Resultados actualizados de terapia CAR-T en linfoma no Hodgkin

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Disclosures

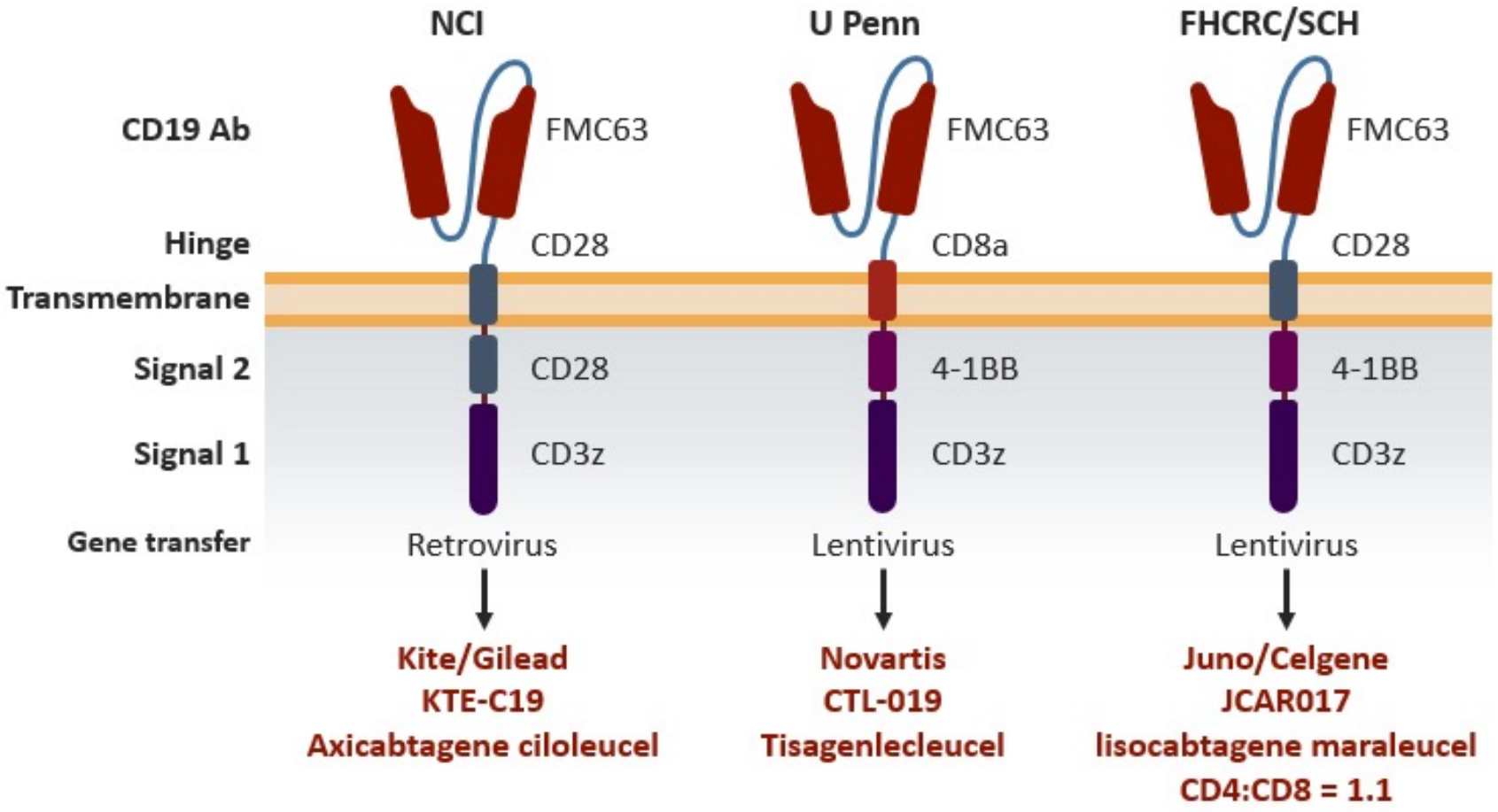
Speaker:

- Celgene / BMS, Novartis, Roche, AbbVie, Janssen and Gilead / Kite

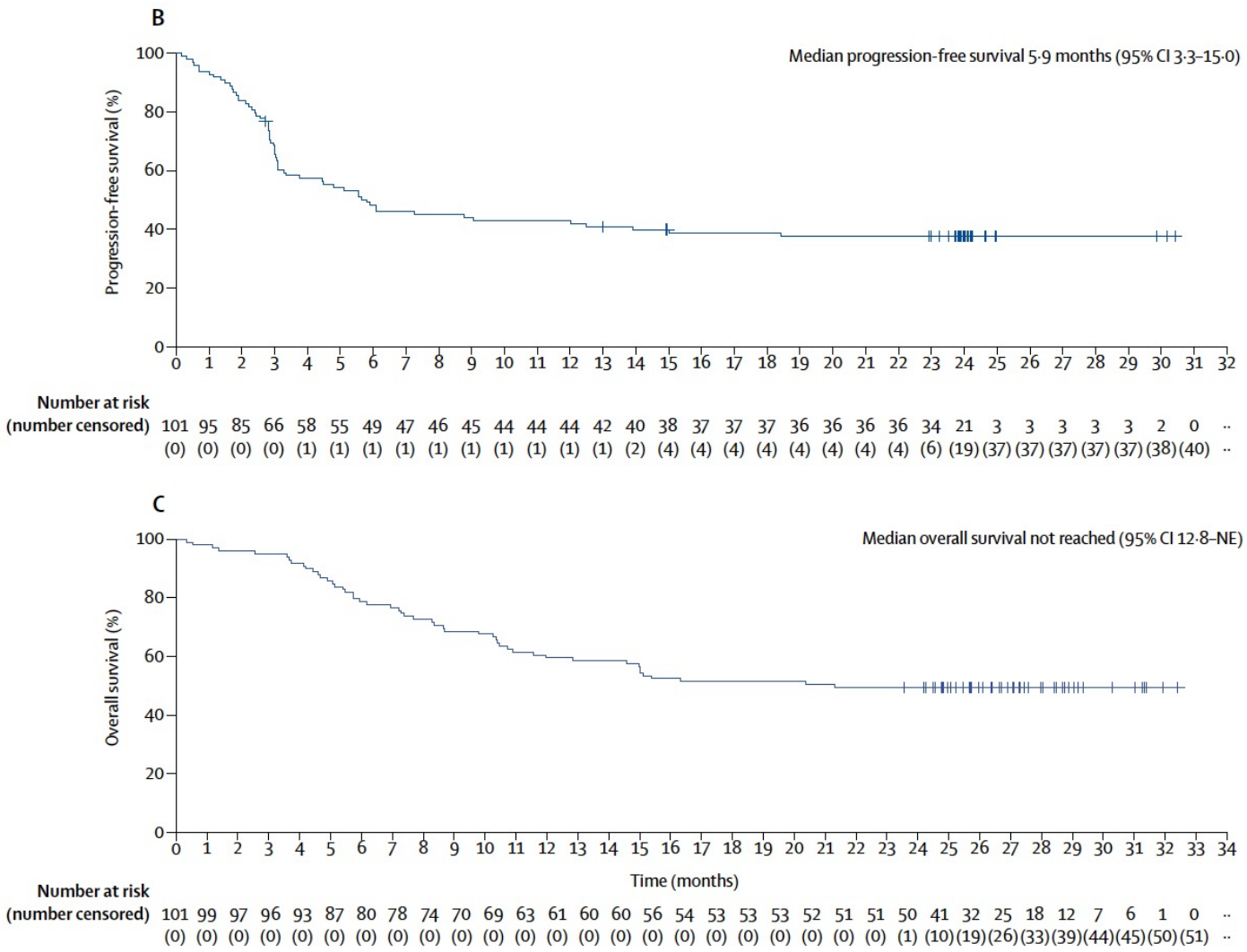
Travel and accommodation:

- Novartis, Roche, Celgene and Gilead

FDA approved CAR T-cell therapies for LBCL



Axicabtagene ciloleucel for R/R LBCL
Long-term results from ZUMA-1 trial



ORR: (n=101): 83%
CR: 58%

Grade ≥ 3 CRS = 11%
Grade ≥ 3 ICANS = 32%

n(%)	N= 111
Patients who died	66 (59)
Primary cause of death	
Progressive disease	52 (47)
Other	8[a] (7)
AEs	5[b] (5)
Secondary malignancy	1 (1)

