THE UNIVERSITY OF CHICAGO MEDICINE

Chimeric Antigen Receptor (CAR) T-Cell Therapy: A Cure for Cancer?

Michael R. Bishop, M.D.
Director, Cellular Therapy Program
University of Chicago

CAR T-Cell Therapy: A Cure for Cancer?

Disclosures

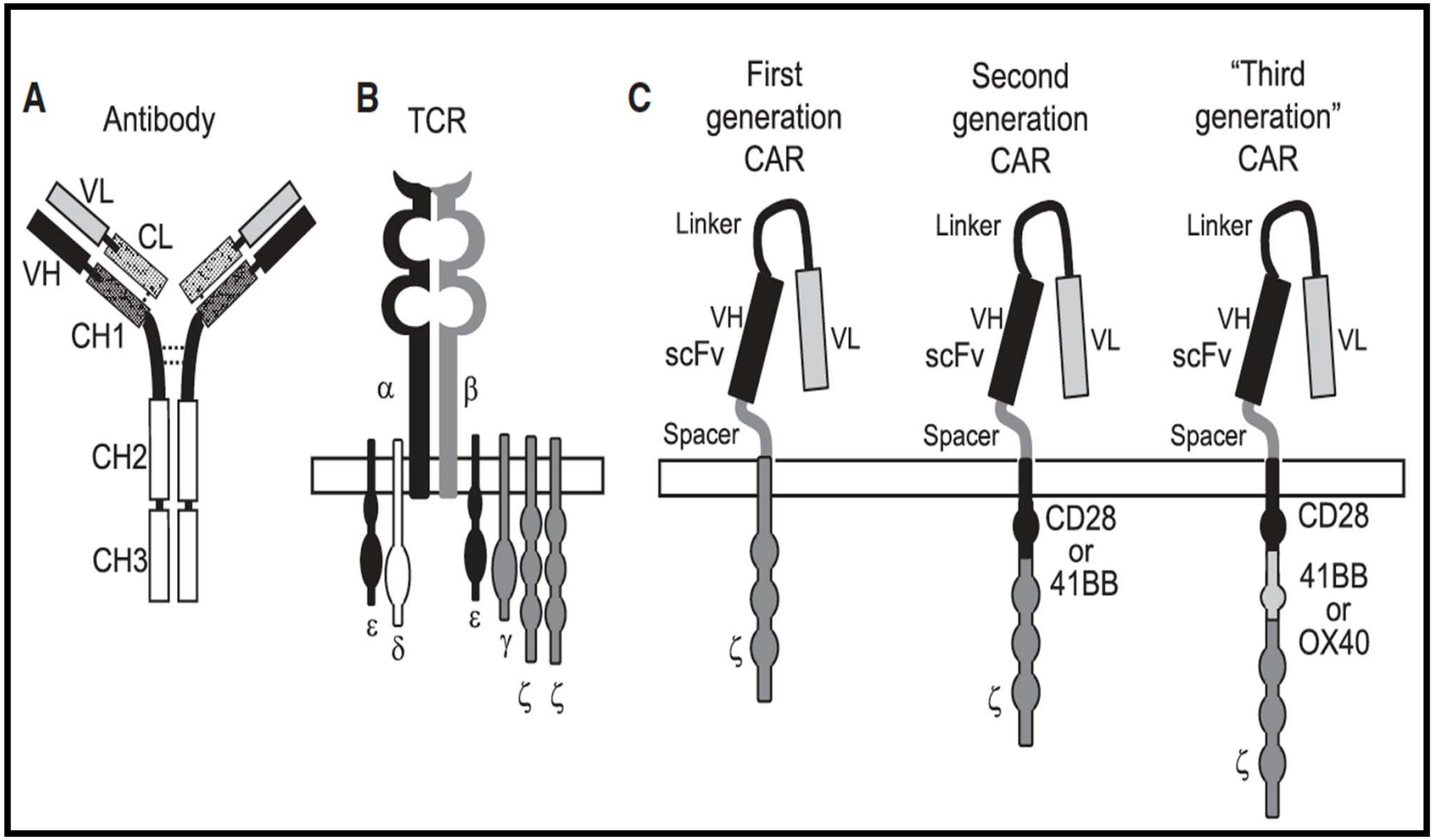
- **Honoraria:** Celgene, OptumHealth, Kite/Gilead
- **Speakers Bureau:** Celgene, Kite/Gilead, Agios
- **Membership on a Advisory Board or Consultant:** JUNO Therapeutics, KITE/Gilead, Novartis, CRISPR Therapeutics, OptumHealth

Discussion of off-label drug use: N/A

CAR T-Cell Therapy: A Cure for Cancer?

- Understand the biology and potential toxicities of CAR T cell therapy
- Review data on the efficacy and safety of chimeric antigen receptor T cells (CAR-T) for patients with relapsed/refractory hematologic malignancies
- Review costs and economic analyses of CAR T cell therapy

