



Update da **ASH 2022**

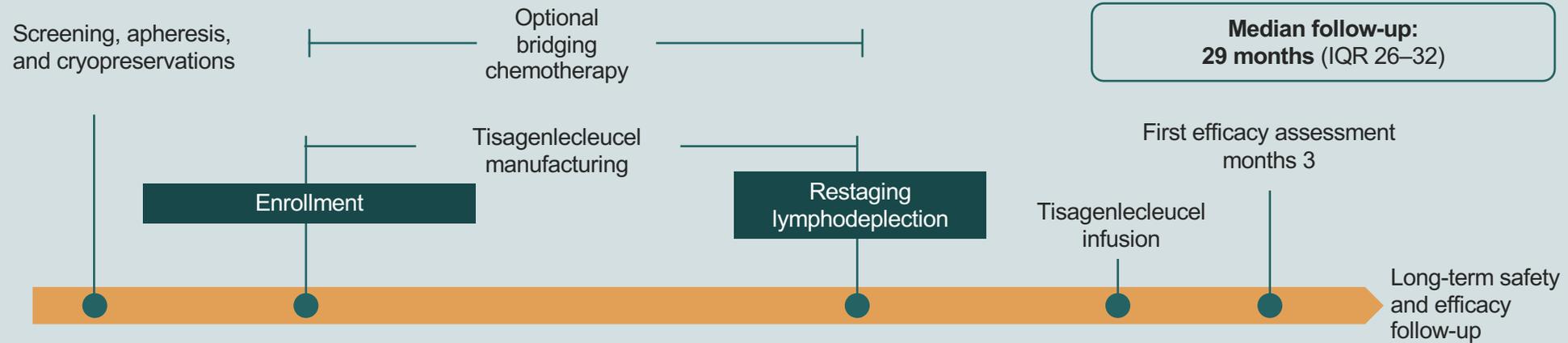
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Long-term clinical outcomes and correlative efficacy analyses in patients with R/R follicular lymphoma (FL) treated with tisagenlecleucel in the ELARA trial

Dreyling M, et al. Presented at ASH 2022; Abstract n. 608

Long-term clinical outcomes and correlative efficacy analyses in patients with R/R follicular lymphoma (FL) treated with tisagenlecleucel in the ELARA trial



Key eligibility criteria

- ≥18 years of age
- FL grade 1, 2, or 3A
- R/R disease
- No evidence of histological transformation/FLT3B
- No prior anti-CD19 therapy or allogeneic HSCT

Study treatment

- Tisagenlecleucel dose range (single IV infusion) was 0.6–0.6 x 10⁸ CAR+ viable T cells

Endpoints

Primary: CRR by IRC

Secondary: ORR, DOR, PFS, OS, safety, cellular kinetics

- Bridging therapy was allowed and was followed by disease re-evaluation before tisagenlecleucel infusion
- 18% (17/97) of patients received tisagenlecleucel in the outpatient setting

ELARA: tisagenlecleucel induced consistently high responses in all patients, including, high-risk patient populations

Endpoints in efficacy analysis set (IRC assessment)	% (95% CI) n=94
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CRR	68 (58–77)
ORR	88 (78–92)

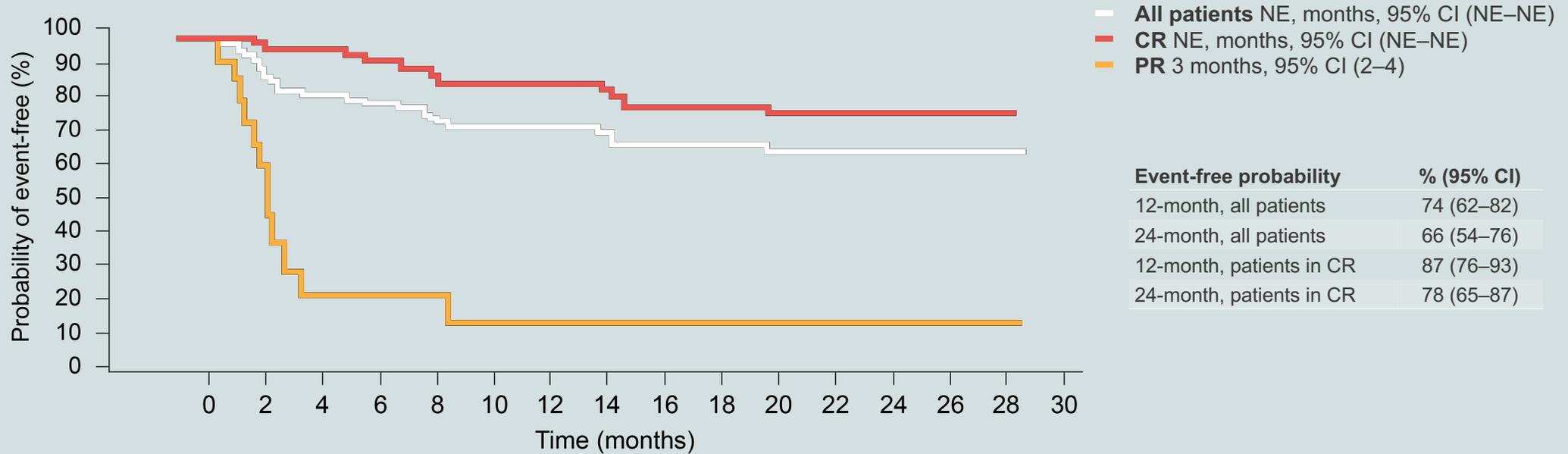
- High ORR (86%) and CRR (69%) are consistent with the primary analysis

