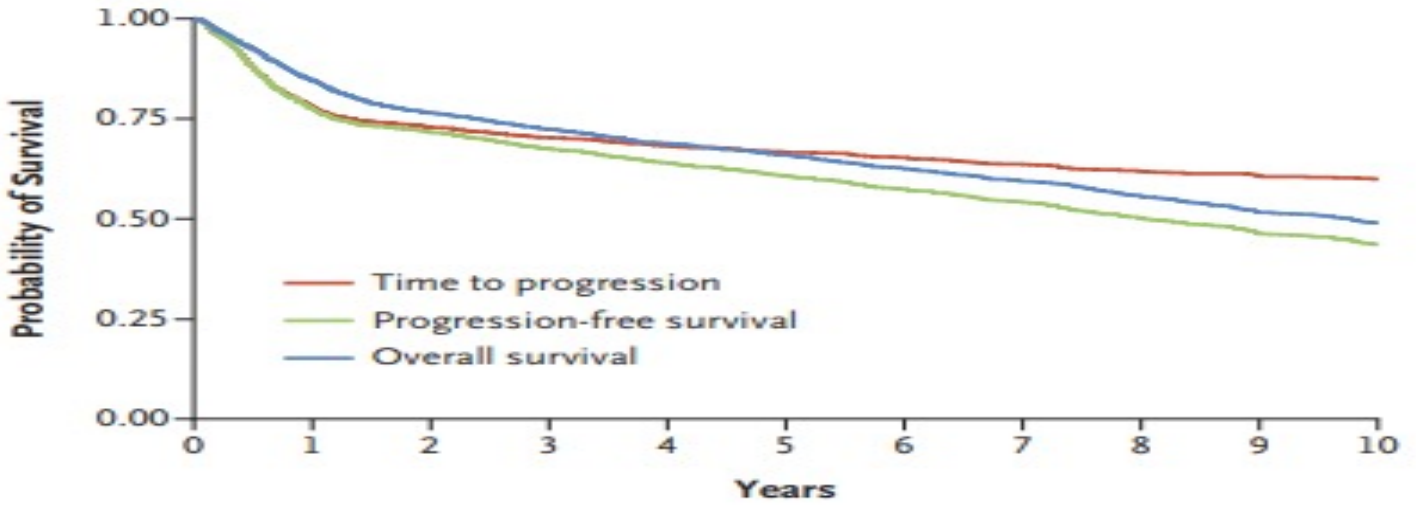
Dati degli studi registrativi delle terapie cellulari

Stefania Bramanti
IRCCS Istituto Clinico Humanitas Rozzano

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
NOVARTIS					x		
BMS					x		
JANSENN					x		
GILEAD					x		

Outcomes of Patients with DLBCL

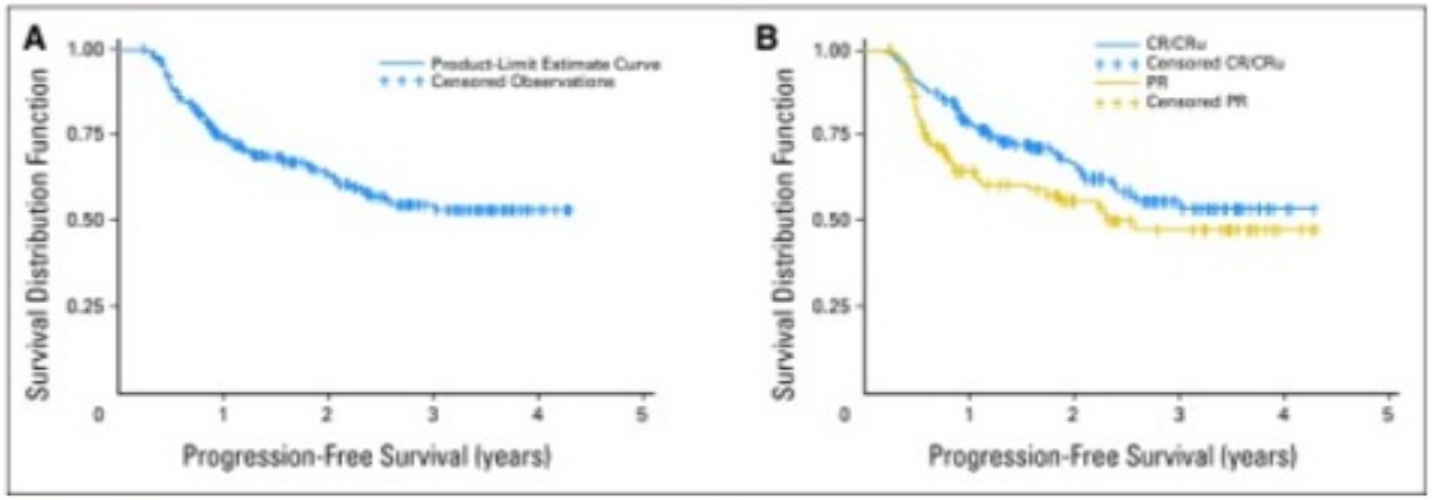


No. at Risk											
Time to progression	3082	2133	1775	1446	1236	1048	830	700	585	468	391
Progression-free survival	3082	2132	1774	1445	1235	1047	829	699	584	467	390
Overall survival	3082	2336	1900	1558	1338	1140	911	767	647	519	437

Sehn LH and Salles G. NEJM. 2021.

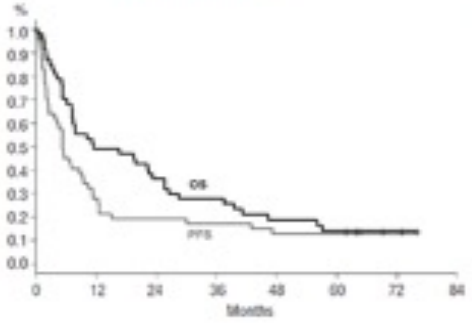
Salvage Regimens With Autologous Transplantation for Relapsed Large B-Cell Lymphoma in the Rituximab Era

R/R DLBCL outcome after first line			
	CR %	2yr PFS%	OS%
All	20-25	30	40
Relapsed	40	50	60-70
Refractory	7	15	20