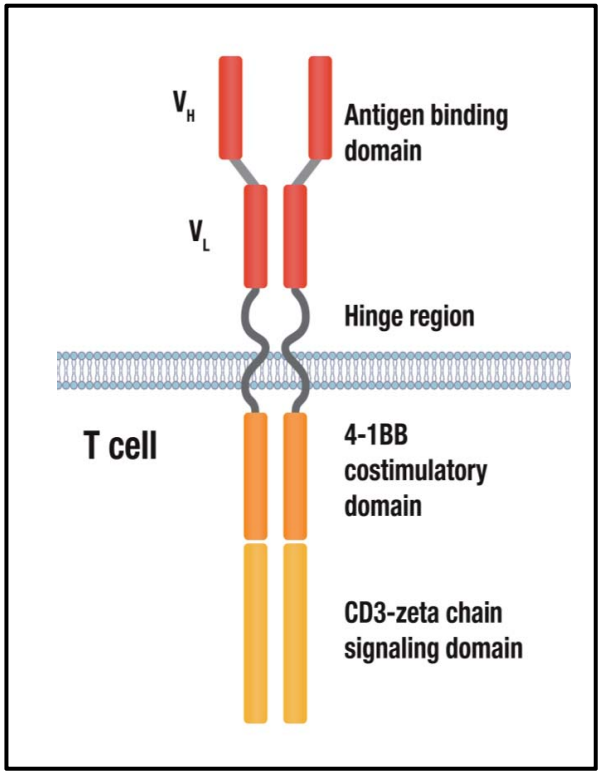
Chimeric Antigen Receptors



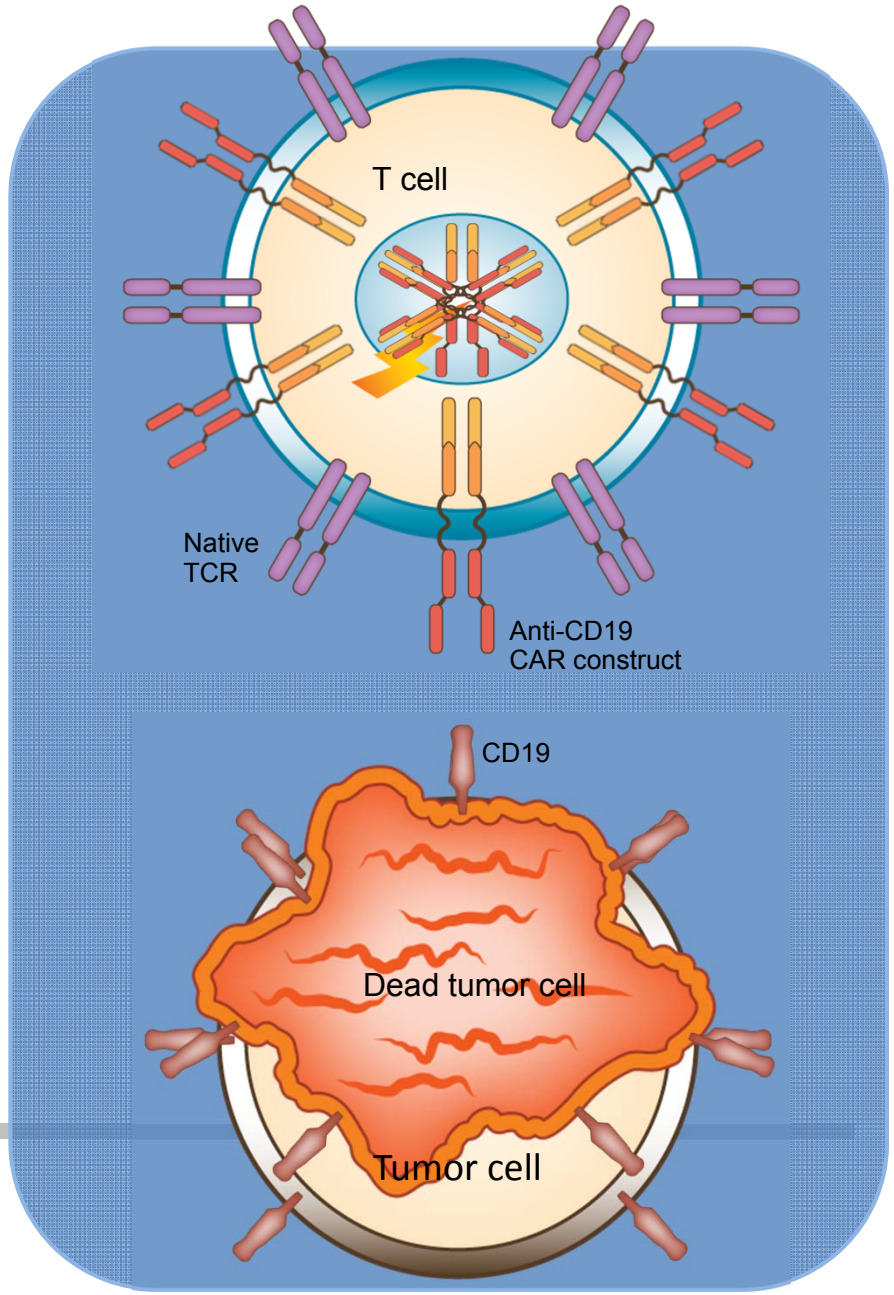
THE UNIVERSITY OF CHICAGO MEDICINE

Dotti et al. Human Gene Ther 2009; 20:1229–1239

Chimeric Antigen Receptor (CAR) T-cells

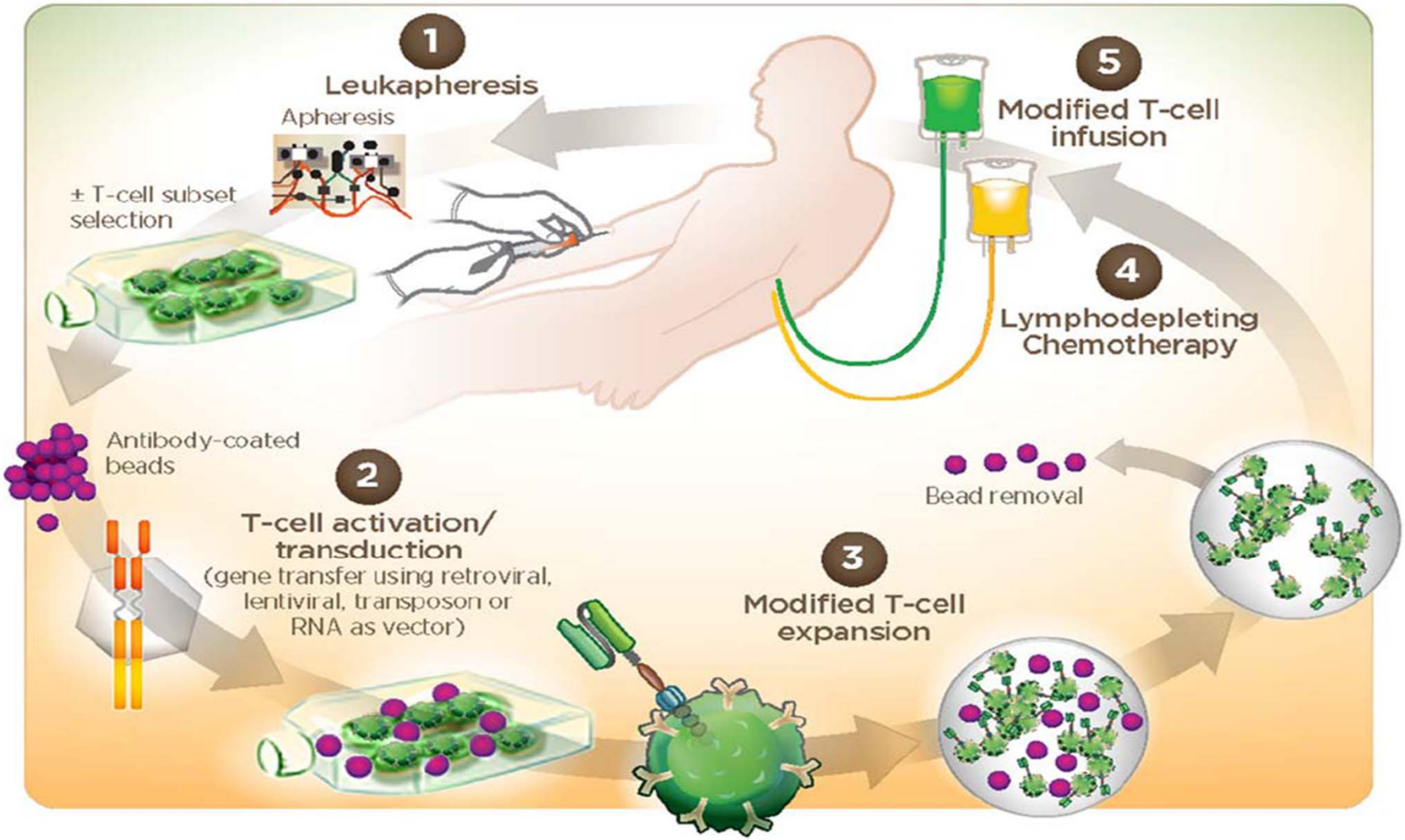


- **Uses patients own cells**
- **Tumor specific**
- **Can be applied to multiple malignancies**



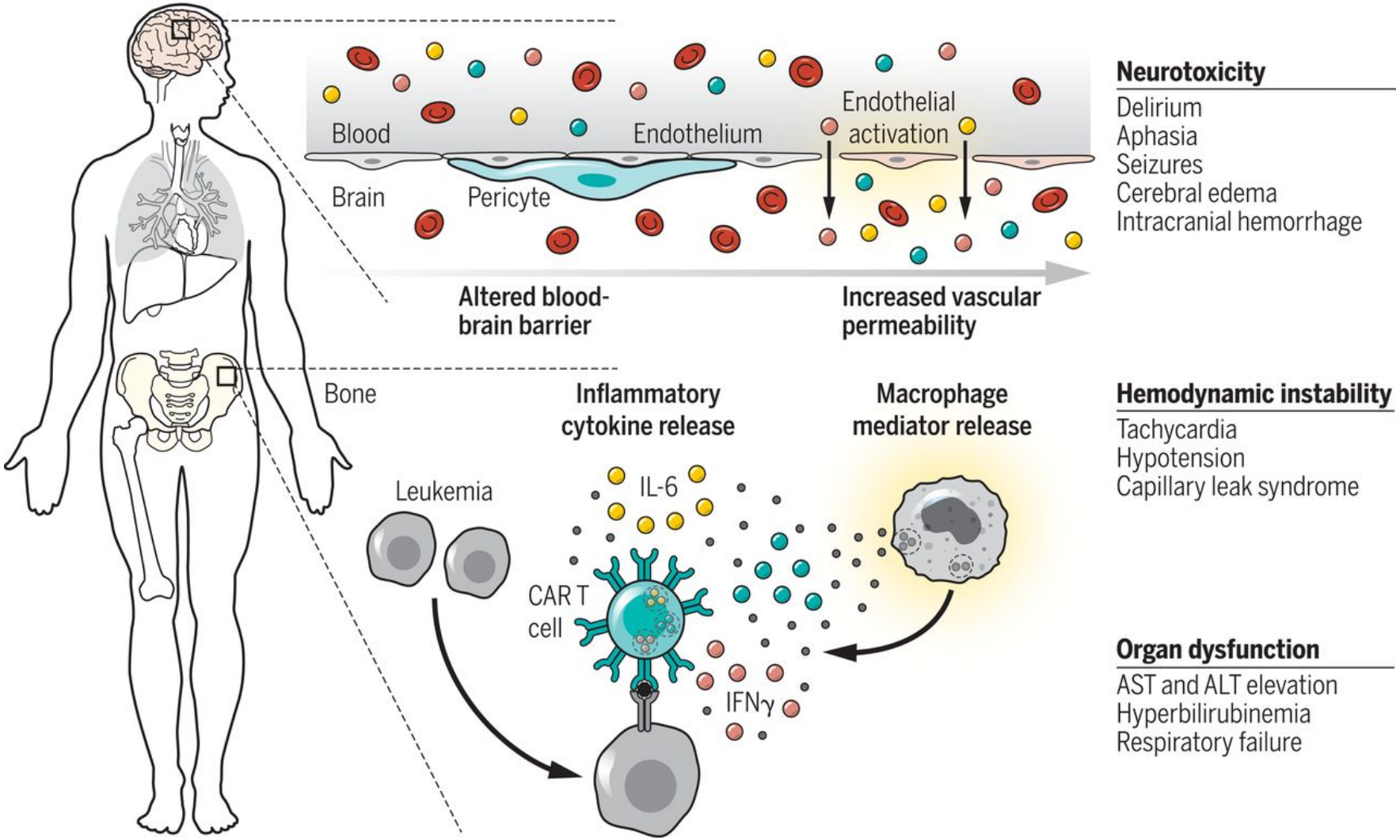
Courtesy N. Frey

CAR T-Cell Clinical Process



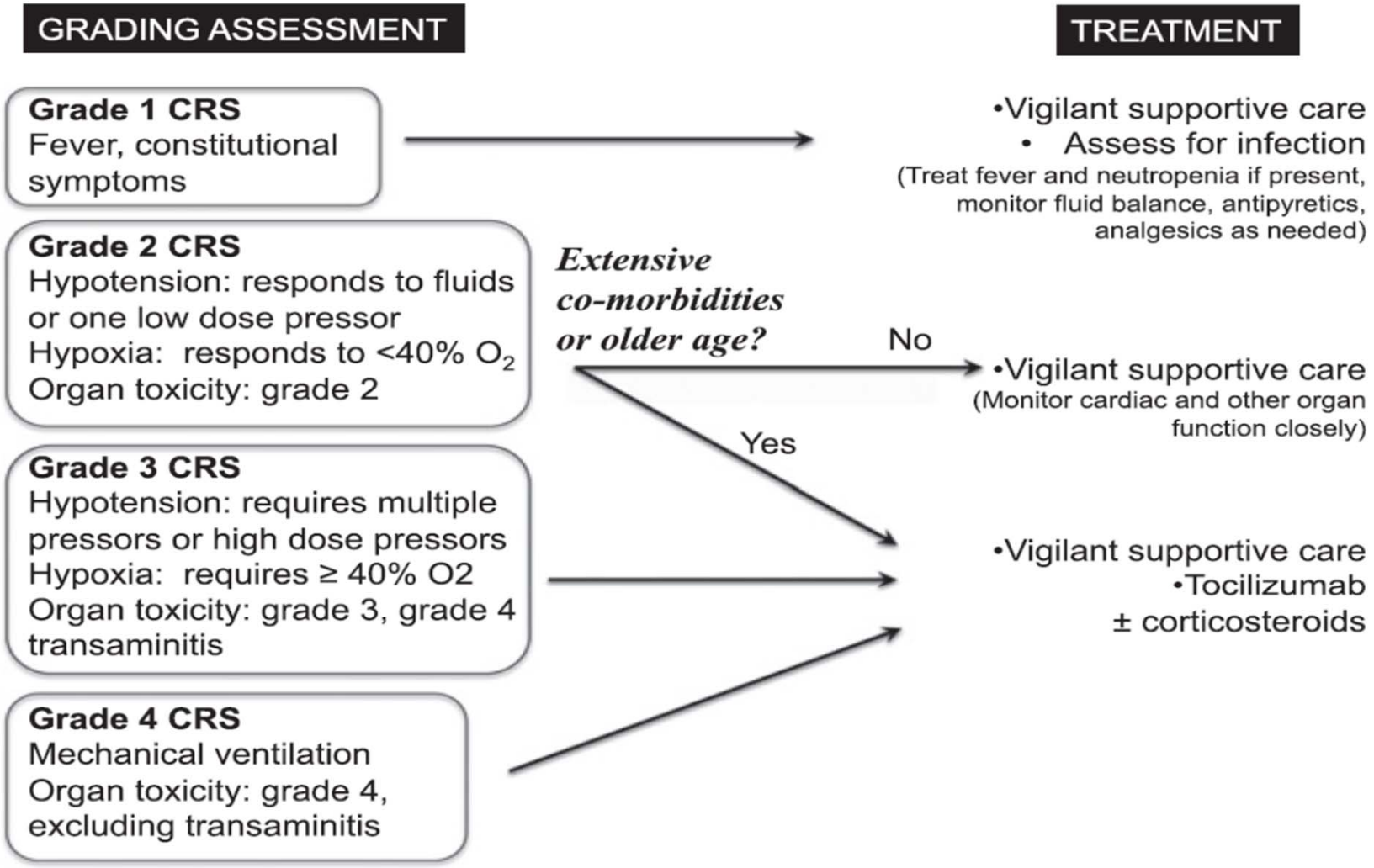
Frey, et al. Am J Hem 2016

Challenges of CAR T-Cell Therapy



June CH et al. Science 359:1361, 2018

Challenges of CAR T-Cell Therapy



Lee et al. Blood 124:188, 2014

Early Clinical Results

CAR T Cells in Chronic Lymphoid Leukemia

Clinical Results

	Baseline Tumor Burden	Estimated Tumor Mass	CART19+ Cells Infused	Response
UPN 01	2.5×10^{12}	2.5 kg	1.13×10^{9}	CR (+19 months)
UPN 02	3.5×10^{12}	3.5 kg	5.8×10^{8}	PR (+9 months)
UPN 03	1.3×10^{12}	1.3 kg	1.42×10^{7}	CR (+17 months)

