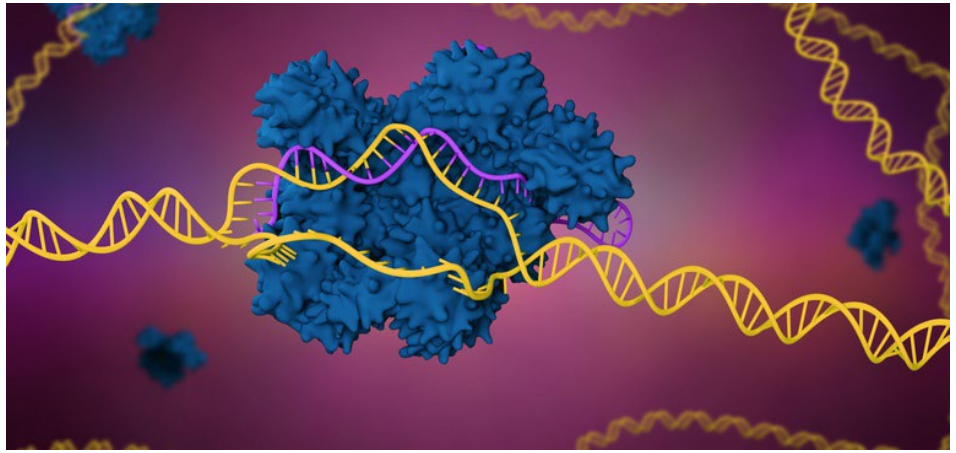
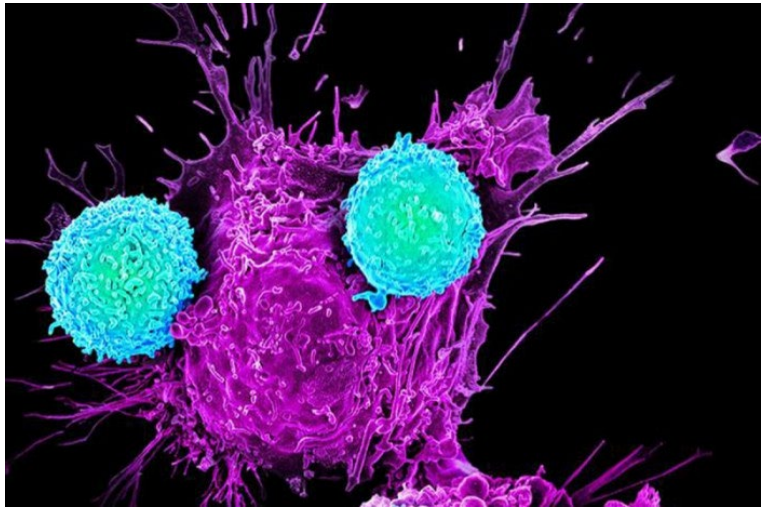
“Cancer Care: The Rapidly Emerging World of Clinical Cellular Immunooncology and how it can integrate with community practices”





Richard Maziarz MD

Director, Adult BMT & Immune Effector Cell Therapy Programs

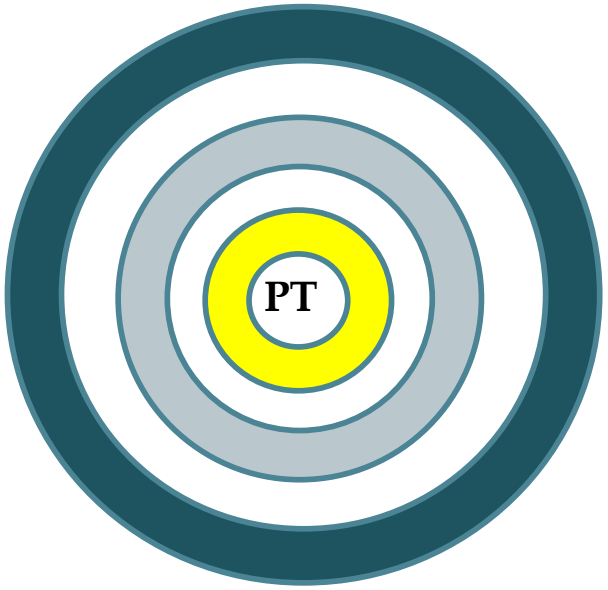
March 18, 2022

Disclosures

- Patents & Royalties: Athersys; Springer Publishers
- Research Funding: Novartis, BMS/ Juno,
- Consultancy: Novartis, Artiva Biotherapeutics, Intellia,
- ASTCT: Chair, Value & Health Econ interest group

