



Society for Immunotherapy of Cancer

Cellular Immunotherapy in the Community Hospital Setting

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Milwaukee, WI

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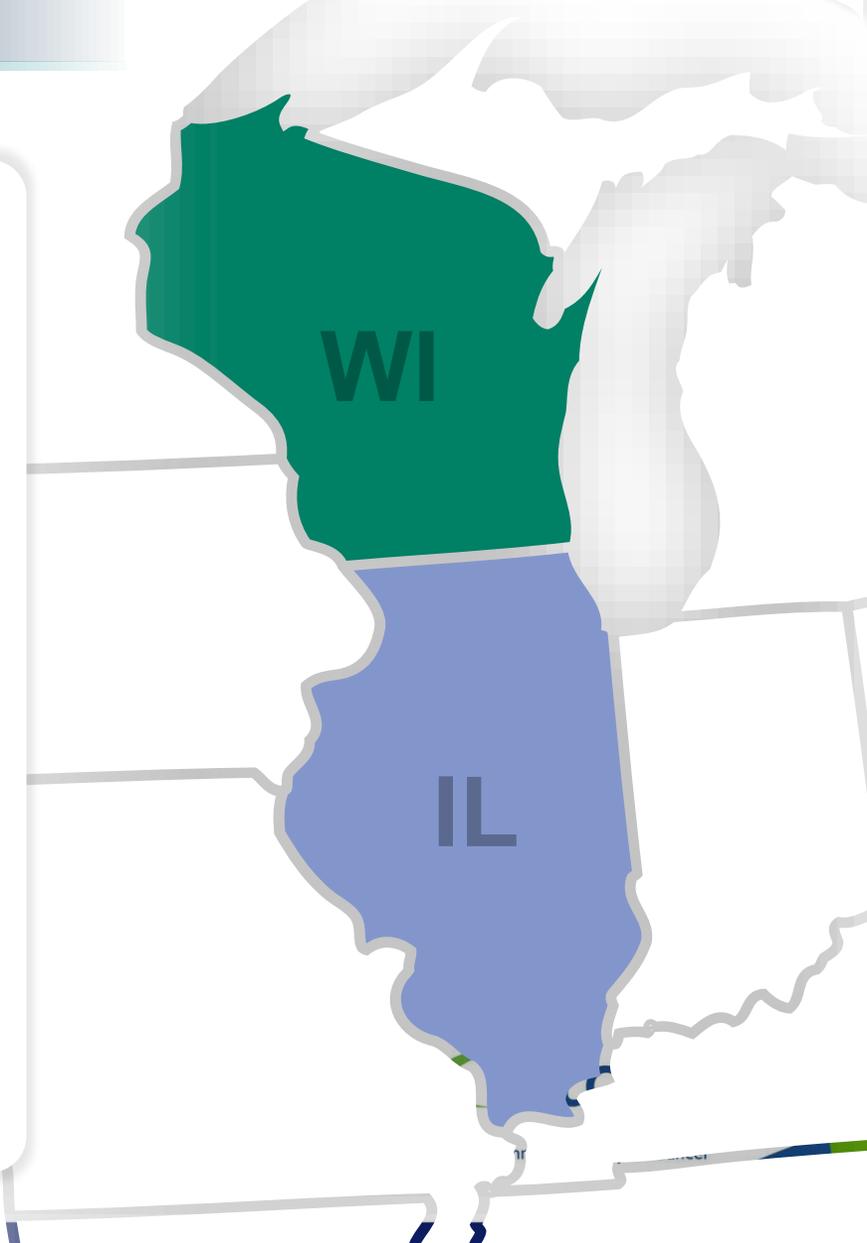
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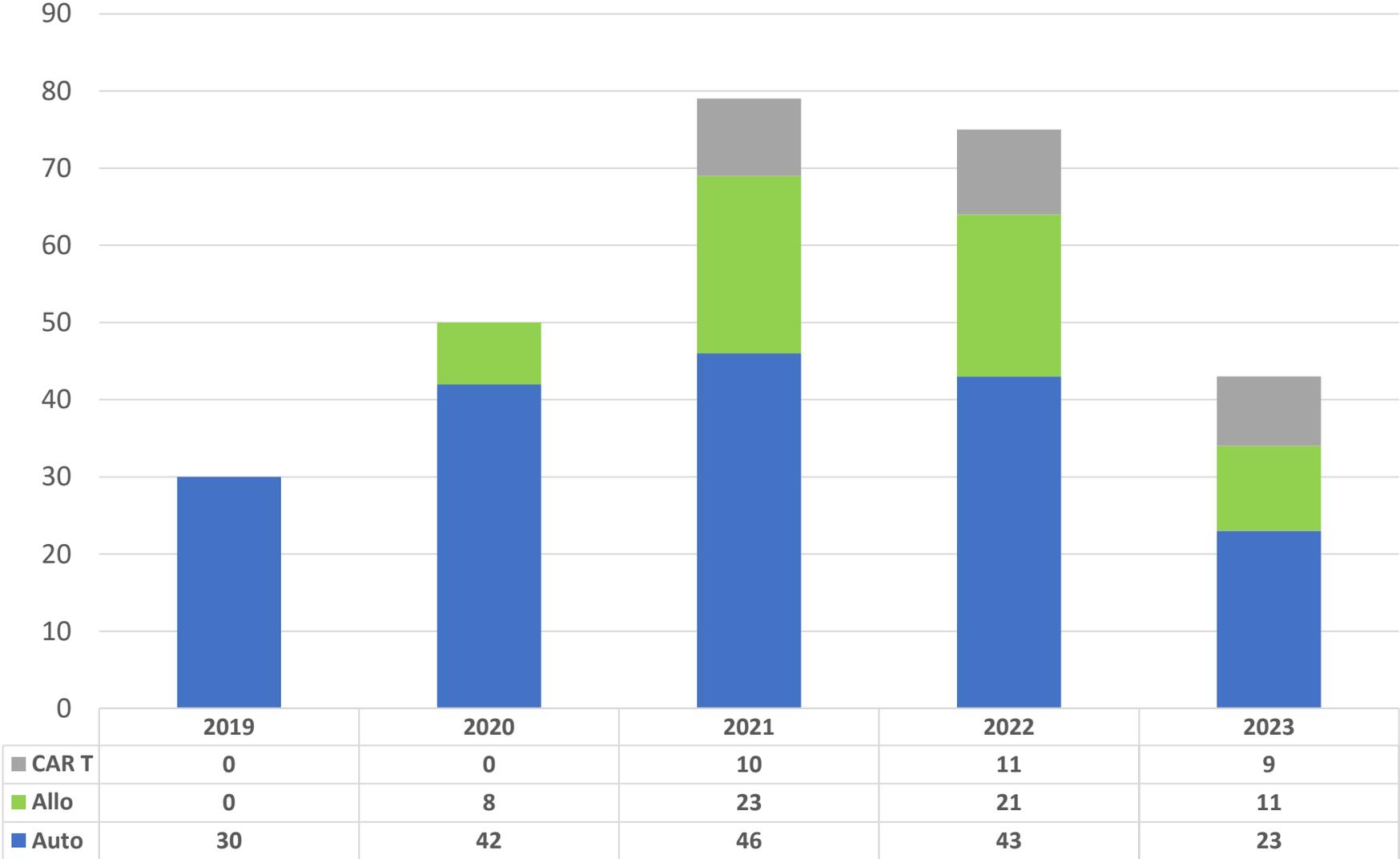