1 kg = ~10^{12} tumor cells

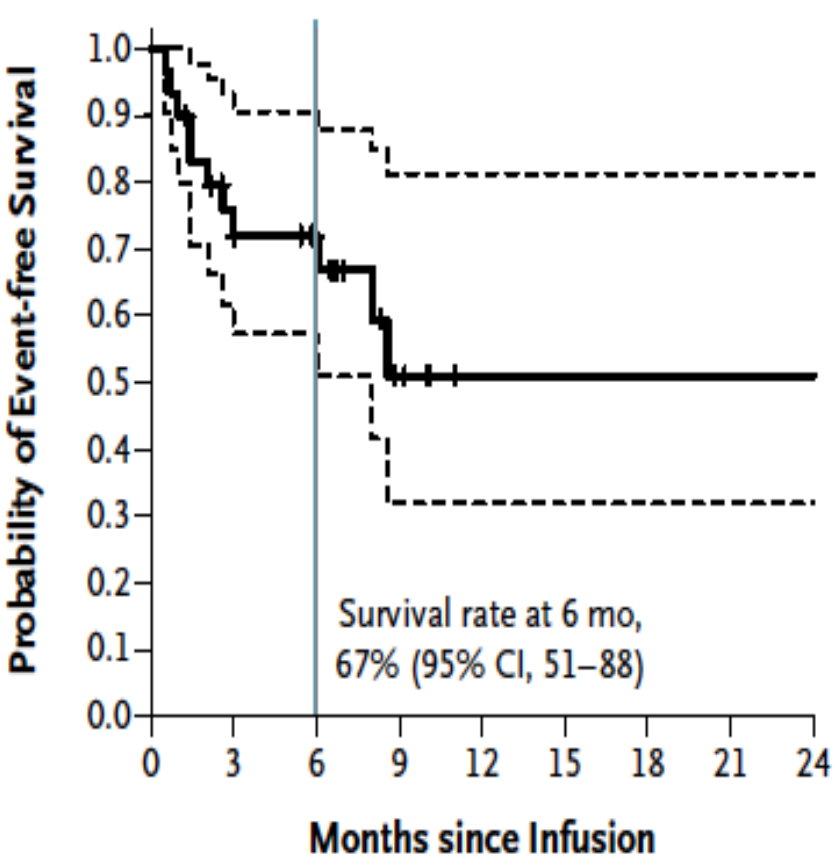
THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

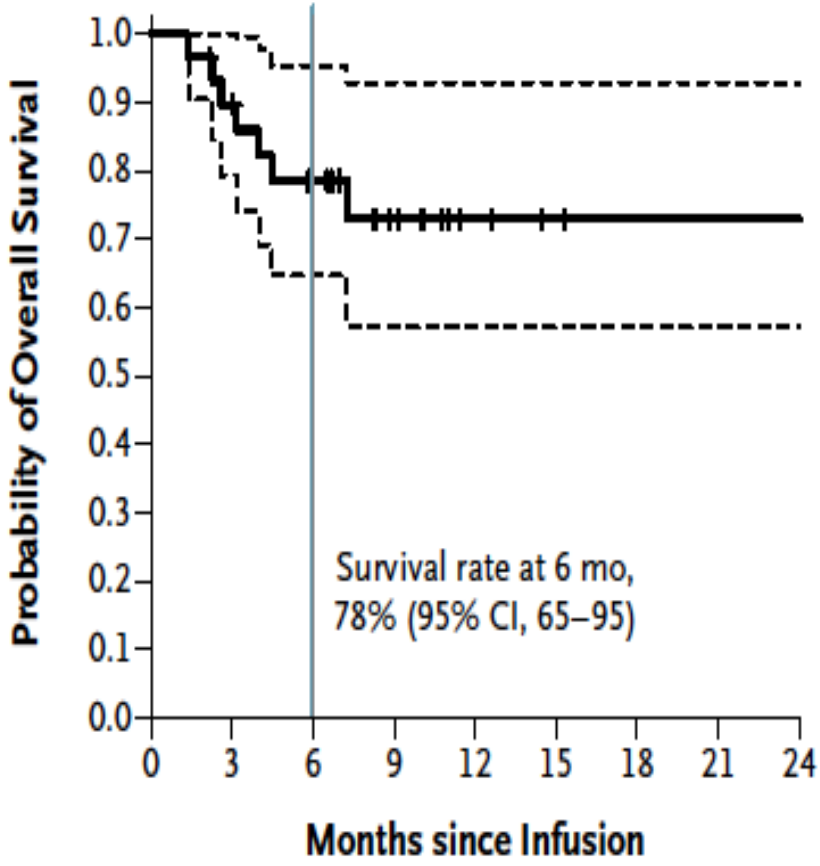
Porter et al, NEJM Aug 2011; Kalos et al, Science Translation Med Aug 2011

Anti-CD19 CAR T Cells for B-cell Acute Lymphoblastic Leukemia

	Number of Patients	Construct	CR (%)	MRD Negativity (%)	Relapse-Free Survival (%)	Follow-Up (months)
Park	24	Retroviral, 19-28z	90[a]	90	N/A[a]	N/A
Grupp	30	Lentiviral, CD19-BB-z	90	73	67	6
Lee	20	Retroviral, FMC63-28z	70	60	79	4.8

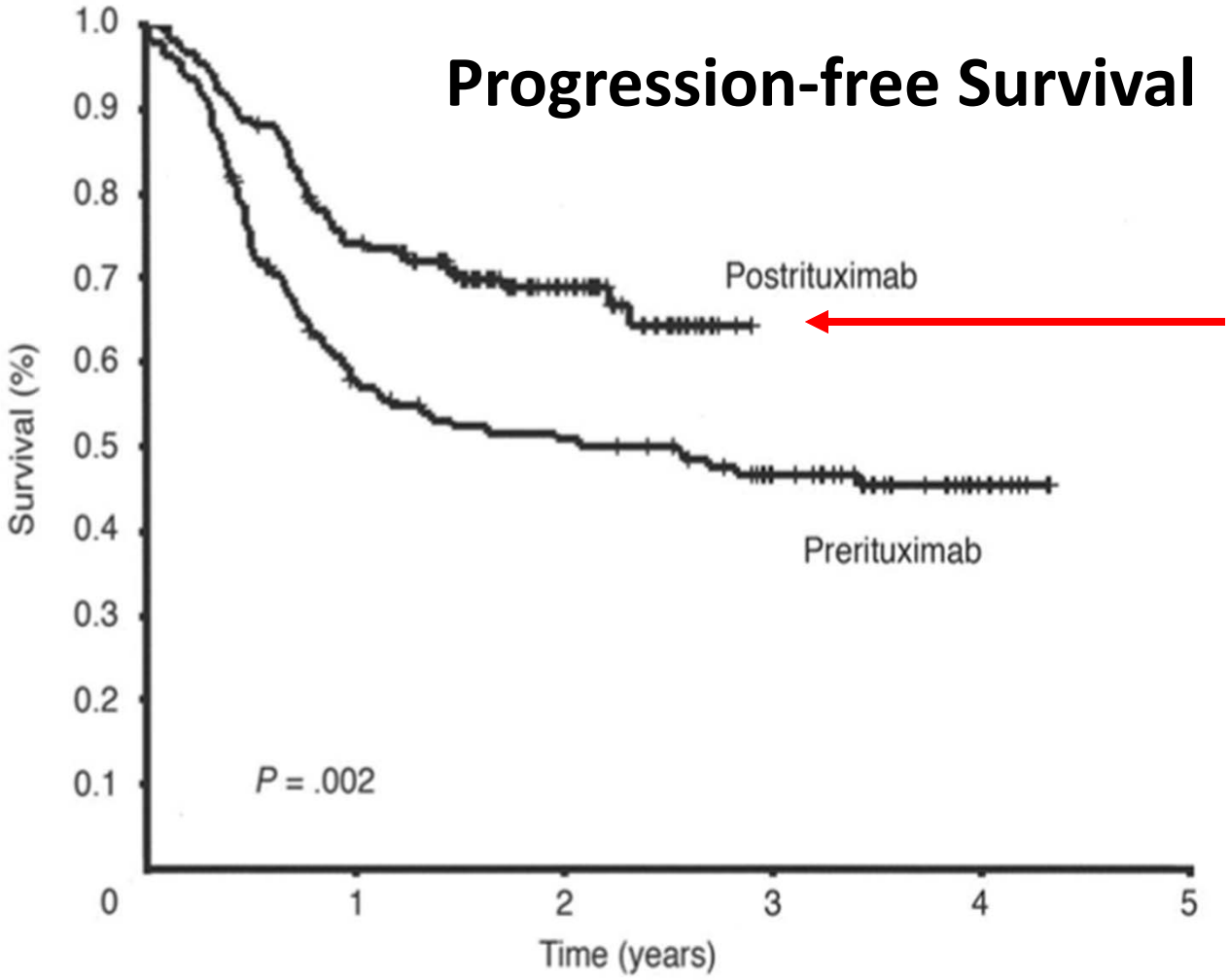
Anti-CD19 CAR T Cells for B-cell Acute Lymphocytic Leukemia





Diffuse Large B-cell Lymphoma

Standard of Care in DLBCL: R-CHOP



67% 3-year PFS

~1/3 of patients suffer relapsed/refractory disease

Auto HSCT is the SOC

Sehn LH, et al. *J Clin Oncol*. 2005;23:5027-33

Collaborative Trial in Relapsed Aggressive Lymphoma (CORAL)

Factor	Total No. of Patients	Response CR/CRu/PR			3-Year Event-Free Survival		3-Year Overall Survival	
		No. of Patients	%	*P*	%	*P*	%	*P*
All patients	398	246	63		31		50	
CR/CRu		148	38		51		70	
Prior rituximab								
No	147	122	83	< .001	47	< .001	66	< .01
Yes	244	124	51		21		40	
Relapse, > 12 months	160	140	88	< .001	45	< .001	64	
Refractory, < 12 months	228	106	46		20		39	< .001
saaIPI								
< 2	224	160	71	< .001	40		62	
> 1	146	76	52		18	< .001	32	< .001

Abbreviations: CR, complete response; CRu, unconfirmed complete response; PR, partial response; saaIPI, secondary age-adjusted International Prognostic Index.

Gisselbrecht C, et al. J Clin Oncol. 2010; 28:4184-90

SCHOLAR-1: Outcomes in Refractory DLBCL

	MDACC (n=152)	MC / IA (n =84)	CCTG LY.12 (n=190)	CORAL (n=171)
Median age[a] (range)	55 (20, 79)	61 (20, 84)	54 (25, 68)	54 (19, 65)
RR (%)	19	23	24	36
CR	7	8	2	18
PR	13	14	23	18
RR by subgroup (%)				
Primary refractory (n=142)	NA	28	24	NA
Refractory to > 2nd line therapy (n=306)	19	26	NA	36
Relapse < 1 year post ASCT (n=149)	21	11	NA	35
Median OS (Q1, Q3) - mos	6.9 (5.8, 8.2)	4.6 (3.9, 5.8)	6.8 (5.8, 8.2)	6.7 (5.6, 8.8)

[a]CORAL included subjects 18 – 65, Ly.12 studies included subjects ≥ 16; subjects > 65 were not recommended for inclusion. NA – due to study design.

- ORR = 24%
- Median OS = ~6 months

Crump M, et al. *Blood*. 2017;130:1800-1808.

