Carolinas HealthCare System

Levine Children's Hospital

CAR T-Cell Management for the ED Provider

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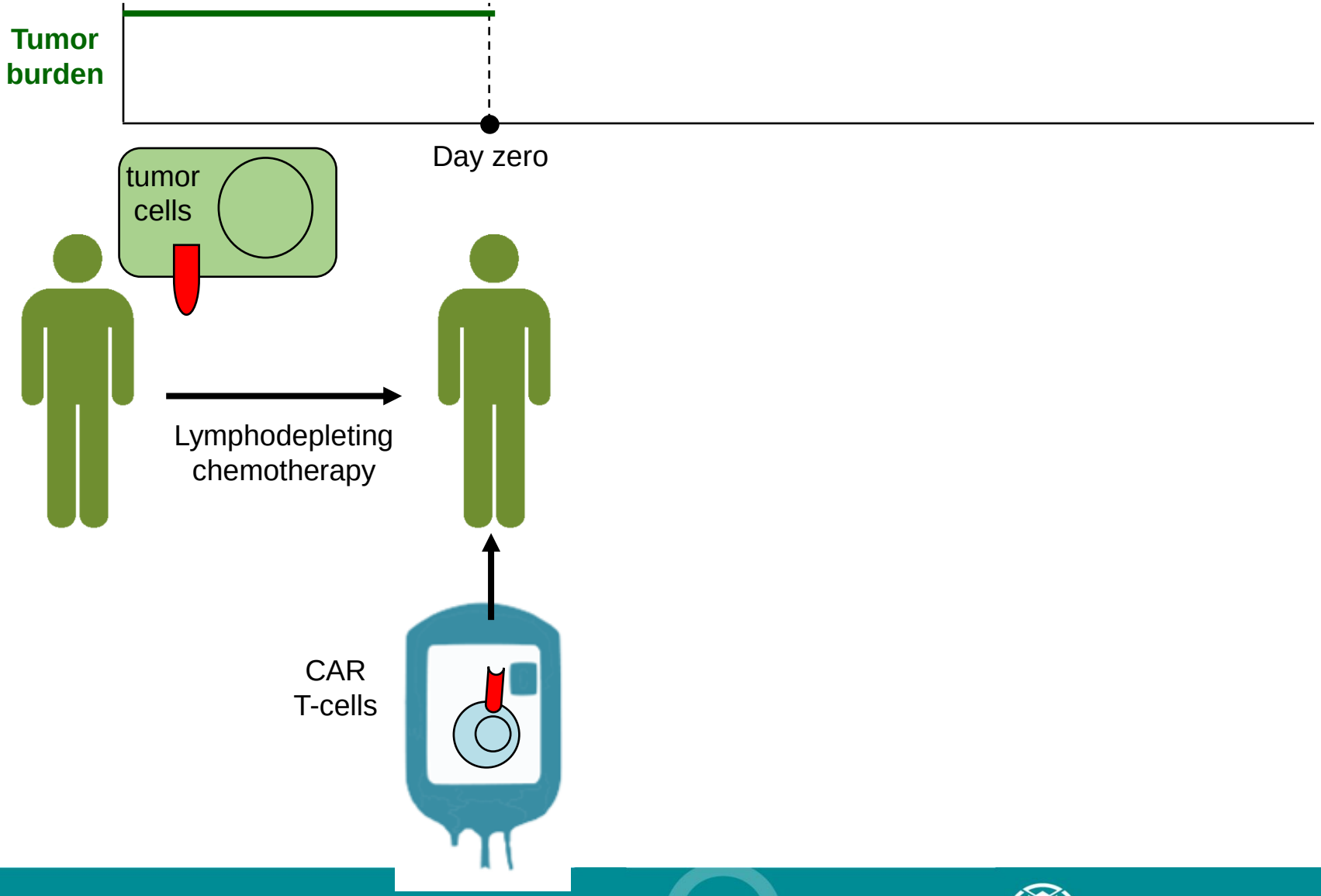
Agenda

- What are CAR T-cells?
- When does CAR T-cell toxicity occur?
- What are CAR T-cell toxicities?
- What do I do about CAR T-cell toxicity?

What are CAR T-cells?



