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OBECABTAGENE AUTOLEUCEL (OBE-CEL, AUTO1) FOR RELAPSED/REFRACTORY ADULT B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (R/R B-ALL): POOLED ANALYSIS OF THE ONGOING FELIX PHASE IB/II STUDY

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Background

- Obecabtagene autoleucel (obe-cel) is an autologous CAR-T cell product, which utilizes a fast off-rate CD19 binder to reduce toxicity and improve persistence[1,2]
- The clinical activity of obe-cel has been evaluated in Phase I studies in R/R pediatric[1] and adult B-ALL,[2] and other B-cell malignancies including B-NHL and B-CLL[3]
- The FELIX study (NCT04404660) is a pivotal study of obe-cel in R/R adult B-ALL; preliminary results from the Phase IIA cohort were recently presented[4]

We present results from the FELIX Phase Ib/II study as a pooled analysis of all patients treated to date with obe-cel, including patients with low leukemic burden* at treatment

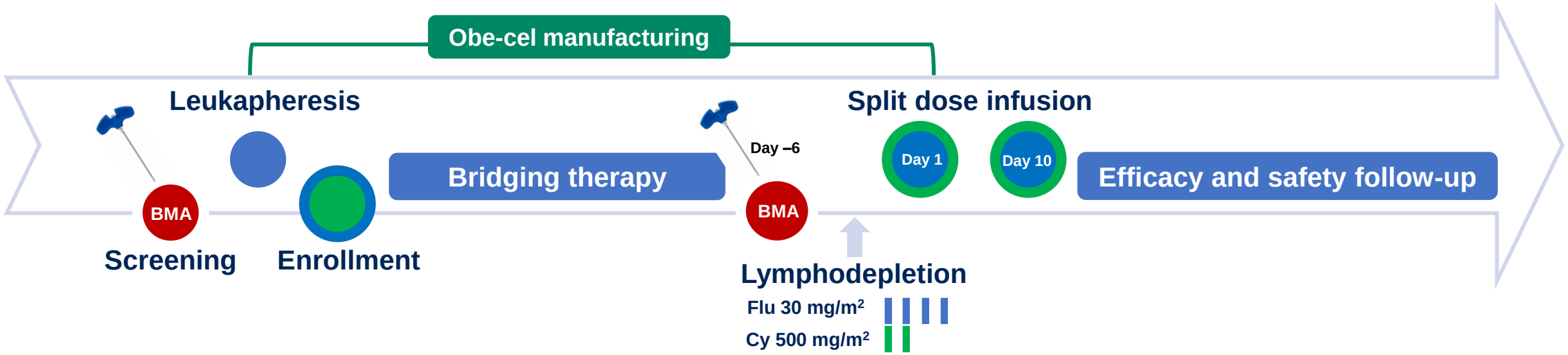
*Defined as morphological remission per investigator assessment (<5% BM blasts without EMD) as measured at screening and lymphodepletion

B-ALL, B-cell acute lymphoblastic leukemia; B-CLL, B-cell chronic lymphocytic leukemia; BM, bone marrow; B-NHL, B-cell non-Hodgkin lymphoma; CAR-T, chimeric antigen receptor T-cell; CD19, cluster of differentiation 19; EMD, extramedullary disease; R/R, relapsed/refractory

1. Ghorashian S, et al. Nat Med 2019;25(9):1408–14; 2. Roddie C, et al. J Clin Oncol 2021;39(30):3352–63; 3. Roddie C, et al. Blood 2022;140(Suppl. 1):7452–3, ASH abstract; 4. Roddie C, et al. J Clin Oncol 2023;41(16 Suppl):7000

FELIX: obe-cel tested in adults with R/R B-ALL

Study design with leukemic burden-adjusted split dosing

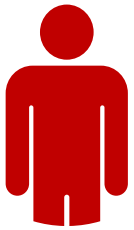


Lymphodepletion → **Leukemia burden-adjusted split dosing based on BM at Day –6**

Lymphodepletion	Leukemia burden-adjusted split dosing based on BM at Day –6		
BM blasts ≤20%	100 × 10^6 CAR-T cells	CRS Grade <2 No ICANS	310 × 10^6 CAR-T cells
BM blasts >20%	10 × 10^6 CAR-T cells		400 × 10^6 CAR-T cells

B-ALL, B-cell acute lymphoblastic leukemia; BM, bone marrow; BMA, bone marrow analysis; CAR-T, chimeric antigen receptor T-cell; CRS, cytokine release syndrome; cy, cyclophosphamide; flu, fludarabine; ICANS, immune effector cell-associated neurotoxicity syndrome; obe-cel, obecabtagene autoleucel; R/R, relapsed/refractory

FELIX: patient eligibility and endpoints



Key eligibility criteria

- R/R adult B-ALL*
- Age ≥18 years

Cohort A
≥5% BM blasts at screening

Cohort B
MRD-positive at screening

Cohort C
Isolated EMD at screening

Selected endpoints‡

- CR/CRi rate per IRRC
- DoR
- EFS§
- OS
- MRD-negativity rate($<10^{-4}$)
- Safety
- CAR-T expansion/persistence
- Manufacture feasibility

*R/R B-ALL: primary refractory; first relapse if first remission ≤12 months; R/R disease after ≥2 lines of systemic therapy; R/R disease after allogeneic transplant; R/R Philadelphia chromosome-positive ALL if intolerant to/failed two lines of any TKI or one line of second-generation TKI, or if TKI therapy is contraindicated