CAR T-cell Products in Clinical Trials

	KTE-C19	CTL-019	JCAR015	JCAR017
Company	KITE	Novartis	Juno	Juno
Binding Domain (All Murine ScFv)	FMC63	FMC63	SJ25C1	FMC63
Indications	DLBCL, TFL PMBCL,MCL, ALL, CLL	NHL, ALL, CLL	Adult ALL	Adult NHL, Pediatric ALL,, CLL
Spacer Domain	CD28	CD8α	CD28	IgG4 hinge
Transmembrane Domain	CD28	CD8α	CD28	CD28
Stimulatory Domain	CD28-CD3ζ	4-1BB-CD3ζ	CD28-CD3ζ	4-1BB-CD3ζ
Starting Cell Population Selection	None	None	CD3+ enriched PBMC	CD4+ and CD8+
Final CD4/CD8 ratio	Variable	Variable	Variable	1:1
Ablation Technology	None	None	None	EGFRt
Viral Vector	Gamma retrovirus	Lentivirus	Gamma retrovirus	Lentivirus

Courtesy of William Go

Global Trial of the Efficacy and Safety of CTL019 in Adult Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma: An Interim Analysis of the JULIET Study

Stephen J. Schuster, Michael R. Bishop, Constantine Tam, Edmund K. Waller, Peter Borchmann, Joseph McGuirk, Ulrich Jäger, Samantha Jaglowski, Charalambos Andreadis, Jason Westin, Isabelle Fleury, Veronika Bachanova, Stephen Ronan Foley, P. Joy Ho, Stephan Mielke, Harald Holte, Oezlem Anak, Lida Pacaud, Rakesh Awasthi, Feng Tai, Gilles Salles, Richard T. Maziarz

On behalf of the JULIET study investigators

JULIET: Eligibility and Endpoints

Key Eligibility Criteria

- ≥ 18 years of age
- ≥ 2 prior lines of therapy for DLBCL
- PD after or ineligible for auto-HSCT
- No prior anti-CD19 therapy
- No active CNS involvement

Endpoints

- Primary endpoint: best overall response rate (ORR: CR + PR)
  - Lugano criteria used for response assessment by IRC[1]
  - Null hypothesis of ORR ≤ 20%
- Secondary endpoints: DOR, OS, safety

1. Cheson BD, et al. *J Clin Oncol.* 2014;32(27):3059-3068.

auto-SCT, autologous stem cell transplant; CNS, central nervous system; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; IRC, Independent Review Committee; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial response.

JULIET: Demographics and Baseline Disease Status

	Patients (N = 99)
Age, median (range), years	56 (22-76)
≥ 65 years, %	23
ECOG perf status 0/1	55/45
Central histology review	
Diffuse large B-cell lymphoma, %	80
Transformed follicular lymphoma, %	19
Double/triple hits in *CMYC/BCL2/BCL6* genes, %	15 [a]
Cell of origin[b]	
Germinal center B-cell type, %	52
Nongerminal center B-cell type, %	42
Number of prior lines of antineoplastic therapy, %	
2/3/4-6	44/31/19
Refractory/relapsed to last therapy, %	52/48
Prior auto-SCT, %	47

- **Bridging chemotherapy: 89/99**
- **Lymphodepleting chemotherapy: 92/99**

THE UNIVERSITY OF CHICAGO MEDICINE

[a] *CMYC* + *BCL2*, n = 4; *CMYC* + *BCL2* + *BCL6*, n = 8; *CMYC* + *BCL6*, n = 3.
[b] Determined by the Choi algorithm.

auto-SCT, autologous stem cell transplant;
ECOG, Eastern Cooperative Oncology Group.

JULIET: Adverse Events of Special Interest

	N = 99		
AESI[a]	**All Grades, %**	**Grade 3, %**	**Grade 4, %**
Cytokine release syndrome[b]	58	15	8
Neurological events	21	8	4
Prolonged cytopenia[c]	36	15	12
Infections	34	18	2
Febrile neutropenia	13	11	2

[a] Occurring within 8 weeks of tisagenlecleucel infusion. [b] Cytokine release syndrome was graded using the Penn scale. [c] At day 28.

- **No deaths due to tisagenlecleucel, CRS or cerebral edema**
- **26 patients (26%) were infused as outpatients**
- **20/26 patients (77%) remained outpatient for ≥ 3 days after infusion**

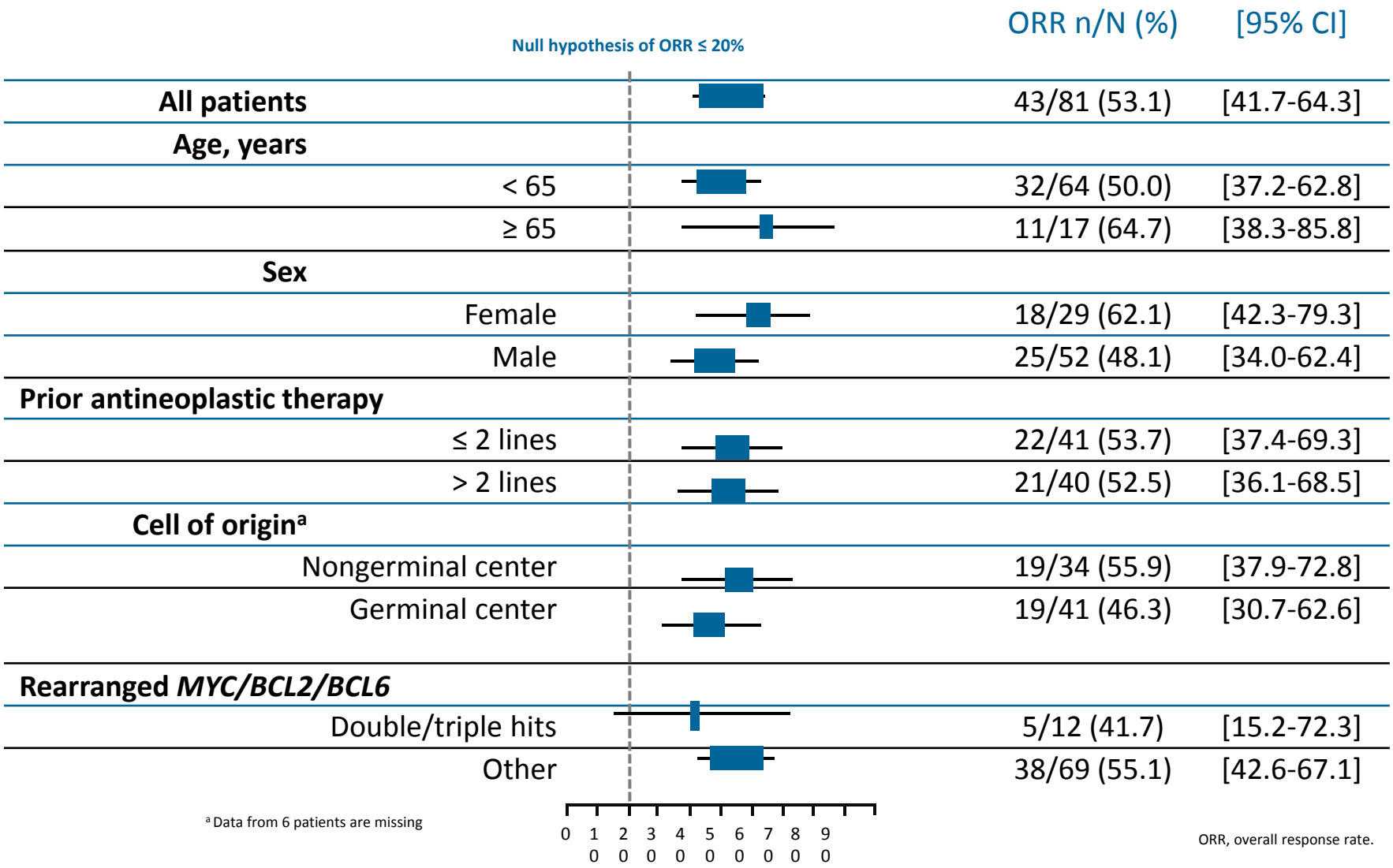
JULIET: Primary Endpoint Met: ORR 53%

Response Rate, %	Best Overall Response Rate (N = 81)	Response at 3 Months (N = 81)	Response at 6 Months (n = 46)
ORR (CR + PR)	53	38	37
CR	40	32	30
PR	14	6	7

[a] *P* < .0001; (95% CI, 42%-64%). Null hypothesis of ORR ≤ 20%.

- Durability of responses shown by stability between 3 and 6 month response rates
- Response at 3 months is indicative of long term benefit

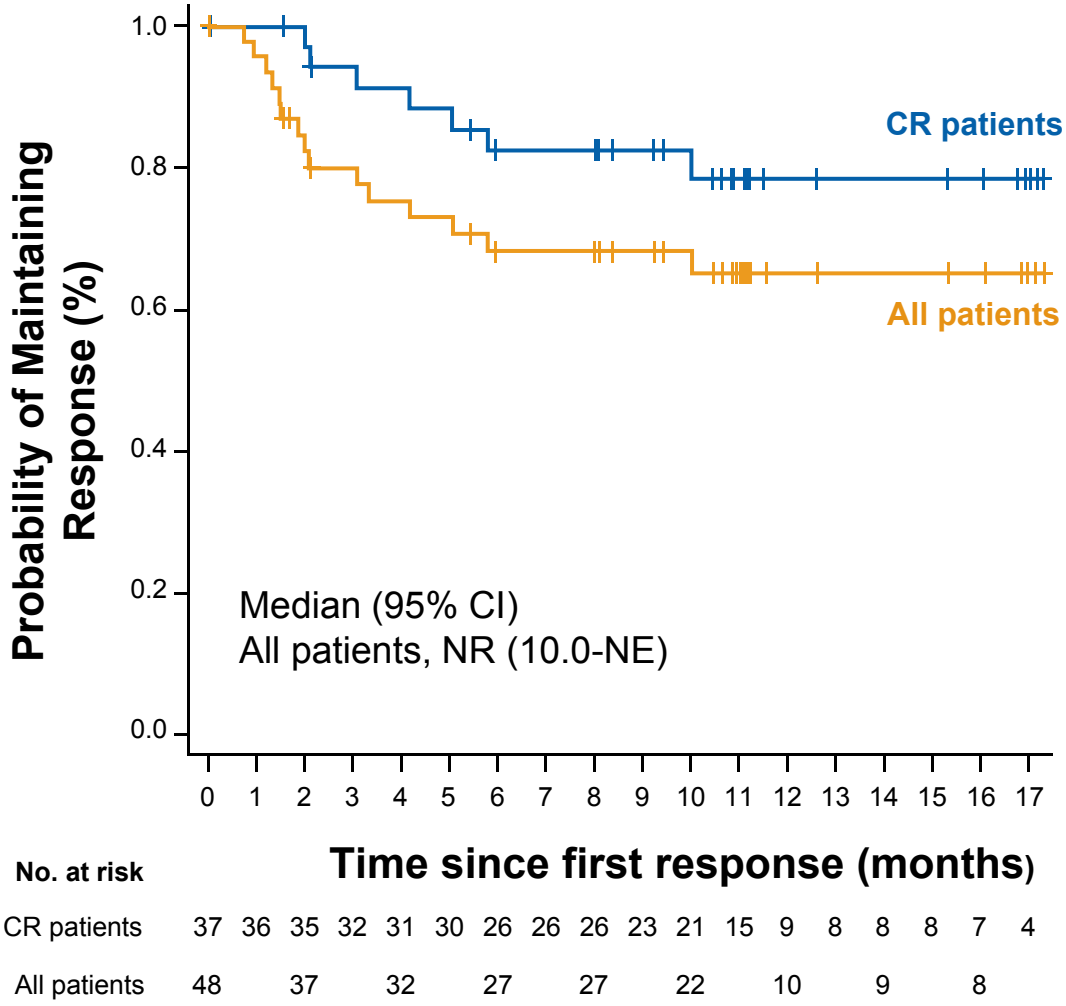
JULIET: ORR Consistent Across Subgroups



[a] Data from 6 patients are missing

ORR, overall response rate.

