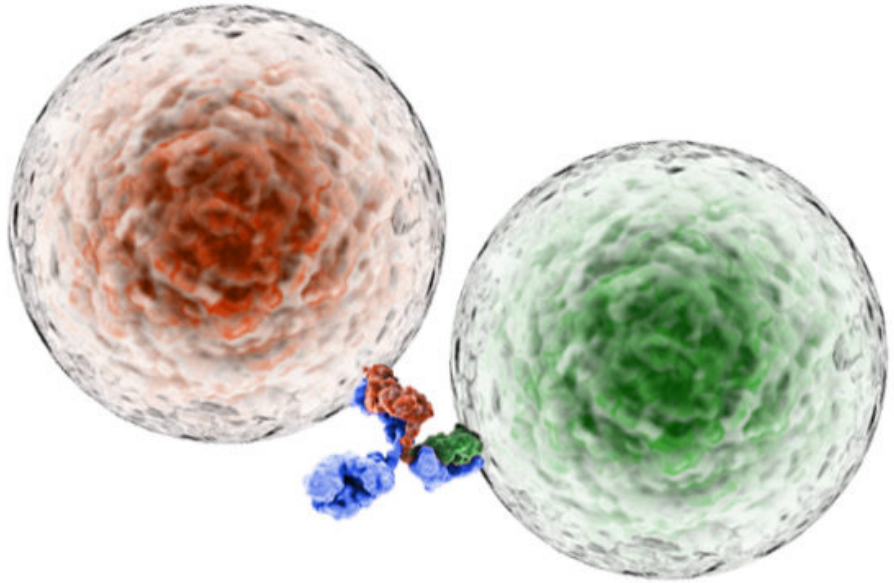


Malignant Hematology and Use of Bispecific Antibodies in Puerto Rico

Alexis M. Cruz Chacón, MD FACP

Director of Bone Marrow Transplantation Program, Hospital Auxilio Mutuo

Hematology and Oncology Fellowship Program Director, San Juan City Hospital

Co-Principal Investigator - Malignant Hematology, Puerto Rico NCORP

Adjunct Assistant Professor of Medicine, UPR Medical Sciences Campus

Medical Oncologist, Division of Cancer Medicine, UPR Comprehensive Cancer Center

Agenda

Introduction

Immunotherapy Basics

Bispecific antibodies (BiAbs)

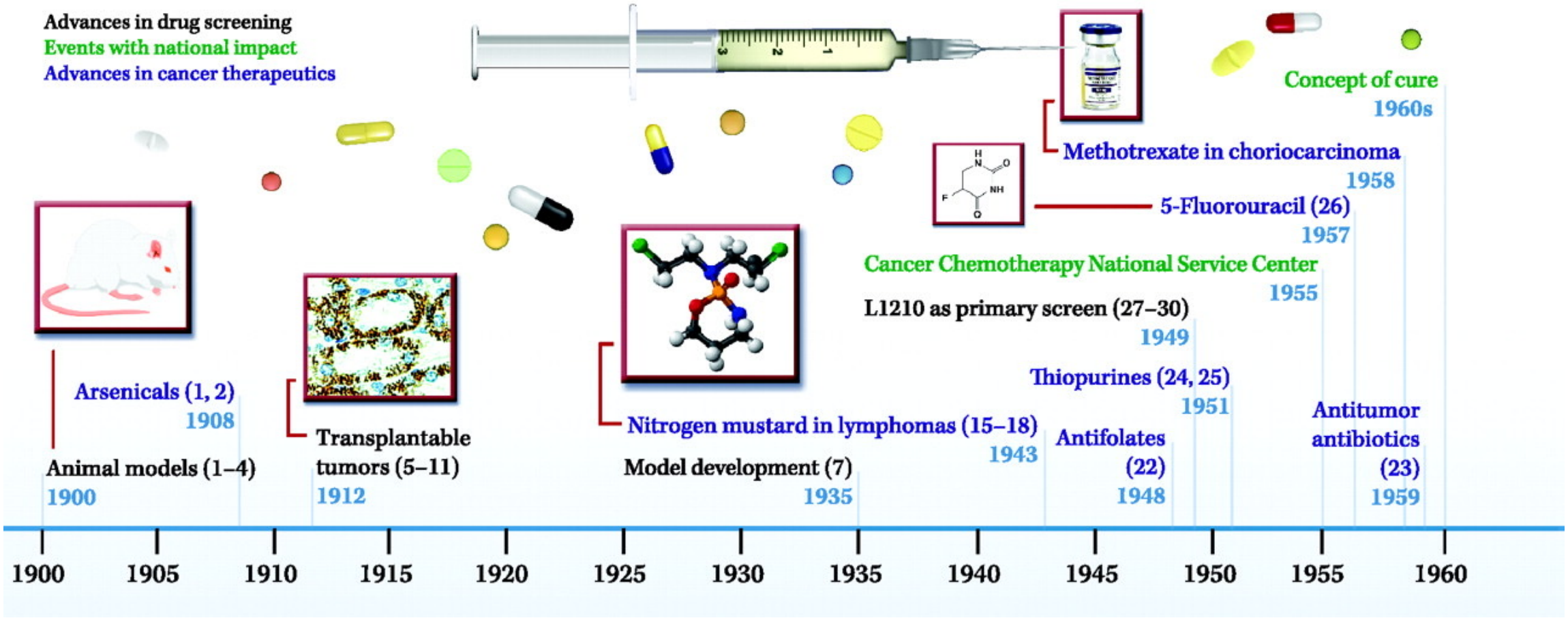
FDA approved BiAbs with indications

BiAbs Adverse Events

Traditional Chemotherapy

- Standard treatment for cancer during the last several decades has been IV chemotherapy
  - Targets rapidly dividing cells, malignant and normal
  - Many successes
  - Serious toxicity and adverse effects

- **Decreasing number of new chemotherapy agents being tested and approved**


Advances in drug screening
Events with national impact
Advances in cancer therapeutics
Concept of cure
1960s
Methotrexate in choriocarcinoma
1958
5-Fluorouracil (26)
1957
Cancer Chemotherapy National Service Center
1955
L1210 as primary screen (27–30)
1949
Thiopurines (24, 25)
1951
Antitumor antibiotics (23)
1959
Antifolates (22)
1948
Nitrogen mustard in lymphomas (15–18)
1943
Model development (7)
1935
Transplantable tumors (5–11)
1912
Arsenicals (1, 2)
1908
Animal models (1–4)
1900
1900
1905
1910
1915
1920
1925
1930
1935
1940
1945
1950
1955
1960

Targeted Therapies

- Drugs or antibodies that block the growth and spread of cancer by interfering with specific molecules (**TARGETS**) involved in cancer growth.
- Promises treatment specific to malignant cells, avoiding toxicity to normal tissues.
- Generally categorized as either monoclonal antibodies or small molecules:
  - **Monoclonal antibodies:** designed to interact with cell surface antigens.
  - **Small molecules:** capable of diffusing into cells and act on intracellular targets.

Special Virus Cancer Program
1964

Cure of ALL & Hodgkin's disease (51–56, 63–66)
1963–70

Vinca alkaloids (50)
1963

Xenografts in nude mice
1975

Adjuvant chemotherapy (79–83)
1968–75

Cure of testicular cancer (86–88)
1976

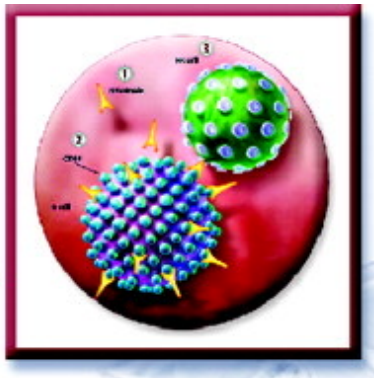
National Cancer Act
1971

NCI investment in molecular biology
1984

Cell culture systems
1990

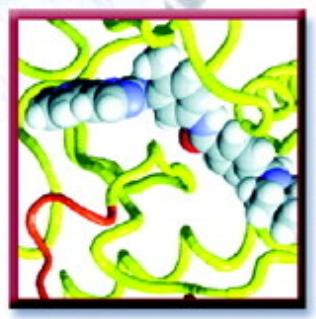
Cancer mortality begins to decline
1990

First monoclonal antibody approved
1997



Imatinib (Gleevec) (95–98)
1996

Tyrosine kinase inhibitors (94–101)
2005



Molecular profiling
2002

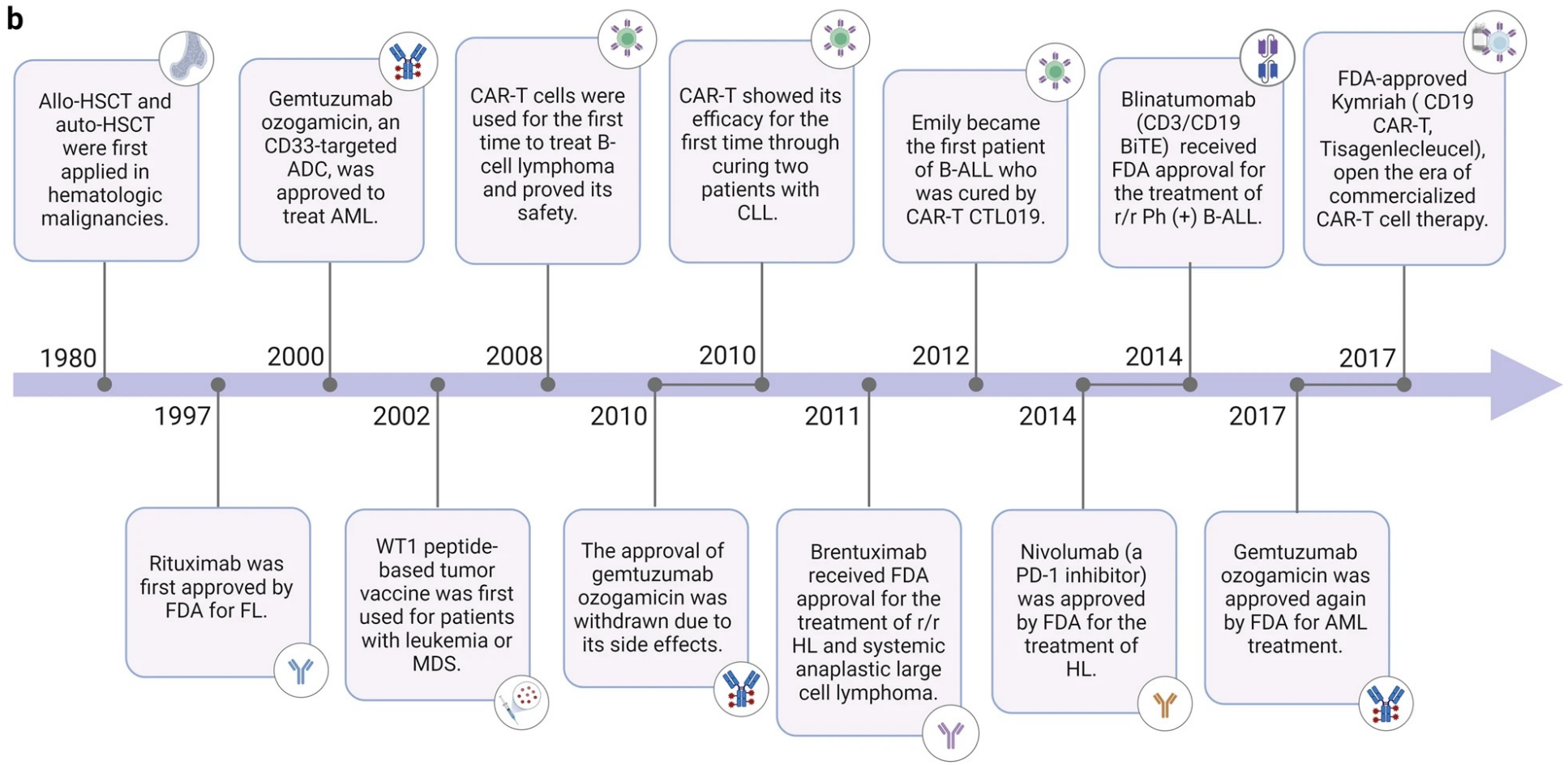
Genome sequenced
2001

Target specific screens
2007

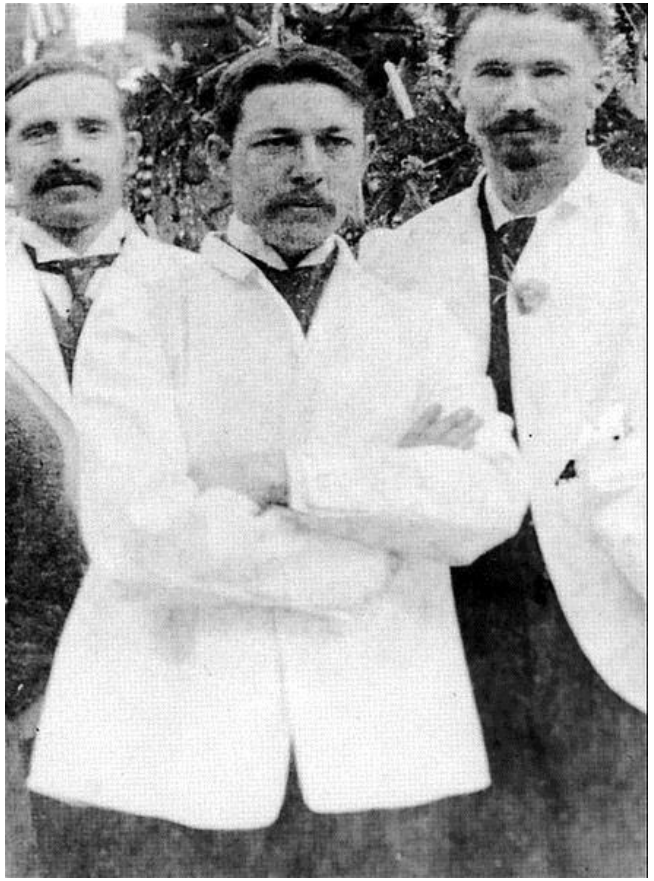
Mortality decline accelerates
2007

1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015

The Immunotherapy Era



William Coley and the birth of cancer immunotherapy



New York Times - July 29, 1908

ERYSIPELAS GERMS AS CURE FOR CANCER

Dr. Coley's Remedy of Mixed Toxins Makes One Disease Cast Out the Other.

MANY CASES CURED HERE

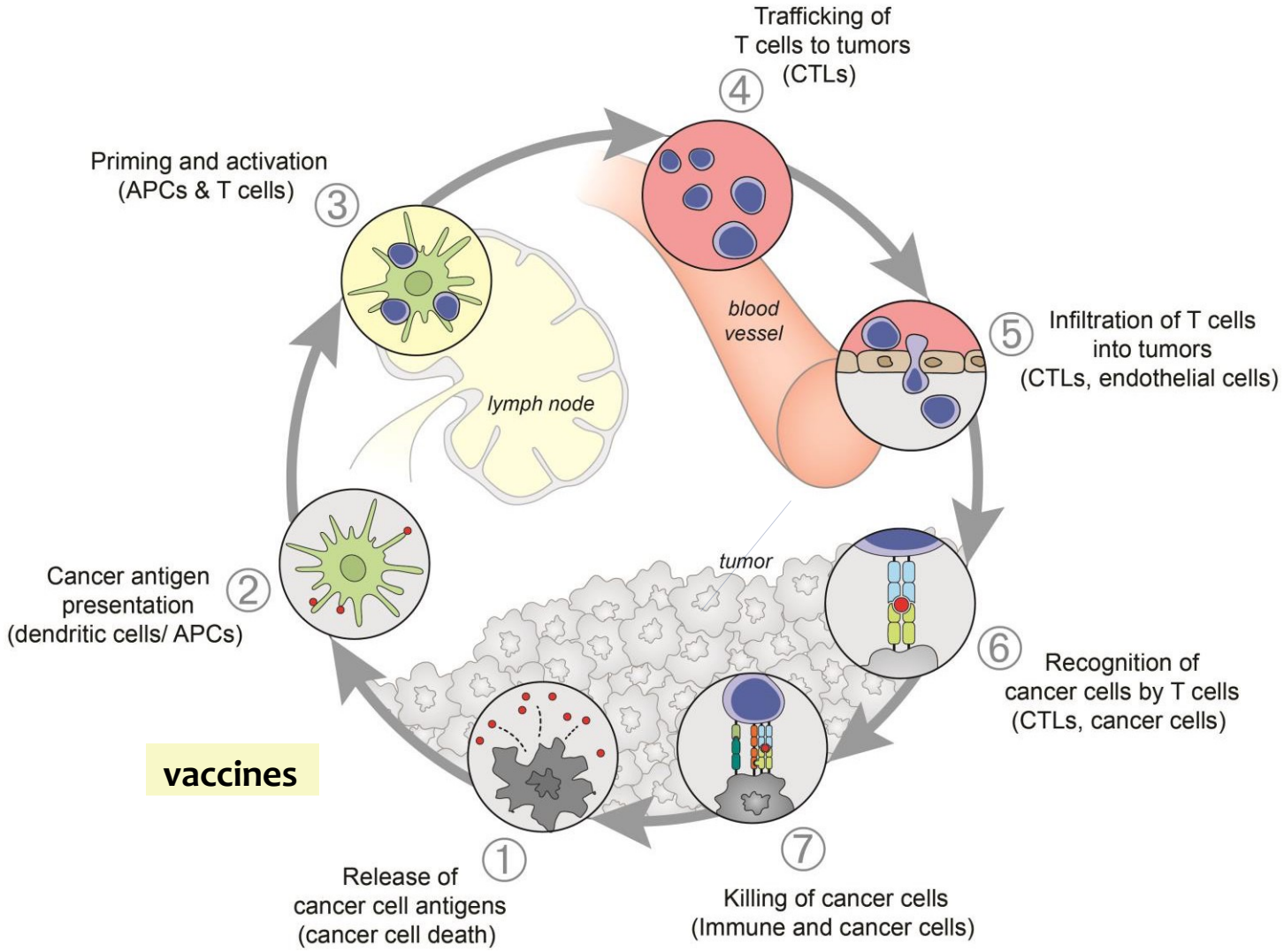
Physician Has Used the Cure for 15 Years and Treated 430 Cases— Probably 150 Sure Cures.