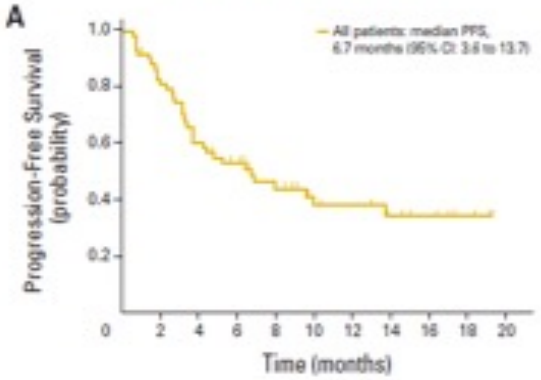


Gisselbrecht C , JCO 2010

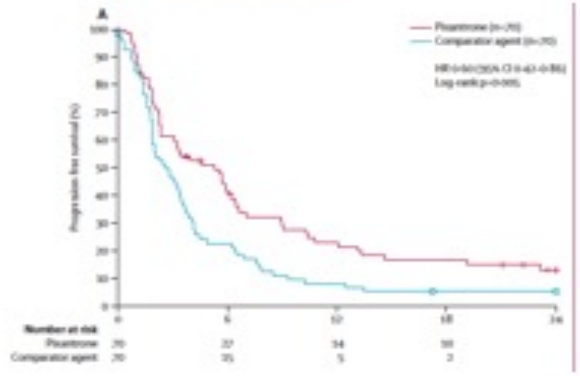
R-GemOx



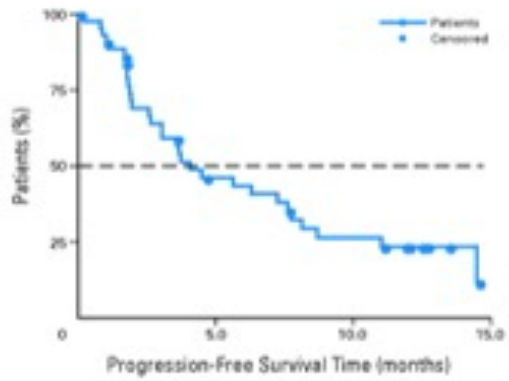
R-bendamustine



Pixantrone

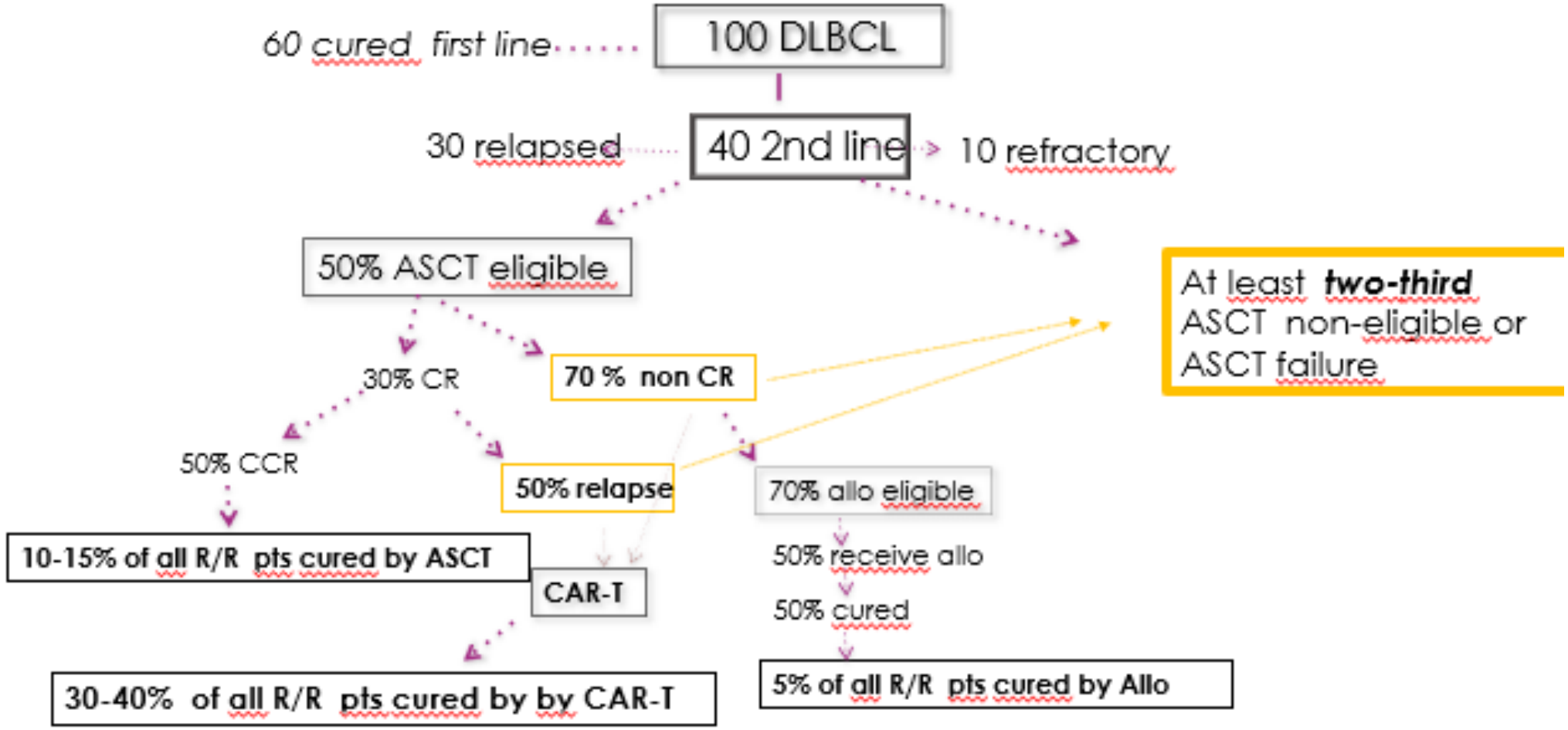


Lenalidomide



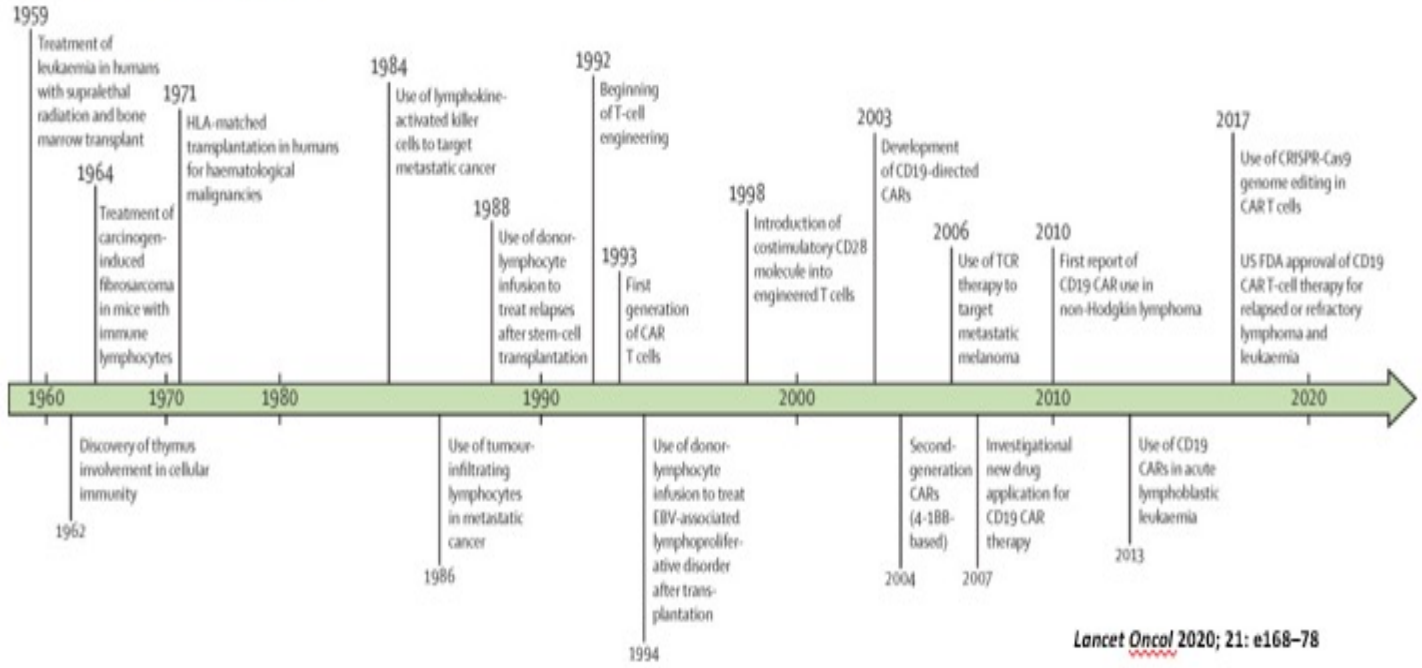
Mounier N, et al. Haematol. 2013; Arcari A, et al. Leuk Lymphoma. 2015; Pettengel R, et al. Lancet Oncol. 2012; Wiernik PH, et al. JCO. 2008.

