C’è una soglia di età anagrafica al di sopra della quale un paziente non dovrebbe essere candidato alla terapia cellulare CAR-T?

Le ragioni del si

Michele Spina
Aviano

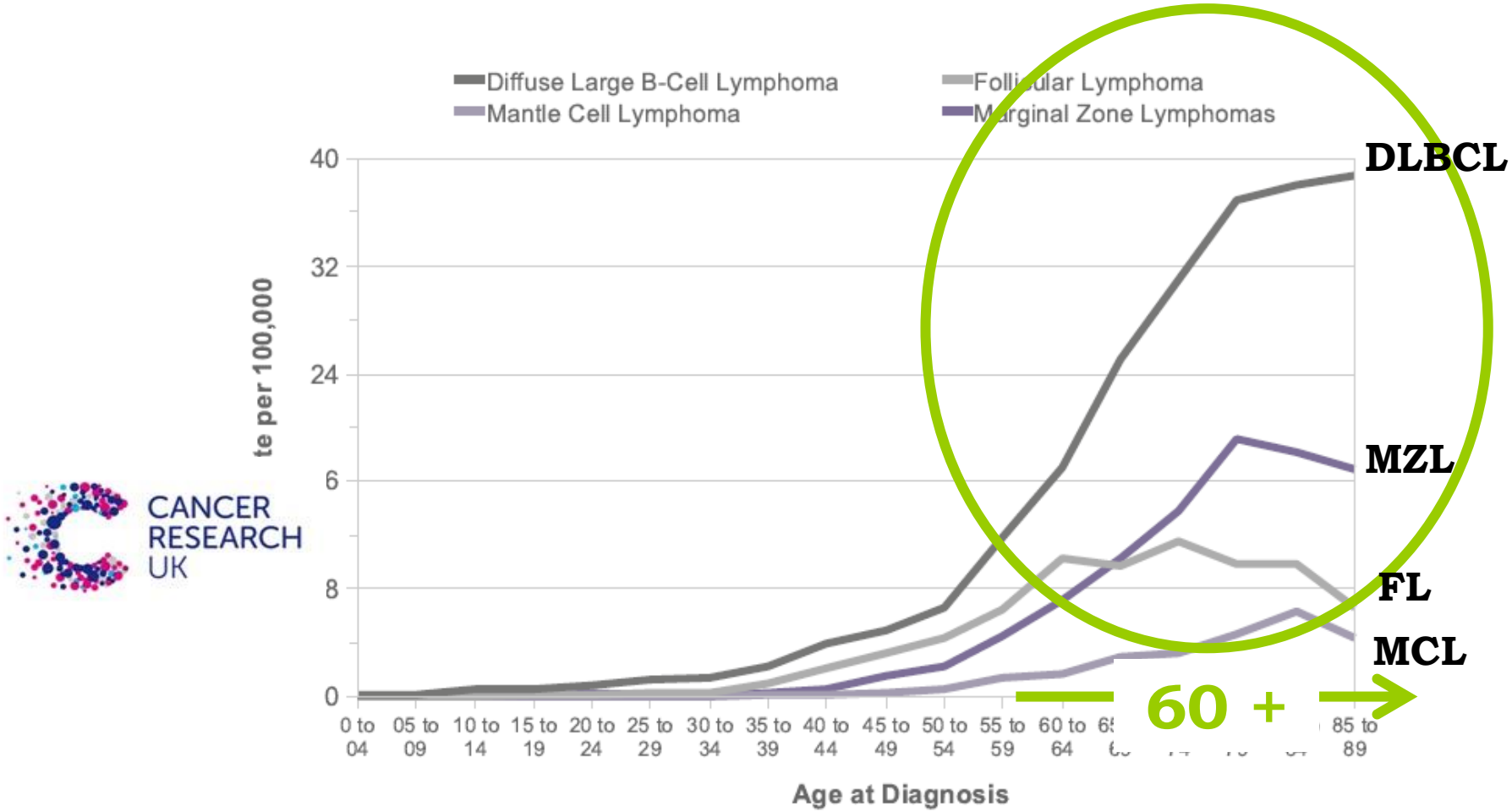
CONVEGNO EDUCAZIONALE GITMO
HOT QUESTIONS IN TRASPLANTATION AND CELLULAR THERAPIES

Disclosures of Michele Spina

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Gilead					X	X	
Abbvie						X	
Servier					X	X	
Novartis						X	
Istituto Gentili						X	
Incyte						X	
BeiGene						X	

Non-Hodgkin Lymphoma Subtypes: 2004-2011

Age-Specific Incidence Rates, UK (Estimates Based on HMRN data)



CANCER RESEARCH UK

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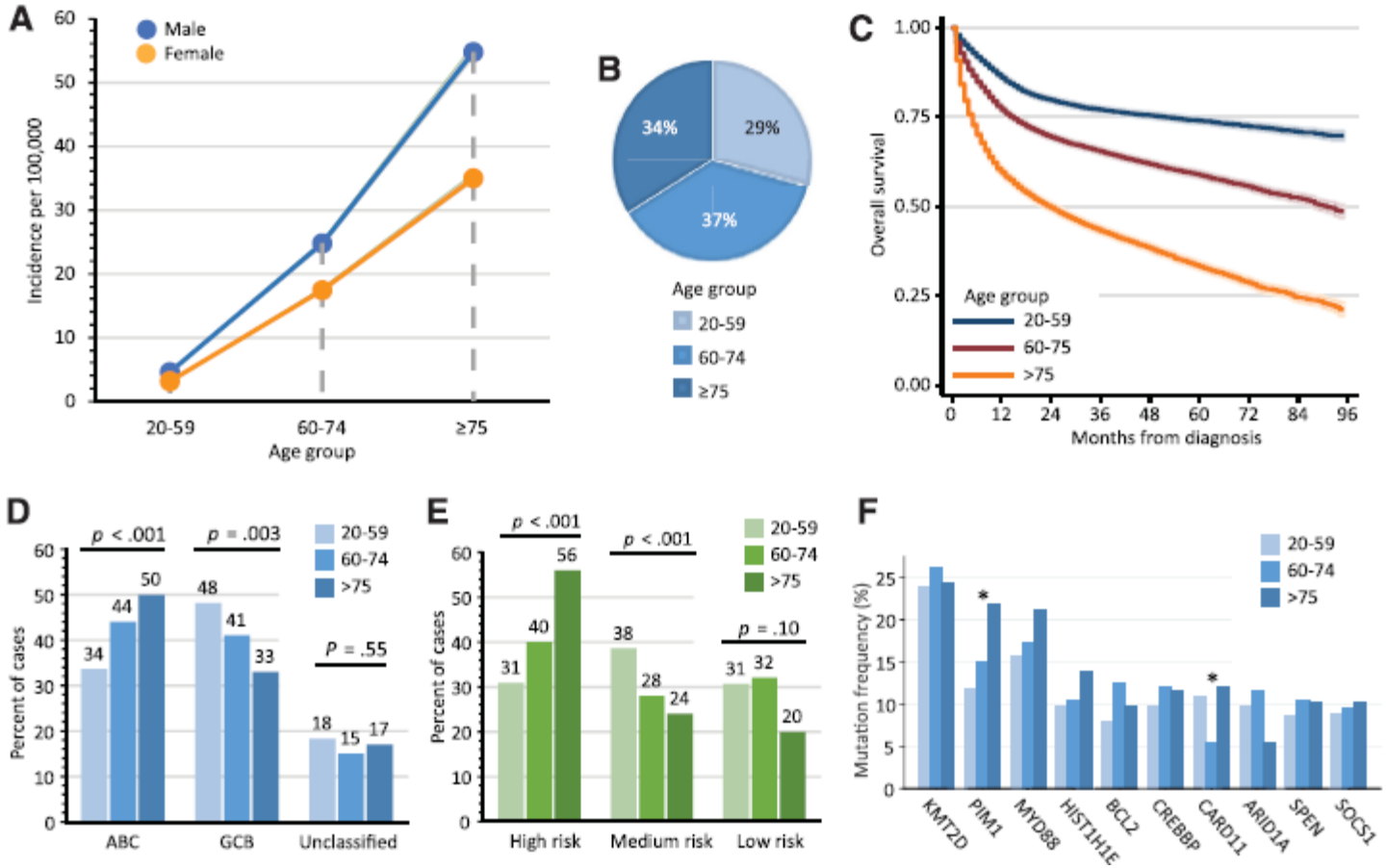
Prepared by Cancer Research UK


A
Male
Female
Incidence per 100,000
0
10
20
30
40
50
60
20-59
60-74
≥75
Age group
B
34%
29%
37%
Age group
20-59
60-74
≥75
C
Overall survival
1.00
0.75
0.50
0.25
0.00
Age group
20-59
60-75
>75
0
12
24
36
48
60
72
84
96
Months from diagnosis
D
p < .001
p = .003
p = .55
20-59
60-74
>75
Percent of cases
34
44
50
48
41
33
18
15
17
ABC
GCB
Unclassified
E
p < .001
p < .001
p = .10
20-59
60-74
>75
Percent of cases
31
40
56
38
28
24
31
32
20
High risk
Medium risk
Low risk
F
20-59
60-74
>75
Mutation frequency (%)
0
5
10
15
20
25
*
*
KMT2D
PIM1
MYD88
HIST1H1E
BCL2
CREBBP
CARD11
ARID1A
SPEN
SOCS1

Changes in the Survival of Older Patients With Hematologic Malignancies in the Early 21st Century

Dianne Pulte, MD[1,2]; Lina Jansen, PhD[1]; Felipe A. Castro, PhD[1]; and Hermann Brenner, MD, MPH[1,3,4]

Cancer, July 2016

TABLE 1. Five-Year Relative Survival of Patients With Hematological Malignancies by Time Period and Age Group

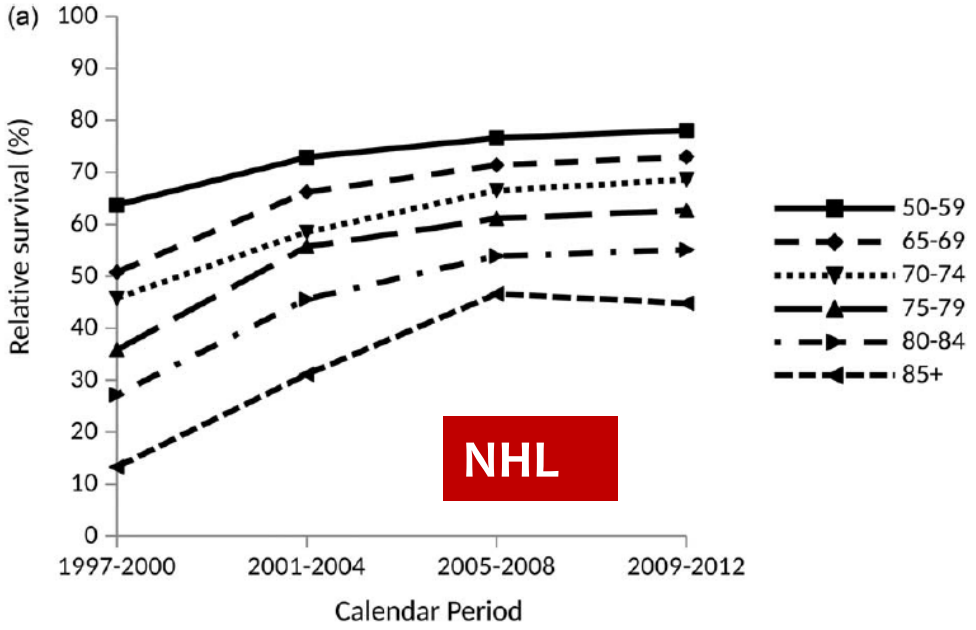
Malignancy	Age, y	5-y Relative Survival, % (Standard Error) 1997-2000	2001-2004	2005-2008	2009-2012	Difference Between 1997-2000 and 2009-2012, %
NHL	50-59	63.7 (0.8)	72.9 (0.7)[a]	76.6 (0.6)[a]	78.1 (0.6)[a]	+14.4
	65-69	50.8 (0.9)	66.2 (1.0)[a]	71.4 (1.0)[a]	73.0 (0.9)[b]	+22.2
	70-74	45.8 (0.9)	58.5 (1.0)[a]	66.5 (1.0)[a]	68.6 (1.0)[b]	+22.8
	75-79	35.8 (0.9)	55.7 (1.1)[a]	61.1 (1.1)[a]	62.7 (1.1)[b]	+26.9
	80-84	27.2 (0.9)	45.6 (1.4)[a]	53.9 (1.3)[a]	55.1 (1.3)[b]	+27.9
	≥85	13.3 (0.8)	31.1 (1.7)[a]	46.6 (1.9)[a]	44.8 (1.6)	+31.5

