation while preserving T-cell cytotoxicity against malignant B cells
- A phase 1, FIH trial in patients with B-NHL (NCT04594642) demonstrated activity and tolerability of surovatamig in R/R FL and DLBCL, with a CR rate of 88%[2,3]



B-ALL, B-cell acute lymphoblastic leukemia; B-NHL, B-cell non-Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; FC, fragment crystallizable; FIH, first-in-human; FL, follicular lymphoma; IgG, immunoglobulin G; R/R, relapsed/refractory.

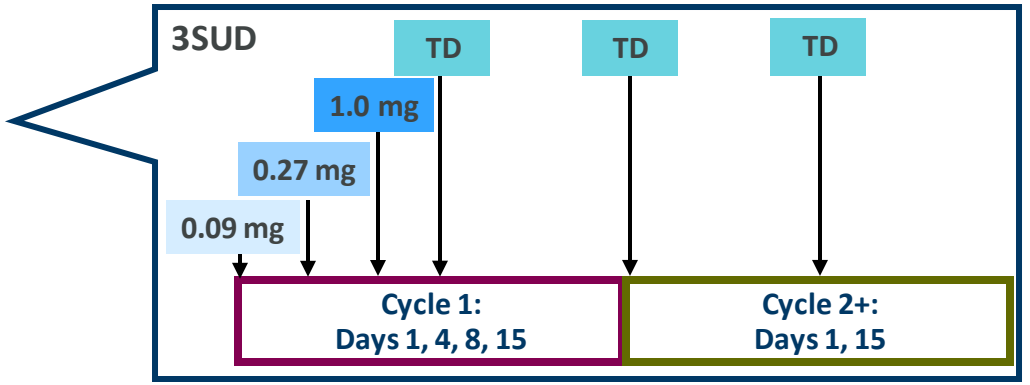
1. Malik-Chaudhry HK, et al. *MAbs*. 2021;313:1890411. 2. Hou JZ, et al. *Blood*. 2024;144(Suppl 1):341. 3. Gaballa S, et al. *Blood*. 2024;144(Suppl 1):868.

Study design



Treatment Schedule

- **Triple step-up dosing (3SUD):**
  Surovatamig (IV infusion) on first cycle: C1D1, C1D4, and C1D8
  - SUD1: 0.09 mg, 0.27 mg, and 1.0 mg – DL1
  - SUD2: 0.27 mg, 1.0 mg, and 2.4 mg – DL2 & DL3
- **Target doses (C1D15): DL1: 2.4 mg; DL2: 7.2 mg; DL3: 15 mg**
  - Cycles 2+: administered every 2 weeks (D1 and D15)
- Patients with high tumor burden (>50% BM blasts or >15,000/mL PB) received dexamethasone (10–24 mg/d) 4–7 days ± 1 dose of vincristine 2 mg prior to D1



BM, bone marrow; C, cycle; D, day; DL, dosing level; mTPI-2, modified Toxicity Probability Interval; IV, intravenous; PB, peripheral blasts; RP2D, recommended phase 2 dose; SUD, step-up dosing; TD, target dose.