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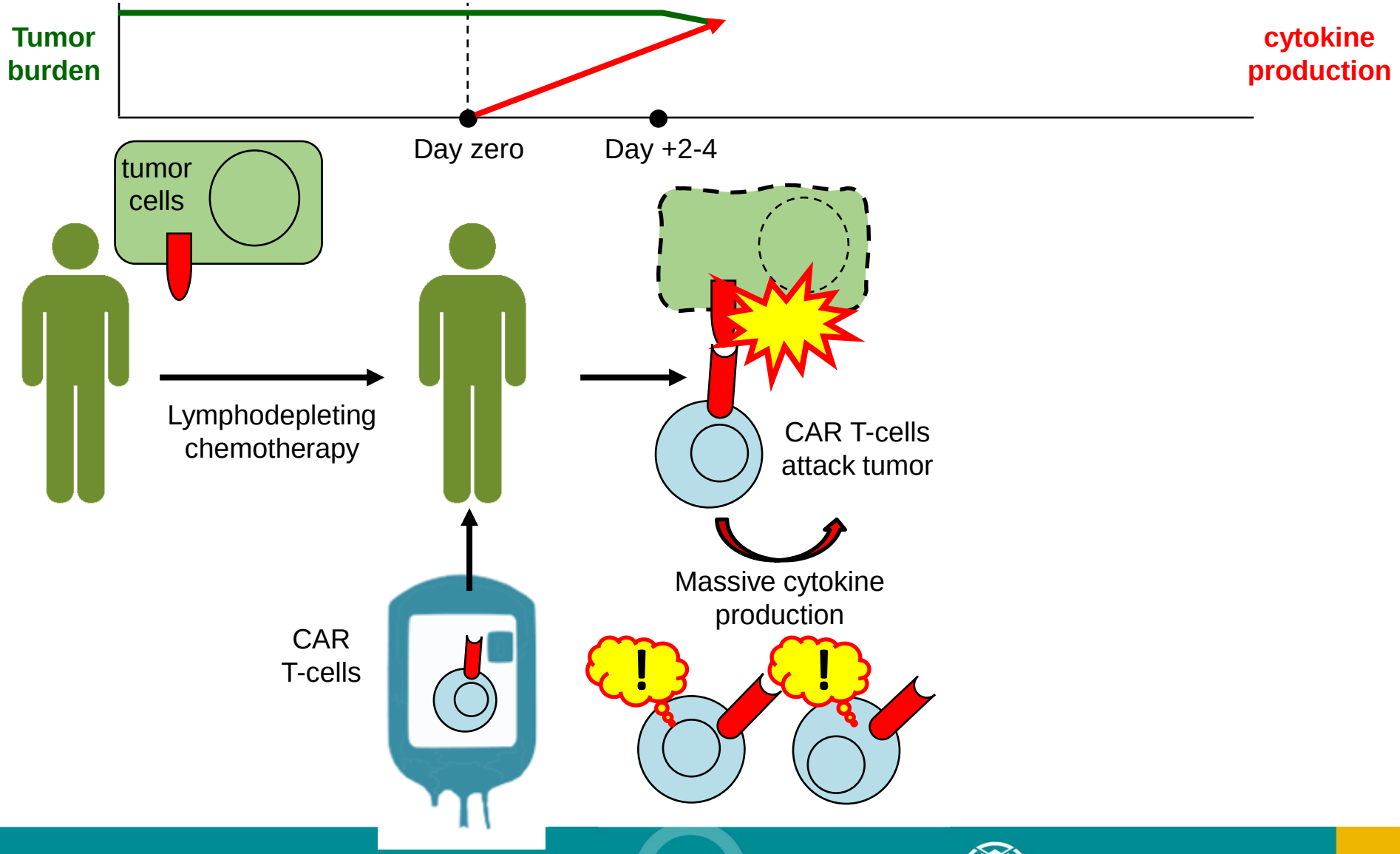