‡Primary endpoints: Cohorts A and C, ORR defined as the proportion of patients achieving CR or CRi; Cohort IIB, the proportion of patients achieving MRD-negative remission ($<10^{-4}$ leukemic cells)

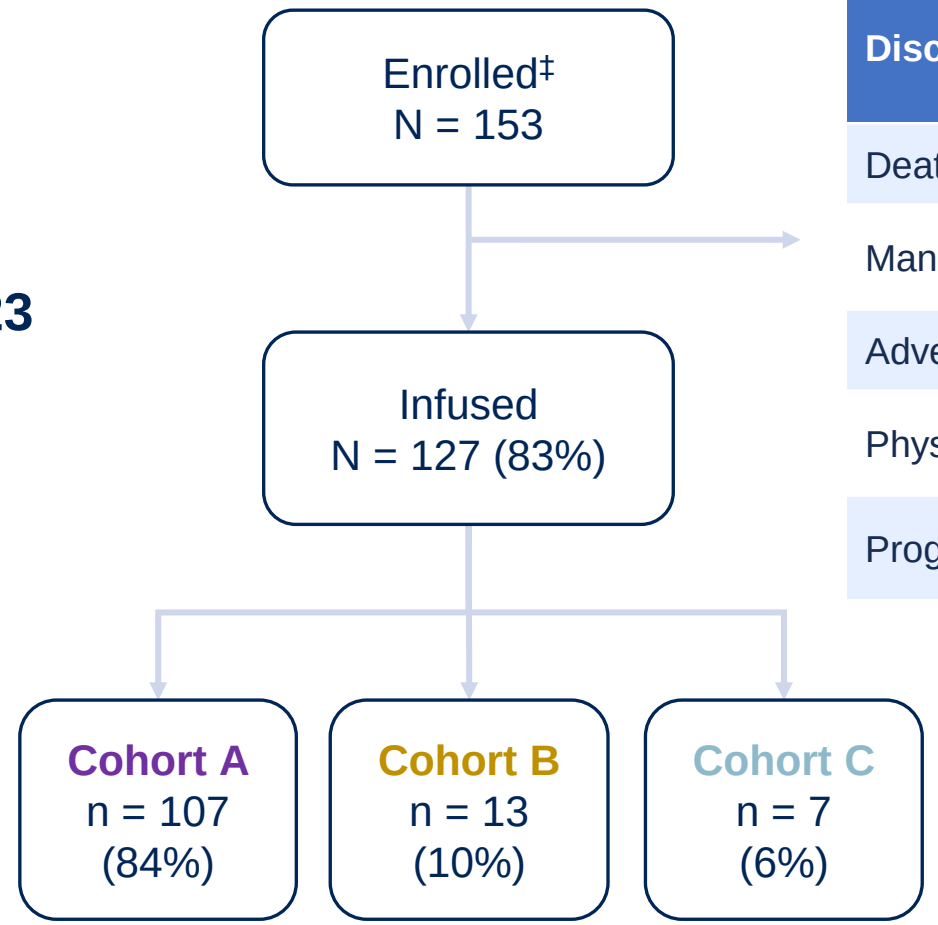
§EFS: the time from date of first infusion to the earliest of treatment failure, relapse, or death from any cause

ALL, acute lymphoblastic leukemia; B-ALL, B-cell acute lymphoblastic leukemia; BM, bone marrow; CAR-T, chimeric antigen receptor T-cell; CR, complete remission; CRi, CR with incomplete hematologic recovery; DoR, duration of remission; EFS, event-free survival; EMD, extramedullary disease; IRRC, Independent Response Review Committee; MRD, measurable residual disease; ORR, overall remission rate; OS, overall survival; R/R, relapsed/refractory; TKI, tyrosine kinase inhibitor

FELIX: patient disposition

127/153 (83%) enrolled patients received obe-cel*

Data cut-off date: September 13, 2023



Discontinued	n (%)
	26 (17)
Death	15 (10)
Manufacturing-related	7 (5)
Adverse event	2 (1)
Physician decision	1 (0.7)
Progressive disease	1 (0.7)

*Seven patients received Dose 1 only
‡All eligibility criteria met and the leukapheresate accepted for manufacturing
obe-cel, obecabtagene autoleucel

FELIX: baseline characteristics

Heavily pre-treated patients (many post-allogeneic SCT)

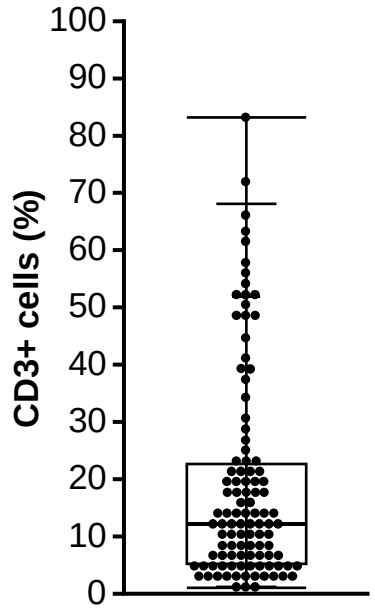
	All treated patients (N = 127)
	n (%)*
Median age, years (range)	47 (20–81)
Male/female	66/61 (52/48)
Asian Black or African American White Unknown Hispanic or Latino	16 (13) 2 (2) 94 (74) 15 (12) 38 (30)
Philadelphia chromosome-positive	36 (28)
Prior therapies, median (range) ≥3 prior lines	2 (1–6) 44 (35)
Prior allogeneic SCT	56 (44)
Prior blinatumomab Prior inotuzumab Prior blinatumomab and inotuzumab	53 (42) 40 (31) 21 (17)
BM blasts % at screening, median (range)	36 (0–100)
EMD at screening	29 (23)