Aldoss I et al, EHA 2025

Dose-Dependent Enhanced Efficacy in ITT and CD19-Exposed Populations

	DL1 (SUD: 0.09/0.27/1.0; TD: 2.4 mg) (n=13)	DL2 (SUD: 0.27/1.0/2.4; TD: 7.2 mg) (n=12)	DL3 (SUD: 0.27/1.0/2.4; TD: 15 mg) (n=6)	Total (n=31)
ORR EoC1 (CR/CRi) (ITT)	**6/13 (46)**	**7/12 (58)**	**5/6 (83)**	**18[a]/31 (58)**
CR/CRi MRDneg (local flow [10^{-4}])	5/6 (83)	7/7 (100)	5/5 (100)	17/18 (94)
Disease relapse	2/6 (33)	0/7	0/5	2/18 (11)
ORR (CR/CRi) by prior therapy subgroup[b,c]				
Blinatumomab-exposed	4/9 (44)	1/4 (25)	3/3 (100)	8/16 (50)
CAR-T-exposed	1/3 (33)	2/3 (67)	4/5 (80)	7/11 (64)
Double-exposed	1/3 (33)	1/2 (50)	3/3 (100)	5/8 (63)
Triple-exposed (+Inotuzumab)	0/2 (0)	1/2 (50)	3/3 (100)	4/7 (57)
ORR (CR/CRi) (among patients with EMD)[b]	**2/3 (67)**	**2/2 (100)**	**0/0**	**4/5 (80)**

Values are n/N (%).
[a]Of the 18 patients with CR/CRi, 11 had high disease burden. [b]Median follow-up: 97 days (range, 35-401 days); [c]Prior therapy subgroups are not mutually exclusive.
CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; CRi, complete response with incomplete count recovery; DL, dosing level; EMD, extramedullary disease; ITT, intent-to-treat; MRDneg, minimal residual disease negative; ORR, overall response rate; SUD, step-up dosing; TD, target dose.

Aldoss I et al, EHA 2025

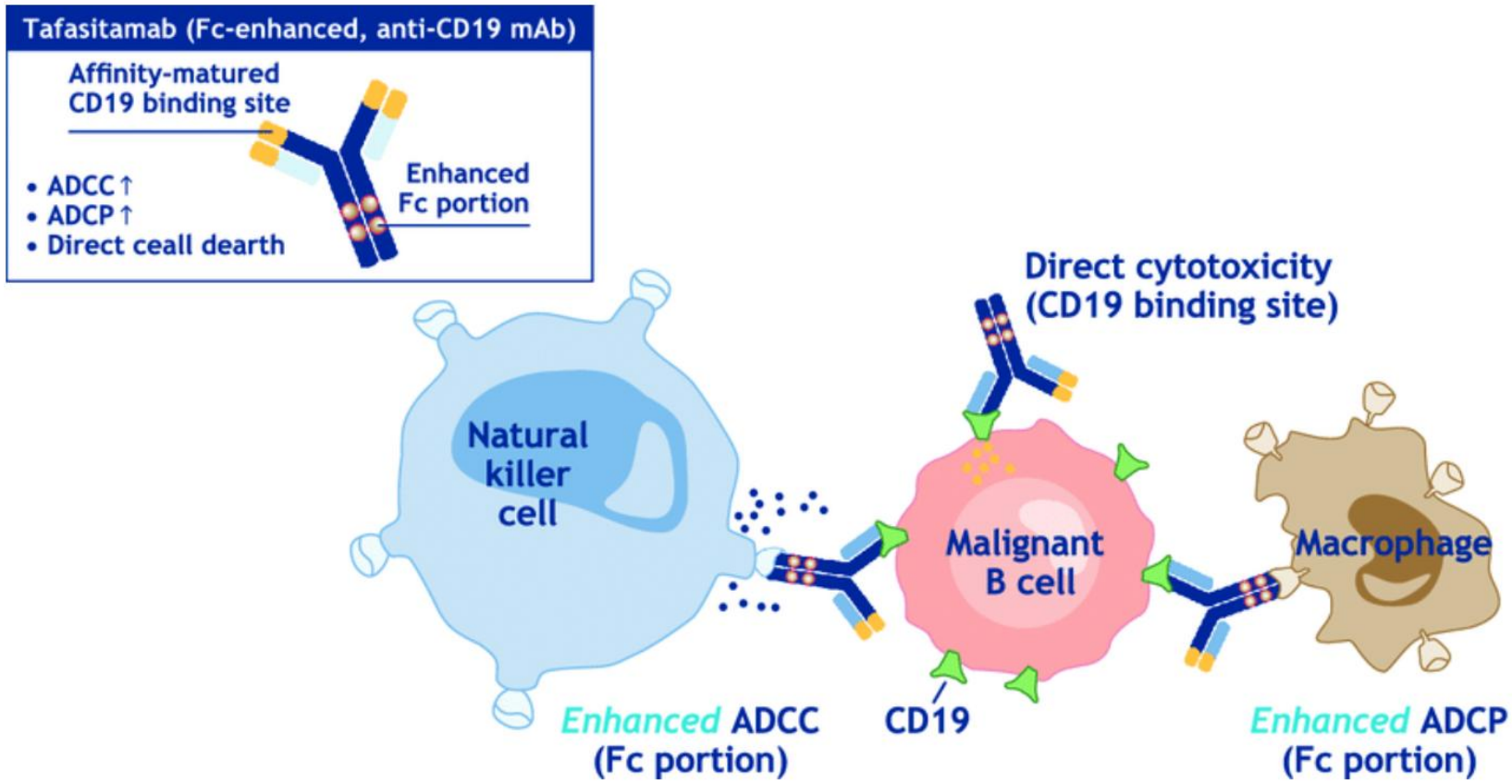
Low Incidence of G2+ Immune-Related Adverse Events (IR-AEs)