JULIET: Global Trial of CTL019 in Patients with Relapsed/Refractory DLBCL



- Median F/U = 14 mos
- ORR = 52%; CR = 40%
- Median DOR not reached
- 12-mo relapse-free survival rate:
  - 78.5% among CR patients
  - 65% among all responders
- No patient proceeded to transplant while in response

THE UNIVERSITY OF CHICAGO MEDICINE

EHA 2018

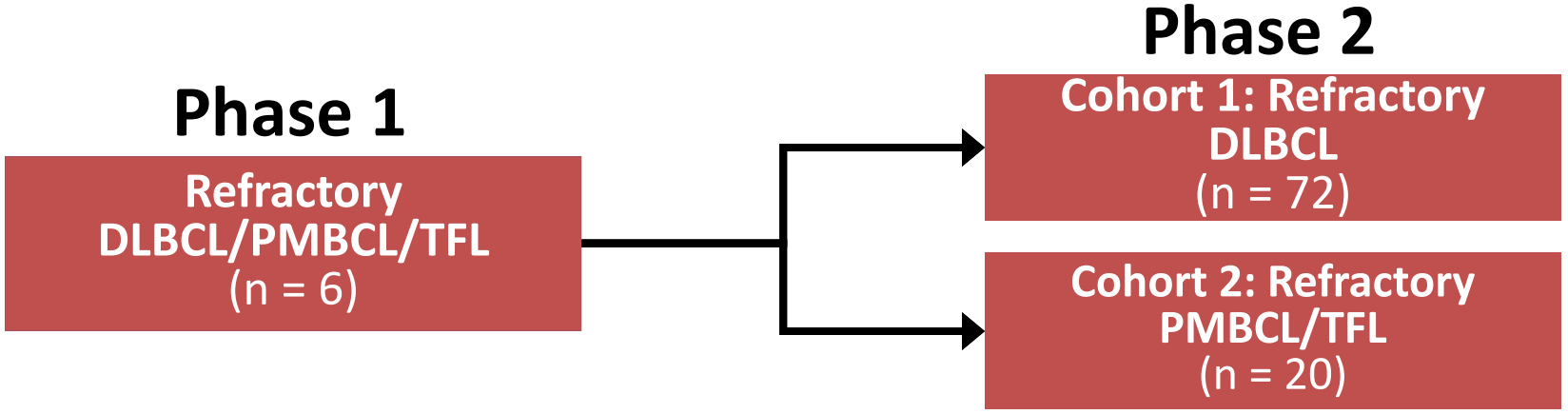
From Borchmann P, et al. In: Proceedings from the European Hematology Association; June 14-17, 2018; Stockholm, Sweden [abstract S799]. Reprinted with author's permission.

Axicabtagene Ciloleucel (axi-cel; KTE-C19) in Patients With Refractory Aggressive Non-Hodgkin Lymphoma (NHL): Primary Results of the Pivotal Trial ZUMA-1

Sattva S. Neelapu,[1*] Frederick L. Locke,[2*] Nancy L. Bartlett,[3] Lazaros J. Lekakis,[4] David Miklos,[5] Caron A. Jacobson,[6] Ira Braunschweig,[7] Olalekan Oluwole,[8] Tanya Siddiqi,[9] Yi Lin,[10] John Timmerman,[11] Patrick Reagan,[12] Lynn Navale,[13] Yizhou Jiang,[13] Jeff Aycock,[13] Meg Elias,[13] Jeff Wiezorek,[13] William Y. Go[13]

THE UNIVERSITY OF CHICAGO MEDICINE

ZUMA-1: Multicenter Trial of Axi-cel in Refractory Aggressive NHL



Eligibility criteria

- Aggressive NHL: DLBCL, PMBCL, TFL
- Chemotherapy-refractory disease: no response to last chemotherapy or relapse ≤12 months post-ASCT
- Prior anti-CD20 mAb and anthracycline
- ECOG PS 0-1

Primary end point

- Phase 2: Objective response rate (ORR) tested in the first 92 patients dosed[a]

Key secondary end points

- DOR, OS, safety, levels of CAR T and cytokines

Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA 1: Patient Characteristics

Characteristic	DLBCL (n = 77)	PMBCL/TFL (n = 24)	All Patients (N = 101)
Median (range) age, y	58 (25–76)	57 (23–76)	58 (23–76)
≥65 y, n (%)	17 (22)	7 (29)	24 (24)
Men, n (%)	50 (65)	18 (75)	68 (67)
ECOG PS 1, n (%)	49 (64)	10 (42)	59 (58)
Disease stage III/IV, n (%)	67 (87)	19 (79)	86 (85)
IPI score 3-4, n (%)	37 (48)	11 (46)	47 (47)
≥3 prior therapies, n (%)	49 (64)	21 (88)	70 (69)
History of primary refractory disease, n (%)	23 (30)	3 (13)	26 (26)
History of refractory to 2 consecutive lines, n (%)	39 (51)	15 (63)	54 (54)
Response to last chemotherapy regimen, n (%)			
Stable Disease	10 (13)	4 (17)	14 (14)
Progressive Disease	51 (66)	15 (63)	66 (65)
Refractory Subgroup Before Enrollment	**DLBCL (n = 77)**	**PMBCL/TFL (n = 24)**	**All Patients (N = 101)**
Refractory to second- or later-line therapy, n (%)	59 (77)	19 (79)	78 (77)
Relapse post-ASCT, n (%)	16 (21)	5 (21)	21 (21)

Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

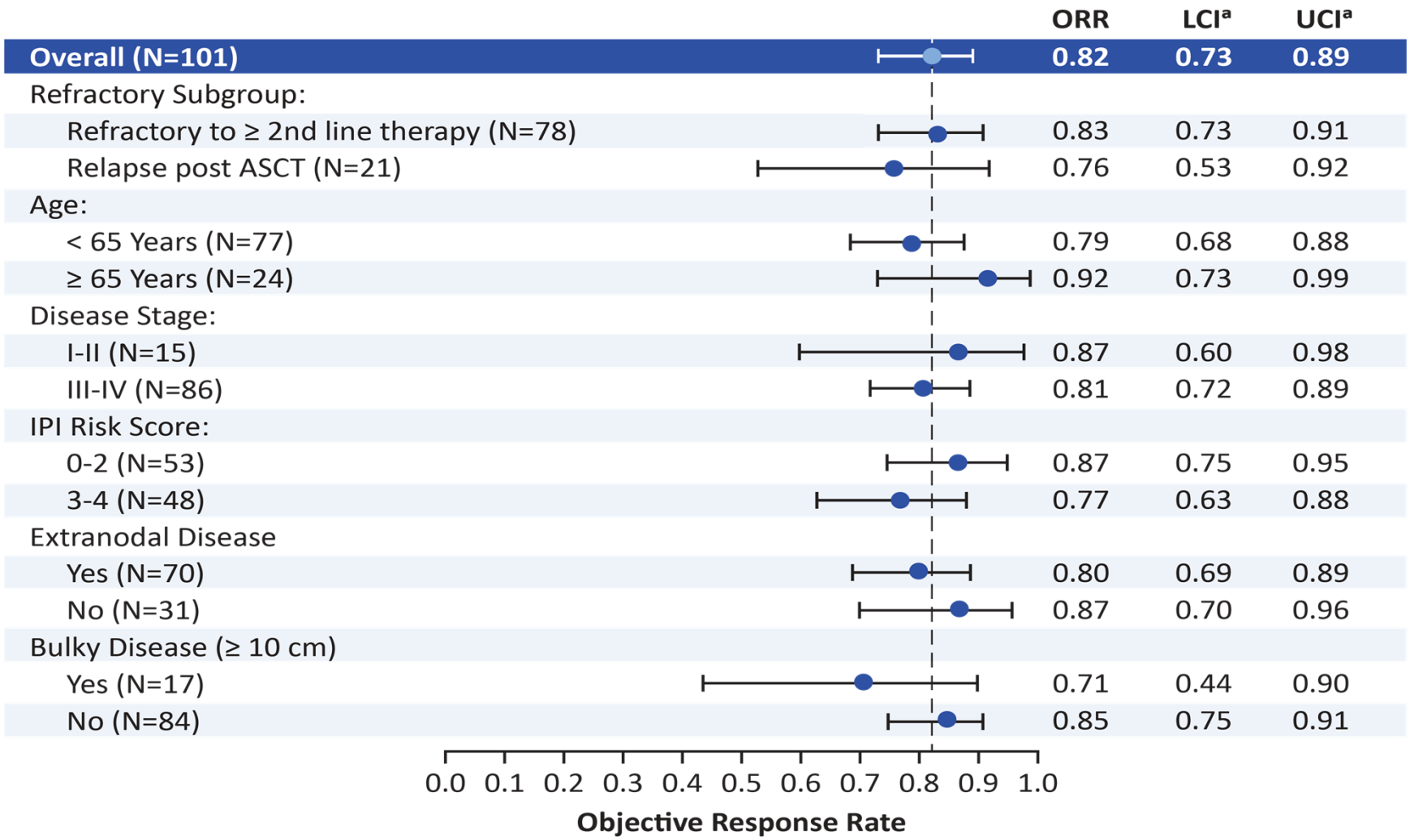
ZUMA-1: Met Primary Endpoint of ORR ($P < 0.0001$)[a] in Combined Group

Best Response	ZUMA-1 Phase 2					
	DLBCL		TFL/PMBCL		Combined	
	ORR (%)	CR (%)	ORR (%)	CR (%)	ORR (%)	CR (%)
mITT[b]	n = 77		n = 24		n = 101	
	82	49	83	71	82	54

[a] Inferential testing when 92 axi-cel–dosed patients had 6 mo of follow-up. ORR 82%, $P<0.0001$. [b] mITT (modified intention-to-treat) set of all patients dosed with axi-cel.

Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA-1: Responses Were Consistent Across Key Covariates



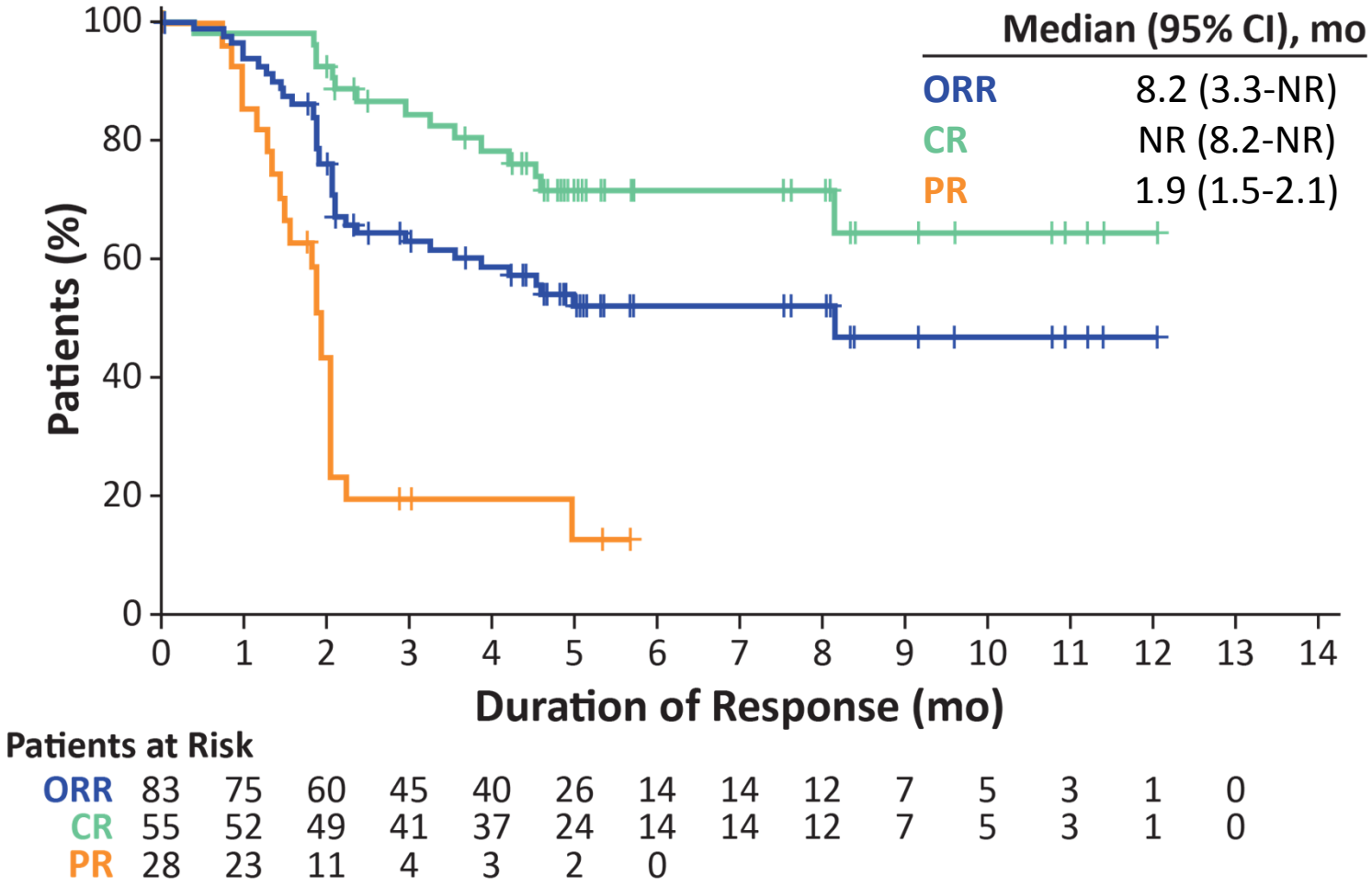
Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA-1: Responses Were Durable: 44% Ongoing At 8.7 Months of Follow Up