- +

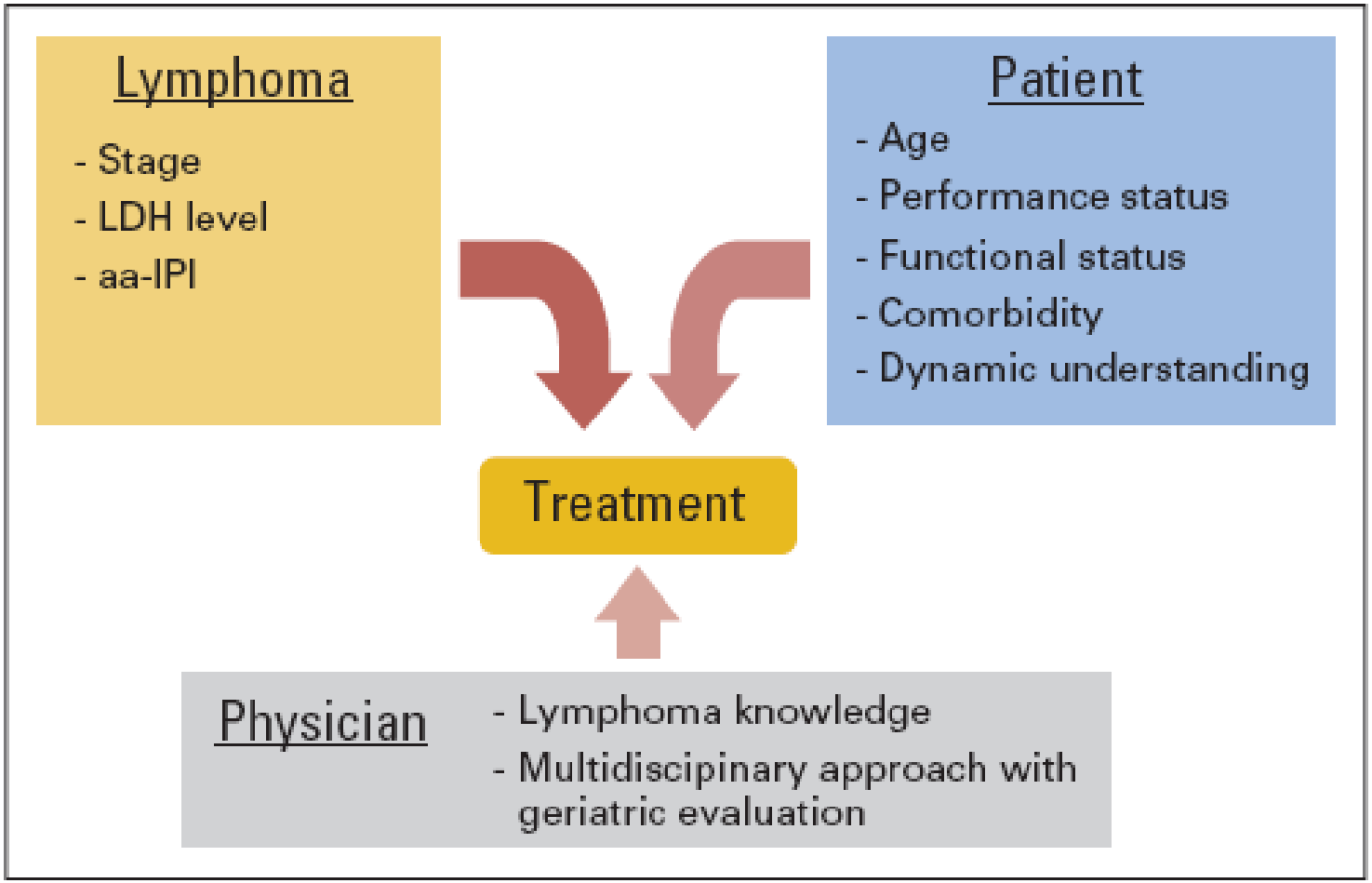
[a] $P \leq .01$ versus the preceding period.
[b] $P \leq .05$ versus the preceding period.

For older patients with NHL survival has, in general, been increasing at least as fast as for younger patients

The age-related disparity in survival has actually been decreasing



Integrated approach to assess therapeutic options in older patients



Thieblemont C. and Coiffier B., JCO May 2007, 25(14): 1916-1923

The relevance of a geriatric assessment for elderly patients with a haematological malignancy – A systematic review

Hamaker ME et al, LEUKEMIA RESEARCH, 2014

- **18 publications from 15 studies**

GA impairments: associated with a shorter OS in a relevant proportion of studies

In a multivariate analysis , when geriatric parameters were included, age and PS lost their predictive value for mortality in most studies

@ **GA can detect multiple health issues,** even in patients with good PS and implements non-oncologic interventions in over 70% of patients

@ Impairments in geriatric domains:

- appear to be associated with toxicity

- **should be integrated in individualised treatment algorithms**

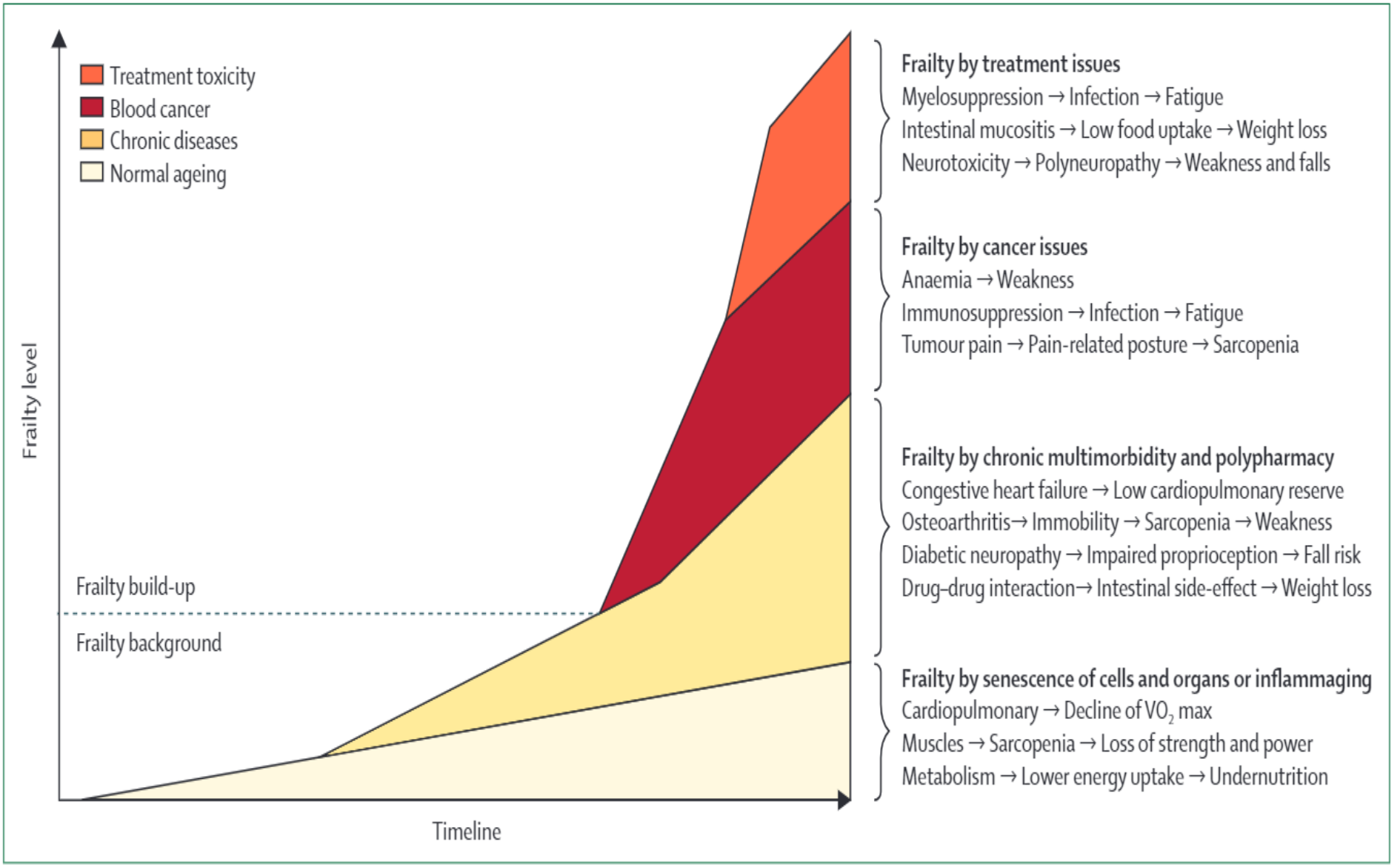


Figure 1: **Components of frailty in older patients with haematological malignancies**
Several examples of pathways to frailty are provided below each of the four scenarios.

Leukemia & Lymphoma, April 2015; 56(4): 921–926

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2014.953142

informa
healthcare

ORIGINAL ARTICLE: CLINICAL

Comprehensive geriatric assessment is an essential tool to support treatment decisions in elderly patients with diffuse large B-cell lymphoma: a prospective multicenter evaluation in 173 patients by the Lymphoma Italian Foundation (FIL)

Alessandra Tucci[1], Maurizio Martelli[2], Luigi Rigacci[3], Paola Riccomagno[4], Maria Giuseppina Cabras[5], Flavia Salvi[6], Caterina Stelitano[7], Alberto Fabbri[8], Sergio Storti[9], Stefano Fogazzi[1], Salvatrice Mancuso[10], Maura Brugiatelli[11], Angelo Fama[2], Paolo Paesano[2], Benedetta Puccini[3], Chiara Bottelli[1], Daniela Dalceggio[1], Francesco Bertagna[12], Giuseppe Rossi[1] & Michele Spina[13]; for the Italian Lymphoma Foundation (FIL)

Table II. Characteristics of patients classified according to CGA*.

CGA category	All	Fit	Unfit	Frail	*p*-Value
No. of evaluable patients (%)	173	79 (46%)	28 (16%)	66 (38%)	
M/F	91/82	52/27	13/15	26/40	
Median age	77	74	79	81	<0.0001
Ann Arbor stage III–IV (%)†	57	57	58	58	NS
B symptoms (%)‡	32	25	24	37	NS
IPI risk class intermediate-high/high (%)§	43	41	44	54	NS

Table IV. Overall survival time according to patient and treatment characteristics (univariate and multivariate Cox regression analysis).

Variables	Univariate HR (95% CI)	*p*-Value	Multivariate HR (95% CI)	*p*-Value
Age < 80 vs. ≥ 80 years	2.67 (1.61–4.44)	0.0002		
Stage I–II vs. III–IV	1.59 (0.92–2.74)	0.09		
IPI (intermediate-low/low vs. intermediate-high/high)	3.72 (1.80–7.68)	0.0003	4.60 (1.35–15.64)	0.008
CGA	5.61 (2.95–10.64)	0.0001	3.69 (1.09–12.51)	0.03
ADL (≤ 5 vs. 6)	0.3 (0.17–0.51)	0.0001		
IADL (≤ 6 vs. ≥ 7)	0.24 (0.14–0.41)	0.0001		
CIRS-G grade 2 (< 5 vs. ≥ 5)	2.89 (1.04–8.03)	0.04		
CIRS-G grade 3–4 (0 vs. ≥ 1)	2.14 (1.22–3.73)	0.007		
Curative vs. palliative treatment approach	0.27 (0.16–0.46)	0.0001		
Treatment dose (< 70% vs. ≥ 70%)	0.38 (0.17–0.86)	0.02		

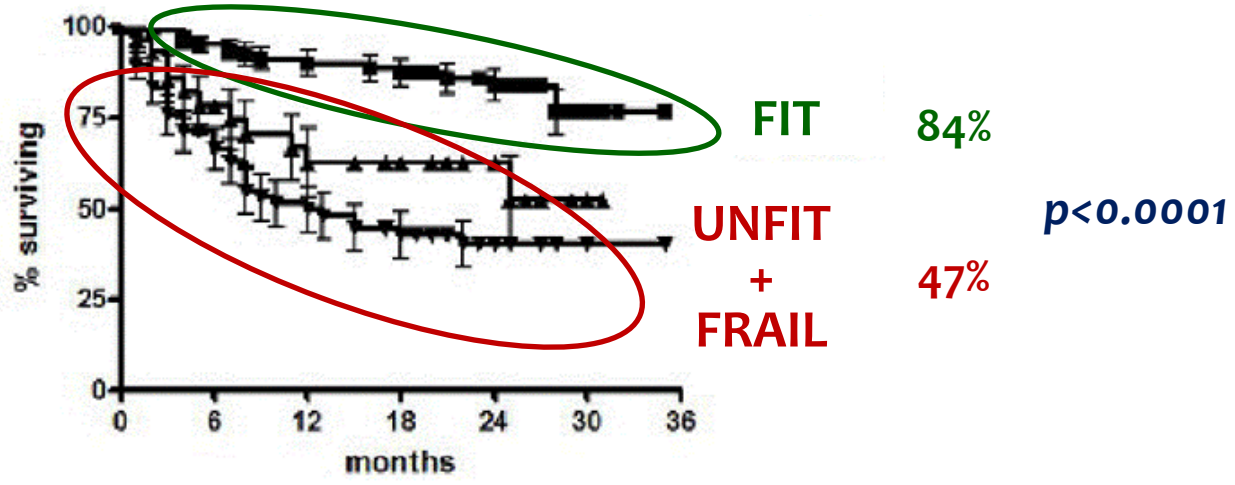


Figure 1. Actuarial overall survival curves of elderly patients with DLBCL classified as "fit," "unfit" and "frail" according to CGA, independent of treatment received.