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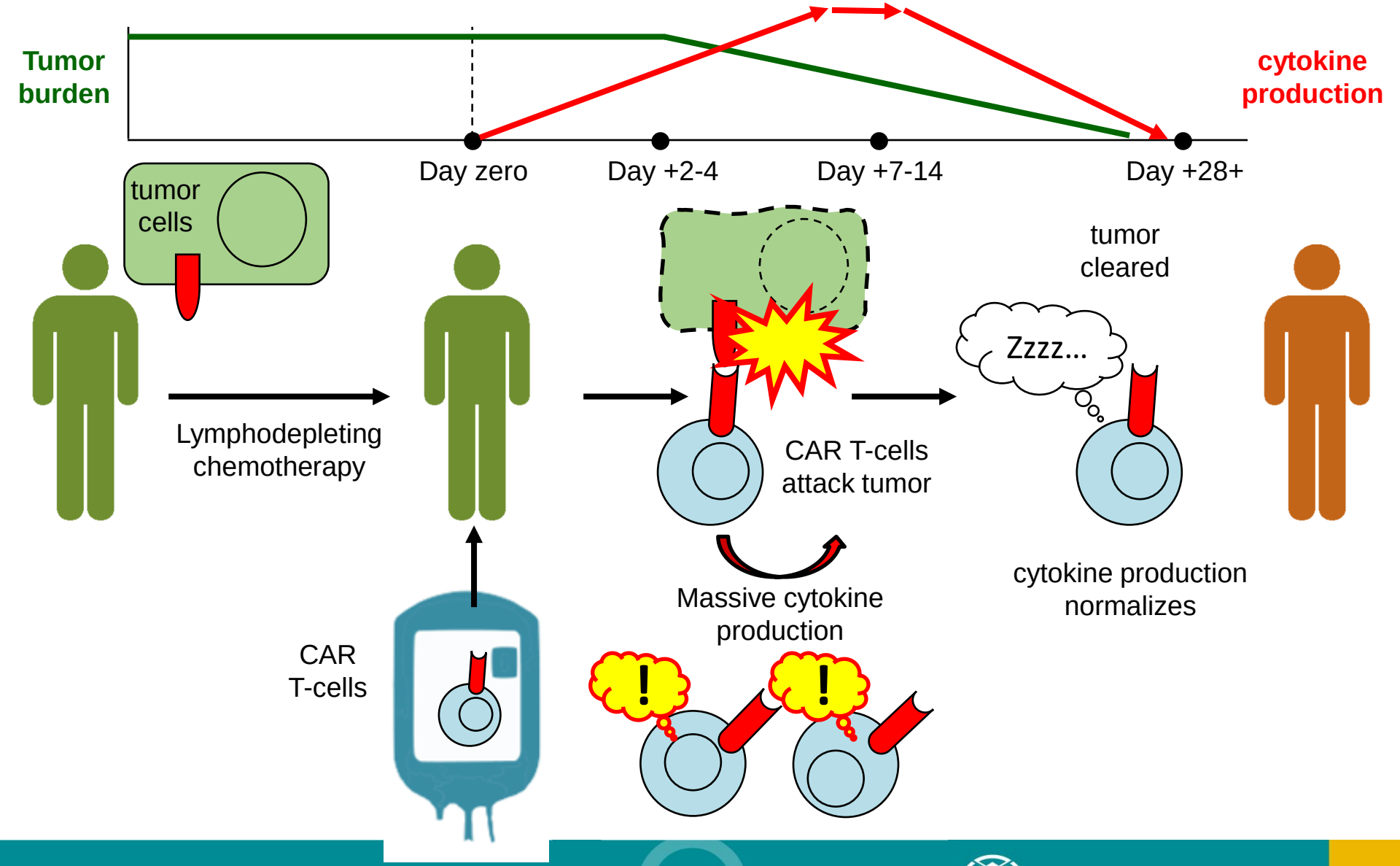
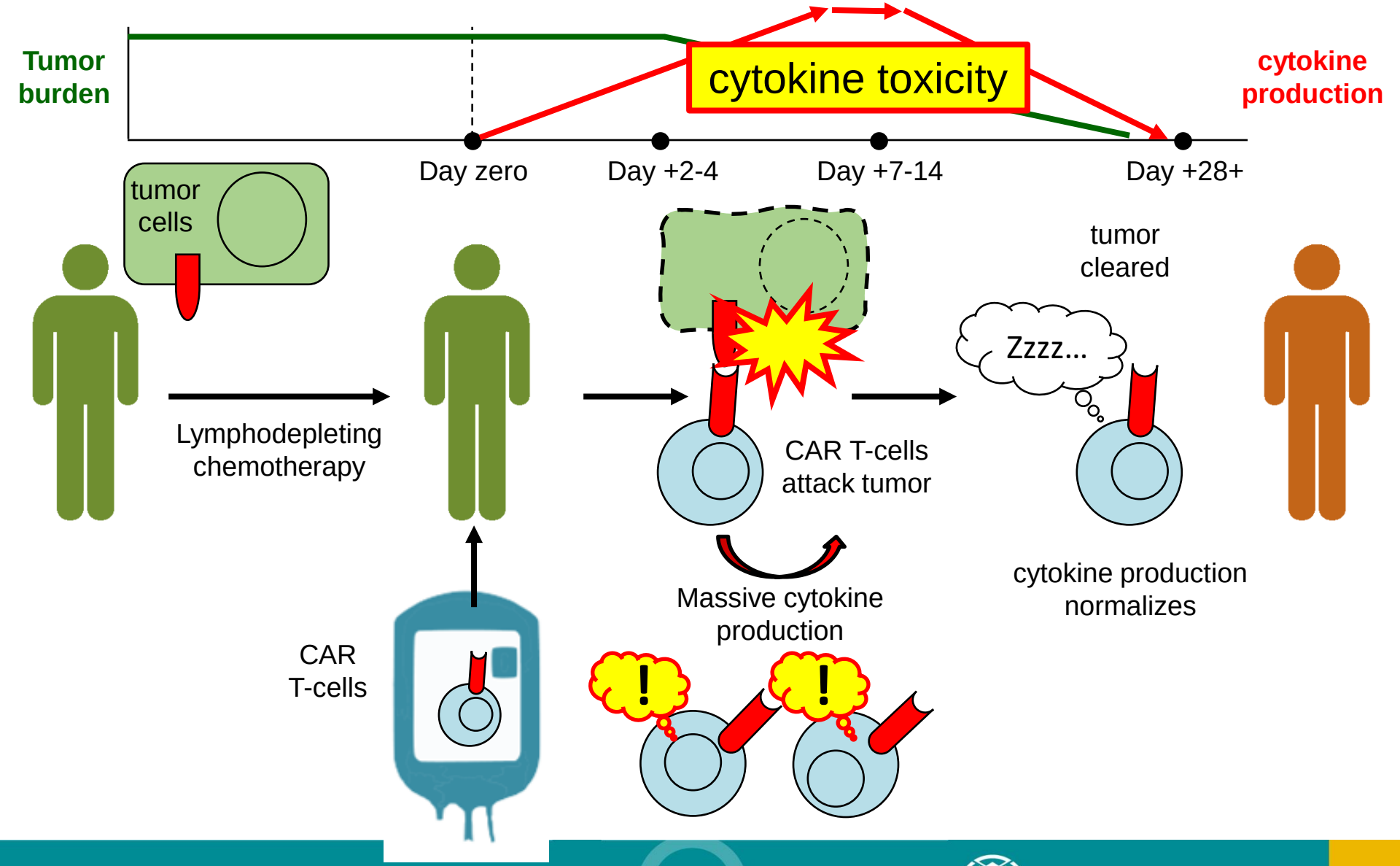


