Understanding and Managing Immune Effector Cell Toxicities in Hematologic Malignancies in 2024

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Objectives & Disclosure

Assess the risk for immune effector toxicity associated with therapies for hematologic malignancies

Propose a strategy to manage a patient experiencing immune effector toxicity

Disclosure

- *I have no conflicts of interest to disclose*
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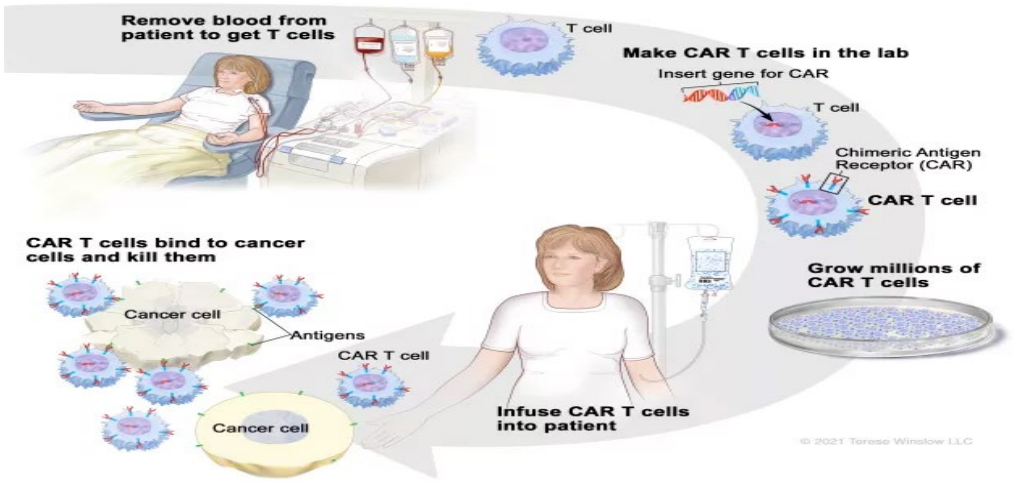
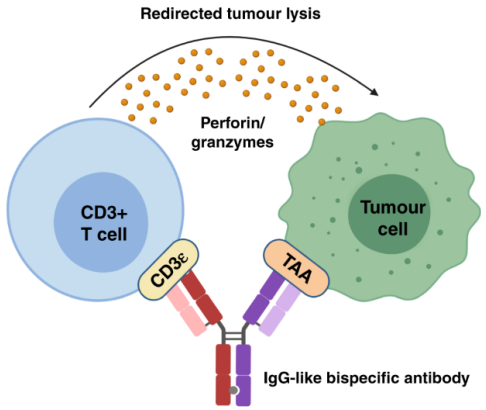
Immune Effector Cell Toxicity

Chimeric Antigen Receptor T-Cell (CAR T-cell)



https://www.cancersupportcommunity.org/car-t-cell-therapy

Bispecific T-Cell Engager (BTCE)



CD3 bispecific T-cell redirection mechanism of action in cancer immunotherapy

Br J Cancer. 2021;124:1037-1048

Cytokine Release Syndrome (CRS)	Immune Effector Cell – Associated Neurotoxicity Syndrome (ICANS)
• Fevers, chills, tachycardia, hypotension, hypoxia, capillary leak, organ dysfunction, hemophagocytic lymphohistiocytosis/ macrophage activation syndrome (HLH/MAS)	• Encephalopathy, delirium, hallucinations, cognitive defects, tremors, ataxia, dysphasia, nerve palsies, focal motor or sensory deficits, myoclonus, somnolence, obtundation, seizures

• Infused T-cells or activated t-cells, host immune effector cells, and/or vascular endothelial activation result in:
  • Hyperinflammation
  • Overproduction of inflammatory cytokines (IL-6, IL-1, INFγ, TNFα)
	• Systemic hyperinflammation affects blood-brain barrier + increased vascular permeability result in:
	  • Accumulation of cytokines (IL-6, INFγ, TNFα) host-immune cells, and CAR T-lymphocytes in brain

Blood Reviews. 2019;34:45-55

https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

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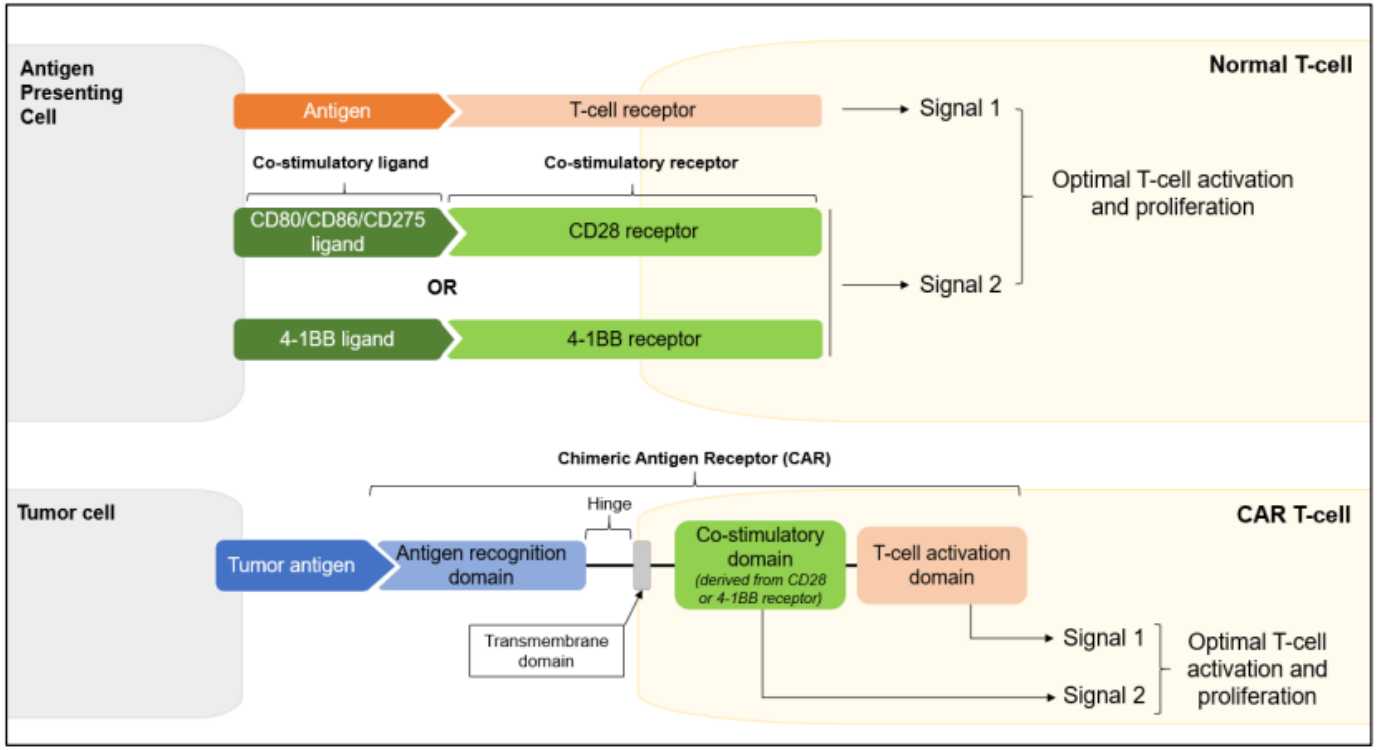
Chimeric Antigen Receptor (CAR) T-cell Therapy