Provider Principles

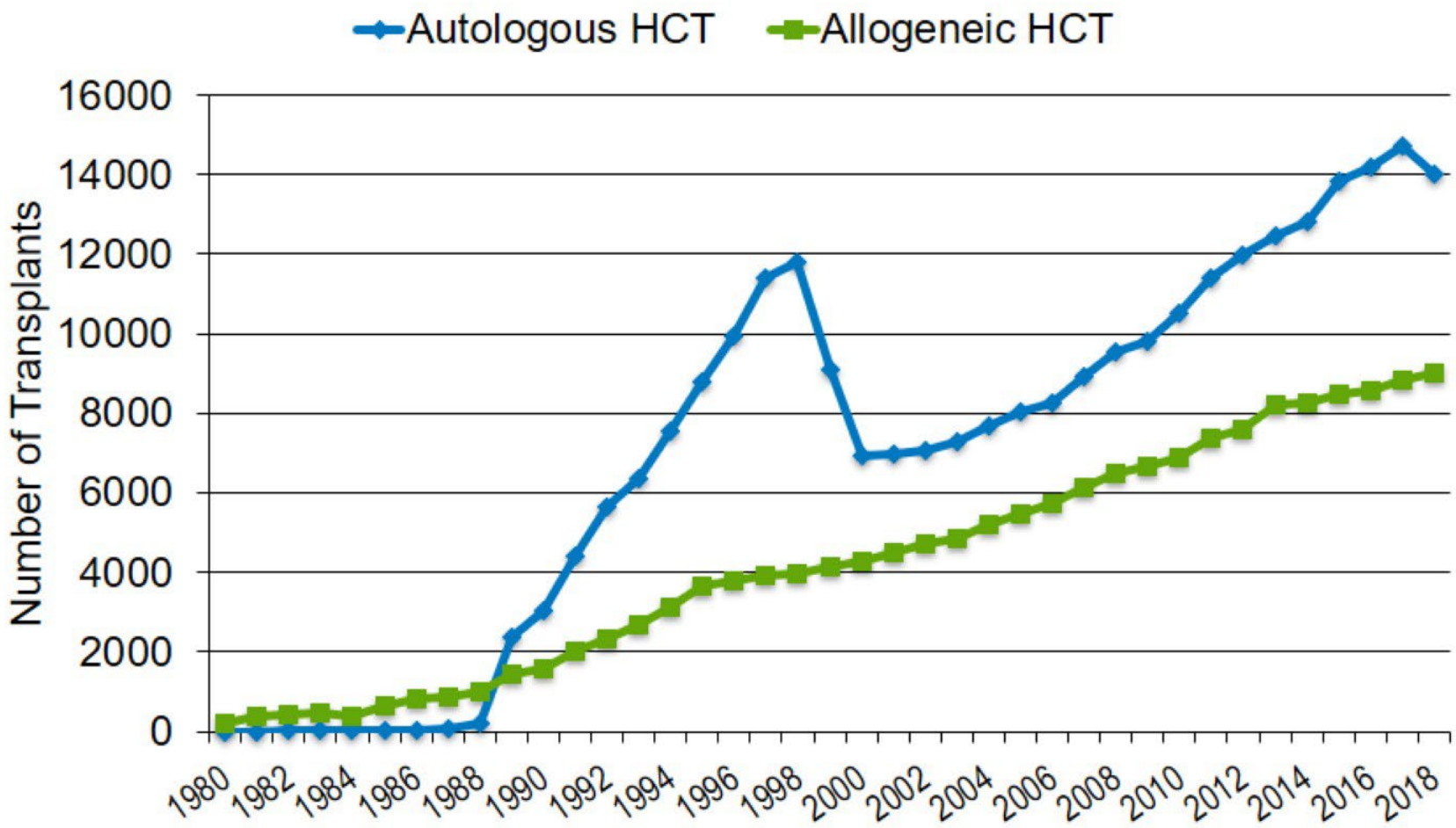
- Primary goal is the direct delivery of care to patients
- The patient is the center of our attention.



Cell Therapy 2022

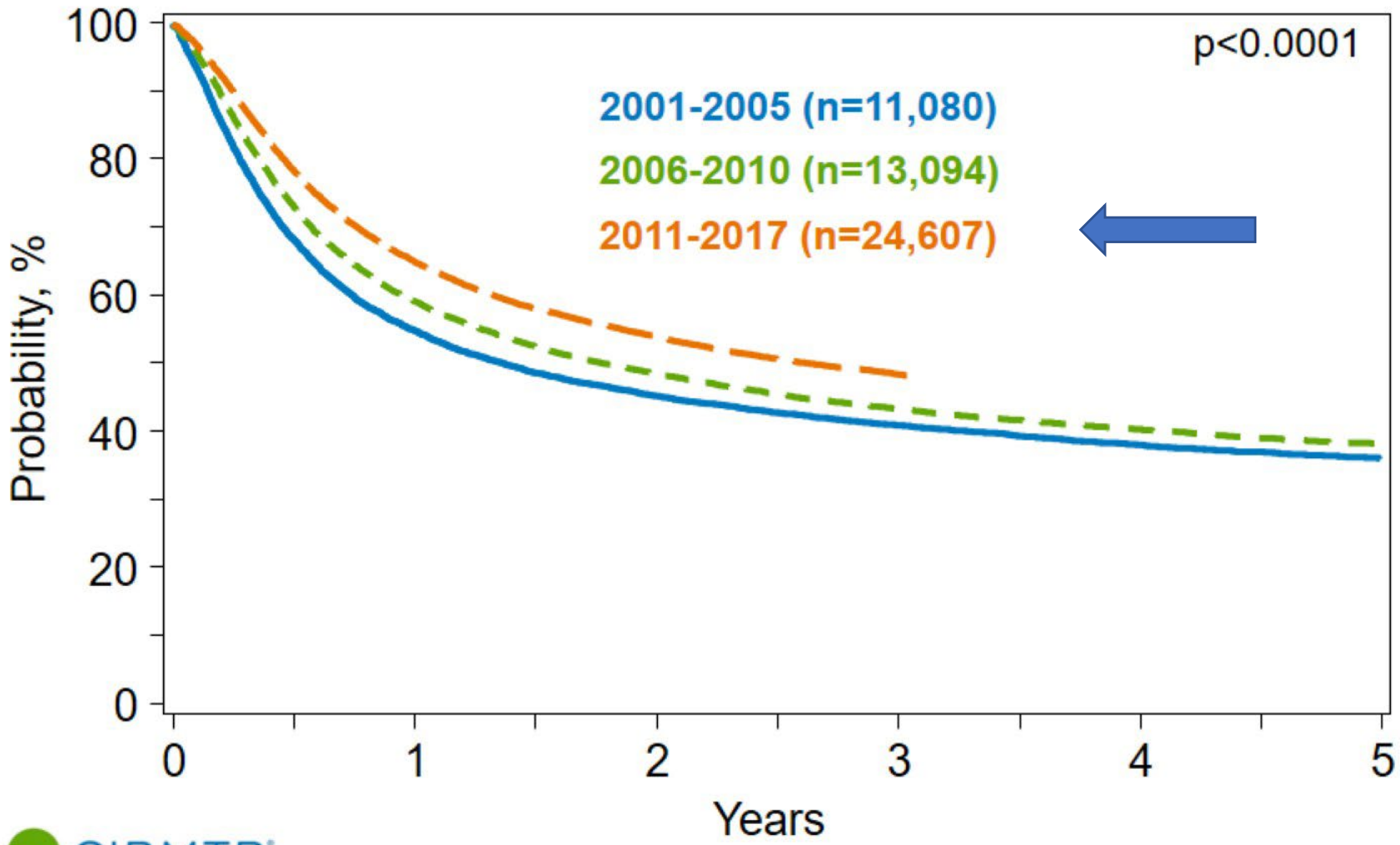
- HCT remains the paradigm for clinical cell therapy
  - Continues to provide important treatment options for patients with hematologic malignancies, as well as other disorders
- Ongoing improvements in supportive care → expansion of application of a safer procedure
- Expansion of cell therapy options → further outcome improvement (adult stem cells, T regs, viral specific T cells, etc)
- Evidence based medicine → dictate expansion of procedures (MDS or NHL in the elderly; scleroderma; sickle cell; multiple sclerosis)