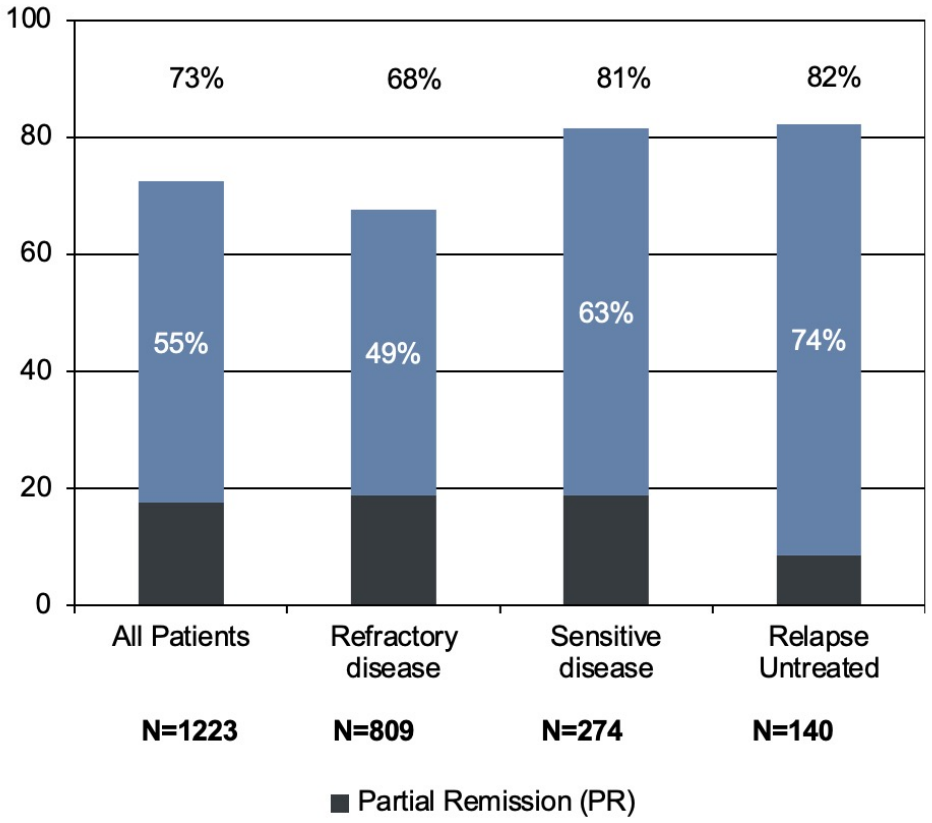
Locke F, Lancet Oncol 2019; Neelapu S, NEJM 2017

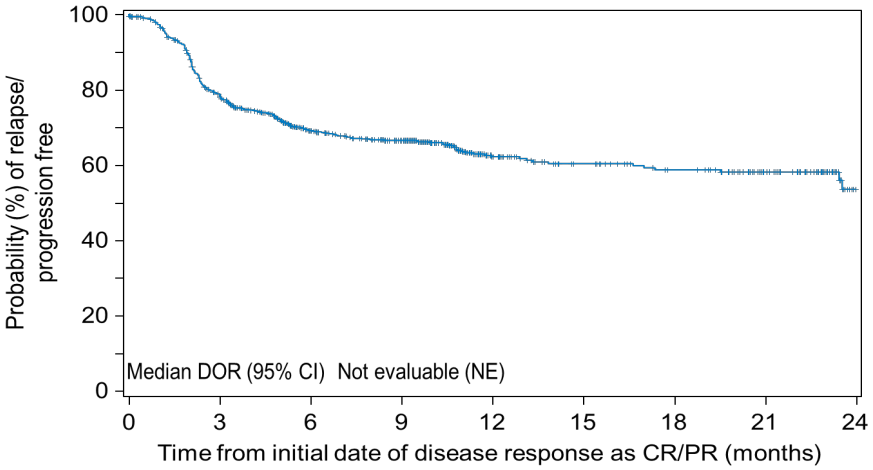
Real-World Evidence of axi-cel for the treatment of LBCL in the US

Characteristic	Total
Number of patients	1,223
Number of US centers	76
Median age, years (range)	62 (19-91)
≥65 years	38%
Male	65%
ECOG performance status 0-1	83%
Prior History of Malignancy	16%
Transformed lymphoma	26%
Double/triple hit lymphoma	15%
Chemotherapy resistant disease	66%
Prior auto-HCT	27%
Time from diagnosis to axi-cel, median months	14

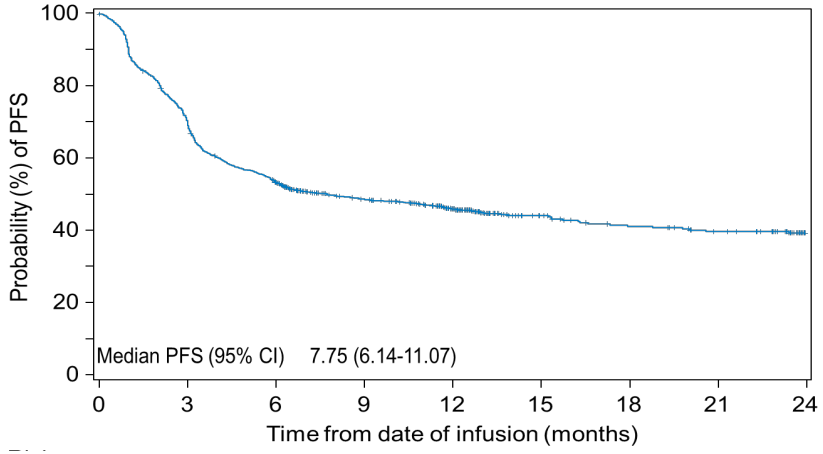
Jacobson CA, et al. ASCO 2021. Abstract #7552

Real-World Evidence of axi-cel for the treatment of LBCL in the US





DoR

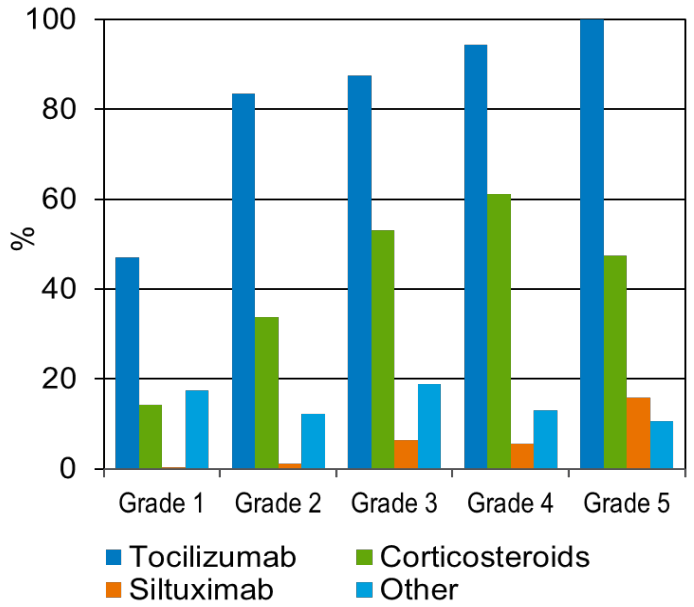


PFS

Jacobson CA, et al. ASCO 2021. Abstract #7552

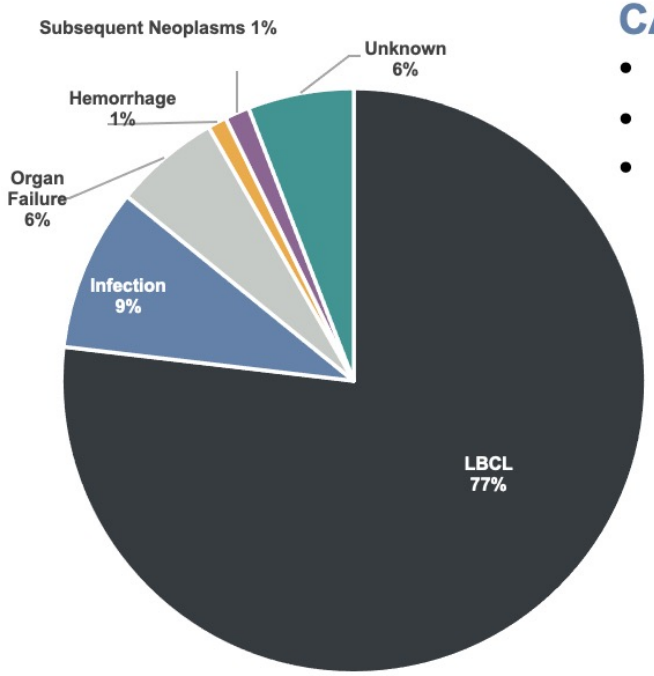
Real-World Evidence of axi-cel for the treatment of LBCL in the US