REGIMEN	N	Median age	ORR%	CR %	PFS
R-GEMOX	49	69	46	38	5-yrs 12.8%
R-Bendamustine	55	76	50	28	Median 8.8 mo
Pixantrone	70	60	37	20	Median 5.3 mo
Lenalidomide	49	65	35	12	Median 4 mo


60 cured first line
100 DLBCL
30 relapsed
40 2nd line
10 refractory
50% ASCT eligible
At least two-third
ASCT non-eligible or
ASCT failure
30% CR
70 % non CR
50% CCR
50% relapse
70% allo eligible
10-15% of all R/R pts cured by ASCT
CAR-T
50% receive allo
50% cured
30-40% of all R/R pts cured by by CAR-T
5% of all R/R pts cured by Allo

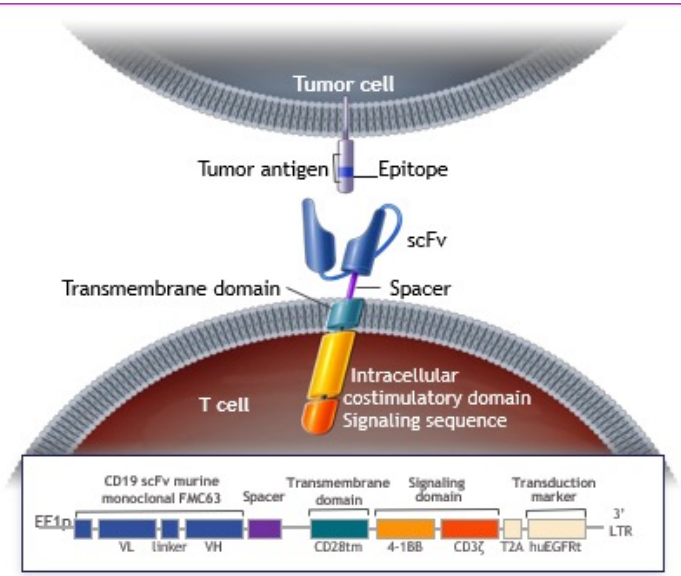
CAR T cells: continuation in a revolution of immunotherapy

Anurag K Singh, Joseph P McGuirk



Lancet Oncol 2020; 21: e168–78

TRANSFORM study (NCT03575351)



Screening + leukapheresis

1:1 randomization

Stratification
- Refractory vs relapsed
- sAAIPI: 0/1 vs 2/3

PET[b] LDC[c]

Bridging therapy allowed[a]

Liso-cel
(100 × 10^6 CAR+ T cells)

SOC[d]
(3 cycles of salvage immunochemotherapy, followed by HDCT + ASCT)

Crossover to liso-cel
Allowed if SOC failed based on IRC-confirmed EFS[e] event

Key patient eligibility criteria
- Age 18–75 years
- Aggressive NHL
  - DLBCL NOS (de novo or transformed from indolent NHL), HGBCL (double/triple hit) with DLBCL histology, FL3B, PMBCL, THRBCL
- Refractory or relapsed ≤ 12 months after 1L treatment containing an anthracycline and a CD20-targeted agent
- ECOG PS ≤ 1
- Eligible for ASCT
- Secondary CNS lymphoma allowed
- LVEF > 40% for inclusion
- No minimum absolute lymphocyte count

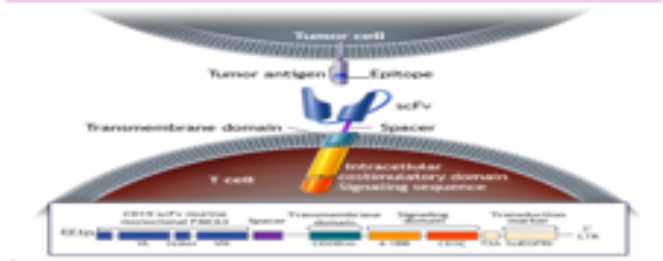
Primary endpoint
- EFS[e] (per IRC)

Key secondary endpoints
- CR rate (per IRC), PFS (per IRC), OS

Other secondary endpoints
- Duration of response, ORR (per IRC), PFS on next line of treatment
- Safety, PROs

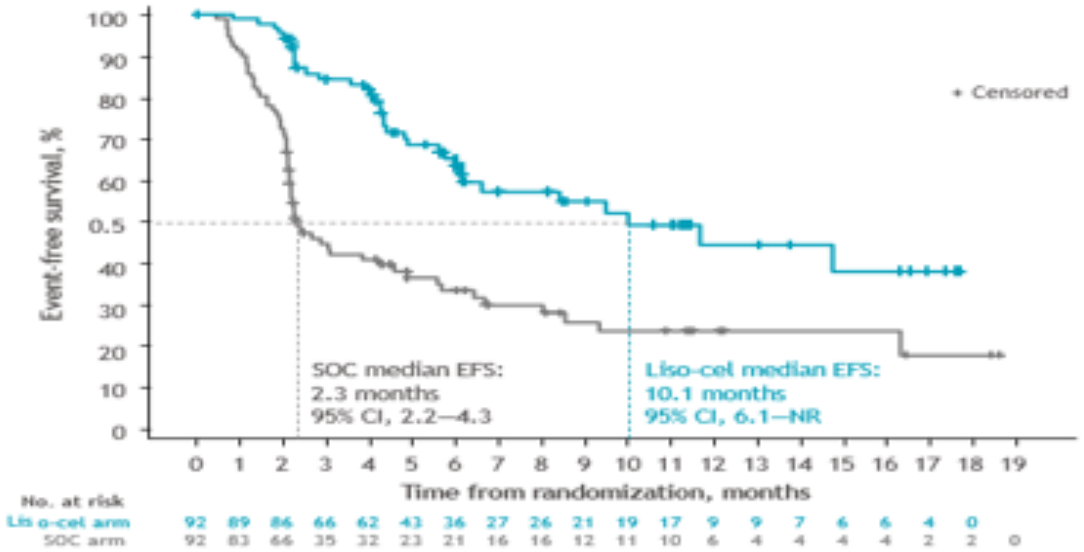
Exploratory endpoints
- Cellular kinetics
- B-cell aplasia