When does CAR T-cell toxicity occur?



Two major acute toxicities of CAR T-cell therapy

- **CRS:** Cytokine Release Syndrome
  - Temporary sepsis-like inflammatory response from hyperactive T-cells killing tumor

- **iCANS**: Immune Effector Associated Encephalopathy
  - Temporary brain inflammation from CAR T-cell therapy

ED Management of CAR T-cell patients

- For any CAR T-cell patient, call/Halo Peds BMT on-call immediately on arrival to ED

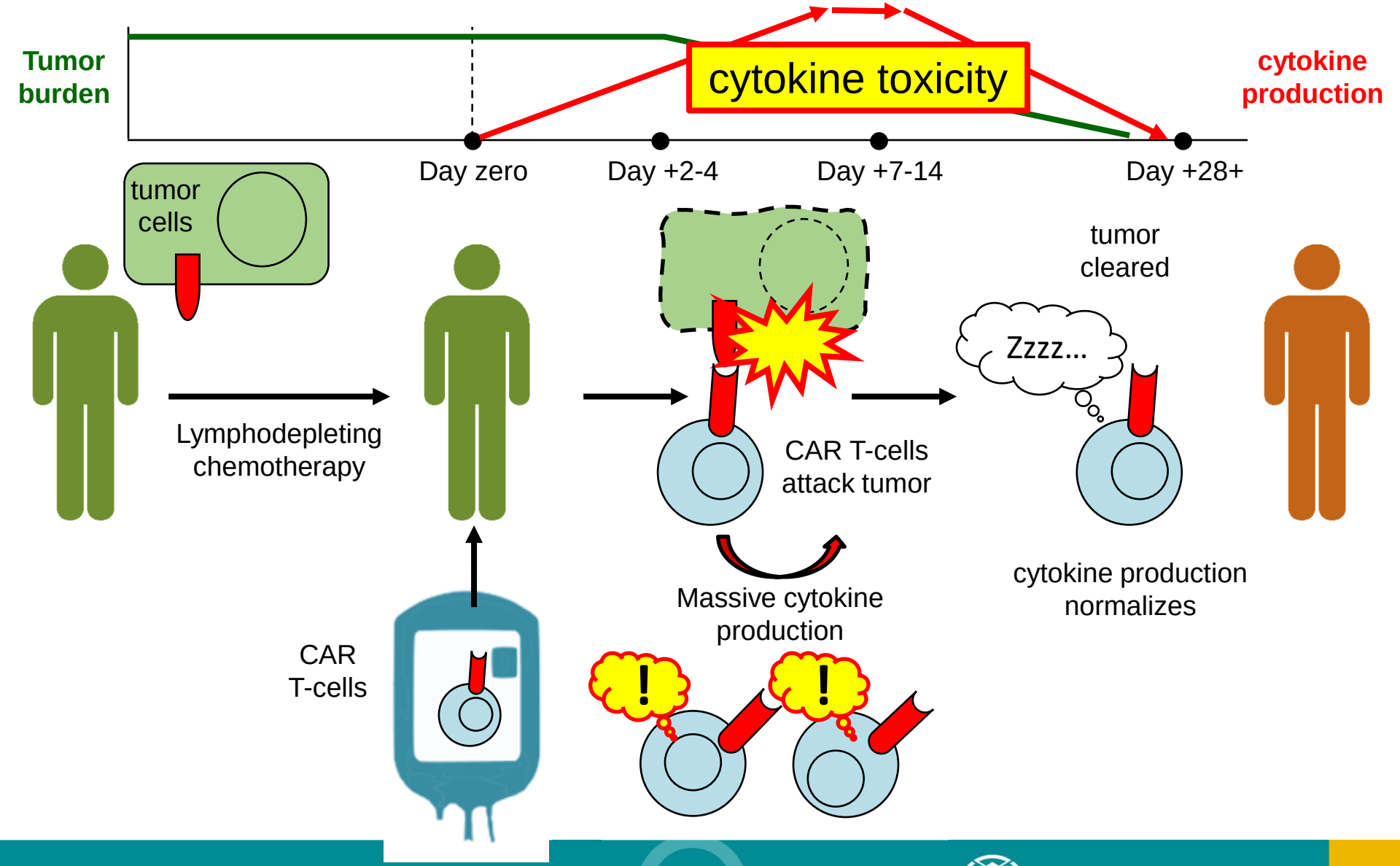
- CAR T-cell patients are just like Onc/BMT patients
  - weak immune systems
  - high risk for infections

  - treat CAR T-cell patients just like any other Onc/BMT patient (room immediately, etc.)

You can have cytokine toxicity and sepsis

- A CAR T-cell patient is also an oncology patient
- Immune system is not normal (2/2 cancer and lymphodepleting chemo)
- Oncology patients with fever, hypotension, etc. have sepsis until proven otherwise
- Get BCx and broad spectrum Abx in ASAP

When does CAR T-cell toxicity occur?



ED Management of CAR T-cell patients

- CAR T-cell patients within first 45 days after cell infusion, with any sign of illness, have cytokine release syndrome (CRS) until proven otherwise

- CAR T-cell patients within first 45 days with mental status changes have iCANS until proven otherwise

- CAR T-cell patients after 45 days – probably *not* CRS/iCANS: talk to your Peds BMT attending

Cytokine Release Syndrome (CRS)

- successfully activated CAR T-cells release copious cytokines as they kill tumor
  - more active CAR T-cells, more CRS
  - more tumor to kill, more CRS
- Occur between 1-14+ days after CAR T-cells

- symptoms resemble sepsis
  - fever, myalgias, nausea/vomiting
  - severe: hypotension, respiratory insufficiency, renal failure, coagulopathy