*Data reported are n (%) unless otherwise stated
BM, bone marrow; EMD, extramedullary disease; SCT, stem cell transplant

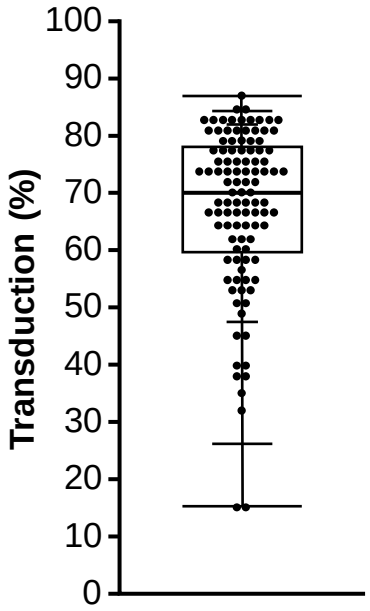
FELIX: obe-cel manufacturing

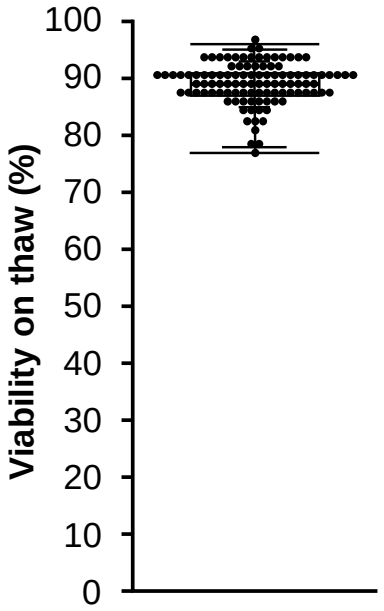
Robust and rapid manufacturing, despite variable starting material

Starting material quality

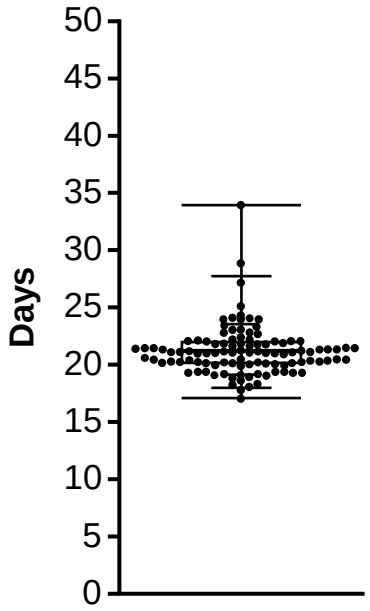


Release parameters





Vein-to-release time



- Obe-cel was released for 95% of patients, with a median time from vein-to-release of 22 days
- Consistent manufacturing was observed, despite leukapheresis from patients with multiple lines of prior therapy (many with prior allogeneic SCT) and high leukemic burden

For more details on obe-cel manufacturing, please see poster 4892

CD3, cluster of differentiation 3; obe-cel, obecabtagene autoleucel; SCT, stem cell transplant

FELIX: remission rate and MRD by status at lymphodepletion

High MRD-negative remission rates were observed after obe-cel

All treated patients (N = 127)

Morphologic disease* (n = 98)

- **74% of patients had CR/CRi (n = 73)**
- **95% of evaluated responders were MRD-negative‡**

No morphologic disease (n = 29)

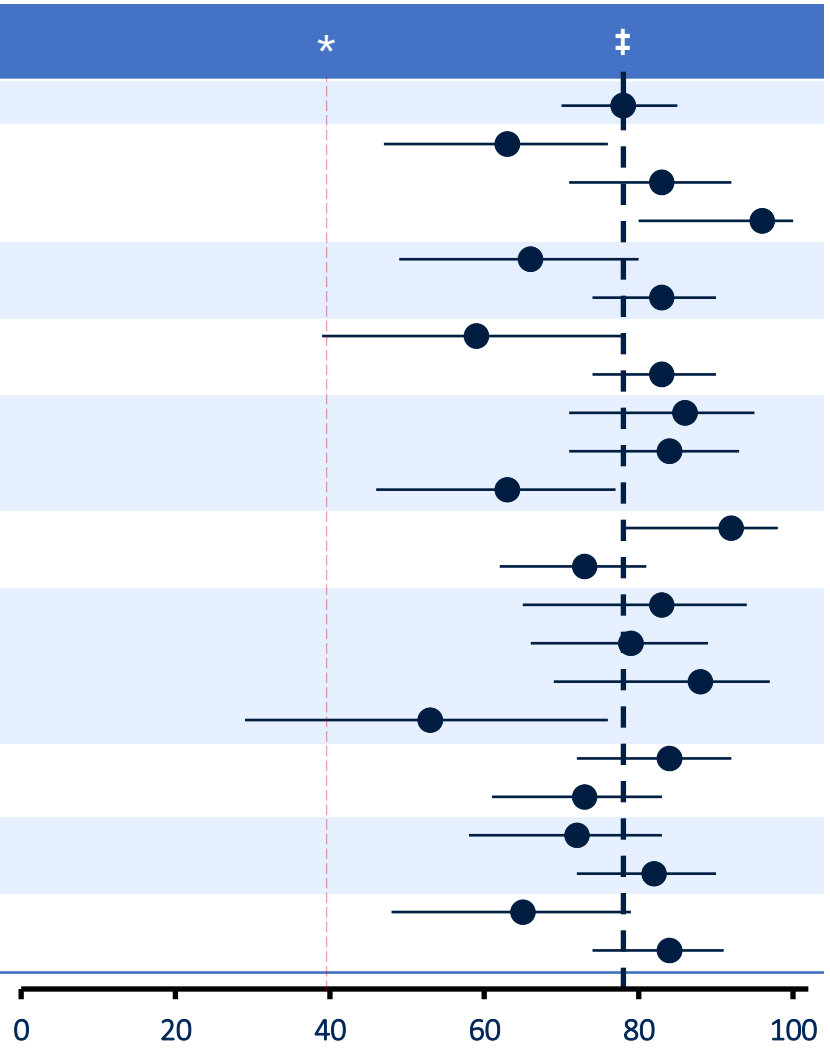
- **100% of evaluable patients were MRD-negative§**