Baseline disease characteristic	All patients n (%) n=97	CRR % (95% CI)	ORR % (95% CI)
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POD24*	61 (63)	59 (46–71)	82 (70–91)
High metabolic tumor volume	20 (21)	40 (19–64)	75 (51–91)
Bulky disease	62 (64)	65 (51–76)	86 (74–93)
Double refractory	65 (67)	66 (53–77)	85 (74–92)
High FLIPI (≥3)	57 (59)	61 (48–74)	81 (68–90)

- High rates of durable responses were observed in most patients in high-risk disease subgroups who have poor prognosis with current non-CAR-T cell therapies

IRC: independent review committee; DOR: duration of response; HSCT: haematopoietic stem cell transplantation; *POD24: progression of disease within 24 months of initial chemoimmunotherapy



KEY RESULTS

- CRR 68%
- ORR 86%
 - POD24:
 - CRR 59%
 - ORR 82%
- Mean DOR, PFS and OS were not reached after >2 years follow-up

CONCLUSIONS

- Tisagenlecleucel induced high rates of durable responses in all patients, including those with high-risk disease characteristics such as POD24 and high baseline tumor burden; tisagenlecleucel was well tolerated and suitable for outpatient administration
- Exploratory biomarkers suggest that a favorable TME and decreased inflammatory status were associated with improved clinical outcomes

CAR T-cell therapy remain effective in patients with R/R B-cell NHL after bispecific antibodies exposure: results of a LYSA study based on the Descar-T registry

Crochet G, et al. Presented at ASH 2022; Abstract n. 2026

AIM AND METHODS

- **Aim:** investigate the outcomes (efficacy and toxicity) of CAR-T cell therapy in R/R B-NHL patients previously treated with BA.
- **Methods:** we retrospectively analyzed adult patients with R/R B-NHL treated with approved CAR-T cells (axi-cel, tisa-cel or brexu-cel) after prior exposure to BA. Patients' data were collected through the French DESCAR-T registry and medical records

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS AT CAR-T INFUSION

Characteristics	Population (n=28)
Median age (range) – years	63.0 (38–77)
Male sex, n (%)	19 (67.9%)
Histologie, n (%)	
• Large B-cell lymphoma	23 (82.1%)
- Diffuse large B-cell lymphoma NOS	20 (71.4%)
- T-cell or histiocyte-rich large B-cell lymphoma	1 (3.6%)
- High-grade B-cell lymphoma, with rearrangement of MYC with BCL2 or BCL6 or both	1 (3.6%)
- Follicular lymphoma grade 3b	1 (3.6%)
• Follicular lymphoma grade 1–3a	2 (7.2%)
• Mantle cell lymphoma	3 (10.7%)
Disease stage III or IV, n (%)	22 (88.0%)
Bulky disease (>5cm), n (%)	10 (35.7%)
Prior therapies	
• Median (range)	
- Before bispecific antibodies	2 (1–6)
- Before CAR-T infusion	4 (2–9)
• Chemoradiotherapy disease, n (%)	27 (96.4%)
• Previous ASCT, n (%)	3 (10.7%)

CAR T-cell therapy remain effective in patients with R/R B-cell NHL after bispecific antibodies exposure: results of a LYSA study based on the Descar-T registry

