CAR-Team

Update da EHA 2022

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Update da EHA 2022

LARGE B-CELL LYMPHOMA

A MATCHED COMPARISON OF TISAGENLECLEUCEL AND AXICABTAGENE CILOLEUCEL CAR-T CELLS IN RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: A REAL-LIFE LYSA STUDY FROM THE FRENCH DESCAR-T REGISTRY

- In a previous propensity score matching (PSM) analysis, *Bachy et al.* (ASH 2021) reported a prolonged progression-free survival (PFS) but a higher toxicity associated with axi-cel compared with tisa-cel. No OS difference was observed but the follow-up was short (6 months).
- The aim of this study is to report PSM analysis with longer follow-up and with additional patients treated with axi-cel or tisa- cel.
- All patients treated in France with axi-cel or tisa-cel from the 1st July 2018 to the 1st October 2021 and included in the DESCAR-T registry were considered.
- Propensity score matching was used to create a balanced covariate distribution between a cohort of patients treated with tisa-cel and a cohort of patients treated with axi-cel.

Abstract S260 (oral presentation), Bachy E. et al. EHA 2022

A MATCHED COMPARISON OF TISAGENLECLEUCEL AND AXICABTAGENE CILOLEUCEL CAR-T CELLS IN RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: A REAL-LIFE LYSA STUDY FROM THE FRENCH DESCAR-T REGISTRY

RESULTS:

In the 1:1 matched population (N=418, 209 pts treated with tisa-cel and 209 with axi-cel):

- best ORR: 66% vs 80% for pts treated with tisa-cel vs axi-cel (P<0.001)
- CRR: 42% vs 60% for pts treated with tisa-cel vs axi-cel (P<0.001)

After a median FU of 11.7 months (95% CI, 10.5-12.0 months):

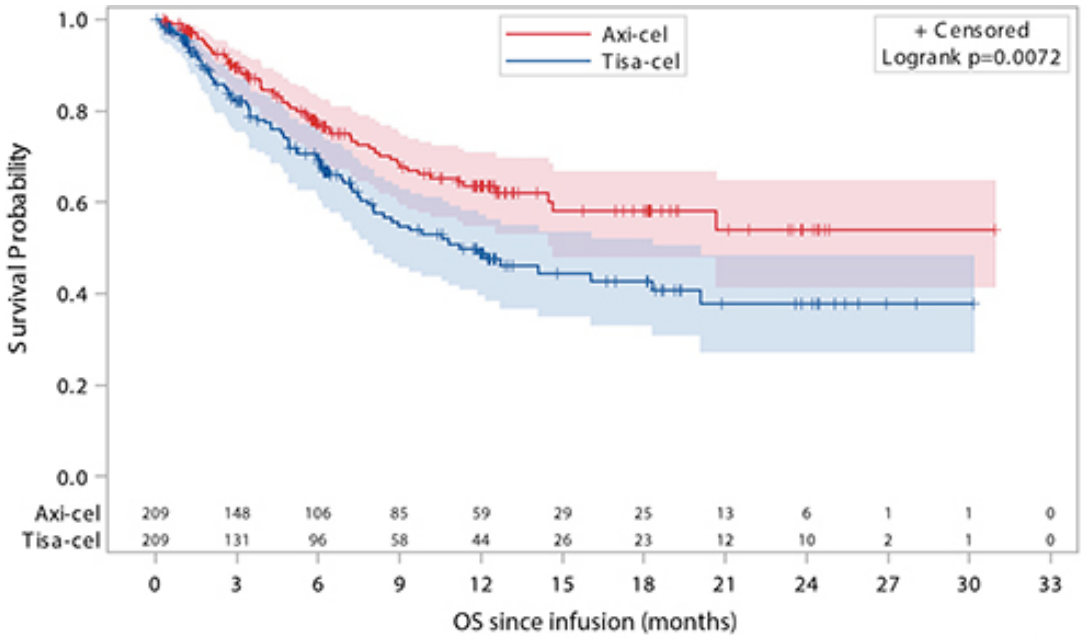
- 1-yr PFS was 33% vs 47% for pts treated with tisa-cel vs axi-cel (HR=1.65, 95% CI 1.26-2.18, P=0.0003)
- 1-yr OS was 49% vs 63% for pts treated with tisa-cel vs axi-cel (HR=1.58, 95% CI, 1.13-2.21; P=0.0072)

TOXICITY:

- Grade 1-2 CRS were significantly more frequent with axi-cel than tisa-cel (P=0.004)
- No significant difference was observed for grade 3 or more CRS (9% vs 5% for tisa-cel and axi-cel, respectively)
- Both all grades and severe (grade ≥3) ICANS were significantly more frequent with axi-cel than tisa-cel (all grade: 48% vs 22% for axi-cel vs tisa-cel, grade ≥3: 14% vs 3% for axi-cel vs tisa-cel)

Abstract S260 (oral presentation), Bachy E. et al. EHA 2022

A MATCHED COMPARISON OF TISAGENLECLEUCEL AND AXICABTAGENE CILOLEUCEL CAR-T CELLS IN RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: A REAL-LIFE LYSA STUDY FROM THE FRENCH DESCAR-T REGISTRY



	No. of Subjects	Event	Censored	Median Survival (95%CL)
Axi-cel	209	28.2 % (59)	71.8 % (150)	Not reached (14.7 ; NA)
Tisa-cel	209	37.8 % (79)	62.2 % (130)	11.2 (8 ; 20.1)

This matched-comparison study, supports:

1. a higher efficacy,

but also

2. higher toxicity

of axi-cel compared with tisa-cel in third or more treatment line for R/R DLBCL.

Abstract S260 (oral presentation), Bachy E. et al. EHA 2022

LISOCABTAGENE MARALEUCEL (LISO-CEL) AS SECOND-LINE THERAPY FOR R/R LARGE B-CELL LYMPHOMA (LBCL) IN PATIENTS NOT INTENDED FOR HSCT: PRIMARY ANALYSIS FROM THE PHASE 2 PILOT STUDY

- PILOT trial (NCT03483103) evaluated liso-cel, an autologous CD19-directed CAR T cell product, as second-line treatment in patients with R/R LBCL not intended for HSCT.

- Eligible patients were:
  - adults with R/R LBCL after first-line treatment who were not deemed candidates for HDCT and HSCT
  - Patients who met ≥ 1 frailty criteria as follows:
    - age ≥ 70 years,
    - ECOG PS of 2,
    - diffusing capacity for carbon monoxide ≤ 60%,
    - left ventricular ejection fraction < 50%,
    - creatinine clearance < 60 mL/min or
    - AST/ALT> 2 × the upper limit of normal.

- Primary endpoint: objective response rate (ORR) per independent review committee;
- All patients had ≥ 6 months of follow-up from first response. Median follow-up 12.3 mo (1.2-26.5).

Abstract S258 (oral presentation), Sehgal A. et al. EHA 2022

LISOCABTAGENE MARALEUCEL (LISO-CEL) AS SECOND-LINE THERAPY FOR R/R LARGE B-CELL LYMPHOMA (LBCL) IN PATIENTS NOT INTENDED FOR HSCT: PRIMARY ANALYSIS FROM THE PHASE 2 PILOT STUDY

Characteristics of liso-cel treated patients (N=61):

- Median age: 74 years (range 53–84) with 79% of patients ≥ 70y;
- 69% of patients had at least 1 frailty criteria;
- ECOG PS of 2: 26%;
- Hematopoietic cell Transplantation-specific Comorbidity Index score ≥ 3: 44%;
- Refractory to first line chemotherapy: 54%;
- Relapsed within 12 months: 21%;
- Relapsed after 12 months: 25%;
- Bridging chemotherapy: 51%

Abstract S258 (oral presentation), Sehgal A. et al. EHA 2022

LISOCABTAGENE MARALEUCEL (LISO-CEL) AS SECOND-LINE THERAPY FOR R/R LARGE B-CELL LYMPHOMA (LBCL) IN PATIENTS NOT INTENDED FOR HSCT: PRIMARY ANALYSIS FROM THE PHASE 2 PILOT STUDY

Efficacy outcome

Table. Efficacy outcomes per IRC assessment

Efficacy, IRC assessed (Lugano 2014 criteria)	Liso-cel treated (N = 61)
ORR, n (%) [95% CI]	49 (80) [68.2–89.4]
CR rate	33 (54) [40.8–66.9]
DOR, median (95% CI), months	12.1 (6.2–NR)
Median (range) follow-up, months	15.5 (0–23.0)
DOR for patients achieving CR, median (95% CI), months	21.7 (12.1–NR)
DOR for patients achieving PR, median (95% CI), months	2.1 (1.4–3.3)
PFS, median (95% CI), months	9.0 (4.2–NR)
Median (range) follow-up, months	13.0 (0.7–23.9)
OS, median (95% CI), months	NR (17.3–NR)
Median (range) follow-up, months	17.6 (1.2–35.4)
Probability of OS at 1 year (95% CI), %	70.0 (56.1–80.3)

CR, complete response; DOR, duration of response; IRC, independent review committee; liso-cel, lisocabtagene maraleucel; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response.

Safety

Most frequent TEAE:

- neutropenia in 51% of pts,
- fatigue in 39% of pts,
- grade ≥ 3 TEAEs in 79% of pts,
- grade 5 TEAEs in 2 pts (COVID-19).

CRS:

- any grade in 38% of pts,
- grade 3 CRS in 1 patient (2%); no grade 4/5 CRS.

NEs:

- any grade in 31% of pts;
- grade 3 in 5% of pts; no grade 4/5 NEs.

In the PILOT study, liso-cel as II line treatment in patients with LBCL who met ≥ 1 frailty criteria and for whom HSCT was not intended, demonstrated substantial and durable overall and complete responses, with no new safety concerns.

Abstract S258 (oral presentation), Sehgal A. et al. EHA 2022

CLINICAL AND PATIENT-REPORTED OUTCOMES IN A PHASE 3 STUDY OF AXICABTAGENE CILOLEUCEL (AXI-CEL) VS STANDARD-OF-CARE IN ELDERLY PATIENTS WITH RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA (ZUMA-7)

- In the global Phase 3, randomized, ZUMA-7 study, axi-cel significantly improved event-free survival (EFS; HR 0.398, P<0.0001; median 8.3 vs 2 months) compared with second-line SOC in R/R LBCL (*Locke FL, et al. N Engl J Med)*

- Patient reported outcomes (PRO) instruments [EORTC QLQ-C30 and the EQ-5D-5L visual analog scale (VAS)], were administered at baseline (prior to treatment), Day 50, Day 100, Day 150, and Month 9, then every 3 months up to 24 months or time of EFS event, whichever occurred first.

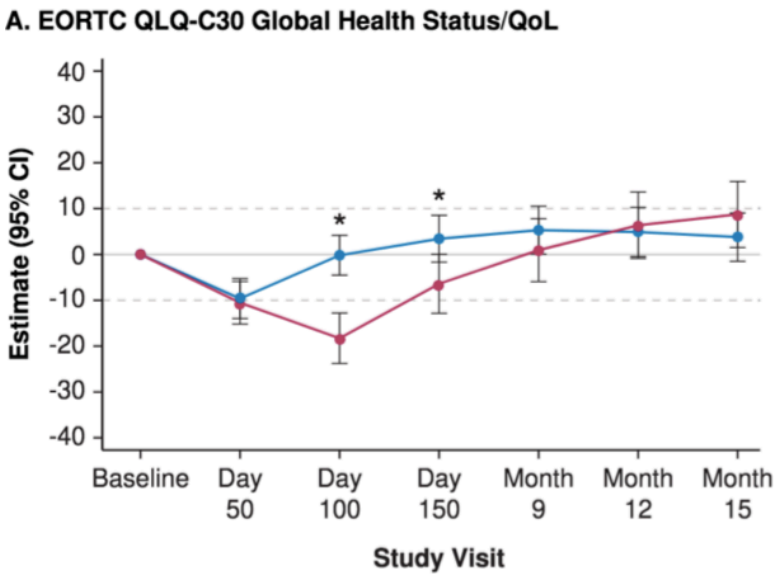
- The quality-of-life analysis set, included all patients who had a baseline PRO and ≥1 completed measure at Day 50, 100, or 150. A clinically meaningful change was defined as 10 points for each EORTC QLQ-C30 score and 7 points for EQ-5D-5L VAS score.