Safety profile	
Any Gr CRS/Gr ≥3, %	82/9
Any Gr NE/Gr ≥3, %	55/24



CRS Grade Incidence by Intervention

All Causes of Death (N=478)

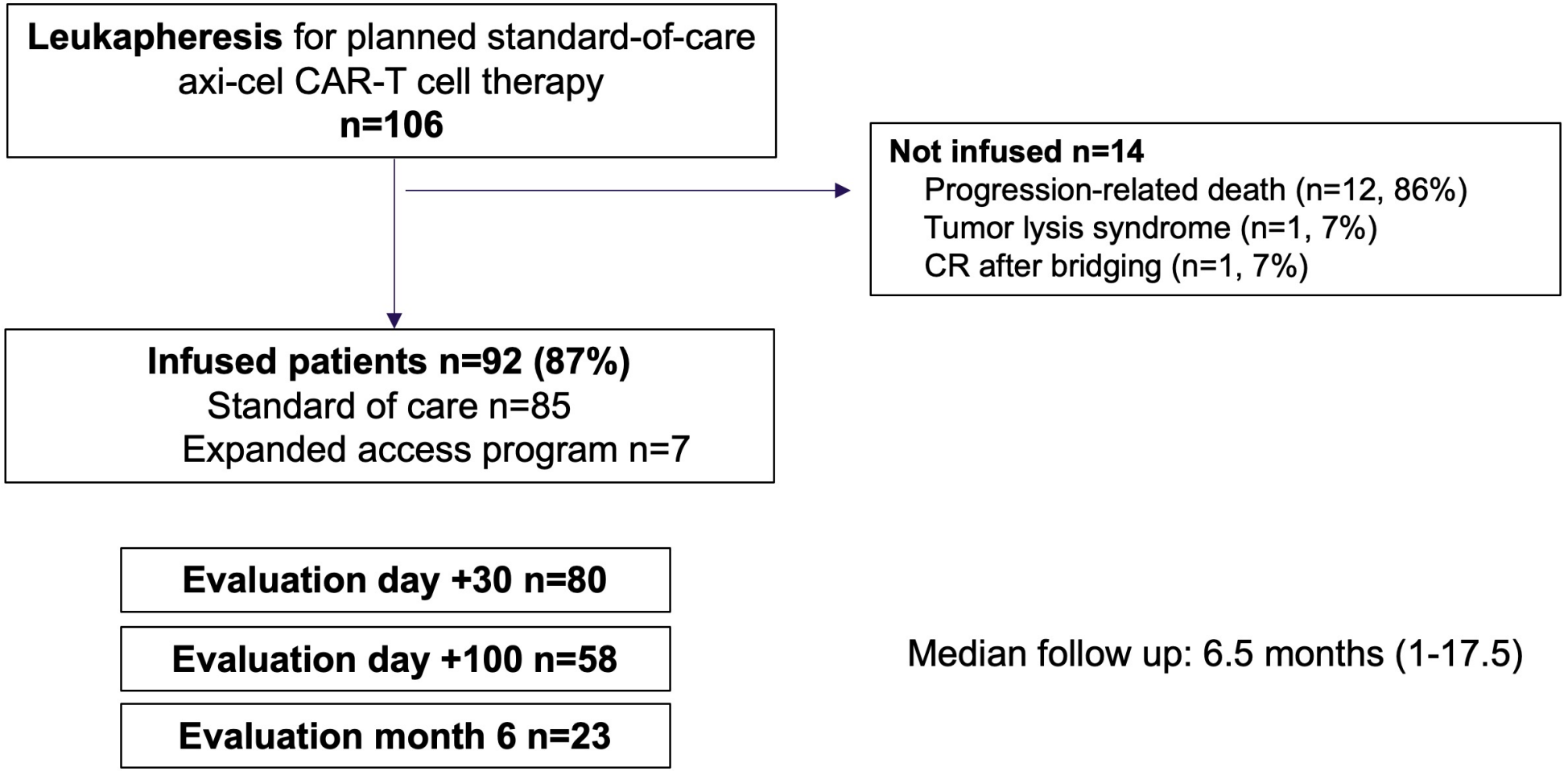


CAR T-Cell Specific Deaths:

- Neurologic Toxicity: N=4
- CRS: N=8
- Hemorrhage:
  - CNS: N=3
  - GI: N=2

Jacobson CA, et al. ASCO 2021. Abstract #7552

Spanish experience with axicabtagene ciloleucel

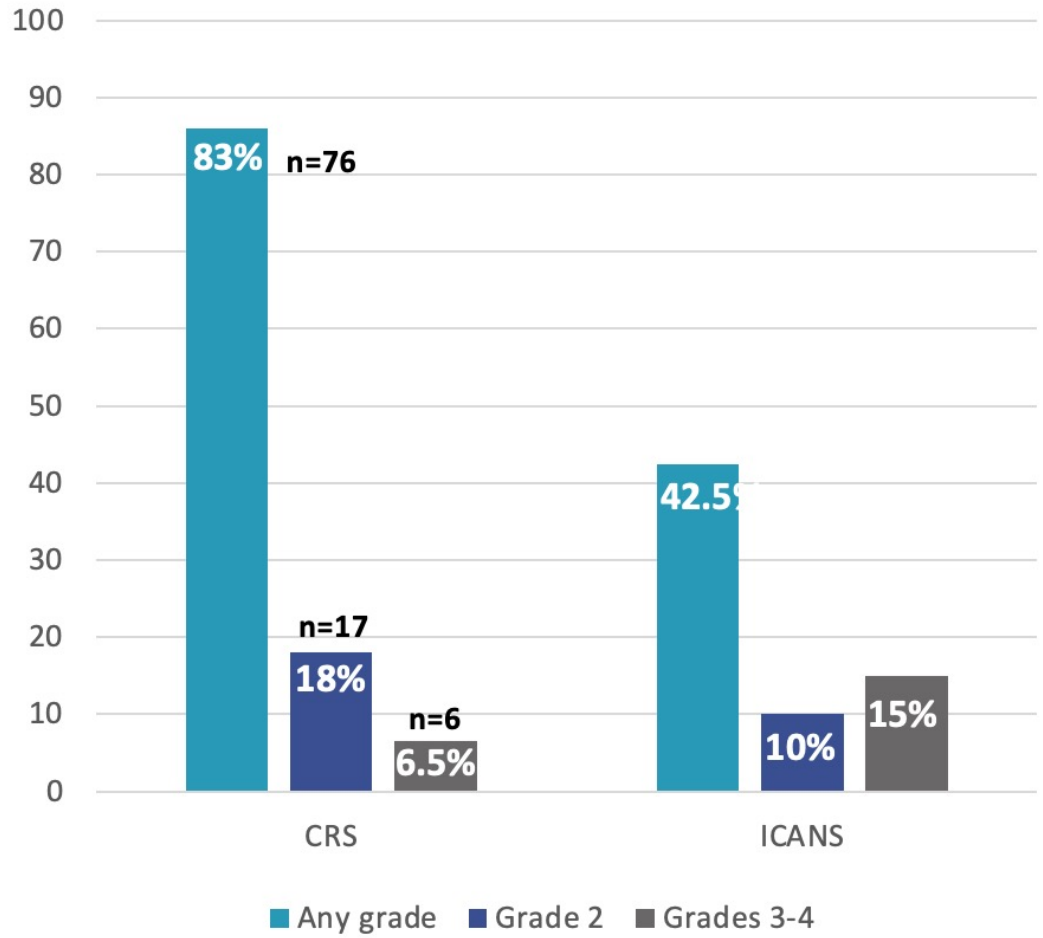


Median follow up: 6.5 months (1-17.5)

