



Society for Immunotherapy of Cancer

# Cellular Immunotherapy in the Community Hospital Setting

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Milwaukee, WI

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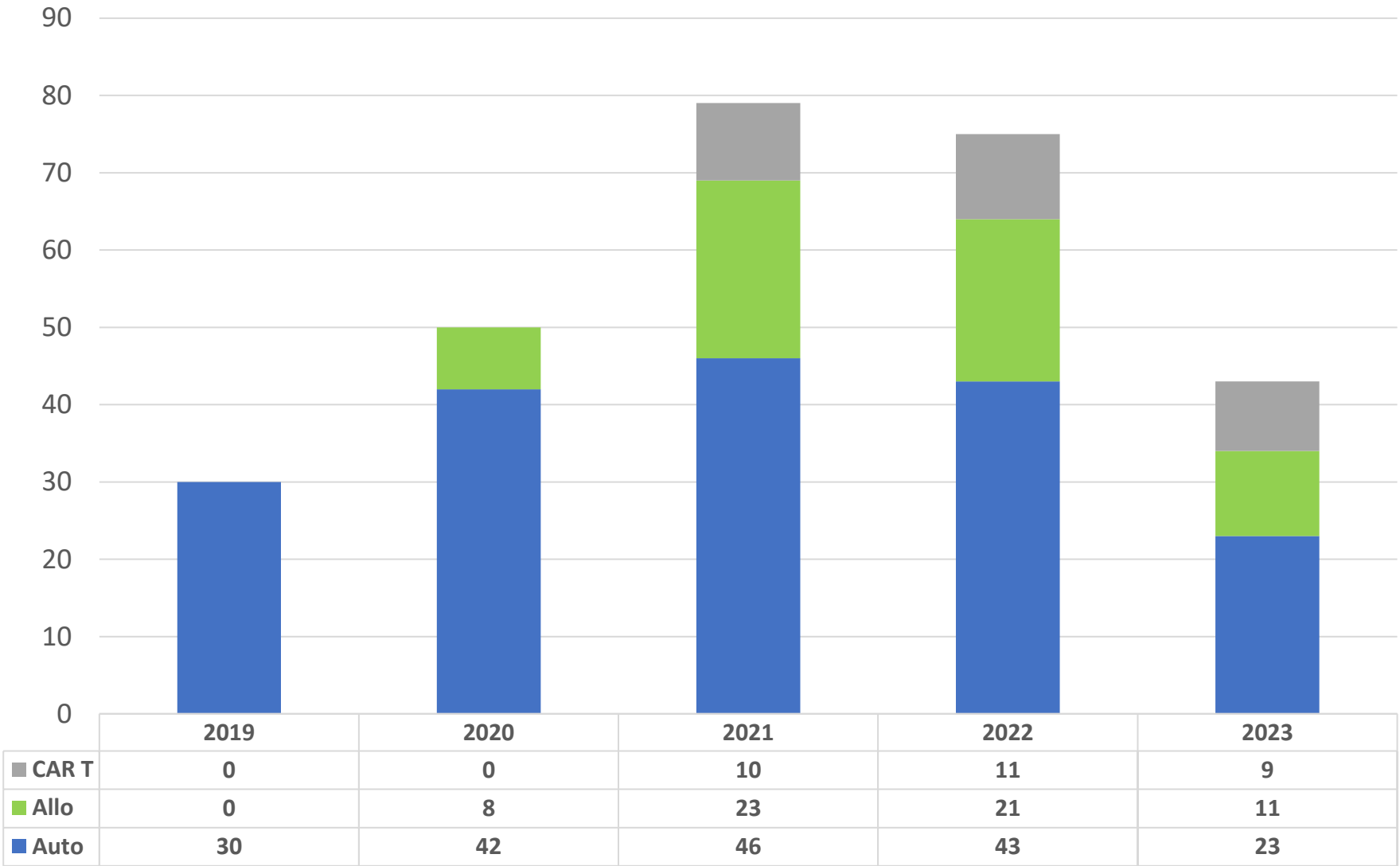