Abramson JS, et al. ASH 2022



- Results of a prespecified interim analysis of the TRANSFORM study (NCT03575351), performed at a median follow-up of 6.2 months, demonstrated superior efficacy of liso-cel compared with SOC as second-line treatment for patients with primary refractory or early relapsed (within 12 months of first-line [1L] therapy) LBCL3

Median follow-up in both arms: 6.2 months



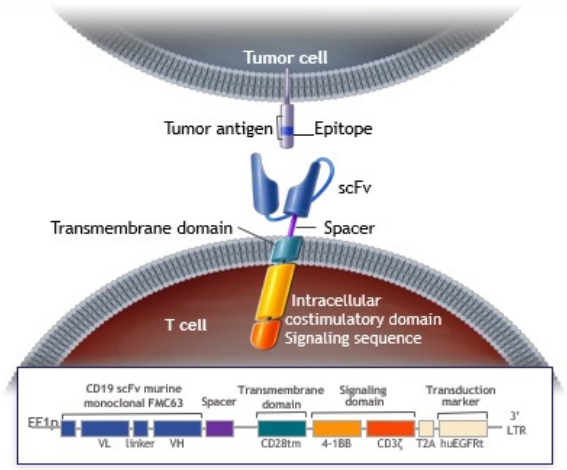
	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	0.349 (0.229–0.530) P < 0.0001	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
Two-sided 95% CI	52.0–74.7	23.0–43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
Two-sided 95% CI	29.4–59.6	13.4–34.1

Kamdar M, et al. Lancet 2022

American Society of Hematology (ASH) Annual Meeting
December 10-13, 2022; New Orleans, LA, USA

Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma: primary analysis of the randomized, phase 3 TRANSFORM study

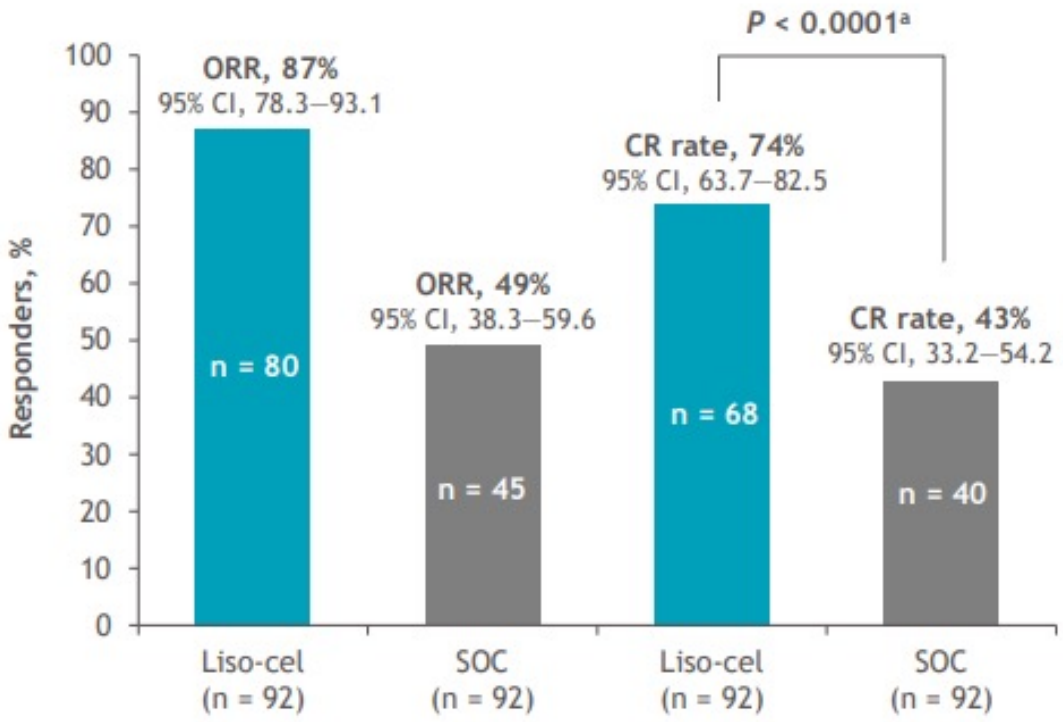
Jeremy S. Abramson,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami Ibrahimi,[7] Stephan Mielke,[8] Pim Mutsaers,[9] Francisco Hernandez-Ilizaliturri,[10] Koji Izutsu,[11] Franck Morschhauser,[12] Matthew Lunning,[13] Alessandro Crotta,[14] Sandrine Montheard,[14] Alessandro Previtali,[14] Manali Kamdar[15]

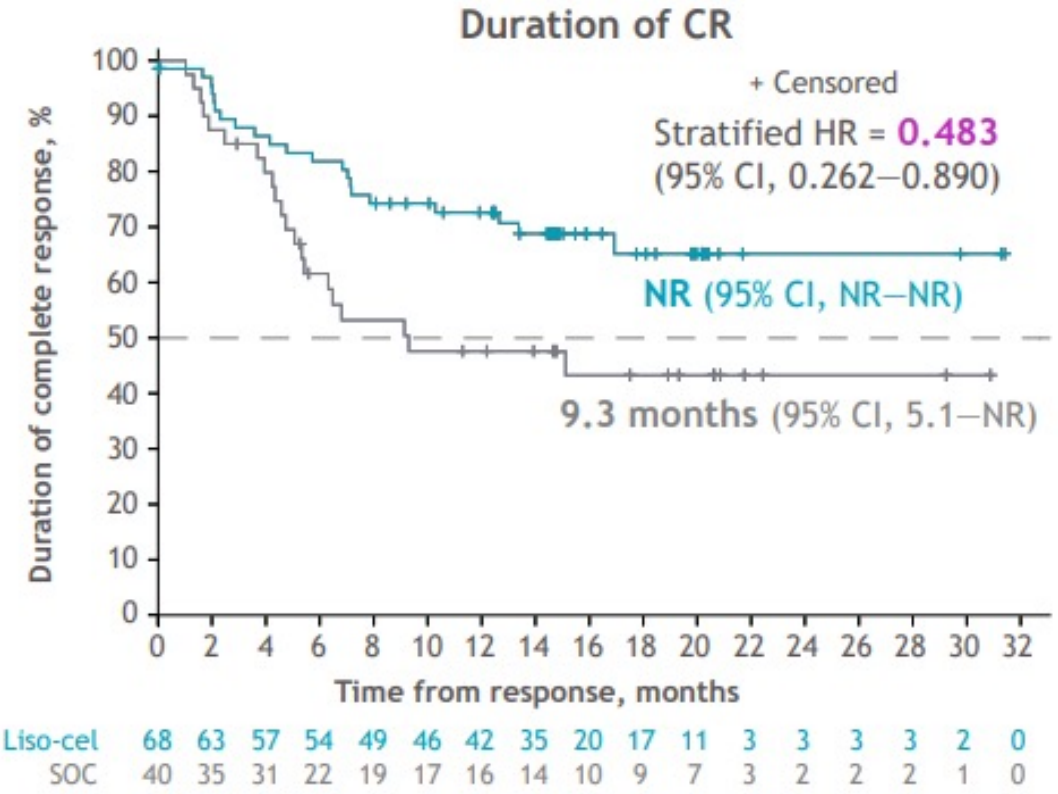


With a median follow-up of 17.5 months, the primary analysis of the TRANSFORM study confirmed the superiority of liso-cel over SOC in patients with primary refractory or early relapsed LBCL