Annual Number of HCT Recipients in the US by Transplant Type



CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Trends in Survival after Allogeneic HCT for AML, ≥18, 2001-2017



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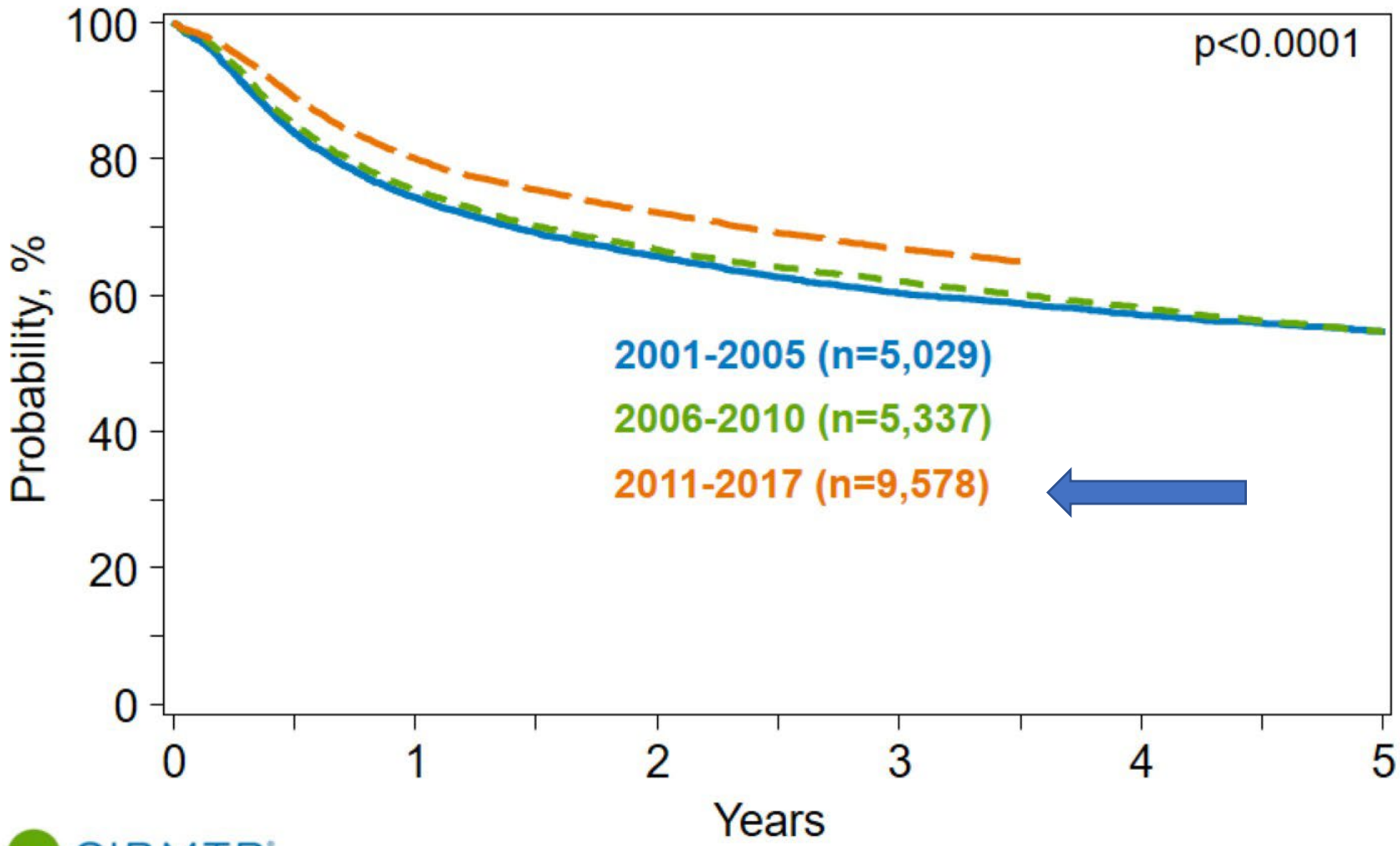
Trends in Survival after Autologous HCT for DLBCL, 2001-2017