# Aurora St. Luke's Medical Center Transplant Program

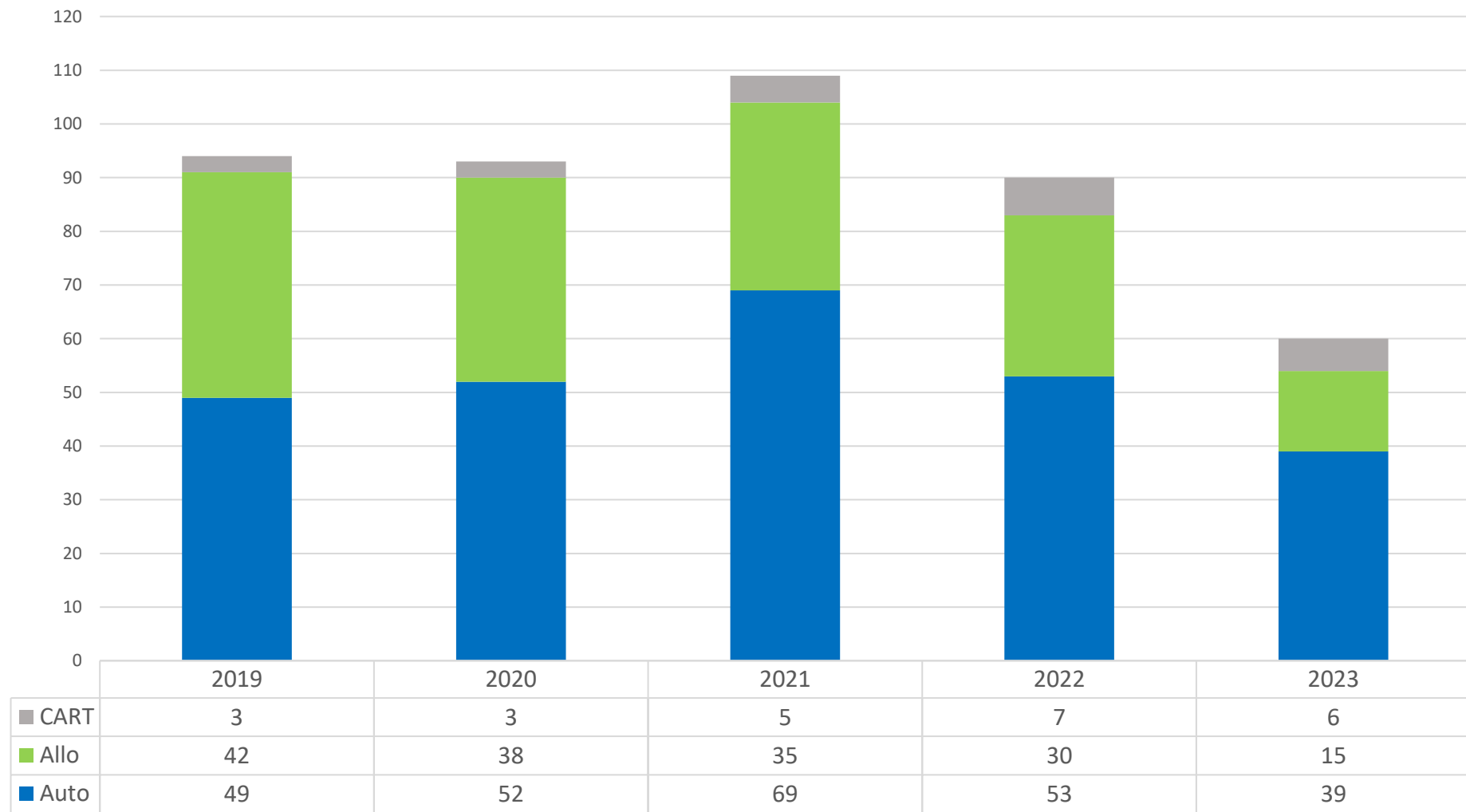
- **Community Hospital-Based Program in Milwaukee, WI (Tertiary Care)**
- **Stem Cell Transplant/Cell Therapy Program established in 1990**
- **>1,000 Total Transplant/CAR-T cases**
  - Autologous Transplants (first case 1990)
  - Allogeneic Transplants (first case 2020)
  - CAR T Cell Therapy (first case 2021)
- **> 30 Commercial CAR-T cell therapy cases to date**
  - Program experienced in Virus-Specific T cells (VST) and Tumor Infiltrating Lymphocytes (TIL)