Tucci A et al. Leuk Lymph 2015

ELDERLY PROJECT

1. General Data
2. Disease Status
3. Activity of Daily Living (ADL)
4. Instrumental Activity of Daily Living (IADL)
5. CIRS-G

Simplified Geriatric Assessment in Older Patien With Diffuse Large B-Cell Lymphoma: The Prospective Elderly Project of the Fondazione Italiana Linfomi

Francesco Merli, MD[1]; Stefano Luminari, MD[1,2]; Alessandra Tucci, MD[3]; Annalisa Arcari, MD[4]; Luigi Rigacci, MD[5]; Eliza Hawkes, MD[6]; Carlos S. Chiattone, MD[7,8]; Federica Cavallo, MD[9]; Giuseppina Cabras, MD[10]; Isabel Alvarez, MD[1]; Alberto Fabbri, MD[11]; Alessandro Re, MD[3]; Benedetta Puccini, MD[5]; Allison Barraclough, MD[12]; Marcia Torresan Delamain, MD[13]; Simone Ferrero, MD[9]; Sara Veronica Usai, MD[10]; Angela Ferrari, MD[1]; Emanuele Cencini, MD[11]; Elsa Pennese, MD[14]; Vittorio Ruggero Zilioli, MD[15]; Dario Marino, MD[16]; Monica Balzarotti, MD[17]; Maria Christina Cox, MD[18]; Manuela Zanni, MD[19]; Alice Di Rocco, MD[20]; Arben Lleshi, MD[21]; Barbara Botto, MD[22]; Stefan Hohaus, MD[23]; Michele Merli, MD[24]; Roberto Sartori, MD[25]; Guido Gini, MD[26]; Luca Nassi, MD[27]; Gerardo Musuraca, MD[28]; Monica Tani, MD[29]; Chiara Bottelli, MD[3]; Sofia Kovalchuk, MD[5]; Francesca Re, MD[30]; Leonardo Flenghi, MD[31]; Annalia Molinari, MD[32]; Giuseppe Tarantini, MD[33]; Emanuela Chimienti, MD[21]; Luigi Marcheselli, MS[34]; Caterina Mammi, PhD[35]; and Michele Spina, MD[21]

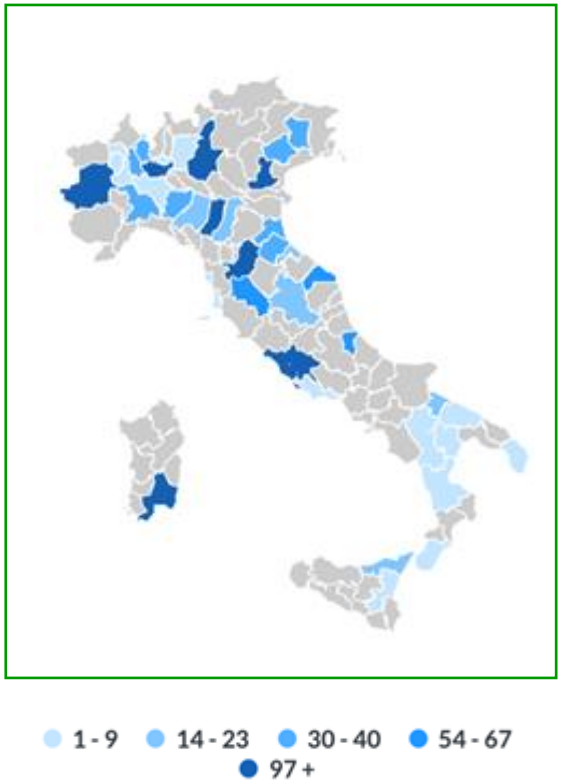
J Clin Oncol 00.

Elderly Project: Clinical Characteristics and sCGA

Enrollment period: Dec 2013 – Dec 2017

- **37 Italian centres**
- **1353 patients (1207 eligible)**

	N. (%)
Age (median) [range]	**76 [65-94]**
Gender (male)	**609 (50%)**
IPI (3-5) [N=1102]	**612 (56%)**



Fitness Status by sCGA

	N. (%)
FIT	**520 (43%)**
UNFIT	**300 (25%)**
FRAIL	**387 (32%)**
Total	**1207 (100%)**

Merli F et al. JCO 2021

The emergence of chimeric antigen receptor (CAR) T-cell therapy has changed the treatment landscape for diffuse large B-cell lymphoma (DLBCL); however, real-world experience reporting outcomes among older patients treated with CAR T-cell therapy is limited.

LEUKEMIA & LYMPHOMA
2022, VOL. 63, NO. 2, 353–361
https://doi.org/10.1080/10428194.2021.1986216

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Evaluation of the safety and efficacy of humanized anti-CD19 chimeric antigen receptor T-cell therapy in older patients with relapsed/refractory diffuse large B-cell lymphoma based on the comprehensive geriatric assessment system

Huan Zhang[a], Man Liu[b], Qing Li[a], Cuicui Lyu[a], Yan-Yu Jiang[a], Juan-Xia Meng[a], Jing-Yi Li[a] and Qi Deng[a]

[a]Department of Hematology, Tianjin First Central Hospital, School of Medicine, Nankai University, Tianjin, China; [b]Department of Surgery Plastic, Tianjin First Central Hospital, School of Medicine, Nankai University, Tianjin, China

Table 1. Grouping criteria for comprehensive geriatric assessment system.

CGA category	Fit	Unfit	Frail
Age (years)	≥65 to <80	≥80	≥80
ADL (score)	6	5	≤4
IADL (score)	8	6–7	≤5
CIRS-G	No comorbidity score 3–4 and <5 comorbidities score 2	No comorbidity score 3–4 and 5–8 comorbidities score 2	≥1 comorbidity score 3–4 or >8 comorbidities score 2

CGA: comprehensive geriatric assessment; ADL: activity of daily living; IADL: instrumental activity of daily living; CIRS-G: Cumulative Illness Rating Score for Geriatrics.

Table 2. Baseline characteristics of the patients ($n = 31$).

CGA category	FIT	Unfit/frail	*p* value
Median age (range), years	68 (65–80)	76 (73–86)	.013
Man	9 (52.9%)	7 (50.0%)	.532
ECOG > 1	1 (0.6%)	5 (35.7%)	<.001
Karnofsky < 90	1 (0.6%)	5 (35.7%)	<.001
ADL			<.001
6	17 (100.0%)	10 (71.4%)	
5	0 (0.0%)	3 (21.4%)	
≤4	0 (0.0%)	1 (7.14%)	
IADL			<.001
8	17 (100.0%)	9 (64.3%)	
6–7	0 (0.0%)	4 (28.6%)	
≤6	0 (0.0%)	1 (7.14%)	
CIRS-G			.006
No comorbidity score 3–4	17 (100.0%)	12 (85.7%)	
≥1 comorbidity score 3–4	0 (0.0%)	2 (14.3%)	
<5 comorbidities score ≤2	17 (100.0%)	0 (0.0%)	
≥5 comorbidities score ≤2	0 (0.0%)	14 (100.0%)	
LDH, pre-lymphodepletion			.071
>upper limit of normal	14 (82.4%)	12 (85.7%)	
<upper limit of normal	3 (17.6%)	2 (14.3%)	
Tumor cross-sectional area (mm^2)			.542
≥4000	8 (47.1%)	9 (64.3%)	
<4000	9 (52.9%)	5 (35.7%)	
Double/triple-hit			.638
Yes	7 (41.2%)	6 (42.9%)	
No	10 (58.8%)	8 (57.1%)	
Disease stage			.735
I/II	3 (17.6%)	2 (14.3%)	
III/IV	14 (82.4%)	12 (85.7%)	
IPI			.953
0–2	8 (47.1%)	6 (42.9%)	
3–5	9 (52.9%)	8 (57.1%)	
Extranodal disease			.631
Yes	5 (29.4%)	3 (21.4%)	
No	12 (70.6%)	11 (78.6%)	
Number of prior therapies			.753
1–4	3 (17.6%)	4 (28.6%)	
≥5	14 (83.4%)	10 (71.4%)	
Refractory category			.052
Refractory to second-line or later therapy	17 (100.0%)	11 (64.7%)	
Best response as progressive disease to last previous therapy	9 (52.9%)	8 (57.1%)	
Relapse after autologous stem-cell transplantation	3 (17.6%)	0 (0.0%)	

CGA: comprehensive geriatric assessment; double/triple-hit MYC rearrangement plus rearrangement of BCL2/BCL6 by fish; IPI: International Prognostic Index; tumor cross-sectional area: sum of the product of the perpendicular diameters of up to six target measurable nodes and extranodal sites.

Table 3. Clinical responses in CGA subgroup.

	Number	ORR	CR	PR
Overall	31	24 (77.4%)	16 (51.6%)	8 (25.6%)
Fit	17	15 (88.2%)	10 (58.8%)	5 (29.4%)
Unfit/frail	14	9 (64.3%)	6 (42.9%)	3 (21.4%)
χ^2		2.542	1.927	1.136
p		.003	.012	.181