Figure 1: Optimal T-cell (and CAR T-cell) activity requires two signals



https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

FDA Approved Agents	Target	Indication
Axicabtagene Ciloleucel (Axi-Cel) (Yescarta)	CD19	r/r FL, r/r LBCL
Brexucabtagene Autoleucel (Brexu-Cel) (Tecartus)		r/r ALL, r/r MCL
Lisocabtagene Maraleucel (Liso-Cel) (Breyanzi)		r/r LBCL
Tisagenlecleucel (Tis-Cel) (Kymriah)		r/r ALL, r/r LBCL, r/r FL
Ciltacabtagene Autoleucel (Cilta-Cel) (Carvykti)	BCMA	r/r MM
Idecabtagene Vicleucel (Ide-Cel) (Abecma)		r/r MM

r/r: relapsed refractory

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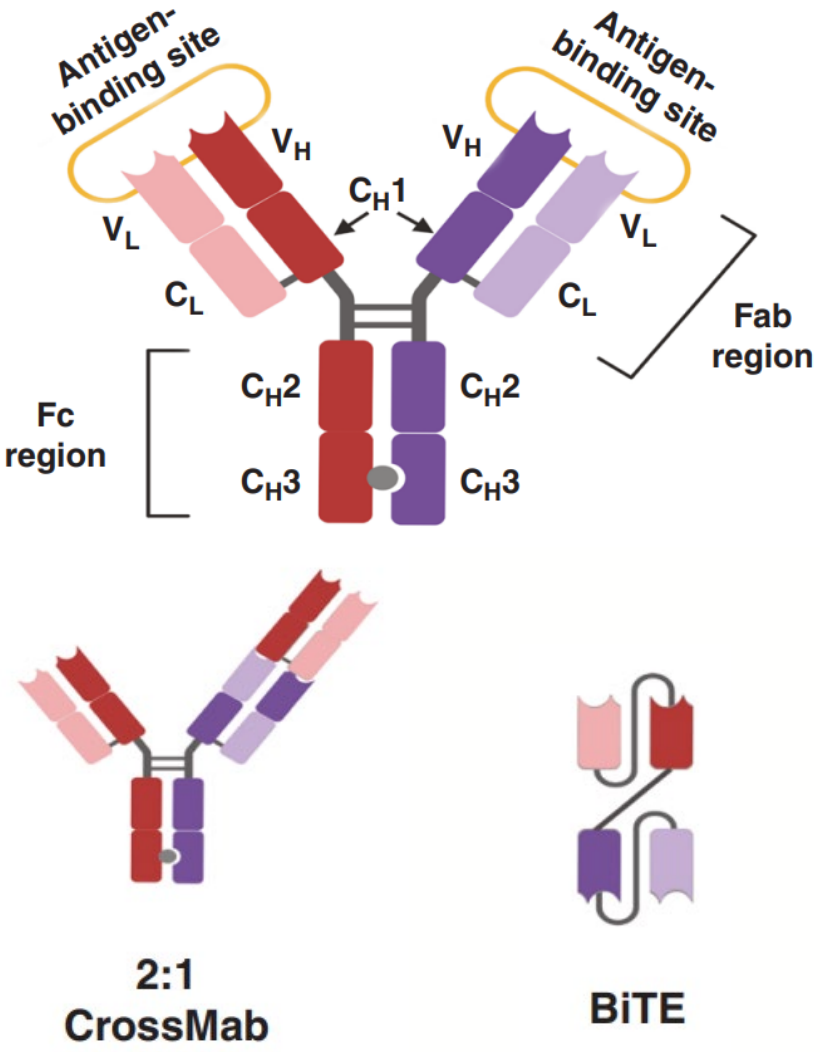
Bispecific T-Cell Engagers (BTCE)



FDA Approved Agents	Target	Indication
Blinatumomab (Blincyto)	CD 19	ALL w/ MRD, r/r ALL
Epcoritamab (Epkinly)	CD20	r/r DLBCL (3rd line)
Glofitamab (Columvi)		r/r DLBCL (3rd line)
Mosunetuzumab (Lunsumio)		r/r follicular lymphoma (3rd line)
Elranatamab (Elrexfio)	BCMA	r/r myeloma (5th line)
Teclistamab (Tecvayli)		r/r myeloma (5th line)
Talquetamab (Talvey)	GPRC5D	r/r myeloma (5th line)

r/r: relapsed refractory

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ASTCT Consensus Grading for CRS/ICANS

CRS	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temp ≥ 38°C	Temp ≥ 38°C	Temp ≥ 38°C	Temp ≥ 38°C
		WITH		
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor w/ or w/o vasopressin	Requiring multiple vasopressors (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 (e.g., CPAP, BiPAP, mechanical ventilation)

ICANS	Grade 1	Grade 2	Grade 3	Grade 4
ICE Score	7-9	3-6	0-2	0 (unarousable)
Awakens to:	Spontaneously	To voice	Only to tactile stimulus	Unarousable or requires vigorous tactile stimuli. Stupor or coma
Seizure	N/A	N/A	Any clinical seizure that resolves rapidly or nonconvulsive seizures on EEG resolving w/ 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
Elevated 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

Biol Blood Marrow Transplant. 2019;25:625-638.

Agent Specific Toxicity Rates

CAR T-Cell

CAR T-cell Therapies	Target	Costimulatory domain	CRS	Severe CRS	ICANS	Severe ICANS
Axi-Cel	CD19	CD28	93%	13%	64%	28%
Brexu-Cel		CD28	89-91%	15-24%	60-63%	25-30%
Liso-Cel		4-1BB	42%	2%	30%	10%
Tis-Cell		4-1BB	58-77%	22-47%	21-40%	12-13%
Ide-Cel	BCMA	4-1BB	84%	5%	18%	3%
Cilta-Cel		4-1BB	95%	4%	21%	9%

NCCN guidelines: Management of Immunotherapy related toxicities; Cancer Treatment Reviews. 2022;111:102479; Lancet. 2021;398:491-502

BTCE

Bispecific T-cell Engagers	Oncologic Target	CRS	Severe CRS	ICANS	Severe ICANS
Blinatumomab (Blincyto)	CD 19	15%	5%	65%*	13%*
Epcoritamab (Epkinly)	CD20	51%	2.5%	6%	0.6%
Glofitamab (Columvi)		70%	4.1%	4.8%	2.1%
Mosunetuzumab (Lunsumio)		39%	2.5%	1%	0
Elranatamab (Elrexfio)	BCMA	58%	0.5%	3.3%	
Teclistamab (Tecvayli)		72%	0.6%	6%	0%
Talquetamab (Talvey)	GPRC5D	76%	1.5%	9%	

*Includes all neurotoxicity

Rates derived from Prescribing Information for each medication as of 12/2023

BTCE Dose Titrations

Blinatumomab
(Continuous IV infusion)

- Cycle 1: 9 mcg/d x 7 days then 28 mcg/d to complete 28 days
- Hospitalize x 9 days cycle 1
- Hospitalize x 3 days for additional cycles

Epcoritamab
(Subcutaneous)

- Day 1: 0.16 mg
- Day 8: 0.8 mg
- Day 15: 48 mg**
- Day 22: 48 mg
- Cycle 2-3: 48 mg on days 1/8/15/22
- Cycle 4-9: 48 mg days 1/15

Glofitamab
(IV infusion)

- Day 1: Obinutuzumab
- Day 8: 2.5 mg over 4h*
- Day 15: 10 mg over 4 h
- Every 21 days: 30 mg over 4 h cycle 2 then over 2 h

Mosunetuzumab
(IV Infusion)

- Day 1: 1 mg over 4 h
- Day 8: 2 mg over 4 h
- Day 15: 60 mg over 4 h
- Cycle 2 Day 1: 60 mg over 2 h
- Every 21 days: 30 mg over 2 h