	During SUD		After TD		
IR-AEs	During SUD1 n=13	During SUD2 n=18	After 2.4 mg n=10	After 7.2 mg n=12	After 15 mg n=6
CRS Any	4 (31)	13 (72)	3 (30)	3 (25)	-
CRS G2	2 (15)	5 (28)	1 (11)	1 (8)	-
CRS G3	-	1 (6)	-	-	-
ICANS Any	-	4 (22)	-	1 (8)	-
ICANS G2	-	3 (17)	-	-	-
ICANS G3	-	-	-	1 (8)	-

Values are n (%). No G4+ CRS or ICANS events were reported.
Dash (-) indicates no patients with an event.
CRS, cytokine release syndrome; G, grade; ICANS, immune effector cell–associated neurotoxicity syndrome; SUD, step-up dosing; TD, target dose.

Aldoss I et al, EHA 2025

Tafasitamab



A Phase 2a, Single-Arm, Open-Label Study of Tafasitamab, a Humanized, Fc-Modified, Anti-CD19 Antibody, in Patients With Relapsed/Refractory B-Precursor Cell Acute Lymphoblastic Leukemia

Rebecca B. Klisovic, MD[1]; Wing H. Leung, MBBS, PhD[2]; Wolfram Brugger, MD, PhD[3]; Maren Dirnberger-Hertweck, PhD[3]; Mark Winderlich, PhD, MSc[3]; Sumeet V. Ambarkhane, MD, MBBS[3]; and Elias J. Jabbour, MD [4]

Characteristic	Patients (N = 22)
Median age, y (range)	52.0 (16.0-79.0)
Male, n (%)	12 (54.5)
Median time since ALL diagnosis, mo (range)	13.0 (1.7-322.5)
ECOG performance status, No. (%)	
0	7 (31.8)
1	10 (45.5)
2	5 (22.7)
ALL subtype, No. (%)	
Acute pre-B-lymphoblastic leukemia	15 (68.2)
Acute pro-B-lymphoblastic leukemia	2 (9.1)
Mature B-lymphoblastic leukemia	1 (4.5)
Common B-lymphoblastic leukemia	1 (4.5)
Philadelphia-positive B-ALL	2 (9.1)
Other (Pre-B-ALL in CR1)	1 (4.5)
ALL cytogenetics, No. (%)	
t(4;11)/11q23	3 (13.6)
t(9;22)	2 (9.1)
t(1;19)	4 (18.2)
14q32	1 (4.5)
Low hypodiploidy/complex karyotype	1 (4.5)
Other	11 (50)
Median prior lines of therapy, No. (range)	2 (1-8)
Prior allogeneic stem cell transplantation, No. (%)	6 (27.3)
Prior umbilical cord blood transplantation, No. (%)	1 (4.5)
Prior ALL therapies, No. (%)	
Chemotherapy/chemoimmunotherapy[a]	22 (100)
Radiation therapy	2 (9.1)
POMP maintenance	2 (9.1)
Best response to last therapy, No. (%)	
Complete remission	7 (31.8)
Stable disease	4 (18.2)
Progressive disease	6 (27.3)
Unknown	5 (22.7)