Aurora St. Luke's Medical Center Transplant Program

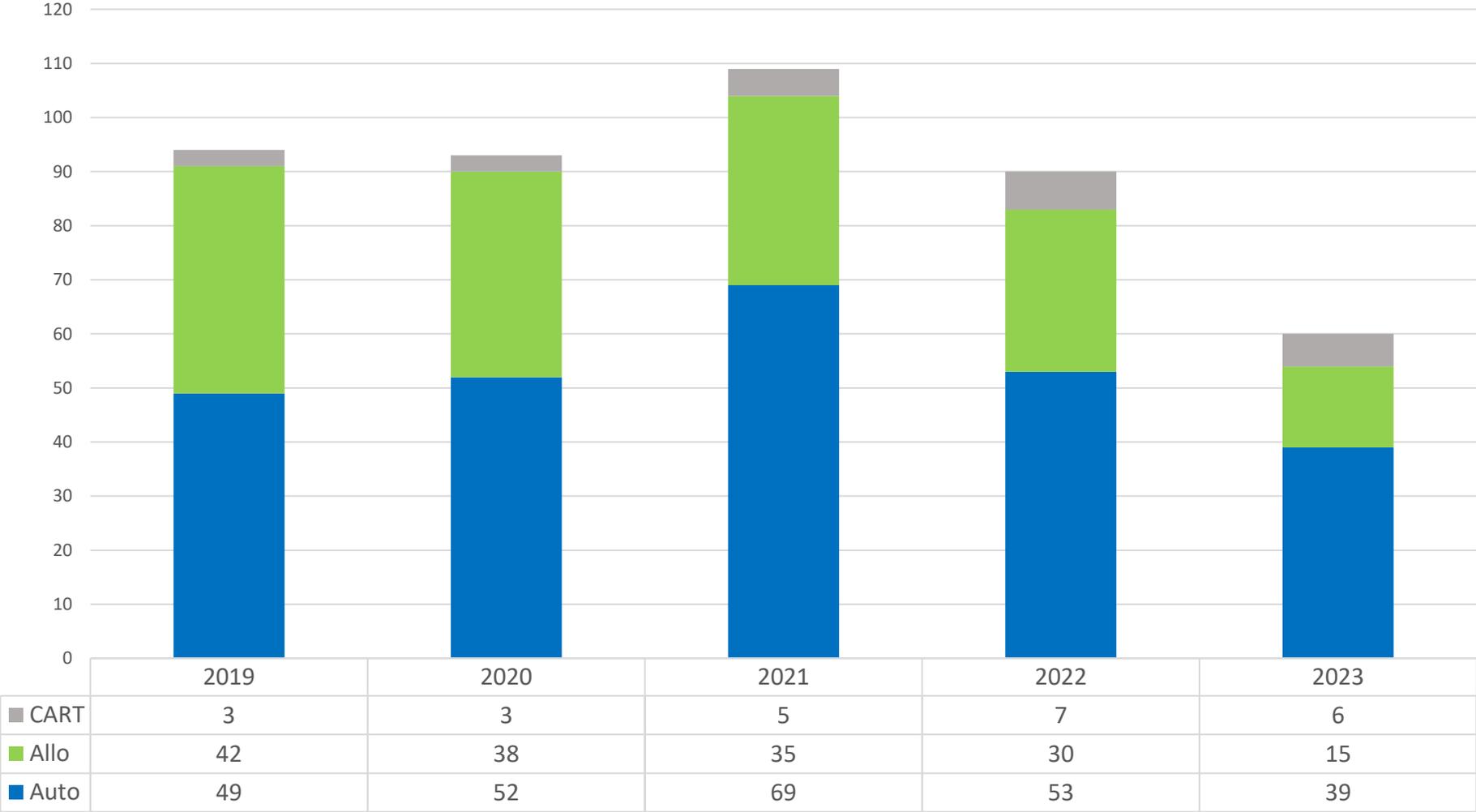
- **Community Hospital-Based Program in Milwaukee, WI (Tertiary Care)**
- **Stem Cell Transplant/Cell Therapy Program established in 1990**
- **>1,000 Total Transplant/CAR-T cases**
 - Autologous Transplants (first case 1990)
 - Allogeneic Transplants (first case 2020)
 - CAR T Cell Therapy (first case 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