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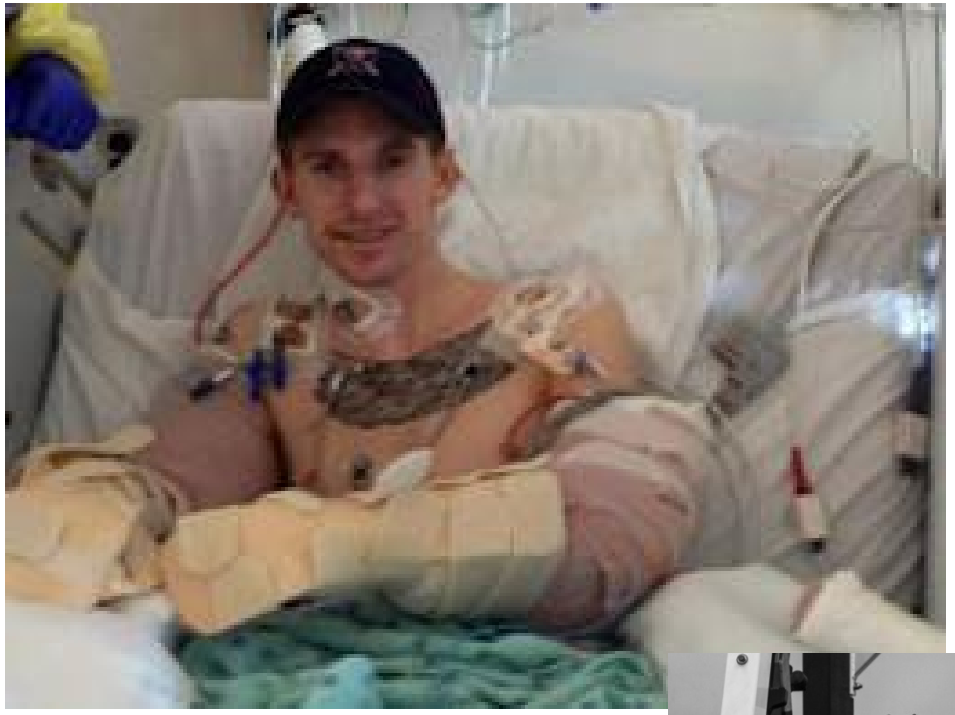
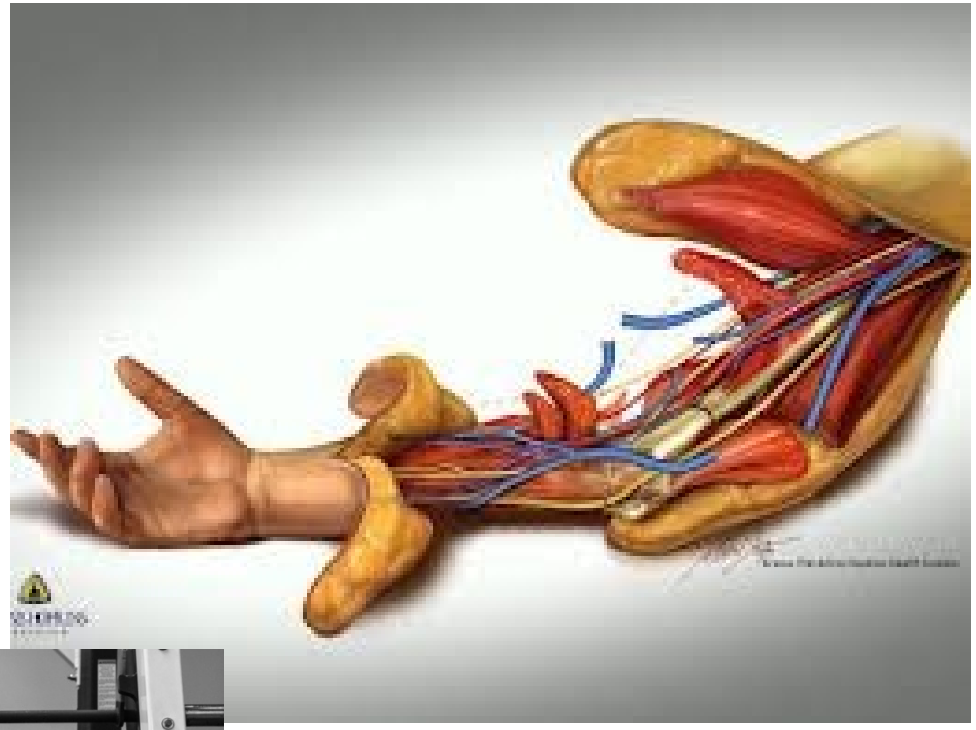
The Future is Now
Novel Therapeutic Interventions:
Vascularized Composite Allotransplantation