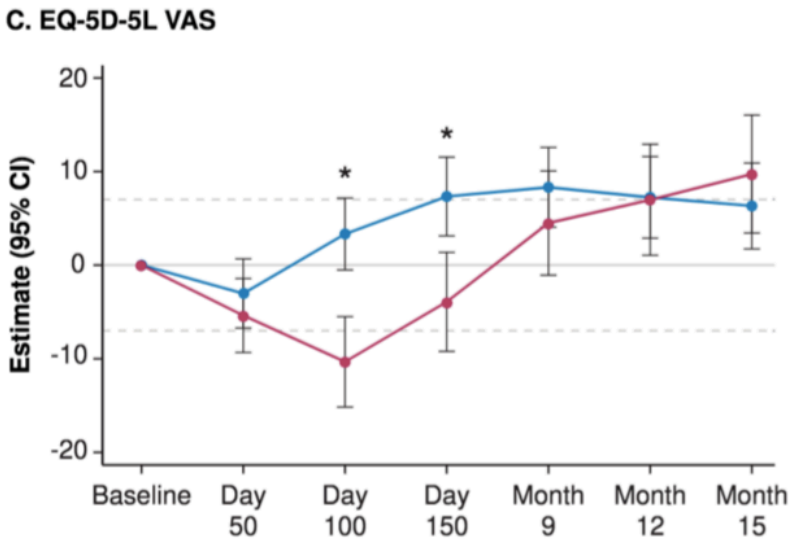
- The authors report results of a planned subgroup analysis of the ZUMA-7 study assessing outcomes, including PROs of second-line axi-cel vs SOC in patients aged ≥65 years

Abstract S211 (oral presentation), Sureda A. et al. EHA 2022

CLINICAL AND PATIENT-REPORTED OUTCOMES IN A PHASE 3 STUDY OF AXICABTAGENE CILOLEUCEL (AXI-CEL) VS STANDARD-OF-CARE IN ELDERLY PATIENTS WITH RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA (ZUMA-7)

- In the QoL analysis (46 axi-cel and 42 SOC patients) there were statistically significant and clinically meaningful differences in mean change of scores from baseline at Day 100 favoring axi-cel for EORTC QLQ-C30 Global Health (P<0.0001, fig. A) Physical Functioning (P=0.0019) and EQ-5D-5L VAS (P<0.0001, fig. C).
- For all 3 domains, scores also favored (P<0.05) axi-cel over SOC at Day 150.

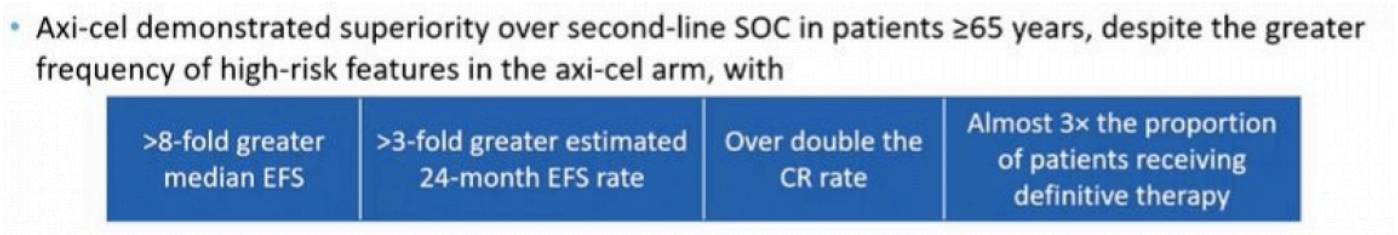




Abstract S211 (oral presentation), Sureda A. et al. EHA 2022

CLINICAL AND PATIENT-REPORTED OUTCOMES IN A PHASE 3 STUDY OF AXICABTAGENE CILOLEUCEL (AXI-CEL) VS STANDARD-OF-CARE IN ELDERLY PATIENTS WITH RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA (ZUMA-7)

- Axi-cel demonstrated superiority over second-line SOC in patients ≥65 years with significantly improved EFS and a manageable safety profile (*Locke FL, et al. N Engl J Med).*

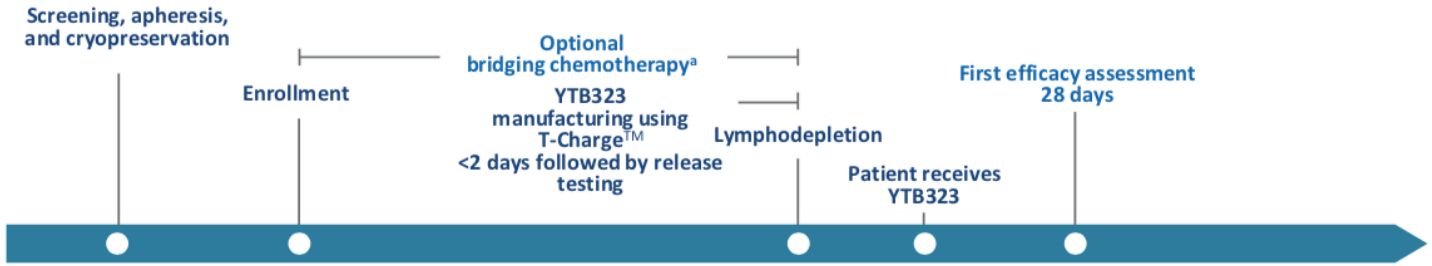


- Axi-cel also showed meaningful improvement in quality of life over SOC, measured by multiple validated PRO instruments, with suggested faster recovery to pretreatment quality of life.
- The superior clinical outcomes and patient experience with axi-cel over SOC should help inform treatment choices in second-line R/R LBCL for patients ≥65 years.

Abstract S211 (oral presentation), Sureda A. et al. EHA 2022

PHASE I STUDY OF YTB323, A CHIMERIC ANTIGEN RECEPTOR CAR-T CELL THERAPY MANUFACTURED USING T-CHARGE™, IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

- YTB323 is an autologous CD19-directed CAR T-cell (II generation, 41BB) generated by the innovative T-Charge™ platform, which demonstrates high potency, preserves T-cell stemness in the final product, and takes <2 d to manufacture.
- T-Charge™ is expected to prolong CAR-T cell persistence and yield higher response rates and durability.
- Here are reported the preliminary results of the Phase I, first-in-human, trial.



Key eligibility criteria	Study treatment	End points
• ≥18 years of age • Measurable disease at enrollment • ECOG PS 0-1 • Relapsed/refractory disease • ≥2 lines of prior therapies, including/or autologous HSCT	• Lymphodepleting chemotherapy: fludarabine (30 mg/m^2 IV daily ×3 days) + cyclophosphamide (500 mg/m^2 IV daily ×3 days) • YTB323 dose levels (single IV dose): – DL1, 2.5×10^6 CAR+ cells – DL2, 12.5×10^6 CAR+ cells – DL3, 25×10^6 CAR+ cells – DL4, 40×10^6 CAR+ cells	**Primary:** Incidence of DLTs[b] and safety to determine a recommended dose **Secondary:** Cellular kinetics, ORR, DOR, OS

Abstract S212 (oral presentation), Dickinson M. et al. EHA 2022

PHASE I STUDY OF YTB323, A CHIMERIC ANTIGEN RECEPTOR CAR-T CELL THERAPY MANUFACTURED USING T-CHARGE™, IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

45 pts with r/r DLBCL treated with YTB323 and followed for a median of 10 months (0.3-29 months) were enrolled.

Baseline Variable	YTB323 Infused (N=45)
Median age (range), years	64.8 (41-79)
Race, n (%)	
Asian	1 (2.2)
White	42 (93.3)
Histology, n (%)	
DLBCL	43 (95.6)
Transformed lymphoma/other	2 (4.4)
Elevated LDH (>ULN),[a] n (%)	25 (55.6)
Prior HSCT, n (%)	13 (28.9)
No. prior lines of therapy, n (%)	
2	30 (66.7)
≥3	15 (33.3)
Time since most recent relapse/progression to YTB323, median (range), months	2.8 (1.4-81.8)
Received bridging therapy,[b] n (%)	30 (66.7)

Abstract S212 (oral presentation), Dickinson M. et al. EHA 2022

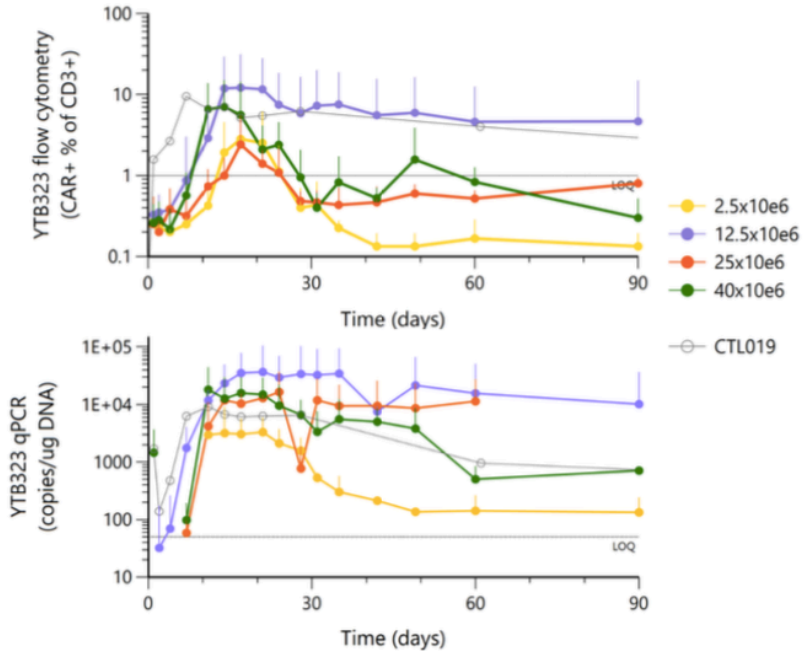
PHASE I STUDY OF YTB323, A CHIMERIC ANTIGEN RECEPTOR CAR-T CELL THERAPY MANUFACTURED USING T-CHARGE™, IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

Table 1: response at different DL

	YTB323 2.5×10⁶ (N=4)	YTB323 12.5×10⁶ (N=26)	YTB323 25×10⁶ (N=6)	YTB323 40×10⁶ (N=6)
	n (%)	n (%)	n (%)	n (%)
Best overall response				
CR	3 (75)	**17 (65)**	4 (67)	4 (67)
CR excluding patients in CR before YTB323[a]	1/2 (50)	**14/23 (61)**	4/6 (67)	3/5 (60)
PR	0	**1 (4)**	0	0
Overall response rate[b]	3 (75)	**18 (69)**	4 (67)	4 (67)
[95% CI][c]	[19.4-99.4]	**[48.2-85.7]**	[22.3-95.7]	[22.3-95.7]

- ORR across all dose levels at Day 28 was 69%

Fig. A



- Responses appear durable, with a median DoR not reached
- Expansion increased from DL1 to DL2; there were no further increases at higher doses
- Time to peak YTB323 expansion was delayed compared to tisagenlecleucel (16 days at DL2 vs 9 days in JULIET, by flow cytometry. Fig. A)

Abstract S212 (oral presentation), Dickinson M. et al. EHA 2022

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Toxicity

CRS	Treated Patients (N=45)			
	YTB323 2.5×10⁶ (N=4)	YTB323 12.5×10⁶ (N=28)	YTB323 25×10⁶ (N=7)	YTB323 40×10⁶ (N=6)
CRS,[a] n (%)	1 (25)	**10 (36)**	2 (29)	2 (33)
Grade 1/2	1 (25)	**9 (32)**	2 (29)	2 (33)
Grade 3/4	0	**1 (4)**	0	0
Management, n (%)				
Tocilizumab	0	**7 (70)**	1 (50)	0
Corticosteroids	0	**3 (30)**	0	0
Vasopressors	0	**1 (10)**	0	0
Admitted to ICU, n (%)	0	**3 (30)**	0	0
Time to onset, days	9	**10 (1-17)[b]**	7, 36	2, 9
Time from onset to resolution, days	5	**4 (1-18)[b]**	5, 10	5, 7

ICANS	Treated Patients (N=45)			
	YTB323 2.5×10⁶ (N=4)	YTB323 12.5×10⁶ (N=28)	YTB323 25×10⁶ (N=7)	YTB323 40×10⁶ (N=6)
ICANS,[a] n (%)	0	**3 (10.7)**	0	2 (33.3)
Grade 1/2	0	**1 (3.6)**	0	2 (33.3)
Grade 3/4	0	**2 (7.1)**	0	0
Management, n (%)	–	**3 (100)**	–	1 (50)
Dexamethasone	–	**2 (66.7)**	–	1 (50)
Methylprednisolone	–	**1 (33.3)**	–	0
Anakinra	–	**1 (33.3)**	–	0
Time to onset, days	–	**10, 16, 28**	–	6, 28
Time from onset to resolution, days	–	**11, 16, 24**	–	1, 36

AEs	Treated Patients (N=45)			
Adverse Events (AE),[a] n (%)	YTB323 2.5×10⁶ (N=4)	YTB323 12.5×10⁶ (N=28)	YTB323 25×10⁶ (N=7)	YTB323 40×10⁶ (N=6)
Any AE				
Any grade	4 (100)	**27 (96)**	6 (86)	6 (100)
Grade ≥3	4 (100)	**24 (86)**	6 (86)	6 (100)
Dose-limiting toxicities	0	**2 (7)[c]**	0	0
Death[b]	2 (50)	**4 (14)**	0	2 (33)
Related to YTB323	0	**0**	0	0
Infections				
Any grade	2 (50)	**6 (21)**	2 (29)	3 (50)
Grade ≥3	1 (25)	**4 (14)**	0	2 (33)

Abstract S212 (oral presentation), Dickinson M. et al. EHA 2022

PHASE I STUDY OF YTB323, A CHIMERIC ANTIGEN RECEPTOR CAR-T CELL THERAPY MANUFACTURED USING T-CHARGE™, IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

- T-CHARGE™ is a novel platform that preserves T-cell stemness in the product and utilizes a rapid manufacturing process.
- Preliminary results of phase 1 study of YTB323 are encouraging, demonstrate early efficacy and a manageable safety profile in R/R DLBCL.
- 12.5×10^6 CAR+ viable T cells is the recommended dose for Phase III studies, based on the CR rate, favorable safety profile, and cellular kinetics

Abstract S212 (oral presentation), Dickinson M. et al. EHA 2022

CAR T-CELLS ASSOCIATED ACUTE TOXICITY IN B-CELL NON-HODGKIN LYMPHOMA: REAL-WORLD STUDY FROM THE DESCAR-T REGISTRY

- CRS and ICANS are common immune-related toxicities associated with CAR T-cell therapy. Their clinical manifestations can be severe and potentially life threatening.
- Here is reported a large cohort study of R/R aggressive B-cell lymphoma patients treated with commercial products in a real world setting.
- All data were collected through the French DESCAR-T registry.
- 705 pts were included for the analysis of toxicity with a median follow-up of 12 months (range: 0.2-39)
- The aim of the study is to report the French experience of CAR-T toxicity. The authors specifically addressed the modifiable risk factors for toxicity and assessed management toxicity in a real-world population.