TABLE 2. ORRs

Response Rates	Patients (N = 22), No. (%)
ORR (CR, CRi, or PR)	2 (9.1) [95% CI, 1.1-29.2]
CR	1 (4.5)
CRi	1 (4.5)
PR	0 (0)
SD	3 (13.6)
PD	16 (72.7)
No response assessment after 2 cycles (PD)	1 (4.5)

Abbreviations: CI, confidence interval; CR, complete remission; CRi, complete remission with incomplete count recovery; ORR, overall response rate; PD, progressive disease; PR, partial remission; SD, stable disease.

Cancer 2021

Tafasitamab ongoing clinical trials

NCT05453500 Recruiting

Chemotherapy (DA-EPOCH+/-R) and Targeted Therapy (**Tafasitamab**) for the Treatment of Newly-Diagnosed Philadelphia Chromosome Negative B Acute Lymphoblastic **Leukemia**

Conditions

B Acute Lymphoblastic **Leukemia**, Philadelphia Chromosome Negative

Locations

Seattle, Washington, United States

NCT05366218 Recruiting

Tafasitamab (MOR00208) in Pediatric Patients with Relapsed or Refractory Acute B Lineage **Leukemia**

Conditions

ALL, Childhood B-Cell | Acute Lymphocytic **Leukemia** Refractory | Acute Lymphoid **Leukemia** Relapse