*Morphologic disease defined as ≥5% BM blasts or presence of EMD regardless of BM blast status
‡MRD status available for 64/73 patients, as assessed by NGS or flow cytometry
§MRD status available for 27/29 patients, as assessed by NGS or flow cytometry
BM, bone marrow; CR, complete remission; CRi, CR with incomplete hematologic recovery; EMD, extramedullary disease; MRD, measurable residual disease; NGS, next-generation sequencing; obe-cel, obecabtagene autoleucel

FELIX: CR/CRi subgroup analysis per IRRC

Obe-cel demonstrated high CR/CRi rates across all subgroups

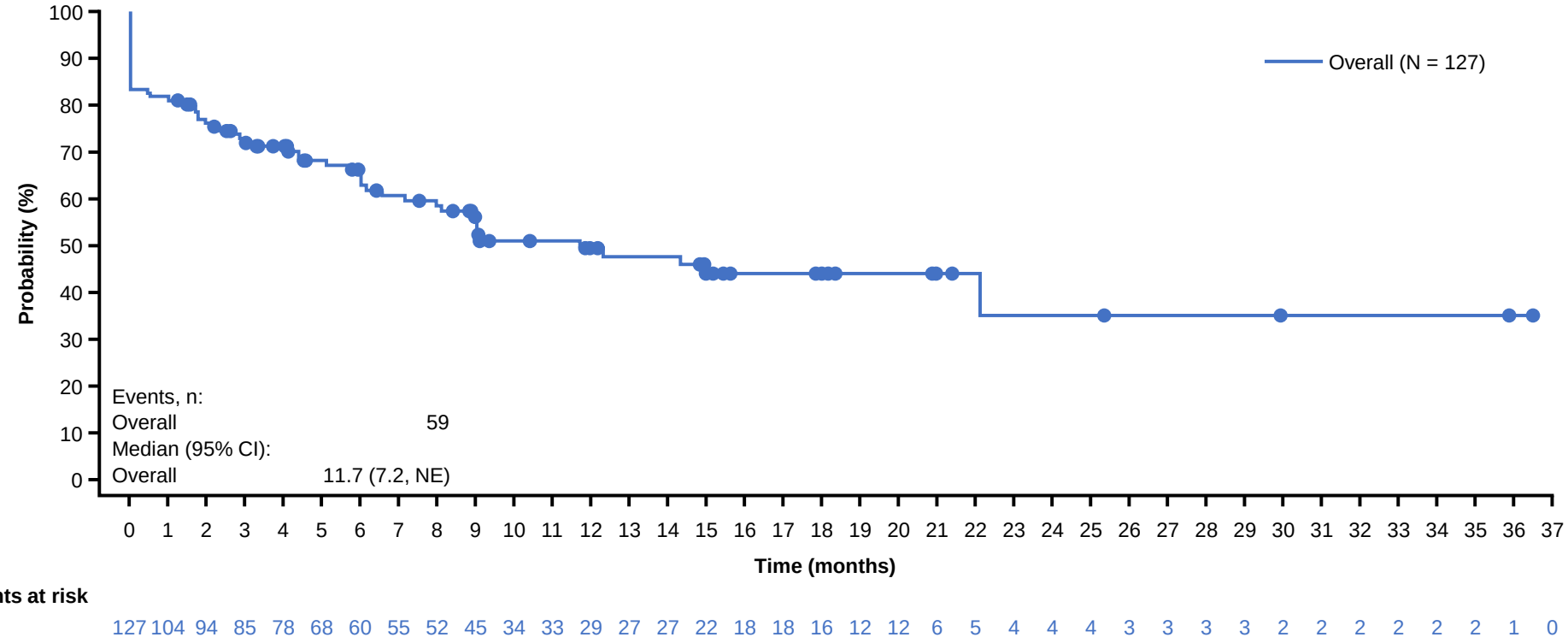
Subgroup		Total, n (%)	ORR, % (95% CI)
Overall		**127 (100)**	**78 (70, 85)**
Age, years	18–39	48 (38)	63 (47, 76)
	40–64	54 (43)	83 (71, 92)
	≥65	25 (20)	96 (80, 100)
Hispanic or Latino	Yes	38 (30)	66 (49, 80)
	No/Unknown	89 (70)	83 (74, 90)
EMD at lymphodepletion	Yes	27 (21)	59 (39, 78)
	No	100 (79)	83 (74, 90)
BM blasts % at lymphodepletion	<5	36 (28)	86 (71, 95)
	≥5−≤75	51 (40)	84 (71, 93)
	>75	40 (31)	63 (46, 77)
Philadelphia chromosome-positive	Yes	36 (28)	92 (78, 98)
	No	91 (72)	73 (62, 81)
Prior therapies	1	30 (24)	83 (65, 94)
	2	53 (42)	79 (66, 89)
	3	25 (20)	88 (69, 97)
	≥4	19 (15)	53 (29, 76)
Prior allogeneic SCT	Yes	56 (44)	84 (72, 92)
	No	71 (56)	73 (61, 83)
Prior blinatumomab	Yes	53 (42)	72 (58, 83)
	No	74 (58)	82 (72, 90)
Prior inotuzumab	Yes	40 (31)	65 (48, 79)
	No	87 (69)	84 (74, 91)