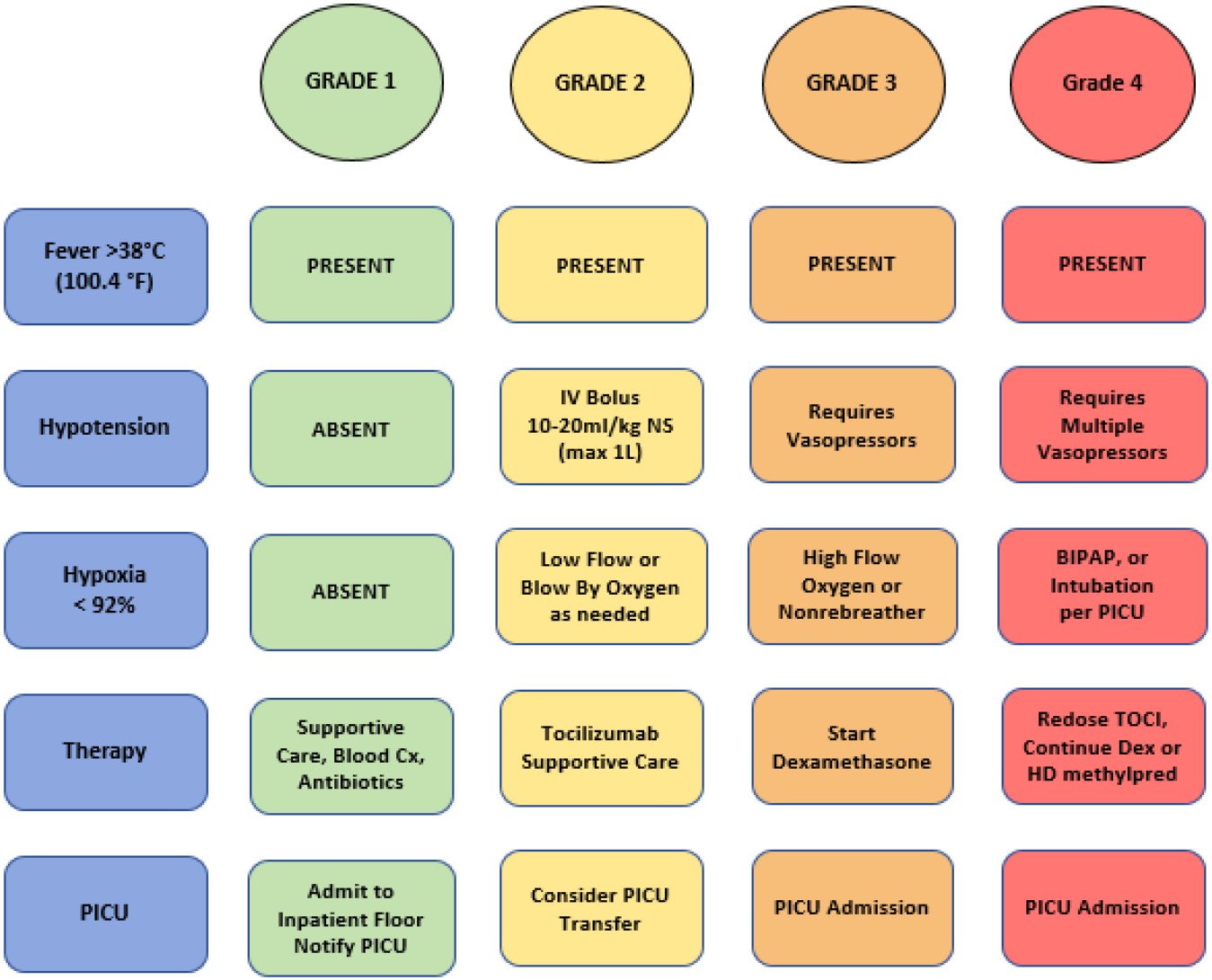
ED Management of Cytokine Release Syndrome (CRS)

- CRS is a medical emergency like sepsis
- CRS acts and is treated just like sepsis
- You know how to treat sepsis
  - ASAP blood cultures, broad spectrum Abx
  - For hypotension, give 1st NS bolus (less volume if hypoxia)
  - Alert PICU for possible transfer
  - Use the CRS management guidelines