ORR: objective response rate; CR: complete response; PR: part response

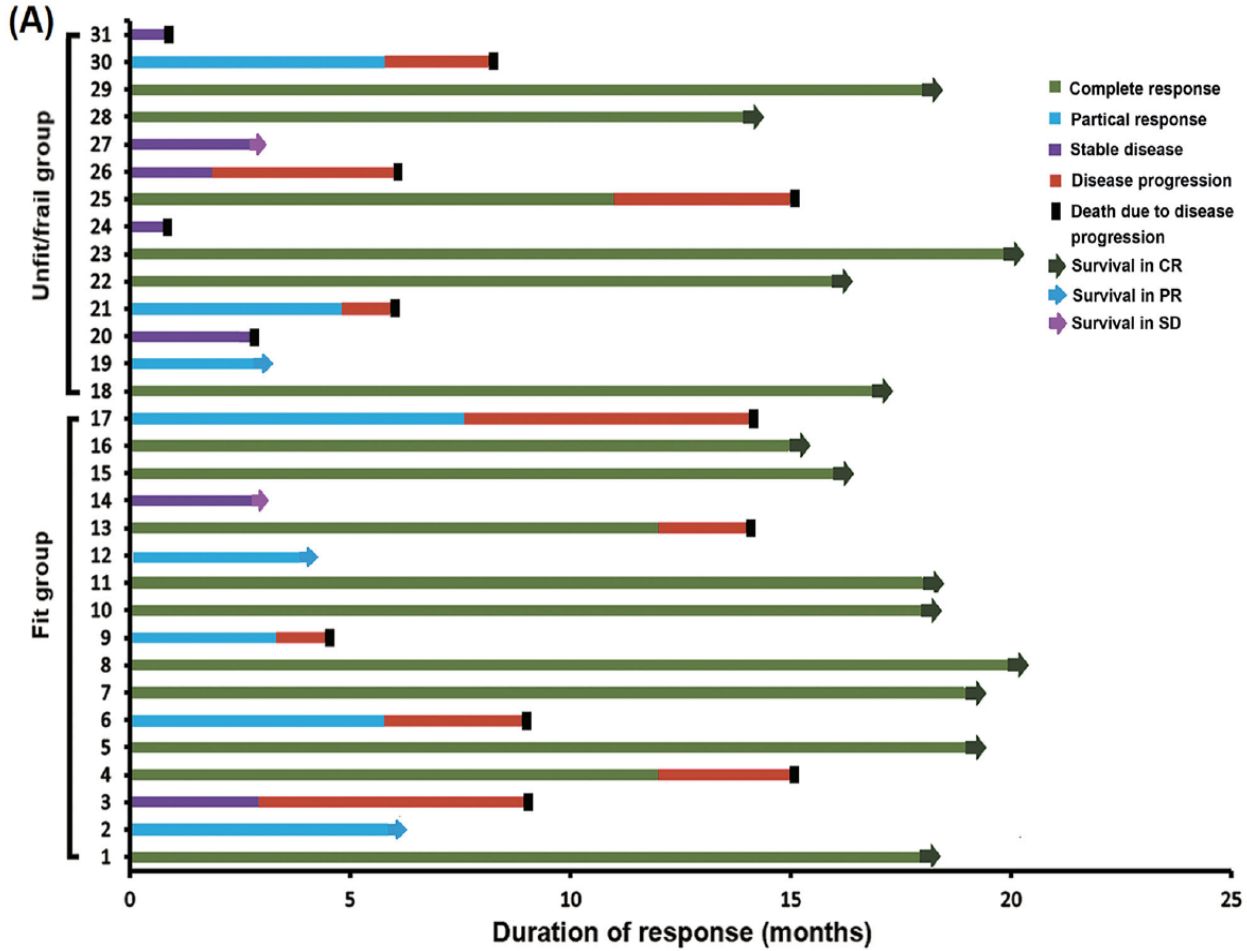
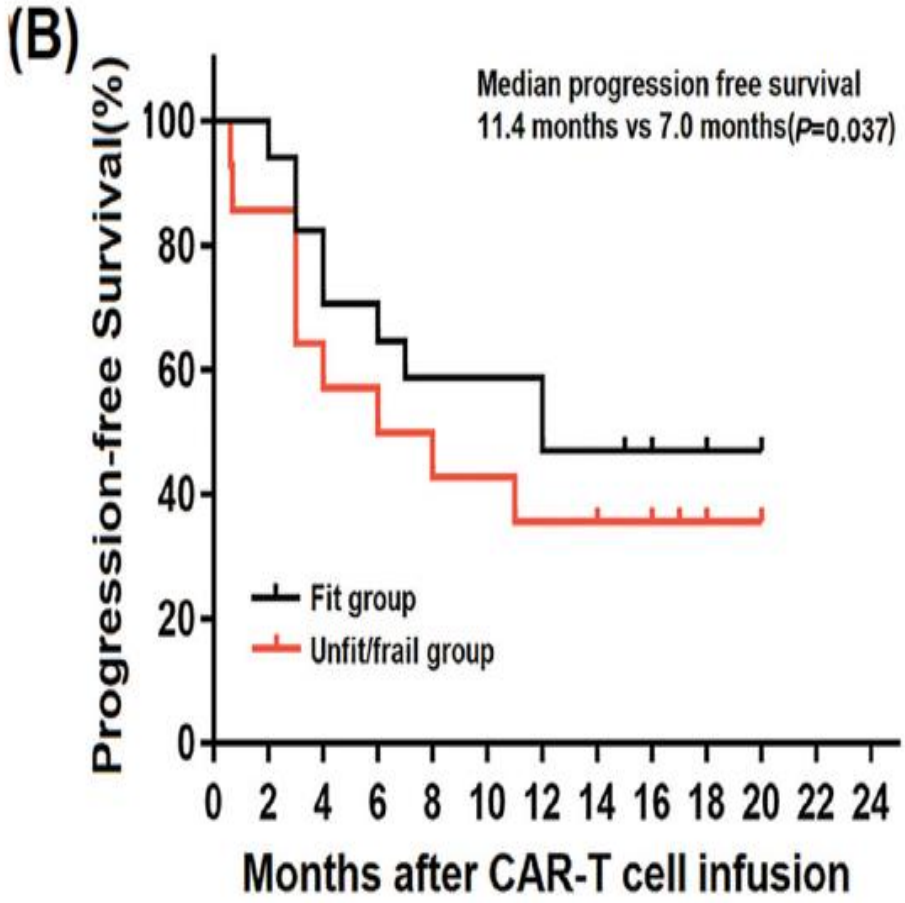
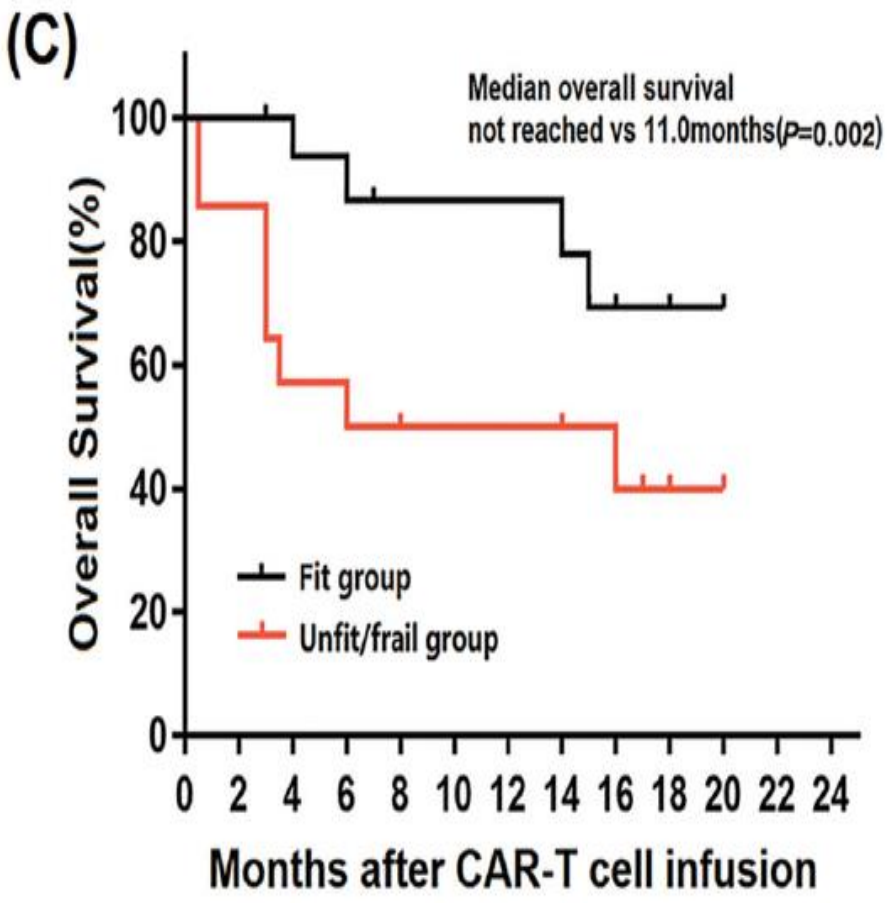


Table 5. CGA subgroup analysis of adverse events, *n* (%).

	Fit group ($n = 17$)	Unfit/frail group ($n = 14$)	χ^2	p
CRS			7.513	.023
Grade 0	12 (70.6%)	3 (21.4%)		
Grade 1–2	4 (23.5%)	8 (57.1%)		
Grade ≥3	1 (5.9%)	3 (21.4%)		
Hematological			8.123	.017
Grade 0	11 (64.7%)	2 (14.3%)		
Grade 1–2	2 (11.8%)	5 (35.7%)		
Grade ≥3	4 (23.5%)	7 (50.0%)		
Cardiovascular events			4.803	.022
Grade 0	15 (88.2%)	8 (57.1%)		
Grade 1–2	2 (14.3%)	2 (14.3%)		
Grade ≥3	0 (0.0%)	4 (28.6%)		
Increased aminotransferase			5.656	.016
Grade 0	13 (76.5%)	6 (42.9%)		
Grade 1–2	3 (17.6%)	6 (42.9%)		
Grade ≥3	0 (0.0%)	3 (21.4%)		
Increased creatinine			3.958	.026
Grade 0	14 (82.4%)	9 (64.3%)		
Grade 1–2	3 (17.6%)	4 (28.6%)		
Grade ≥3	0 (0.0%)	1 (7.1%)		


(B)
Median progression free survival
11.4 months vs 7.0 months(P=0.037)
Progression-free Survival(%)
100
80
60
40
20
0
Fit group
Unfit/frail group
0 2 4 6 8 10 12 14 16 18 20 22 24
Months after CAR-T cell infusion


(C)
Median overall survival
not reached vs 11.0months(P=0.002)
Overall Survival(%)
100
80
60
40
20
0
Fit group
Unfit/frail group
0 2 4 6 8 10 12 14 16 18 20 22 24
Months after CAR-T cell infusion

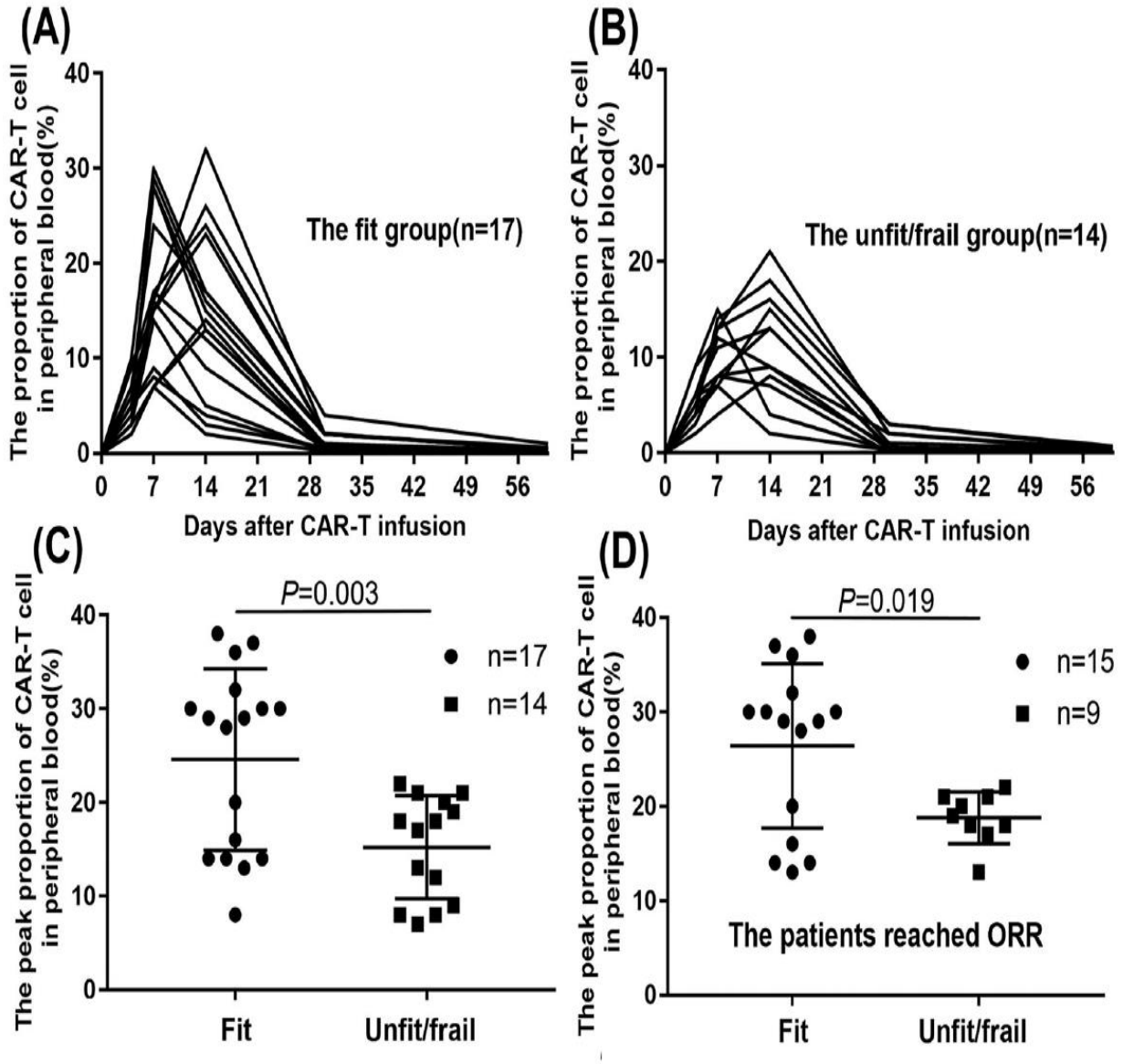


Figure 3. The expansion of anti-CD19 CAR T-cells. (A) The proportions of anti-CD19 CAR T-cells changed within 60 days after infusion in the fit group ($n = 17$). (B) The proportions of anti-CD19 CAR T-cells changed within 60 days after infusion in the unfit/frail group ($n = 14$). (C) The peak proportion of anti-CD19 CAR T-cells in the fit group was significantly higher than that in the unfit/frail group (24.59%±9.39% vs. 15.21%±5.30%; $p = .003$). (D) The proportion of anti-CD19 CAR T-cells in patients with an ORR was higher in the fit group than in the unfit/frail group (29.12%±8.41%% vs. 18.78%±2.57%; $p = .019$).

In conclusion, despite the limitations of a small sample size and short follow-up time, our results demonstrate positive efficacy and controlled side effects of humanized anti-CD19 CAR T-cell therapy in elderly patients. Elderly patients should not be excluded from receiving CAR T-cell therapy. The CGA system is used to stratify elderly patients with R/R DLBCL under CAR T-cell therapy to effectively predict their treatment response, adverse reactions, and long-term survival. In the future, we look forward to more prospective randomized controlled studies that will guide treatment through CGA stratification, and this will help develop a combination of CGA scales suitable for elderly R/R DLBCL patients and standardize them to help more effectively stratify patients and guide treatment.