*The red dashed line denotes the Phase IIA null hypothesis (40%)
‡The black dashed line denotes the ORR among all treated patients (ORR=CR+CRi)
BM, bone marrow; CR, complete remission; CRi, CR with incomplete hematologic recovery; EMD, extramedullary disease; IRRC, Independent Response Review Committee; obe-cel, obecabtagene autoleucel; ORR, overall remission rate; SCT, stem cell transplant

FELIX: EFS in all treated patients*

The event-free survival estimate at 12 months was 50%



All treated patients (N = 127)	
Median EFS (95% CI), months	**11.7** (7.2, NE)
6-month EFS (95% CI), %	**65** (56, 73)
12-month EFS (95% CI), %	**50** (39, 59)

Patients at risk

127	104	94	85	78	68	60	55	52	45	34	33	29	27	27	22	18	18	16	12	12	6	5	4	4	4	3	3	3	3	2	2	2	2	2	2	1	0

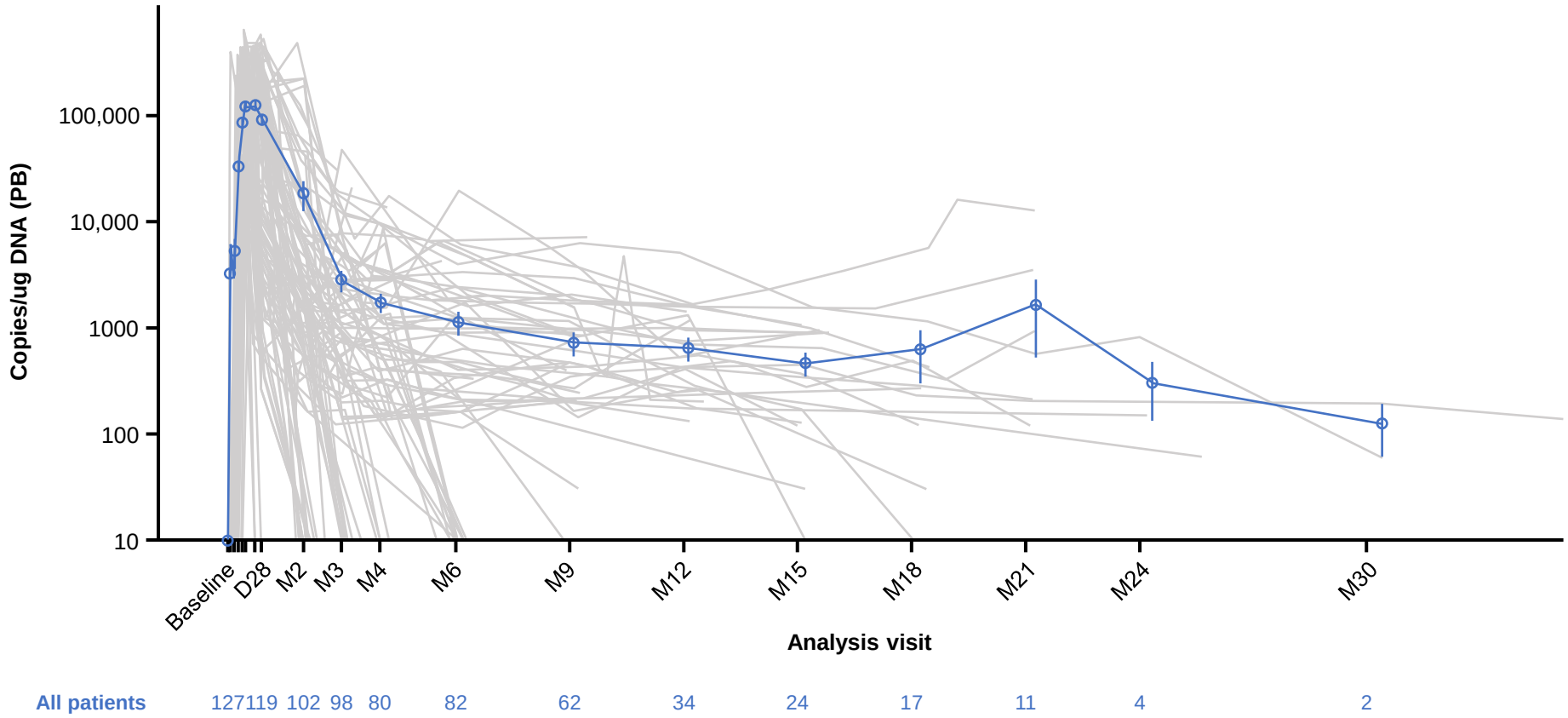
- The median follow-up time was 16.6 months (range: 3.7−36.6 months)
- 17/99 (17%) responders proceeded to SCT while in remission
- A pooled analysis from the ALLCAR19 and FELIX Phase Ib studies will be presented as a poster on Saturday, December 9, 2023 5:30–7:30pm (Roddie C, et al. Abstract 2114)