Abstract S210 (oral presentation), Sesques P. et al. EHA 2022

CAR T-CELLS ASSOCIATED ACUTE TOXICITY IN B-CELL NON-HODGKIN LYMPHOMA: REAL-WORLD STUDY FROM THE DESCAR-T REGISTRY

RESULTS

CRS

- any grade: 83.3% (587 pts)
- grade ≥ 3: 10.5% (62 pts)
- median time from the infusion to the onset of CRS was 2 days (range: 0-34); median time to resolution was 6 days (range: 1-30).
- 38% of pts with CRS grade 1, 53 % with grade 2 and 65% with grade 3+ developed ICANS subsequently.

ICANS

- any grade: 41% (289 pts)
- grade > 3: 27% (78 pts)
- median time from the infusion to the onset was 6 days (range: 0-379); median time to resolution was 7 days (range: 1-100).
- most patients (94.5%) with ICANS had previously experienced CRS.

89 pts (29.9%) required admission to intensive care unit.
Tocilizumab was the most common treatment for toxicity (411 pts, 68%) and 272 pts (45%) received corticosteroids.

Abstract S210 (oral presentation), Sesques P. et al. EHA 2022

CAR T-CELLS ASSOCIATED ACUTE TOXICITY IN B-CELL NON-HODGKIN LYMPHOMA: REAL-WORLD STUDY FROM THE DESCAR-T REGISTRY

CRS

- The parameters which statistical predict any CRS (multivariable analysis) were Axi-cel ($p < 0.0001$), and elevated LDH ($p < 0.03$);
- The parameters which increased the risk of developing a grade 3+ CRS were bulky mass (> 5 cm), age <65 years and higher s-EASIX score (LDH/Platelets).

ICANS

- The parameters which statistical predict any ICANS were Axi-cel ($p < 0.0001$), ECOG ≥2 ($p = 0.004$), age ≥65 $p < 0.0001$) and higher s-EASIX score ($p = 0.01$).
- The parameters which increased the risk of developing a grade 3+ ICANS were Axi-cel ($p < 0.001$), ECOG ≥2 ($p = 0.04$) and higher s-EASIX score ($p = 0.0067$).

Abstract S210 (oral presentation), Sesques P. et al. EHA 2022

CAR T-CELLS ASSOCIATED ACUTE TOXICITY IN B-CELL NON-HODGKIN LYMPHOMA: REAL-WORLD STUDY FROM THE DESCAR-T REGISTRY

- No survival impact (OS and PFS) was detected for pts who experimented any grade or grade 3+ of ICANS or CRS (Figure 1 and 2).
- Cumulative dose and duration of tocilizumab or corticosteroids were not significantly associated with adverse PFS or OS.

Fig.1 OS since 1st administration by CRS grade

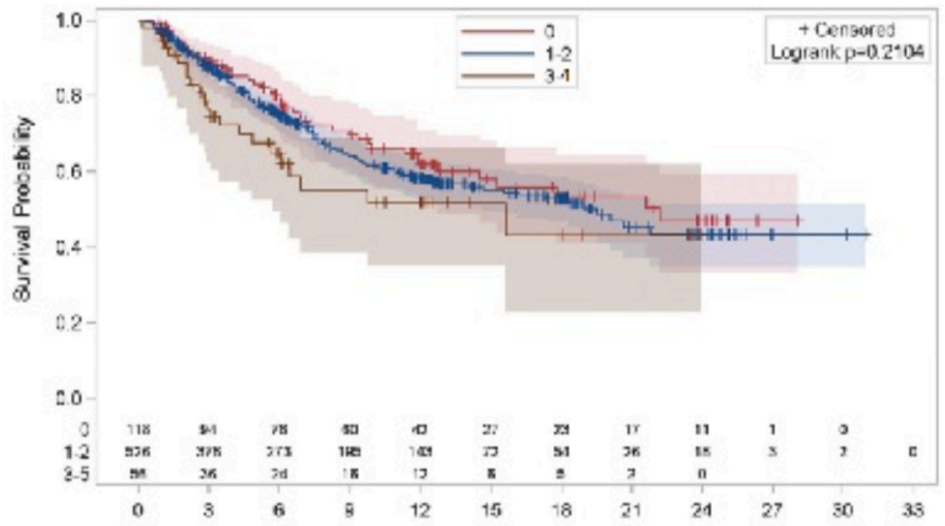
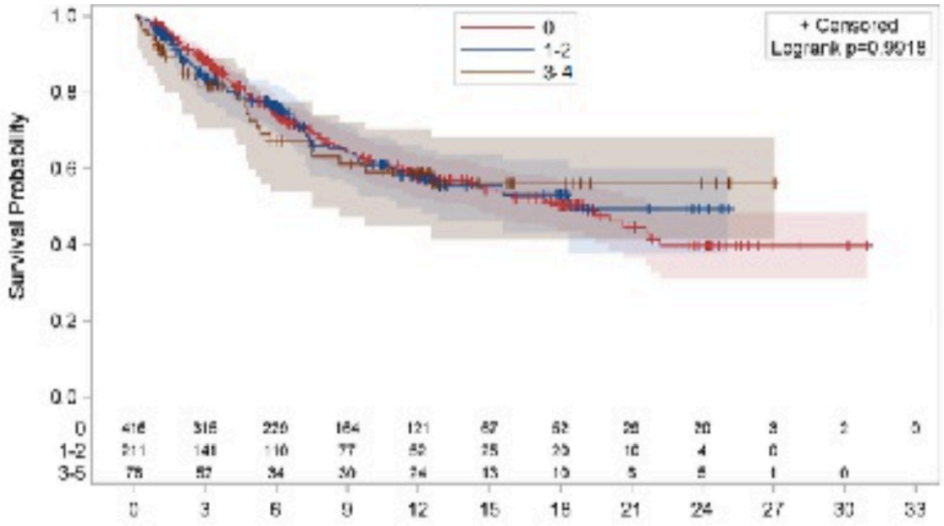


Fig.2 OS since 1st administration by ICANS grade



Abstract S210 (oral presentation), Sesques P. et al. EHA 2022

PHASE 1/2 STUDY OF ANBAL-CEL, NOVEL ANTI-CD19 CAR-T THERAPY WITH DUAL SILENCING OF PD-1 AND TIGIT IN RELAPSED OR REFRACTORY LARGE B CELL LYMPHOMA

- Anbal-cel is a novel 2nd generation autologous CD19 CAR T-cell therapy which has been knock-downed for PD-1 and TIGIT, using OVIS platform.
- The knock-down of PD-1 and TIGIT at CD19 CAR-T cells exerts the superior T-cell functionality by delaying the exhaustion of CAR-T cells.
- Here are reported the preliminary results from the phase 1 dose escalation part of Anbal-cel trial (NCT04836507) in patients with r/r LBCL

Abstract S214 (oral presentation), Won Seog K. et al. EHA 2022

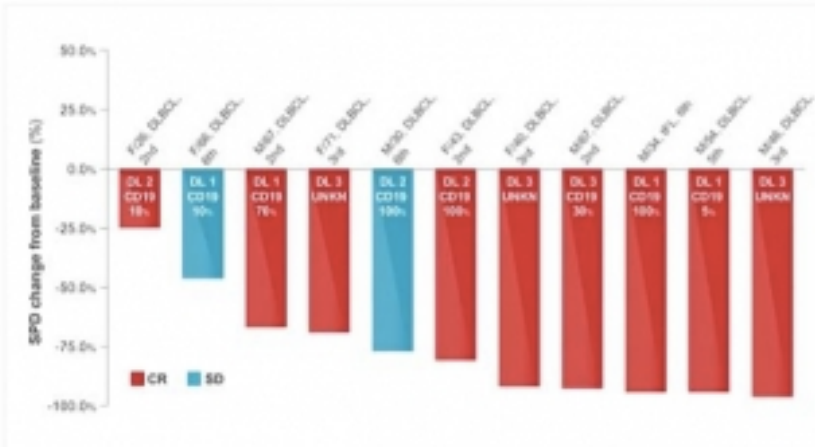
PHASE 1/2 STUDY OF ANBAL-CEL, NOVEL ANTI-CD19 CAR-T THERAPY WITH DUAL SILENCING OF PD-1 AND TIGIT IN RELAPSED OR REFRACTORY LARGE B CELL LYMPHOMA

Baseline characteristic of 11 evaluable pts

	2×10^5 cells/kg N=4	7×10^5 cells/kg N=3	2×10^6 cells/kg N=4	Total N=11
Age (years), median (range)	60 (34 – 67)	30 (26 – 43)	56.5 (40 – 71)	46 (26 – 71)
≥ 65 – no. (%)	2 (50)	0	2 (50)	4 (36)
Male – no. (%)	3 (75)	1 (33)	2 (50)	6 (55)
ECOG performance status 1 – no. (%)	2 (50)	1 (33)	1 (25)	4 (36)
Disease subtype – no. (%)				
DLBCL	3 (75)	3 (100)	4 (100)	10 (91)
transformed Follicular Lymphoma (tFL)	1 (25)	0	0	1 (9)
Cell of origin of cancer – no. (%)				
GCB	2 (50)	3 (100)	1 (25)	6 (55)
non-GCB	2 (50)	0	3 (75)	5 (45)
Double expressor type – no. (%)	1 (25)	1 (33)	3 (75)	5 (45)

	2×10^5 cells/kg N=4	7×10^5 cells/kg N=3	2×10^6 cells/kg N=4	Total N=11
Previous Line of Therapy – no. (%)				
1 & 2	1 (25)	2 (67)	1 (25)	4 (36)
3	0	0	3 (75)	3 (27)
≥ 4	3 (75)	1 (33)	0	4 (36)
Refractory to Last Line of Therapy – no. (%)	4 (100)	1 (33)	3 (75)	8 (73)
Previous ASCT – no. (%)	0	2 (67)	2 (50)	4 (36)
Refractory to 1st Line of Therapy – no. (%)	2 (50)	2 (67)	2 (50)	6 (55)
SPD (mm^2) - median (range)	3,693 (673 – 5,990)	3,520 (570 – 7,719)	3,526 (693 – 6,125)	3,520 (570 – 7,719)
SPD ≥ 5,000mm^2 – no. (%)	2 (50)	1 (33)	2 (50)	5 (45)

82% Complete Response Rate across All Dose Levels



Cells/kg	2×10^5 (N=4)	7×10^5 (N=3)	2×10^6 (N=4)	Total (N=11)
CR	75%	67%	100%	82%
PR	0	0	0	0
ORR	75%	67%	100%	82%

ORR: 82% (9/11), with all 9 pts reaching a CR

Abstract S214 (oral presentation), Won Seog K. et al. EHA 2022

PHASE 1/2 STUDY OF ANBAL-CEL, NOVEL ANTI-CD19 CAR-T THERAPY WITH DUAL SILENCING OF PD-1 AND TIGIT IN RELAPSED OR REFRACTORY LARGE B CELL LYMPHOMA

Treatment related AEs (TRAE) of any grade

TRAE	2 x 10^5 cells/kg (N=4)	7 x 10^5 cells/kg (N=3)	2 x 10^6 cells/kg (N=4)	TOTAL (N=11)
Cytokine Release Syndrome	0	3 (100%)	2 (50%)	5 (46%)
Anaemia	0	0	2 (50%)	2 (18%)
Neutropenia	0	0	2 (50%)	2 (18%)
Fever	1 (25%)	0	1 (25%)	2 (18%)
Thrombocytopenia	0	0	2 (50%)	2 (18%)

CRS (ASCT grading 2019)

Dose level	2 x 10^5 cells/kg (N=4)			7 x 10^5 cells/kg (N=3)			2 x 10^6 cells/kg (N=4)			All patients (N=11)		
Grade	1	2	3	1	2	3	1	2	3	1	2	3
CRS – no. (%)	0	0	0	2 (67)	1 (33)	0	0	0	2 (50)	2 (18)	1 (9)	2 (18)
Fever	0	0	0	2 (67)	1 (33)	0	2 (50)	0	0	4 (36)	1 (9)	0
Hypotension	0	0	0	1 (33)	0	0	0	1 (25)	1 (25)	1 (9)	1 (9)	1 (9)
Hypoxia	0	0	0	0	0	0	0	0	2 (50)	0	0	2 (18)
Pleural effusion	0	0	0	0	0	0	0	0	1 (25)	0	0	1 (9)
CRS onset time (day) – median (range)		N/A			7 (6 – 11)			8.5 (1 – 16)			7 (1 – 16)	
CRS duration (day) – median(range)		N/A			2 (1 – 5)			16.5 (14 – 19)			5 (1 – 19)	
Rescue medication – no. (%) Tocilizumab		1 (25)			3 (100)			2 (50)			6 (55)	
Rescue medication – no. (%) Steroids		0			0			1 (25)			1 (9)	
Rescue medication – no. (%) Vasopressor		0			0			2 (50)			2 (18)	