Current Oncology Reports (2022) 24:1189–1199
https://doi.org/10.1007/s11912-022-01272-6

GERIATRIC ONCOLOGY (L BALDUCCI, SECTION EDITOR)

CAR T-Cell Therapy in the Older Person: Indications and Risks

Geoffrey Shouse[1] · Alexey V. Danilov[1,2] · Andy Artz[1]

Accepted: 25 February 2022 / Published online: 14 April 2022

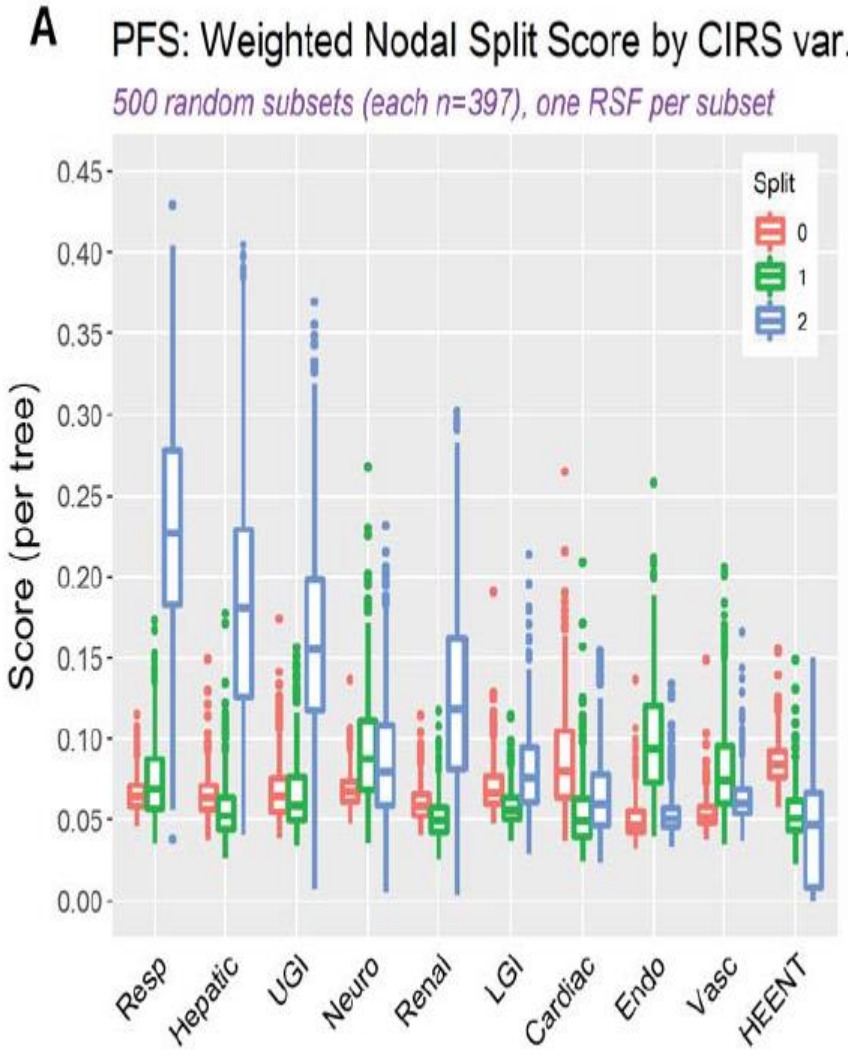
Table 2 Outcomes in older adults from clinical trial and real-world evidence for approved CART products comparing patients ≥ 65 years to < 65 years of age. *Axi-Cel* axicabtagene ciloleucel, *Tisa-Cel* tisagenlecleucel, *Liso-Cel* lisocabtagene maraulecel, *Brexu-Cel* brexucabtageneautoleucel, *Ide-Cel* idecabtagenevicleucel, *DLBCL* diffuse large B cell lymphoma, *MCL* mantle cell lymphoma, *MM* multiple myeloma, *B-ALL* B-cell acute lymphoblastic leukemia, *ORR* objective response rate, *CR* complete response, *G* grade, *CRS* cytokine release syndrome, *NTX* neurotoxicity, *Infxn* infection, *NR* not reported, *n* number of patients

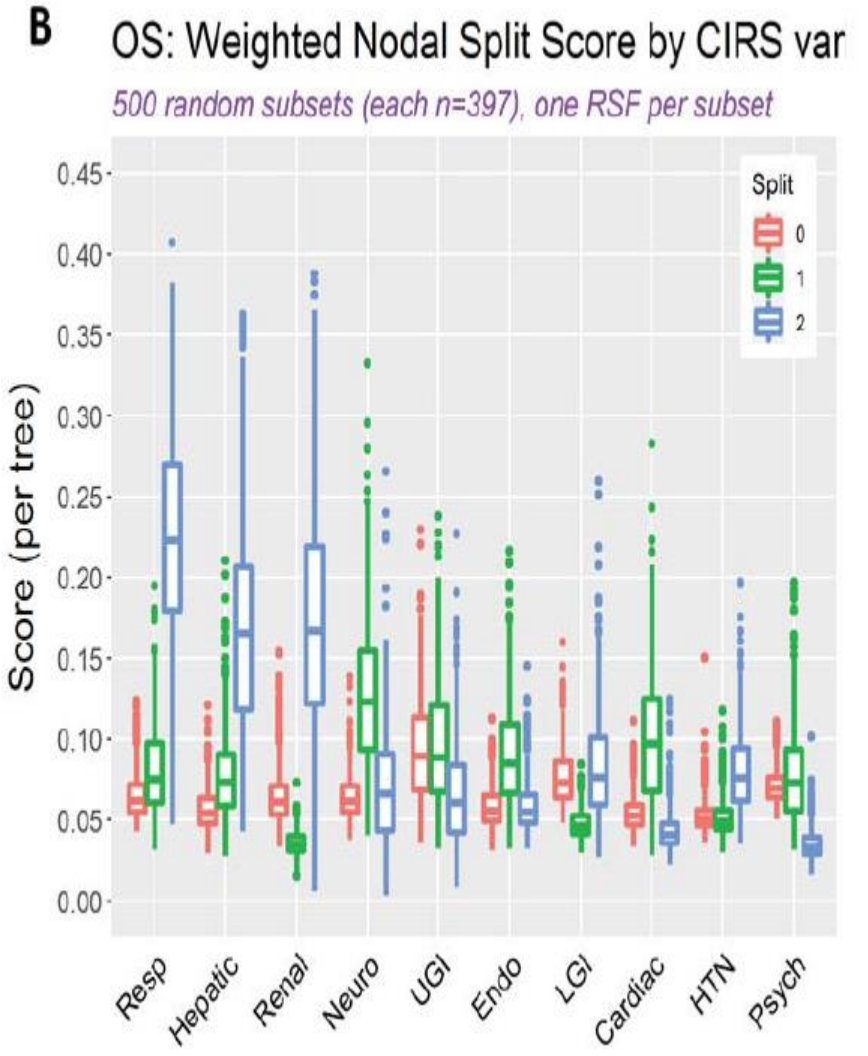
Product	Disease	Reference	Number of patients	% Patients age ≥ 65 years	ORR ≥ 65 vs < 65 years *n* (%)	CR ≥ 65 vs < 65 years *n* (%)	G ≥ 3 CRS ≥ 65 vs < 65 years *n* (%)	G ≥ 3 NTX ≥ 65 vs < 65 years *n* (%)	G ≥ 3 Infxn ≥ 65 vs < 65 years *n* (%)
Axi-Cel	DLBCL	(6)	108	25%	22 (92%) vs 62 (81%)	18 (75%) vs 41 (53%)	2 (7%) vs 10 (12%)	12 (44%) vs 23 (28%)	5 (19%) vs 25 (31%)
Tisa-Cel	DLBCL	(7)	111	23%	13 (59%) vs 35 (49%)	NR	NR	NR	NR
Axi-Cel and Tisa-Cel	DLBCL	(26)	49	51%	NR	51% overall and not different among groups	2 (8%) vs 3 (12%)	6 (25%) vs 4 (16%)	10 (42%) vs 15 (60%)
Axi-Cel and Tisa-Cel	DLBCL	(25)	804	41%	NR	NR	(All grades) 197 (59%) vs 302 (64%)	(All grades) 142 (43%) vs 171 (36%)	(Sepsis) 11 (3%) vs 5 (1%)
Liso-Cel	DLBCL	(5)	269	42%	82 (76%) vs 104 (70%)	65 (60%) vs 71 (48%)	NR	NR	NR
Brexu-Cel	MCL	(10)	60	53%	30 (94%) vs 26 (93%)	NR	NR	NR	NR
Ide-Cel	MM	(8)	128	35%	45 (70%) vs 83 (90%)	NR	NR	NR	NR
Axi-Cel	Follicular	(11)	86	31%	NR	NR	NR	NR	NR
Brexu-Cel	B-ALL	(9)	65	15%	NR	8 (100%) vs 47 (71%)	NR	NR	NR

blood advances

A validated composite comorbidity index predicts outcomes of CAR T-cell therapy in patients with diffuse large B cell lymphoma

Geoffrey Shouse[1]*, Andy Kaempf[2]*, Max J. Gordon[3], Andy Artz[1], David Yashar[1], Audrey M. Sigmund[4], Gordon Smilnak[5], Steven Bair[6], Agrima Mian[7], Lindsey Fitzgerald[8], Amneet Bajwa[4], Samantha Jaglowski[4], Neil Bailey[9], Mazyar Shadman[10], Krish Patel[9], Deborah M. Stephens[8], Manali Kamdar[6], Brian Hill[7], Jordan Gauthier[10], Reem Karmali[5], Loretta J. Nastoupil[3]*, Adam S. Kittai[4]* and Alexey V. Danilov[1]*

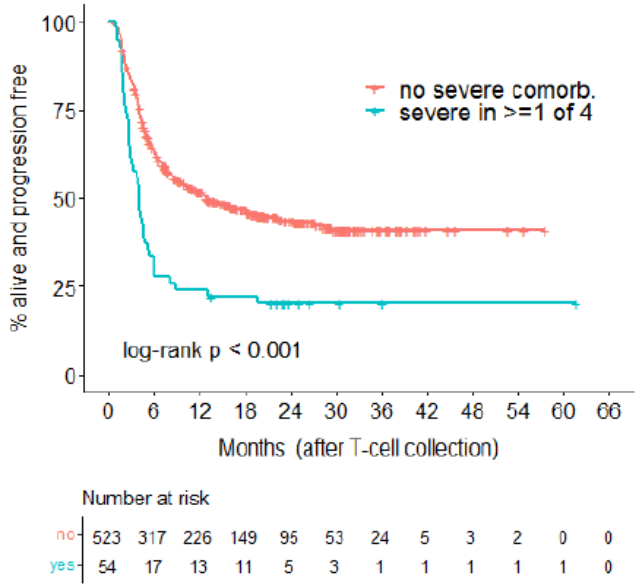




Severe CIRS score (>2) in the respiratory, upper GI, renal and hepatic system "SEVERE 4" had the strongest impact on PFS and OS

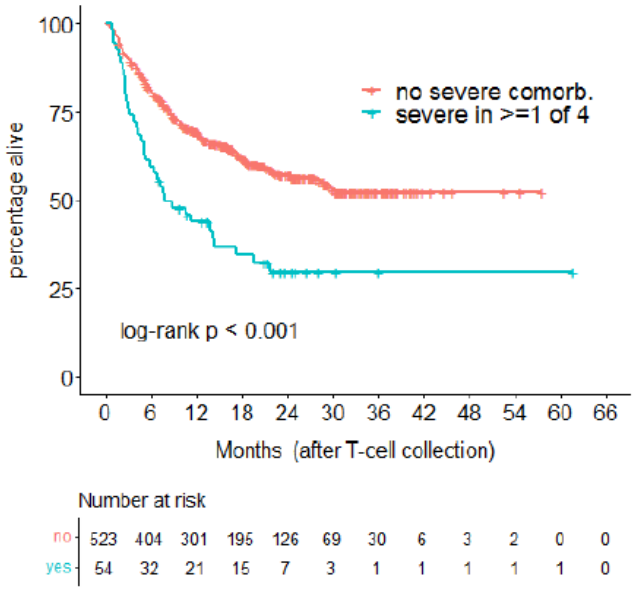
ure 2

LC: PFS Kaplan-Meier curves by Severe4 (n=577)



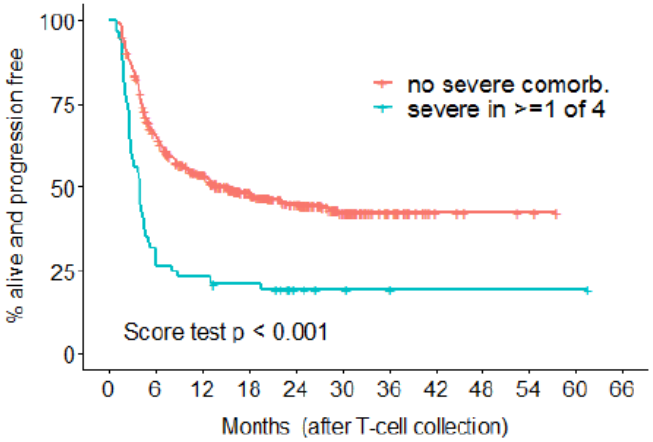
B

LC: OS Kaplan-Meier curves by Severe4 (n=577)