# Aurora St. Luke's Medical Center Transplant Program Volumes



# Advocate Lutheran General Transplant Program Volumes

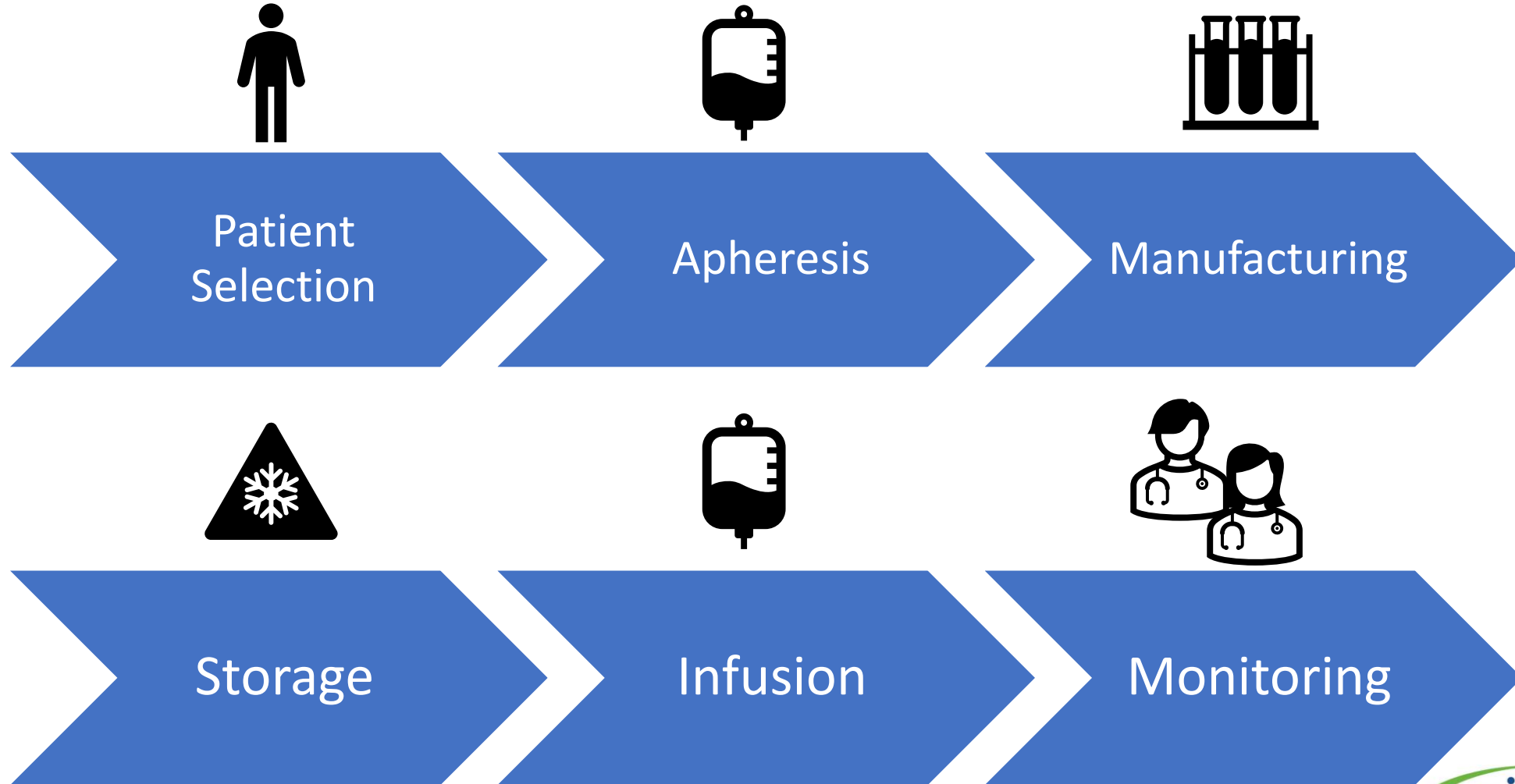


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# The Three Pillars:

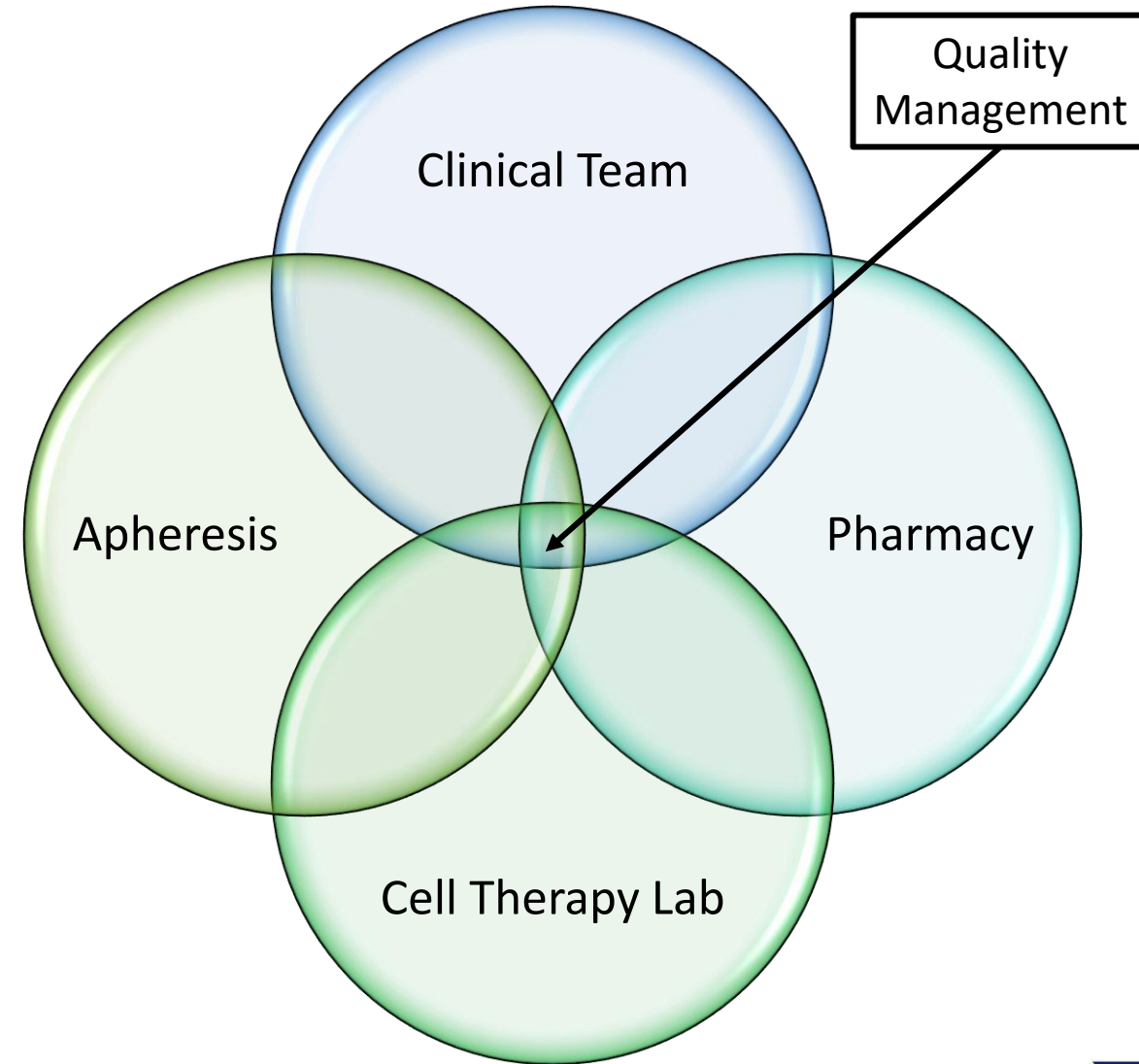
- **Clinical: Education Across the Care Continuum**
- **Operational: Coordinate Continuity of Care and Team Management**
- **Financial: Facilitate Coding, Billing, and Economics**