Following news from St. Louis that two men have been cured of cancer in the City Hospital there by the use of a fluid discovered by Dr. William B. Coley of New York, it came out yester-

Elie Metchnikoff & Paul Ehrlich won the Nobel Prize 3 months later

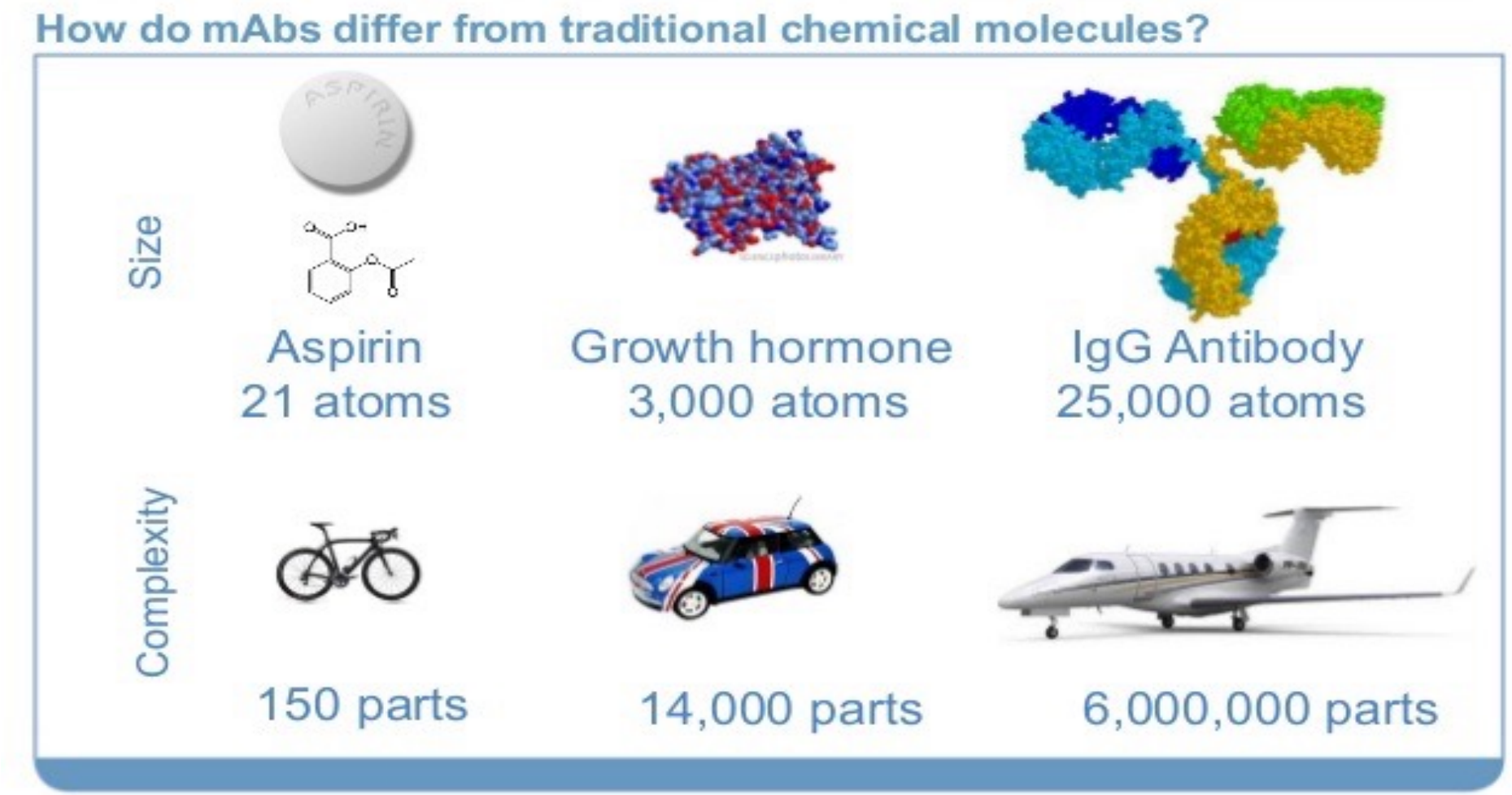
What we have learned:

Our Immune System is capable of Recognize and Attack Cancer Cells

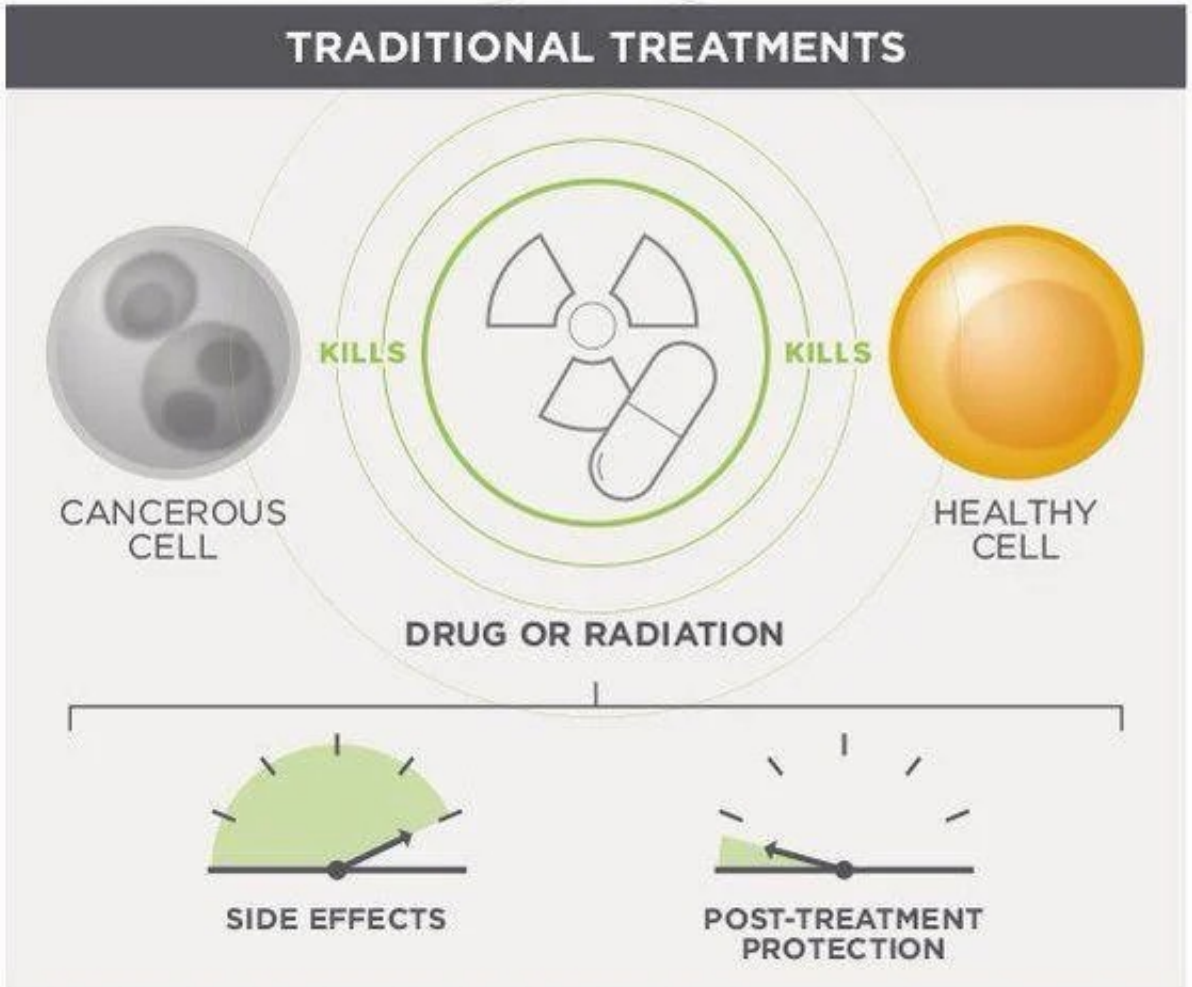


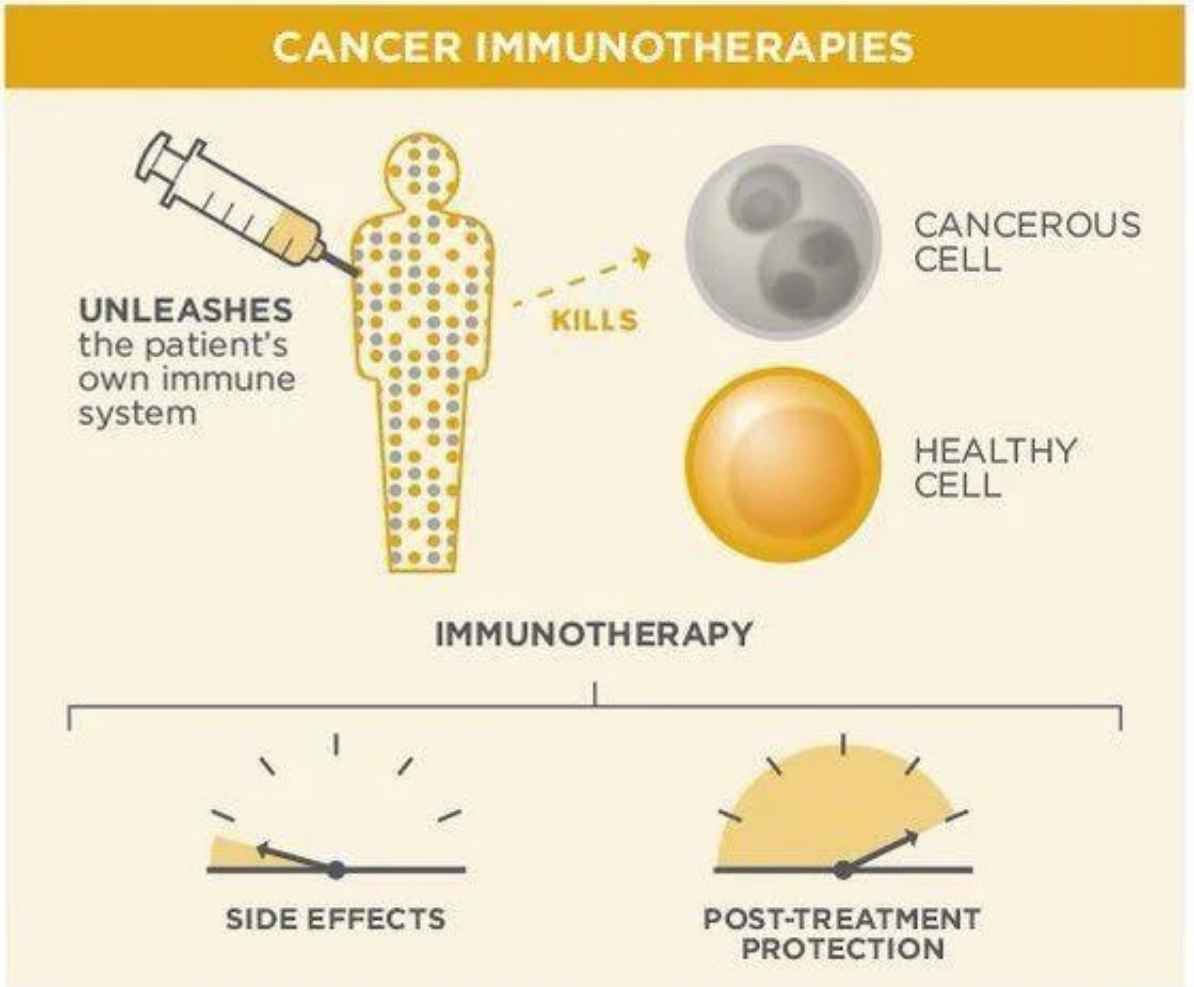
Chen & Mellman (2013) Immunity

Complexity of Immunotherapy

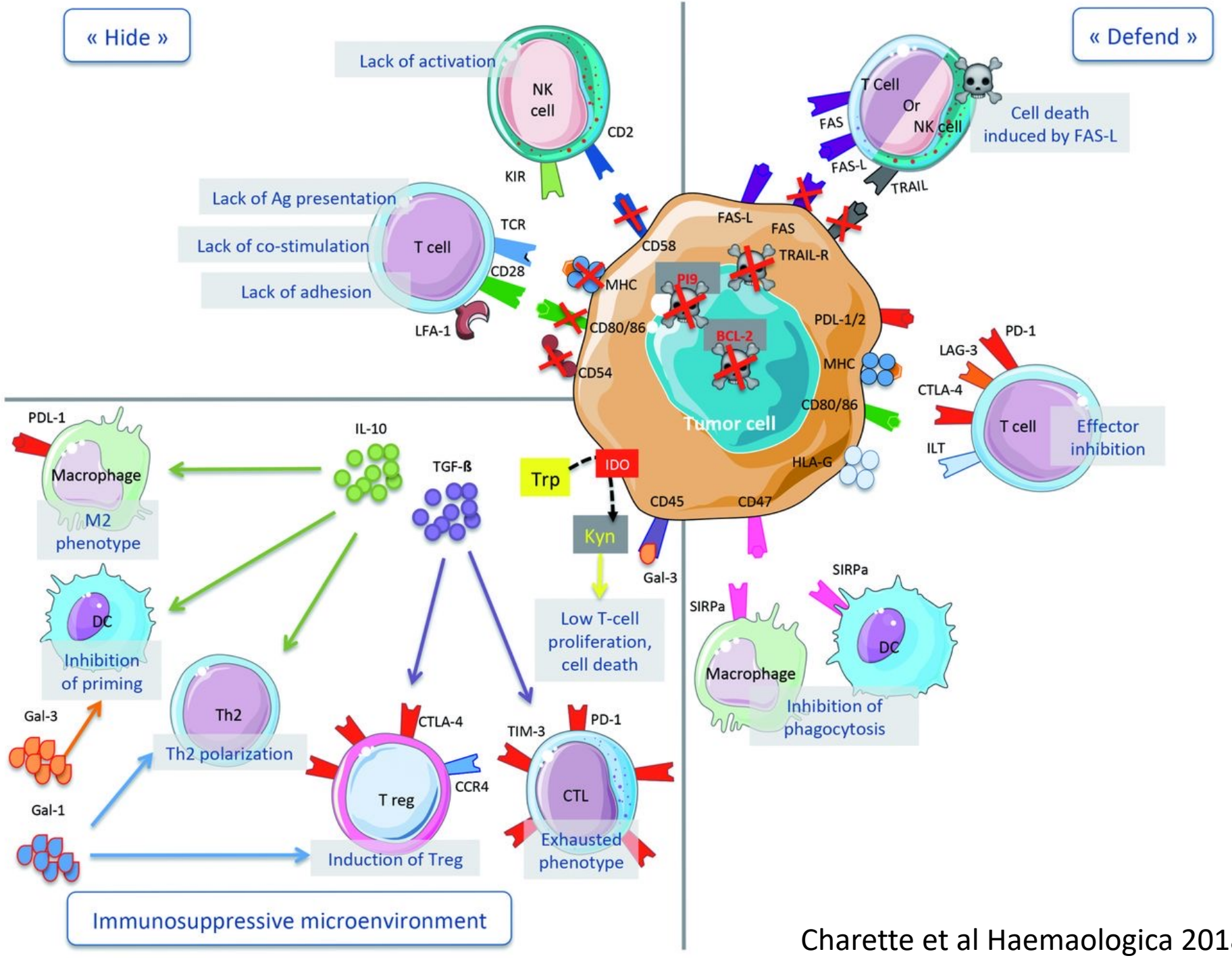


IMMUNOTHERAPY VS. CHEMOTHERAPY



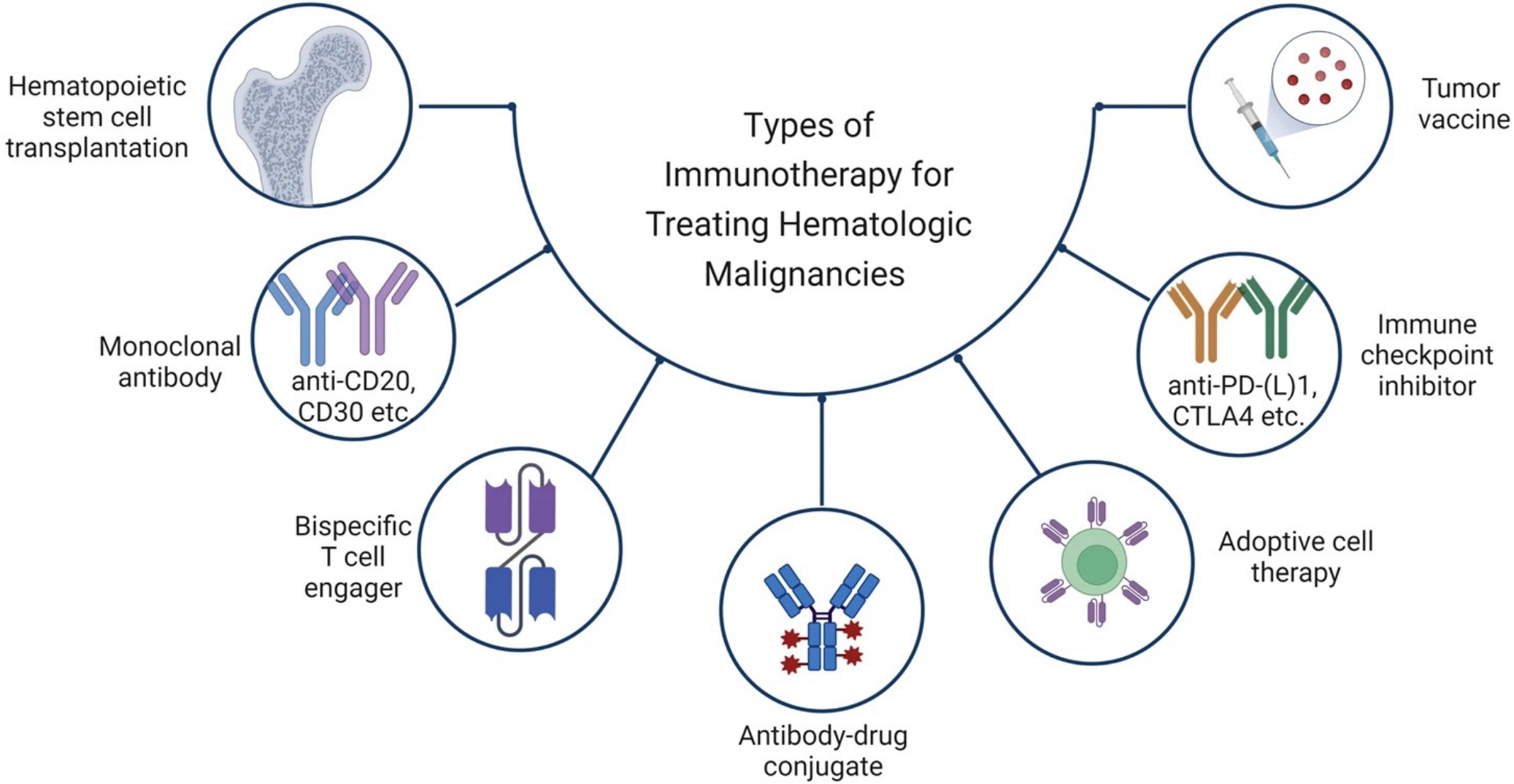


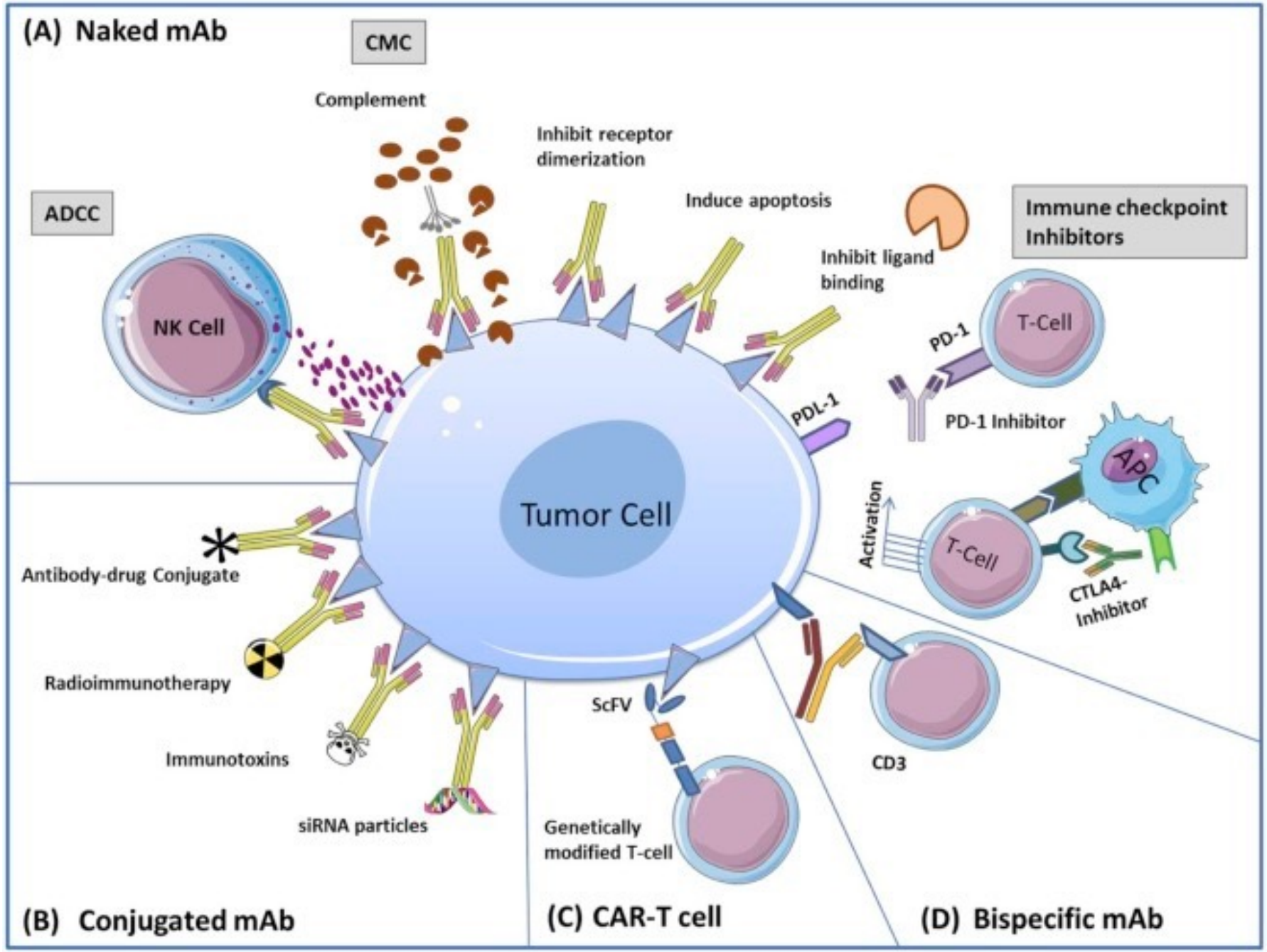
However, Cancer Resists…



Charette et al Haemaologica 2018

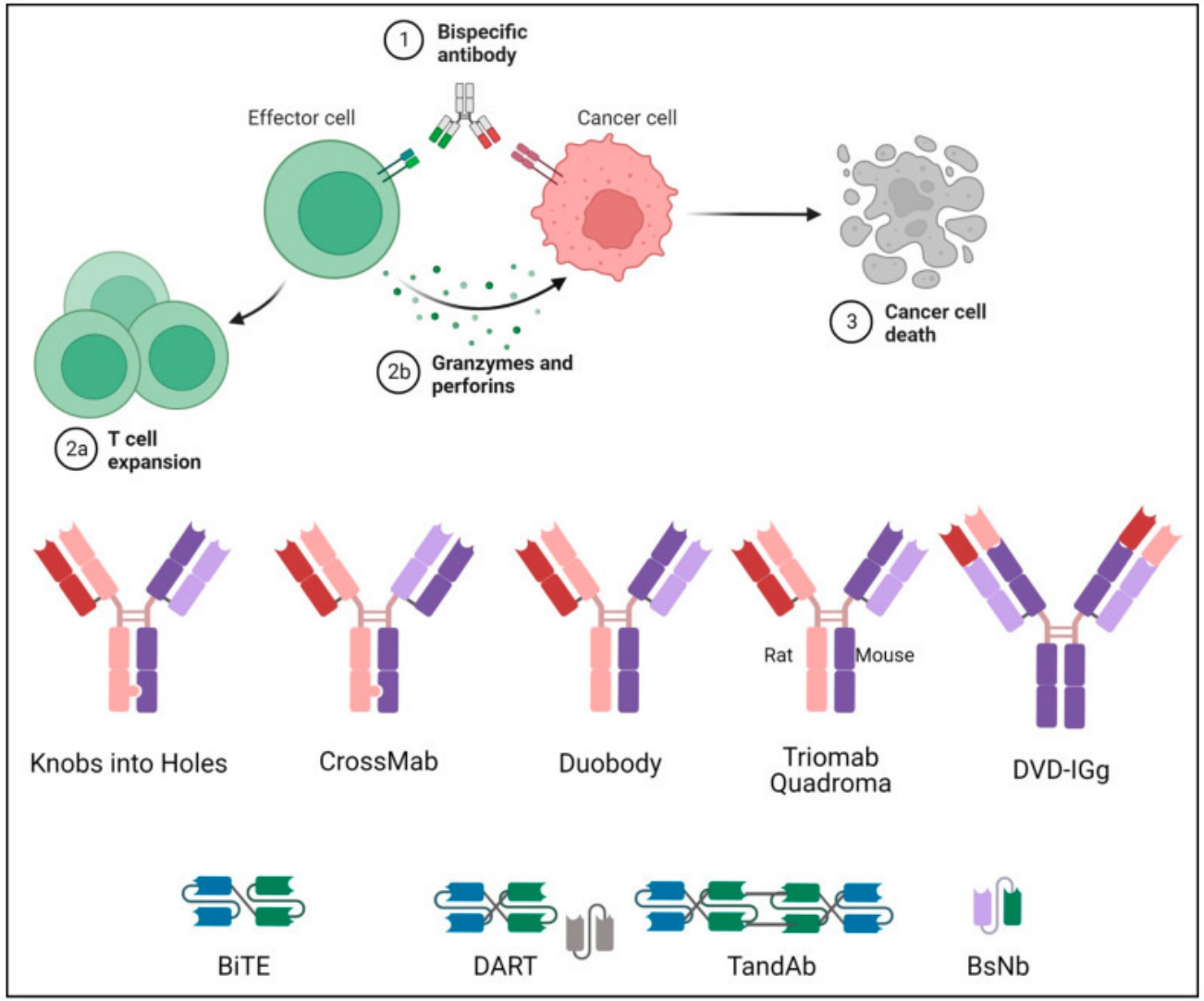
Immunotherapy Modalities for Hematologic Malignancies




(A) Naked mAb
CMC
Complement
Inhibit receptor dimerization
Induce apoptosis
ADCC
NK Cell
Inhibit ligand binding
Immune checkpoint Inhibitors
PD-1
T-Cell
PDL-1
PD-1 Inhibitor
Tumor Cell
Activation
APC
T-Cell
CTLA4-Inhibitor
Antibody-drug Conjugate
Radioimmunotherapy
Immunotoxins
siRNA particles
ScFV
CD3
Genetically modified T-cell
(B) Conjugated mAb
(C) CAR-T cell
(D) Bispecific mAb

Bispecific Antibodies (BiAbs)

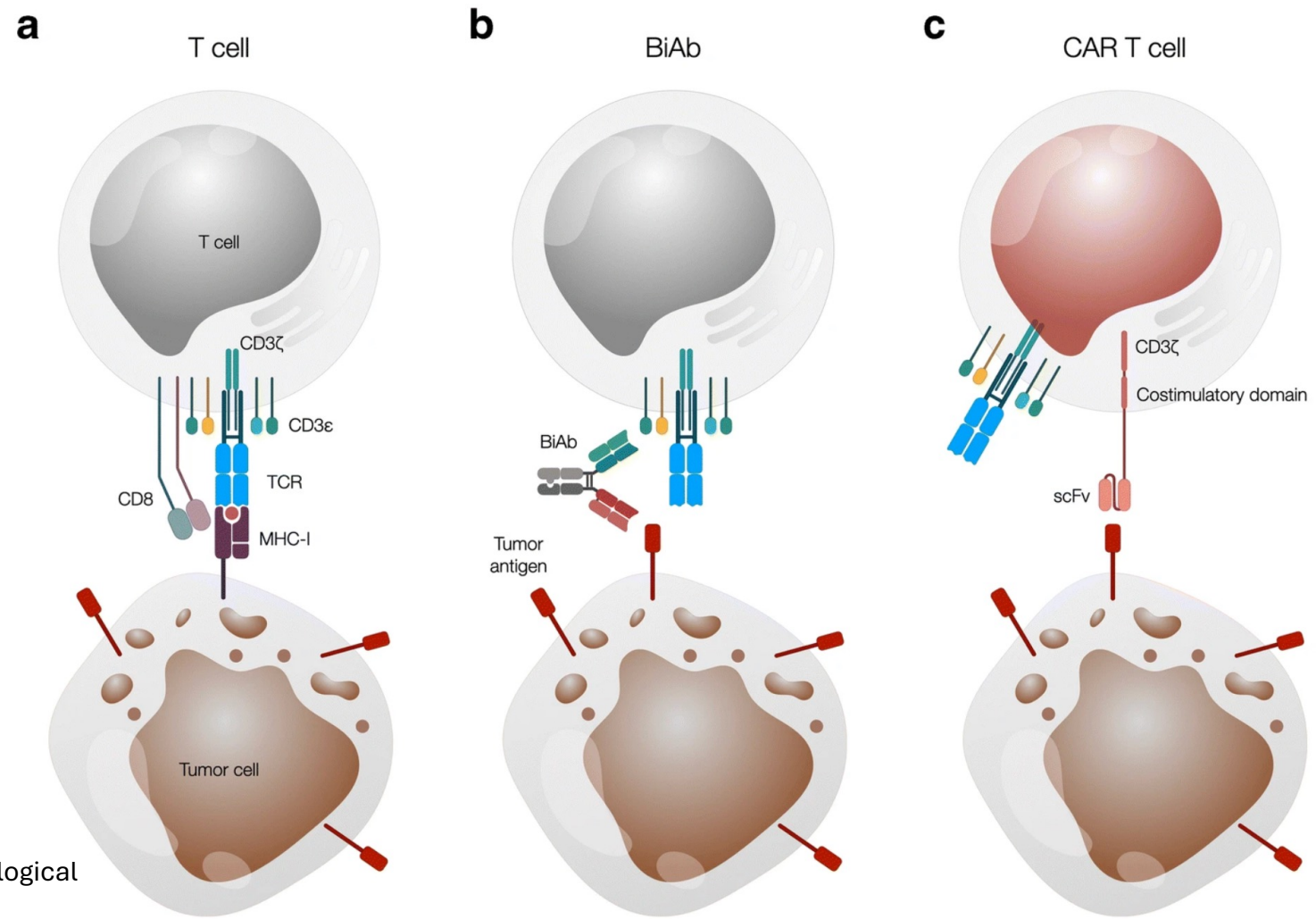
- CD3-targeted bispecific antibodies recruit T-cells to target cancer cells
  - One arm of the bispecific molecule binds to CD3 (antigen on T-cells)
  - The other arm binds to a tumor-associated antigen (eg, CD19, CD20, BCMA)
- Once bound, a synapse forms and T-cells release perforin, as granzymes flow through open pore—leading to cell death



FDA Approved Bispecific Antibodies

DRUG	INDICATION	TARGET	YEAR OF APPROVAL
Tarlatamab	SCLC	DLL3	2024
Talquetamab	Multiple Myeloma	GPRC5D	2023
Elrantamab	Multiple Myeloma	BCMA	2023
Glofitamab	Diffuse large B-cell lymphoma	CD20	2023
Epcoritamab	Diffuse large B-cell lymphoma	CD20	2023
Teclistamab	Multiple Myeloma	BCMA	2022
Mosunetuzumab	Follicular lymphoma	CD20	2022
Amivantamab	NSCLC	EGF/MET	2021
Blinatumomab	ALL	CD19	2014

Bispecific Antibodies vs CART



Schwerdtfeger et al., Current Hematological Malignancy 2021

Bispecific Antibodies vs CART

	CAR T-Cell	Bispecific mAbs
Convenience factors	Specialized center Caregiver needed Prolonged manufacturing time	"Off the shelf"
Hospitalization	At most centers	For step-up doses
Length of treatment	1-time administration	Ongoing weekly
Toxicities	CRS, neurotoxicity, cytopenias, infection	CRS, cytopenias, infection
REMS	Yes	Yes
Cost	>$400K	~400K per yr Must consider length of treatment

- No randomized data on sequencing bispecific antibodies and CAR-T cell therapies

Bispecific Antibodies in B-ALL

ALL Relapse

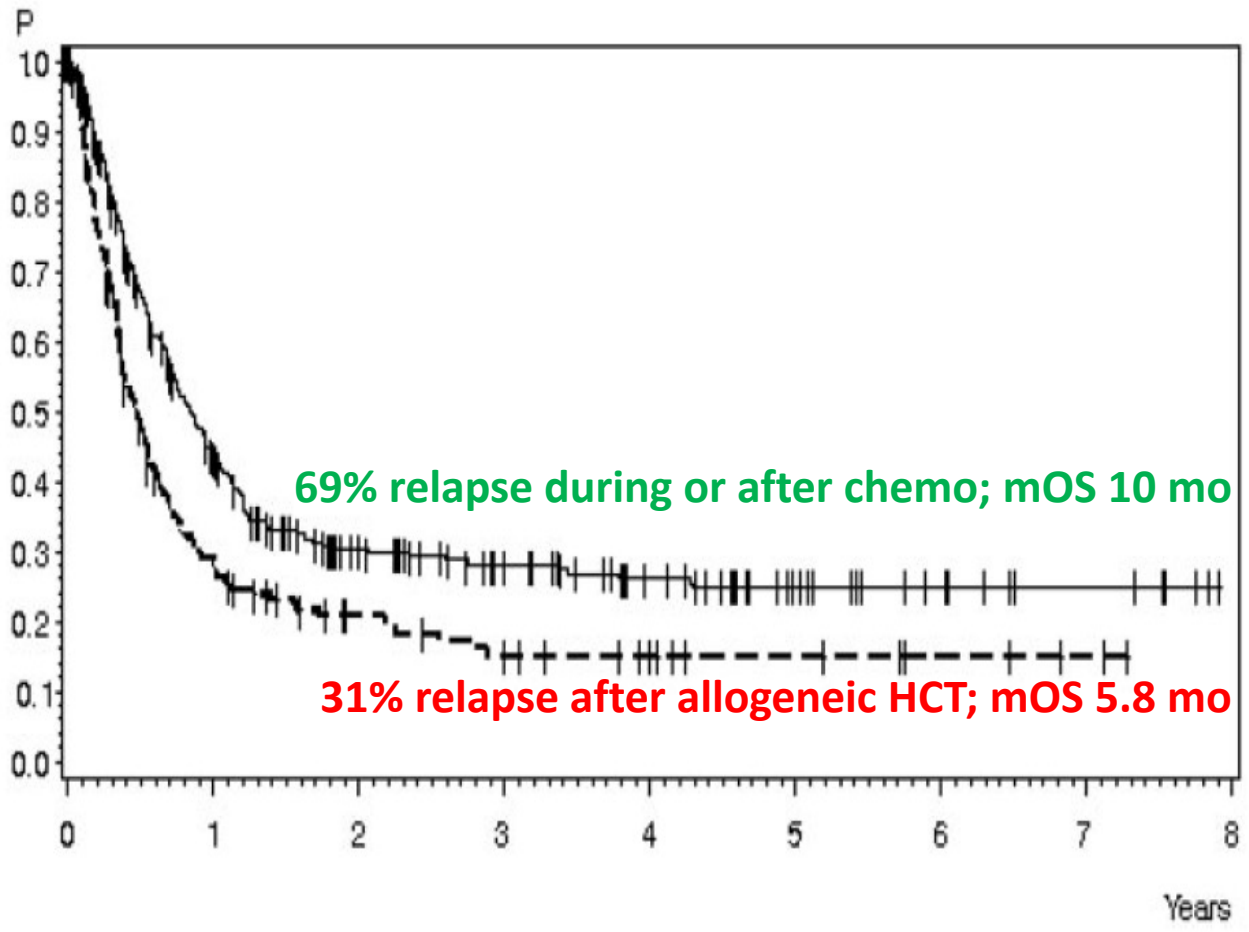


Figure 1. Survival in patients with relapsed ALL according to first-line therapy. Relapse during or after chemotherapy, n = 378 (solid line), 28% ± 3% after 3 years, 25% ± 3% after 5 years; median 10 months; relapse after SCT, n = 169 (dashed line), 15% ± 3% after 3 and 5 years, median 5.8 months ($P < .0001$).