Elranatamab
(Subcutaneous)

- Day 1: 12 mg**
- Day 4: 32 mg *
- Day 8: 76 mg
- Weekly thru week 48: 76 mg
- Every 2 weeks week 49+: 76mg

Teclistamab
(Subcutaneous)

- Day 1: 0.06 mg/kg**
- Day 4: 0.3 mg/kg**
- Day 7: 1.5 mg/kg
- Weekly 1.5 mg/kg

Talquetamab
(Subcutaneous)

- Day 1: 0.01 mg/kg**
- Day 4: 0.06 mg/kg**
- Day 7: 0.4 mg/kg**
- Weekly: 0.4 mg/kg

Pretreat step up doses with steroid, diphenhydramine, acetaminophen (except blinatumomab, steroid only)

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* = 24 hours of hospitalization suggested

Information derived from Prescribing Information for each medication as of 12/2023

Timing of CRS & ICANS

CAR T-cell Therapies

CRS	ICANS
• Onset: 2-3 d • Duration: 7-8 d	• Onset: 4-10 d • Duration: 14-17 d

Bispecific T-cell Engagers

	CRS		CRS Incidence During Titration					ICANS	
	Onset (Range)	Duraion (Range)	Dose 1	Dose 2	Dose 3	Dose 4	Recurrent CRS	Onset (Range)	Duration (Range)
Blinatumomab	2d	5d						W/in 1st 2 wks	
Epcoritamab	24h (0-10d)	2 d (1-27d)	9%	16%	61%*	6%	16%	3 (1-3d)	4d (0-8 d)
Glofitamab	14h (5-74h)	2d (1-14d)	56%*	35%	29%	2.8%^	34%		
Mosunetuzumab	5-46h@	3d (1-21d)	15%	5%	33%	5%	11%		
Elranatamab	2d (1-9d)	2d (1-19d)	43%**	19%*	7%	1.6%^	13%	3d (1-4d)	2d (1-18 d)
Teclistamab	2d (1-6d)	2d (1-9d)	42%**	35%**	24%**	<3%^	33%	4d (2-8d)	
Talquetamab	27h (0-7d)	17h (0-26d)	29%**	44%**	33%**	12%!	30%	2.5d (1-16d)	2d (1-22 d)

Information derived from Prescribing Information for each medication as of 12/2023
NCCN guidelines: Management of Immunotherapy related toxicities V1.2024
^ all subsequent doses
@ onset longer with progressive doses
*24 h of hospitalization recommended
! For the addtl step up dose necessary for biweekly dosing

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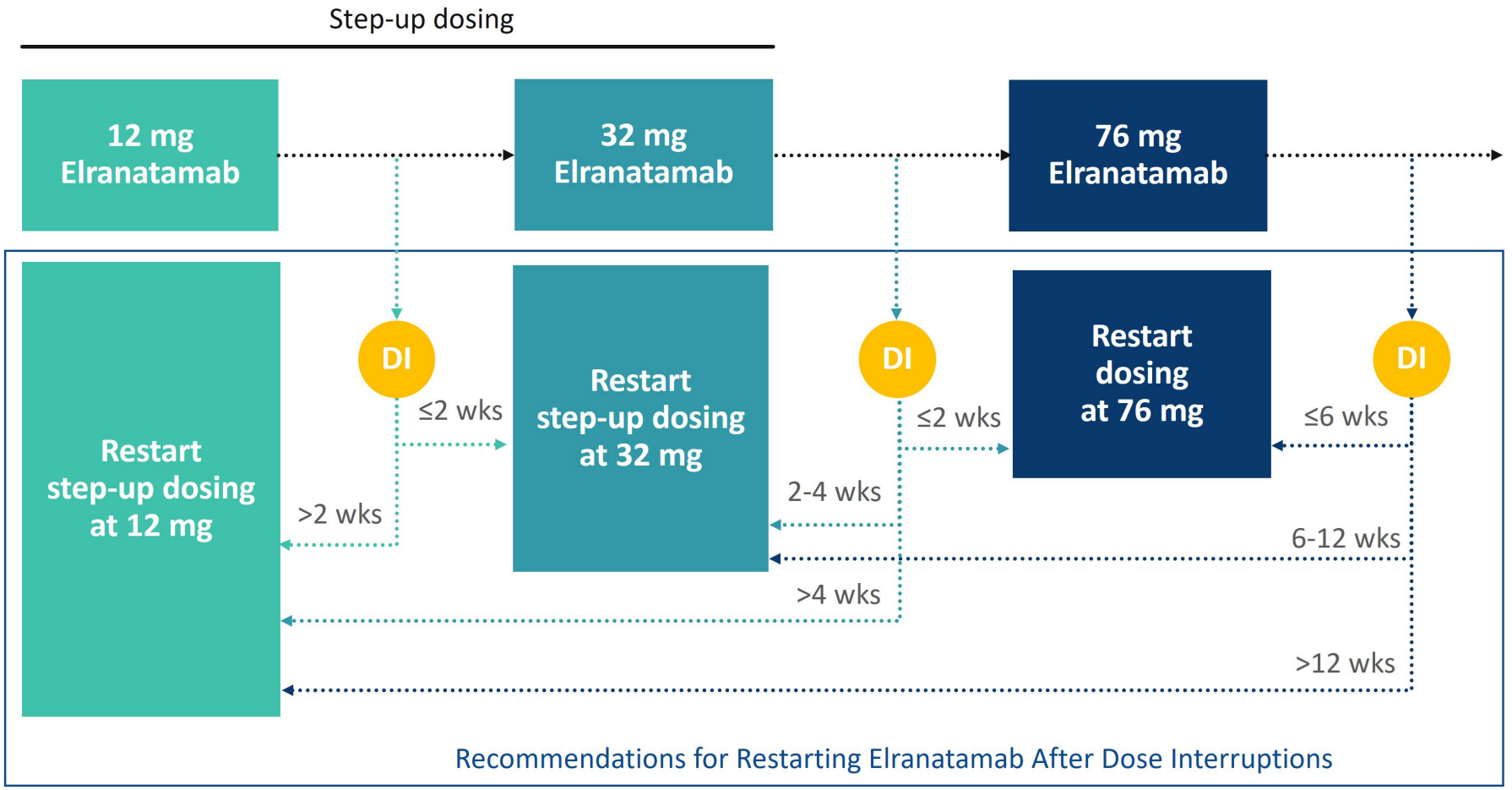
BTCE Dose Interruptions

Figure. Dosing Recommendations for Restarting Elranatamab Following a Dose Interruption (DI)



Blood. 2023;142(S1):3384

Immune Effector Toxicity Management Overview

- Immunosuppression to counter overactive immune effector cells and increased cytokine levels

Tocilizumab	Corticosteroids	Anakinra	Supportive Care
• Humanized IgG1κ anti-IL6R antibody • Binds both soluble and membrane-bound IL-6R • Insufficient CNS penetration • May increase CSF IL-6 levels • Generally limited to 2 doses during a CRS episode	• CONCERN – higher doses could suppress CAR T-cell expansion and persistence • Detrimental impact on efficacy not supported in most studies • Dexamethasone may be preferred for ICANS due to better CNS penetration • Rapid taper once symptoms begin to improve	• Interleukin 1 Receptor antagonist • Limited data • Consider in patients with tocilizumab refractory CRS	• Antipyretics • IV hydration • Vasopressors • Seizure prophylaxis (i.e., levetiracetam)

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https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

J Clin Oncol. 2021;39:3978-92

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Management of CAR T-cell Induced Cytokine Release Syndrome (CRS)