Neurological events (ASCT grading 2019)

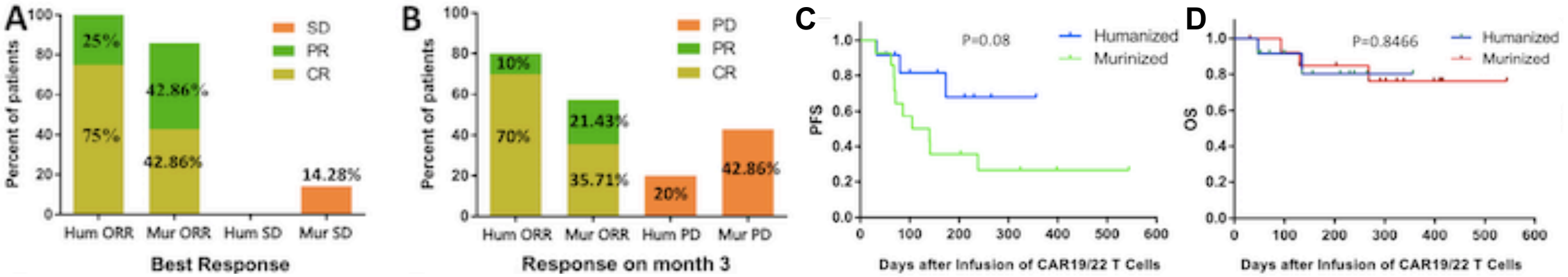
Dose level	2 x 10^5 cells/kg (N=4)			7 x 10^5 cells/kg (N=3)			2 x 10^6 cells/kg (N=4)			All patients (N=11)		
Grade	1	2	3	1	2	3	1	2	3	1	2	3
NEs – no. (%)	0	0	0	0	0	0	0	1 (25)	0	0	1 (9)	0
Confusion	0	0	0	0	0	0	0	1 (25)	0	0	1 (9)	0
Delirium	0	0	0	0	0	0	1 (25)	0	0	1 (9)	0	0
NEs onset time (day) – median		N/A			N/A			7			7	
NEs duration (day) – median		N/A			N/A			13			13	
Rescue medication – no. (%) Tocilizumab		0			0			1 (25)			1 (9)	
Rescue medication – no. (%) Steroids		0			0			1 (25)			1 (9)	
Rescue medication – no. (%) Anti-epileptics		0			0			0			0	

- CRS is one of the most frequent TRAE of any grade and of grade $\geq$ 3
- 2/11 (18%) pts had grade 3 CRS, all of them were treated with DL3 (2x10^6 cells/Kg)
- 1/11 (9%) pts had NE of grade 2, he was treated with DL3
- No CRS and NE of grade 4 or 5 occurred

Based on this phase 1 study, phase 2 patient enrollment will be commenced in Mar 2022 to evaluate the response rate, duration of response of CR as well as safety

Abstract S214 (oral presentation), Won Seog K. et al. EHA 2022

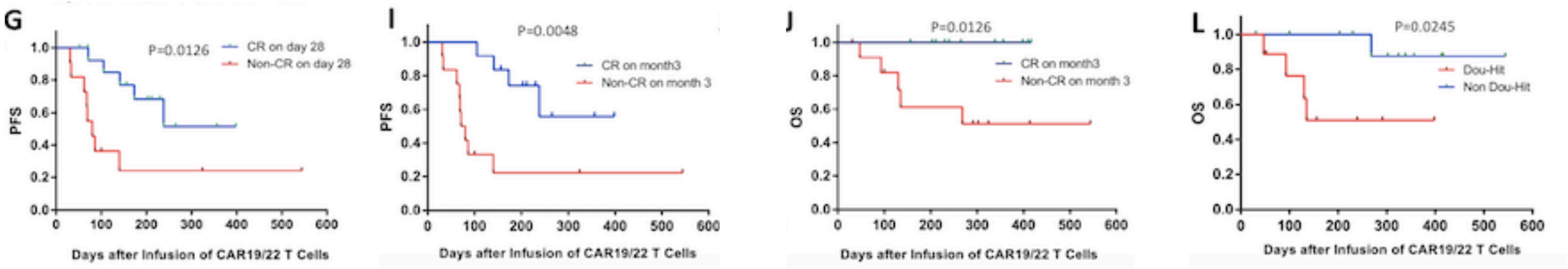
EFFICACY AND SAFETY OF HUMANIZED VERSUS MURINIZED CD19 AND CD22 CAR-T CELL COCKTAIL THERAPY FOR REFRACTORY/RELAPSED B-CELL LYMPHOMA



- ORR Humanized (hum) CART: 100% (12/12), fig A.
- ORR murinized (mur) CART: 87.5% (12/14), fig A.
- All 4 BL pts in both groups had CR
- ORR Hum CART at 3 months (10/12 pts valuable): 80%, fig B.
- ORR Mur CART at 3 months (14/14 pts valuable): 57% , fig B.
- At a median follow-up of 291 days (31- 544), pts in the hum group had a favorable PFS than those in the mur (1-year PFS of 67.9% vs. 26.8%), although there was no statistical significance (p=0.08) due to the limited number of pts (fig C).

Abstract S213 (oral presentation), Huang L. et al. EHA 2022

EFFICACY AND SAFETY OF HUMANIZED VERSUS MURINIZED CD19 AND CD22 CAR-T CELL COCKTAIL THERAPY FOR REFRACTORY/RELAPSED B-CELL LYMPHOMA



- Achieving CR on day 28 (HR: 0.21; P=0.012) and maintaining it till the 3rd month (HR: 0.18; P=0.004) is an independent prognostic factors associated with favorable PFS (fig. G and I).
- Maintaining CR till the 3rd month (HR: 0.10; P=0.012) and non-double hit (HR: 0.11; P=0.024) predicted a longer OS (fig. J-L).
- Majority of patients had mild CRS (grade 1-2) in both group. Only 2 pts experienced grade 3 CRS and grade 3 NE.

CD19/CD22 CAR-T cocktail therapy demonstrates promising efficacy and safety for the treatment of R/R aggressive B-cell lymphoma. Patients in the humanized group showed better results than those in the murinized one, although this is not a randomized trial.

Abstract S213 (oral presentation), Huang L. et al. EHA 2022

Update da EHA 2022

INDOLENT, HODGKIN and T-CELL LYMPHOMAS

EFFICACY AND SAFETY OF A THIRD GENERATION CD20 CART (MB-106) FOR TREATMENT OF RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL)

- MB-106 is a fully human 3rd-generation CD20-targeted CAR-T product with both 4-1BB and CD28 costimulatory domains.
- Eligibility criteria:
  - Pts with R/R B-cell malignancies including FL
  - FL after at least 1 prior line of treatment
  - Elegibility was confirmed after CD20 expression testing
  - Prior treatment with a CD19 CAR is allowed after recovery of normal B cells (≥ 20 B cells/μL)
- CAR-T cells are administered at one of 4 dose levels (DL) [DL1: 3.3x105, DL2: 1x106, DL3: 3.3x106, DL4: 1x107 CAR T cells/kg].
- Here are presented the results of the FL cohort from ongoing phase I/II clinical trial investigating MB-106 for B- cell lymphoma/CLL.

Pts Characteristics	N=28
Age, median (range)	61.8 (44.7–81.3)
> 65, n (%)	7 (25%)
> 80, n (%)	2 (7%)
Female sex, n (%)	10 (55.5%)
Stage at initial diagnosis	
1-2	2 (11%)
3-4	16 (89%)
Histologic grade at diagnosis	
1-2	11 (61%)
3A	5 (28%)
Prior lines of treatment (range)	5 (1–12)
History of transformation	3 (17%)
POD24	12 (67%)
Prior CD19 CAR-T	1 (5.5%)

Abstract S207 (oral presentation), Shadman M. et al. EHA 2022

EFFICACY AND SAFETY OF A THIRD GENERATION CD20 CART (MB-106) FOR TREATMENT OF RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL)

SAFETY (18 PTS)

- All CRS events were grade 1 (n=4; 22%) or 2 (n=1; 5.5%).
- No occurrence of ICANS of any grade.
- The most common AEs of grade 3+ were lymphopenia (Gr 3-4: 100%) trombocytopenia (Gr 3-4: 11%) and neutropenia (Gr 3-4: 94%).

AEs (N= 18)	Grade				
	1	2	3	4	Any
CRS	4 (22%)	1 (5.5%)	-	-	5 (27.5%)
ICANS	-	-	-	-	0 (0%)
Lymphopenia	-	-	2 (11%)	16 (89%)	18 (100%)
Neutropenia	-	-	6 (33%)	11 (61%)	17 (94%)
Anemia	-	4 (22%)	7 (39%)	-	11 (61%)
Thrombocytopenia	-	3 (17%)	-	2 (11%)	5 (28%)
Febrile neutropenia	1 (5.5%)	-	2 (11%)	-	3 (16.5%)

Abstract S207 (oral presentation), Shadman M. et al. EHA 2022

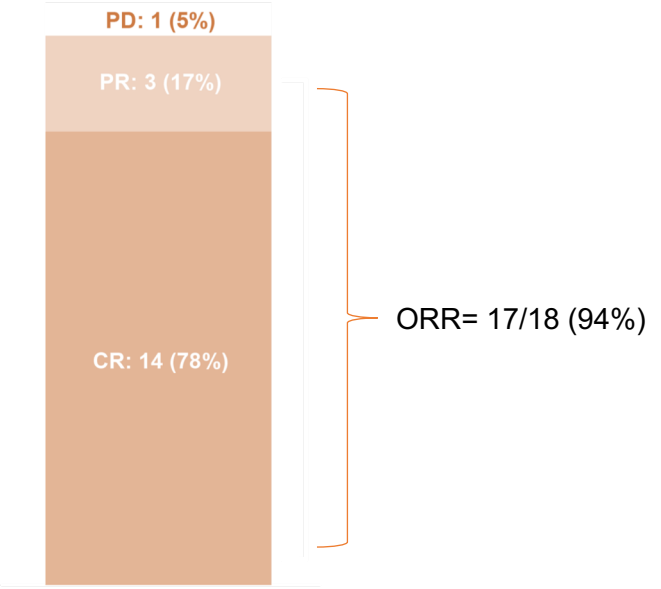
EFFICACY AND SAFETY OF A THIRD GENERATION CD20 CART (MB-106) FOR TREATMENT OF RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL)

EFFICACY (18 pts)

- Treatment with MB-106, a third generation CD20 targeting CAR-T, resulted in high ORR and CR rates and CAR-T persistence in FL pts and was associated with favorable safety profile with no grade 3+ CRS or ICANS occurred.