*Censoring new non-protocol anti-cancer therapies including SCT with disease assessment by IRRC (data cut-off date: September 13, 2023)
Median EFS: ITT population − 9.8 months (95% CI: 5.9, 12.9)
CI, confidence interval; EFS, event-free survival; IRRC, Independent Response Review Committee; ITT, intent-to-treat; NE, not evaluable; obe-cel, obecabtagene autoleucel; SCT, stem cell transplant

FELIX: obe-cel persistence in responders

Obe-cel has high expansion and long-term persistence

	All treated patients (N = 127)
C_{max}, copies/ug Geo-Mean, CV%	110,896 (254)
T_{max}, days Median, range	14 (2–55)
$AUC_{0–28d}$, copies/ug×d Geo-Mean, CV%	1,105,176 (212)



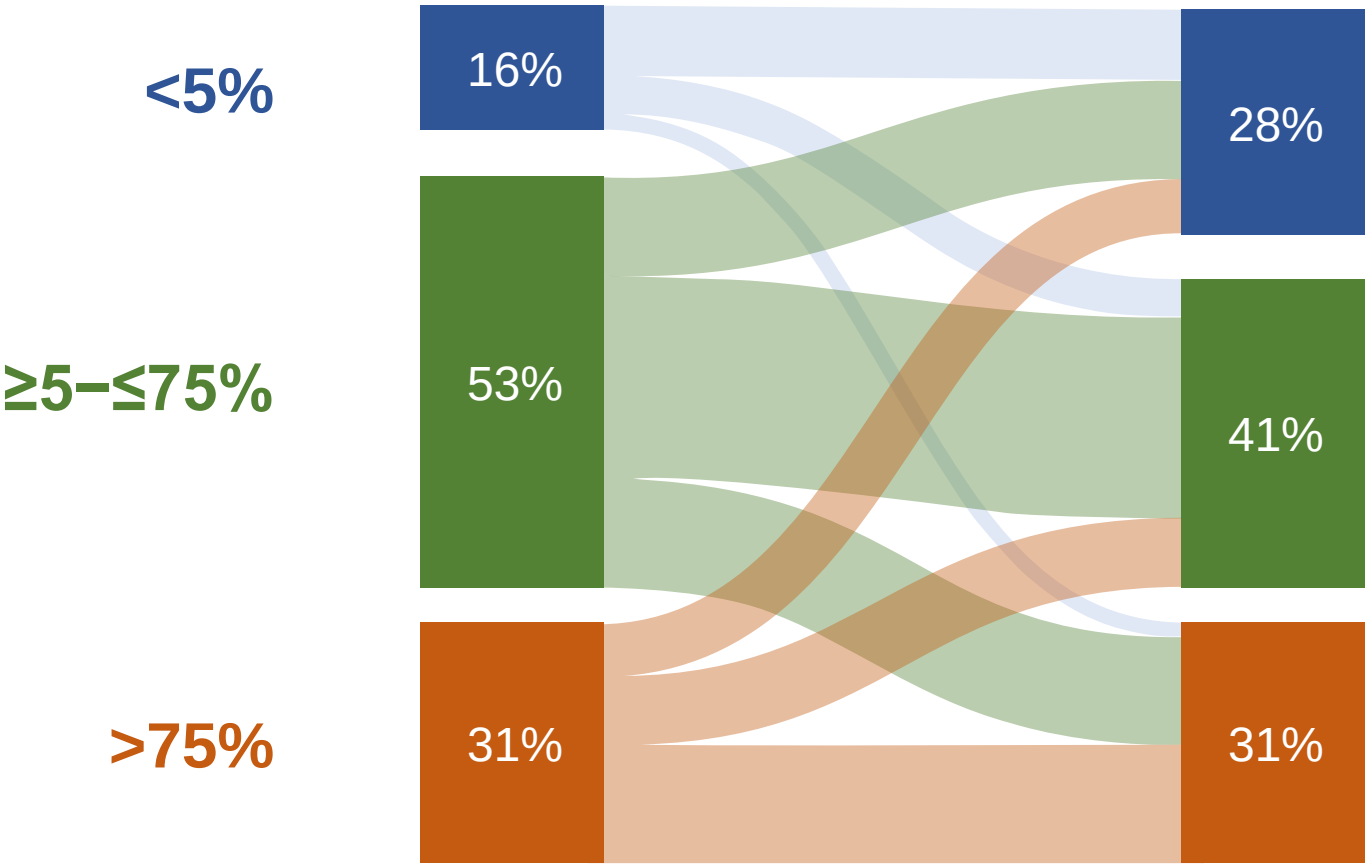
- CAR-T persistence was detected in 72% of ongoing responders at the latest follow-up