Grade 1	Grade 2	Grade 3	Grade 4
• Tocilizumab for prolonged CRS (>72 h) • Consider dexamethasone for early onset CRS (<72 h) if liso-cel or ida-cel	• Tocilizumab • Dexamethasone 10 mg q12-24 h if hypotension resistant to 1-2 doses of tocilizumab	• Tocilizumab • Dexamethasone 10 mg q6-12 h	• Tocilizumab • Dexamethasone 10 mg q6 h or methylprednisolone 1-2g/d x 3 doses

Management of CAR T-cell Induced Immune Effector Cell Associated Neurotoxicity (ICANS)

Grade 1	Grade 2	Grade 3	Grade 4
• Monitor for progression • Consider tocilizumab if concurrent CRS • Sz prophylaxis	• Dexamethasone 10 mg x 1, repeat q6-12 h if no improvement • Sz prophylaxis	• Dexamethasone 10 mg q6 h or methylprednisolone 1 mg/kg q12 h • Sz prophylaxis	• Methylprednisolone 1-2 g/d x 3 days then rapid taper • Consider Anakinra 100 mg q6 h • Sz prophylaxis

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NCCN Guidelines: Management of Immunotherapy Related Toxicity. V1.2024
See individual CAR T-cell agent prescribing information for agent specific CRS/ICANS management toxicity.

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CAR T-cell Therapy Toxicity: Real World Experience

	DLBCL N=185	FL N=67	MCL N=92	MM N=42
CAR-T treatment setting				
Academic	81%	90%	83%	95%
Community	14%	5%	12%	5%
CAR-T therapy				
Axi-Cel	53%	70%		
Tis-Cel	32%	19%		
Liso-Cel	12%	9%		
Brexu-Cel			99%	
Ide-Cel				81%
Cilta-Cel				17%
Unknown	3%	2%	1%	2%
CRS incidence				
Any CRS	56%	60%	72%	57%
Grade 1	27%	30%	27%	43%
Grade 2	23%	22%	35%	14%
Grade ≥ 3	3%	5%	3%	0%
Median CRS time to onset, days (range)	3 (0-15)	4 (0-15)	4 (0-12)	1 (0-16)
Median CRS duration, days (range)	4 (1-33)	5.5 (1-20)	5 (1-18)	2 (0-8)

Data source: Flatiron Health US, nationwide EHR database

Data cut off: 8/31/2022

Grade 1 CRS Treatment	DLBCL N=49	FL N=20	MCL N=25	MM N=18
Tocilizumab	37%	40%	48%	39%
Corticosteroids	16%	25%	28%	6%
Grade ≥ 2 CRS Treatment	**DLBCL N=47**	**FL N=18**	**MCL N=35**	**MM N=6**
Tocilizumab	75%	67%	86%	100%
Corticosteroids	45%	44%	63%	50%
Anakinra			1 patient	

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Blood. 2023;142(S1):5150

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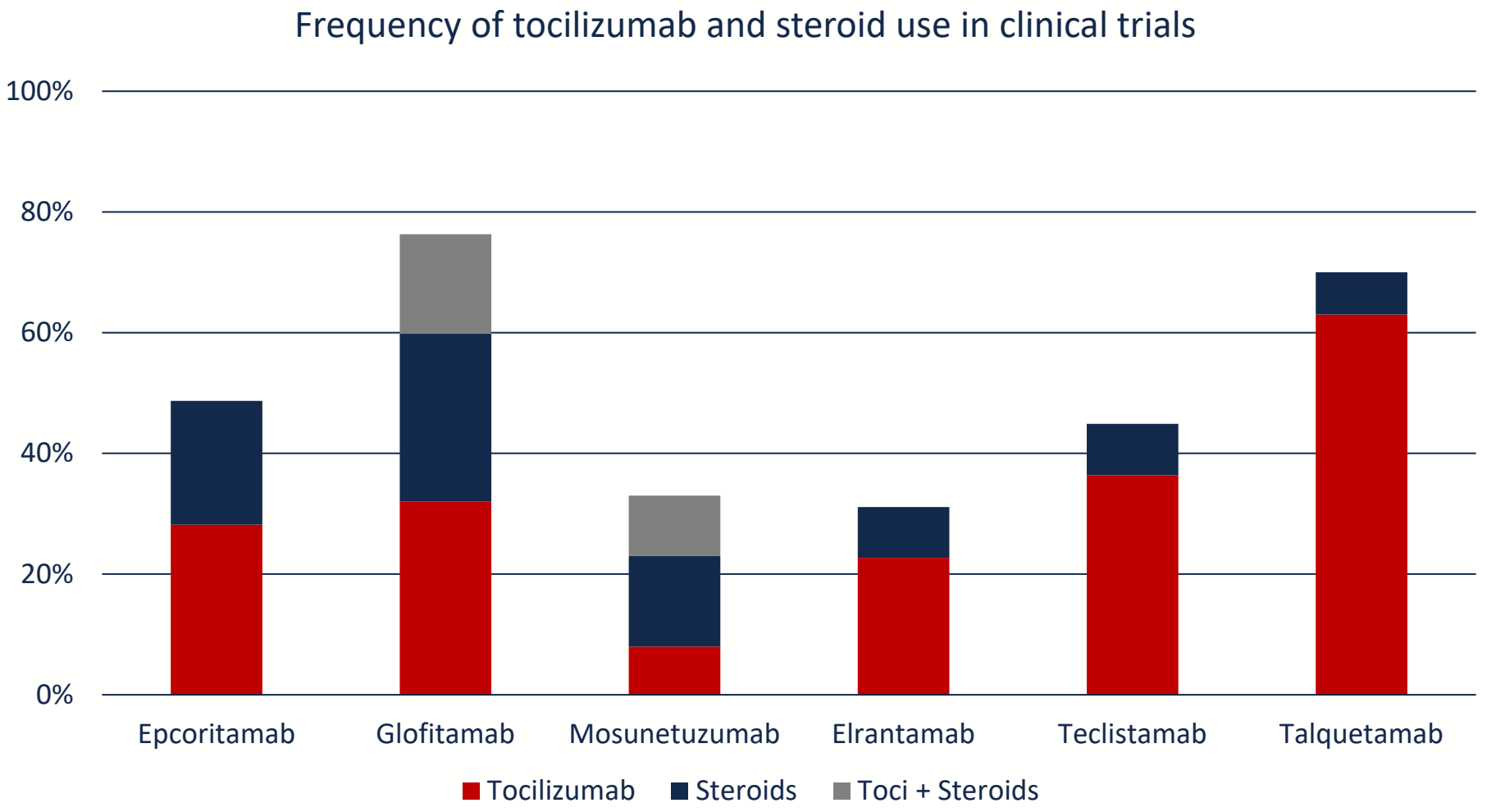
Management of BTCE CRS and ICANS

- CRS
  - Prescribing information: Treat per current practice guidelines
    - Blinatumomab: dexamethasone 8 mg q8h if grade 3 or 4
    - Pretreat with next dose and consider hospitalization for next dose
    - D/C if grade 4
  - NCCN guidelines: *Consider providing one dose of dexamethasone 8 mg to take if needed for severe CRS (shaking, chills, felling severely ill) at home prior to going to ED*
- ICANS
  - D/C if grade 4 or recurrent grade 3 (glofitamab: d/c if grade 3 > 7d)
  - 4 products have more prescriptive recommendations (epcoritamab, elranatamab, teclistamab, talquetamab)

Sz prophylaxis	Grade 2-4: dex 10 mg IV q6h until ≤ grade 1 then taper	Grade 4: consider methylprednisolone 1g/d x 3d	D/C if grade 4 or recurrent grade3