Abramson JS, et al. ASH 2022

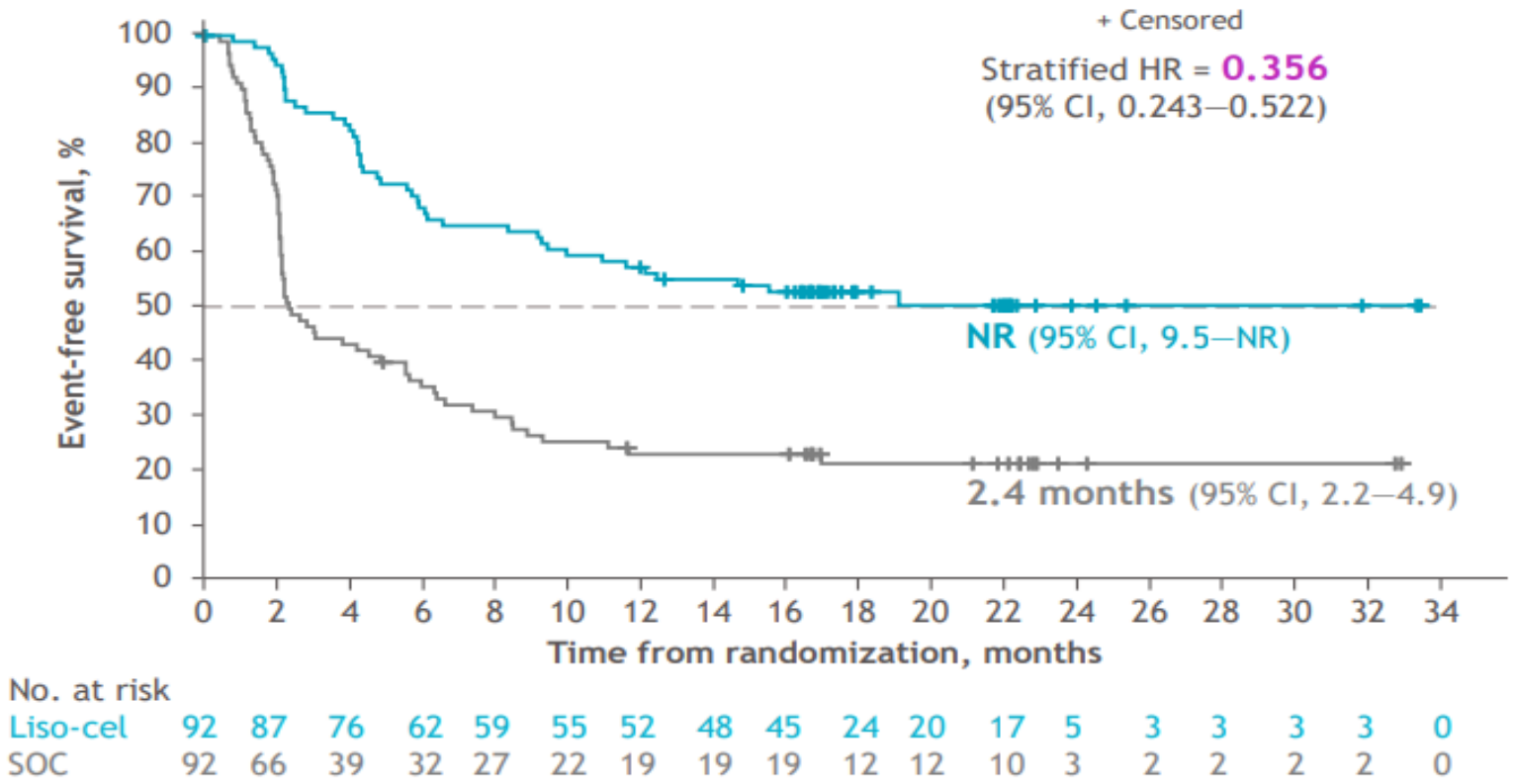
TRANSFORM: response rates





- Of 26 patients with a best overall response of PR at the interim analysis, the response deepened to CR for 9 patients at the primary analysis (6/18 in the liso-cel group; 3/8 in the SOC group)

EFS per IRS (ITT set; primary endpoint)