Histology	Best response by Lugano PET criteria	All dose levels	Dose level 0 (n=1)	Dose level 1 (n=2)	Dose level 2 (n=4)	Dose level 3 (n=8)	Dose level 4 (n=3)
			$1x10^5$ cells/kg	$3.3x10^5$ cells/kg	$1x10^6$ cells/kg	$3.3x10^6$ cells/kg	$1x10^7$ cells/kg
FL (n=18)	ORR, n (%)	17/18 (94%)	1	1	4	8	3
	CR, n (%)	14/18 (78%)	1	1	2	7	3
	PR, n (%)	3/18 (17%)	-	-	2	1	-
	SD, n (%)	-	-	-	-	-	-
	PD, n (%)	1/18 (5%)	-	1	-	-	-

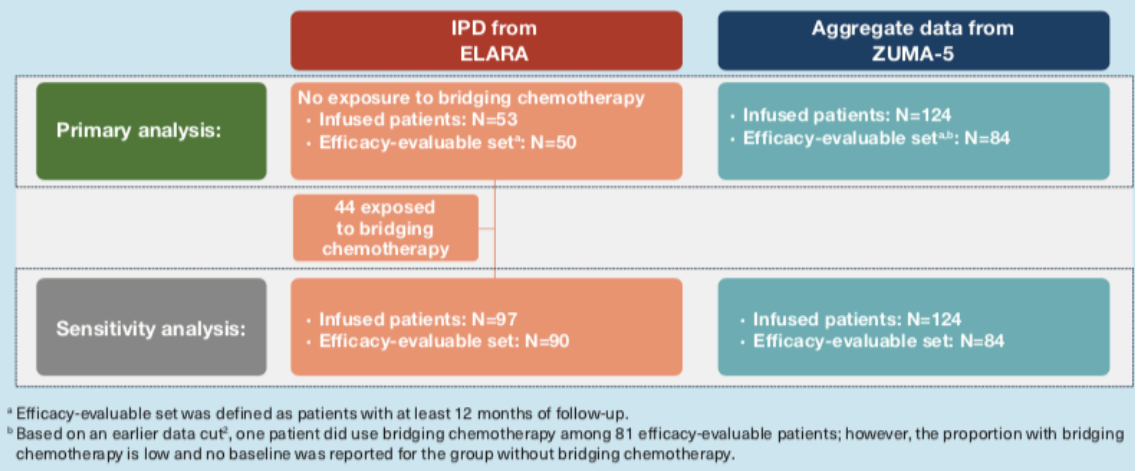
BEST RESPONSE (n=18)



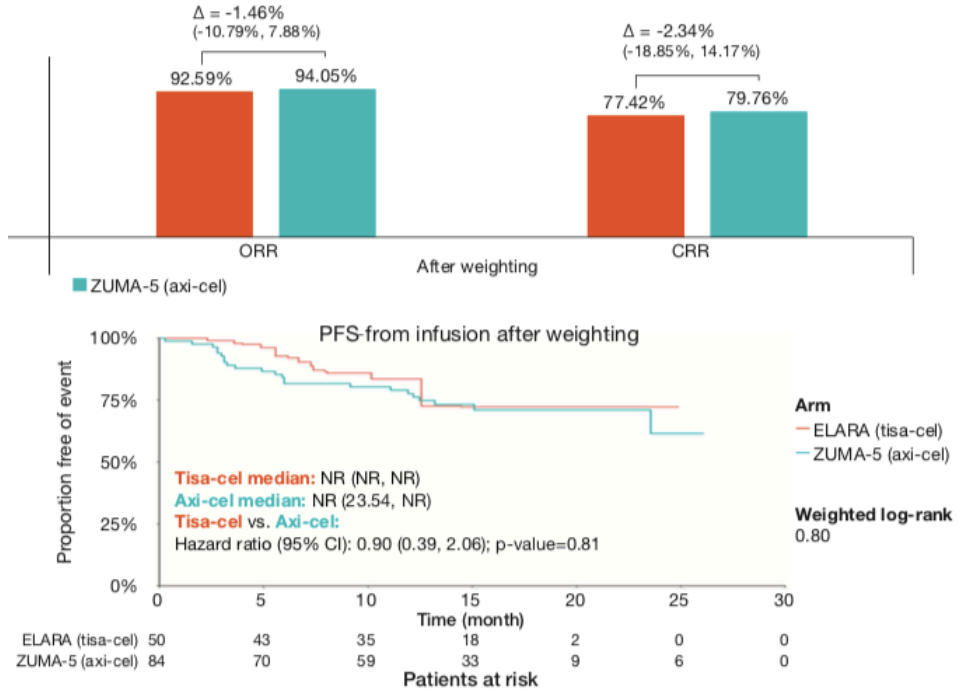
Abstract S207 (oral presentation), Shadman M. et al. EHA 2022

COMPARATIVE EFFICACY AND SAFETY OF TISAGENLECLEUCEL AND AXICABTAGENE CILOLEUCEL IN RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA

Aim: To compare the efficacy and safety outcomes of tisa-cel and axi-cel in r/r FL using matching-adjusted indirect comparison (MAIC).



IPD: individual-level patient data



The MAIC results indicated that tisa-cel and axi-cel were comparable in response rates and PFS, while tisa-cel was associated with better safety outcomes than axi-cel. These results confirm and reinforce the relevance of CAR-T therapies for r/r FL.

Abstract P1111 (poster presentation),Dickinson M. et al. EHA 2022

BREXUCABTAGENE AUTOLEUCEL FOR RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA IN ROUTINE PRACTICE: UPDATED REPORT FROM THE US LYMPHOMA CAR T CONSORTIUM

189 underwent leukapheresis
(8/18/20–12/31/21)

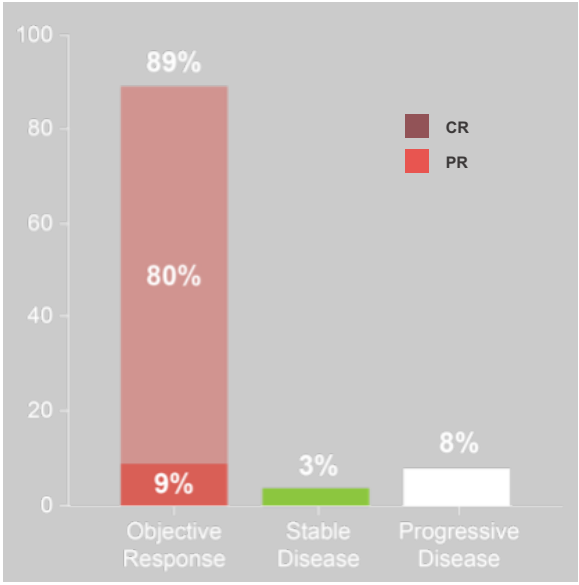
22 did not receive CAR-T infusion

- CR to bridging therapy (n=1)
- Manufacture failure (n=7)
- Organ dysfunction (n=2)
- Disease progression (n=5)
- Death (n=6)
- Patient declined (n=1)

167 received CAR-T infusion

- Standard of care (n=159)
- Expanded access program (n=2)
- Single case IND (n=6)

Best response (159)



Survival:

- Median OS: 15.3 months
- **6-mo OS rate:** 85%
- 12-mo OS rate: 75%
- Median PFS: NR
- **6-month PFS rate 63%**
- 12-month PFS rate 54%

Safety	CRS, n (%)	ICANS, n (%)	ZUMA-2 CRS (%)	ZUMA-2 NE (%)
Total	147 (90%)	100 (61%)	91%	63%
Grade 1-2	135 (82%)	48 (29%)	76%	32%
Grade 3-4	11 (7%)	52 (32%)	15%	31%
Grade 5	1 (1%)			
Days to onset	4 (0–13)	6 (1–18)	2 (1–13)	7
Duration	5 (1–33)	6 (1–144+)	11	12

KEY RESULTS (n=189)

- Day 30 ORR: 89%, CR: 70% (159 evaluable patients)
- Best ORR: 89%, CR: 80%
- At median FU of 5.6 mo; 6-mos DOR: 67%, PFS: 63%, OS: 85%
- CRS: 90% (8% Gr ≥3, 1 Gr 5), and ICANS: 61% (32% Gr ≥3, 0 Gr 5)
- Comparable to ZUMA-2

Abstract P1155 (poster presentation), Wang Y. et al. EHA 2022

A PHASE 1, FIRST-IN-HUMAN, DOSE-ESCALATION CLINICAL TRIAL OF MEMORY-ENRICHED CD30-CAR T-CELL THERAPY FOR THE TREATMENT OF RELAPSED OR REFRACTORY HODGKIN LYMPHOMA AND CD30+ T-CELL LYMPHOMA

- Alvarez-Fernandez and collegues developed a second generation (4-1BB costimulated) CD30-CAR-T (HSP-CAR30) targeting an epitope within the CD30 molecule to overcome soluble CD30 and generated products enriched in memory T-cells to ensure efficient engraftment, persistence and enhancement of antitumor efficacy
- Here, are reported the results of the Phase 1, dose escalation, study evaluating HSP-CAR30 for the treatment of R/R HL and CD30+ T-NHL (NCT04653649).
- Primary endpoints: assess safety of HSP-CAR30 and establish maximum tolerated dose (MTD) recommended for the following Phase 2.
- Secondary objectives include best response rates after infusion

Abstract S257 (oral presentation), Caballero A.C. et al. EHA 2022

A PHASE 1, FIRST-IN-HUMAN, DOSE-ESCALATION CLINICAL TRIAL OF MEMORY-ENRICHED CD30-CAR T-CELL THERAPY FOR THE TREATMENT OF RELAPSED OR REFRACTORY HODGKIN LYMPHOMA AND CD30+ T-CELL LYMPHOMA

Patient N°	Cohort	Demographic characteristics and baseline disease features						Adverse events						
		Age (years)	Diagnosis	Stage	Extra-nodal sites	Prior treatment N°	Bridging therapy	CRS (Grade)	CRS onset day	CRS duration (days)	ICANS (Grade)	Infections (Grade)	Infections (Type)	Rash (BS%)
HSP-CAR30-01	-	38	HL	IIA	-	8	Yes	-	-	-	-	-	-	-
HSP-CAR30-02	DL1	42	HL	IVA	Subcutaneous tissue, muscle, bone	4	No	Yes (1)	1	1	No	Yes (4)	Mycobacteria (TB)	No
HSP-CAR30-03	DL1	65	NHL-T	IVA	GI (stomach), lung	7	Yes	Yes (1)	21	2	No	Yes (1)	Viral (Rhinovirus)	Yes (27)
HSP-CAR30-04	DL1	49	HL	IIA	-	5	No	No	-	-	No	Yes (1)	Viral (SarsCov2)	No
HSP-CAR30-05	DL2	48	HL	IIA	-	4	No	No	-	-	No	No	-	No
HSP-CAR30-06	DL2	43	HL	IVA	Bone, lung	5	No	No	-	-	No	No	-	No
HSP-CAR30-07	DL2	38	HL	IVB	Bone	4	No	Yes (1)	0	2	No	Yes (3)	Viral (CMV)	Yes (18)
HSP-CAR30-08	DL3	63	HL	IVA	Bone	5	No	No	-	-	No	No	-	Yes (45)
HSP-CAR30-09	DL3	65	NHL-T	IVA	Skin, subcutaneous tissue, muscle	3	No	Yes (1)	1	2	No	No	-	Yes (36)
HSP-CAR30-10	DL3	65	HL	IVA	Bone	5	Yes	Yes (1)	0	3	No	No	-	No
HSP-CAR30-11	DL3	21	HL	IIIA	-	4	No	Yes (1)	2	2	No	No	-	No

11 patients (9 HL; 2 T-NHL) underwent apheresis, 10 received treatment
Median age: 49.9. years; median number of prior lines 4.6. No DLTs.

Abstract S257 (oral presentation), Caballero A.C. et al. EHA 2022

A PHASE 1, FIRST-IN-HUMAN, DOSE-ESCALATION CLINICAL TRIAL OF MEMORY-ENRICHED CD30-CAR T-CELL THERAPY FOR THE TREATMENT OF RELAPSED OR REFRACTORY HODGKIN LYMPHOMA AND CD30+ T-CELL LYMPHOMA

SURVIVAL:

- Best objective response: 100%, including 5 (50%) patients with complete response (CR), all HL.
- 3 patients have died of progressive disease (2 T-NHL and 1 HL).
- Median PFS and median OS was not reached.
- Six-month PFS for HL patients was 75%.

This is the first European academic CART clinical trial evaluating a T-cell memory-enriched CART 30. HSP-CAR30 has shown promising efficacy in heavily pre-treated HL patients that is being explored in a phase 2 trial already started.

Abstract S257 (oral presentation), Caballero A.C. et al. EHA 2022

SAFETY AND PRELIMINARY EFFICACY FINDINGS OF AUTO4, A TRBC1-TARGETTING CAR, IN RELAPSED/REFRACTORY TRBC1 POSITIVE SELECTED T CELL NON-HODGKIN LYMPHOMA

- *Maciocia and collegues*, described a targeting strategy for the treatment of T-cell NHL, based on the mutually exclusive expression of T cell receptor beta-chain constant domains 1 and 2 (TRBC1 and TRBC2) which can spare a proportion of the normal T cell compartment (*Maciocia PM. et al, Nat Med 2017*).

- Here are describe early clinical findings of AUTO4, a TRBC1 directed autologous CAR T-cell therapy, tested against relapsed/refractory (r/r) TRBC1+ PTCL in a phase 1/2 multicenter, single-arm trial (NCT03590574).

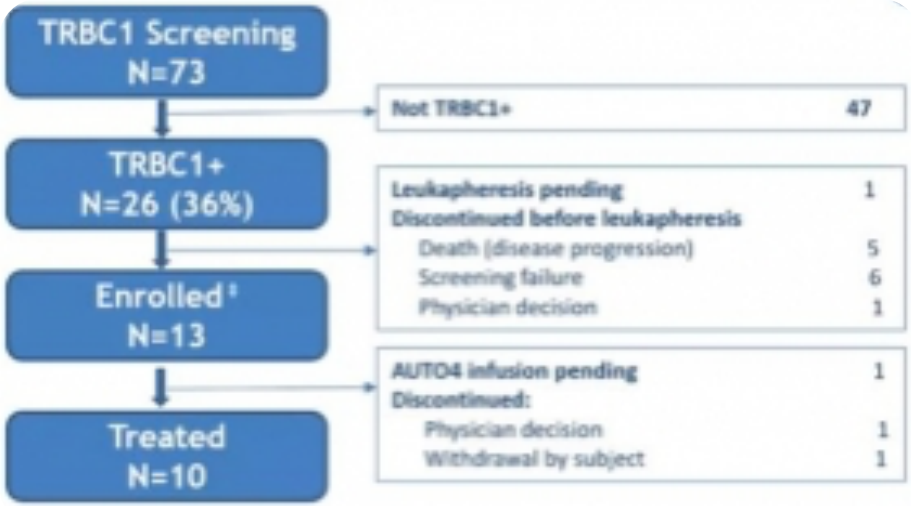
- Primary endpoints: incidence of Grade $\geq$ 3 toxicity occurring within 60 days of AUTO4 infusion and the frequency of DLT within 28 days of AUTO4 infusion.