LC: PFS Kaplan-Meier curves by Severe4 (n=550)

Left Truncation time from T-cell collection to CART infusion



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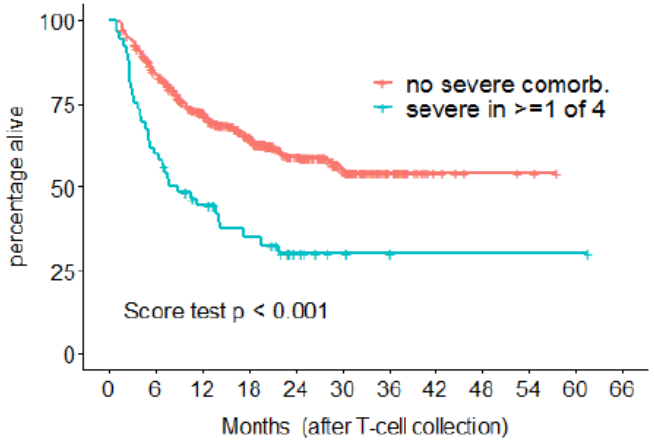
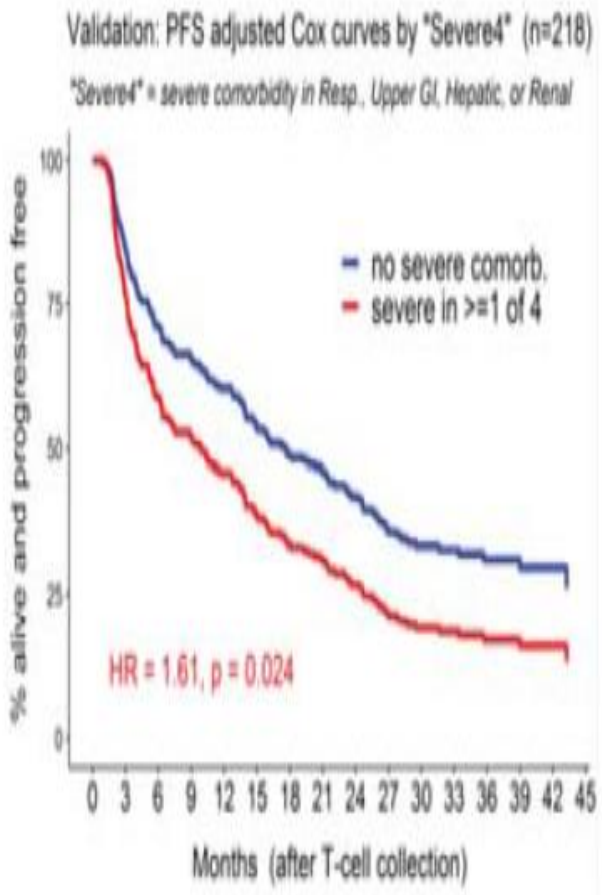
LC: OS Kaplan-Meier curves by Severe4 (n=550)

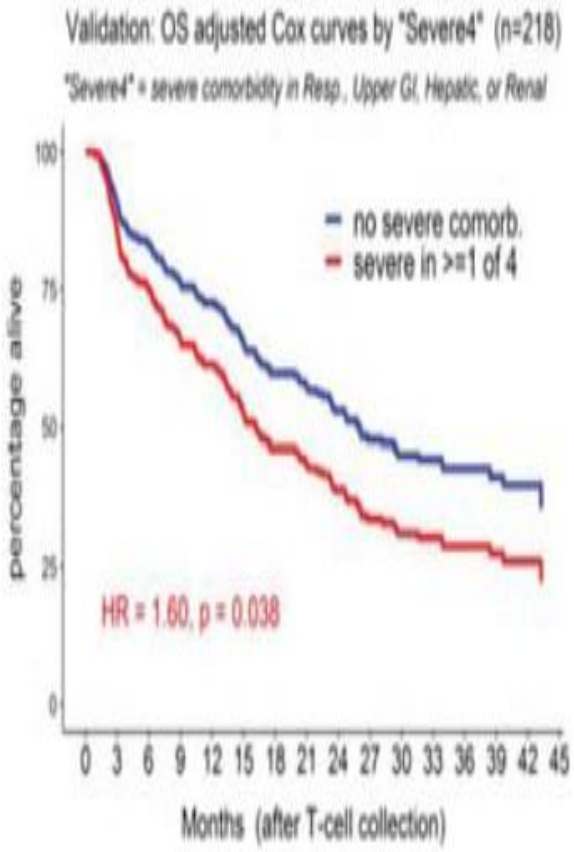
Left Truncation time from T-cell collection to CART infusion



A


Validation: PFS adjusted Cox curves by "Severe4" (n=218)
"Severe4" = severe comorbidity in Resp., Upper GI, Hepatic, or Renal
% alive and progression free
100
75
50
25
0
no severe comorb.
severe in >=1 of 4
HR = 1.61, p = 0.024
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45
Months (after T-cell collection)

B


Validation: OS adjusted Cox curves by "Severe4" (n=218)
"Severe4" = severe comorbidity in Resp., Upper GI, Hepatic, or Renal
percentage alive
100
75
50
25
0
no severe comorb.
severe in >=1 of 4
HR = 1.60, p = 0.038
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45
Months (after T-cell collection)

Comorbidities Predict Inferior Survival in Patients Receiving Chimeric Antigen Receptor T Cell Therapy for Diffuse Large B Cell Lymphoma: A Multicenter Analysis

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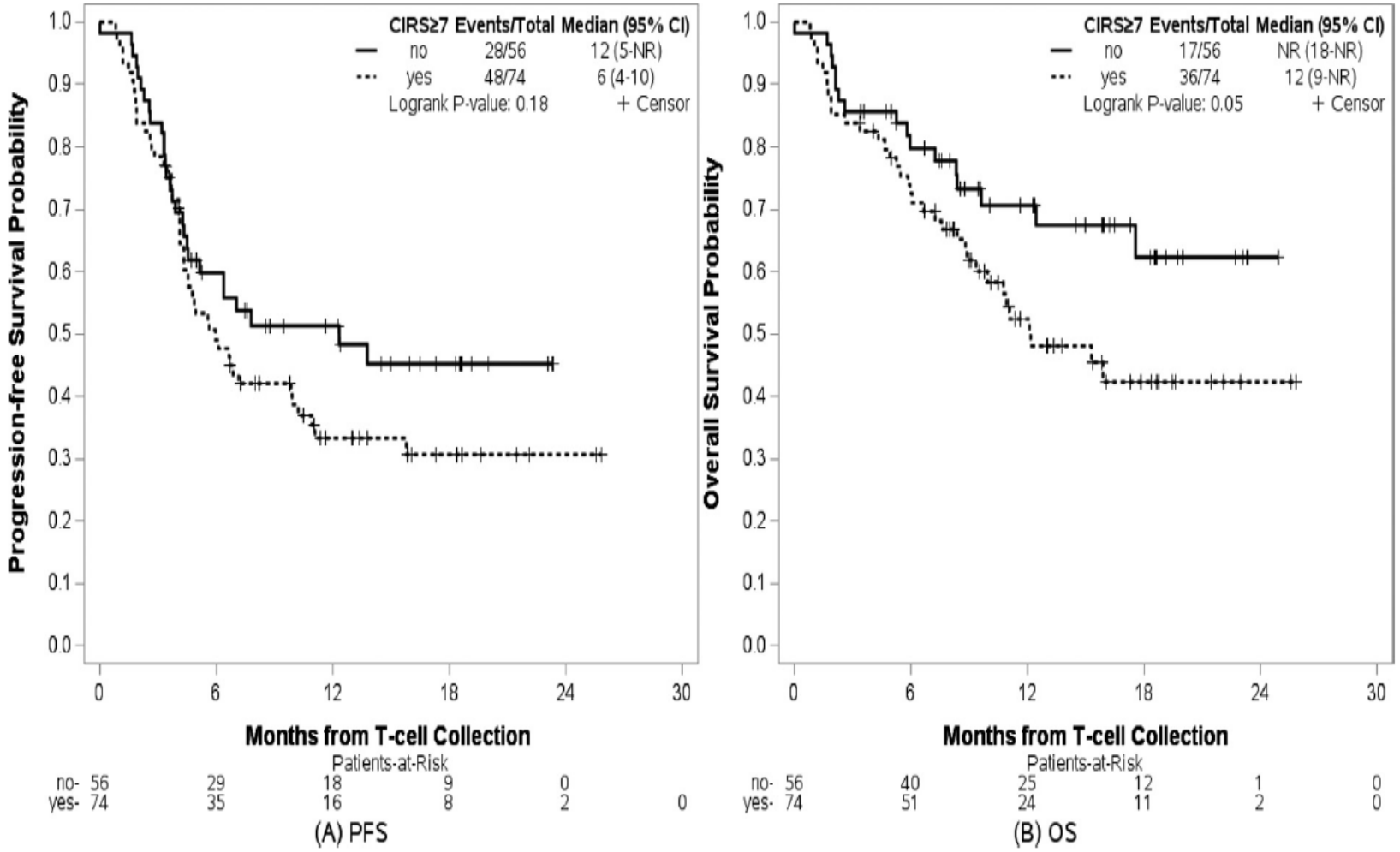


Figure 2. PFS and OS of patients with DLBCL treated with CAR-T therapy by CIRS ≥7.

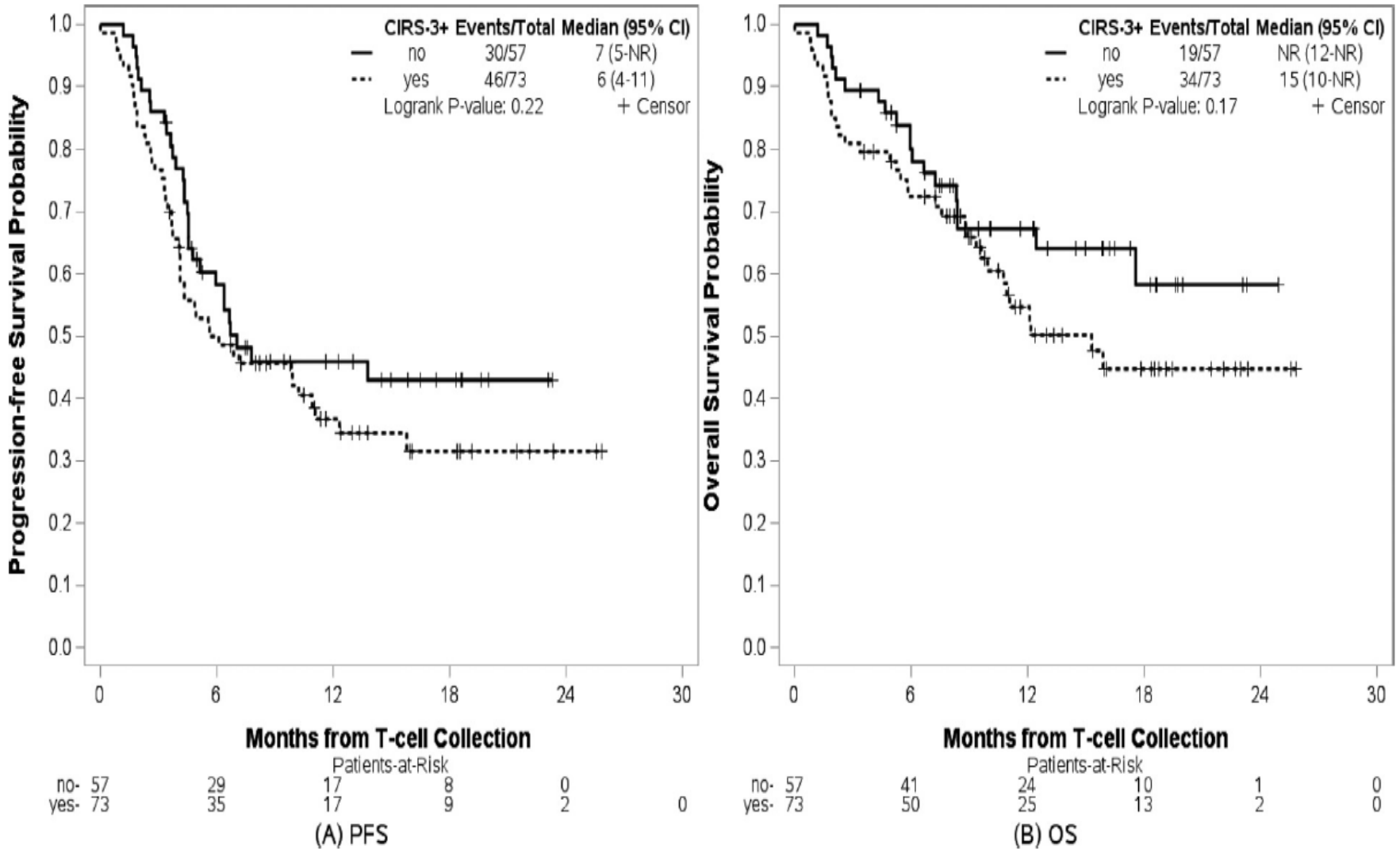


Figure 3. PFS and OS of patients with DLBCL treated with CAR-T therapy by CIRS-3+.