CELLS ARE DRUGS*

- Autologous HCT- PBSC are used to enhance Hematopoietic Recovery after high-dose chemoradiotherapy
- Allogeneic HCT - Allogeneic stem cells are used to enhance hematopoietic recovery after high-dose chemoradiotherapy and critical to the intervention, donor derived, adoptively transferred mature lymphocytes are used to establish a graft versus malignancy effect
- Immune effector cells/ CAR–T – Graft engineered autologous (? allogeneic) T cells targeting surface B-cell antigens that activate the cytotoxic capacity of the ex vivo manufactured, reintroduced T-cell products
- *Regulated by FDA- exempt or non-exempt (e.g. more than minimally manipulated; heterologous use)

Cancer Therapy Evolves

Surgery

Radiation

Chemotherapy

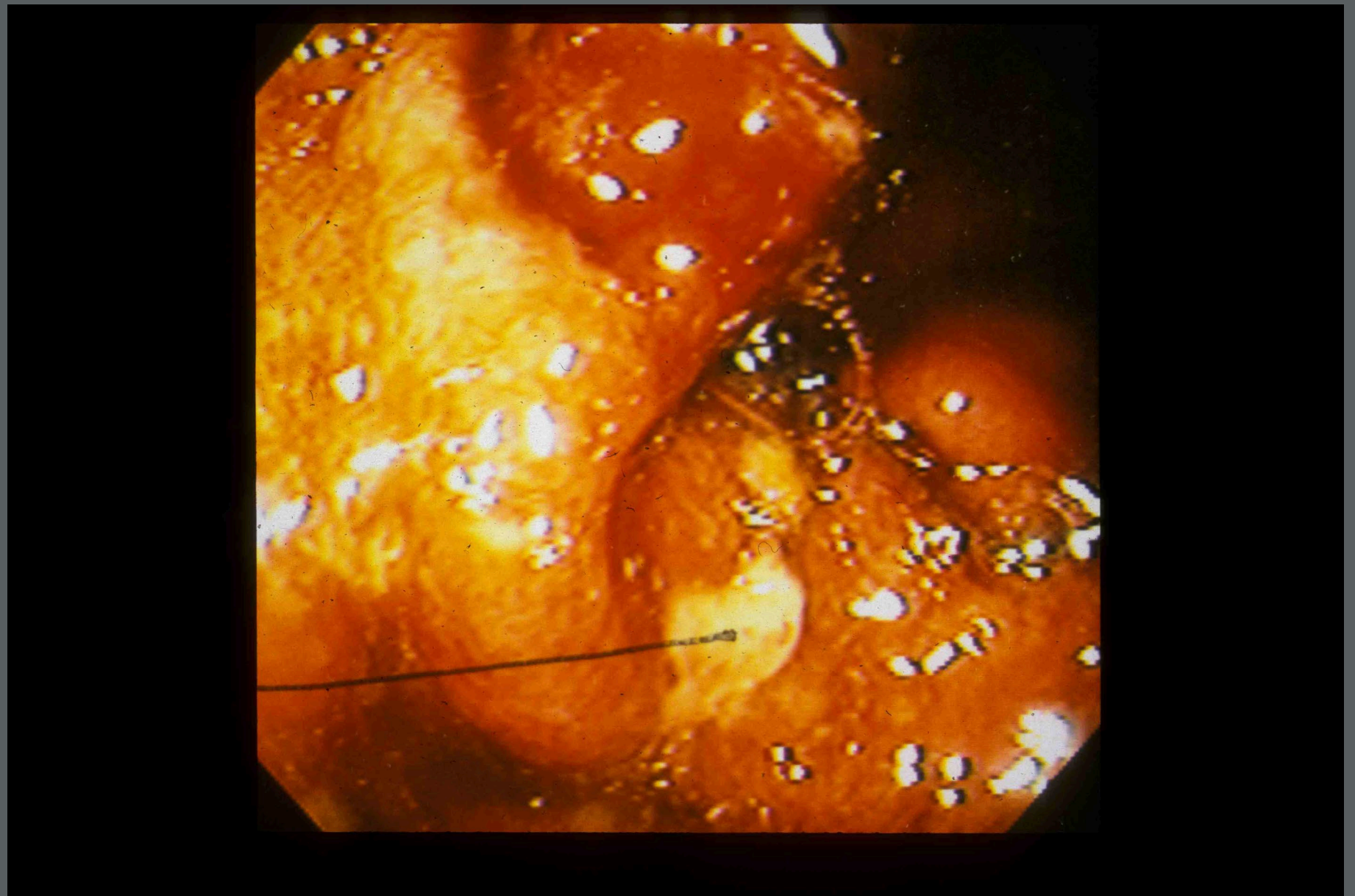
Immunotherapy/
Cellular Therapy

History:

Do T cells really make an impact in a clinical scenario

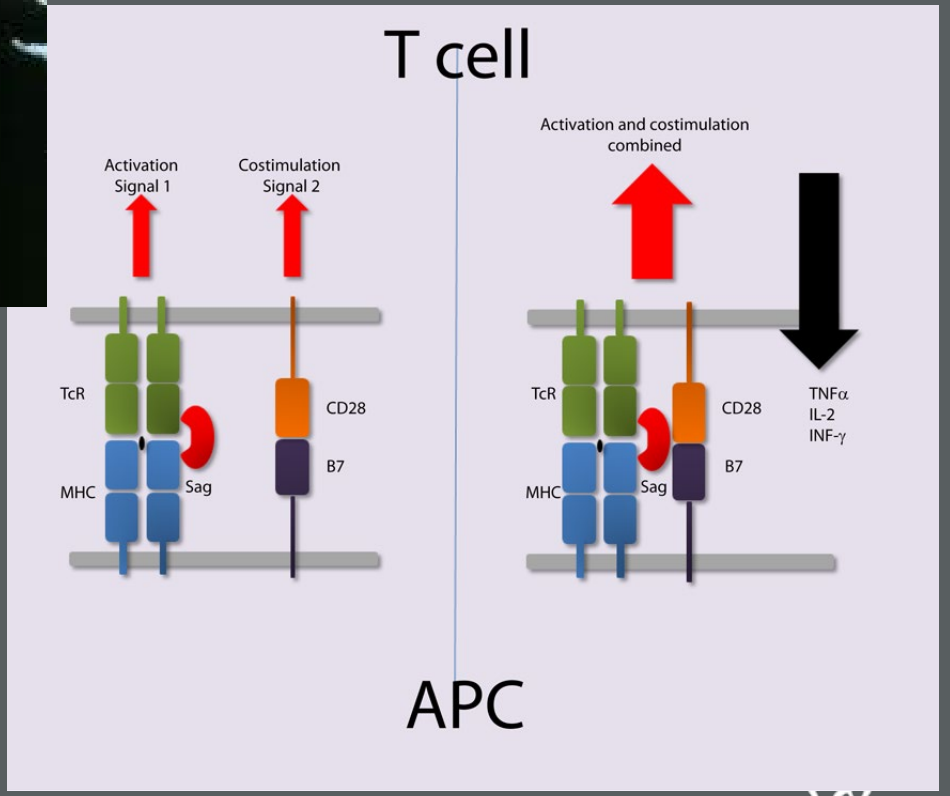
OHSU

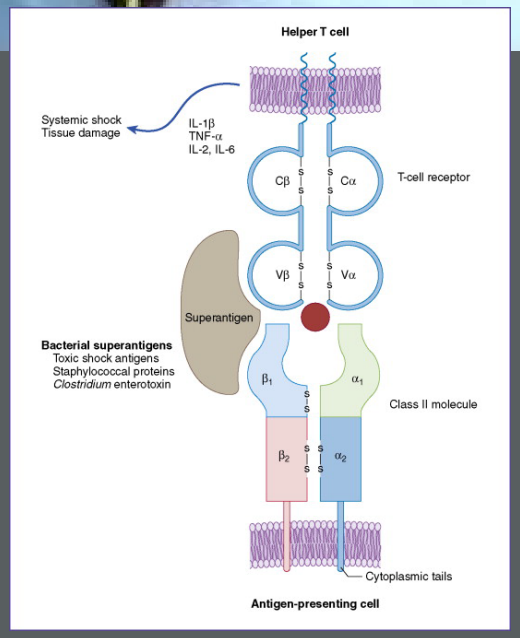
Grade IV Acute GVHD of the G I Tract is a T cell Disease

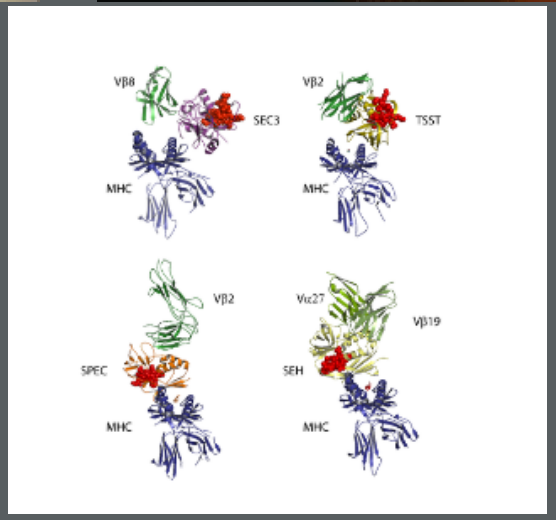


Toxic Shock Syndrome:

a T cell disorder of Superantigens





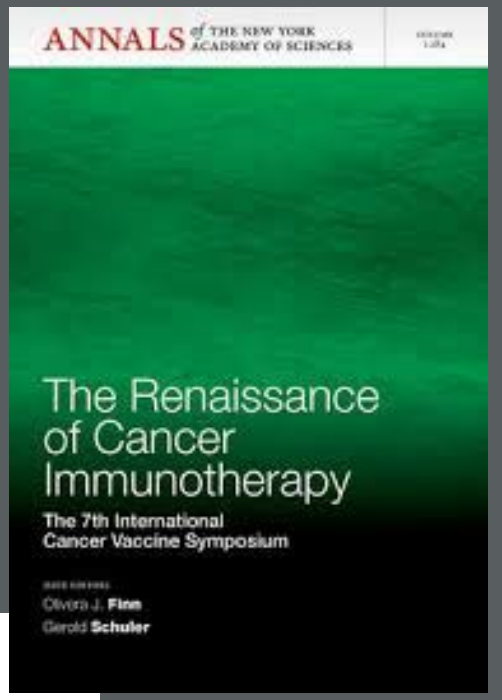


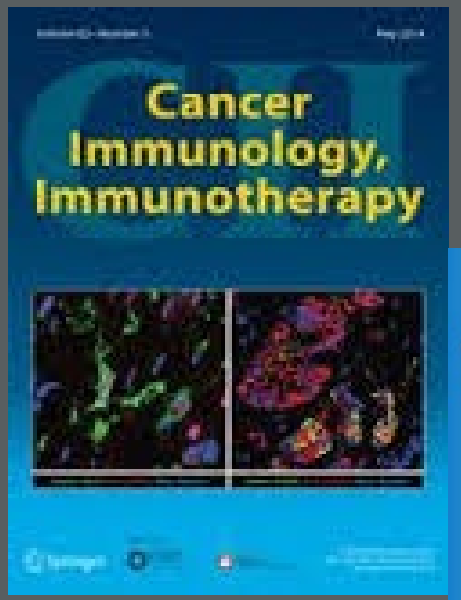
Fraser, PLOS Bio, 2011

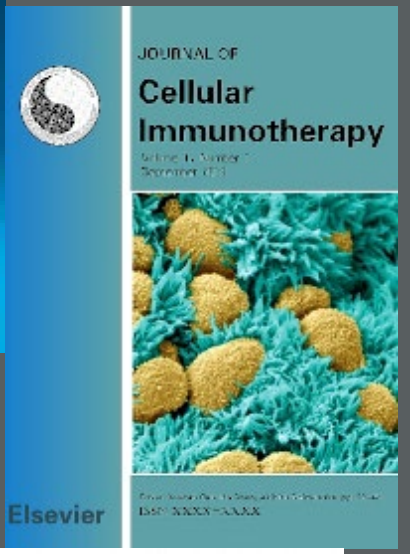
OHSU


Science
Breakthrough of the Year
Cancer Immunotherapy
T cells on the attack

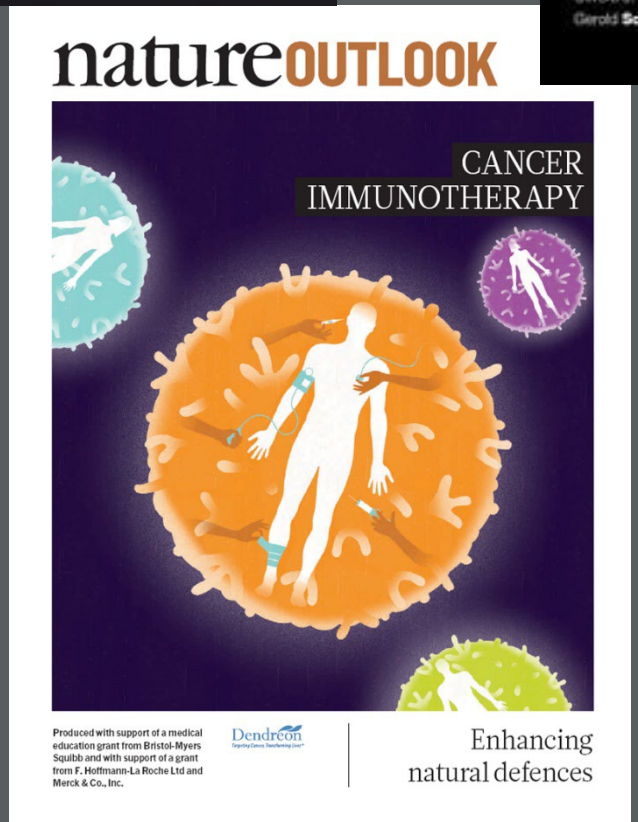

nature REVIEWS
Tumour immunology & immunotherapy
CANCER
STIMULATING DEBATE
Strategies to target the immune checkpoint


ANNALS of THE NEW YORK ACADEMY OF SCIENCES
The Renaissance of Cancer Immunotherapy
The 7th International Cancer Vaccine Symposium
Olivera J. Finn
Gerold Schuler

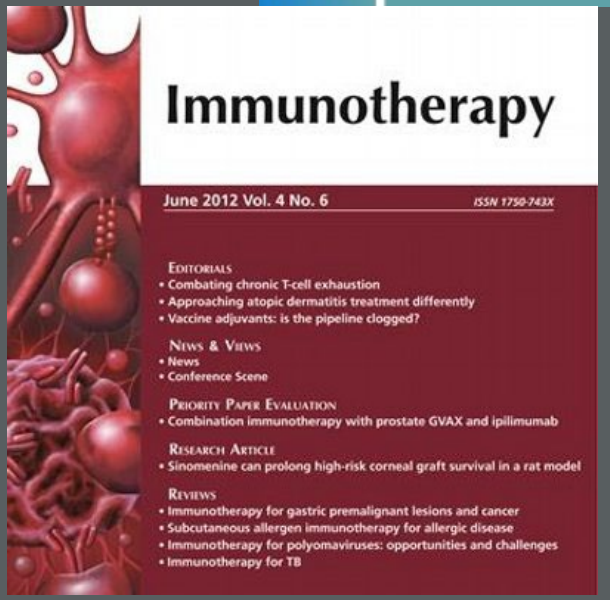

Cancer Immunology, Immunotherapy


JOURNAL OF
Cellular Immunotherapy
Elsevier


The lingering legacy of Deepwater Horizon
The future of human genome editing
Drilling into engine oil antiwear films
Science
$10
3 APRIL 2015
AAAS
SPECIAL ISSUE
Cancer Immunology and Immunotherapy


natureOUTLOOK
CANCER IMMUNOTHERAPY
Produced with support of a medical education grant from Bristol-Myers Squibb and with support of a grant from F. Hoffmann-La Roche Ltd and Merck & Co., Inc.
Dendreon
Enhancing natural defences