AUC, area under the curve; CAR-T, chimeric antigen receptor T-cell; C_{max}, maximum concentration; CV, coefficient of variation; d, day; D, day; Geo, geometric; M, month; obe-cel, obecabtagene autoleucel; PB, peripheral blood; T_{max}, time to maximum concentration

FELIX: leukemic burden in all treated patients

Leukemic burden at screening is not predictive of leukemic burden prior to lymphodepletion

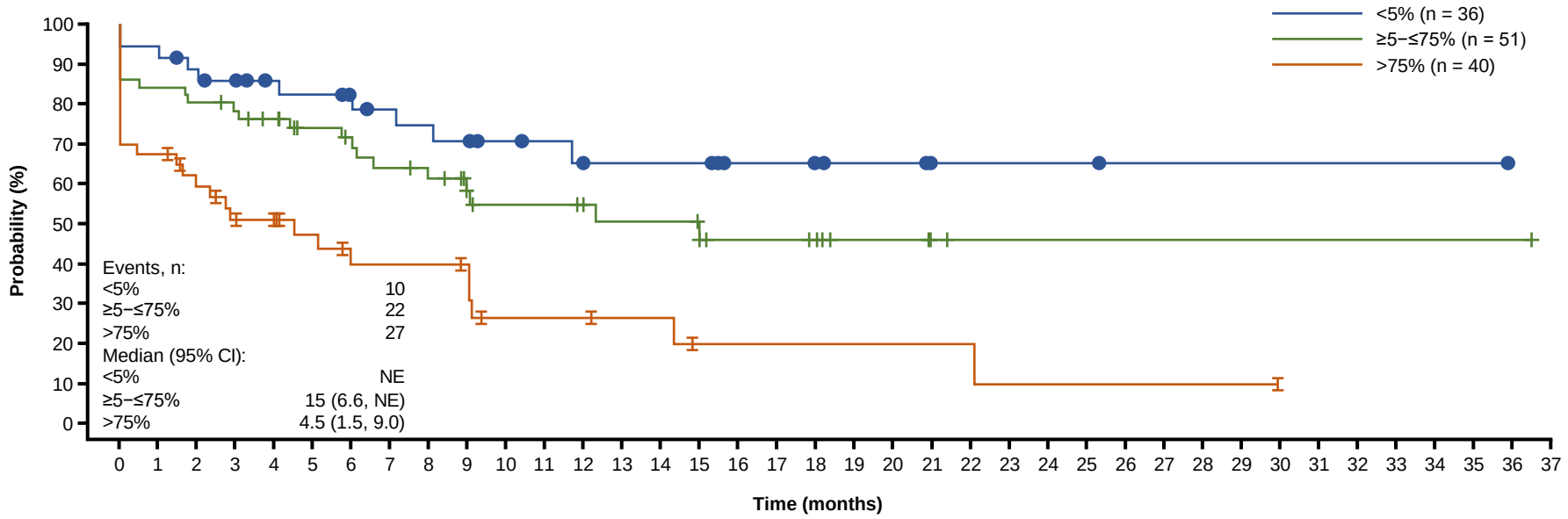
118/127 (93%) patients received bridging therapy*



*Bridging therapy per physician's choice, including inotuzumab ozogamicin
BM, bone marrow

FELIX: EFS by leukemic burden prior to lymphodepletion*

Lower leukemic burden is associated with better outcomes



Patients at risk

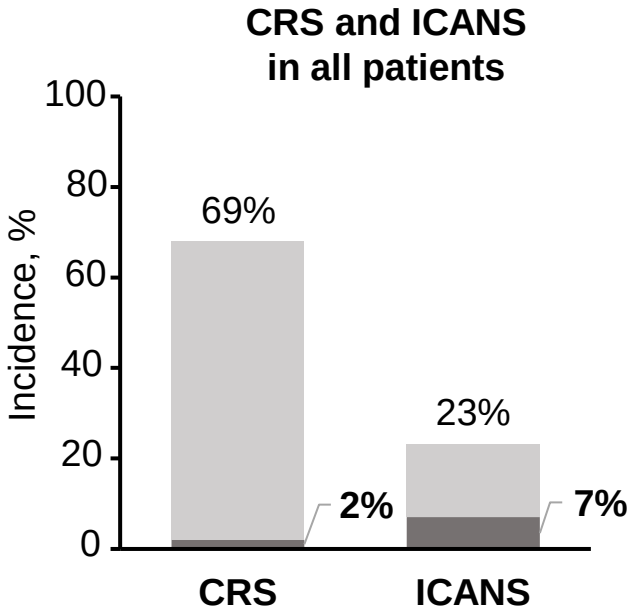
<5% (n = 36)	36	34	31	28	25	24	22	20	19	18	14	13	11	11	11	11	8	8	7	6	6	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	0	0
≥5–≤75% (n = 51)	51	43	41	39	36	31	28	25	23	18	15	15	13	12	12	9	8	8	7	4	4	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
>75% (n = 40)	40	27	22	18	17	13	10	10	10	9	5	5	5	4	4	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0