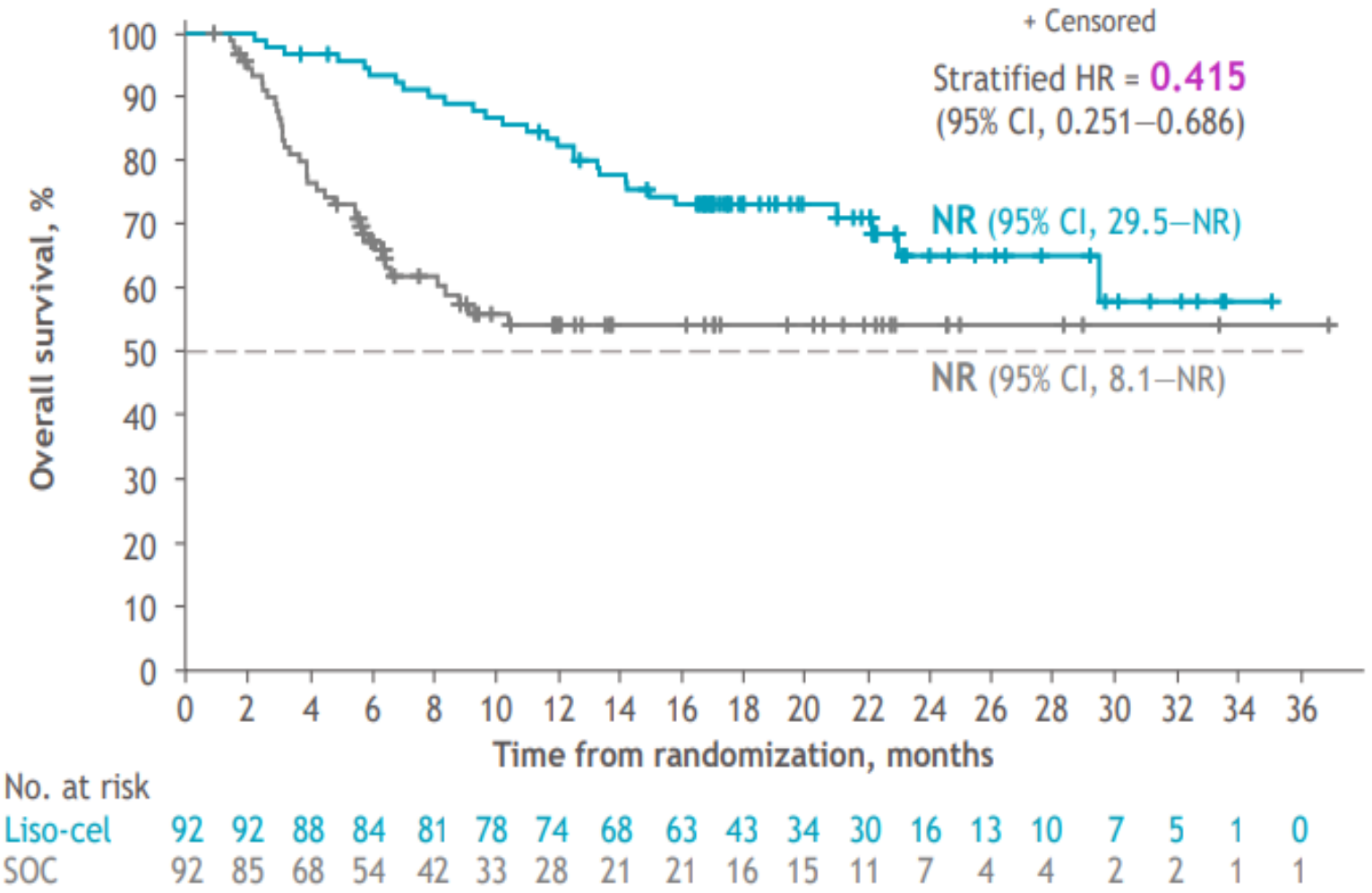
18-month EFS rate	
Liso-cel	SOC
52.6%	20.8%
(95% CI, 42.3–62.9)	(95% CI, 12.2–29.5)

Median follow-up: 17.5 months

At 18 months, EFS and PFS rates with liso-cel were more than double those with SOC – With longer follow-up, there was a deepening of response

Abramson JS, et al. ASH 2022

OS adjusted for crossover effect



18-month OS rate	
Liso-cel	SOC
73.1%	54.1%
(95% CI, 63.9–82.3)	(95% CI, 43.1–65.2)

Median follow-up: 17.5 months

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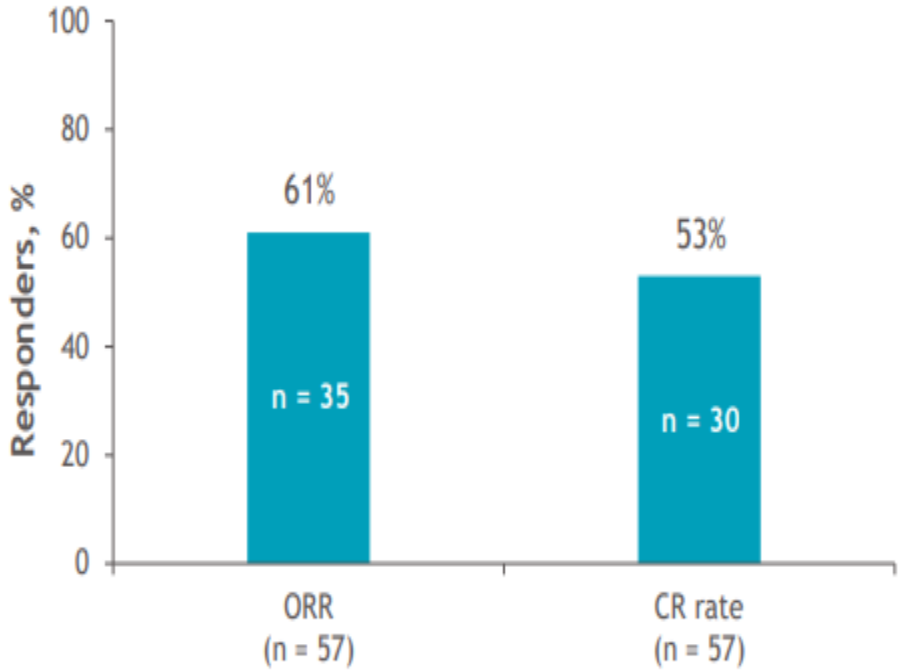
Efficacy outcomes in the crossover subgroup



	Crossover subgroup (n = 57)[a]
Median (range) follow-up, months[b]	12.0 (1.4–28.1)
Median (95% CI) EFS, months[c]	5.9 (3.1–15.1)
Median (95% CI) PFS, months[c]	5.9 (3.2–26.5)
Median (95% CI) OS, months[c]	15.8 (11.8–NR)

All endpoints were evaluated from the time of liso-cel infusion.

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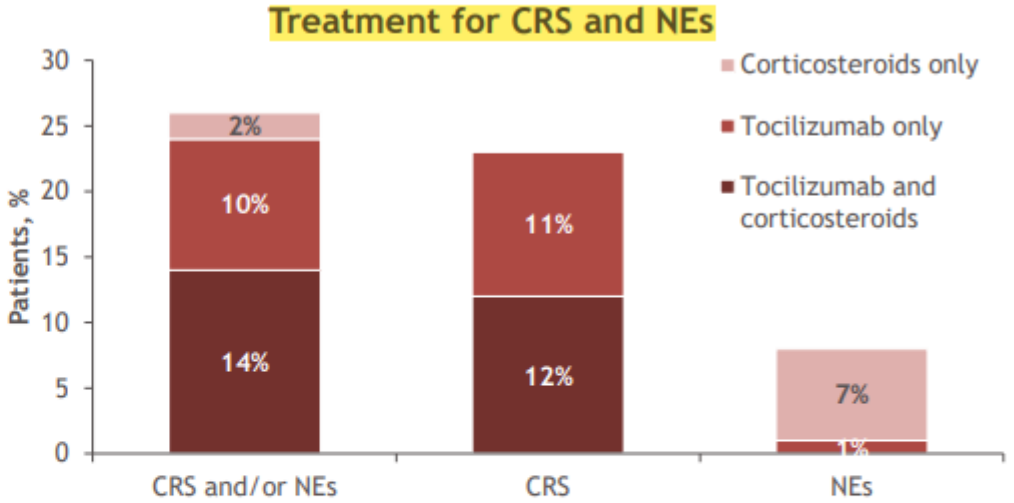
Safety

