Anti-CD19 chimeric antigen receptor T-cell therapy has less efficacy in Richter transformation than in *de novo* large B-cell lymphoma and transformed low-grade B-cell lymphoma

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Table S1 Univariate and multivariate analysis to identify prognostic factors for progression free survival.

Variable	Univariate analysis			Multivariate analysis		
	N, Event	HR(95% CI)	p-value	N, Event	HR(95% CI)	p-value
Cohort	454,252		<0.001	419,232		<0.0001
De novo LBCL		-	-		-	-
Transformed iNHL		0.71(0.59-0.86)			0.75(0.65-0.86)	
Transformed CLL		1.23(1.03,1.47)			1.55(1.29,1.87)	
Age at CAR-T infusion	454,252		0.36	419,232		0.19
		1.00(0.99-1.0)			0.99(0.98-1.00)	
LDH range pre-lymphodepletion	427,237		0.027	419,232		0.064
normal		-	-		-	-
elevated		1.63(1.06-2.50)			1.62(0.97-2.69)	
CAR-T costimulatory domain	454,252		0.16	419,232		0.1
4-1BB		-	-		-	-
CD28		0.87(0.71-1.06)			0.8(0.6-1.05)	
Pre-apheresis treatment lines	446,247		0.15	419,232		0.071
≤3		-	-		-	-
4-5		1.07(0.77-1.48)			0.95(0.65-1.37)	
≥6		1.25(1.00-1.56)			1.21(0.89-1.65)	

[1]HR = Hazard Ratio, CI = Confidence Interval, PFS progression free survival

Table S2 Univariate and multivariate analysis to identify prognostic factors for relapse.

Variable	Univariate analysis			Multivariate analysis		
	N, Event	HR(95% CI)	p-value	N, Event	HR(95% CI)	p-value
Cohort	454,252		<0.001	419,225		<0.0001
De novo LBCL		- -			- -	
Transformed iNHL		0.75(0.71-0.80)			0.79(0.73-0.86)	
Transformed CLL		1.38(1.17,0.80)			1.76(1.36,2.29)	
Age at CAR-T infusion	454,252		0.40	419,225		0.13
		1.00(0.99-1.0)			0.99(0.98-1.00)	
LDH range pre-lymphodepletion	427,229		0.012	419,225		0.031
normal		- -			- -	
elevated		1.71(1.13-2.60)			1.73(1.05-2.83)	
CAR-T costimulatory domain	454,242		0.038	419,225		0.010
4-1BB		- -			- -	
CD28		0.81(0.66-0.99)			0.71(0.55-0.92)	
Pre-apheresis treatment lines	446,238		0.62	419,225		0.31
≤3		- -			- -	
4-5		1.06(0.74-1.54)			0.94(0.61-1.45)	
≥6		1.17(0.85-1.61)			1.15(0.80-1.65	

[1]HR = Hazard Ratio, CI = Confidence Interval, PFS progression free survival

Table S3 Univariate exploratory analysis to identify prognostic factors for survival and progression free survival in patients with Richters transformation.

Variable	Univariate analysis - OS			Univariate analysis - PFS		
	N, Event	HR(95% CI)	p-value	N, Event	HR(95% CI)	p-value
Age at CAR-T infusion	30,17	0.96(0.91-1.0)	0.075	30,18	0.93(0.87-1.00)	0.046

LDH range pre-lymphodepletion
    normal
    elevated
	29,17	- -
		1.60(0.89-2.88)
			0.12	29,18	- -
					1.72(0.76-3.89)
						0.19

Pre-apheresis treatment lines ≤3 4-5 ≥6	28,17	- - 0.68(0.39-1.19) 2.00(1.25-3.19)	<0.001	28,17	- - 0.51(0.24-1.08) 1.48(1.01-2.16)	0.002

Bridging BTK exposure
    No exposed
    Exposed
	30,17	- -
		1.51(0.51-4.44)
			0.45	30,18	- -
					1.18(0.26-5.27)
						0.83

Disease stage at apheresis
    ≤II
    ≥III-IV
	27,16	- -
		1.61(0.70-3.71)
			0.26	30,17	- -
					1.58(0.81-3.06)
						0.18

Pre-CAR-T KPS (categorized) ≥90 <90	30,17	- - 1.29(0.76-2.19)	0.34	30,17	- - 0.96(0.41-2.26)	0.34

[1]HR = Hazard Ratio, CI = Confidence Interval, OS overall survival, PFS progression free survival, KPS Karnofsky performance status

Table S4 Univariate and multivariate analysis to identify prognostic factors for overall survival excluding patients treated with POC CAR T .