BTCE CRS Management in Clinical Trials



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NEJM 2022;387:2220—2231
NEJM 2022;387:2232-2244
Lancet Oncol 2022;23:1055-1065

NEJM 2022;387:495-505
J Clin Oncol 2023;41:2238-2247
Nature Medicine 2023;29:2259-2267

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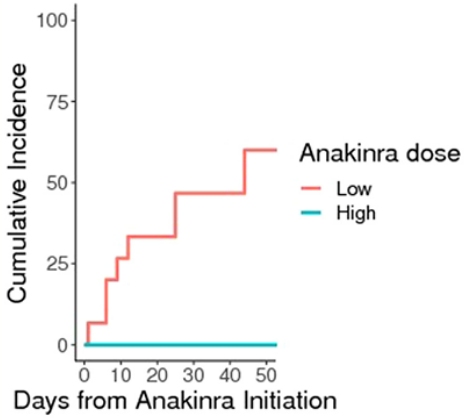
Anakinra Treatment

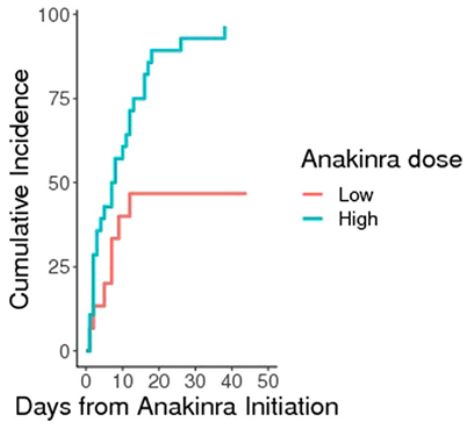
- Refractory CRS or ICANS after CAR-T, N=43
- High dose anakinra: >200 mg/day IV
- Low dose anakinra: 100-200 mg/d SQ or IV

	Low Dose	High Dose	P-value
Peak CRS Grade, median (IQR)	2 (1-2)	2 (1-2)	0.4
Peak ICANS grade, median (IQR)	4 (4-4)	4 (3-4)	0.069
Time to first anakinra, d, median (IQR)	9 (8-14)	8 (6-11)	0.13
Steroid duration, d, median (IQR)	13 (4-24)	12 (8-20)	0.9
Cumulative anakinra dose, mg, median	700	4200	0.0001
Duration of anakinra, d, median (IQR)	6 (4.5-10)	7.5 (4.75-12.2)	0.41

Treatment Related Mortality



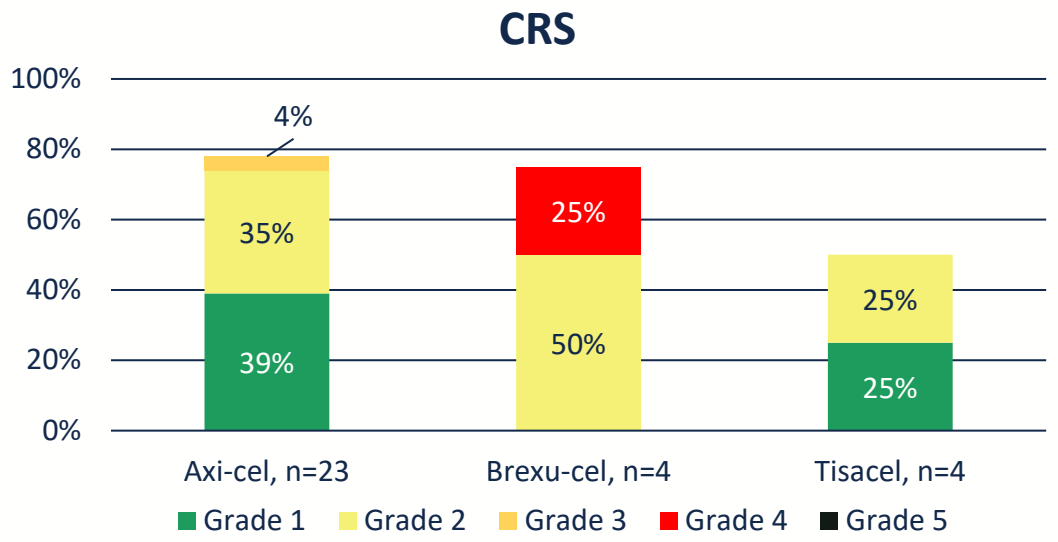
CRS Symptom Resolution

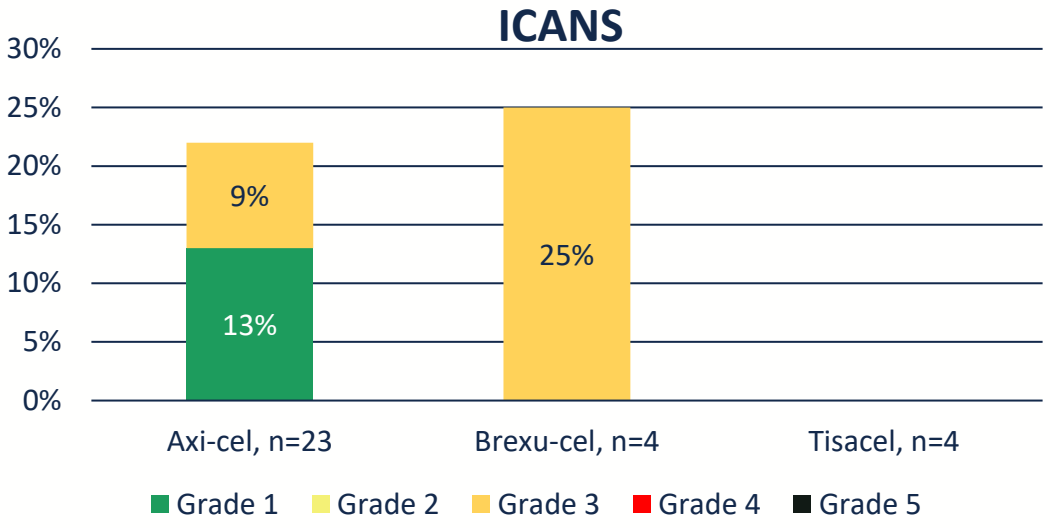


Transplantation and Cellular Therapy. 2023;29:430-7

Prophylactic anakinra w/ CAR-T

- 100 mg SQ Q12 h days 2-10, N=31





Nature Medicine 2023;29:1710-1717

Alternative Therapies for Immune Effector Toxicity

Treatment Strategies Under Investigation

- Siltuximab (IL-6 antagonist)
- Ruxolitinib (JAK 1 and 2 inhibitor)
- Cyclophosphamide
- Intravenous Immune Globulin
- Anti-thymocyte Globulin
- Extracorporeal cytokine adsorption with CRRT

Prophylaxis Strategies Under Investigation

- Corticosteroid prophylaxis
- Anakinra prophylaxis
- JAK1 inhibition (Itacitinib)
- Lenzilumab (GM-CSF inhibitor)
- Fractionation of CAR T-cell dose
- Simvastatin
- Early tocilizumab
- PolB-001 (broad spectrum anti-inflammatory)

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Cancer Treatment Reviews. 2022;111:102479
Annals Oncol. 2021;32:34-48
https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