	ZUMA-1 Phase 2 (mITT population[a])					
	DLBCL (n = 77)		TFL/PMBCL (n = 24)		Combined (N = 101)	
	ORR (%)	CR (%)	ORR (%)	CR (%)	ORR (%)	CR (%)
Month 6	36	31	54	50	41	36
Ongoing	36	31	67	63	44	39

Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

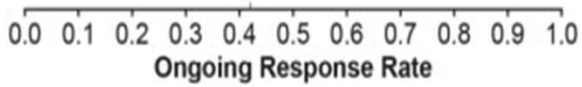
ZUMA-1: Duration of Responses At a Median Follow-Up of 8.7 Months



Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA-1: Consistent Ongoing Responses (> 1 year) Across Key Covariates

		n[a]	ORR	LCI[b]	UCI[b]
Overall (N=108)		45	0.42	0.32	0.52
Refractory Subgroup	Refractory to ≥ 2nd line therapy (N=80)	31	0.39	0.28	0.50
	Relapse post ASCT (N=25)	14	0.56	0.35	0.76
Age	< 65 Years (N=81)	32	0.40	0.29	0.51
	≥ 65 Years (N=27)	13	0.48	0.29	0.68
Disease Stage	I-II (N=18)	11	0.61	0.36	0.83
	III-IV (N=90)	34	0.38	0.28	0.49
IPI Risk Score	0-2 (N=60)	30	0.50	0.37	0.63
	3-4 (N=48)	15	0.31	0.19	0.46
Treatment History	Primary Refractory Disease (N=27)	11	0.41	0.22	0.61
	Refractory to 2 Consecutive Lines (N=55)	19	0.35	0.22	0.49
CD19 Status	Positive (N=77)	33	0.43	0.32	0.55
	Negative (N=10)	5	0.50	0.19	0.81
Cell of Origin	Germinal Center B Cell-like (GCB) (N=52)	23	0.44	0.30	0.59
	Activated B-Cell like (ABC) (N=18)	6	0.33	0.13	0.59
CD4/CD8 Ratio	>1 (N=51)	21	0.41	0.28	0.56
	≤1 (N=57)	24	0.42	0.29	0.56
Tocilizumab Use	Yes (N=49)	17	0.35	0.22	0.50
	No (N=59)	28	0.47	0.34	0.61
Corticosteroid Use	Yes (N=30)	10	0.33	0.17	0.53
	No (N=78)	35	0.45	0.34	0.57



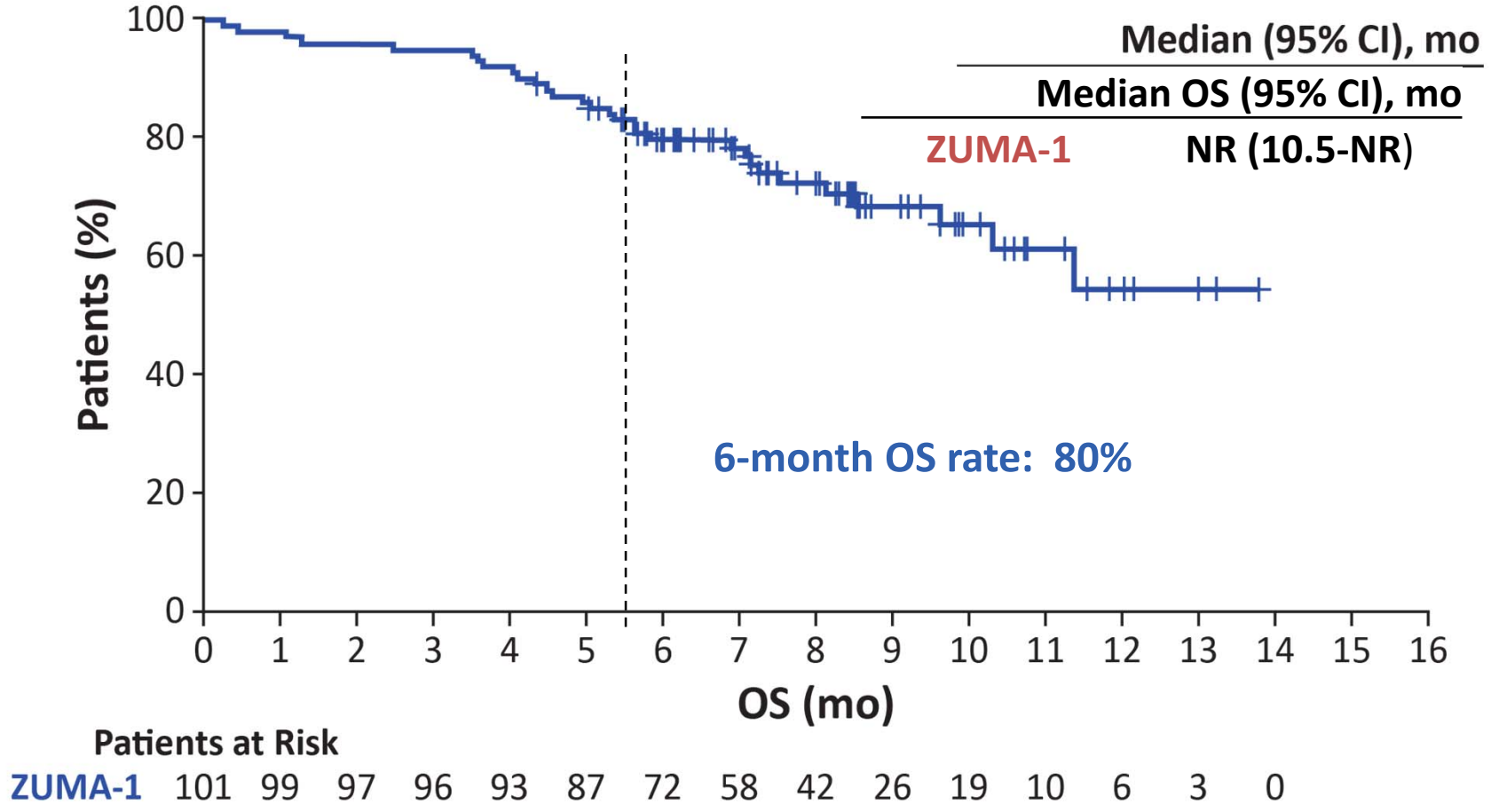
- Median follow-up: 15.4 mo

[a]Indicates the number of evaluable patients. [b]The 95% lower confidence interval (LCI) and upper confidence interval (UCI) of the ongoing response rate were calculated using the Clopper-Pearson method. ASCT, autologous stem cell transplant; IPI, International Prognostic Index.

THE UNIVERSITY OF CHICAGO MEDICINE

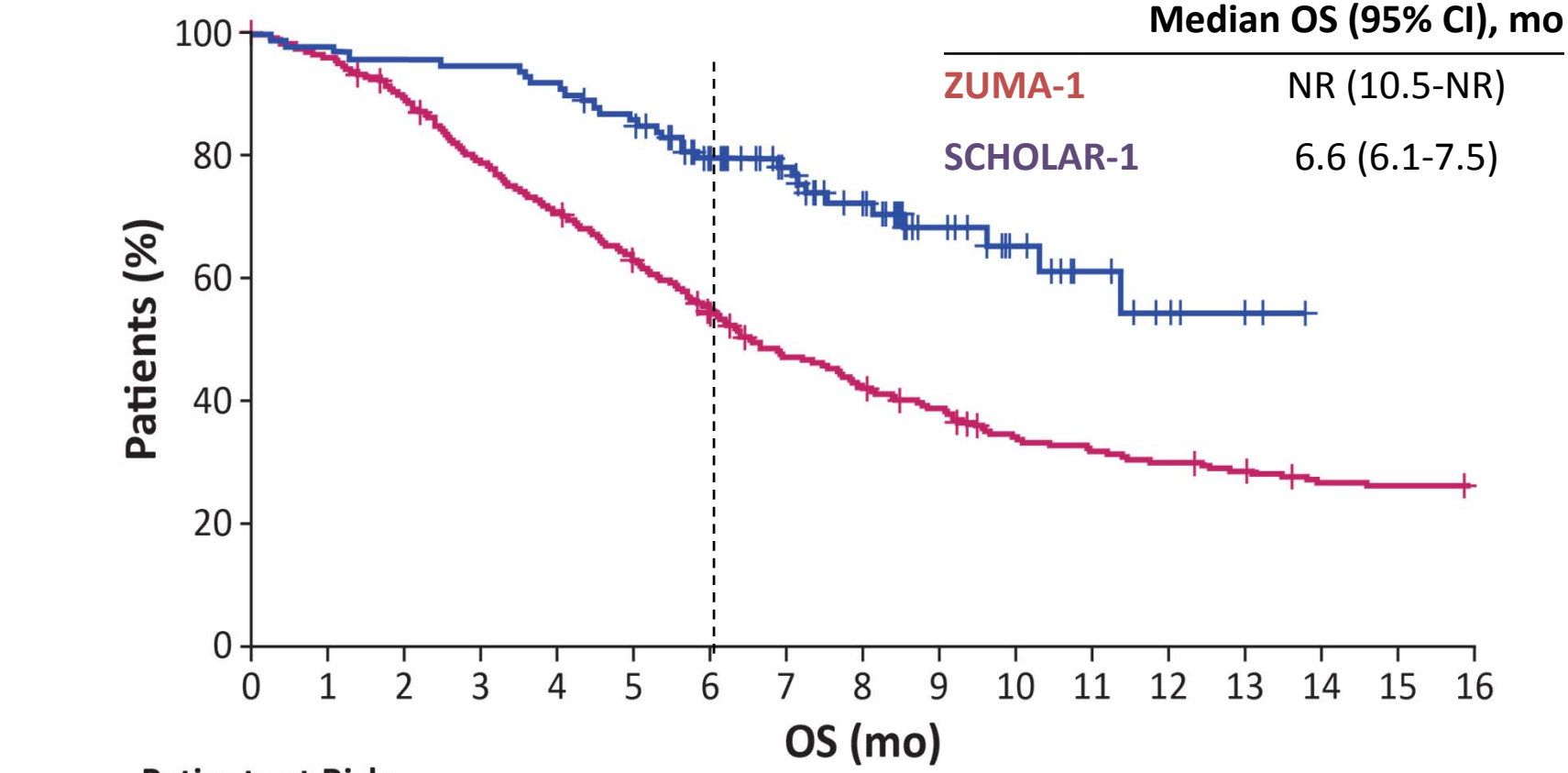
Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA-1: Median OS Not Reached At a Median Follow-Up of 8.7 Months



Neelapu SS, et al. N Engl J Med 2017; 377:2531-2544.