| Variable	Univariate analysis			Multivariate analysis		
	N, Event	HR(95% CI)	p-value	N, Event	HR(95% CI)	p-value
Cohort	373,141		<0.001	342,131		<0.001
De novo LBCL		- -			- -	
Transformed iNHL		0.65(0.56-0.76)			0.61(0.50-0.75)	
Transformed CLL		1.98(1.12-3.50)			2.26(1.68,3.06)	
Age at CAR-T infusion	373,141	1.01(1.01-1.02)	<0.001	342, 131	1.01(1.00-1.02)	0.021
LDH range pre-lymphodepletion	350,134		<0.001	342, 131		<0.001
normal		- -			- -	
elevated		3.01(2.07-4.38)			3.08(2.00-4.74)	
CAR-T costimulatory domain	373,141		0.074	342, 131		0.60
4-1BB		- -			- -	
CD28		0.82(0.65-1.02)			0.94(0.74-1.19)	
Pre-apheresis treatment lines	365,138		0.080	342, 131		<0.001
≤3		- -			- -	
4-5		1.12(0.79-1.59)			0.97(0.55-1.70)	
≥6		1.65(1.04-2.61)			1.56(1.04-2.34)	

[1]HR = Hazard Ratio, CI = Confidence Interval, PFS progression free survival

Table S5 Univariate and multivariate analysis to identify prognostic factors for progression free survival excluding patients treated with POC CAR T .

Variable	Univariate analysis			Multivariate analysis		
	N, Event	HR(95% CI)	p-value	N, Event	HR(95% CI)	p-value

Cohort
   De novo LBCL
   Transformed iNHL
   Transformed CLL
	374,208	- -
		0.77(0.66-0.90)
		1.43(1.07-1.91)
			<0.001	343,191	- -
					0.81(0.68-0.96)
					1.56(0.99,2.46)
						<0.001

Age at CAR-T infusion	374,208	1.00(1.00-1.01)	<0.76	343, 191	1.00(0.99-1.00)	0.19

LDH range pre-lymphodepletion
   normal
   elevated
	351,196	- -
		1.67(1.01-277)
			<0.045	343, 191	- -
					1.65(0.89-3.06)
						0.11

CAR-T costimulatory domain
   4-1BB
   CD28
	374,208	- -
		0.77(0.60-1.03)
			0.083	343, 191	- -
					0.78(0.58-1.04)
						0.0.92

Pre-apheresis treatment lines ≤3 4-5 ≥6	366,203	- - 0.98(0.69-1.40) 1.25(0.95-1.65)	0.17	343, 191	- - 088(0.54-1.44) 1.21(0.82-1.8)	<0.001

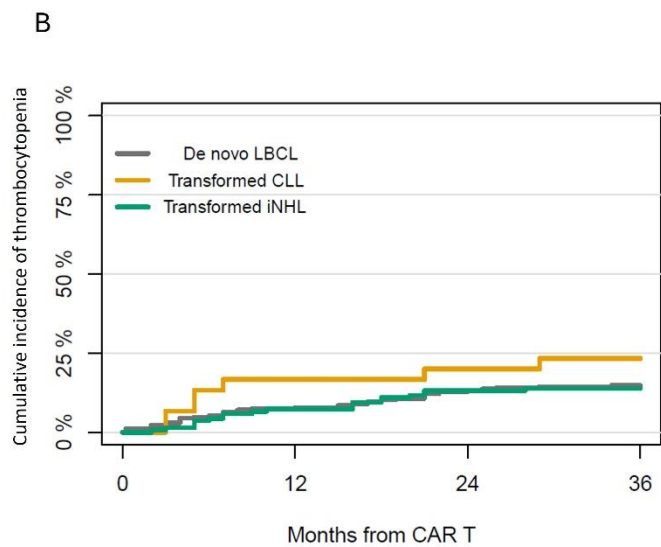[1]HR = Hazard Ratio, CI = Confidence Interval, PFS progression free survival

Supplementary figure S1 Cumulative incidence of neutropenia and thrombocytopenia.

A
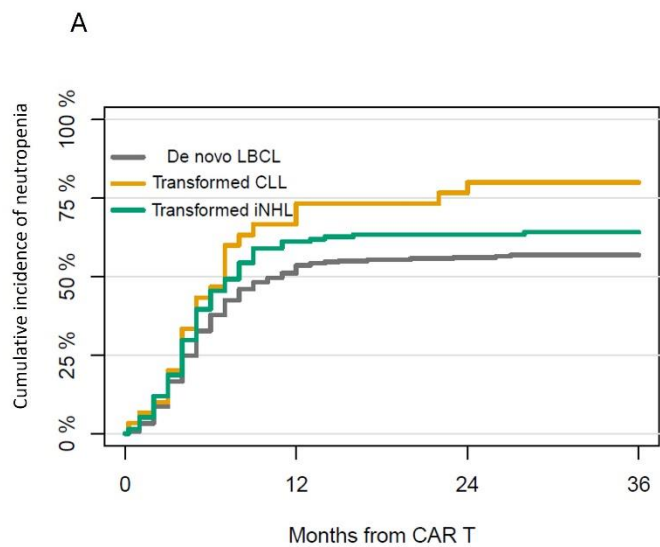
Characteristic	N	Days 30	Days 60	p-value[1]
cohort	442			0.025
DeNovo LBCL		57% (51%, 62%)	58% (52%, 63%)	
RT		80% (59%, 91%)	80% (59%, 91%)	
Transformed iNHL		64% (55%, 72%)	66% (57%, 73%)	