# CAR-T Cell Process



## Before starting a new program...

- Evaluate whether your volume supports the work
  - Will you have enough referrals to support competency requirements and minimum numbers for accreditation?
- Think about your patient population
  - Are your patients mostly high risk cases?  
Good mixture?
- Consider your payer mix
  - CAR-T is expensive and payer mix is crucial for staying afloat
- Get input from key stakeholders (apheresis, cell therapy lab, pharmacy, ICU, ED, administration, billing, research, etc)





# REMS

- All CAR-T cell products and some bispecific T cell engagers (BiTEs) have REMS program requirements
  - REMS training must be completed by all team members performing the functions of prescribe, dispense, or administer
- REMS programs for each product vary and attention is needed to the details, for example:
  - How close to the facility must the patient stay and for how long
  - Management of adverse events

# Commercially Available CAR-T Products

Product	Manufacturer	Disease	Onsite cryopreservation required?	Water bath/Dry Thaw Device Required?
Kymriah (tisagenlecleucel)	Novartis	FL; LBCL; pediatric ALL	Yes	Yes
Yescarta (axicabtagene ciloleucel)	Kite (Gilead)	FL; LBCL	No	Yes
Tecartus (brexucabtagene autoleucel)	Kite (Gilead)	MCL; adult ALL	No	Yes
Breyanzi (lisocabtagene maraleucel)	Bristol Myers Squibb	LBCL	No	No
Abecma (idecabtagene vicleucel)	Bristol Myers Squibb	MM	No	Yes
Carvykti (ciltacabtagene autoleucel)	Janssen/Legend Biotech	MM	Yes	Yes

ALL = Acute Lymphoblastic Leukemia; FL = Follicular Lymphoma; LBCL = Large B Cell Lymphoma; MCL = Mantle Cell Lymphoma; MM = Multiple Myeloma

# Clinical Team Considerations

- ☐ Need a Quality Management Program (if not already established)
  - ☐ SOPs on patient selection & education, treatment protocols, management of cytokine release syndrome (CRS) & neurotoxicity
  - ☐ Validations of infusion processes, Maintenance of equipment, etc.
- ☐ Determine whether preparative regimen and cell infusion will be given inpatient or outpatient
- ☐ Patient must remain close to hospital for 30 days
  - ☐ May need housing?
- ☐ Caregiver required; patient unable to drive for 8 weeks
- ☐ Training/Competency needed for Physicians, APCs, RNs to CAR-T cell administration as well as detection and management of adverse events
  - ☐ 24/7 availability of Cell Therapy Physician
  - ☐ CRS & Neurotox assessments
- ☐ Training and communication with the ED and ICU

# Pharmacy Considerations

- ☐ Pharmacy MUST be involved
- ☐ CAR-T REMS programs require 2 doses of tocilizumab on-hand for each patient
- ☐ Some programs choose to have Pharmacy order and dispense the CAR-T products
  - ☐ Our program uses our Cell Therapy Lab for ordering and dispensing
- ☐ Build EMR structure for treatment plans including preparative chemotherapy regimen

## Tocilizumab Inventory Reservation

- Place four (4) vials of tocilizumab 400 mg in a bag and label with custom patient specific label.
- Place labeled bag with vials in the refrigerator in bin labeled "For CAR-T Patients ONLY"
- Do not remove bag from bin until notified by RPH

Patient: \*\*\*

MRN: \*\*\*

Date of admission: \*\*\*

# Apheresis Considerations

Have an  
established  
Apheresis  
Program?