Patients with CRS and NEs	Liso-cel arm (n = 92)
CRS,[a] n (%)	
Any grade	45 (49)
Grade 1	34 (37)
Grade 2	10 (11)
Grade 3	1 (1)
Grade 4/5	0
Time to onset, days, median (range)	5.0 (1–63)
Time to resolution, days, median (range)	4.0 (1–16)
NE,[b] n (%)	
Any grade	10 (11)
Grade 1	4 (4)
Grade 2	2 (2)
Grade 3	4 (4)
Grade 4/5	0
Time to onset, days, median (range)	11.0 (7–17)
Time to resolution, days, median (range)	4.5 (1–30)



- No vasopressors or prophylactic corticosteroids were used

Other adverse events of special interest	Liso-cel arm (n = 92)	SOC arm (n = 91)
Prolonged cytopenia[c]	40 (43)	3 (3)
Grade ≥ 3 infection	14 (15)	19 (21)

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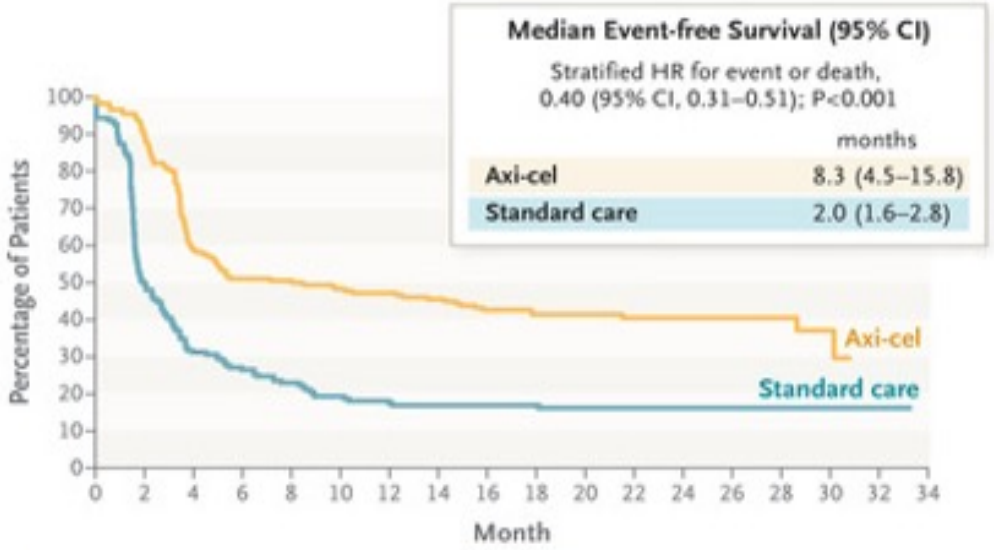
RESEARCH SUMMARY

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

Event-free Survival



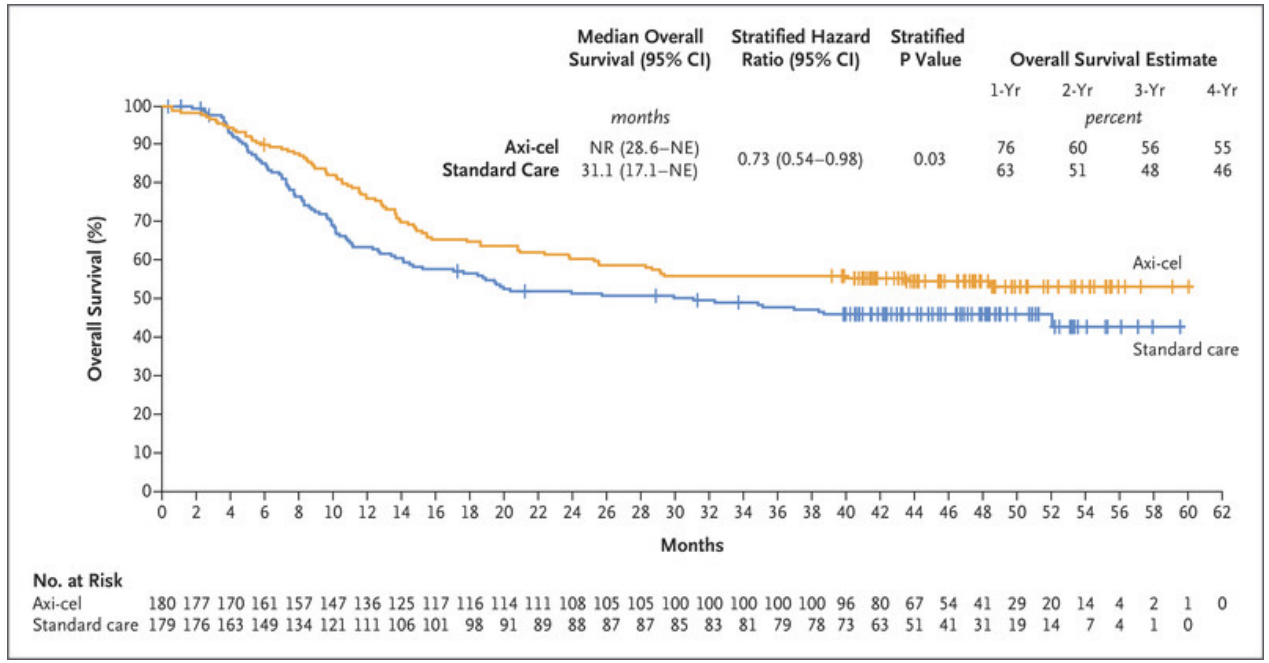
Adverse Events of Grade 3 or Higher

Percentage of Patients

	Axi-cel (N=170)	Standard Care (N=168)
Any adverse event	91%	83%
Neutropenia	69%	41%
Cytokine release syndrome	6%	—
Any neurologic event	21%	1%