Kwon M, et al. *EBMT 2021*

Spanish experience with axicabtagene ciloleucel

Safety profile



CRS treatment

- Tocilizumab in 58%
- Corticosteroids in 19%

ICANS treatment

- Steroids in 78%
- Tocilizumab in 31%
- Anakinra in 21%
- Siltuximab in 15%

ICU in 20 patients (22%)

Toxicity associated deaths n=6 (6.5%)

4 ICANS

- 1 Sepsis during ICU admission due to ICANS
- 1 ICANS + HLH/MAS
- 2 ICANS (cerebral edema)

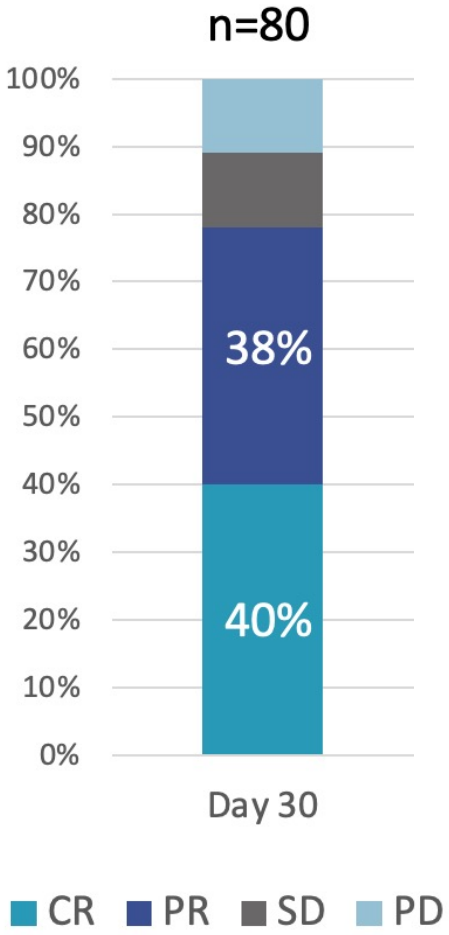
1 Sepsis

1 Refractory CRS

Kwon M, et al. *EBMT 2021*

Spanish experience with axicabtagene ciloleucel

Efficacy results



Of 39 with PR/SD at day 30 → 9 (23%) converted to CR

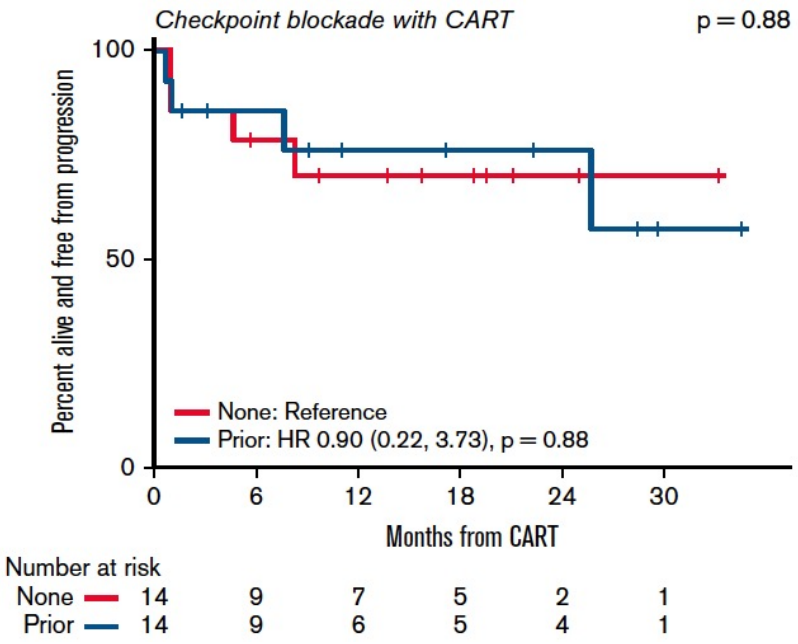
	CR30	CR90
Histology group (tFL, DBCL, PMBL)	0.395	0.585
Stage (I, II, III, IV)	0.619	0.473
IPI risk score (low, int-low, int-high, high, very high)	0.745	0.588
Bulky disease	**0.029**	**0.039**
Number of prior lines (n)	0.199	0.969
Prior autologous HSCT	1.000	0.190
Primary refractory disease	0.465	0.455
Status at lymphodepletion (CR, PR, PD, SD)	0.091	0.885
Bridging therapy	0.590	0.850

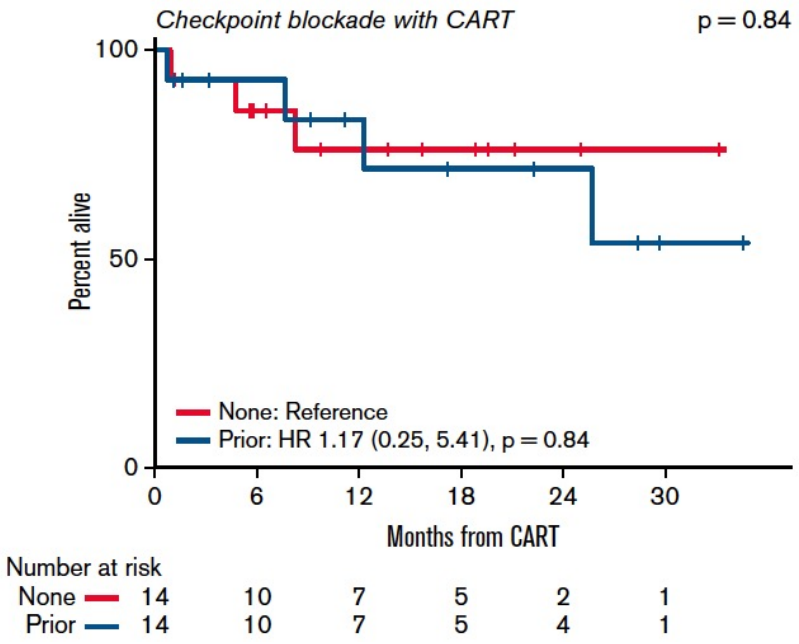
Kwon M, et al. *EBMT 2021*

Real-world outcomes of axi-cel in adult patients with primary mediastinal B-cell lymphoma

ORR: (n=33): 76%
CR: 67%

CRS, any grade/G ≥3 = 88%/6%
ICANS, any grade/G ≥3 = 39%/27%





Median age: 32y (range 18-46)

Median prior lines: 3 (range, 1-9)