- Secondary endpoint: overall response (CR+PR) rate post AUTO4 infusion by PET-CT (Lugano 2014 criteria)

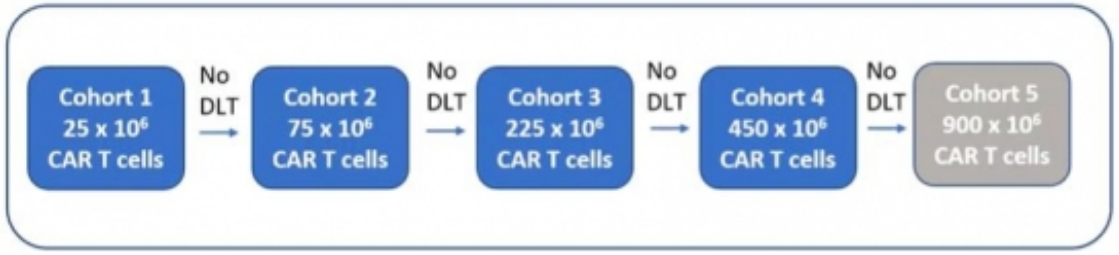
Abstract S261 (oral presentation), Cwynarski K. et al. EHA 2022

SAFETY AND PRELIMINARY EFFICACY FINDINGS OF AUTO4, A TRBC1-TARGETTING CAR, IN RELAPSED/REFRACTORY TRBC1 POSITIVE SELECTED T CELL NON-HODGKIN LYMPHOMA.

Patients disposition



Safety set: 10 pts
Efficacy set, ≥ 1 mo f-up: 9 pts



Baseline characteristics

	Total (N=10)
Age, median (range)	55 (34 – 63)
Median prior lines of treatment (range)	3 (1 – 5)
Stage of Lymphoma at screening	
• I/II	2 (20%)
• III/IV	8 (80%)
Lymphoma Subtype, n (%)	
• Peripheral T-cell lymphoma NOS	5 (50%)
• Anaplastic large cell lymphoma, ALK-negative	1 (10%)
• Angioimmunoblastic T cell lymphoma (AITL)	4 (40%)
Prior Autologous Stem Cell Transplant, n (%)	3 (30%)
ECOG 0/1, n (%)	3 (30%), 7 (70%)
Bridging therapy YES, n (%)	7 (70%)

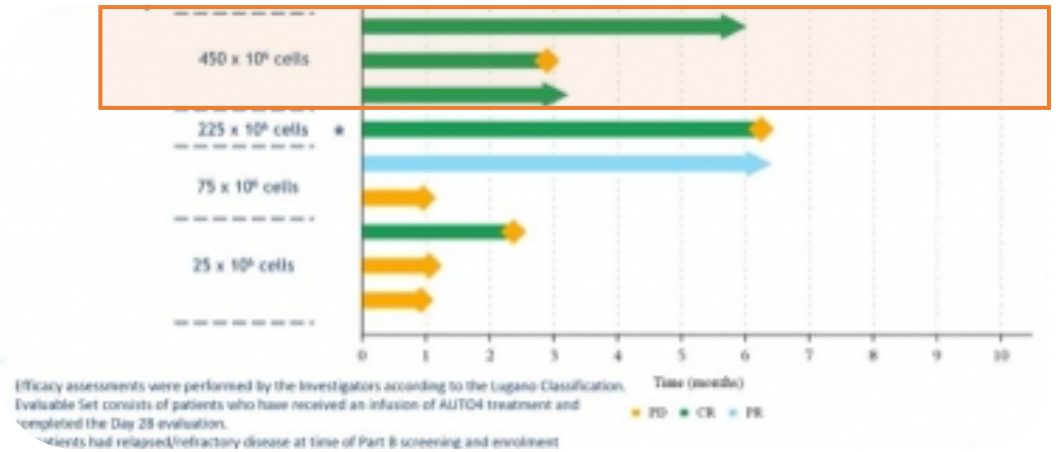
Abstract S261 (oral presentation), Cwynarski K. et al. EHA 2022

SAFETY AND PRELIMINARY EFFICACY FINDINGS OF AUTO4, A TRBC1-TARGETTING CAR, IN RELAPSED/REFRACTORY TRBC1 POSITIVE SELECTED T CELL NON-HODGKIN LYMPHOMA.

SAFETY DATA

	Cohort 1 $25x10^6$ cells (N = 3)	Cohort 2 $75x10^6$ cells (N = 2)	Cohort 3 $225x10^6$ cells (N = 1)	Cohort 4 $450x10^6$ cells (N = 4)	Total (N = 10)
Dose Limiting Toxicity (DLT)	0	0	0	0	0
Grade 3 or 4 TEAE within 60 days	3 (100%)	2 (100%)	1 (100%)	4 (100%)	10 (100%)
Neutropenia	3 (100%)	2 (100%)	0	3 (75%)	8 (80%)
Infections and Infestations	0	0	0	0	0
Serious TEAE	2 (67%)	0	0	2 (50%)	4 (40%)
Any grade CRS	0	0	0	4 (100%)	4 (40%)
Grade 3 CRS	0	0	0	1 (25%)	1 (10%)
Any grade ICANS	0	0	0	0	0

SURVIVAL DATA (Fig.1)



- 3 pts (33%) experienced CRS (1 Grade 1, 1 Grade 2, and 1 Grade 3).
- None of the pts experienced ICANS.
- The most common treatment-emergent adverse events were cytopenias (anemia and neutropenia).
- 5/9 pts achieved a CR at 1 months (green line, Fig 1), of them 3 progressed at 2.5, 3 and 6 months respectively.
- 1 pts remains with a PR at 6 months post AUTO4 (light-blue line, Fig. 1) and 3 pts did not respond (yellow line, Fig.1)

AUTO4 has a tolerable safety profile in patients with r/r TRBC1+ peripheral T-cell lymphoma.
Early data shows encouraging response rates.

Abstract S261 (oral presentation), Cwynarski K. et al. EHA 2022

THE COBALT-LYM STUDY OF CTX130: A PHASE 1 DOSE ESCALATION STUDY OF CD70-TARGETED ALLOGENEIC CRISPR-CAS9–ENGINEERED CAR T CELLS IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) T- CELL MALIGNANCIES

- Adapting CAR T-cell therapy for TCL continues to be challenging due to poor function of donor T cells, fratricide effect, and risk of infusing transduced malignant CAR T cells into pts.
- CTX130™ is a first-in-class, CD70-targeting allogeneic CAR T that may allow for CAR T therapy in pts whose own T cells are not ideal to manufacture auto CAR T-cells.
- CD70 is a co-stimulatory protein with temporally limited expression on activated lymphocytes and is highly expressed in many TCLs.
- Here are reported the preliminary results of the COBALTTM-LYM trial (NCT04502446), a phase 1 open-label, multicenter, global study evaluating the safety and efficacy of CTX130 in pts ≥18 y with CD70+ (≥10% by immunohistochemistry) R/R TCL (PTCL or CTCL).
- Primary endpoint: safety (incidence of dose limiting toxicities [DLTs]).
- Key secondary endpoints: overall response rate, disease control rate (DCR; ≥stable disease [SD]), duration of response and OS.

Abstract S262 (oral presentation), Swaminathan P. I. et al. EHA 2022

THE COBALT-LYM STUDY OF CTX130: A PHASE 1 DOSE ESCALATION STUDY OF CD70-TARGETED ALLOGENEIC CRISPR-CAS9–ENGINEERED CAR T CELLS IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) T- CELL MALIGNANCIES

Adverse Events of Interest, N (%)

	DL1 $3x10^7$ N=4		DL2 $1x10^8$ N=4		DL3 $3x10^8$ N=5		DL4 $9x10^8$ N=5		DL≥3 N=10	
	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3
CRS	1 (25)	-	1 (25)	-	4 (80)	-	4 (80)	-	**8 (80)**	-
ICANS	-	-	-	-	3 (60)	-	-	-	**3 (30)**	-
GvHD	-	-	-	-	-	-	-	-	-	-
Infections	2 (50)	1 (25)	-	1 (25)	2 (40)	1 (20)	1 (20)	1 (20)	**3 (30)**	**2 (20)**

Best overall response, n (%)

Cell dose (CAR+ T cells)	DL1 $3x10^7$ N=4	DL2 $1x10^8$ N=4	DL3 $3x10^8$ N=5	DL4 $9x10^8$ N=5	DL≥3 N=10
Overall Response Rate (ORR)	2 (50)	0	3 (60)	4 (80)	**7 (70)**
CR	1 (25)	0	2 (40)*	1 (20)	**3 (30)**
PR	1 (25)	0	1 (20)	3 (60)	**4 (40)**
Disease Control Rate (DCR = CR + PR + SD)	3 (75)	1 (25)	5 (100)	4 (80)	**9 (90)**

	PTCL		CTCL	
	DL≥3 N=5	Total N=8	DL≥3 N=5	Total N=10
ORR	4 (80)	5 (63)	3 (60)	4 (40)
CR	2 (40)	3 (38)	1 (20)	1 (10)
PR	2 (40)	2 (25)	2 (40)	3 (30)
DCR	4 (80)	5 (63)	5 (100)	8 (80)

- Total of 18 pts were treated ans evaluable for day28 (8 with PTCL and 10 with CTCL); median age was 67 (39-78), the median prior lines of therapy was 3 (1-8)
- Pts were treated with CTX130 at 4 DLs (from $3x10^7$ to $9x10^8$). Pts could receive a second course of CTX130.

CTX130, the first CAR T directed against CD70, shows clinically meaningful responses, including CRs, with has an acceptable safety profile in pts with heavily pretreated R/R TCL and will be investigated further in an expansion phase of the study.

Abstract S262 (oral presentation), Swaminathan P. I. et al. EHA 2022

Update da EHA 2022

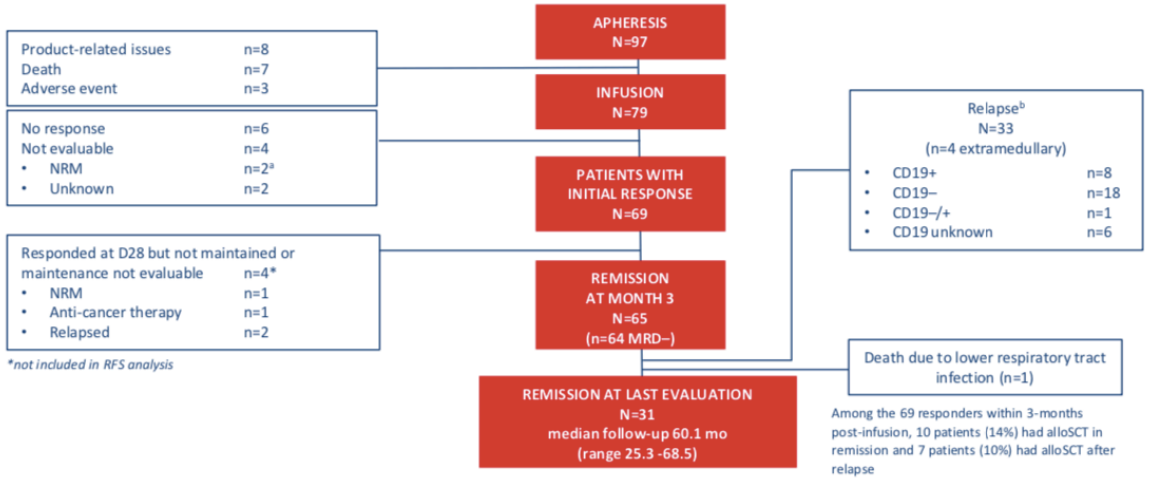
PEDIATRIC AND YOUNG ADULT PATIENTS

TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: FINAL ANALYSES FROM THE ELIANA STUDY.