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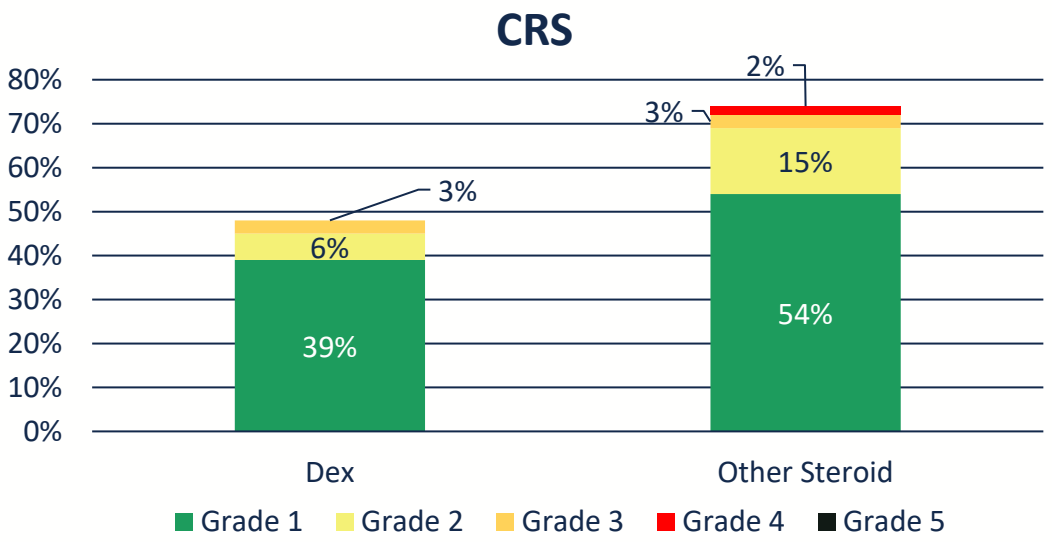
Preventing CRS/ICANS – New Data with BTCEs

- Teclistamab: Prophylactic tocilizumab vs. standard of care

	No Toci n=48	Toci 8 mg/kg 4 h prior to 2nd step up dose n=33
CRS	73%	30%
ICANS	20%	6%
Readmissions w/in 14 d	0%	20%

Toci 8 mg/kg 4 h prior to 1st step up dose n=31	
CRS	13%
ICANS	10%

- Glofitamab: Preferred premedication



	Other steroid n=112	Dexamethasone 20 mg n=33
Median time to CRS from C1D8 dose	14h	12h
Time to CRS resolution	31h	27h
Tocilizumab use	34%	25%

Blood. 2023;142(S1):2008
Blood 2023;142(S1):4709
Blood 2023;142(S1): 3130

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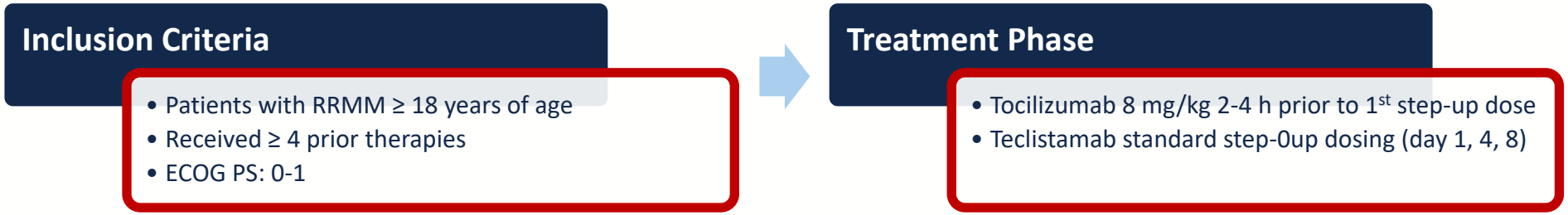
Outpatient Bispecific T-cell Engager Administration - Teclistamab

- Mayo Clinic Experience (n=39)
  - Premedication: acetaminophen, diphenhydramine, dexamethasone during step-up dosing
  - CRS: 32%; all admitted to hospital
    - Total admissions: 19; median length of stay: 1.7d
  - Safe and feasible to administer outpatient
- French Experience (n=8)
  - Temp, BP, O_2 sat by homecare nurse BID x 15 days
  - Oral dexamethasone available in case of emergency
  - CRS: 38%, no grade 3/4; no ICANS ≥ grade 2
  - No toxicity related deaths
- Ongoing phase 2 study, single arm, goal = 50 participants



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Blood. 2023;142(S1):5154
Blood 2023;142(S1):4736
Blood 2023;142(S1): 3374

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Outpatient CAR T-cell Therapy ?

- Mayo Clinic Experience (n=123)
  - In-home, electronic health-record integrated technology to monitor vital signs and neurologic symptoms x 30 days post CAR-T infusion
  - 84% required hospitalization
  - Outpatient CAR T-cell treatment is feasible

- Sarah Cannon Transplant and Cellular Therapy Program Experience (n=40)
  - Daily engagement with virtual nurse
  - In-person clinic visits days 1-14
  - Remote monitoring kit
    - Continuous pulse, resp rate, O_2 sat, skin temp
    - Axillary temp and BP 3x/d
  - 68% required hospitalization
  - Time to admission from infusion: 5 days

Alarm Type	Alarm	Clinic Hours	Non-Clinic Hours
Operational	No data > 240 min	85	122
	Low battery	28	109
Clinical	Bradycardia	12	88
	Tachycardia	19	49
	Hypoxia/Tachypnea	16	131
	Hypoxia/bradypnea	0	1
	Fever	4	79
	Hypertension	1	3
	Hypotension	9	23
	Patient initiated	1	0

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Blood. 2023;142(S1):5075
Blood 2023;142(S1):254

Managing CRS/ICANS – New Data with CAR T-cell Therapies

- Siltuximab – binds circulating IL-6

Axi-cel, n=52, 81% with CRS (10% G3/4), 65% with ICANS (31% G3/4) Toci refractory: 15%; Steroid refractory: 33%	
Improved CRS grade, all patients (toci refractory)	86% (50%)
Time to CRS resolution	1.5 d
Improved ICANS grade, all patients (steroid refractory)	68% (76%)
Time to ICANS resolution	5d

- Intrathecal chemotherapy to treat ICANS, n=12

IT Methotrexate n=10

IT Cytarabine n=2

Grade 1: 4, Grade 2: 2, Grade 3: 6
All received steroids, 6 received anakinra
Time to IT chemo: 1 day
Resolution of ICANS: 92%
Complete resolution of symptoms w/in 24 h: 42%

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Blood. 2023;142(S1):4502
Blood 2023;142(S1): 2138

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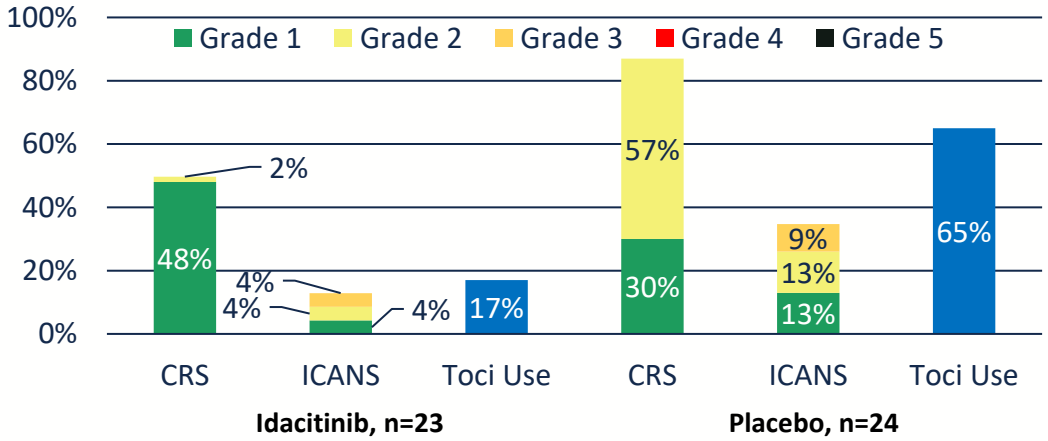
Prophylaxis of CRS/ICANS – New Data with CAR T-cell Therapies