N= 547
CR after 1st salvage 42%
CR after 2nd salvage 33%
CR after SCT 25%
mOS at relapse 8.4 mo
3 years survival 24%

Gökbuget N, Stanze D, Beck J, et al. Outcome of relapsed adult lymphoblastic leukemia depends on response to salvage chemotherapy, prognostic factors, and performance of stem cell transplantation. *Blood*. 2012;120(10):2032-2041. doi:10.1182/blood-2011-12-399287

Relapse after Allo-HCT for B-ALL

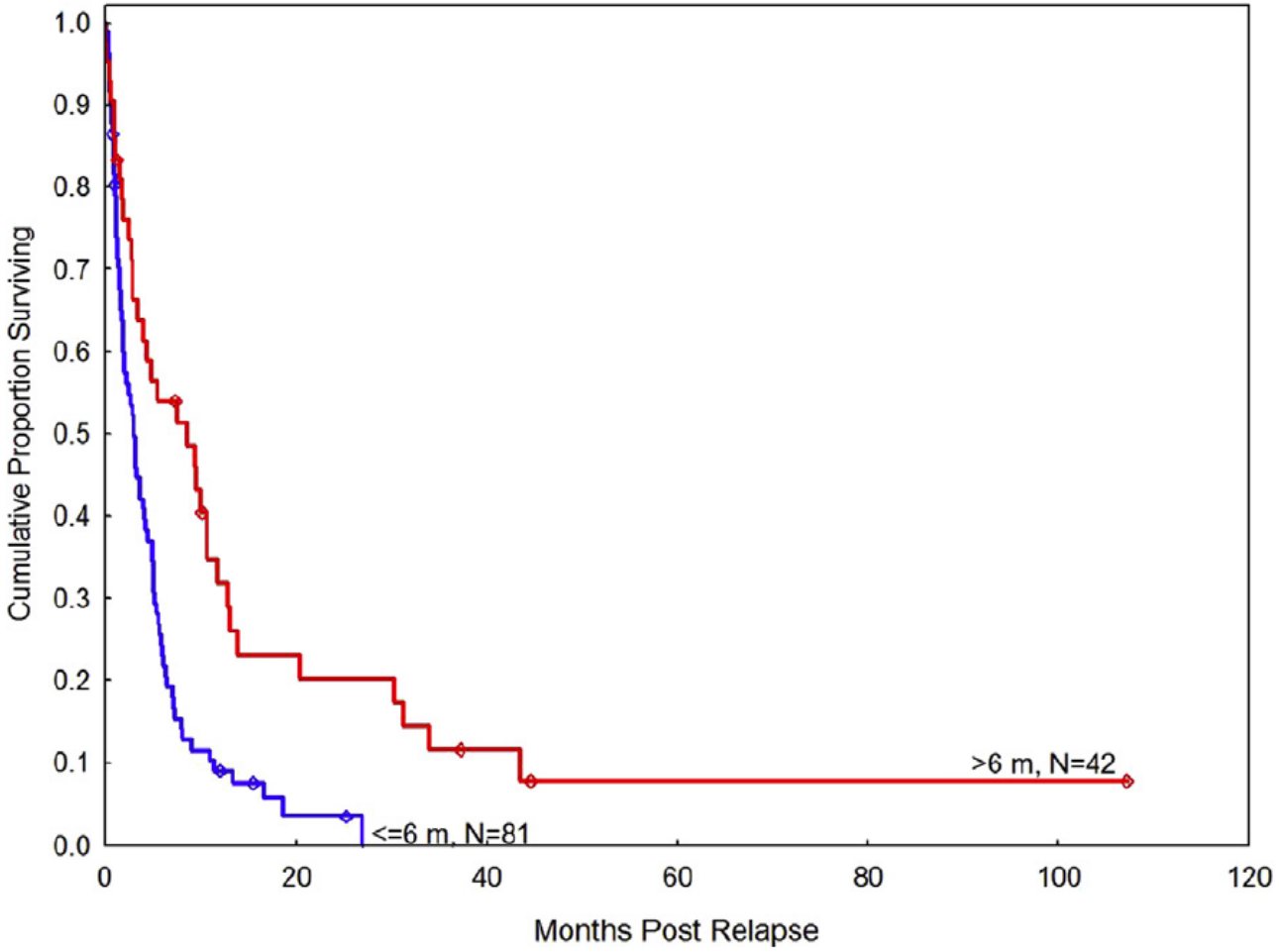
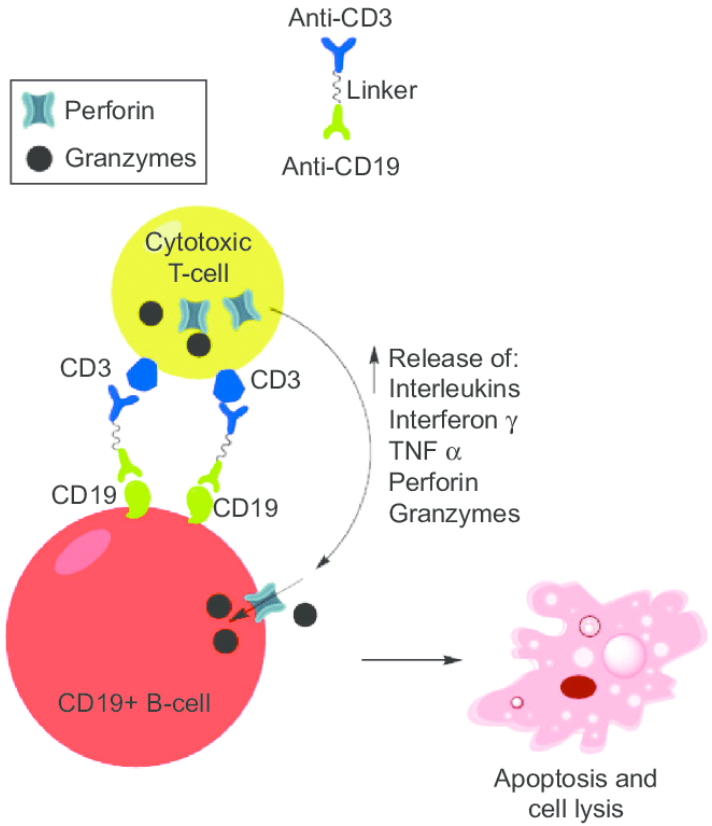


Figure 1. Comparison of OS between patients who relapsed within 6 months of HSCT and those who relapsed after 6 months.

Poon LM, Hamdi A, Saliba R, et al. Outcomes of Adults with Acute Lymphoblastic Leukemia Relapsing after Allogeneic Hematopoietic Stem Cell Transplantation. *Biol Blood Marrow Transplant*. 2013;19(7):1059-1064. doi:10.1016/j.bbmt.2013.04.014

Blinatumomab: The First Approved BiAbs (AKA BiTE)

- Approved by FDA on July 2017 for adults and children with relapsed or refractory Ph positive B-cell precursor ALL
- Special monoclonal antibody that attach to 2 different proteins at same time
  - CD19 – found on leukemia cells
  - CD3 – found on T-cells
- Given as a continuous IV infusion (28 days)
- Common side effects:
  - **Cytokine Release Syndrome**
  - Neurologic problems
  - Leukopenia
  - Infusion reactions



By binding to CD19 and CD3 this drug brings the leukemia cells and immune cells together, causing the immune system to attack cancer cells.

Blinatumomab Clinical Trials for Treatment of B-ALL

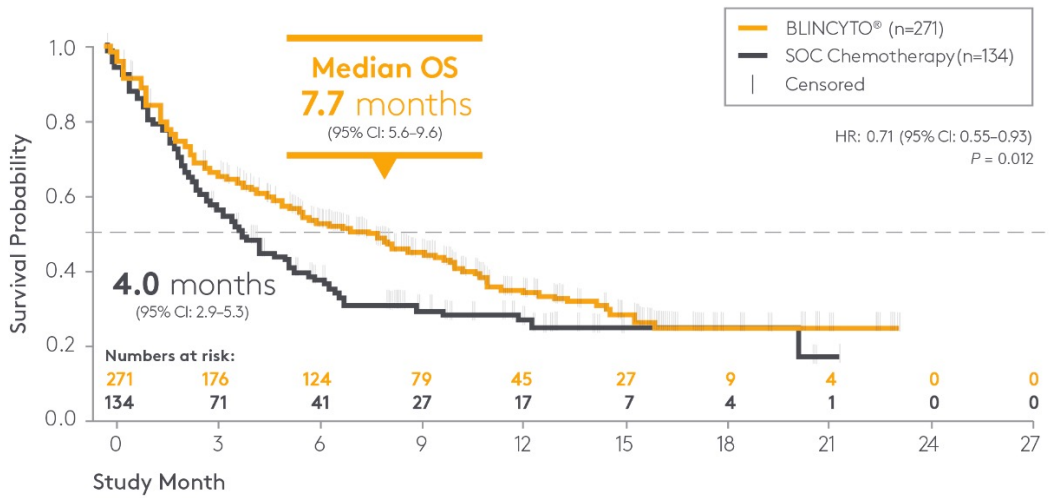
Trial	Study design	Patient population	Enrolled patients	Primary endpoint	Results
TOWER (NCT02013167)	Prospective, randomized phase III	Adults with Ph– RR B-ALL	405	OS	Median OS 7.7 months in blinatumomab group versus 4.0 months in the chemotherapy group (HR 0.71; 95% CI, 0.55 to 0.93; p=0.01)
ALCANTARA (NCT02000427)	Open-label-, single-arm phase II	Adults with Ph+ RR B-ALL	45	CR or CRh	CR or CRh rate 36% (95% CI, 22% to 51%) with 88% MRD–
MT103-205 (NCT01471782)	Phase I/II	Children with RR B-ALL	93 total (49 phase I) (44 phase II)	MTD (phase I) CR (phase II)	CR rate 39% (95% CI, 27% to 51%) with 52% MRD–
BLAST (NCT01207388)	Open-label, single-arm phase II	Adults with B-ALL in first or later hematological CR and persistent or recurrent MRD $\geq 10^{-3}$	113	Complete MRD response	78% achieved MRD–

B-ALL, B-cell acute lymphoblastic leukemia; CR, complete response; CRh, CR with partial hematologic recovery; FDA, Food and Drug Administration; MRD, minimal/measurable residual disease; MTD, maximum-tolerated dosage; OS, overall survival; Ph, Philadelphia chromosome; RR, relapsed/refractory.

TOWER
Randomized Phase 3 Study
R/R B-ALL
Blinatumomab vs SOC Chemo

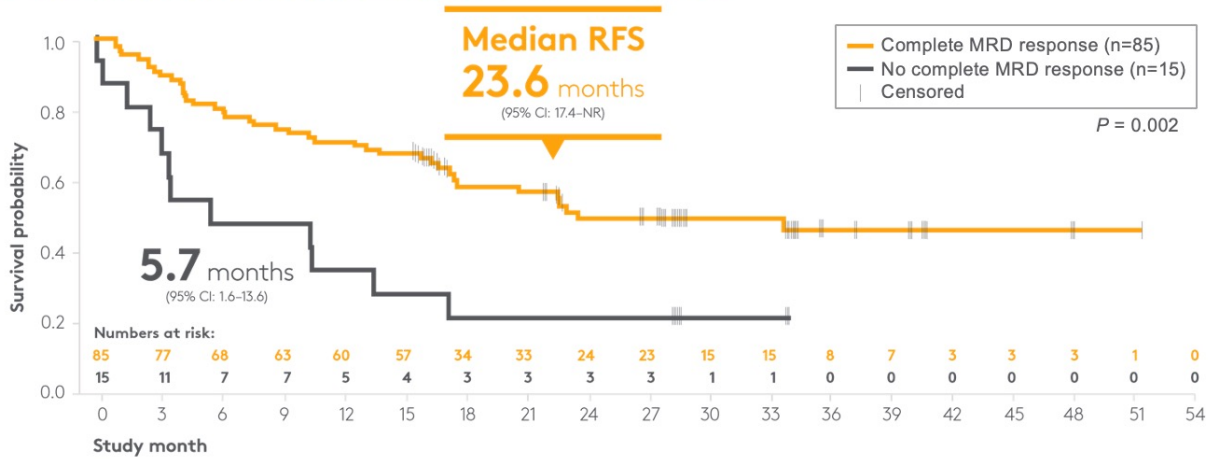
BLAST
Single Arm Phase 2 Study
MRD+ B-ALL
Blinatumomab single agent

Primary Endpoint in TOWER: Overall Survival (Intent-to-Treat Population)[1,2]



- Median OS 7.7 vs 4.0 months

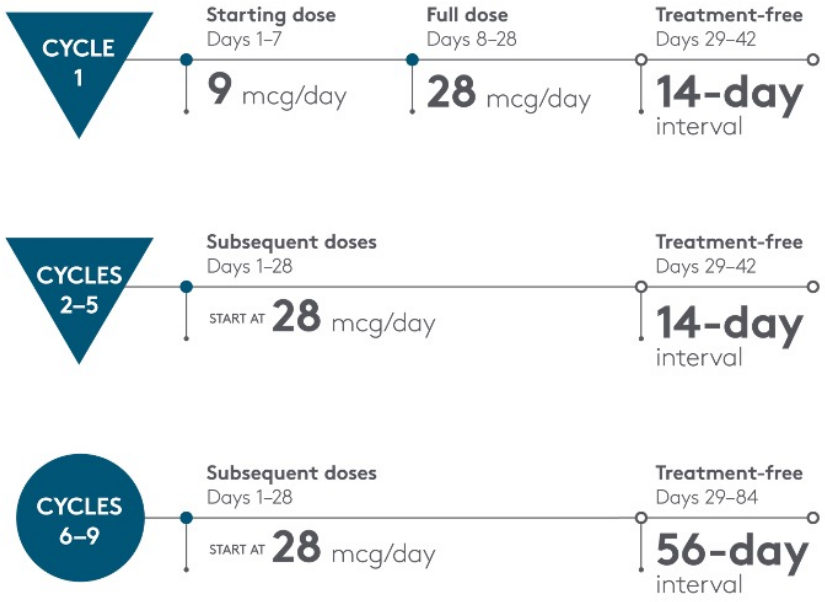
RFS* in Patients With vs Without Complete MRD Response†



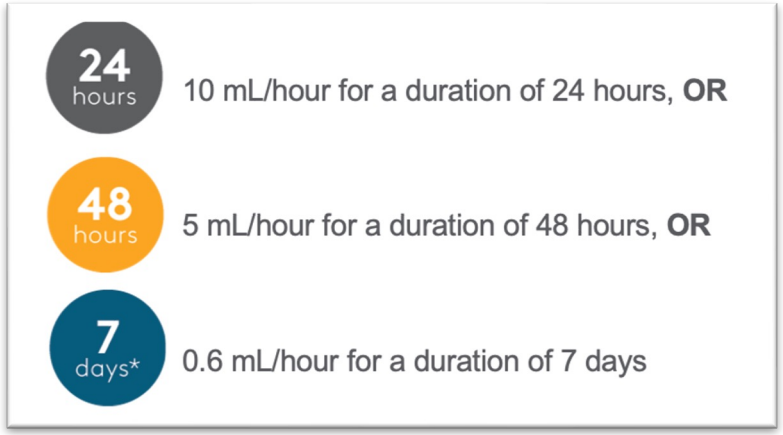
- 81% MRD negative (median 2 cycles)
- Median RFS 23.6 vs 5.7 months