- Need SOPs for collection and labeling
- Possibly packaging of cells and sending to manufacturer

Plan to establish  
Apheresis  
Program?

- Establish a quality management plan
- Purchase/Qualify equipment and supplies
- Validate procedures

Will contract with  
an apheresis  
facility?

- Can perform procedures on-campus or off-campus
- Need agreements in place
- Ensure contracted facility is involved with onboarding process

# Cell Therapy Lab Considerations

☐ Do you NEED a cell therapy lab?

☐ Depends on the CAR-T cell product

☐ If no cell therapy lab:

☐ Who will package fresh apheresis product to send to manufacturer?

☐ Who will receive frozen product for storage until use?

☐ Who will thaw cells for administration?

☐ Facility needs:

☐ Vapor phase nitrogen storage ( $\leq -150^{\circ}\text{C}$ ) with continuous temperature and level monitoring

☐ Water bath or dry thaw device that is qualified and maintained for thawing cells

☐ If cells need to be cryopreserved prior to sending to manufacturer:

☐ Biosafety cabinet, centrifuge, tube welder, etc.

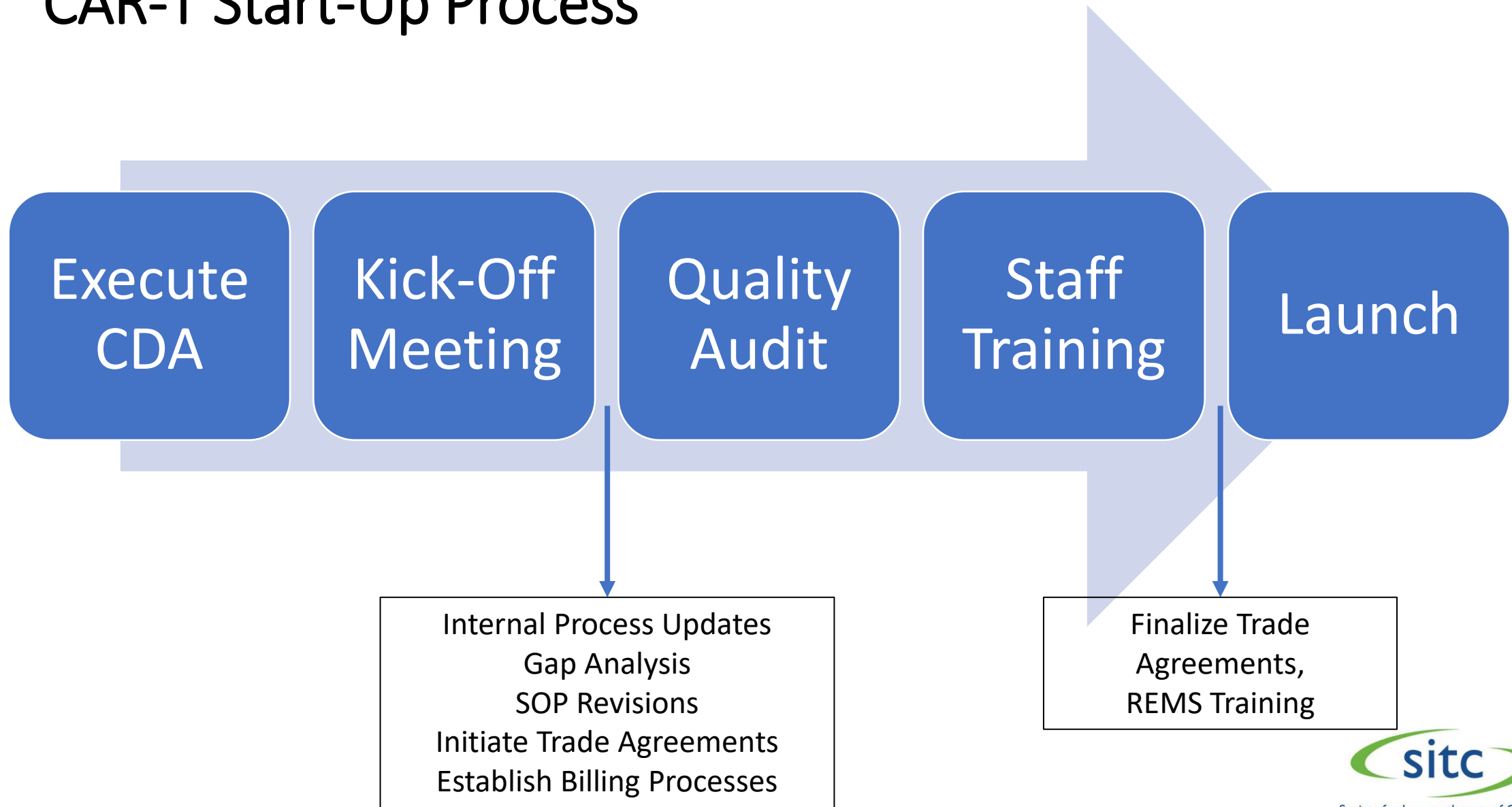
☐ Validated cryopreservation processes

☐ Environmental monitoring

# Other things to keep in mind....

- If CAR-T products do not meet manufacturer's specifications, a research protocol (expanded access) will be needed if you choose to administer the cells
- Apply for FACT Accreditation for Immune Effector Cell Therapy
- RN Coordinator role is key for keeping track of process, consenting, coordinating between manufacturer, apheresis, cell lab, infusion team

# CAR-T Start-Up Process





# Considerations for BiTE

- Develop standards for management of BiTE administration and adverse event management
- Read package inserts carefully for instructions on day of admission, as all products are different