Locations

Berlin, Germany
Essen, Germany
Frankfurt, Germany
Hamburg, Germany

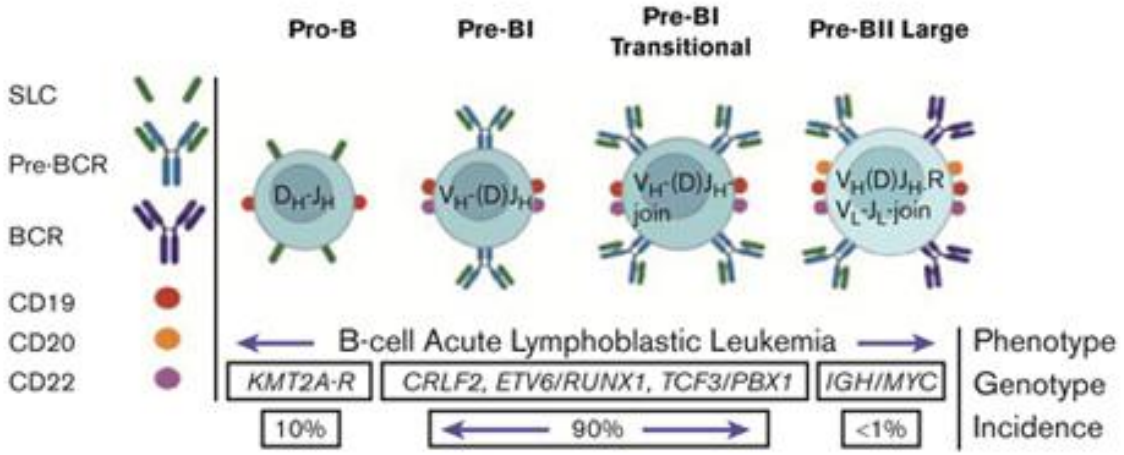
Show all 11 locations

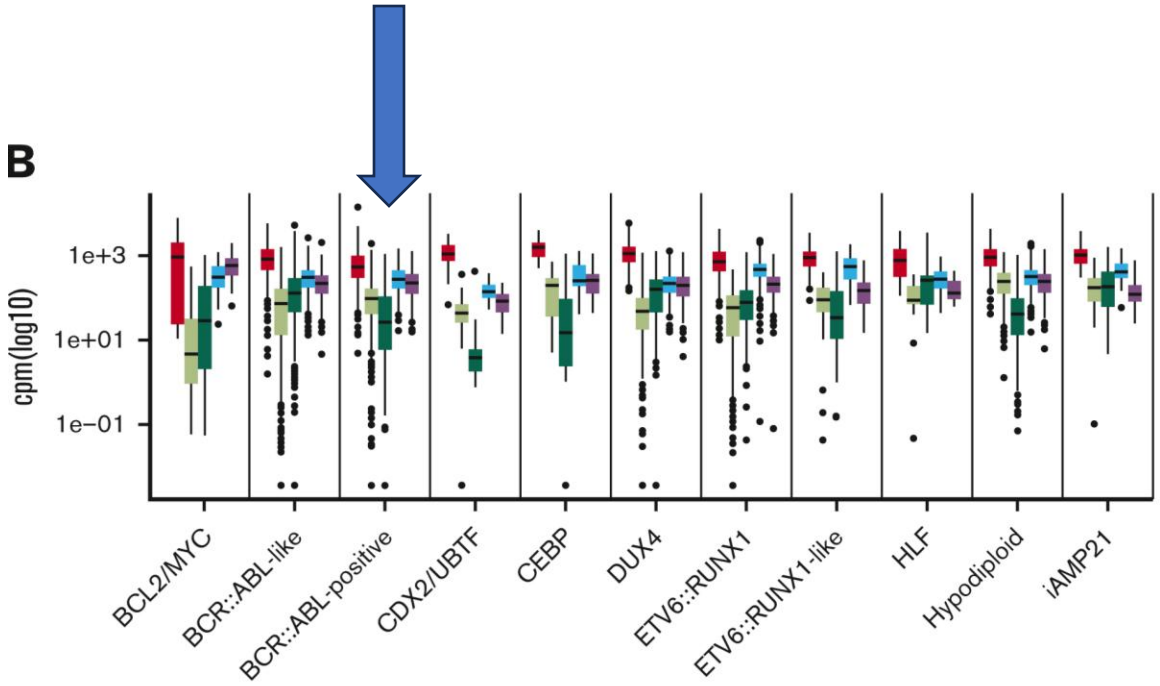
www.clinicaltrials.gov

Antibodies in R/R Ph+ ALL: state of the art

Today	Today in clinical trials	Tomorrow
• Blinatumomab • Inotuzumab Ozogamicin	• s.c. Blinatumomab • Surovatamig • Tafasitamab (US)	• VpreB1 ADC • Trispecific TCE • ???