Blinatumumab Dosing

R/R B-ALL



MRD+ B-ALL



ECOG-ACRIN E1910

Randomized Phase 3 study

Newly Diagnosed B-ALL

Consolidation Therapy With Blinatumomab

Figure 1. Schema

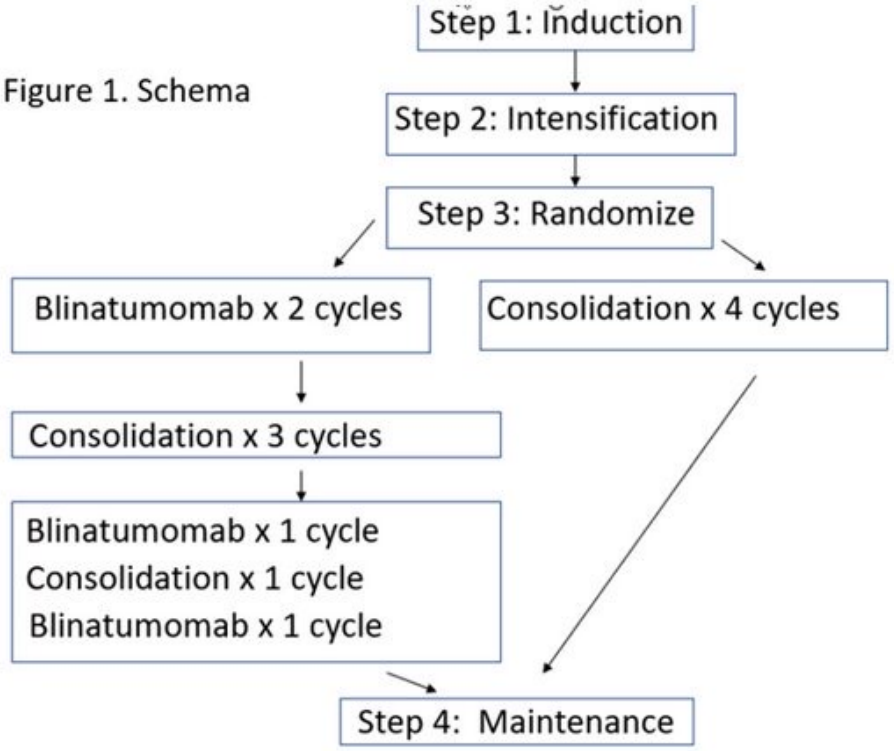
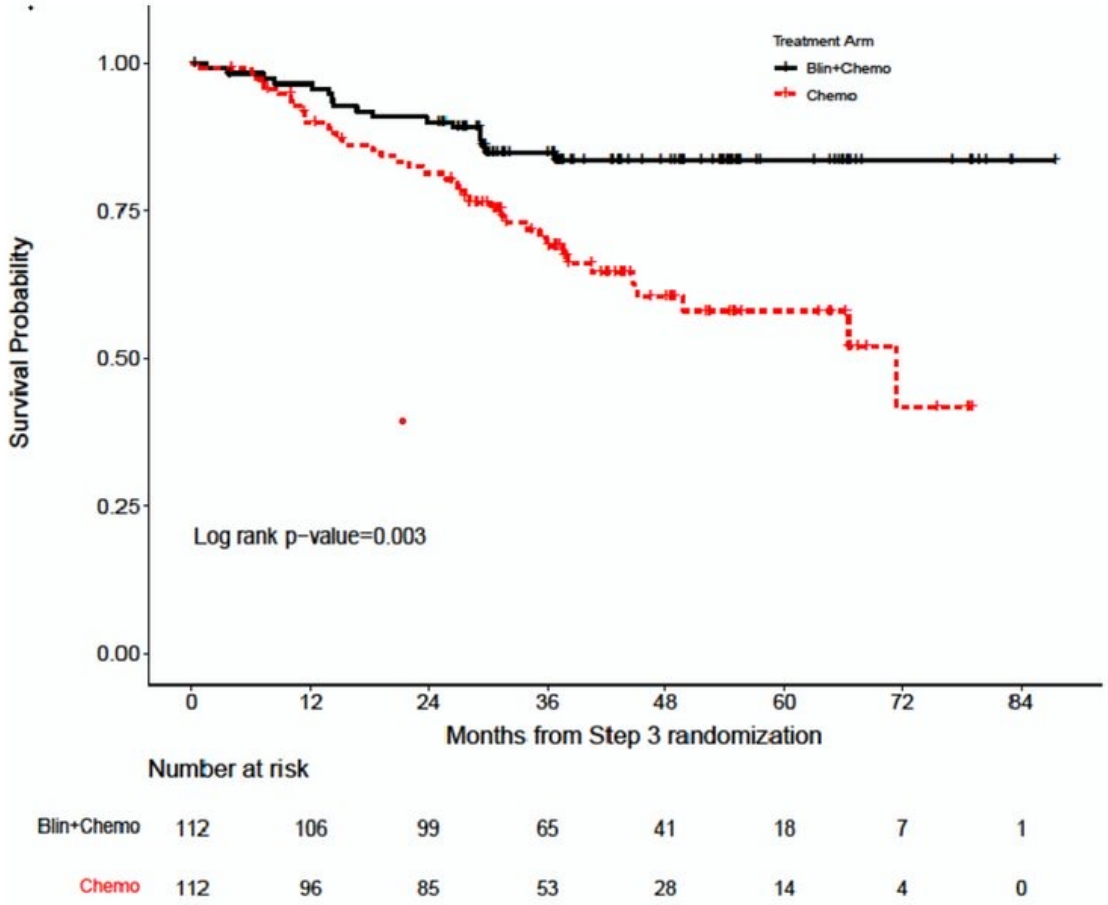


Figure 2: Overall Survival



FDA approves blinatumomab as consolidation for CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia

Resources for Information | Approved Drugs

Oncology (Cancer) / Hematologic Malignancies Approval Notifications

On June 14, 2024, the Food and Drug Administration approved blinatumomab (Blincyto, Amgen Inc.) for adult and pediatric patients one month and older with CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia (Ph-negative BCP ALL) in the consolidation phase of multiphase chemotherapy.

Full prescribing information for Blincyto will be posted on Drugs@FDA.

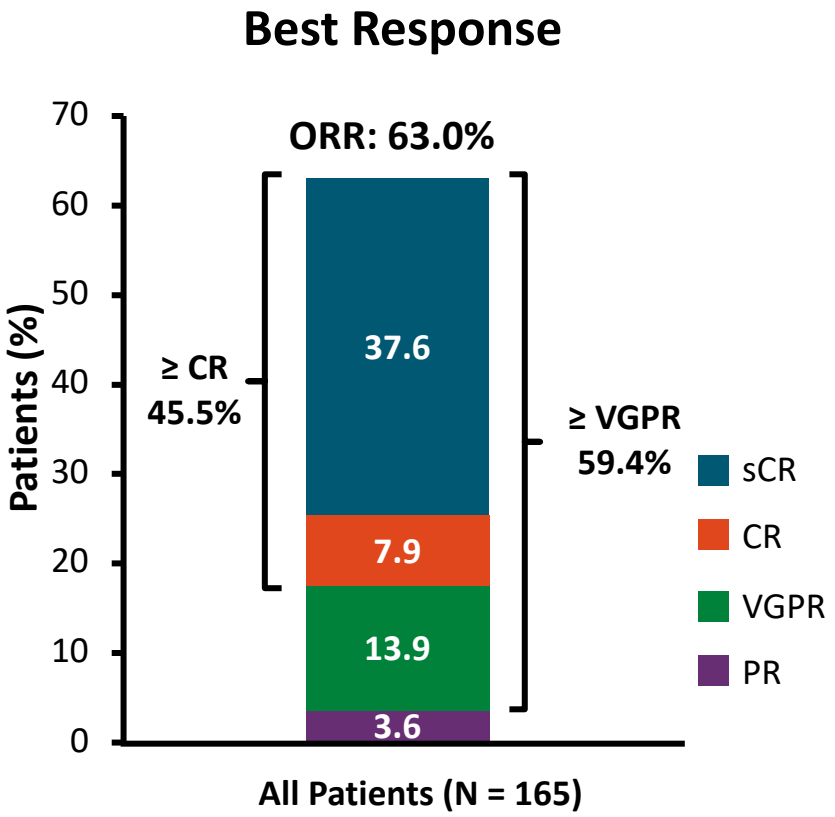
Content current as of:
06/14/2024

Bispecific Antibodies in Multiple Myeloma

Teclistamab: Subcutaneously Administered CD3 x BCMA Bispecific Antibody

- **Indication:** R/R MM after ≥4 prior lines of therapy, including an IMiD, PI, and anti-CD38 mAb (accelerated approval)
- **MajesTEC-1:** pivotal, open-label, phase I/II trial of teclistamab in R/R MM
  - Median time to first response: 1.2 mo
  - Median time to best response: 3.8 mo
  - Long-term median follow-up: 23 mo

Event, Mo (95% CI)	All Patients (N = 165)
Median DoR	22 (16-NE)
Median PFS	11 (9-16)
Median OS	22 (15-NE)



Moreau. NEJM. 2022;387:495. Teclistamab-cqyv PI. van de Donk. ASCO 2023. Abstr 8011.

Teclistamab: CRS and ICANS

- Only available through REMS to mitigate CRS and neurotoxicity risk

Cytokine-Release Syndrome	Neurotoxicity
▪ Rate of CRS: 72% (recurrent: 33%) – Step-up dose 1: 42% – Step-up dose 2: 35% – Initial treatment dose: 24% – Mostly grade 1 (50%) or grade 2 (21%) – <3% with subsequent doses – Median onset: 2 days (range: 1-6) – Median duration: 2 days (range: 1-9)	▪ Most frequent: headache (25%), motor dysfunction (16%), encephalopathy (13%) ▪ 1 patient with grade 4 seizure and 1 fatal case of Guillain-Barré syndrome ▪ ICANS: 6% (recurrent: in 1.8%) – Step-up dose 1: 1.2% – Step-up dose 2: 0.6% – Initial treatment dose: 1.8% – <3% subsequent dosing – Median onset: 4 days (range: 2-8) – Median duration: 3 days (range: 1-20)

Teclistamab-cqyv PI.

Teclistamab: Other AEs of Interest

- Hepatotoxicity (elevated LFTs)
  - Any grade: 28%-34%
  - Grade 3/4: 1%-2%
- Neutropenia:
  - Any grade: 84%
  - Grade 3/4: 56%
- Infection
  - Serious infection: 30%
  - Fatal infection: 4%
- Injection-site reaction: 35% (grade 1/2)

Teclistamab-cqyv PI.

Teclistamab: Dosing and Administration

- Hospitalization recommended for 48 hr after administration of step-up and first treatment doses
- Premedication: PO/IV acetaminophen 650-1000 mg or equivalent, dexamethasone 16 mg, diphenhydramine 50 mg or equivalent

Schedule	Day	Dose
Step up:		
▪ 1	1	0.06 mg/kg SC
▪ 2*	4	0.3 mg/kg SC
▪ 3 (first treatment dose)†	7	1.5 mg/kg SC
Weekly dosing	1 wk after first treatment dose, then QW	1.5 mg/kg SC
Biweekly dosing	Q2W for those who achieve and maintain ≥ CR for ≥6 mo	1.5 mg/kg SC

*May be given 2-4 days after step-up dose 1 or ≤7 days after for AE resolution. †May be given 2-4 days after step-up dose 2 or ≤7 days after for AE resolution.

Teclistamab-cqyv PI.

Talquetamab: Subcutaneously Administered GPRC5D-Directed CD3 T-Cell Engager

- **Indication:** R/R MM after ≥4 prior lines of therapy, including an IMiD, PI, and anti-CD38 mAb (accelerated approval)
- **MonumenTAL-1:** pivotal, open-label, multicenter, dose-escalation and expansion phase I/II trial of talquetamab in R/R MM

Outcome	0.4 mg/kg QW (n = 143)	0.8 mg/kg Q2W (n = 145)
ORR, %	74.1	71.7
≥CR, %	33.6	38.7
Median DoR, mo	9.5	NR
Median PFS, mo	7.5	14.2
Median follow-up, mo	18.8	12.7

Chari. NEJM. 2022;387:2232. Talquetamab-tgvs PI. Touzeau. EHA 2023. Abstr S191.

Talquetamab: Toxicity/Adverse Events

- Only available through REMS to mitigate CRS and neurotoxicity risk

Cytokine-Release Syndrome

- Rate of CRS: 76% (recurrent: 30%)
  - Step-up dose 1: 29%
  - Step-up dose 2: 44%
  - Step-up dose 3: 33%
  - Initial treatment dose: 30% in 0.4 mg/kg QW vs 12% in 0.8 mg/kg Q2W
  - Mostly grade 1 (57%) or grade 2 (17%)
  - <3% with subsequent doses
  - Median onset: 27 hr (range: <1-167)
  - Median duration: 17 hr (range: 0-622)

Neurotoxicity

- Most frequent: headache (20%), sensory neuropathy (14%), encephalopathy (15%), and motor dysfunction (10%)
- ICANS: 9% (recurrent: 3%)
  - Step-up dose 1: 3%
  - Step-up dose 2: 3%
  - Step-up dose 3: 1.8%
  - Initial treatment dose: 2.6% in 0.4 mg/kg QW vs 3.7% with 8.0 mg/kg Q2W
  - Median onset: 2.5 days (range: 1-16)
  - Median duration: 2 days (range: 1-22)

Talquetamab-tgvs PI.

Talquetamab: Other AEs of Interest

- Weight loss: 62%
- Oral toxicity (dysgeusia, dry mouth, dysphagia, stomatitis)
  - Any grade: 80%
  - Grade 3: 2.1%
- Infection
  - Serious infection: 16%
  - Fatal infection: 1.5%
- Cytopenia
  - Grade 3/4 neutropenia: 35% (median onset: 22 days)
  - Grade 3/4 thrombocytopenia: 22% (median onset: 12 days)
- Skin toxicity
  - Any grade: 62%
  - Grade 3: 0.3%
  - Median time to onset: 25 days

Talquetamab-tgvs PI.

Talquetamab Dosing Schedules: Weekly or Biweekly

- Hospitalization recommended for 48 hr after administration of step-up and first treatment doses
- Premedication: PO/IV dexamethasone 16 mg, diphenhydramine 50 mg, and acetaminophen 650-1000 mg or an equivalent of each

Weekly Dosing		
Schedule	**Day**	**Dose**
Step up ▪ 1 ▪ 2* ▪ 3 (first treatment dose)*	1 4 7	0.01mg/kg SC 0.06 mg/kg SC 0.4 mg/kg SC
Weekly dosing	1 wk after first treatment dose, then QW	0.4 mg/kg SC

Biweekly Dosing		
Schedule	**Day**	**Dose**
Step up ▪ 1 ▪ 2* ▪ 3* ▪ 4 (first treatment dose)†	1 4 7 10	0.01mg/kg SC 0.06 mg/kg SC 0.4 mg/kg SC 0.8 mg/kg SC
Biweekly dosing	2 wk after first treatment dose, then Q2W	0.8 mg/kg SC

*May be given 2-4 days after prior dose or ≤7 days after for AE resolution.
†May be given 2-7 days after administering step-up dose 3.

Talquetamab-tgvs PI.

Talquetamab Modified Dosing: Efficacy and Safety

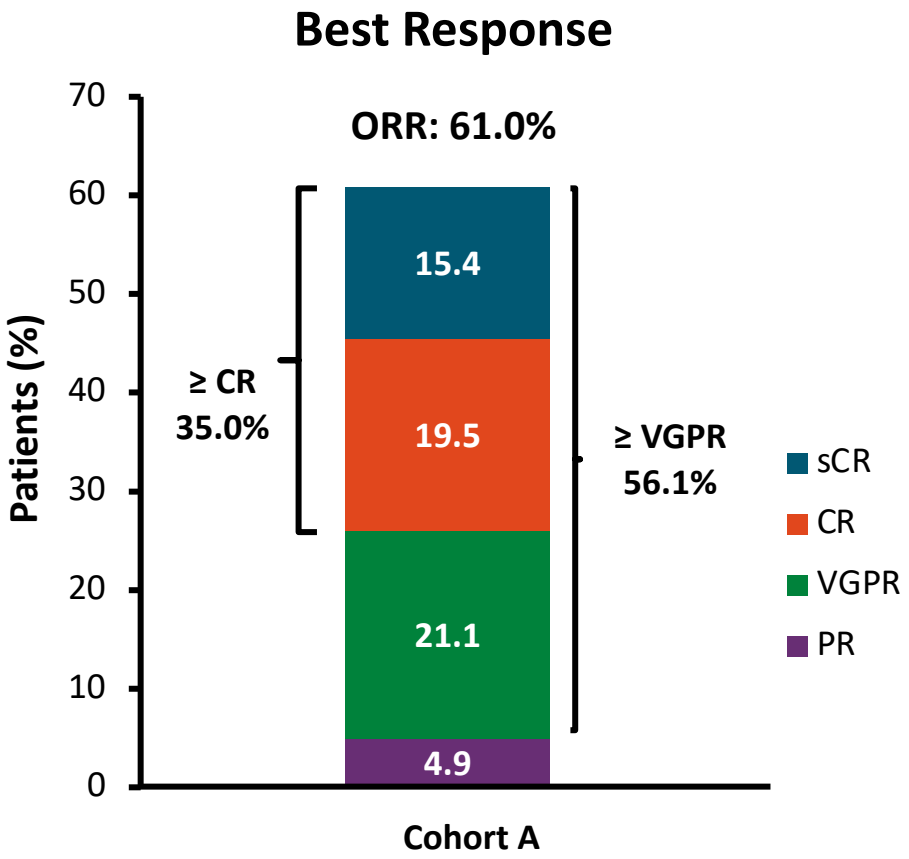
- Prospective dose-reduction cohorts (pooled), prespecified in phase I (N = 24):
  - Patients in these cohorts switched TAL dose after achieving ≥ PR (n = 19)
    - TAL 0.8 mg/kg Q2W → TAL 0.4 mg/kg Q2W (n = 9) after confirmed ≥ PR at next cycle
    - TAL 0.8 mg/kg Q2W → TAL 0.8 mg/kg Q4W (n = 10) after confirmed ≥ PR at next cycle
- Median time to dose reduction following response: 3.1 mo (range: 2.3-4.2)[1]
- Response maintained following prospective dose reduction, with some patients achieving deepening responses[1]:
  - ORR: 79.2% (19/24); sCR: 25%; CR: 29.2%; VGPR: 20.8%; PR: 4.2%
- Outcomes in these cohorts are in line with those observed in TAL 0.8 mg/kg Q2W registrational cohort[2]
- With modified dosing, most GPRC5D-related AEs (oral toxicity, skin toxicity, nail toxicity) trended toward improvement or resolution, except for weight loss

1. Chari. ASH 2023. Abstr 1010. 2. Touzeau. EHA 2023. Abstr S191.

Elranatamab: Subcutaneously Administered CD3 x BCMA Bispecific Antibody

- **Indication:** R/R MM after ≥4 prior lines of therapy, including an IMiD, PI, and anti-CD38 mAb (accelerated approval)
- **MagnetisMM-3:** multicenter, open-label, single-arm phase II study of elranatamab in R/R MM
  - Cohort A: BCMA-directed therapy-naive R/R MM
  - Median follow-up: 14.7 mo

Outcome, mo (95% CI)	Cohort A (n = 123)
Median DoR	NR (NE-NE)
Median PFS	NR (9.9-NE)
Median OS	NR (13.9-NE)



Slide credit: clinicaleducationalliance.com:

cea clinical education alliance

Elranatamab: CRS and ICANS

- Only available through REMS to mitigate CRS and neurotoxicity risk

Cytokine-Release Syndrome	Neurotoxicity
▪ Rate of CRS: 58% (recurrent: 13%) – Step-up dose 1: 43% – Step-up dose 2: 19% – Initial treatment dose: 7% – Mostly grade 1 (44%) or grade 2 (14%) – <2% with subsequent doses – Median onset: 2 days (range: 1-9) – Median duration: 2 days (range: 1-19)	▪ Most frequent: headache (18%), sensory neuropathy (13%), encephalopathy (15%), and motor dysfunction (13%) ▪ Guillain-Barré syndrome: 0.5% ▪ ICANS: 3.3% (recurrent, 1.1%) – Step-up dose 1: 2.7% – Step-up dose 2: 0.5% – Subsequent doses: 0.5% – Median onset: 3 days (range: 1-4) – Median duration: 2 days (range: 1-18)

Elranatamab-bcmm PI.