The NEW ENGLAND JOURNAL of MEDICINE

Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma



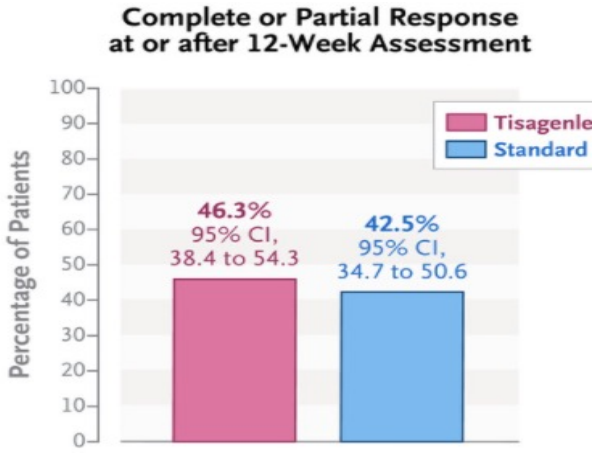
Jason R. Westin,June 2023

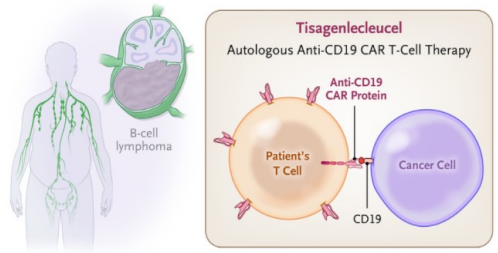
The NEW ENGLAND JOURNAL of MEDICINE

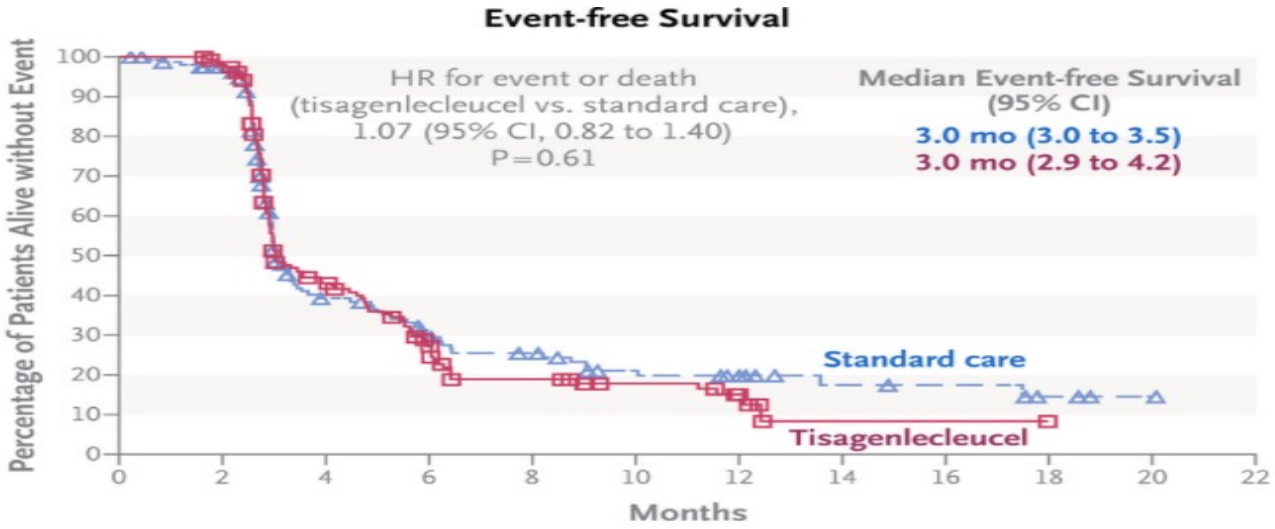
RESEARCH SUMMARY

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

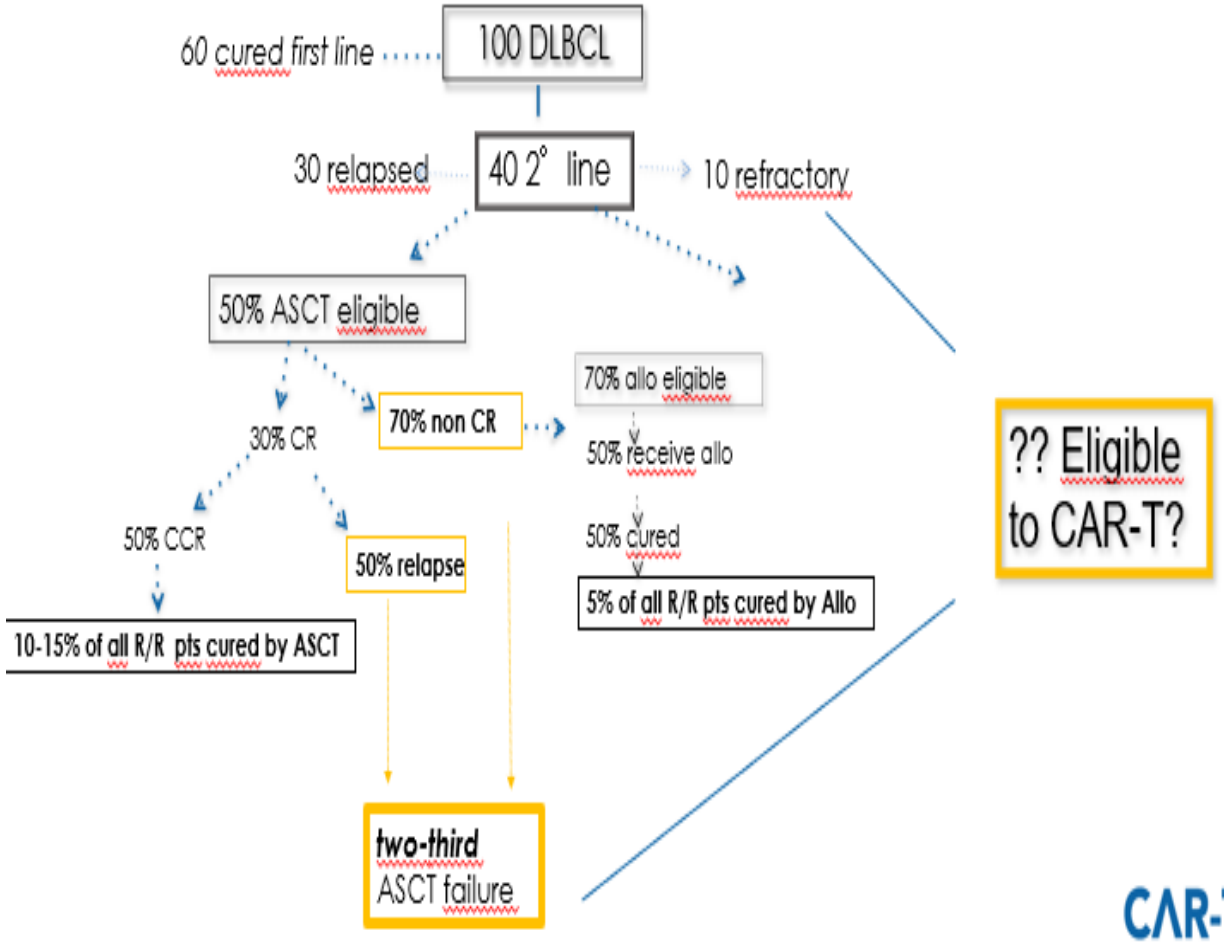
Bishop MR et al. DOI: 10.1056/NEJMoa2116596







	All Grades no. (%)	Grade ≥3 no. (%)
CRS[b]	95 (58.6)	8 (4.9)
NE[d]	16 (10.3)	3 (1.9)



?? Eligible to CAR-T?

Speaker's Experience

CAR-T ACADEMY

HUMANITAS
CANCER CENTER

CAR-T TEAM

Unità Clinica
Armando Santoro
Stefania Bramanti
Chiara De Philippis
Daniele Mannina

Laboratorio di manipolazione cellulare
Rossana Capizzutto
Inna Timofeeva
Laura Rondini

Farmacia
Gabriella Pieri
Martina Roperti

Trial Office
Laura Rossi
Elisa Carra

Unità di aferesi
Daniele Girardi
Elena Tirea
Annalisa Palladina

Anestesisti e Neurologi
Elena Costantini
Simona Marcheselli
Umberto Pensato

Radioterapia
Pierina Navarria

Infermieri di ricerca
Francesca Roveroni
Sergio Ferrante