Tocilizumab: the CAR T-cell toxicity magic bullet

- Unlike sepsis, in CRS you know exactly what the problem is (CAR T-cell toxicity)
- Tocilizumab (anti IL-6 antibody) blunts CRS without harming CAR T-cell action
- If you're giving a fluid bolus, give tociluzumab
- If you need oxygen, give tocilizumab
- IV infusion over 60 minutes, available 24/7

LCH Cytokine Release Syndrome Cheat Sheet



iCANS (immune effector-cell neurotoxicity syndrome)

- appears to be widely dependent on the specific CAR T-cell product (some have lots, some have little); less common with Kymriah

- Mild: headaches, delirium, altered consciousness, language disturbances
- Severe: seizures, brain swelling, brain herniation and death
- Early detection and early treatment is key to survival

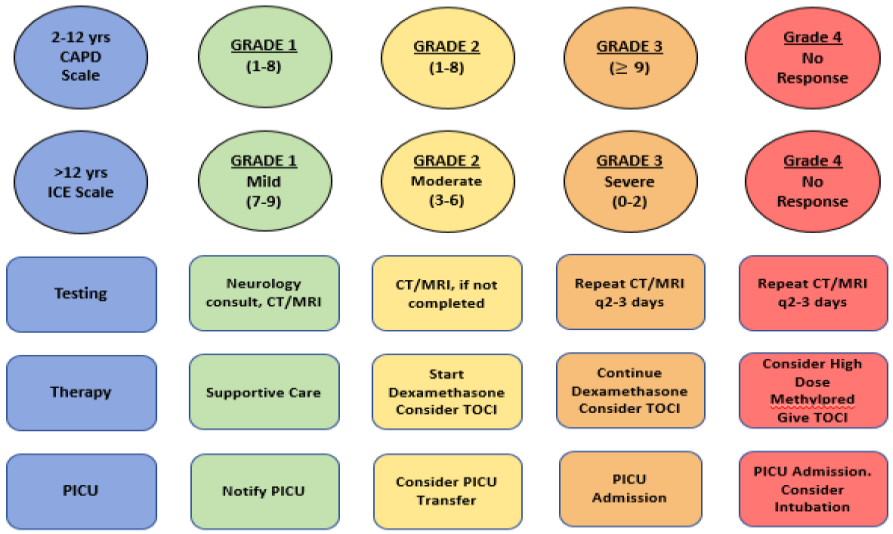
ED Management of iCANS

- CAR T-cell patients within first 45 days with mental status changes have iCANS until proven otherwise
- Call the Peds BMT Attending on arrival to ED
- Alert PICU
- Get the LCH iCANS cheat sheet
- Perform the (age-appropriate) mental status exam on the cheat sheet
- Discuss with Peds BMT attending and treat

LCH iCANS Cheat Sheet

Cornell Assessment of Pediatric Delirium (CAPD) Neurological Assessment. Patients 2 to ≤12 yr old					
	Never 4	Rarely 3	Sometimes 2	Often 1	Always 0
Does the child make eye contact with the caregiver?					
Are the child's actions purposeful?					
Is the child aware of their surroundings?					
Does the child communicate needs and wants?					
	Never 0	Rarely 1	Sometimes 2	Often 3	Always 4
Is the child restless?					
Is the child inconsolable?					
Is the child underactive - very little movement while awake?					
Does it take the child a long time to respond to interactions?					

Immune Effector Cell Associated Encephalopathy (ICE) Score Neurological Assessment. Patients >12yr old		
Orientation	Orientation to year, month, city, and hospital	**4 Points**
Naming	Name 3 objects (ex. Points to clock, pen, button)	**3 Points**
Following Commands	Ability to follow simple command (ex. show me 2 fingers)	**1 Point**
Writing	Ability to write a standard sentence (ex. Our national bird is the bald eagle)	**1 Point**
Attention	Count backwards from 100 to 10	**1 Point**



- Worst case is cerebral edema and brain herniation
- Call the Peds BMT attending and alert PICU

Summary

- Any CAR T-cell patient who arrives in ED – call the Peds BMT attending on arrival
- Any CAR T-cell patient within 45 days of cell infusion with any sign of illness has CRS until proven otherwise
- Any CAR T-cell patient within 45 days of cell infsuion with mental status changes, has iCANS until prove otherwise
- Reference the LCH CAR T-cell toxicity cheat sheets