Elranatamab: Other AEs of Interest

- Infection
  - Serious: 42%
  - Grade 3/4: 31%
  - Fatal: 7%
- Neutropenia
  - Any grade: 62%
  - Grade 3/4: 51%
  - Febrile: 2.2%
- Hepatotoxicity (elevated LFTs)
  - Any grade: 36%-40%
  - Grade 3/4: 3.8%-6%
  - Grade 3/4 elevated bilirubin: 0.5%

Elranatamab-bcmm PI.

Elranatamab: Dosing and Administration

- Hospitalization recommended for 48 hr after step-up dose 1 and 24 hr after step-up dose 2
- Premedication: PO acetaminophen 650 mg, PO/IV dexamethasone 20 mg, PO diphenhydramine 25 mg or an equivalent of each

Schedule	Day	Dose
Step-up		
▪ 1	1	12 mg SC
▪ 2	4	32 mg SC
▪ 3 (first treatment dose)	8	76 mg SC
Weekly dosing	1 wk after first treatment dose, then QW through Wk 24	76 mg SC
Biweekly dosing	At Wk 25, Q2W thereafter for those who achieve a response	76 mg SC

Elranatamab-bcmm PI.

Comparing Bispecific Antibodies for Multiple Myeloma

	Teclistamab	Talquetamab		Elranatamab
Target	CD3/BCMA	CD3/GPRC5D		CD3/BCMA
Dosing/Route	Weight-based/SQ	Weight-based/SQ		Fixed dosing/SQ
Schedule	C1: Days 1,4, 7 C2: Weekly* Biweekly dosing after ≥6 mo in ≥CR	Weekly	C1: Days 1,4, 7 C2+: Weekly	C1: Days 1,4,8 C2+: Weekly through Wk 24, then Q2W
		Biweekly	C1: Days 1,4, 7, 10 C2+: Biweekly	
Hospitalization	48 hr after all doses in step-up	48 hr after all doses in step-up		48 hr after 1st step-up dose and 24 hr after 2nd step-up dose
Efficacy	ORR: 63%; CR 45.5%	ORR: ~70% CR: ~35%		ORR: 61% CR: 35%
CRS Occurrence	72%: Gr 1: 50% Gr 2: 21%	76%: Gr 1: 57% Gr 2: 17%		58%: Gr 1: 44% Gr 2: 14%
ICANS Occurrence	Gr 1/2: 3% Gr 3/4: 0%	Gr 1/2: 3% Gr 3/4: 3%		Gr 1/2: 3% Gr 3/4: 0%
Neutropenia	Gr 3/4: 56%	Gr 3/4: 35%		Gr 3//4: 51%
Infection	Gr 3/4: 35%	Gr 3/4: 17%		Gr 3/4: 31%
Skin/Nail Toxicity		62%		
Oral Toxicity		80% (dysgeusia: 49%, dry mouth: 34%, dysphagia: 23%, ageusia: 18%)		

Moreau. NEJM. 2022;387:495. Teclistamab-cqyv PI. van de Donk. ASCO 2023. Abstr 8011. Chari. NEJM. 2022;387:2232. Talquetamab-tgvs PI. Touzeau. EHA 2023. Abstr S191. Elranatamab-bcmm PI. Lesokhin. Nat Med. 2023;29:2259.

Choosing Between Bispecific Antibodies for MM

- **Target:** Talquetamab is the only GPRC5D-targeting therapy and is a clear choice for patients progressing on BCMA-targeted therapy
  - Emerging data on BCMA antigen escape as a mechanism of resistance to bispecific therapies like elranatamab and teclistamab
  - Different point mutations on the BCMA extracellular domain can have variable effects on the binding affinity for elranatamab and teclistamab
    - Just because one BCMA-directed bispecific doesn't work, doesn't mean that another one won't
- **Dosing:** Teclistamab and talquetamab use weight-based dosing, while elranatamab dosing is fixed
  - Potential for overtreating?
- **Hospitalization:** Less hospitalization recommended with elranatamab (48 hr after step-up dose 1 and 24 hr after step-up dose 2, followed by outpatient administration)
  - Teclistamab and talquetamab require hospitalization for 48 hr after each step-up dose (includes first treatment dose)
  - From a bed and resource utilization standpoint, elranatamab would be favored

Slide credit: clinicaleducationalliance.com:

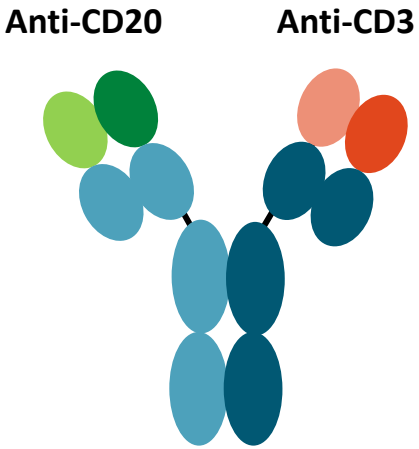
Elranatamab-bcmm PI. Lee. Nat Med. 2023;29:2295. Teclistamab-cqyv PI. Talquetamab-tgvs PI.

Bispecific Antibodies in B-Cell Lymphomas

Mosunetuzumab: CD20-Directed CD3 T-Cell Engager

- **Indication:** R/R FL after ≥2 lines of therapy (accelerated approval)
- **MoA:** Binds CD20 on B-cells and CD3 on T-cells
- **NCT02500407:** Multicenter, open-label, pivotal phase I/II dose escalation trial in NHL and CLL (n = 90 patients with R/R FL)
  - Median follow-up: 37.4 mo

Outcome, Mo	Mosunetuzumab Monotherapy (n = 90)
ORR, %	77.8
CR, %	60.0
Median DoCR	NR
Median DoR	35.9
Median PFS	24.0
Median OS	NR



Mosunetuzumab (IV/SC)

Mosunetuzumab-axgb PI. NCT02500407. Schuster. ASH 2023. Abstr 603.

Mosunetuzumab: AEs of Interest

- CRS:
  - Any grade: 39%
  - Grade 1: 28%
  - Grade 2: 15%
  - Most CRS with 1 mg on cycle 1 Day 1 (15%), 2 mg on cycle 1 Day 8 (5%), and 60 mg on cycle 1 Day 15 (33%)
  - Median time to onset of from cycle 1 Day 15: 25 hours
  - Median duration of CRS: 3 days, range 1 to 29 days
- Neurotoxicity:
  - Any grade: 39%
  - ICANS: 1% (grade 1 or 2)
- Cytopenia (Grade 3/4):
  - Neutropenia: 38%
  - Anemia: 19%
  - Thrombocytopenia: 12%
- Tumor flare:
  - Any grade: 4%
- Infection:
  - Serious: 17%
  - Fatal: 0.9%

Mosunetuzumab-axgb PI.

Mosunetuzumab: Dosing and Administration

- Intravenously administered in 21-day cycles for 8-17 cycles total, no hospitalization required
  - If CR after cycle 8, discontinue treatment
  - If PR after cycle 8, continue through cycle 17

Treatment Cycle	Day	Dose	IV Infusion Rate	Premedication
Cycle 1	1 8 15	1 mg IV 2 mg IV 60 mg IV	≥4 hr	▪ IV dexamethasone 20 mg or methylprednisolone 80 mg ≥1 hr before infusion ▪ IV/PO diphenhydramine hydrochloride 50-100 mg (or equivalent) ▪ PO acetaminophen 500-1000 mg ≥30 min before infusion
Cycle 2	1	60 mg IV	2 hr if previous dose tolerated	▪ Same as cycle 1
Cycle 3+	1	30 mg IV	2 hr if previous dose tolerated	▪ Same as cycle 1 for any grade CRS with prior dose

Mosunetuzumab-axgb PI.

Slide credit: clinicaleducationalliance.com:

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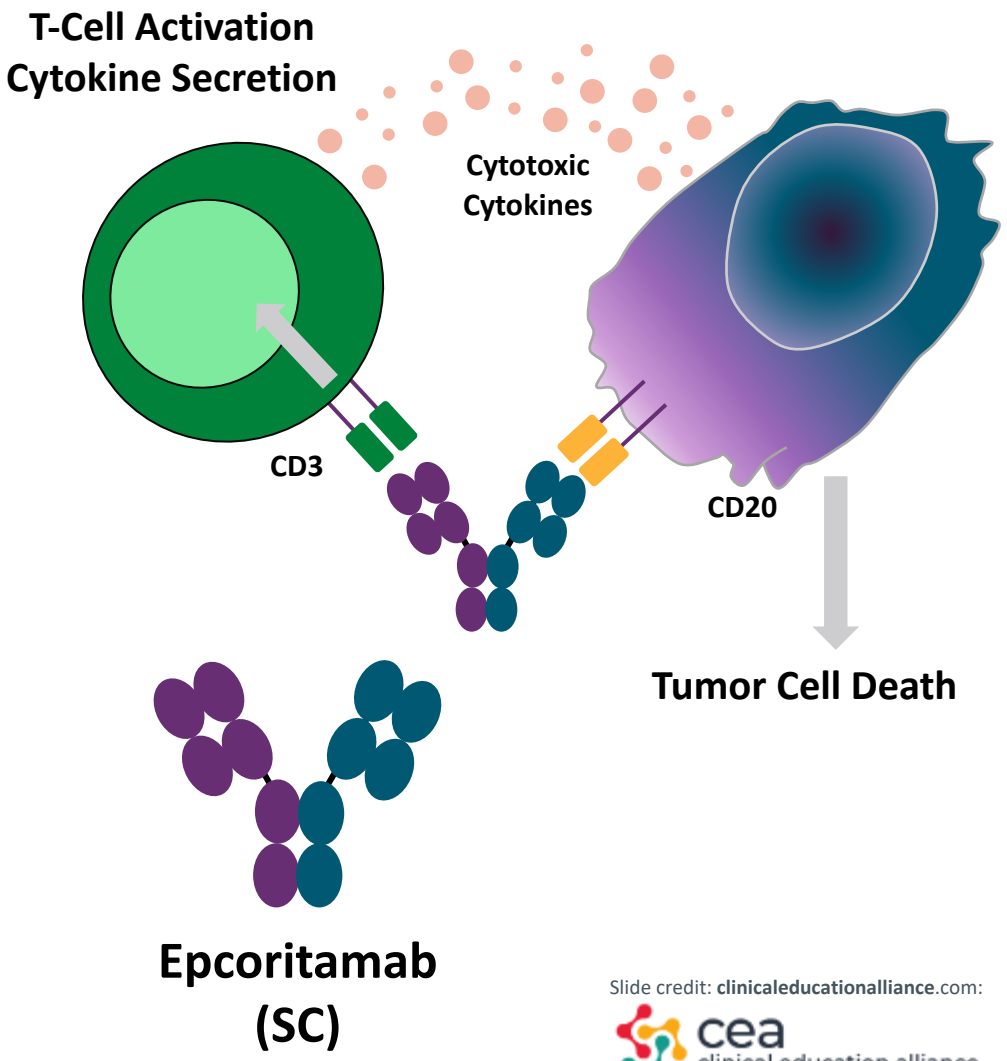
Epcoritamab: Subcutaneously Administered CD20-Directed CD3 T-Cell Engager

- **Indication:** R/R DLBCL, tFL, or high-grade B-cell lymphoma after ≥2 prior lines of therapy (accelerated approval)
- **EPCORE NHL-1:** multicenter, single-arm, dose-escalation/expansion phase I/II study in R/R or PD B-cell lymphoma
  - Median follow-up: 20 mo

Outcome	LBCL (N = 157)
ORR, %	63
CR, %	39
PR, %	24
Median time to CR, mo	2.7
Median PFS,* mo	4.4
Median DoR,* mo	15.5
Median OS,* mo	18.5

*Not reached in patients with CR.



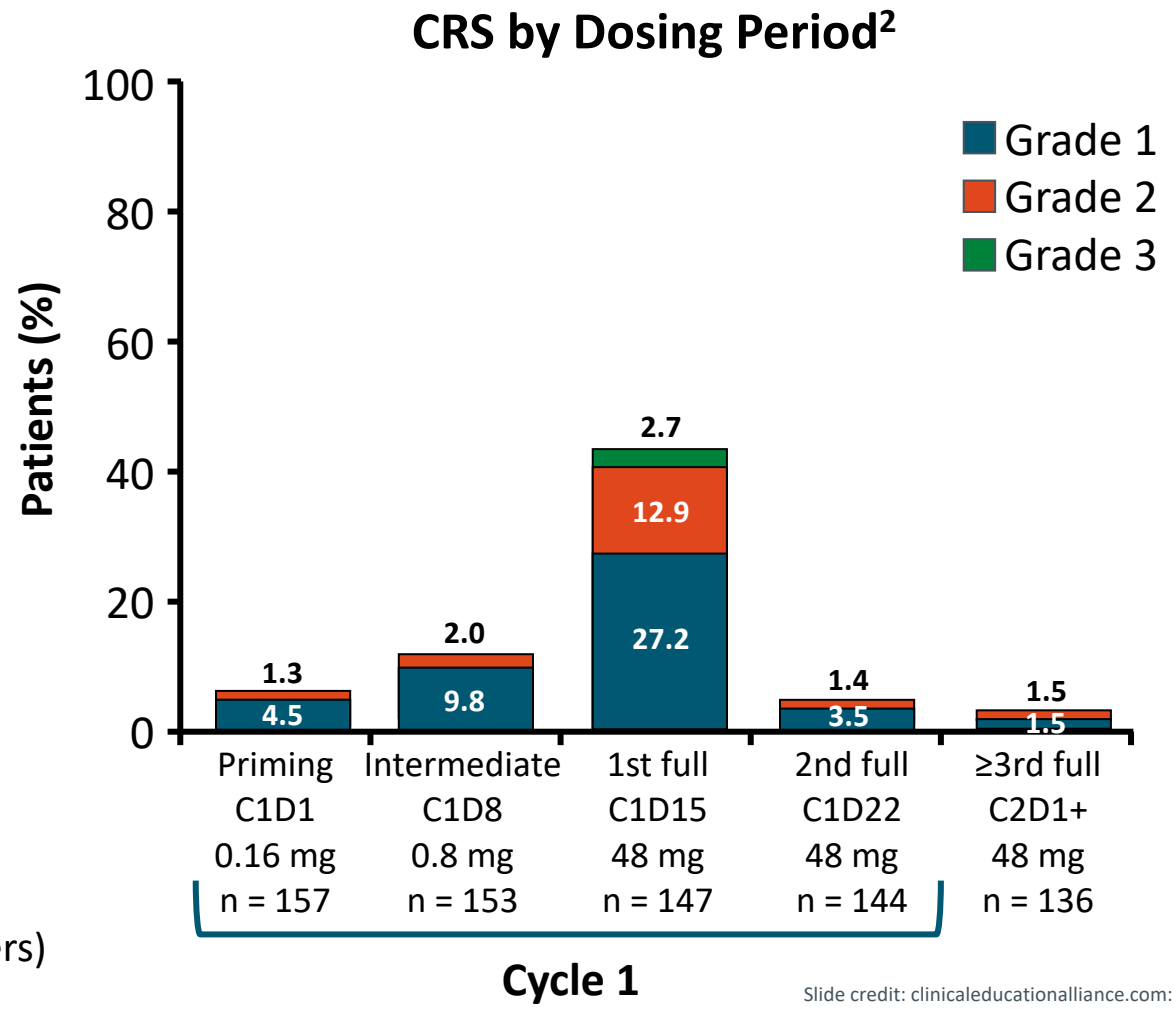
Slide credit: clinicaleducationalliance.com:

Epcoritamab-bysp PI. Karimi. ASCO 2023. Abstr 7525. Thieblemont. JCO. 2023;41:2238.