VpreB1 (CD179a) as a target in B-ALL

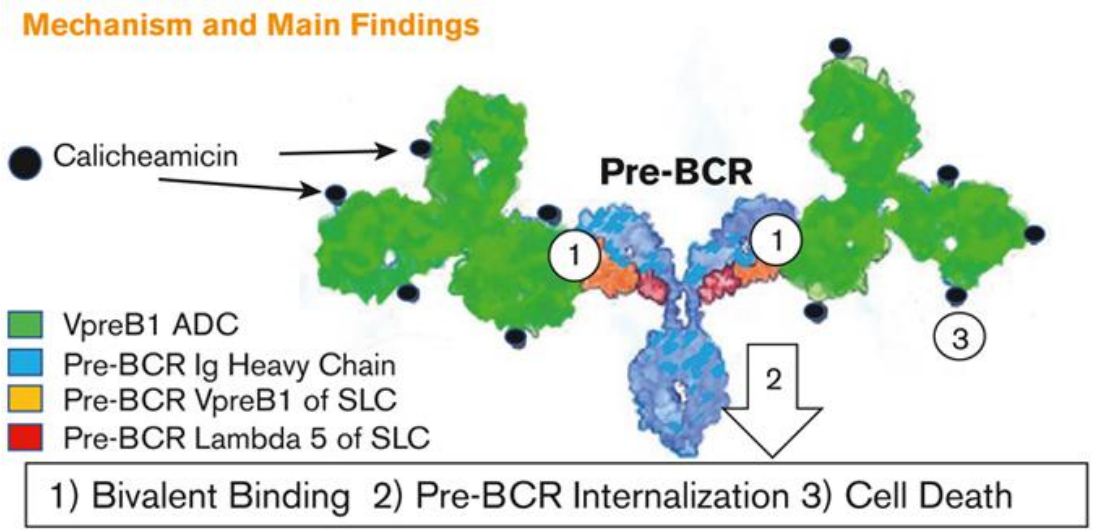


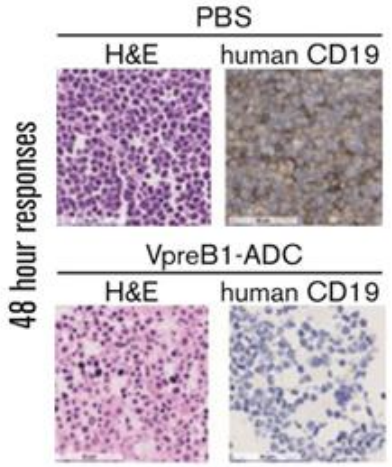


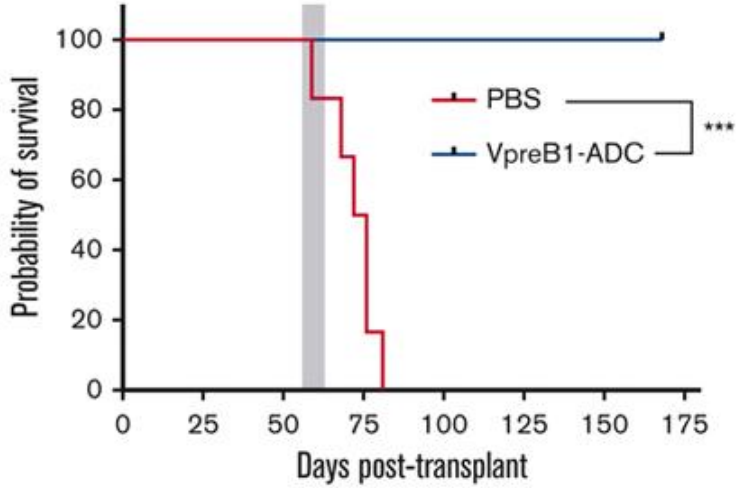
VpreB1 is a unique component of the pre–B-cell receptor and is expressed by most B-ALLs, but not by mature lymphocytes.