OUTCOMES AFTER BA TREATMENT OUTCOMES AFTER CAR-T INFUSION

Response rate (%)		Response rate (%)	
ORR	53.6	ORR	92.3
CR	25	CR	50.0
PR	28.6	PR	42.3
SD	10.7	SD	0
PD	35.7	PD	7.7
Median PFS (95% CI) (mo)	3.2 (3.0–4.2)	Median FU (95% CI) (mo)	8.4 (3.1–18.5)
Median duration of bispecific antibodies treatment (range)	89.5 (20–267)	Median PFS (95% CI) (mo)	10.2 (2.6–NA)
Median time to next treatment (range) (days)	142.5 (37–482)	6 months PFS (95% CI)	57.3 (33.6–75.2)
Reason for bispecific antibodies discontinuation	Progression 96.4 (n=27)	6 months DOR (95% CI)	62.3 (36.7–80)
CRS (grade ≥3), %	67.9 (0)	6 months OS (95% CI)	66.7 (5.4–94.5)
ICANS (grade ≥3), %	0 (0)	CRS (grade ≥3) %	92.9 (10.7)
		ICANS (grade ≥3) %	32.1 (3.6)
		Death after CAR-T infusion, n (%)	7 (25)
		Toxicities	3 (10.7)
		Disease progression	4 (14.3)

Bispecific antibodies, n (%) (combination with lenalidomide in 1 patient)	
Glofitamab (CD20/CD3)	18 (64.3%)
Mosunetuzumab (CD20/CD3)	1 (3.6%)
Odronebamab (CD20/CD3)	3 (10.7%)
Epcoritamab (CD20/CD3)	1 (3.6%)
Plamotamab (CD20/CD3)	3 (10.7%)
JNJ-75348780 (CD22/CD3)	1 (3.6%)
Blinatumomab (C19/CD3)	1 (3.6%)
CAR-T cells, n (%)	
Axi-cel	16 (57.1%)
Tisa-cel	9 (32.1%)
Brexu-cel	3 (10.7%)
Bridging therapy, n (%)	23 (82.1%)

	BA therapy	CAR-T cells
Treatment description	(CD20xCD3) 91.4%	Axi-cel 72%
	(CD19xCD3) 4.3%	Tisa-cel 28%
	(CD22xCD3) 4.3%	
Response rate (%)		
ORR	43.5	91.6
CR	21.7	45.8
PR	21.7	45.8
SD	13.0	0
PD	43.5	8.3
Median follow-up (95% CI) (mo)	/	12.3 (3.7–23.7)
Median PFS (95% CI)	3.1 (2.9–4.2)	3.3 (2.2–NR)
6-months PFS	17.4 (5.4–35)	44.6 (22.4–64.7)
1-year PFS	4.3 (0.3–18.2)	37.2 (15.9–58.7)
Median DOR (95% CI)	2.7 (1.6–4)	2.4 (1.4–NR)
1-year DOR	10 (0.6–35.8)	40.7 (17.4–63.1)
1-year OS	/	53.5 (27–74.2)

KEY RESULTS

BA

ORR 53.6%; CR 25.0%; mPFS 3.2; mTTNT 142 d

- LBCL subgroup: 6 months PFS 17.4%; mPFS 3.1 months; mDOR 2.7 months

AFTER CAR-T INFUSION

ORR 92.9%; CR 50.0%;

- LBCL subgroup: 72% received axi-cel; 28% received tisa-cel; Best ORR 91.6%; best CR 45.8%
- LBCL subgroup: 1-year PFS 37.2%; 1-year OS 53.5%. 1-year DOR was 40.7%

CONCLUSIONS

- The efficacy of CAR-T appears preserved in B-NHL patients whose disease progressed after prior treatment with bispecific antibodies
- No new toxicity signals have been identified