Epcoritamab: CRS and Neurotoxicity in EPCORE NHL-1

CRS Parameter,[1] n (%)	LBCL (N = 157)
Events	80 (51)
▪ Grade 1	50 (32)
▪ Grade 2	25 (16)
▪ Grade 3	5 (3)
Resolution, n/n (%)	79/80 (99)
Median onset from first full dose, hr	20
Median duration, days (range)	2 (1-27)
Received anticytokine treatment	23 (15)
Led to treatment discontinuation	1 (1)

- Median follow-up: 20 mo
- Tocilizumab primarily used to address grade 2/3 CRS
- **ICANS**: 6.4%[2,3]
  - Median follow-up: ~11 mo
  - All grade 1/2, except 1 grade 5 (with multiple confounders)



Slide credit: clinicaleducationalliance.com:

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1. Karimi. ASCO 2023. Abstr 7525. 2. Thieblemont. EHA 2022. Abstr LBA 2364. 3. Thieblemont. JCO. 2023;41:223.

Epcoritamab: Other AEs of Interest

- Cytopenias (grade 3/4):
  - Neutropenia: 32%
  - Anemia: 12%
  - Thrombocytopenia: 12%
  - Febrile neutropenia: 2.5%
- Infection
  - Serious: 15%
  - Fatal: 1.3%

Epcoritamab-bysp PI.

Epcoritamab Dosing and Administration

- Administered in 28-day cycles for ≥10 cycles total
- Hospitalization recommended for 24 hr after C1D15 dose

Treatment Cycle	Day	Dose	Premedication
Cycle 1 ▪ Step-up dose 1 ▪ Step-up dose 2 ▪ Step-up dose 3 (first full dose) ▪ Target dose	 1 8 15 22	 0.16 mg SC 0.8mg SC 48 mg SC 48 mg SC	▪ PO/IV prednisolone 100 mg or dexamethasone 15 mg (or an equivalent) for 30-120 min before weekly administration *and* for 3 consecutive days after each dose ▪ PO/IV diphenhydramine 50 mg and PO acetaminophen 650-1000 mg for 30-120 min before weekly administration
Cycle 2-3	1, 8, 15, 22	48 mg SC	▪ *For grade 2/3 CRS with prior dose:* PO/IV prednisolone 100 mg or dexamethasone 15 mg (or an equivalent) for 30-120 min before weekly administration *and* for 3 consecutive days after dose
Cycle 4-9	1, 15	48 mg SC	▪ Same as cycle 2-3
Cycle 10 and beyond	1	48 mg SC	▪ Same as cycle 2-3

Epcoritamab-bysp PI.

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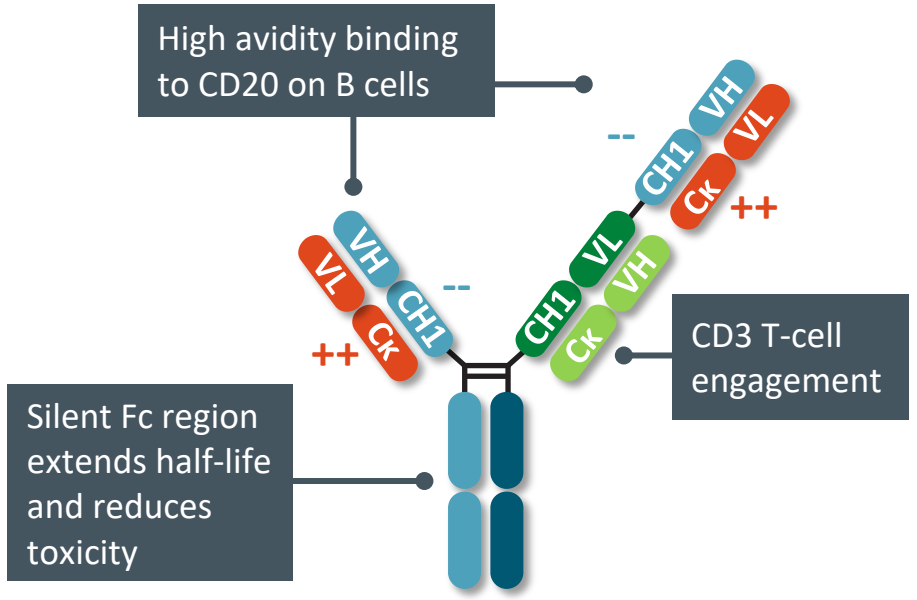
Glofitamab: CD20-Directed CD3 T-Cell Engager

- Unique 2:1 molecular configuration allows “double binding” to CD20 (highlighted in the blue zones)
- **Indication**: R/R DLBCL or tFL after ≥2 prior lines of therapy (accelerated approval)
- **NCT03075696:** Multicenter, open-label phase I/II trial in R/R large B-cell lymphoma
  - Median follow-up: 18.3 mo

Outcome	LBCL (n = 154)
ORR, %	52
CR, %	40
Median DoCR, mo	26.9
18-mo OS, %	41



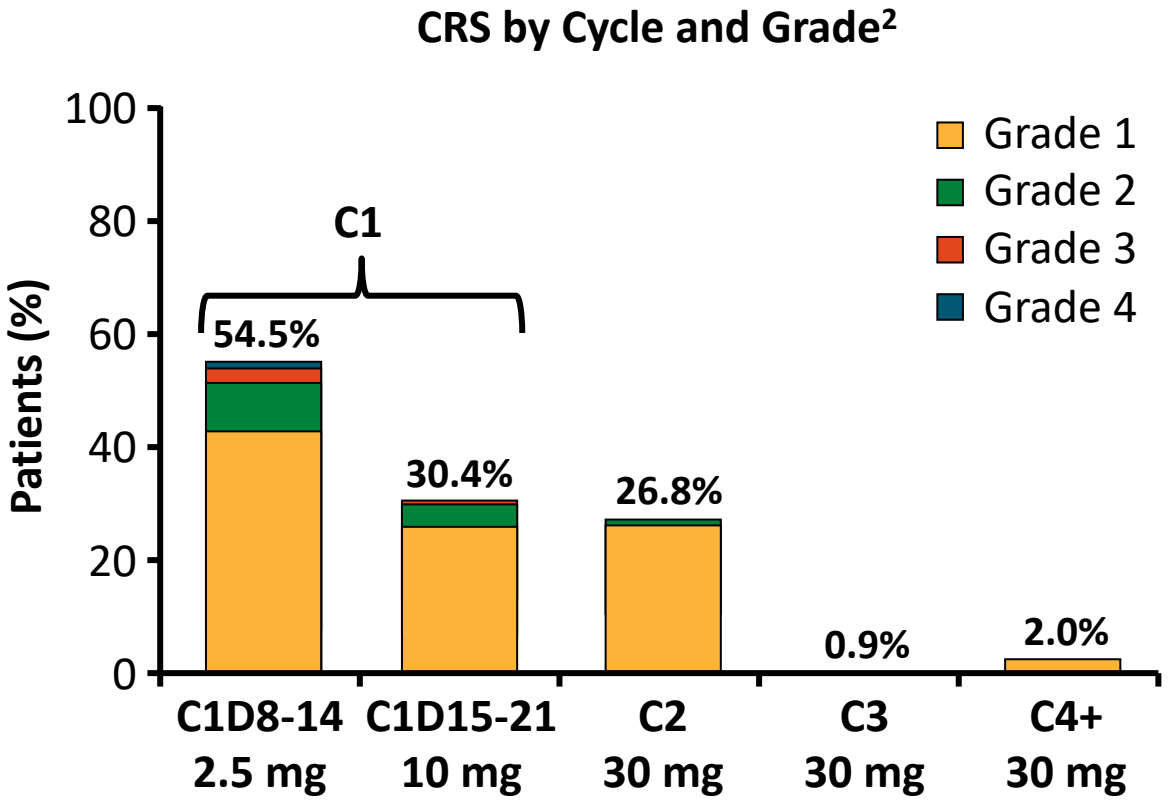
Slide credit: **clinicaleducationalliance**.com:

cea clinical education alliance

Bacac. Clin Cancer Res. 2018;24:4785. Falchi. ASCO 2023. Abstr 7550. Glofitamab-gxbm PI. NCT03075696.

Glofitamab: CRS and Neurotoxicity

CRS Parameter[1,2]	LBLC (N = 154)
CRS, % ▪ Grade 1 ▪ Grade 2 ▪ Grade 3 ▪ Grade 4	64 48 12 3 1
Median onset after C1D8 dose, hr (range)	13.5 (6.0-52.0)
Median duration, hr (range)	30.5 (0.5-317.0)
Treated with corticosteroids, n/N (%)	27/97 (27.8)
Treated with tocilizumab, n/N (%)	31/97 (32.0)
ICANS, n (%) ▪ Grade ≥3	12 (8.0) 4 (3.0)



Slide credit: clinicaleducationalliance.com:

cea clinical education alliance

1. Falchi. ASCO 2023. Abstr 7550. 2. Dickinson. NEJM. 2022;387:2220.

Glofitamab: Other AEs of Interest

- Cytopenias (grade 3/4):
  - Neutropenia: 26%
  - Anemia: 8%
  - Thrombocytopenia: 8%
  - Lymphopenia: 83%
- Infection:
  - Serious: 16%
  - Fatal: 4.8%

- Tumor flare:
  - Any grade: 12%
  - Most occurred in cycle 1
  - Median onset after first dose: 2 days (range: 1-16)
  - Median duration: 3.5 days (range: 1-35)

Glofitamab-gxbm PI.

Glofitamab: Dosing & Administration

- Intravenously administered in 21-day cycles for 12 cycles
- Hospitalization recommended for 24 hr after step-up dose 1 and if CRS with prior dose

Treatment Cycle	Day	Dose	Infusion Duration	Premedication
Cycle 1	1	Obinutuzumab 1,000 mg at 50-400 mg/hr (deplete circulating B-cells)		▪ N/A
▪ Step-up dose 1 ▪ Step-up dose 2	8 15	2.5 mg IV 10 mg IV	4 hr 4 hr†	▪ IV dexamethasone* 20 mg completed ≥1 hr before infusion ▪ PO/IV diphenhydramine 50 mg (or an equivalent) and PO acetaminophen 500-1000 mg ≥30 min before infusion
Cycle 2	1	30 mg IV	4 hr†	▪ Same as Cycle 1 Day 8 and 15 guidance
Cycle 3	1	30 mg IV	2 hr‡	▪ Same as Cycle 1 Day 8 and 15 guidance
Cycle 4-12	1	30 mg IV	2 hr‡	▪ PO/IV diphenhydramine 50 mg (or an equivalent) and PO acetaminophen 500-1000 mg ≥30 min before infusion ▪ *If CRS occurred with previous dose,* add IV dexamethasone* 20 mg completed ≥1 hr before infusion

*If dexamethasone unavailable, administer IV prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg. †Infusion time may be extended to up to 8 hr, if CRS occurred with previous dose. ‡Infusion time should be kept at 4 hours, if CRS occurred with previous dose.

Glofitamab-gxbm PI.

Choosing Between Glofitamab vs Epcoritamab for DLBCL

- Safety and efficacy were similar in pivotal trials
- Inpatient observation recommended for both
- Glofitamab has a fixed duration (21-day cycle x 12) and less frequent administration
- Glofitamab does not require steroids for CRS mitigation

Epcoritamab-bysp PI. Glofitamab-gxbm PI.

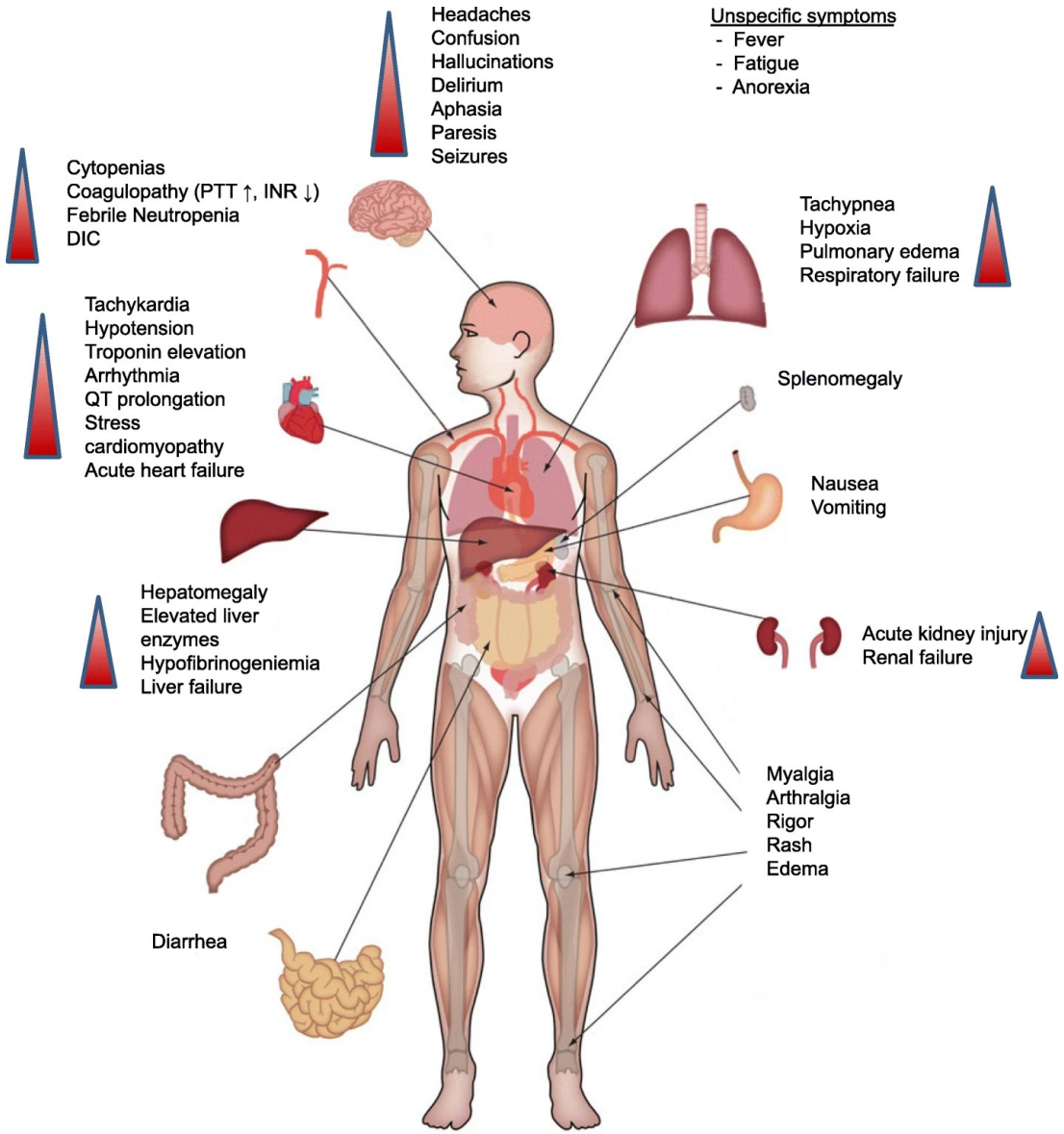
Bispecific Antibodies Adverse Events

Summary of Key AEs With Bispecific Antibodies

- Cytokine-release syndrome
  - American Society of Transplant and Cellular Therapy grading
  - Incidence and timing of onset vary by disease subtype, product, administration route, and dosing schedule
  - Incidence across products: 40%-65%
    - Grade 1/2: 43%-70%
    - Grade 3/4: 2%-4%
- Neurotoxicity: immune effector–cell associated neurotoxicity syndrome
  - Incidence across products: 1%-8%
- Cytopenias/infections
- Tumor flare (with FL and DLBCL FDA-approved bispecific antibodies)
- Hypersensitivity reactions

Cytokine Release Syndrome (CRS)

"**Supraphysiologic** response following **any immune** therapy that results in the activation or engagement of **endogenous or infused T cells and/or other immune effector cells**." Immune efector cell associated neurotoxicity should be excluded from the definition of CRS.


Headaches
Confusion
Hallucinations
Delirium
Aphasia
Paresis
Seizures
Unspecific symptoms
- Fever
- Fatigue
- Anorexia
Cytopenias
Coagulopathy (PTT ↑, INR ↓)
Febrile Neutropenia
DIC
Tachypnea
Hypoxia
Pulmonary edema
Respiratory failure
Tachykardia
Hypotension
Troponin elevation
Arrhythmia
QT prolongation
Stress cardiomyopathy
Acute heart failure
Splenomegaly
Nausea
Vomiting
Hepatomegaly
Elevated liver enzymes
Hypofibrinogeniemia
Liver failure
Acute kidney injury
Renal failure
Myalgia
Arthralgia
Rigor
Rash
Edema
Diarrhea

GRADING OF CYTOKINE RELEASE SYNDROME

(Assess daily and any time there is a change in patient status)

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temp ≥ 38 °C	Temp ≥ 38 °C	Temp ≥ 38 °C	Temp ≥ 38 °C
With either:				
Hypotension	**None**	Not requiring vasopressors	Requiring one vasopressor (with or without vasopressin)	Requiring multiple vasopressor (excluding vasopressin)
†And/or:				
Hypoxia	**None**	Requiring low flow nasal cannula	Requiring high flow nasal cannula, facemask, nonrebreather mask or Venturi mask	Requiring positive pressure (eg: CPAP, BiPAP, intubation and mechanical ventilation)

Adapted from Lee DW, et al. Biol Blood Marrow Transplant. 2018 Dec 25

† CRS grade is determined by the most severe event: hypotension or hypoxia not attributable to any other cause

Organ toxicities associated with CRS may be graded according to CTCAE v5.0, but do not influence CRS grading.