- Simvastatin/Intrathecal dexamethasone (N=15, axi-cel or brexu-cel)
  - Simvastatin 40 mg PO daily starting 5 days prior to apheresis thru day +30 and IT dexamethasone 8 mg days -1 and +6
  - ICANS: 27%, ≥ grade 3: 13%

- Duvelisib 25 mg PO BID day -2 thru +28 (N=17)
  - CRS 76% (71% had onset after day 3); grade 1: 65%, no grade ≥3
  - ICANS 41%, Grade 3/4 12%
  - 75 adverse effects possibly due to duvelisib (15 severe adverse effects)

- Itacitinib prophylaxis
  - 200mg PO bid day -3 to day 26 of axi-cel treatment vs. placebo



Blood. 2023;142(S1):3493
Blood 2023;142(S1):3470
Blood 2023;142(S1):356

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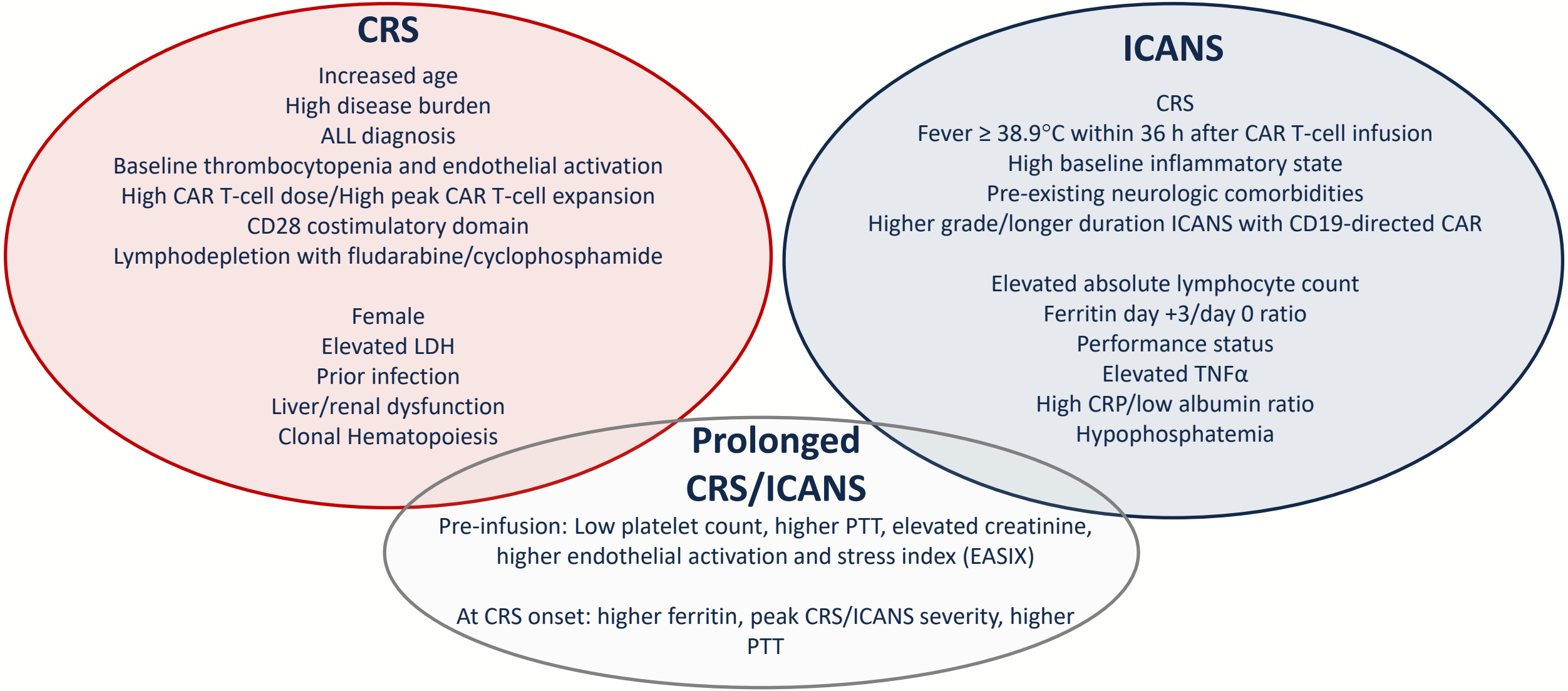
Immune Effector Toxicity Risk Factors



https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf
Cancer Treatment Reviews. 2022;111:102479
Front Pharmacol. 2022;13:950923
Ann Oncol. 2021;32:34-48

Blood. 2023;142(S1):1004
Blood. 2023;142(S1):3626
Blood. 2023;142(S1):92
Blood. 2023;142(S1):4814

Blood. 2023;142(S1):3629
Blood. 2023;142(S1):355
Blood. 2023;142(S1):3495
Blood. 2023;142(S1):2126

The Future of CAR T-cell Therapies

World Report

FDA investigating safety risks in CAR T-cell recipients

The US regulator has received 20 reports of T-cell malignancies following immunotherapy. Roxanne Nelson reports.

By the summer of 2010, Doug Olson and Bill Ludwig had run out of treatment options. Diagnosed with chronic lymphocytic leukaemia in 1996 and 2000, respectively, their cancers were no longer responding to standard therapies. But as luck would have it, a clinical trial with an experimental therapy using chimeric antigen receptor (CAR) T cells was getting underway, and both men were able to enrol in it. They became

Henry Fung (Fox Chase Cancer Center, Philadelphia, PA, USA) does feel that the risks being investigated are a concern, but not likely to have any impact on current indications for treatment. "These patients have limited options, if any", he said. "A causal relationship has not yet been demonstrated. I will also be very cautious in interpreting the data to avoid generalisation as CAR-T is a class of therapy and in fact there are

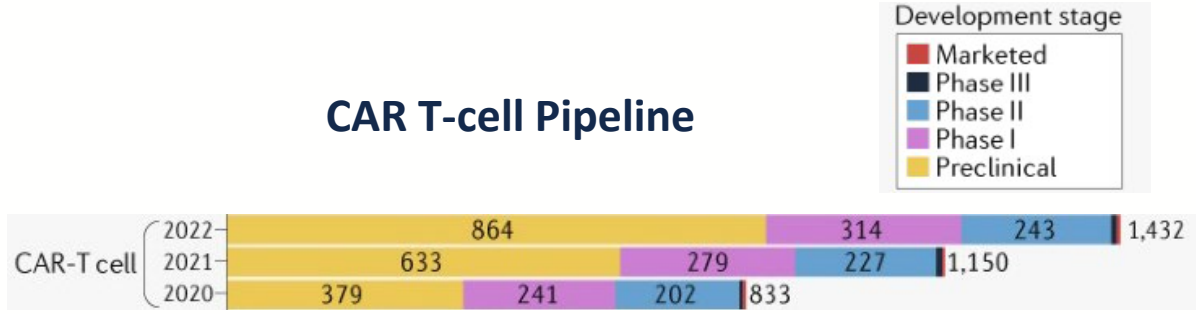
That said, he pointed out that this will be something to take seriously for trials and efforts to move CAR T cells to earlier lines of therapy when the risks might be of more concern when compared with other established therapies.