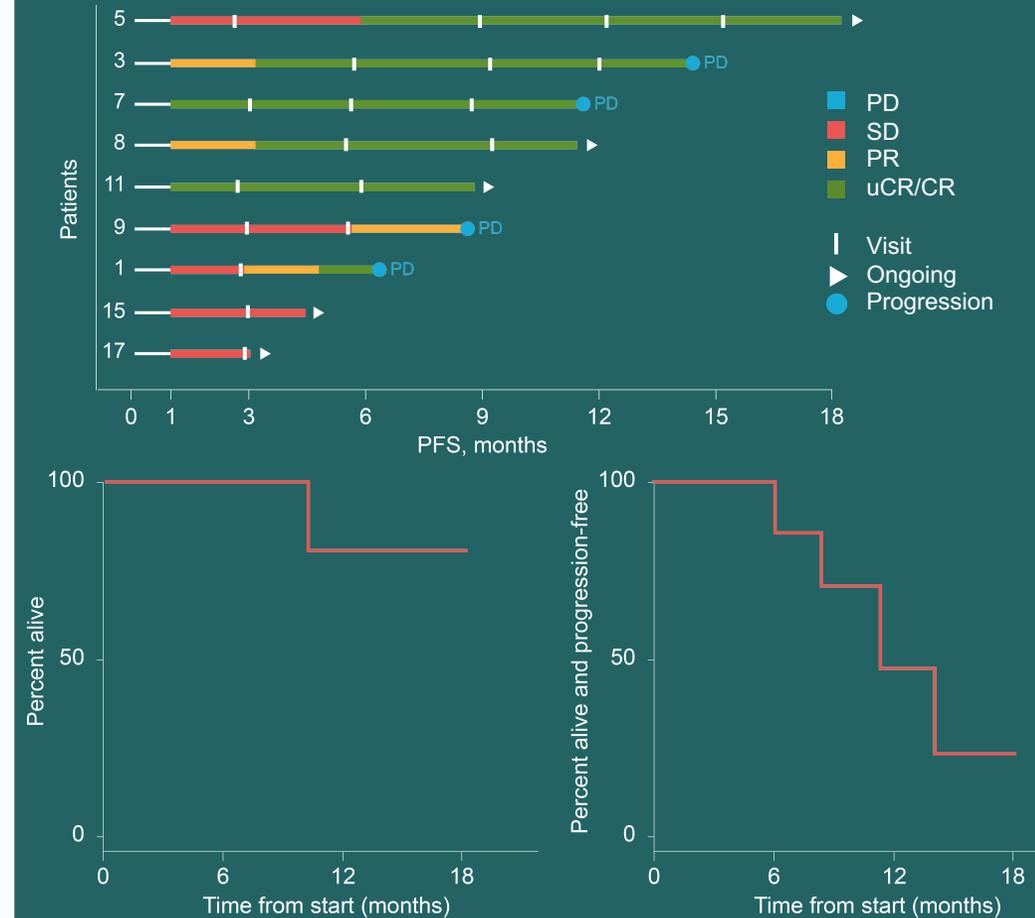
A pilot study of axicabtagene ciloleucel (AXI-CEL) for the treatment of R/R primary and secondary central nervous system lymphoma (CNSL)

Jacobson C, et al. Presented at ASH 2022; Abstract n. 440

BASELINE CHARACTERISTICS

Characteristic		N=9 (%)
Gender	Male	4 (44)
	Female	5 (56)
Age (years)	Median (range)	60 (33–74)
Primary vs secondary CNSL	Primary	6 (67)
	Secondary	3 (33)
Cell of origin (Hans)	GCB	1 (11)
	Non-GCB	5 (56)
	Unknown	3 (33)
DHL or THL	Yes	0 (0)
	No	6 (67)
	Unknown	3 (33)
Double expressor	Yes	3 (33)
	No	4 (44)
	Unknown	2 (22)
Tumor location	<u>Parenchymal</u>	<u>9 (100)</u>
	<u>CSF cytology positive</u>	<u>2 (22)</u>
Number of prior systemic therapies	Median (range)	2 (1.6)
Disease status to last line of therapy	Relapsed	4 (44)
	Refractory	5 (56)
Time from CNSL diagnosis to enrollment	Days (range)	281 (121–8666)
Time from last systemic therapy to enrollment	Days (range)	57 (16–392)

EFFICACY



KEY RESULTS

- Median follow-up: 11.3 months (3.0–19.0 months)
- mDOR: 11.3 months
- Peak serum CAR-T cell levels in the first 7 treated patients were comparable to that seen on ZUMA-1, despite the lack of systemic disease
- Best ORR: 78%; uCR/CR: 67%
- 6 months ORR: 78%

CONCLUSIONS

- Axi-cel has an acceptable safety profile for the treatment of both primary and secondary CNS lymphoma with no increased risk of neurologic events, including high-grade ICANS or cerebral edema
- Axi-cel has promising efficacy in R/R primary and secondary CNS lymphoma with a CR rate of 67% and a mDOR and mPFS of 9.9 and 11.5 months, respectively
- Despite all patients having no systemic lymphoma burden, axi-cel PK was similar to that observed on ZUMA-1