MANAGEMENT OF CYTOKINE RELEASE SYNDROME

CRS Grade	Sign or Symptom	Management
Grade 1	**Fever**	• Symptomatic management of constitutional symptoms and organ toxicities • Acetaminophen and hypothermia blanket as needed for fever • Assess for infection, empiric broad spectrum antibiotics • IV fluids as needed • Consider tocilizumab for persistent fever lasting >3 days in patients with significant comorbidities or if patient is deteriorating
Grade 2 All Grade 2 require: Cardiac telemetry and pulse oximetry, consider ECHO	**Hypotension** *Not requiring vasopressors* **Hypoxia** *(Low-flow nasal cannula: O2 delivered at < 6 L/min)*	• Supportive care as in grade 1 • IV fluid bolus of NS 500-1000 mL • For hypotension: consider tocilizumab 8 mg/kg IV +/- dexamethasone 10 mg IV x one • If no response, consider redosing tocilizumab 8 mg/kg IV (may be repeated every 8 h for up to 3 doses in a 24 h period) • If hypotension persists after fluids boluses or If oxygen requirement increases and 1-2 doses of tocilizumab, or if patient is not improving or deteriorating: Consider dexamethasone 10 mg IV every 6 hours. Manage as grade 3 CRS (start vasopressors, transfer to ICU and obtain ECHO) Symptomatic management of constitutional symptoms and organ toxicities Supplemental oxygen as needed

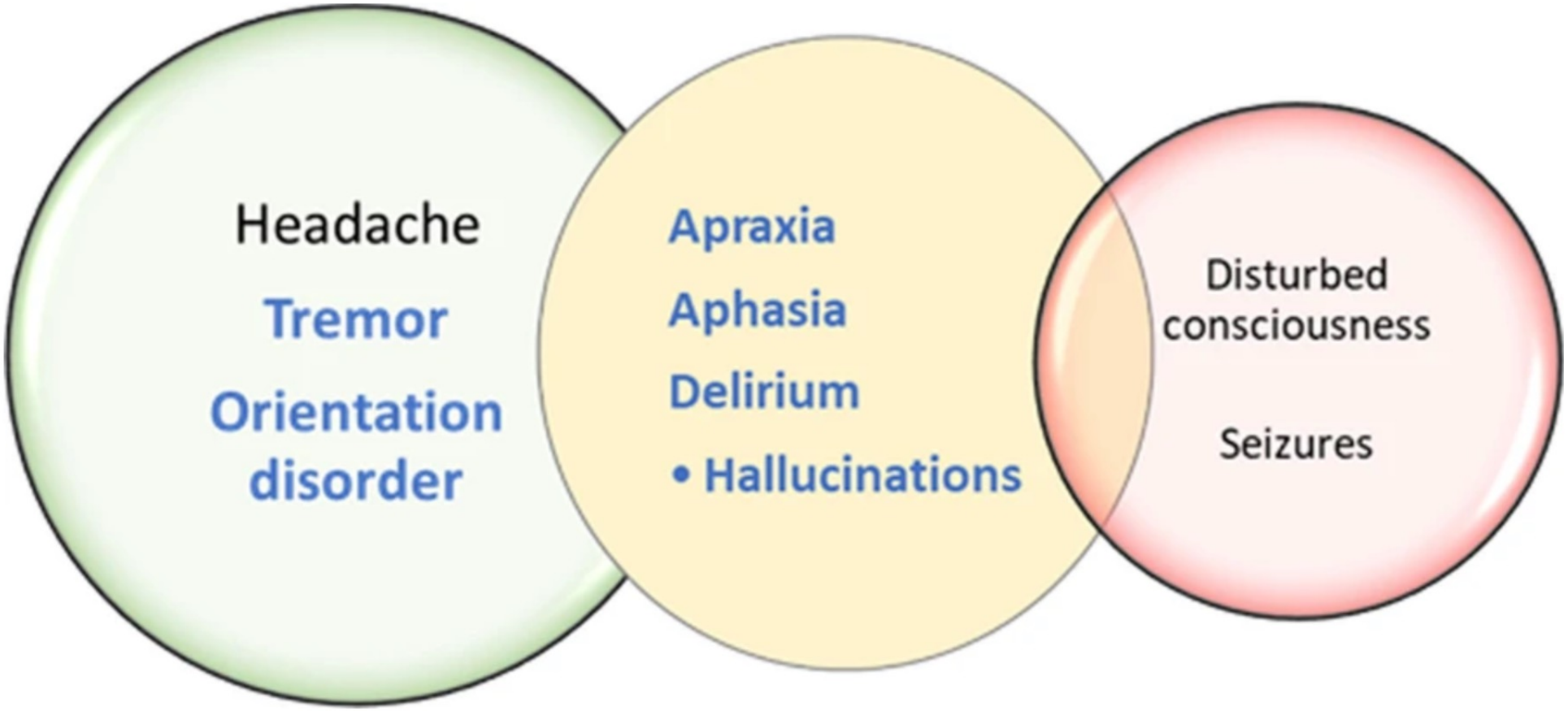
Adapted from Neelapu S, et al. Nat Rev Clin Oncol. 2018;15:47-62, Lee DW, et al. Biol Blood Marrow Transplant. 2018 Dec 25.
High risk for CRS: bulky disease, co-morbidities, early onset of CRS within 3 days of infusion.

MANAGEMENT OF CYTOKINE RELEASE SYNDROME

CRS Grade	Sign or Symptom	Management
Grade 3	**Hypotension** *Requiring one vasopressor +/- vasopressin* **Hypoxia** *(High-flow nasal cannula: O2 delivered at >6 L/min)*	• Supportive care as in grades 1 & 2 • IV fluid boluses as needed, vasopressors as needed • Transfer to ICU, obtain ECHO if not performed already • Tocilizumab if not administered previously as grade 2 • Start dexamethasone 10 mg IV every 6 hours if not started previously. Alternatively, methylprednisolone 1 mg/kg IV every 12 hours may be used. • Symptomatic management of constitutional symptoms and organ toxicities.
Grade 4	**Hypotension** *Requiring multiple vasopressors* **Hypoxia** *Requiring positive pressure*	• Supportive as in grade 2 • Vasopressors, tocilizumab and ECHO as above • Supplemental oxygen requiring positive pressure ventilations: (CPAP, BiPAP, intubation and mechanical ventilation) • Consider changing corticosteroids to high dose methylprednisolone 1000mg/day IV • Symptomatic management of constitutional symptoms and organ toxicities

Adapted from Neelapu S, et al. Nat Rev Clin Oncol. 2018;15:47-62, Lee DW, et al. Biol Blood Marrow Transplant. 2018 Dec 25.
High risk for CRS: bulky disease, co-morbidities, early onset of CRS within 3 days of infusion.

Neurotoxicity



IMMUNE EFFECTOR CELL-ASSOCIATED ENCEPHALOPATHY (ICE) ASSESSMENT SCORE

	Task	Points
Orientation	**Orientation to year, month, city, hospital**	**4**
Naming	**Name 3 objects (e.g., point to clock, pen, button)**	**3**
Commands	**Following commands (e.g., show me 2 fingers or close your eyes and stick out your tongue)**	**1**
Writing	**Ability to write a sentence**	**1**
Attention	**Count backwards from 100 by 10**	**1**
Total		**10**

IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME (ICANS)

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE Score	**7-9**	**3-6**	**0-2**	**0 (patient is unarousable and unable to perform ICE)**
Depressed level of consciousness	**Awakens spontaneously**	**Awakens to voice**	**Awakens only to tactile stimulus**	**Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse.** Stupor or coma
Seizure	**N/A**	**N/A**	**Any clinical seizure focal or generalized that resolves rapidly; or Non- convulsive seizures on EEG that resolve with intervention**	**Life-threatening prolonged seizure (>5 min); or** Repetitive clinical or electrical seizures without return to baseline in **between.**
Motor findings	**N/A**	**N/A**	**N/A**	**Deep focal motor weakness such as hemiparesis or paraparesis**
Raised ICP/ Cerebral edema	**N/A**	**N/A**	**Focal/local edema on neuroimaging**	**Diffuse cerebral edema on neuroimaging; Decerebrate or decorticate posturing; or Cranial nerve VI palsy; or Papilledema; or Cushing's triad**

Adapted from Lee DW, et al. Biol Blood Marrow Transplant. 2018 Dec 25.

•Tremors and myoclonues associated with IEC therapies may be graded according to CTCAE v5.0, but no not influence ICAN grading.

•Intracranial hemorrhage is not considered a neurotoxicity feature and should only be graded according to CTCAE v5.0.

MANAGEMENT OF IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Grade	Management
Grade 1 • ICE score 7-9 and/or depressed level of consciousness but awakens spontaneously. • No seizures, motor weakness, or raised ICP/cerebral edema.	• Vigilant supportive care, aspiration precautions. • Consider neurology consultation. Seizure prophylaxis with levetiracetam. • Consider EEG or Imaging of the brain. • Consider tocilizumab if there is concurrent CRS. • Consider administering Dexamethasone 10mg. intravenously, for both concurrent & non-concurrent CRS. • If not improving after 2 days, consider repeating dexamethasone 10 mg intravenously, for both concurrent & non-concurrent CRS.
Grade 2 • ICE score 3-6 and/or depressed level of consciousness but awakens to voice. • No seizures, motor weakness, or raised ICP/cerebral edema.	• Dexamethasone 10 mg IV every 6 hours. • If associated with concurrent CRS add tocilizumab 8 mg/kg IV x one Neurology consultation. • EEG, MRI brain. • Consider lumbar puncture as per table.

MANAGEMENT OF IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Grade 3 • ICE score 0-2 and/or depressed level of consciousness but awakens to tactile stimulus. • Any clinical seizure focal or generalized that resolves rapidly, or non-convulsive seizure on EEG that resolve with intervention. • No motor weakness. • Focal/local edema on neuroimaging.	• Consider ICU transfer. • Corticosteroids and/or tocilizumab (if associated with CRS) if not previous administered. • Consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent grade >3 ICANS. • Control seizures with benzodiazepines (for short-term control) and levetiracetam +/- phenobarbital and/or lacosamide. • Consider High-dose methylprednisolone 1000 mg/day.
Grade 4 • ICE score 0 and patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse or stupor or coma. • Life-threatening prolonged seizure (>5 minutes), or repetitive clinical or electrical seizures without return to baseline in between. • Deep focal motor weakness such as hemiparesis or paraparesis. • Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad.	• ICU monitoring, consider mechanical ventilation for airway protection. • Methylprednisolone 1000 mg/day IV continued until improvement to grade 1 and then taper. • Consider high-dose methylprednisolone 1000 mg/twice per day. If not improving, consider 1000 mg 3 times per day or alternate therapy (anakinra, siltuximab, ruxolitinib, cyclophosphamide, IVIG, and ATG). • Control seizures with benzodiazepines (for short-term control) and levetiracetam +/- phenobarbital and/or lacosamide. • Imaging of spine for focal motor weakness. • Lower ICP by hyperventilation, hyperosmolar therapy with mannitol/hypertonic saline, and/or neurosurgery consultation for ventriculoperitoneal shunt in patients with cerebral edema.

MANAGEMENT OF IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Diagnostic Considerations for Neurotoxicity
• Fundoscopic exam to assess for papilledema if possible • MRI brain with and without contrast • CT of the brain may be performed if MRI brain is not feasible • Diagnostic lumbar puncture • MRI spine if the patient has focal peripheral neurological deficits • Daily EEG until toxicity symptoms resolve; if no seizures detected on EEG, continue levetiracetam prophylaxis 750 mg every 12 hours
Other Supportive Care Considerations
• Seizure prophylaxis with levetiracetam 750 mg by mouth every 12 hours from day -1 to day 30 • Elevate head of the patient's bed by at least 30 degrees to minimize aspiration risks and to improve cerebral blood flow • Withhold oral intake of food, medicines, and fluids, and assess swallowing • Convert all oral medications and/or nutrition to IV if swallowing is impaired • Avoid medications that cause central nervous system depression • Lorazepam or haloperidol may be used for agitated patients with careful monitoring

Monitoring and Managing Cytopenias

- Monitor CBC at baseline and periodically during treatment
- Withhold agent if severe anemia, thrombocytopenia, and neutropenia per PI
- Severe and long-lasting neutropenia poses increased infection risk
  - Administer appropriate infection prophylaxis
- Administer growth factor support per institutional guidelines

Crombie. Blood. 2024;143:1565. Ludwig. Lancet Oncol. 2023;24:e255.

Infection Prophylaxis and Vaccinations

- Complete outstanding vaccinations ≥2 wk prior to therapy start (eg, influenza, pneumococcal, COVID-19)
  - Delay postinfusion vaccinations for 3-6 mo after chemotherapy
- Optimal prophylaxis duration has not been established, but recommended for up to 6 months following treatment
- Monitor immunoglobulin levels

Antibacterial Prophylaxis	Antiviral Prophylaxis	Antifungal Prophylaxis
Recommend for patients at high risk of infection	HSV/VZV prophylaxis in all patients	▪ PJP prophylaxis recommended ▪ Other antifungal prophylaxis recommended for patients at high risk of fungal infection

Crombie. Blood. 2024;143:1565. Ludwig. Lancet Oncol. 2023;24:e255. Raje. Blood Ca J. 2023;13:116.

Managing Infections Associated With Bispecific Antibodies

- Withhold until resolution; consider permanent discontinuation for grade 4 infections
- Manage infections in accordance with institutional policies and susceptibility patterns
  - Consult with infectious diseases specialist
- Utilize targeted therapy if the infectious organism can be identified
- Consider IVIG for recurrent infections in accordance with institutional policies

Bacterial Infections	Viral Infections	Fungal Infections
▪ Empiric antibacterial agents based on infection site ▪ Concomitant neutropenia: broad spectrum agents (third- or fourth-generation cephalosporin or carbapenem) ▪ Reserve vancomycin for specific indications	▪ Management based on type of virus and institutional protocol ▪ Examples include influenza, VZV, CMV, EBV, RSV, COVID-19	▪ Localized candidiasis: fluconazole ▪ Invasive candidiasis: echinocandin ▪ PJP: trimethoprim-sulfamethoxazole or atovaquone or primaquine with sulfonamide

Crombie. Blood. 2024;143:1565. Ludwig. Lancet Oncol. 2023;24:e255. Raje. Blood Ca J. 2023;13:116.

Managing Talquetamab Skin and Nail Toxicities

- Rash, hand–foot syndrome, pruritus, nail dystrophy:
  - Warn patient of possible palmar/plantar desquamation
  - Ammonium lactate lotion for peeling
  - Heavy moisturizers (eg, petroleum based)
  - Nail hardeners, no nail soaks
  - Lukewarm/cool showers
  - Steroid creams (triamcinolone)
  - Antihistamine for pruritus
  - Adequate hydration
  - Dermatology consultation

Aronson. IMS 6th Annual Nursing Symposium 2022. Abstr NS-001. Mancia. Blood. 2021;138(suppl 1): 1658.

Managing Talquetamab Oral Toxicities

- Dysphagia, dysgeusia, dry mouth
  - Early treatment of candidiasis (glossitis, “burning”)
  - Saliva substitutes
  - Mouth moisturizers
  - Zinc
  - Hydration
  - Good oral hygiene; mouth rinses
  - Eating in upright position

Aronson. IMS Annual Nursing Symposium 2022. Abstr NS-001. Mancia. Blood. 2021;138(suppl 1): 1658.

Patient Communication Recommendations

- Patients and caregivers should be educated on the signs/symptoms of CRS and neurotoxicity, when to contact their HCP, and when to present to the ED
- CRS: at-home monitoring for signs of hypoxia/hypotension, changes in body temperature, blood pressure, pulse oximetry
  - Monitor body temperature 3x/day for 2 days after step-up doses that are provided in the outpatient setting
- Neurotoxicity: monitor for confusion, changes in speech, trouble staying awake, seizures, abnormal actions
- Providing a wallet card with contact information is *strongly* recommended

Crombie. Blood. 2024;143:1565.

Use of Bispecific Antibodies in Puerto Rico

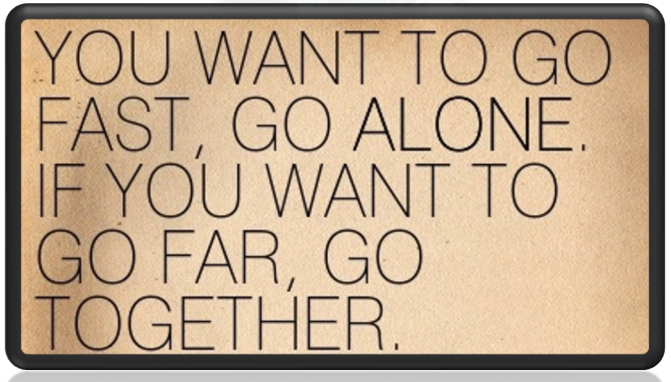
- **Blinatumomab (since 2017)**
  - Most experience in Acute Leukemia Units (Academic Centers)
  - Patient need to be admitted for 28 days
  - No center or specialized pharmacy providing 7-days infusion
- **Newer Bispecific Antibodies (since 2023)**
  - Most patients treated initially at Hospital Auxilio Mutuo
    - Admitted at BMT Unit during first doses (CRS and ICANS monitoring)
    - Some lymphoma patients treated under Clinical Trials – Outpatient dosing
  - Few able to continue their treatment at community oncology practices
- **No major issues with Healthcare insurance approval**
- **Availability at several local Specialty Pharmacies**

Success Stories with Use of Bispecific Antibodies in PR

Teclistamab Patient

Blinatumomab Patient

THANKS



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