- In the primary analysis of the Phase II ELIANA trial (NCT02435849), tisa-cel provided high rates of remission (>80%) in children and young adults with r/r B-ALL, with 62% of responders remaining relapse-free at 24 months *(Grupp et al, Blood 2018)*
- Here, the authors report the efficacy and safety analyses in patients followed up for a maximum of 5.9 years post tisa-cel infusion

Patient Flow Chart

Includes patients who had remission (CR/CRi) within 3 months post infusion



*not included in RFS analysis

Characteristic	All Patients (N=79)
Median age (range), years	11 (3-24)
Sex, male, n (%)	45 (57)
Prior alloSCT, n (%)	48 (61)
Lines of prior therapies, median (range), n	3 (1-8)
Disease status, n (%)	
Primary refractory	6 (8)
Relapsed	73 (92)
Morphologic blast count in bone marrow, median (range),[a] %	74 (5-99)
CNS status classification, n (%)	
CNS-1	67 (85)
CNS-2	10 (13)
CNS-3[b]	1 (1)
Unknown	1 (1)

Abstract S112 (oral presentation), Rives S. et al. EHA 2022

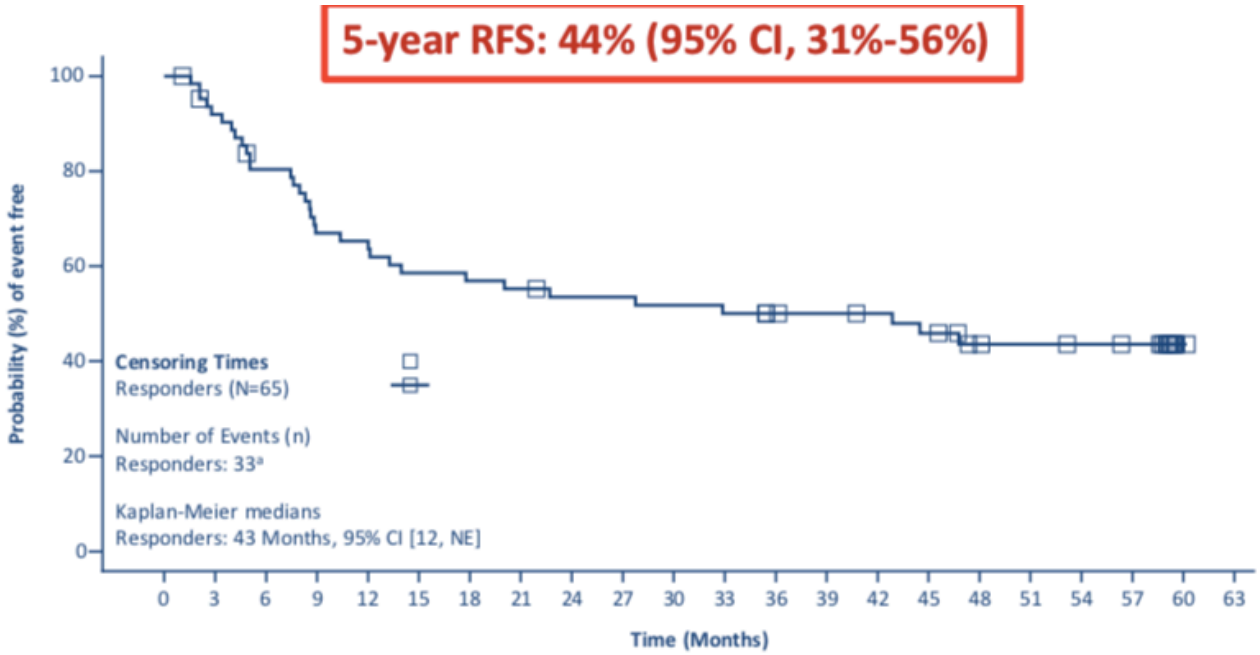
TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: FINAL ANALYSES FROM THE ELIANA STUDY.

First endpoint: ORR

BOR Within 3 Months by IRC assessment	All Patients N=79 n (%)
CR	49 (62)
CRi	16 (20)
No response	7 (9)
Not evaluable	7 (9)
ORR[a]	65 (82)

98% of pts who achieved a remission were MRD- at 3 mo

Secondary endpoint: RFS



Median RFS: 43 months

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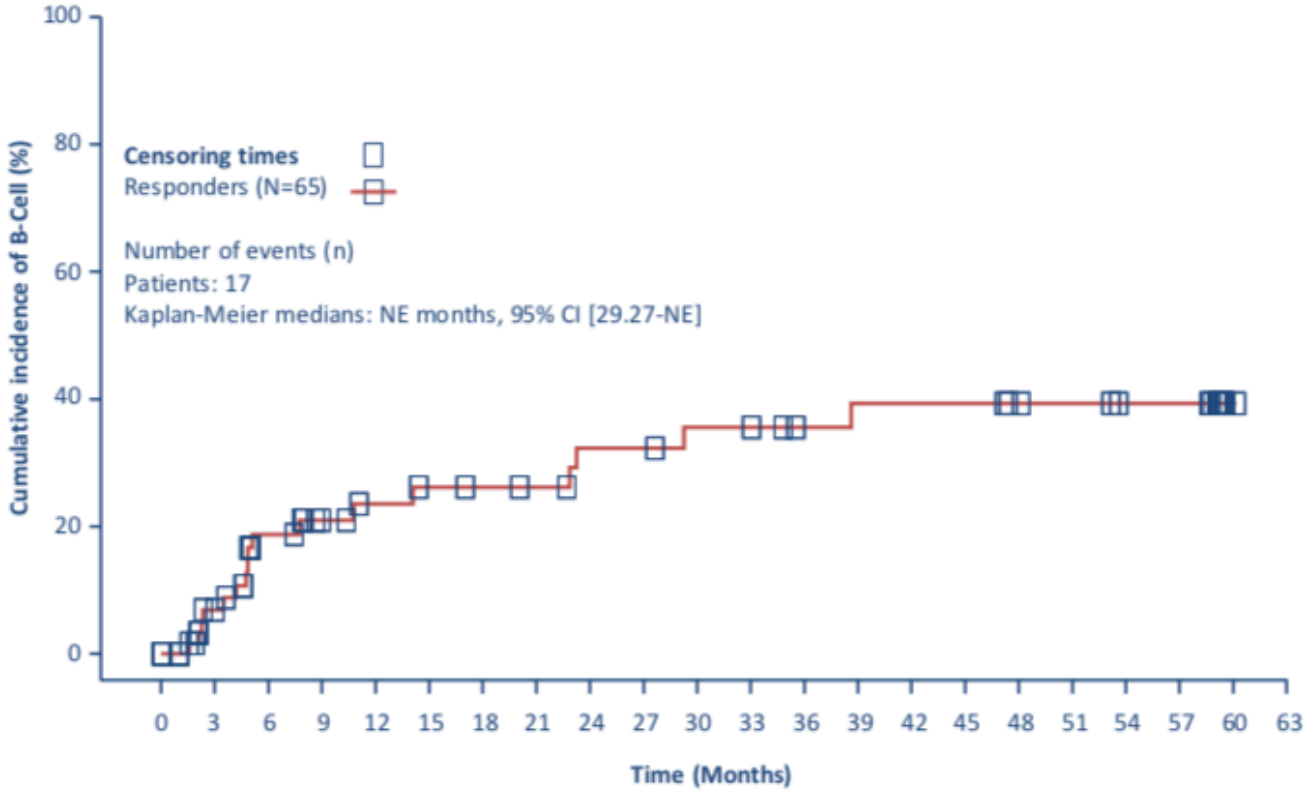
TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: FINAL ANALYSES FROM THE ELIANA STUDY.

Secondary endpoint: B-cell recovery



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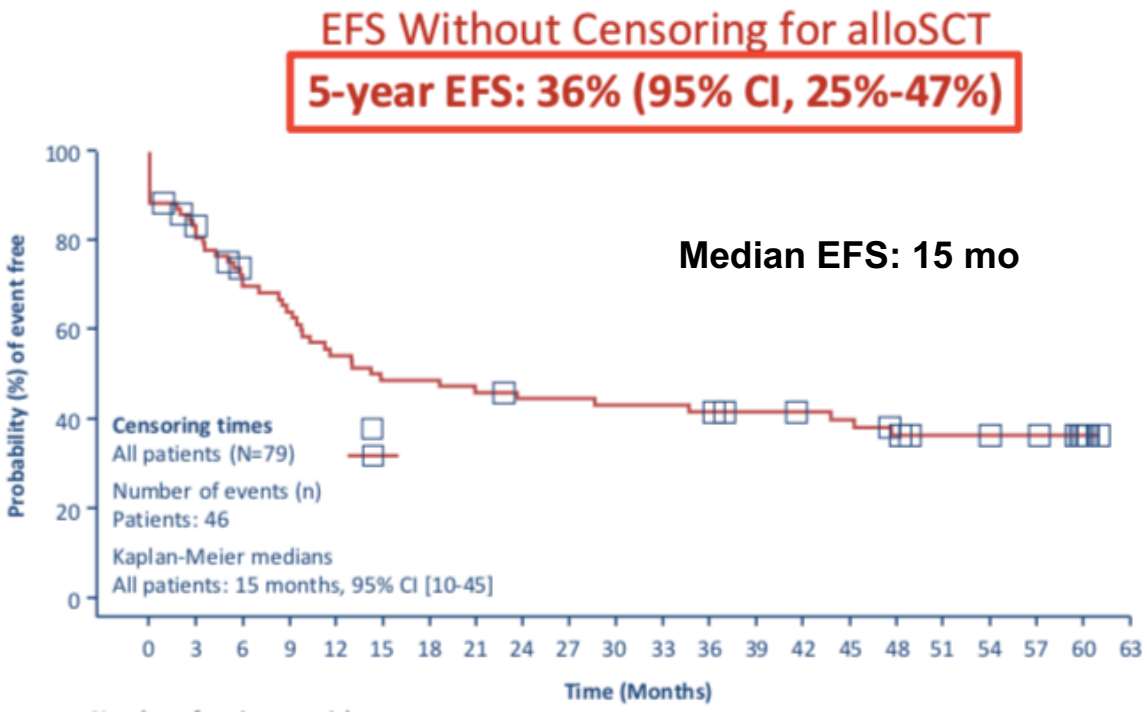
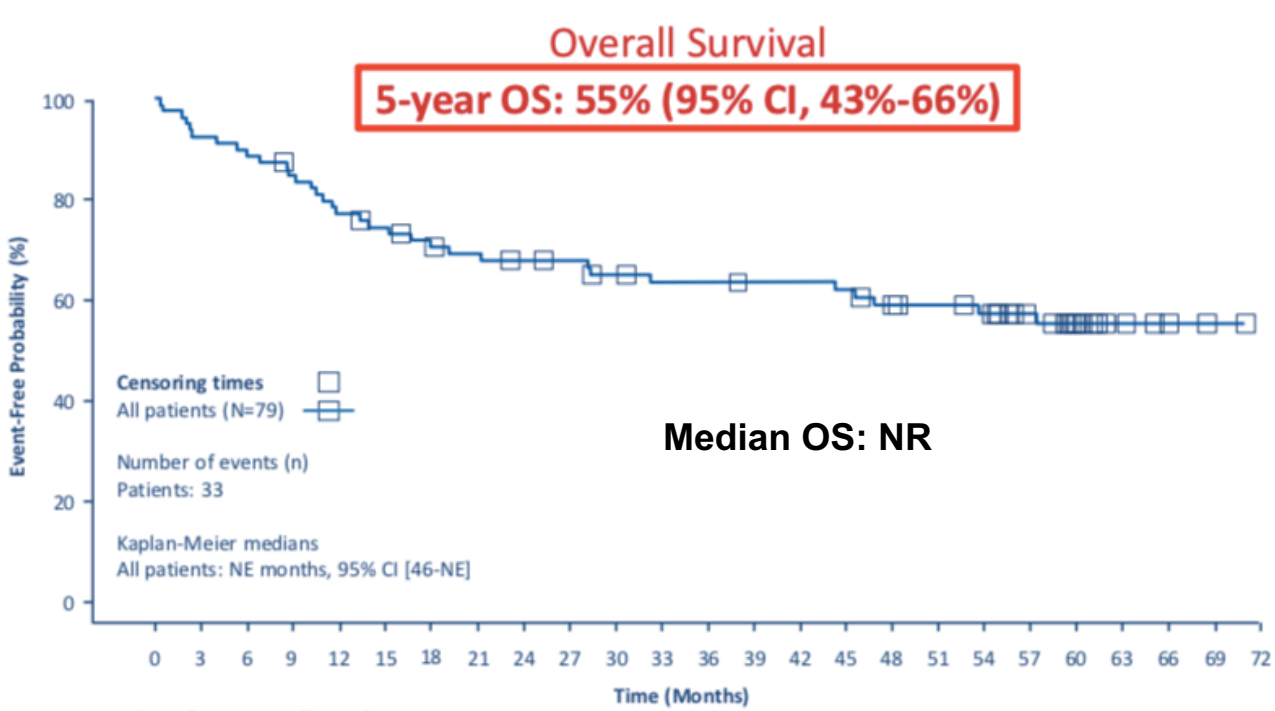
TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: FINAL ANALYSES FROM THE ELIANA STUDY.

Secondary endpoint: EFS and OS





Abstract S112 (oral presentation), Rives S. et al. EHA 2022

TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: FINAL ANALYSES FROM THE ELIANA STUDY.