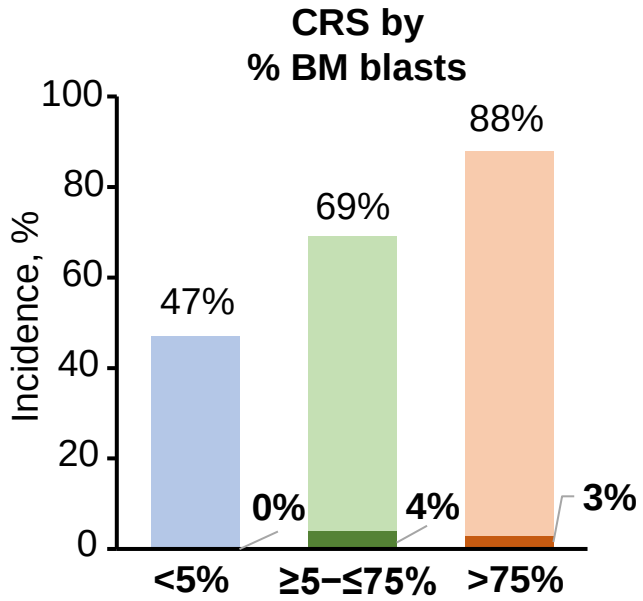
BM blasts % prior to lymphodepletion	<5% (n = 36)	≥5–≤75% (n = 51)	>75% (n = 40)
Median EFS (95% CI), months	**NE**	**15.0** (6.6, NE)	**4.5** (1.5, 9.0)
6-month EFS (95% CI), %	**83** (65, 92)	**72** (57, 82)	**40** (23, 56)
12-month EFS (95% CI), %	**65** (44, 80)	**55** (38, 69)	**27** (12, 44)

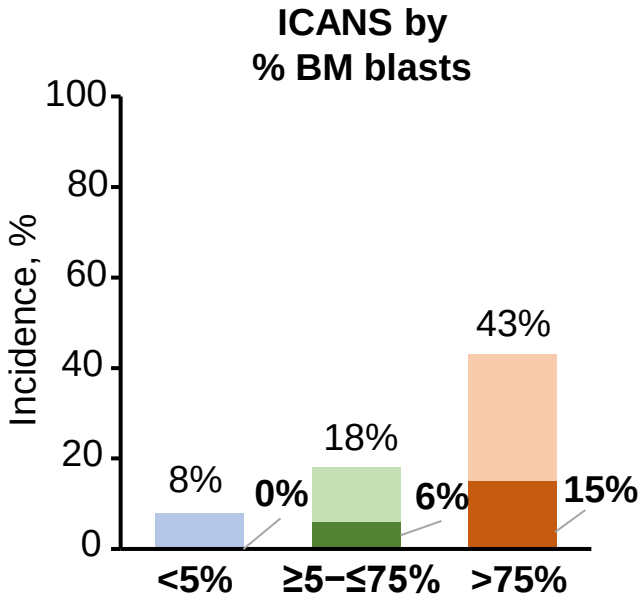
*Censoring new non-protocol anti-cancer therapies including SCT with disease assessment by IRRC (data cut-off date: September 13, 2023)
BM, bone marrow; CI, confidence interval; EFS, event-free survival; IRRC, Independent Response Review Committee; NE, not evaluable; SCT, stem cell transplant

FELIX: CRS and ICANS

Low rates of Grade ≥3 CRS and/or ICANS were observed







Light colors = grade ≤2
Dark colors = grade ≥3

BM blasts % at lymphodepletion

- No grade ≥3 CRS and/or ICANS were observed in patients with <5% BM blasts at lymphodepletion
- Vasopressors were used to treat CRS in 2.4% of patients

BM, bone marrow; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit

FELIX: TEAEs

Favorable safety profile

TEAEs that occurred in ≥20% of patients regardless of causality	All treated patients (N = 127)	
	Any grade, %	Grade ≥3, %
Patients with any TEAE	100	81
CRS	69	2
Pyrexia	29	2
Nausea	26	2
Diarrhea	25	2
Febrile neutropenia	24	24
Anemia	24	21
Headache	24	0
Neutropenia	23	21
ICANS	23	7
Hypotension	22	5
Hypokalemia	21	6
Neutrophil count decreased	20	20

- 15% of patients were admitted to the ICU
- Two deaths were considered treatment-related per investigator assessment: neutropenic sepsis (n = 1); acute respiratory distress syndrome and ICANS (n = 1)

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment emergent adverse event

FELIX: Phase Ib/II conclusions

- Obe-cel successfully manufactured in 95% of leukapheresed patients
- High remission rates independent of leukemic burden at lymphodepletion
- 50% EFS estimate at 12 months, with only 17% of responders proceeding to SCT while in remission
- Favorable safety profile: 2% grade ≥3 CRS and 7% grade ≥3 ICANS
  - Severe toxicity mostly limited to patients with high leukemic burden at lymphodepletion
- Durable remission rates and toxicity inversely correlated with leukemic burden at lymphodepletion
  - Assessment of leukemic burden at lymphodepletion is essential for risk/benefit stratification

Obe-cel is effective treatment for R/R adult B-ALL, with better outcomes observed in patients with lower leukemic burden at lymphodepletion; longer follow-up is required

B-ALL, B-cell acute lymphoblastic leukemia; CRS, cytokine release syndrome; EFS, event-free survival; ICANS, immune effector cell-associated neurotoxicity syndrome; obe-cel, obecabtagene autoleucel; R/R, relapsed/refractory; SCT, stem cell transplant

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