Prior ASCT in 30%

Bulky disease in 42%

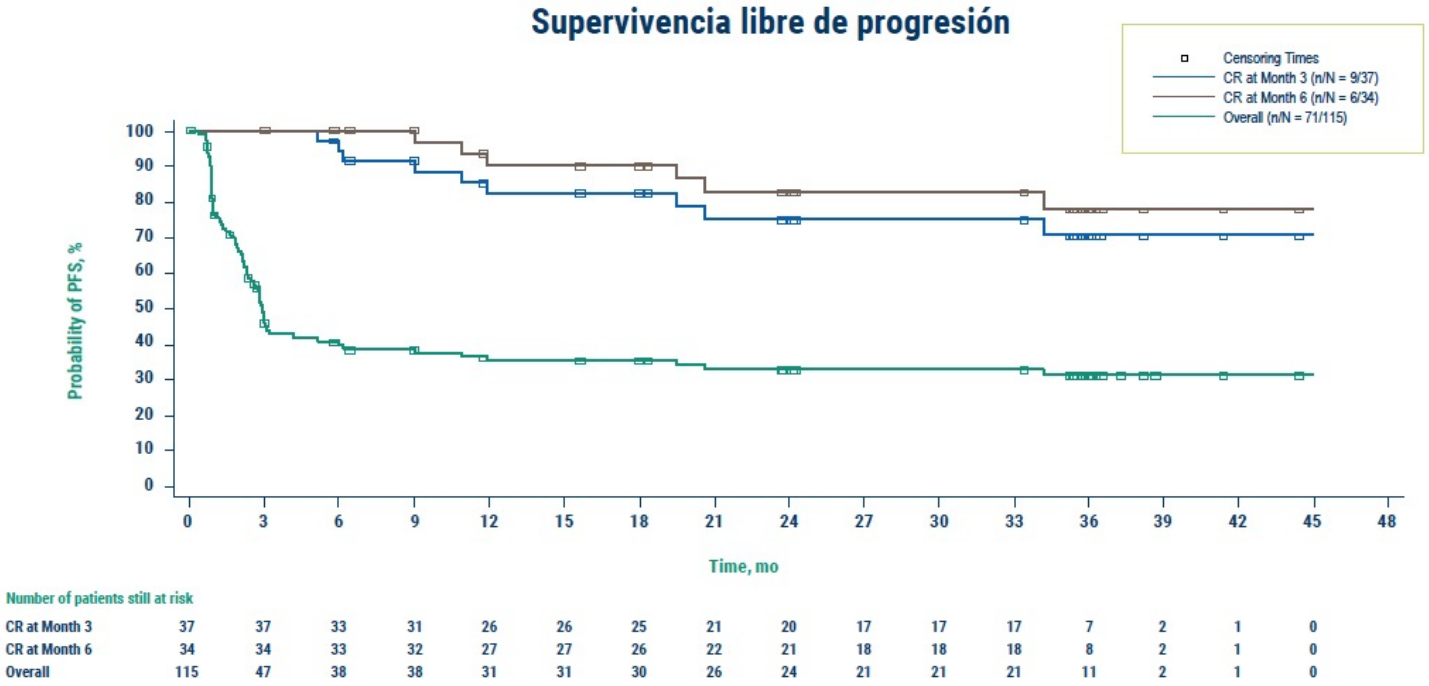
Median FU was 13.8 mo

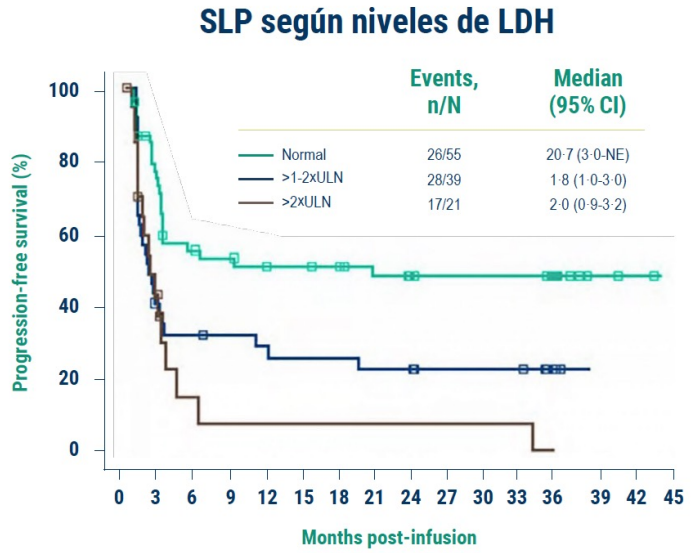
Crombie JL et al, Blood Advances 2021

Tisagenlecleucel for R/R LBCL
Long-term results from JULIET trial

ORR: (n=115): 53%
CR: 39%

CRS, any grade/G ≥3 = 57%/23%
ICANS, any grade/G ≥3 = 20%/11%





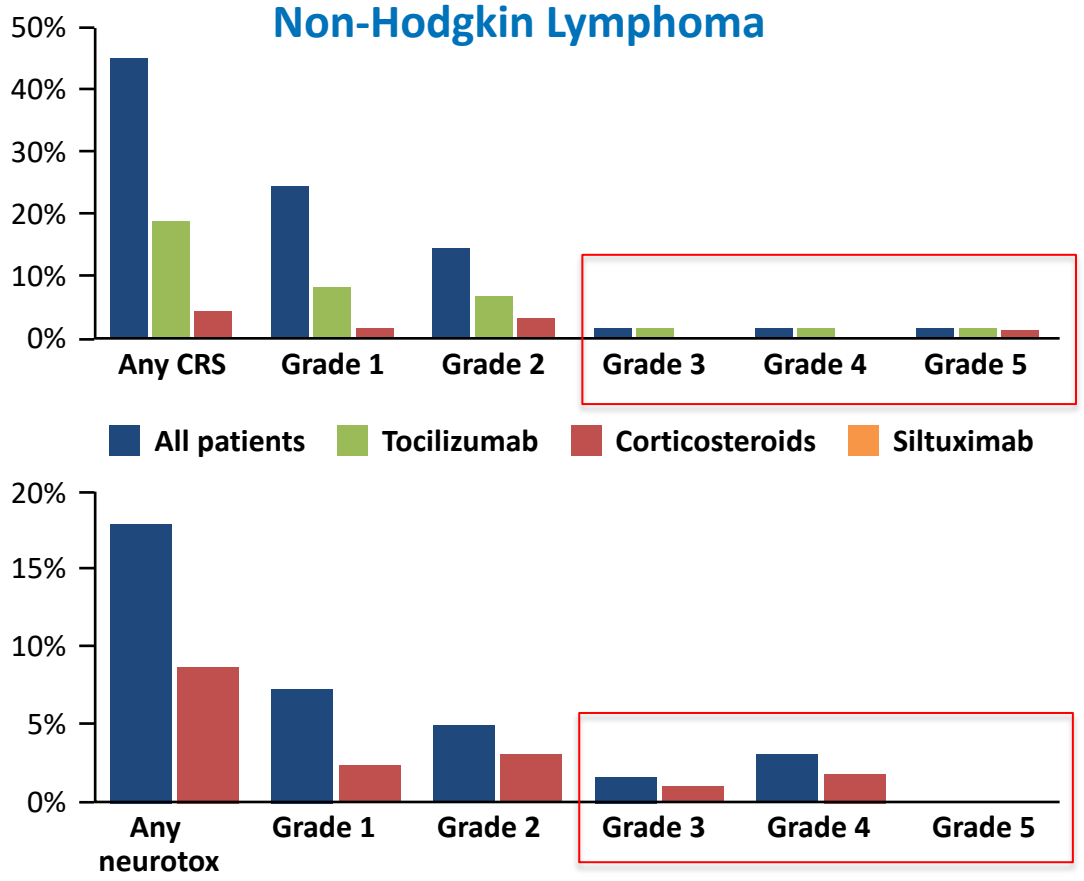
Mediana seguimiento: 40.3 meses

SLP a los 36 meses: 31% en todos los pacientes y 78% en los pacientes con RC a los 6 meses

Schuster S, Lancet Oncol 2021

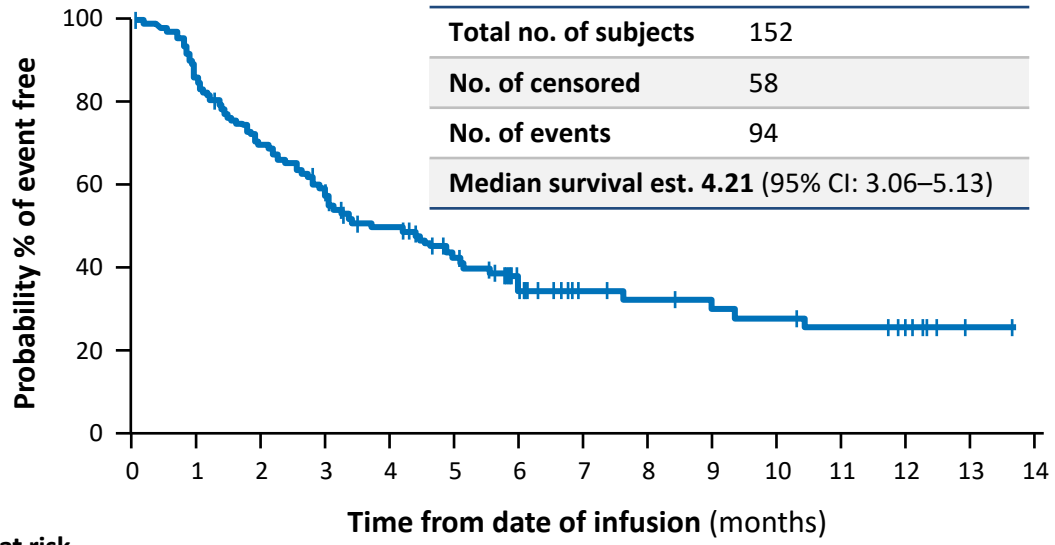
Real-world analysis of tisa-cel in R/R large B-cell lymphoma