ZUMA-1 vs SCHOLAR-1: 6-month OS



Patients at Risk

ZUMA-1	101	99	97	96	93	87	72	58	42	26	19	10	6	3	0		
SCHOLAR-1	635	594	555	487	436	392	337	286	259	233	202	191	177	167	156	151	151

CAR T Cell Trials in Relapsed/Refractory DLBCL

Company		Juno		Novartis		Gilead	
Product		JCAR017		KYMRIAH Tisagenlecleucel		YESCARTA Axicabtagene ciloleucel	
US Status		P1-2		Approved		Approved	
Trial		Transcend		Juliet		ZUMA-1	
Efficacy	Follow-Up	3 Mon	6 Mon	3 Mon	6 Mon	3 Mon	6 Mon
	Patients	N=19	N=14	N=81		N=101	
	Objective Response Rate (ORR)	74%	50%	38%	37%	54%	41%
	Complete Response (CR)	68%	50%	32%	30%	36%	36%
Safety	Patients	N=67		N=81		N=101	
	Cytokine Release Syndrome (CRS)	1% Severe 40% Any		23% Severe 58% Any		13% Severe 94% Any	
	Neurotoxicity	15% Severe 21% Any		12% Severe 58% Any		31% Severe 84% Any	

Multiple Myeloma

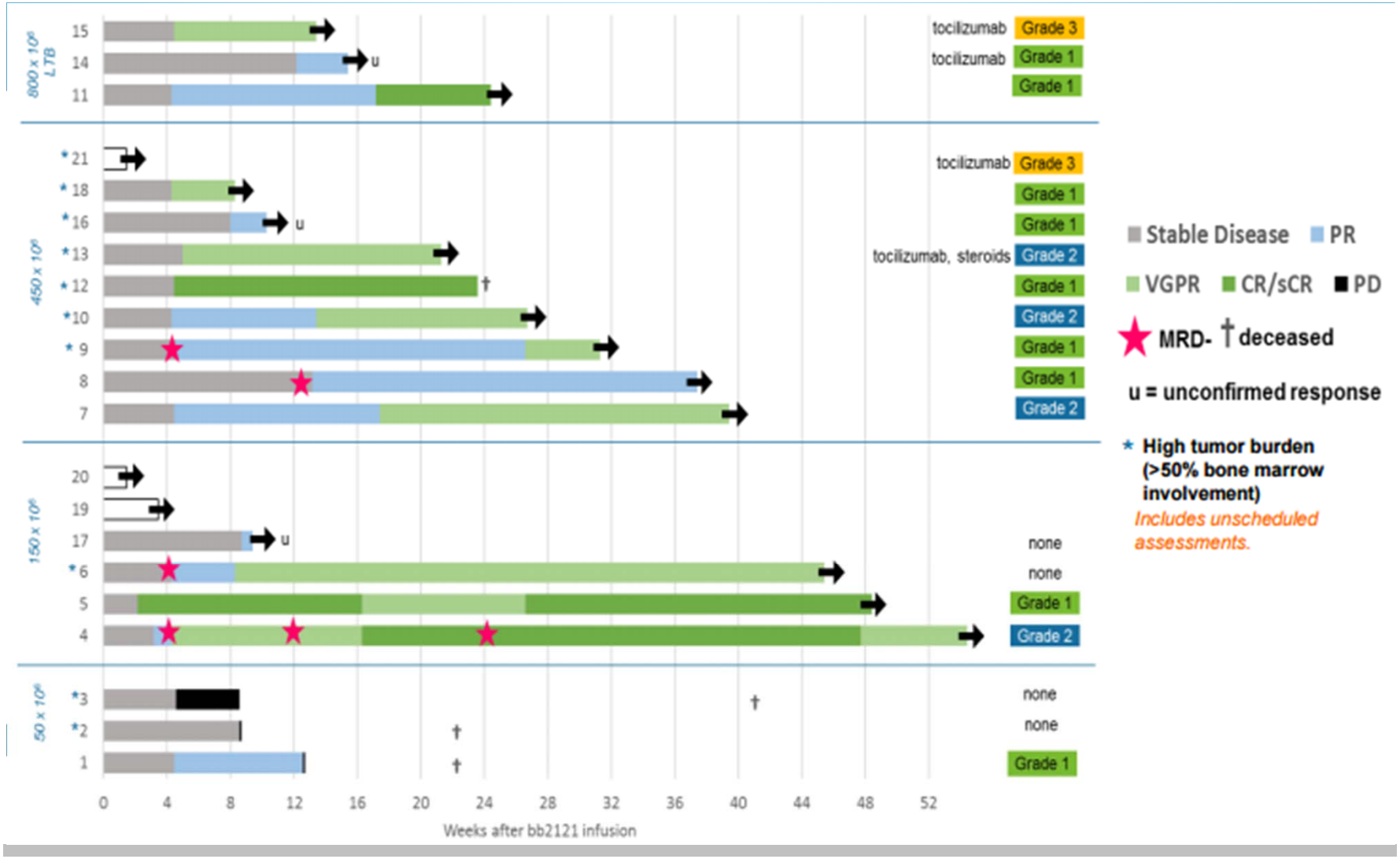
B-cell Maturation Antigen in Multiple Myeloma

Background

- B-cell maturation antigen (BCMA): protein in TNF superfamily that binds B-cell activating factor (BAFF) and a proliferation inducing ligand (APRIL)
- BCMA is expressed by B cells and normal and malignant plasma cells [1]
- BCMA is expressed uniformly on malignant plasma cells in >60-70% of patients with MM and is also present in serum

1. Carpenter RO, et al. Clin Cancer Res. 2013; 19:2048-2060

CRB-401: Phase 1 Trial of bb2121 (Anti-BCMA CAR T Cells) in Relapsed Refractory Myeloma



THE UNIVERSITY OF CHICAGO MEDICINE

Berdeja JG et al. J Clin Oncol 35(suppl 15): 3010

www.bluebirdbio.com

CRB-401: Phase 1 Trial of bb2121 (Anti-BCMA CAR T Cells) in Relapsed Refractory Myeloma Update

Toxicity:

Treatment-Emergent AE, n (%)	All Patients (N = 43)	
	Any Grade	Grade ≥ 3
CRS	27 (63)	2 (5)
Neurotoxicity	14 (33)	1 (2)
Neutropenia	35 (81)	34 (79)
Thrombocytopenia	26 (61)	22 (51)
Anemia	24 (56)	19 (44)
Infection	26 (61)	9 (21)
▪First month	10 (23)	2 (5)

Raje NS, et al. ASCO 2018. Abstract 8007.

CRB-401: Phase 1 Trial of bb2121 (Anti-BCMA CAR T Cells) in Relapsed Refractory Myeloma Update

Efficacy:

Response, %	Dose of CAR T-Cells			BCMA Expression*	
	50×10^6 (n = 3)	150×10^6 (n = 14)	$> 150 \times 10^6$ (n = 22)	< 50% (n = 8)	≥ 50% (n = 11)
ORR	33.3	57.1	95.5	100	91
▪ sCR/CR	0	42.9	50.0	37.5	54.5
▪ VGPR	0	7.1	36.4	50.0	27.3
▪ PR	33.3	7.1	9.1	12.5	9.1
Median DoR, mos	1.9	NE	10.8	--	--
Median follow-up, days range)	84 (59-94)	87 (36-638)	194 (46-556)	168 (121-184)	311 (46-556)

Raje NS, et al. ASCO 2018. Abstract 8007.

Solid Tumors

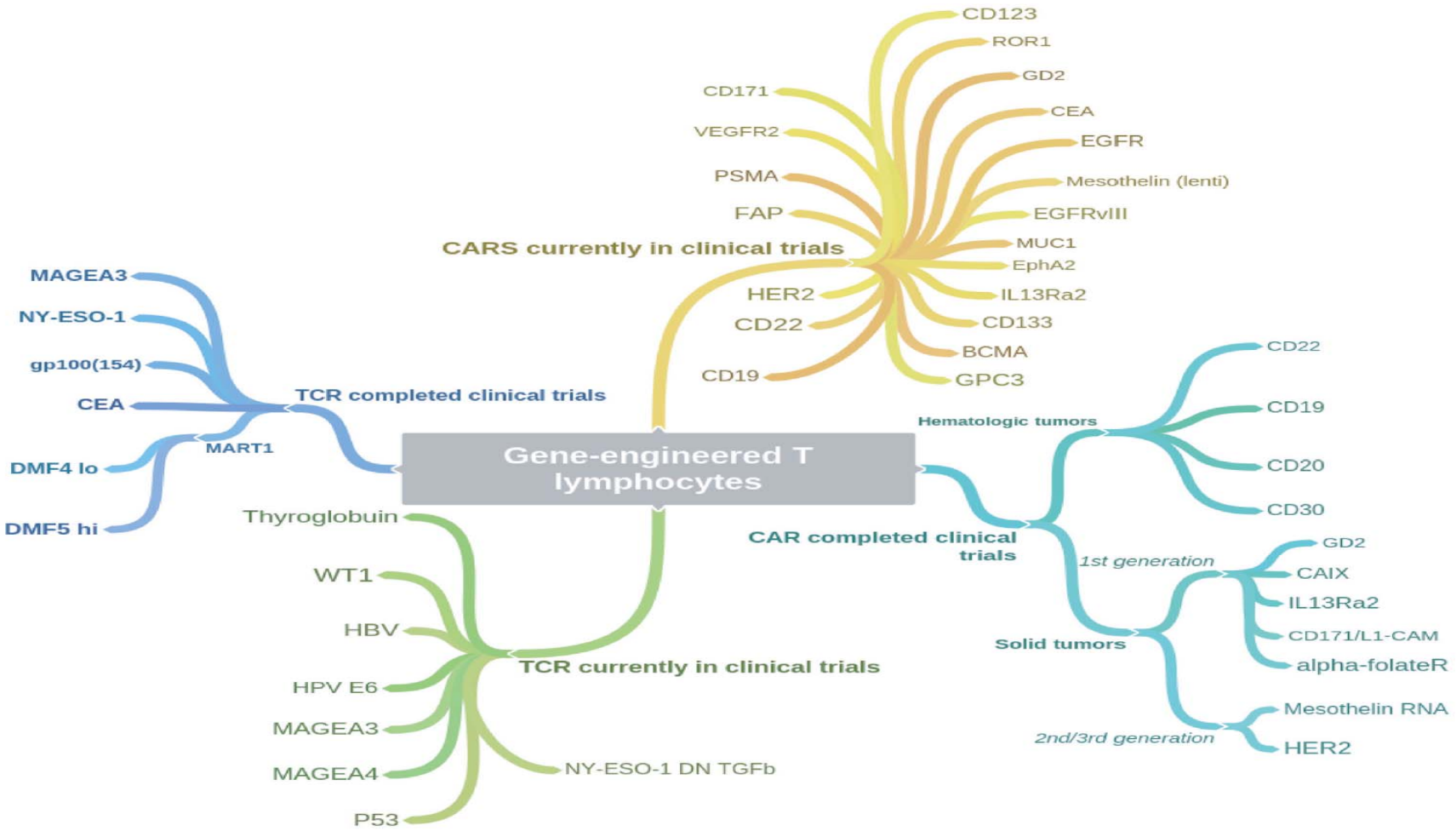
Completed CAR T Cell Trials in Solid Tumors

Target (CAR generation #)	Tumor histology	Patient number	Response rate	Toxicity	Potential mechanism of toxicity
Alpha folate receptor (1) [34]	Ovarian cancer	14	0%	None	N/A
CD171/L1-CAM (1) [36]	Neuroblastoma	6	0%	None	N/A
CAIX (1) [35]	Renal cell carcinoma	3	0%	Biliary toxicity	On-target, off-tumor toxicity in bile duct
GD2 (1) [37, 38]	Neuroblastoma	11	27%	None	N/A
IL13Rα2 (zetakine) (1) [81]	Glioblastoma multiforme	3	0%	None	N/A
Mesothelin (2) [80]	Mesothelioma/Pancreatic cancer	1/1	0%	None	N/A
HER2/ERBB2 (2) [79]	Sarcoma	19	0%	None	N/A
HER2/ERBB2 (3) [49]	Metastatic melanoma	1	N/A	Fatality	On-target, off-tumor toxicity in lung and other normal tissues

N/A, not applicable or not available

Johnson and June. Cell Res 2017

Ongoing and Completed CAR and TCR T Cell Trials in Solid Tumors



Johnson and June. Cell Res 2017

Are Chimeric Antigen Receptor T cells Worth the Cost?