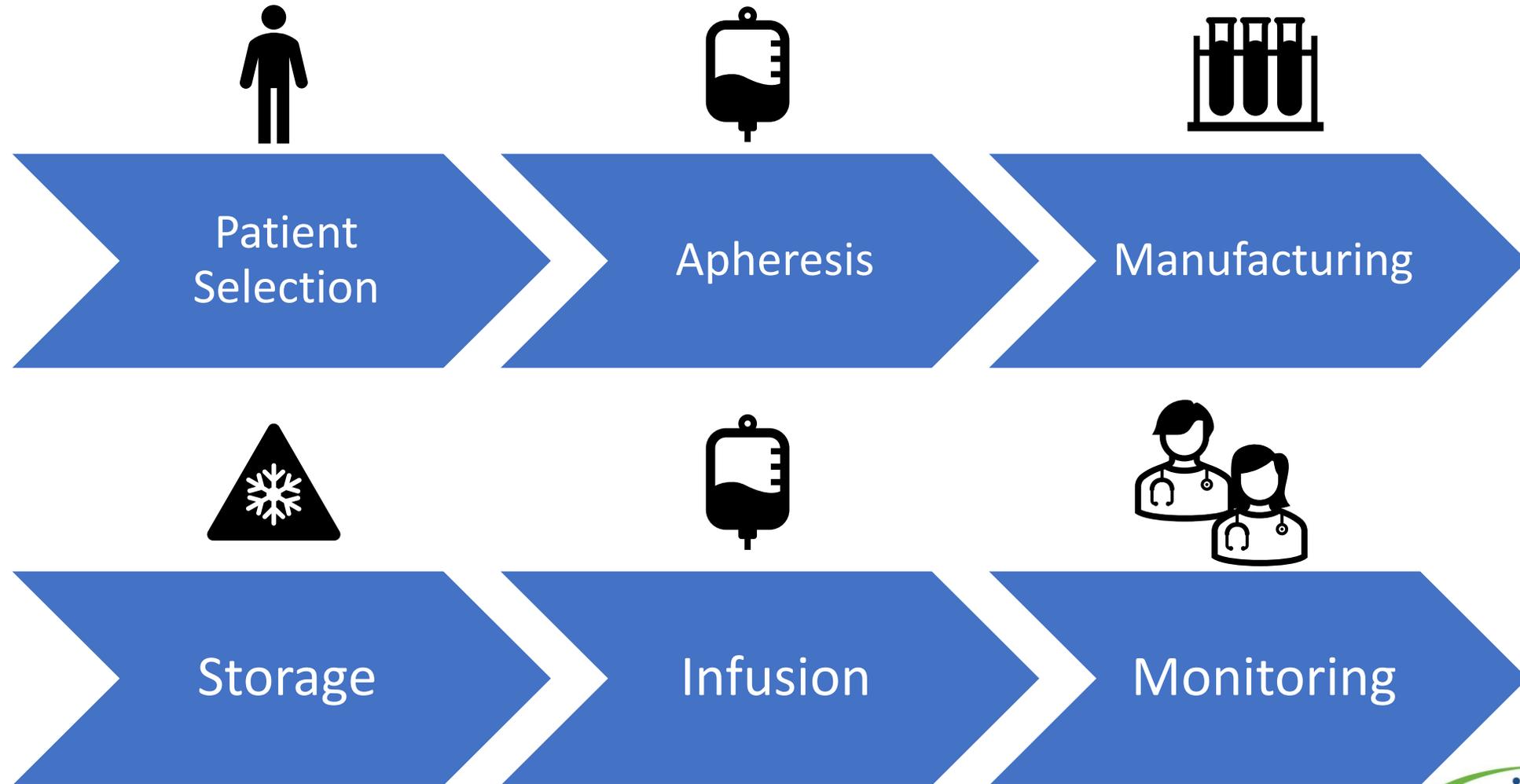
Advocate Lutheran General Transplant Program Volumes



The Three Pillars:

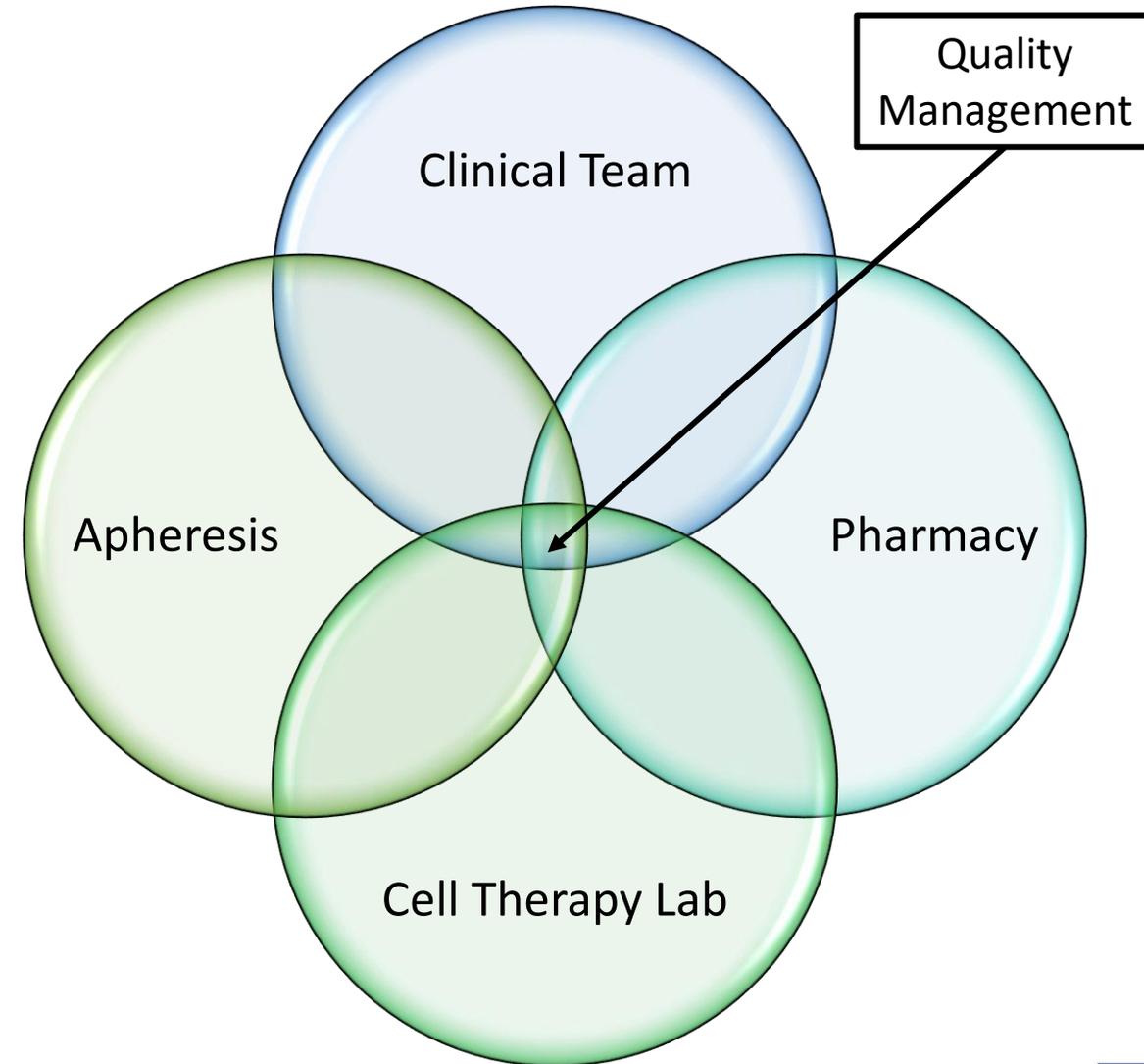
- **Clinical: Education Across the Care Continuum**
- **Operational: Coordinate Continuity of Care and Team Management**
- **Financial: Facilitate Coding, Billing, and Economics**

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.