Safety



Efficacy

Endpoint	CIBMTR, % (95% CI)	Pivotal trial, % (95% CI)
CIBMTR vs JULIET	N=152	N=155
ORR (CR + PR)	61.8 (53.6-69.6)	52.2 (42.7-61.6)
BOR of CR	39.5 (31.6-47.7)	38.3 (29.4-47.8)



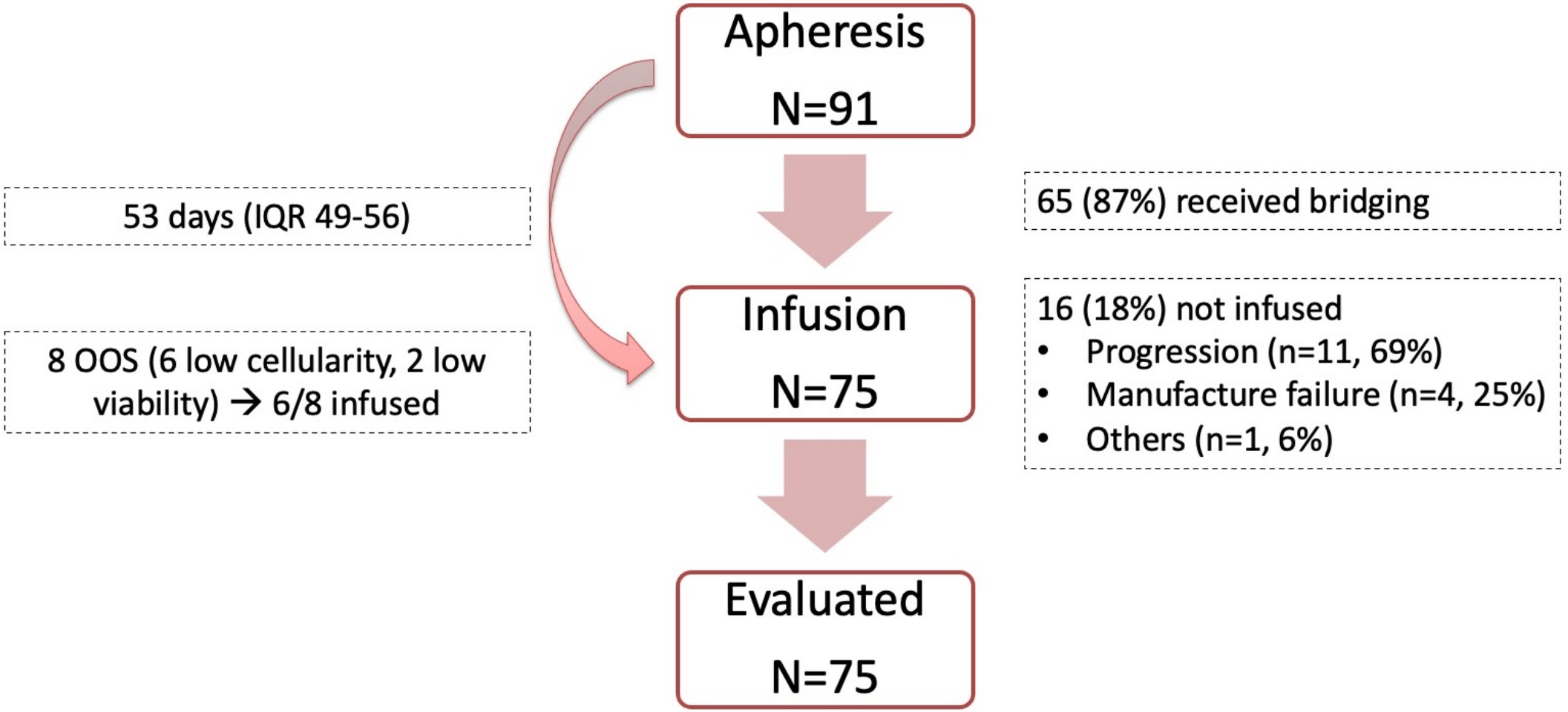
No. at risk

All subjects	152	129	104	87	67	51	34	18	16	15	13	11	9	1	0

BOR, best overall response; CI, confidence interval; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory.

Pasquini M, et al. *Blood Adv* 2020;4:5414–24.

Spanish experience with tisagenlecleucel
10 Spanish sites from December 2018 - June 2020