Gordon P M et al Blood Neoplasia 2025

VpreB1 (CD179a) as a target in B-ALL



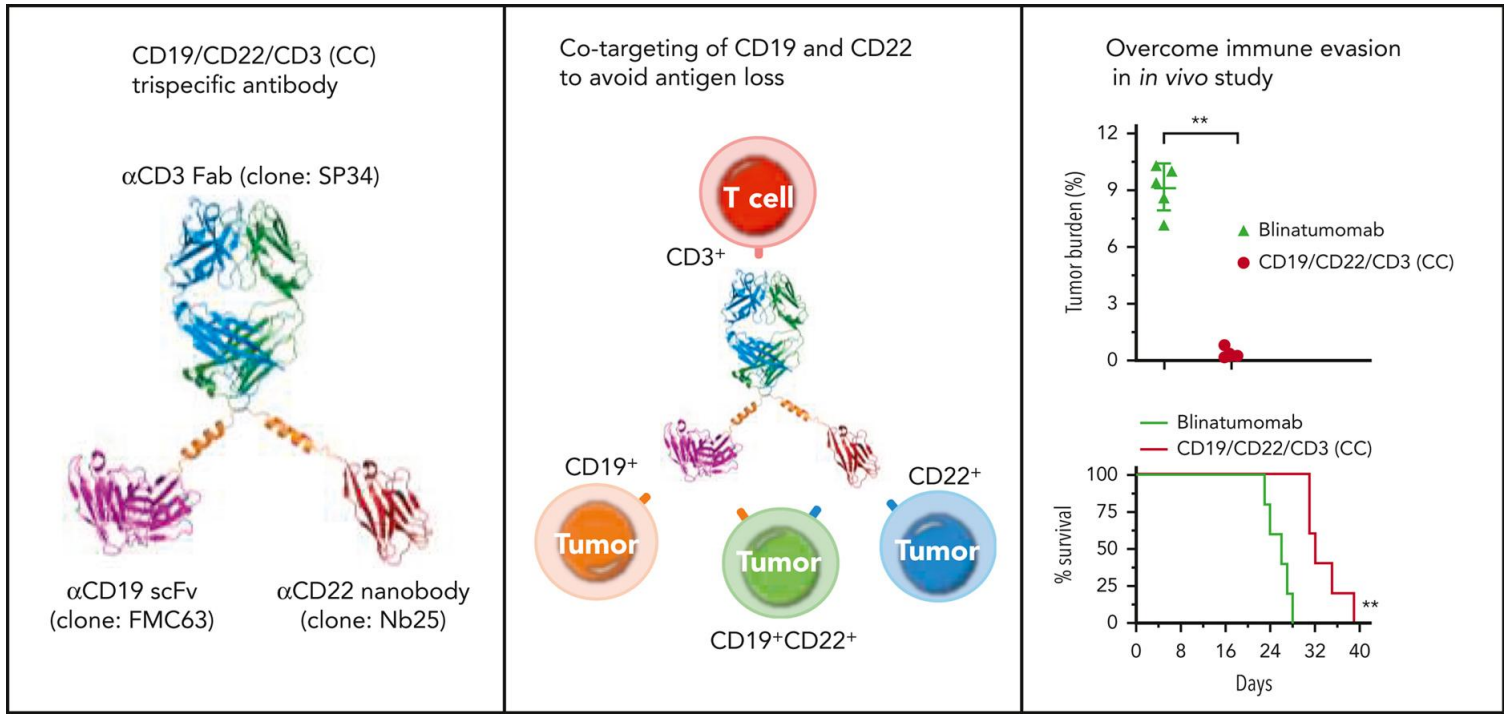




•An ADC targeting VpreB1 demonstrated preclinical efficacy against B-ALL cell lines and patient-derived xenograft models.

Gordon P M et al Blood Neoplasia 2025

CD19/CD22/CD3 trispecific antibody



•A site-specific recombinant strategy guarantees the precise structural and functional optimization of CD19/CD22/CD3 trispecific antibody.

•The optimized CD19/CD22/CD3 exhibited impressive activities in overcoming immune escape and enhancing clearance of B-cell malignancies.

Zhao L et al, Blood 2022

Take home messages and open issues

- **Inotuzumab and blinatumomab paved the way:** they are the first antibody-based therapies to significantly change the treatment of ALL and remain the current standards in the R/R setting. However, duration of response is short.
- **New formulations (s.c. Blinatumomab) and new generations (Surovatamig) are emerging**
- **Trispecific antibodies** are being developed to overcome antigen escape (targeting CD19 and CD22 simultaneously). What about toxicity?
- **Future strategies** will likely rely on combinations (antibodies with CAR-T cells or checkpoint inhibitors) to deepen responses and prolong remission.
- **An earlier use of these approaches**, within combinations treatments, is the first step to improve long term outcome.

Thank you!

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