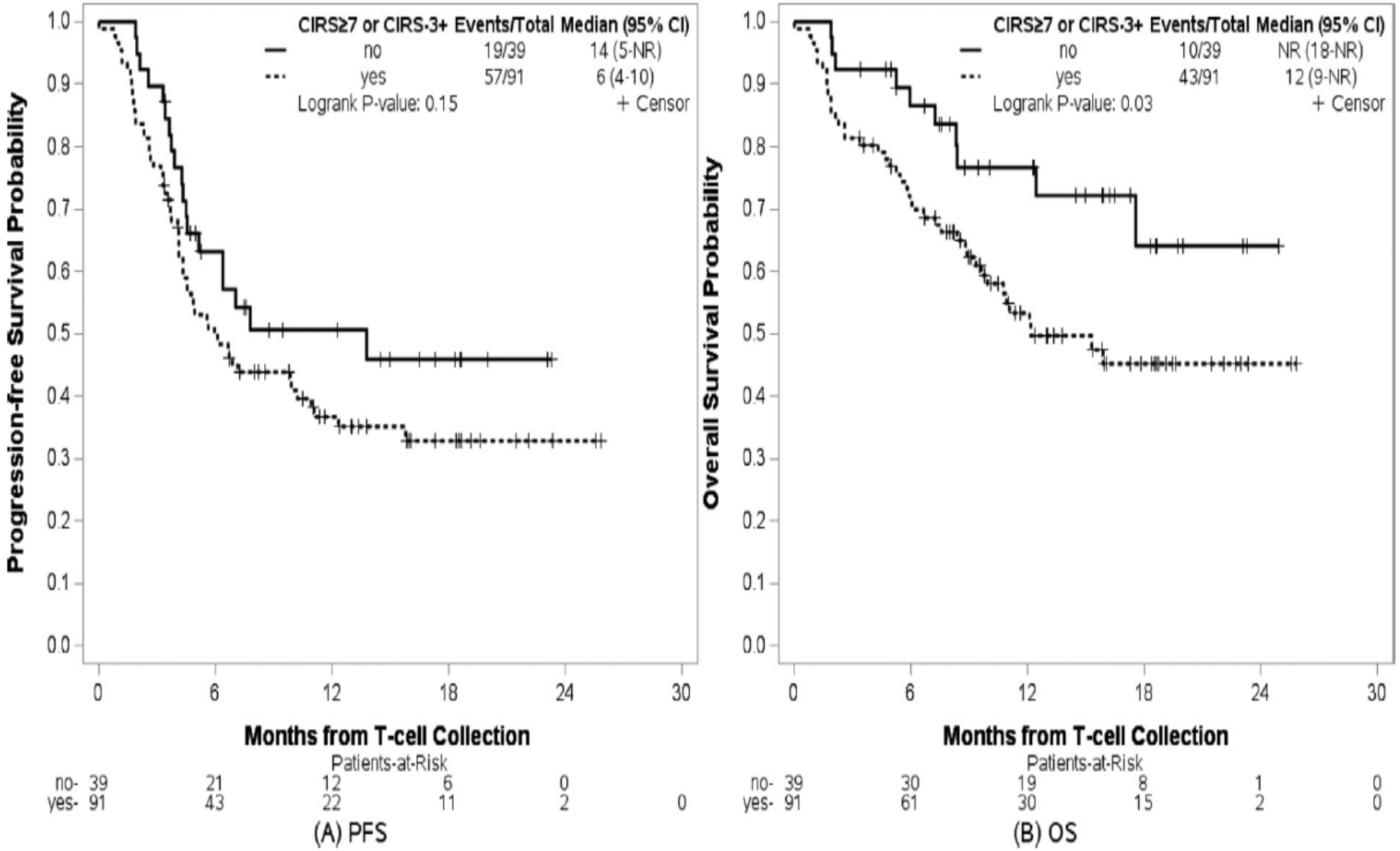
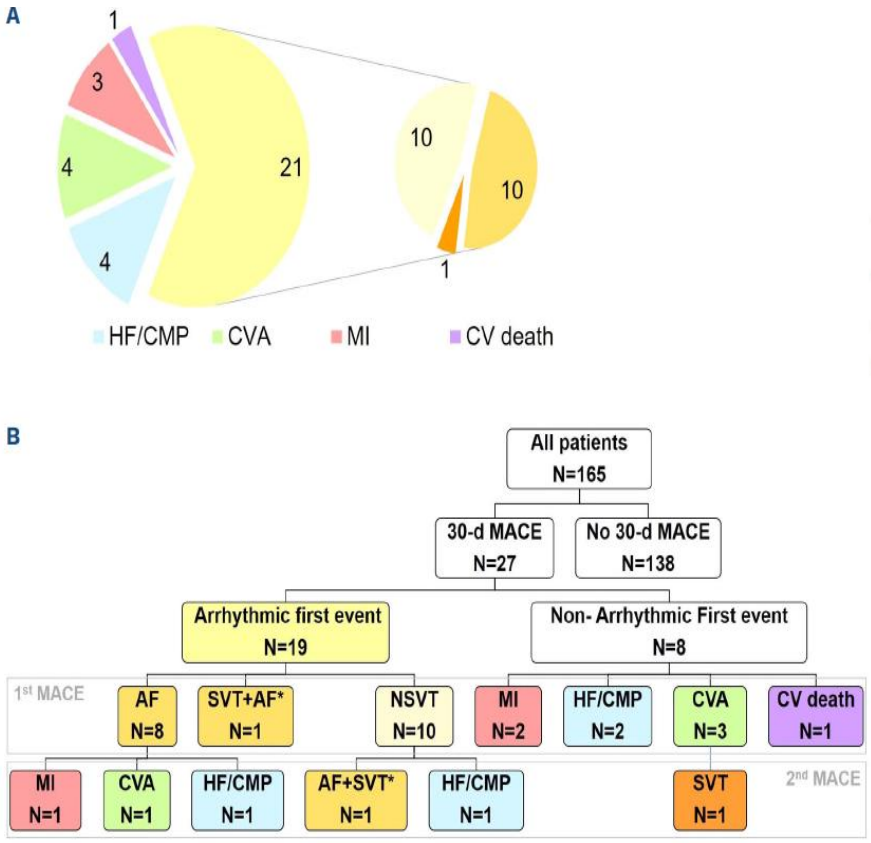
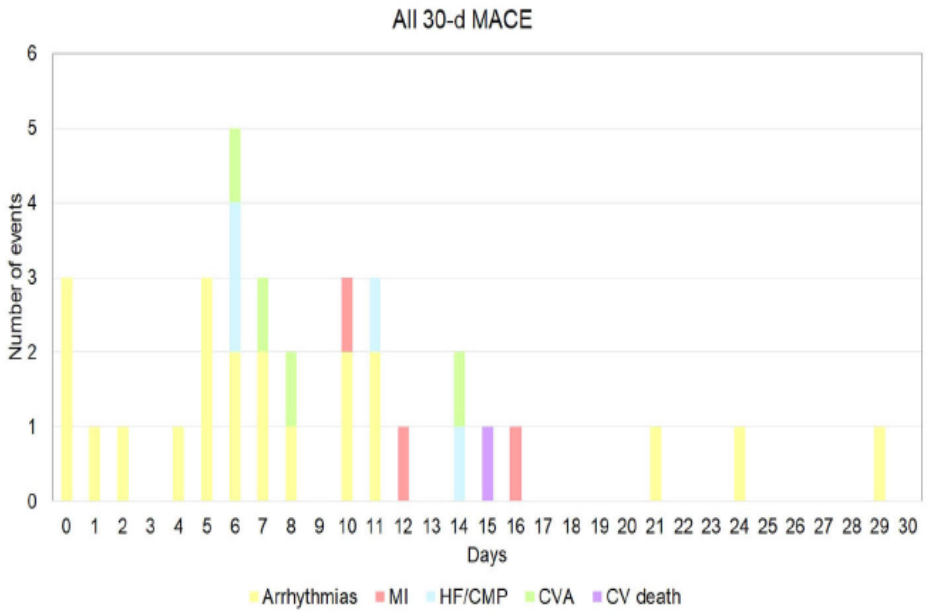


Figure 4. PFS and OS of patients with DLBCL treated with CAR-T therapy by either CIRS ≥7 or CIRS-3+.

Cardiovascular events in patients treated with chimeric antigen receptor T-cell therapy for aggressive B-cell lymphoma





27/165 (16%)

Figure 1. Nature, recurrences, and timing of 30-day major adverse cardiovascular events (A) Cumulative occurrences of 30-day major adverse cardiovascular event (30-d MACE). (B) Nature and recurrences of 30-d MACE. *Events happened on the same day, counted as 1 atrial fibrillation (AF) event. The patients who presented clinical heart failure had a decrease in left ventricular ejection fraction. (C). Timing of 30-d MACE. Day 0 represents the day of chimeric antigen receptor T-cell therapy infusion. AF: atrial fibrillation; CMP: cardiomyopathy; HF: heart failure; CV: cardiovascular; CVA: cerebrovascular accident; MI: myocardial infarction; NSVT: non-sustained ventricular tachycardia; SVT: supraventricular tachycardia.

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					Patients who presented at least one 30-d MACE (N = 27)	
Characteristics/ Outcomes	**All patients (N= 165)**	**Patients who did not present 30-d MACE (N = 138)**	**Patients who presented at least one 30-d MACE (N = 27)**	***P***	**Arrhythmic event(s) only (N = 15)**	**At least one non-arrhythmic event (N = 12)**
Cohort						
Age, median [range], y	60 [18-88]	59 [18-88]	69 [24-83]	**0.001**	68 [42-82]	70 [24-83]
Age >60 years	87 (53%)	66 (48%)	21 (78%)	**0.004**	13 (48%)	8 (30%)
Age <60 years	78 (47%)	72 (52%)	6 (22%)		2 (7%)	4 (15%)
Baseline echocardiographic features#						
Left ventricular ejection fraction, median [range]	58% [38-75]	58% [38-75]	53% [39-68]	0.131	58% [39-66]	50% [44-68]
Presence of diastolic dysfunction	49%	43%	82%	**0.004**	89%	75%

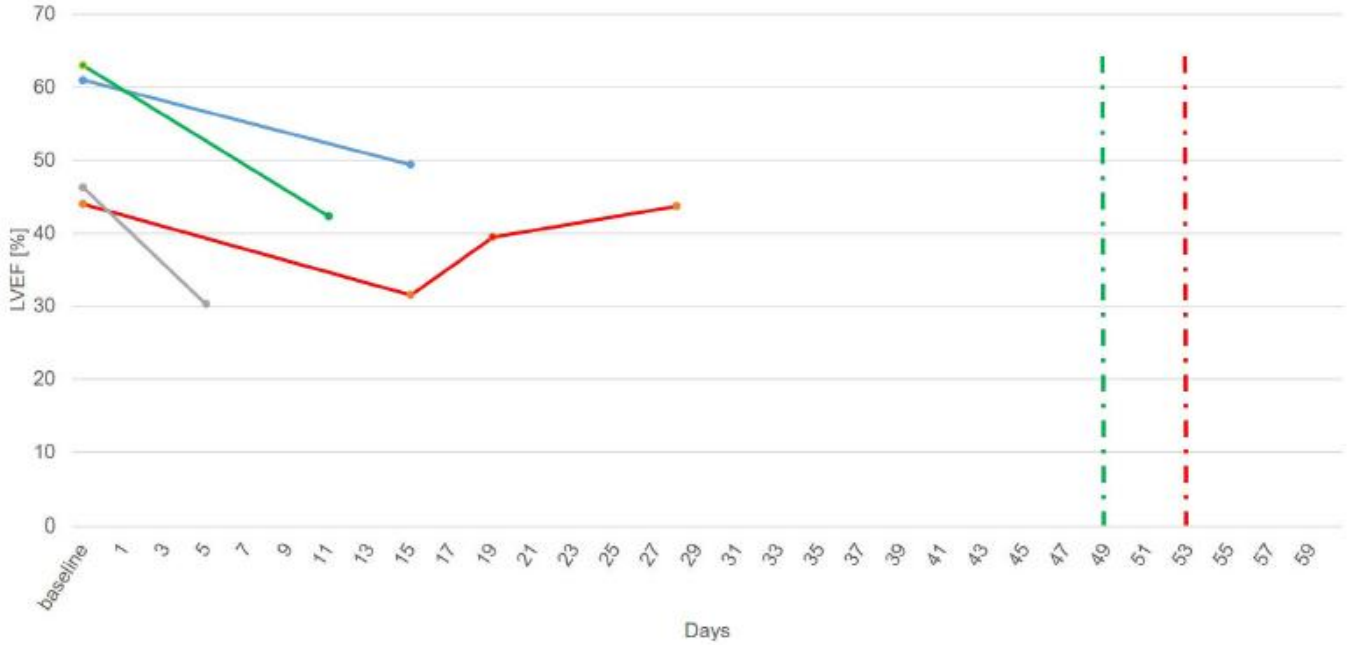


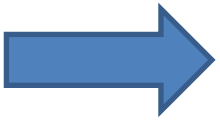
Figure 3. Evolution of left ventricular ejection fraction of patients who presented a drop of ejection fraction of at least 10% during day 0-30. LVEF: left ventricular ejection fraction. Day 0 represents the day of chimeric antigen receptor T-cell therapy infusion. The colored dashed lines indicate the day of death for the patient of the corresponding color.

Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma

Sattva S. Neelapu,[1] Caron A. Jacobson,[2] Olalekan O. Oluwole,[3] Javier Munoz,[4] Abhinav Deol,[5] David B. Miklos,[6] Nancy L. Bartlett,[7,8] Ira Braunschweig,[9] Yizhou Jiang,[10] Jenny J. Kim,[10] Lianqing Zheng,[10] John M. Rossi,[10] and Frederick L. Locke[11]

Table 1. Patient characteristics, efficacy, and safety

Characteristic	≥65 y (n = 27)	<65 y (n = 81)
Grade ≥3 AEs*		
Any grade ≥3 AE, n (%)	27 (100)	79 (98)
Neutropenia†	20 (74)	66 (81)
Anemia	13 (48)	36 (44)
Thrombocytopenia‡	12 (44)	31 (38)
Decreased white blood cell count	9 (33)	22 (27)
Encephalopathy	8 (30)	17 (21)
Lymphocyte count decreased	8 (30)	14 (17)
Grade ≥3 infection		
Infection, n (%)	5 (19)	25 (31)
Grade ≥3 CRS§		
Any grade ≥3 CRS, n (%)	2 (7)	10 (12)
Pyrexia	3 (12)	9 (12)
Hypotension	2 (8)	8 (11)
Hypoxia	3 (12)	6 (7)
Grade ≥3 neurologic event§		
Any grade ≥3 neurologic event, n (%)	12 (44)	23 (28)
Encephalopathy	8 (30)	17 (21)
Confusional state	2 (7)	8 (10)
Aphasia	0	8 (10)
Agitation	3 (11)	2 (2)
Delirium	3 (11)	0

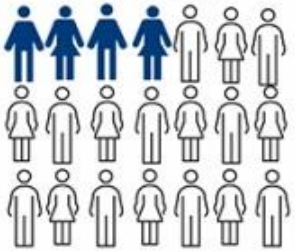


Blood 2020

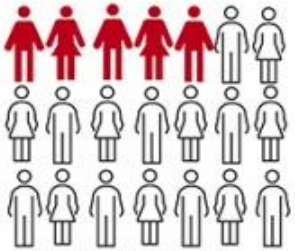
CAR T-Cell Therapy Utilization and Outcomes in Older Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL)

CAR T-cell utilization in patients with DLBCL who received two or more lines of treatments among Medicare Fee-for-Service beneficiaries:

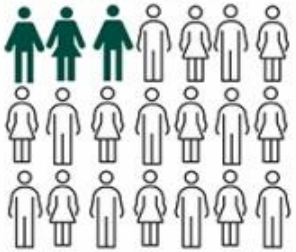
19% of DLBCL Patients Aged 65-69 Utilize CAR T



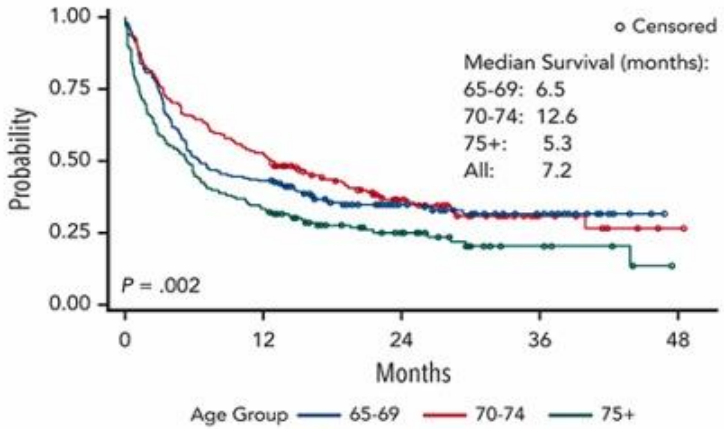
22% of DLBCL Patients Aged 70-74 Utilize CAR T

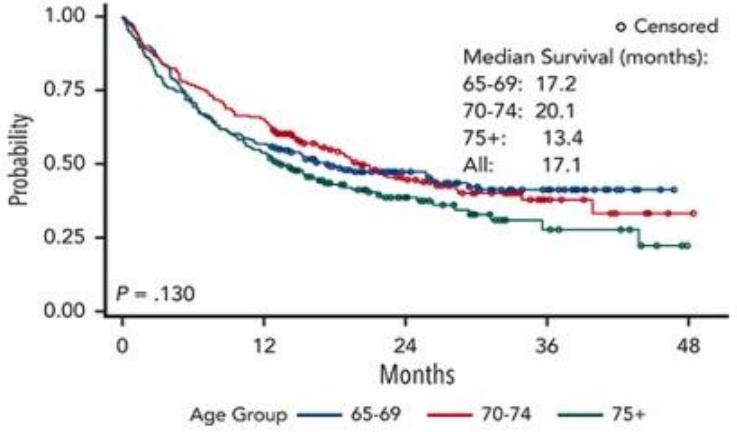


13% of DLBCL Patients Aged 75+ Utilize CAR T



Event-free survival and overall survival from CAR T-cell therapy:





Conclusion: **While CAR T-cell therapy in older patients is associated with favorable event-free survival comparable to outcomes in younger patients, CAR T-cell usage is low in older patients with DLBCL, which suggests an unmet need for more accessible, effective, and tolerable therapy.**

Blood Visual Abstract

*Chihara et al. DOI: 10.1182/**blood**.2023020197*

Table 2. Cox proportional hazards model for EFS and OS

Characteristic	Categories	EFS						OS					
		Univariate			Multivariate			Univariate			Multivariate		
		HR	95% CI	*P* value	HR	95% CI	*P* value	HR	95% CI	*P* value	HR	95% CI	*P* value
Age groups	≥75 vs 65-69 y	1.37	1.07-1.74	.011	1.41	1.10-1.82	.007	1.25	0.96-1.62	.105	1.2	0.91-1.58	.188
	≥75 vs 70-74 y	1.54	1.19-1.98	.001	1.46	1.13-1.89	.004	1.29	0.98-1.70	.066	1.2	0.90-1.58	.207
Sex	Male vs female	0.99	0.81-1.22	.943	0.92	0.75-1.14	.449	1.06	0.85-1.33	.577	1	0.80-1.26	.973
Urban/suburban residence	Rural vs urban	1.14	0.88-1.47	.317		—	—	1.22	0.93-1.60	.158		—	—
Bridging therapy	Present vs absent	1.34	1.09-1.64	.005	1.27	1.03-1.56	.028	1.49	1.19-1.86	<.001	1.39	1.11-1.75	.005
Charlson Comorbidity Index	≥5 vs 0-4	1.57	1.28-1.94	<.0001	1.56	1.26–1.92	<.0001	1.63	1.30-2.05	<.0001	1.58	1.26-1.99	<.0001

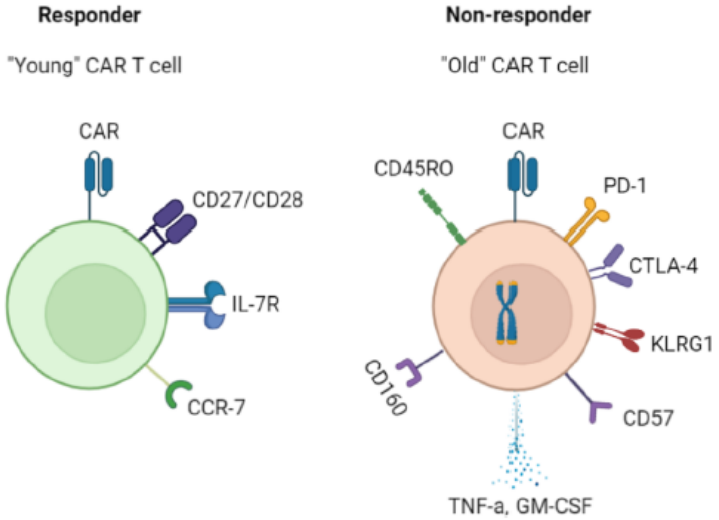


Fig. 2. Features of young and old CAR T cells that determine therapy outcome. CAR T cells of responding patients have higher expression of co-stimulatory receptors and markers associated with a central memory T cell phenotype. Non-responding CAR T cells display higher levels of exhaustion and terminally differentiated markers. Created with BioRender.com.

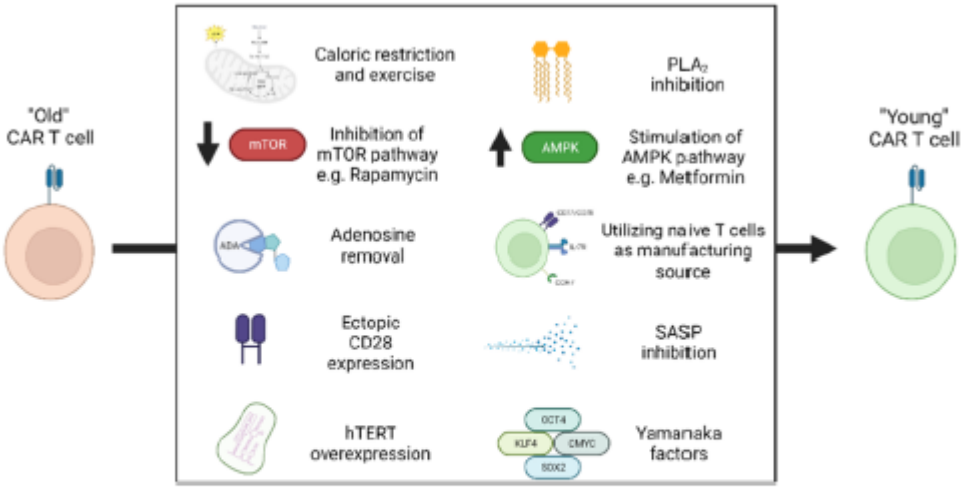


Fig. 3. Rejuvenation approaches for CAR T cells. Proposed methods for T cell rejuvenation include lifestyle changes (CR and exercise), pharmacological intervention (Rapamycin, Metformin, SASP and PLA2 inhibition) and gene editing approaches (ADA, CD28, hTERT, OSKM). Created with BioRender.com.

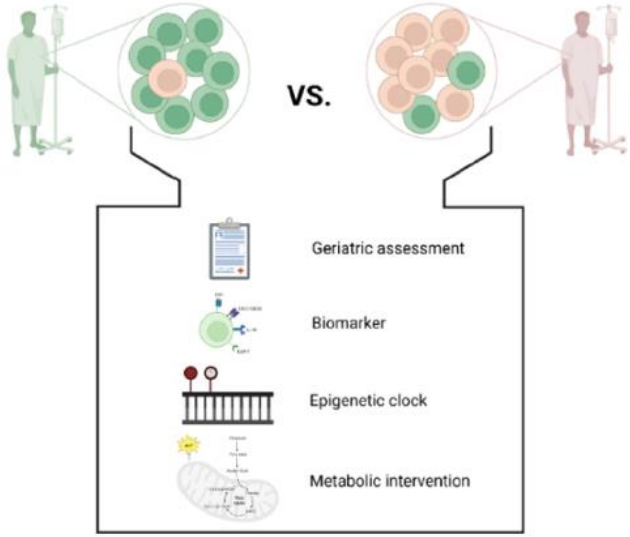


Fig. 4. Possible clinical approaches for differentiating and ameliorating aging phenotypes. These include improved geriatric assessment, biomarker analysis, age prediction with epigenetic clock and metabolic intervention for patients. Created with BioRender.com.

CONCLUSIONS

- Elderly patients (i.e. >75 yrs) are at increasing risk of toxicity
- CGA can be an useful tool to select patients
- Limited data are available regarding the long term efficacy of CAR-T cells in elderly patients in a RWE
- More data on immunological aspect of these patients are warranted
- A better selection of patients will lead to a better use of this treatmant in order to maximaze the outcome and minimaze the side effects and costs.