Iacoboni G, Cancer Medicine 2021

Spanish experience with tisagenlecleucel

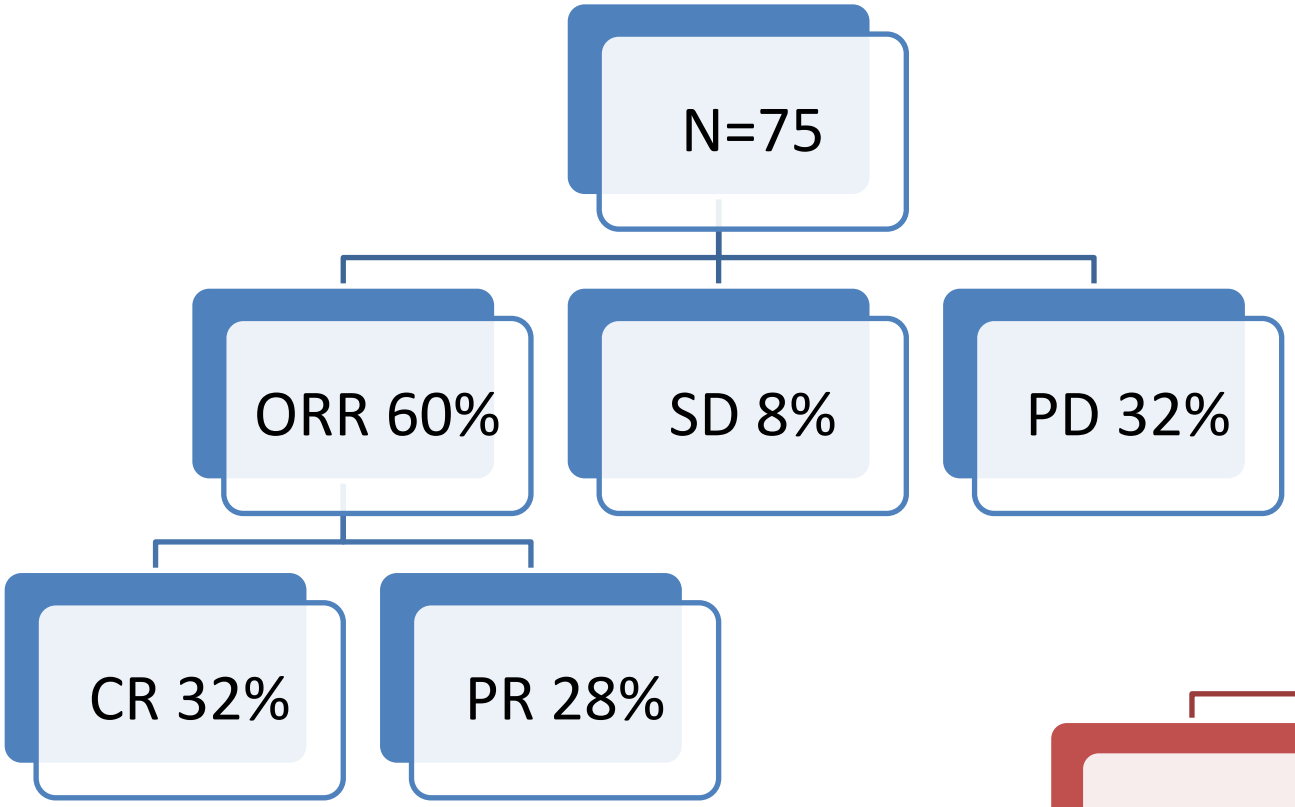
Safety

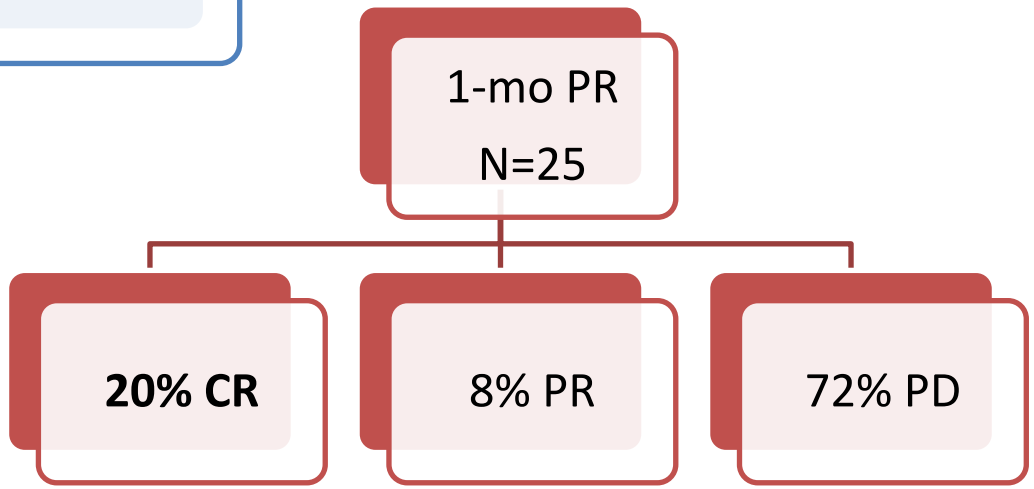
CRS	
• Any grade; n (%)	53 (71)
• Grade ≥2; n (%)	21 (28)
• Grade ≥3; n (%)	**4 (5)**
• Time from infusion to start of CRS; median days (IQR)	2 (1 – 4)
ICANS	
• Any grade; n (%)	11 (15)
• Grade ≥2; n (%)	6 (8)
• Grade ≥3; n (%)	**1 (1)**
• Time from infusion to start of ICANS; median days (IQR)	7 (5 – 9)
ICU, n (%)	10 (13)
Tocilizumab; n (%)	24 (32)
Corticosteroids; n (%)	16 (21)