The issue of developing a second primary cancer from a treatment is also not unique to CAR T-cell therapies. "We have a similar situation

For the **FDA announcement** see https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-investigating-serious-risk-t-cell-malignancy-following-bcma-directed-or-cd19-directed-autologous

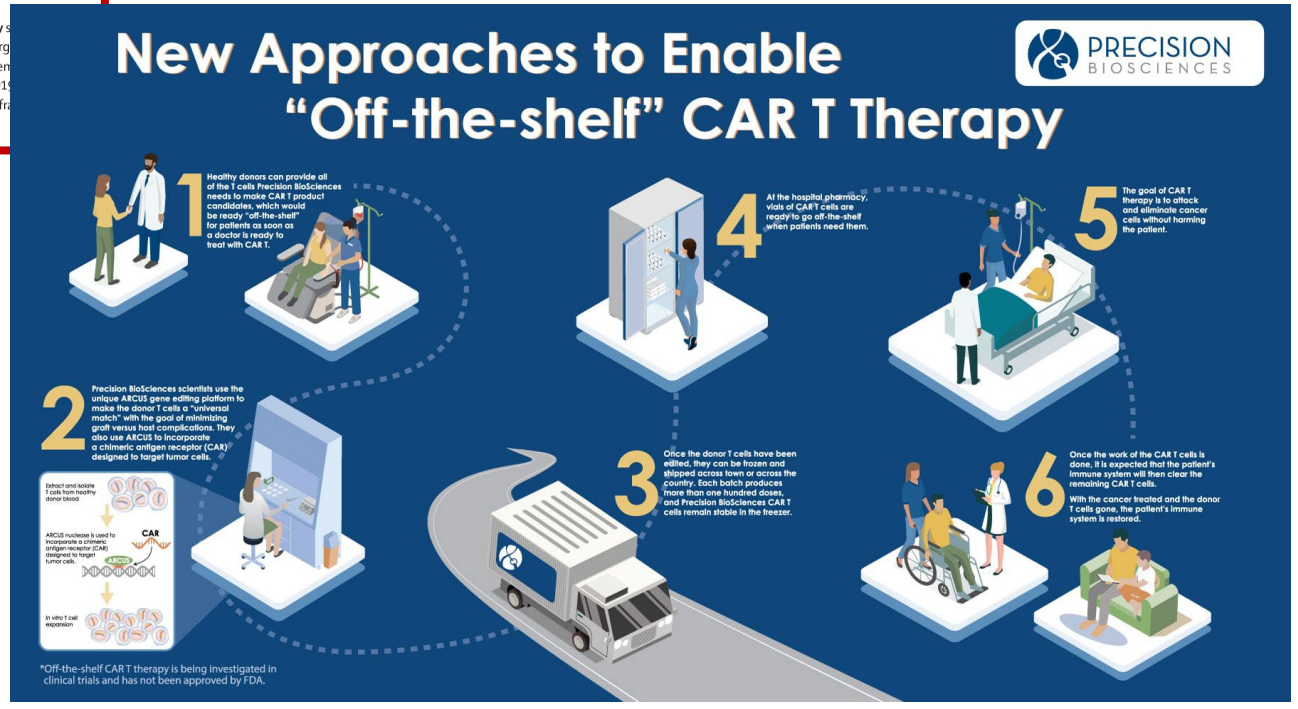
For the **ASH study** s ashpublications.org article/142/Supplen 1/220/501523/CD1 CAR-T-Cells-in-Refra Systemic

CAR T-cell Pipeline



Novel CAR T-cells to mitigate CRS/ICANS risk

- Inclusion of a chimeric inhibitor receptor to inhibit CAR T-cells
- Silencing IL-6 gene



Lancet 2023;402:2181
Nature Reviews. 2022;21:631-32
https://precisionbiosciences.com/pipeline/cancer-immunotherapy/
Blood. 2023;142(S1):889
Blood. 2023;142(S1):3436

The Future of BTCE

1734 *Feasibility and Safety of the First-in-Human Chemotherapy-Light Combination of Rituximab, Polatuzumab Vedotin and Glofitamab in Previously Untreated Aggressive B-Cell Lymphoma Patients Above 60 Years of Age Ineligible for a Fully Dosed R-CHOP - R-Pola-Glo/Ikf-t062, a Study of the Austrian Group for Medical Tumor Therapy (AGMT-NHL-16) and the German Lymphoma Alliance (GLA2022-10)*

4457 Epcoritamab SC + R-Mini-CHOP Leads to High Comple
with Previously Untreated Diffuse Large B-Cell Lymphoma In
Disclosure from Arm 8 of the Epcore NHL-2 Trial

3092 Epcoritamab SC + GemOx Leads to High Complete Met
Relapsed/Refractory Diffuse Large B-Cell Lymphoma Ineligib
Updated Results from Epcore NHL-2

3053 EPCORE FL-1: Phase 3 Trial of Subcutaneous Epcorita
(R^2) Vs R^2 Alone in Patients with Relapsed or Refractory Fol

1014 Talquetamab + Pomalidomide in Patients with Relapse
and Preliminary Efficacy Results from the Phase 1b Monum

855 Mosunetuzumab and Polatuzumab Vedotin Demonst
Unfit/Frail Patients with Previously Untreated Diffuse Larg

438 Subcutaneous Epcoritamab Plus Lenalidomide in Pati
Large B-Cell Lymphoma from EPCORE NHL-5

The future of BTCE is combinations!

1508 "Dose-Dense" Mini-Hyper-CVD, Inotuzumab Ozogamicin and Blinatumomab Achieves High Rates of Rapid MRD-Negativity in Patients with Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia: A Retrospective Analysis

emonstrate Frequent and Durable
ith ≥2L Relapsed/Refractory DLBCL,
: Updated Results from a Phase Ib/II

armacokinetics, and Efficacy of Glofitamab As
with R-ICE Chemoimmunotherapy in Children and Young Adults
on-Hodgkin Lymphoma (iMATRIX-GLO)

uces High Response Rates with a Manageable Safety Profile in
Diffuse Large B-Cell Lymphoma (DLBCL): A 12-Month Analysis

First-in-Human Chemotherapy-Light Combination of Rituximab,
ab in Previously Untreated Aggressive B-Cell Lymphoma Patients
r a Fully Dosed R-CHOP - R-Pola-Glo/Ikf-t062, a Study of the
Therapy (AGMT-NHL-16) and the German Lymphoma Alliance

OP Has a Favorable Safety Profile and Induces High Response Rates in Patients with Previously Untreated (1L) Large B-Cell Lymphoma (LBCL) Defined As High Risk By Circulating Tumor DNA (ctDNA) Dynamics: Preliminary Safety and Efficacy Results

605 Preliminary Findings of a Phase Ib/II Trial Indicate Manageable Safety and Promising Efficacy for Mosunetuzumab in Combination with Lenalidomide (M+Len) in Previously Untreated (1L) Follicular Lymphoma (FL)

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All abstract titles presented at 65th ASH Annual Meeting and Exposition

Conclusions

- Number of therapies with CRS/ICAN risk increasing rapidly
- Immune effector cell toxicities (CRS/ICAN) occur commonly and require prompt recognition and grading
- Early, grade-based management with tocilizumab and/or steroids is necessary to prevent progression
- Most respond to guideline/grade driven management
- Novel therapeutic and prophylactic approaches under investigation to decrease the impact of toxicity as number of FDA approved agents and indications continue to increase

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Understanding and Managing Immune Effector Cell Toxicities in Hematologic Malignancies in 2024

David Reeves, PharmD, BCOP

Professor of Pharmacy Practice
Butler University

Clinical Pharmacy Specialist – Hematology/Oncology
Franciscan Health Indianapolis

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