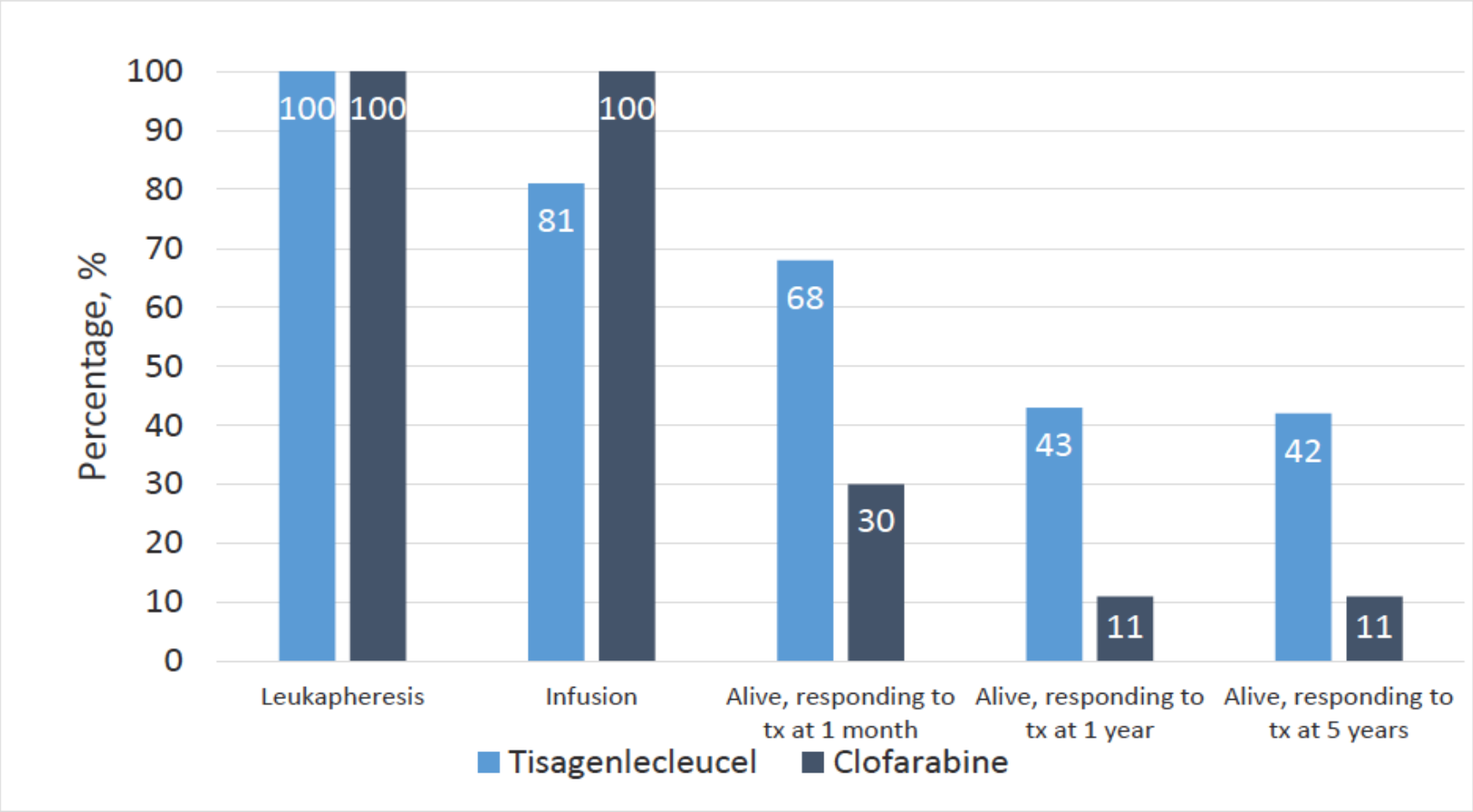
The comparative clinical effectiveness of CAR-T therapies with other salvage therapies for ALL or DLBCL has been challenged because:

• All of the clinical studies are small, single-arm designs with limited follow-up and incomplete reporting

•No trial had control groups. As such, it was not possible to estimate the comparative benefits (or harms) of these novel therapies in relation to prior therapies with FDA indications for the same patient populations using either direct or indirect comparisons.

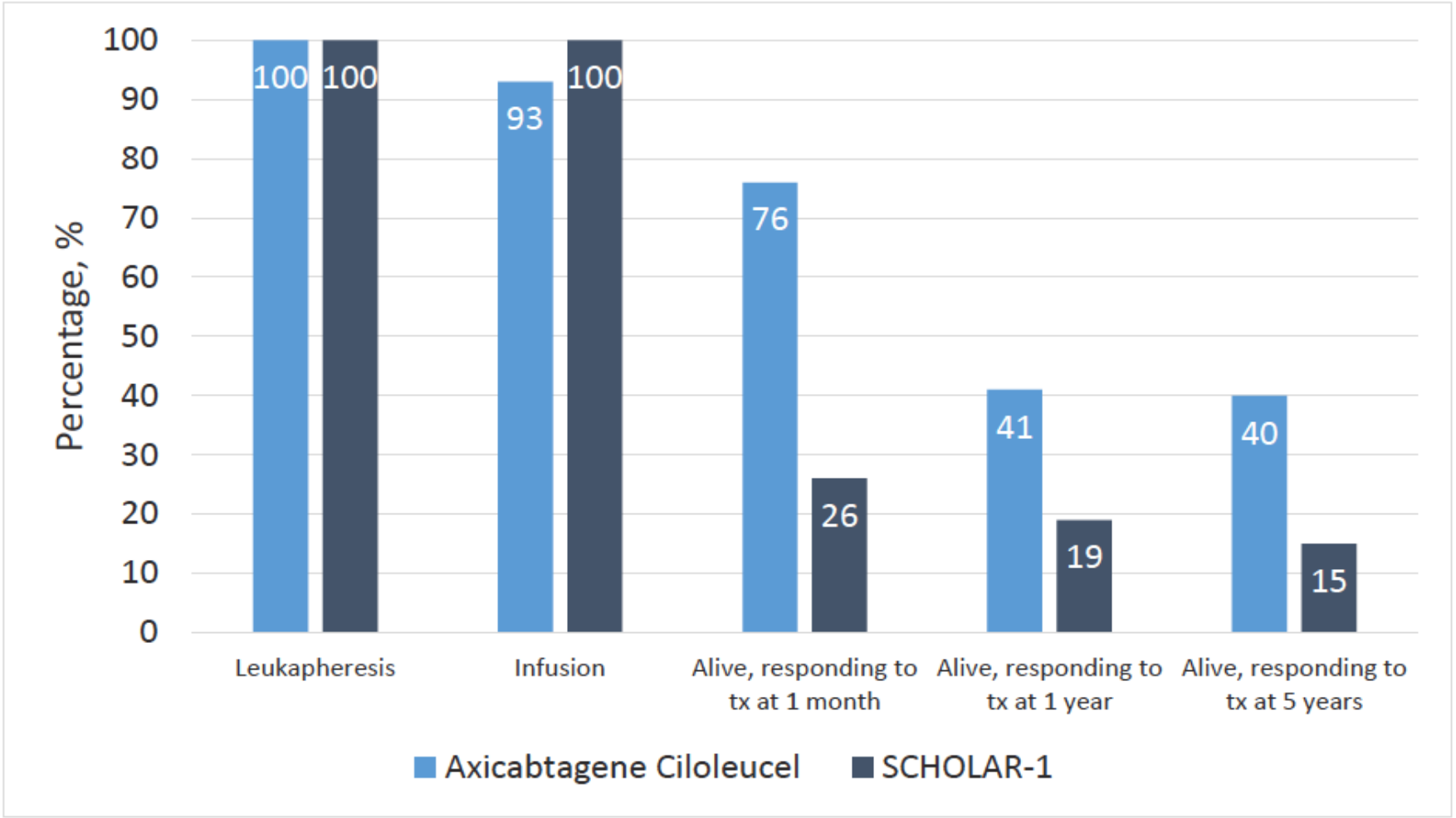
CAR T Cell Therapy in B-cell ALL in Children and Young Adults

Figure ES1. Comparison of Estimated Outcomes for Tisagenlecleucel and Clofarabine*



CAR T Cell Therapy in Relapsed/Refractory DLBCL

Figure ES2. Comparison of Estimated Outcomes for Axicabtagene Ciloleucel and SCHOLAR-1*



THE UNIVERSITY OF CHICAGO MEDICINE

Institute for Clinical and Economic Review
February 2017

Base-case Lifetime Costs and Outcomes

	B-ALL		B-cell Lymphoma	
	Tisagenlecleucel	Clofarabine	Axicabtagene Ciloleucel	Chemotherapy
Total Cost	$666,754	$337,256	$616,927	$154,884
Life Years	10.34	2.43	7.35	3.23
QALYs	9.28	2.10	5.87	2.48

B-ALL: B-cell acute lymphoblastic leukemia, QALYs: quality-adjusted life year

Threshold Analysis Results

	Price	Net Price (with Mark-Up)	Price* to Achieve $50,000 per QALY	Price* to Achieve $100,000 per QALY	Price* to Achieve $150,000 per QALY
Tisagenlecleucel (B-ALL)	$475,000	$575,000	$636,894	$1,162,563	$1,688,232
Axicabtagene Ciloleucel (B-cell Lymphoma)	$373,000	$473,000	$157,578	$340,797	$524,015

Payment assumed for tisagenlecleucel was payment for responders at one month. Payment assumed for axicabtagene ciloleucel was payment at infusion.

*Price needed to achieve the thresholds includes both the acquisition cost and associated mark-up.

QALY: quality-adjusted life year, WAC: wholesale acquisition cost

Are Chimeric Antigen Receptor T cells Worth the Cost?

- In terms of efficacy, it may depend upon the disease
- In terms of cost-effectiveness, possibly
- In terms of value, “no” although this depends upon to whom it is valuable
- Will cost change?
- Who is going to pay?

CAR T-Cell Therapy: A Cure for Cancer?

Summary:

- **CAR T cells induce higher rates of durable complete remissions and prolonged survival compared to historical controls**
- **CAR-T therapy represents an option for B-ALL and B-cell NHL patients who are transplant-ineligible or have relapsed after transplant**
- **In terms of value, it depends upon to whom it is valuable**
- **The indications continue to increase**
- **Are CAR T cells a cure for cancer?**