[1]Gray's Test

B

Characteristic	N	Days 30	Days 60	p-value[1]
cohort	438			0.5
DeNovo LBCL		14% (11%, 19%)	15% (11%, 20%)	
RT		23% (10%, 40%)	23% (10%, 40%)	
Transformed iNHL		14% (8.7%, 20%)	15% (9.3%, 21%)	

[1]Gray's Test

Supplementary figure S2 Survival outcomes according excluding patients treated with POC CAR
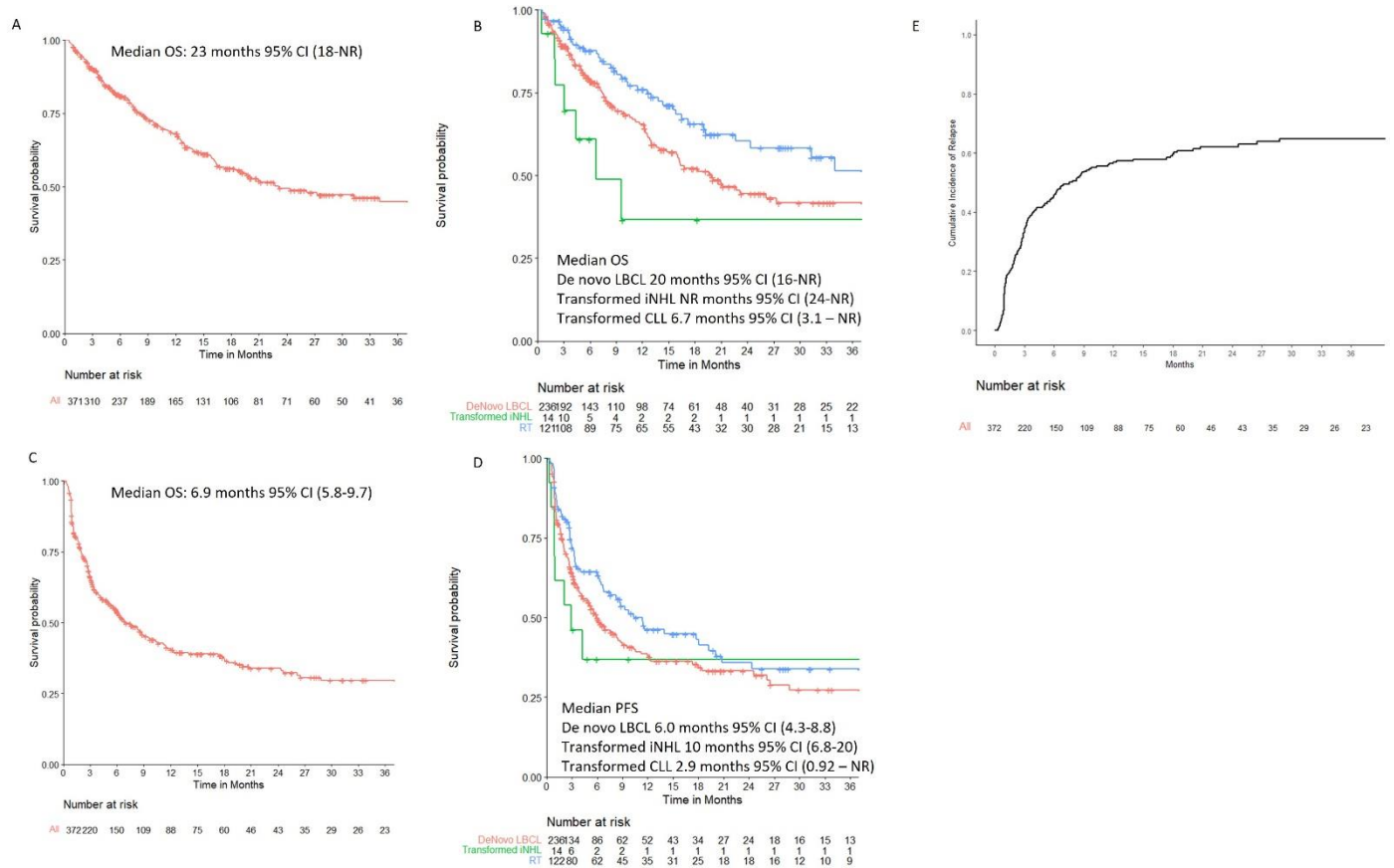
Survival outcomes according excluding patients treated with POC CAR T . (A) Overall survival of the cohort. (B) Overall survival according to histology. (C) Progression Free Survival of the cohort. (D) Progression Free Survival according to histology. (E)cumulative incidence of relapse for the cohort De novo LBCL: Transformed Low grade NHL and transformed CLL