- Prepare to comply with REMS when needed
- Educate providers and RNs both inpatient and outpatient
- Involve ED and ICU

# Commercially Available BiTEs

Product Name	Year Approved	Indication
Blincyto (blinatumomab)	2014	To treat Philadelphia chromosome-negative relapsed or refractory B cell precursor acute lymphoblastic leukemia
Hemlibra (emicizumab-kxwh)	2017	To prevent or reduce the frequency of bleeding episodes in hemophilia A with factor VIII inhibitors
Rybrevant (amivantamab-vmjw)	2021	To treat locally advanced or metastatic non-small cell lung cancer with certain mutations
Kimmtrak* (tebentafusp-tebn)	2022	To treat a form of unresectable or metastatic uveal melanoma
Vabysmo (faricimab-svoa)	2022	To treat neovascular (wet) age-related macular degenerated and diabetic macular edema
Tecvayli (teclistamab-cqyv)	2022	To treat relapsed or refractory multiple myeloma
Lunsumio (mosunetuzumab-axgb)	2022	To treat relapsed or refractory follicular lymphoma
Epkinly (epcoritamab-bysp)	2023	To treat relapsed or refractory diffuse large B-cell lymphoma
Columvi (glofitamab-gxbm)	2023	To treat relapsed or refractory diffuse large B-cell lymphoma or large B-cell lymphoma

\*Kimmtrak is technically a bispecific molecule, not a bispecific antibody. Like some of the other bispecific antibodies used to treat some cancers, Kimmtrak has one arm using an antibody fragment to bring killer T cells to the tumor. Kimmtrak's other arm is an analogous structure found on T cells, the T cell receptor, instead of an antibody fragment to target a tumor antigen.

# Final Thoughts

- Confirm patient volumes support cellular therapy program
- Focus on adverse event management
  - Do you have the infrastructure to support this?
- Education at all levels is critical
  - Differences in REMS programs
  - Include ED and ICU clinical staff