Conclusions:

- These long-term follow-up data demonstrate continued durable efficacy of tisagenlecleucel in heavily pretreated pediatric and young adult patients with r/r B-ALL

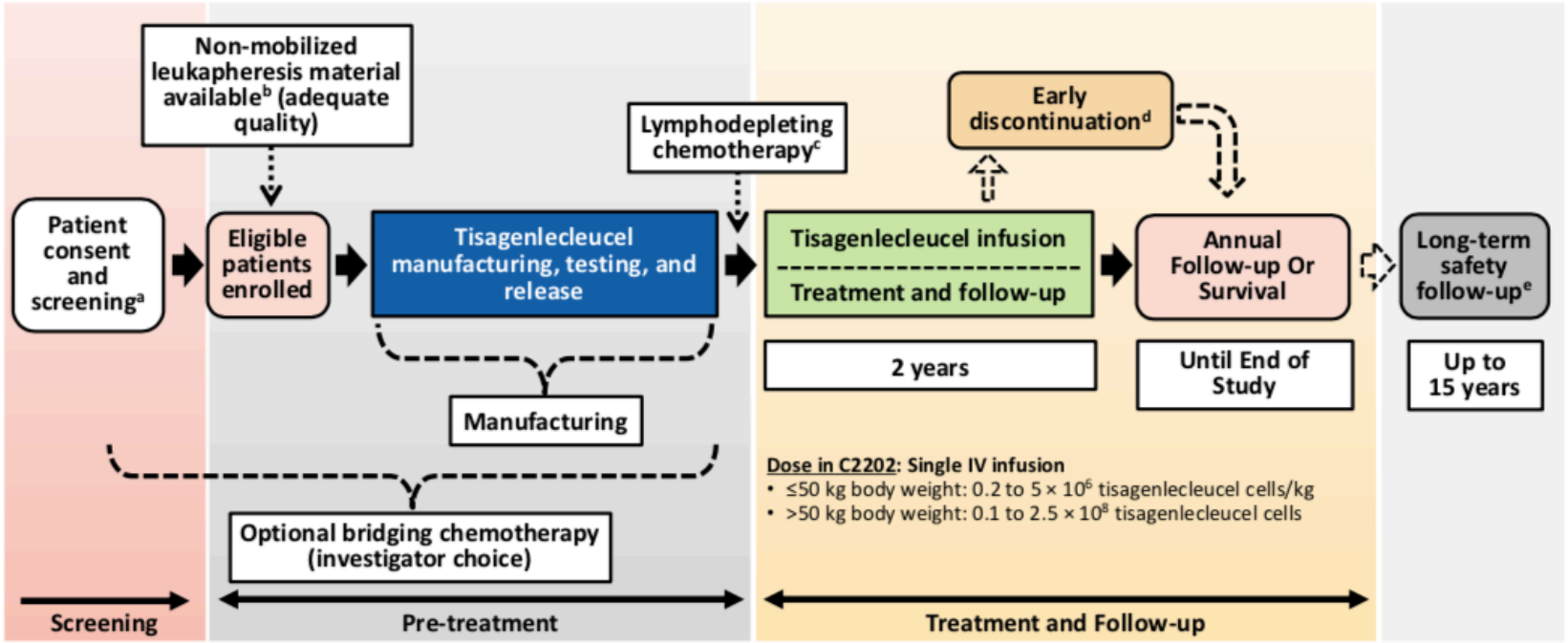
- No new long-term treatment-related safety events were observed in this longer-term >5-year follow-up (Among pts in remission, the most reported grade ≥3 AEs occurring >1 y post-infusion were infection (20%) and cytopenias (6%). Ten (14%) pts in remission experienced long-term cytopenias persisting for >1 y (median 2 y; range, 1.1-5y). Eighty-two percent of pts received IVIG any time post- infusion).

- Long-term remission rates up to 5.9-years of follow-up from ELIANA demonstrate that tisagenlecleucel may be a curative treatment option for heavily pretreated pediatric and young adult patients with r/r B-ALL

Abstract S112 (oral presentation), Rives S. et al. EHA 2022

EFFICACY AND SAFETY OF TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY MATURE B-CELL NON-HODGKIN LYMPHOMA: THE PHASE II BIANCA STUDY

Screened 38 pts → enrolled 34 pts → received bridging 32 pts → infused 33 pts → efficacy analysis set 28 pts
Median follow-up 8 months



Primary endpoint: ORR (CR+PR) by local investigator assessment, which excludes patients with pre-infusion CR

Secondary endpoints: PFS, OS, EFS, DOR, RFS, safety, CAR-T cell kinetics

Abstract S255 (oral presentation), Minard-Colin V. et al. EHA 2022

EFFICACY AND SAFETY OF TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY MATURE B-CELL NON-HODGKIN LYMPHOMA: THE PHASE II BIANCA STUDY

Characteristic at Study Entry		All *Infused* Patients (N=33)
Age, median (range), years		13.0 (3-22)
Sex, male, n (%)		23 (69.7)
Disease at diagnosis, n (%)	Aggressive B-NHL	33 (100.0)
	Burkitt lymphoma	18 (54.5)
	DLBCL	10 (30.3)
	PMBCL	3 (9.1)
	Gray-zone lymphoma	1 (3.0)
	HGBCL with *MYC* and *BCL2* rearrangements	1 (3.0)
Disease stage III or IV at study entry, n (%)		29 (87.9)
Extralymphatic sites involved by lymphoma		18 (54.5)
Disease status, n (%)	Primary refractory	5 (15.2)
	Refractory at relapse	10 (30.3)
	Relapsed or progression	18 (54.5)
Previous lines of therapy, median (range)		2.0 (1-3)
Prior autologous HSCT, n (%)		6 (18.2)

Abstract S255 (oral presentation), Minard-Colin V. et al. EHA 2022

EFFICACY AND SAFETY OF TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY MATURE B-CELL NON-HODGKIN LYMPHOMA: THE PHASE II BIANCA STUDY

First endpoint: ORR

	All Patients (N=28)	
	n (%)	[95% CI]
CR	2 (7.1)	
PR	7 (25.0)	
MR	2 (7.1)	
NR	1 (3.6)	
PD	15 (53.6)	
Unknown	1 (3.6)	
ORR: CR+PR	**9 (32.1)**	**[15.9-52.4]**

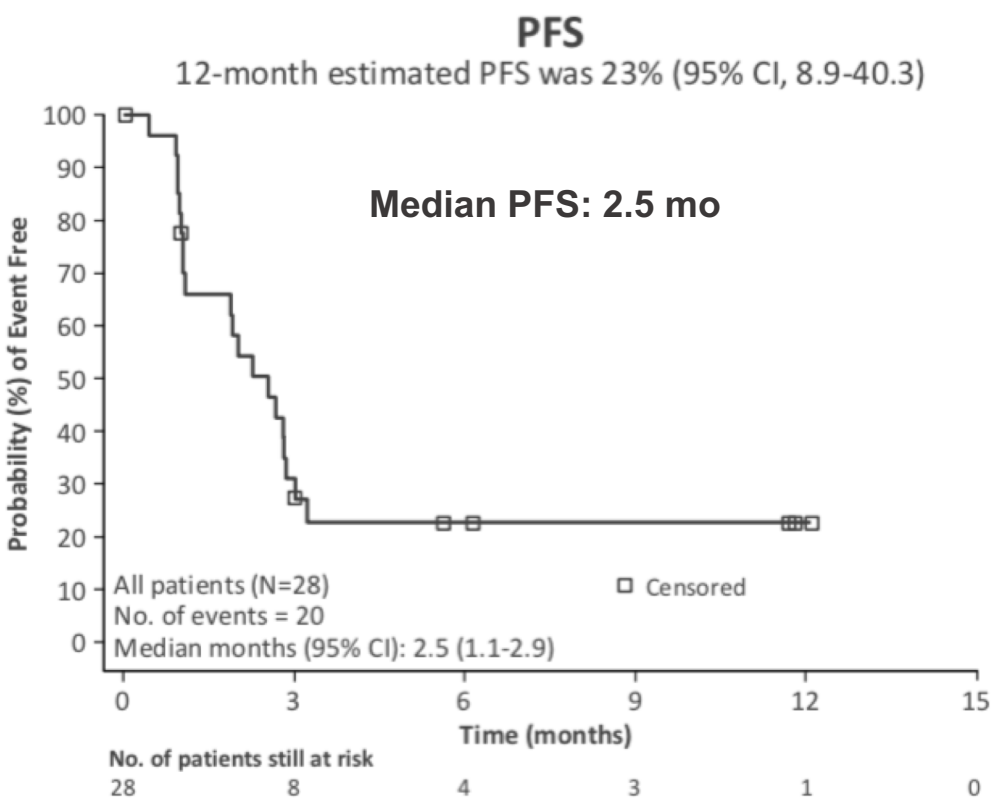
Efficacy Analysis Set (EAS) includes all patients infused with tisagenlecleucel that had measurable disease at baseline (5 infused patients excluded due to CR before infusion [n=4] and no baseline scan after bridging [n=1])

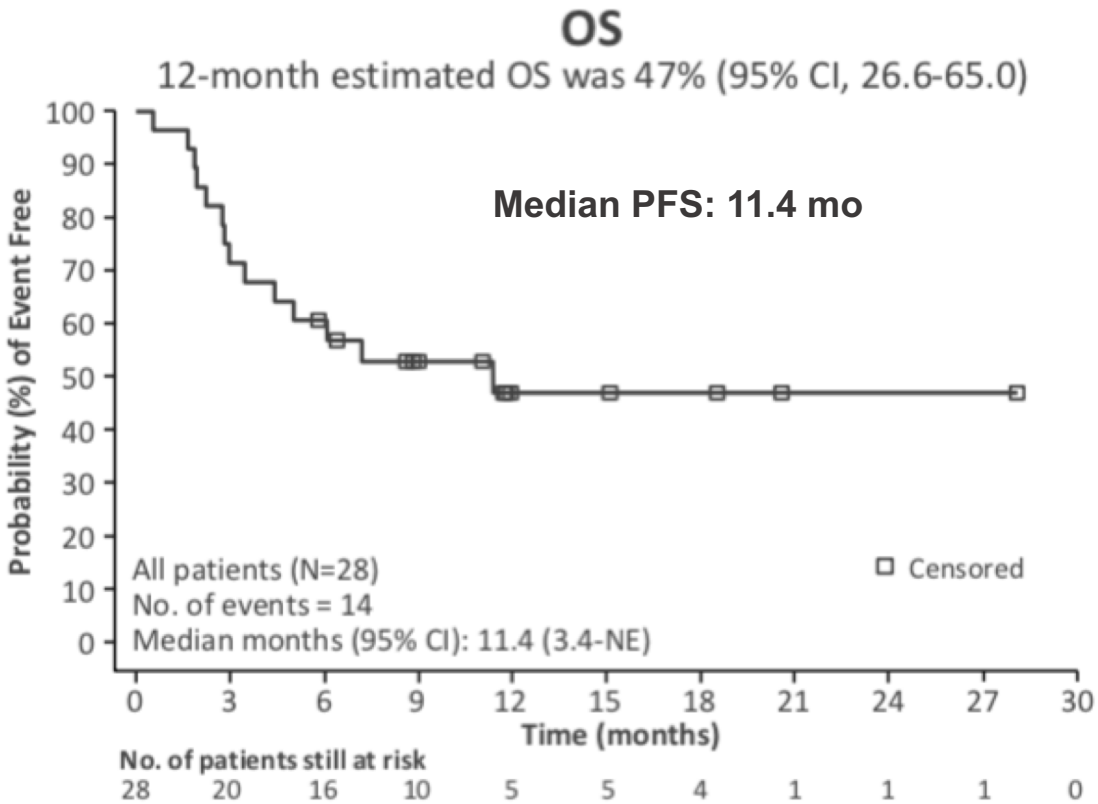
- Subgroup analysis suggested that patients with elevated LDH as well as those with Burkitt lymphoma had a lower ORR than those with DLBCL or other diagnoses (3/15, 20% vs 6/13, 46%);
- 3/5 (60%) patients who did not have measurable disease at infusion and who were excluded from the EAS remained in CR (1 of the 3 had Burkitt lymphoma)

Abstract S255 (oral presentation), Minard-Colin V. et al. EHA 2022

EFFICACY AND SAFETY OF TISAGENLECLEUCEL IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY MATURE B-CELL NON-HODGKIN LYMPHOMA: THE PHASE II BIANCA STUDY

Secondary endpoints: PFS and OS





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Secondary endpoint: Safety

Full Analysis Set		All Patients (N=33)
CRS,[a] n (%)		23 (69.7)
Max grade CRS, n (%)	Grade 1	13 (39.4)
	Grade 2	7 (21.2)
	Grade 3	3 (9.1)
Time to CRS onset from infusion, median (range), days		6 (1-130)
Duration of CRS, median (range), days		5 (1-13)
Admitted to ICU, n (%)		4 (17.4)

Full Analysis Set, NEs any time post infusion[a]	All Patients (N=33)
Patients with at least 1 NE, any grade, n (%)	9 (27.3)
Depressed level of consciousness	3 (9)[b]
Seizure	3 (9)[c]
Aphasia	1 (3)
Confusional state	1 (3)
Delirium	1 (3)[c]
Disturbance in attention	1 (3)
Hallucination	1 (3)[c]
Irritability	1 (3)
Memory impairment	1 (3)
Tremor	1 (3)
Time to onset of NE, median (range), days	8.0 (3-48)
Duration of NE, median (range), days	9.0 (1-21)
Time to onset of grade ≥3 NE, median (range), days	38.0 (3-151)

- The most frequently reported grade ≥3 AEs were anemia and neutropenia (each n=7, 21%)
- CRS occurred in 70% of patients and was generally low grade (no grade 4-5 reported)
  Ne occurred in 27% of patients, 5 (15%) had a grade ≥ 3 NE

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Conclusions

- The BIANCA trial demonstrated feasibility and efficacy of tisacel in some pediatric and young adult patients with r/r mature B-NHL, including Burkitt lymphoma
- 12-month estimated OS was 47%, and 6/15 patients with Burkitt lymphoma are alive post infusion
- The overall safety profile of infused patients was consistent with that already reported in patients given tisagenlecleucel; no new safety signals were observed
- **The role of CAR T-cell therapy in the overall strategy of treating pediatric and young adult patients with r/r Burkitt lymphoma remains to be determined**

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