Iacoboni G, Cancer Medicine 2021

Spanish experience with tisagenlecleucel

Response evaluation

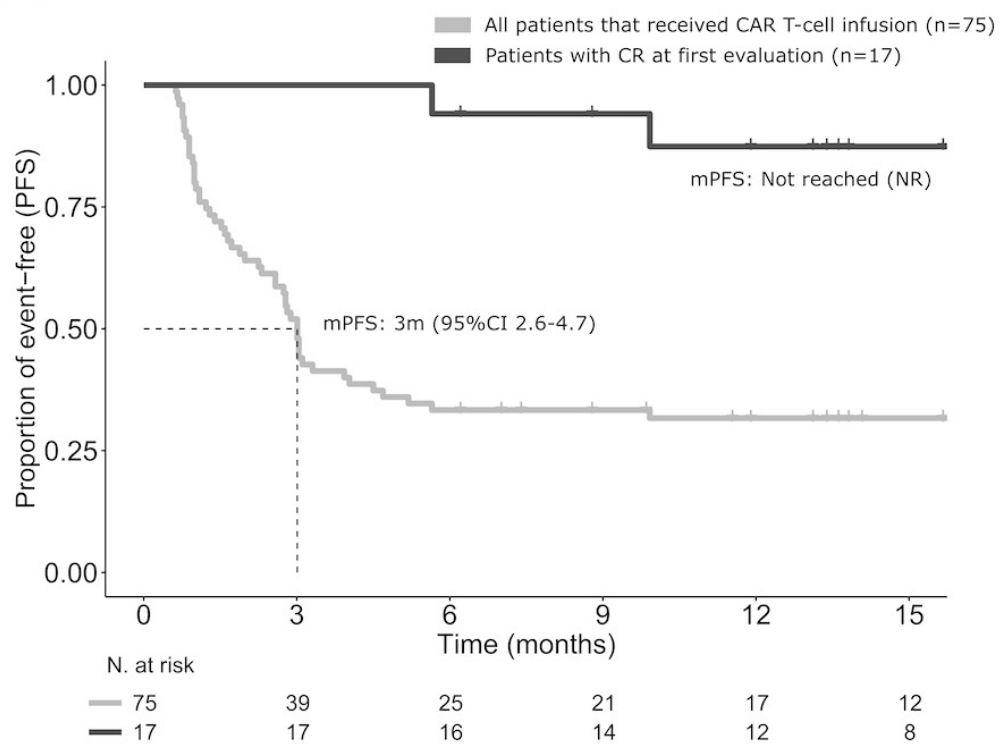




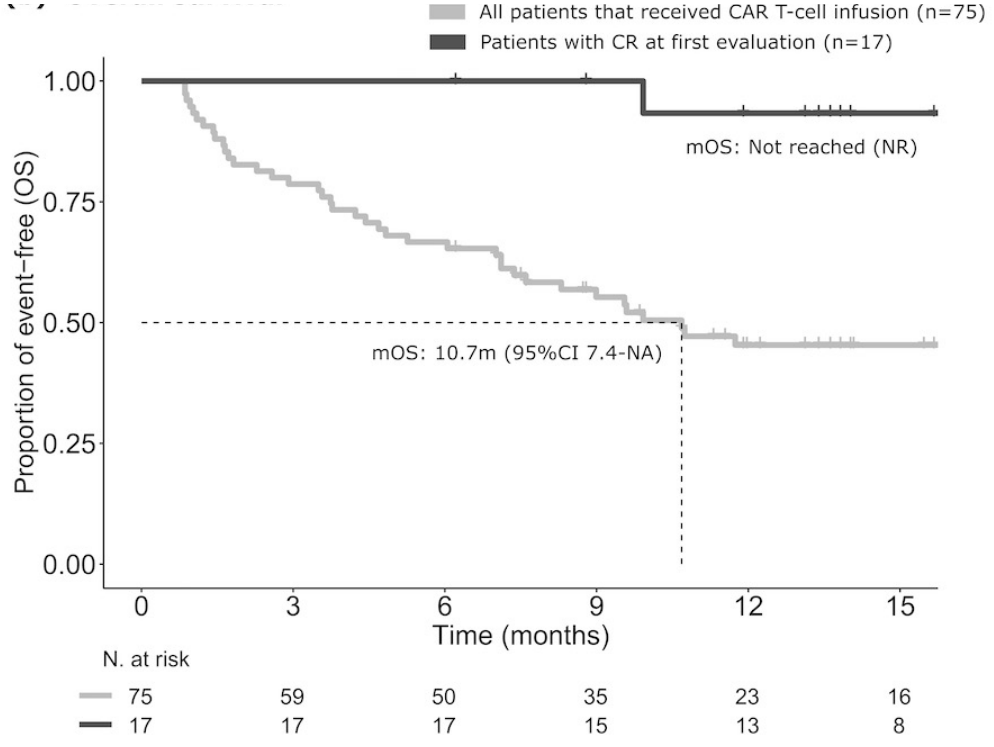
Iacoboni G, Cancer Medicine 2021

PFS and OS for infused patients and patients who achieved an initial CR

Progression-free survival



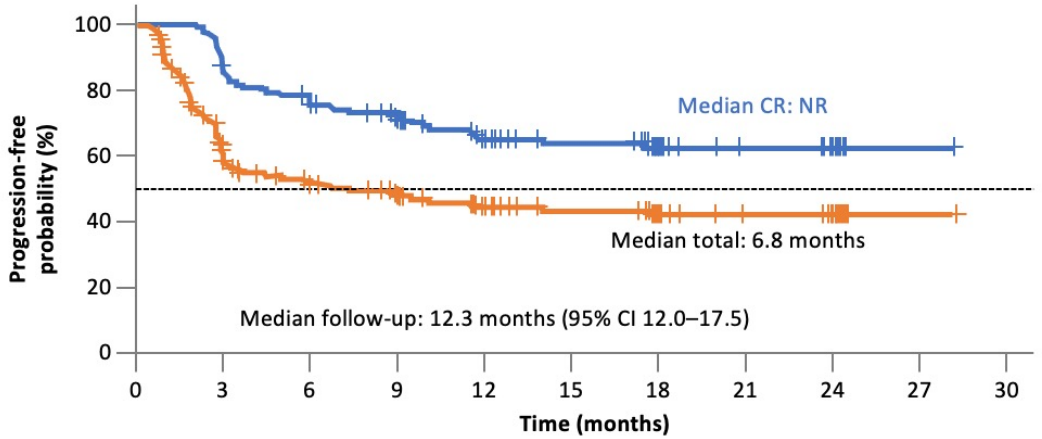
Overall survival

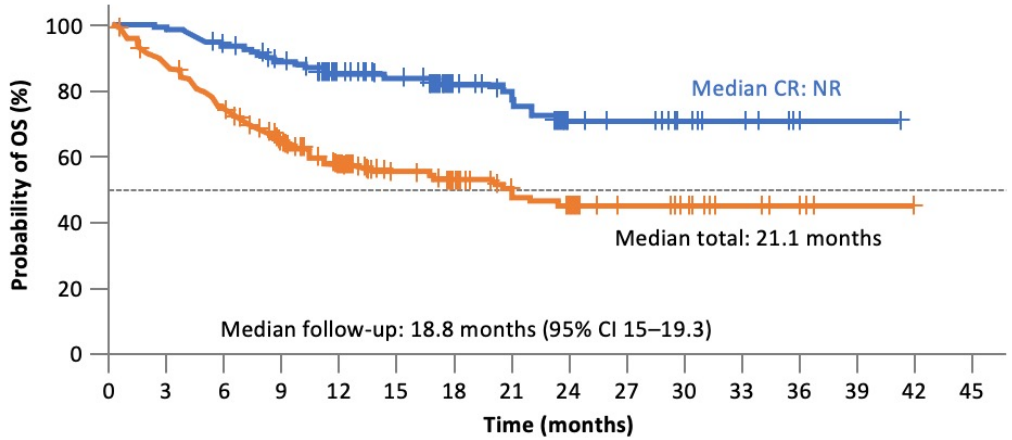


The overall 6-month and 12-month PFS was 33.3% and 31.7%, respectively

Iacoboni G, Cancer Medicine 2021

Lisocabtagene maraleucel for R/R LBCL TRANSCEND trial





Best response	Patients (N = 256)
Best ORR, %	73
Best CR, %	53

	N=269
Any CRS, %	42
Grade ≥ 3 CRS, %	**2**
Any neurological toxicity, %	30
Grade ≥ 3 neurotoxicity, %	**10**

Abramson JS, et al. Lancet. 2020 Sep; 396:839-852.

Brexu-cel real-world data (European)

ORR: (n=74): 85%
CR: 59%

CRS, G ≥3 = 15%
ICANS, G ≥3 = 31%

Apheresis
N=28

Bridging in 79%
- Ibrutinib 53%
- Chemo 47%
- RT 40%

- PD in 4
- Manufacture in 4
- CR in 1

Infusion
N=19

Wang M et al, NEJM 2020; Iacoboni et al (Submitted to ASH2021)

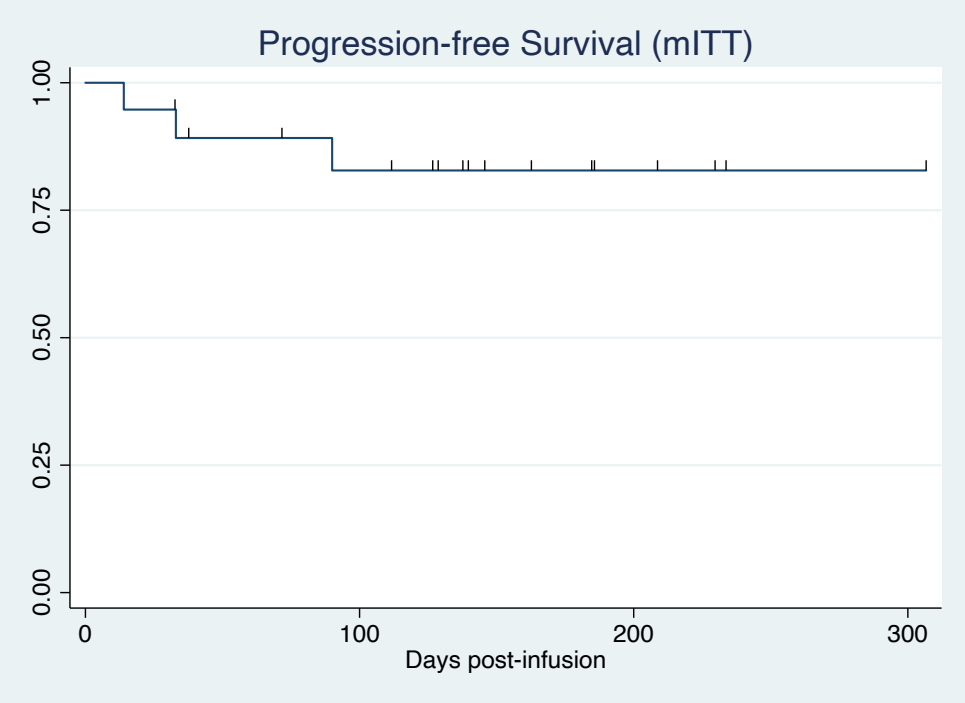
Tecartus real-world data (European)

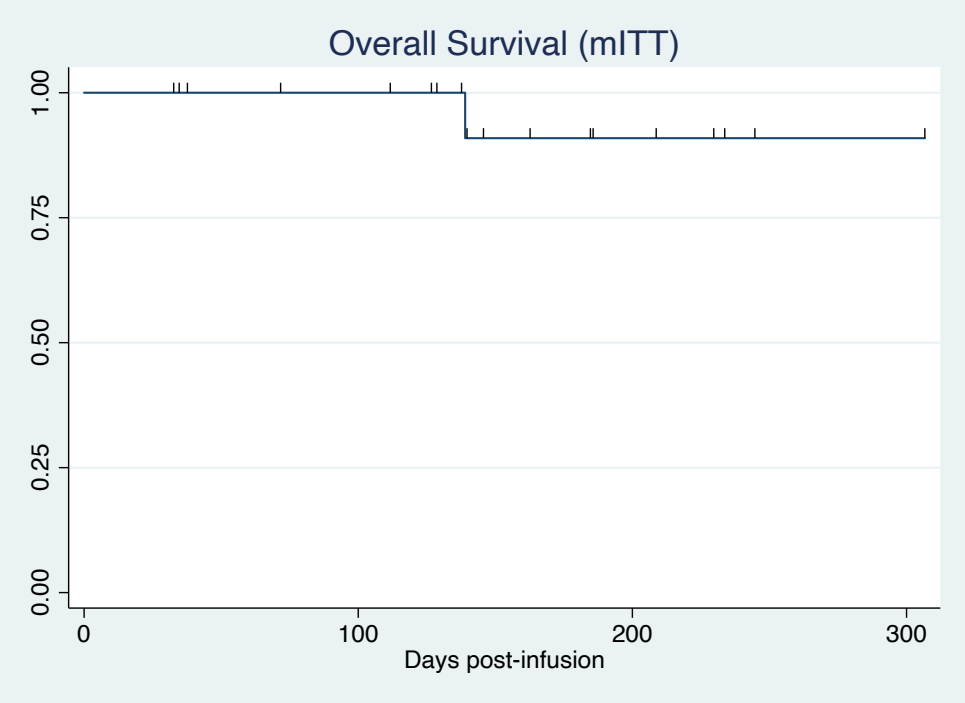
Characteristics	Infused (N=19)
CRS, patients (%)	17 (89)
- **Grade >2**	1 (5)
- **Time from infusion to CRS, median days (range)**	5 (0-9)
ICANS, patients (%)	12 (63)
- **Grade >2**	5 (26)
- **Time from infusion to ICANS, median days (range)**	8 (3-12)
Tocilizumab, patients (%)	16 (84)
Corticosteroids, patients (%)	12 (63)
ICU, patients (%)	2 (11)
Infections, patients (%)	6 (32)
Non-relapse mortality by day 100, patients (%)	0

Iacoboni et al (Confidential, submitted to ASH2021)

Tecartus real-world data (European)

Complete remission in 13 (68%) patients and partial remission in 4 (21%) patients





Estimated 6-month OS was 91% and 6-month PFS was 83%

Iacoboni et al (Confidential, submitted to ASH2021)

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