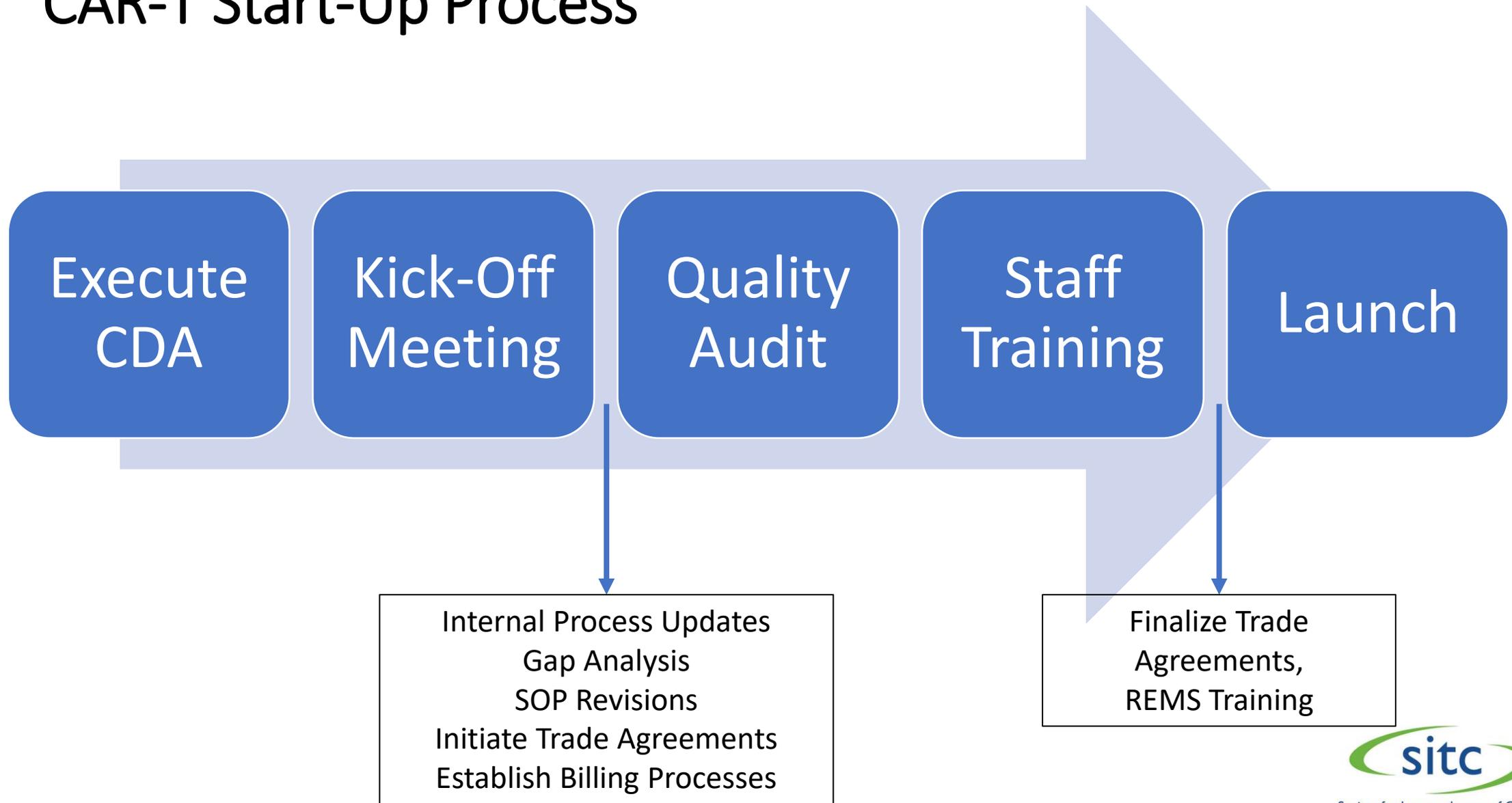
Validated cryopreservation processes

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