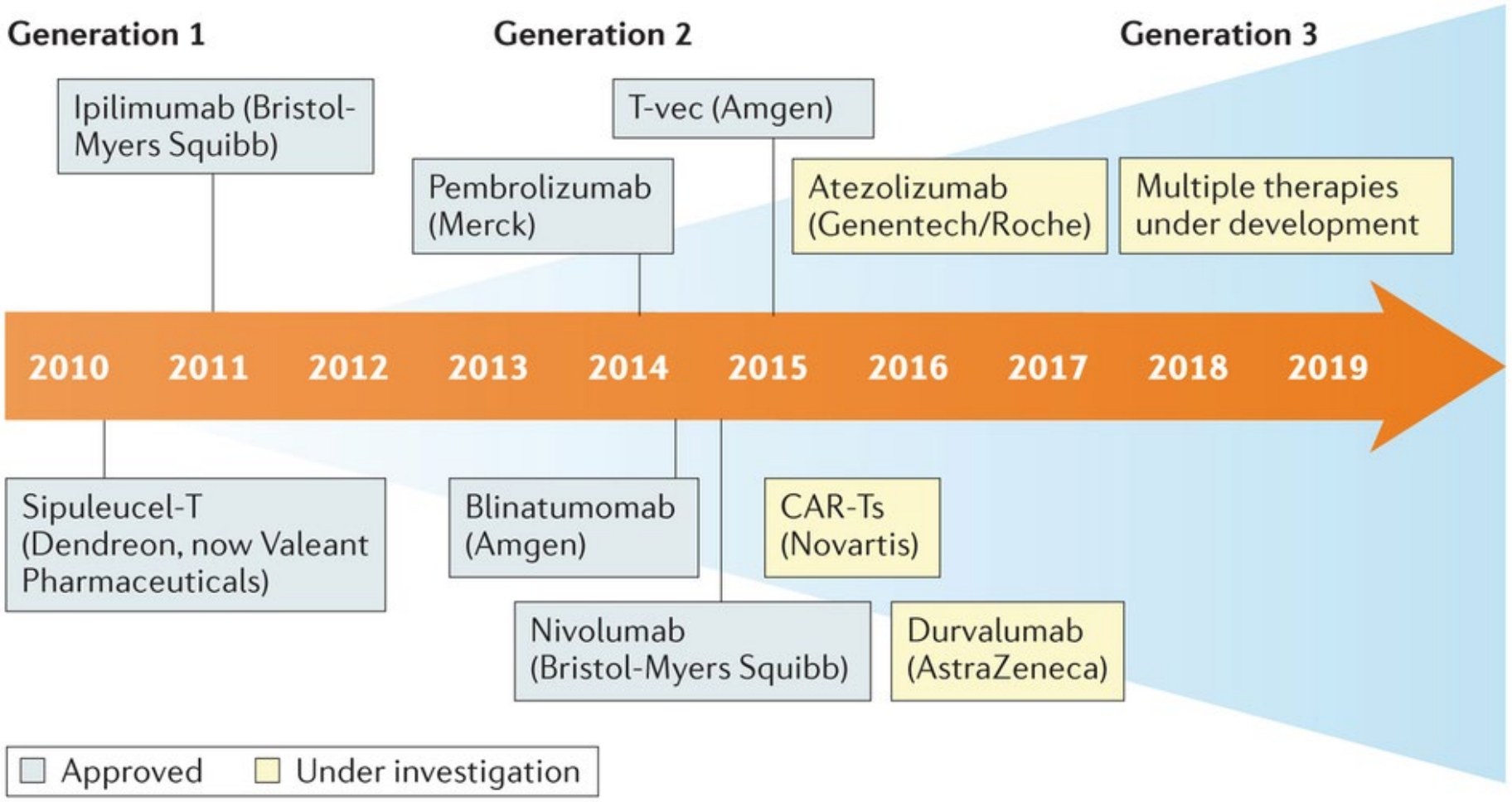

OUTLOOK
Haemophilia
nature
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE
Antitumour immunity enhanced by inhibiting PD-L1/PD-1 and identifying mutant neo-antigens
IMMUNE-CHECKPOINT BLOCKADE IN CANCER
PEER REVIEW
ACCEPT YOUR OWN PAPER
MICROSCOPY
THE CASE FOR AIMING HIGHER
ENERGY
'NIGHT-TIME' COOLING BY DAY


Immunotherapy
June 2012 Vol. 4 No. 6
ISSN 1750-743X
Editorials
• Combating chronic T-cell exhaustion
• Approaching atopic dermatitis treatment differently
• Vaccine adjuvants: is the pipeline clogged?
News & Views
• News
• Conference Scene
Priority Paper Evaluation
• Combination immunotherapy with prostate GVAX and ipilimumab
Research Article
• Sinomenine can prolong high-risk corneal graft survival in a rat model
Reviews
• Immunotherapy for gastric premalignant lesions and cancer
• Subcutaneous allergen immunotherapy for allergic disease
• Immunotherapy for polyomaviruses: opportunities and challenges
• Immunotherapy for TB

Current Day: Immuno-oncology

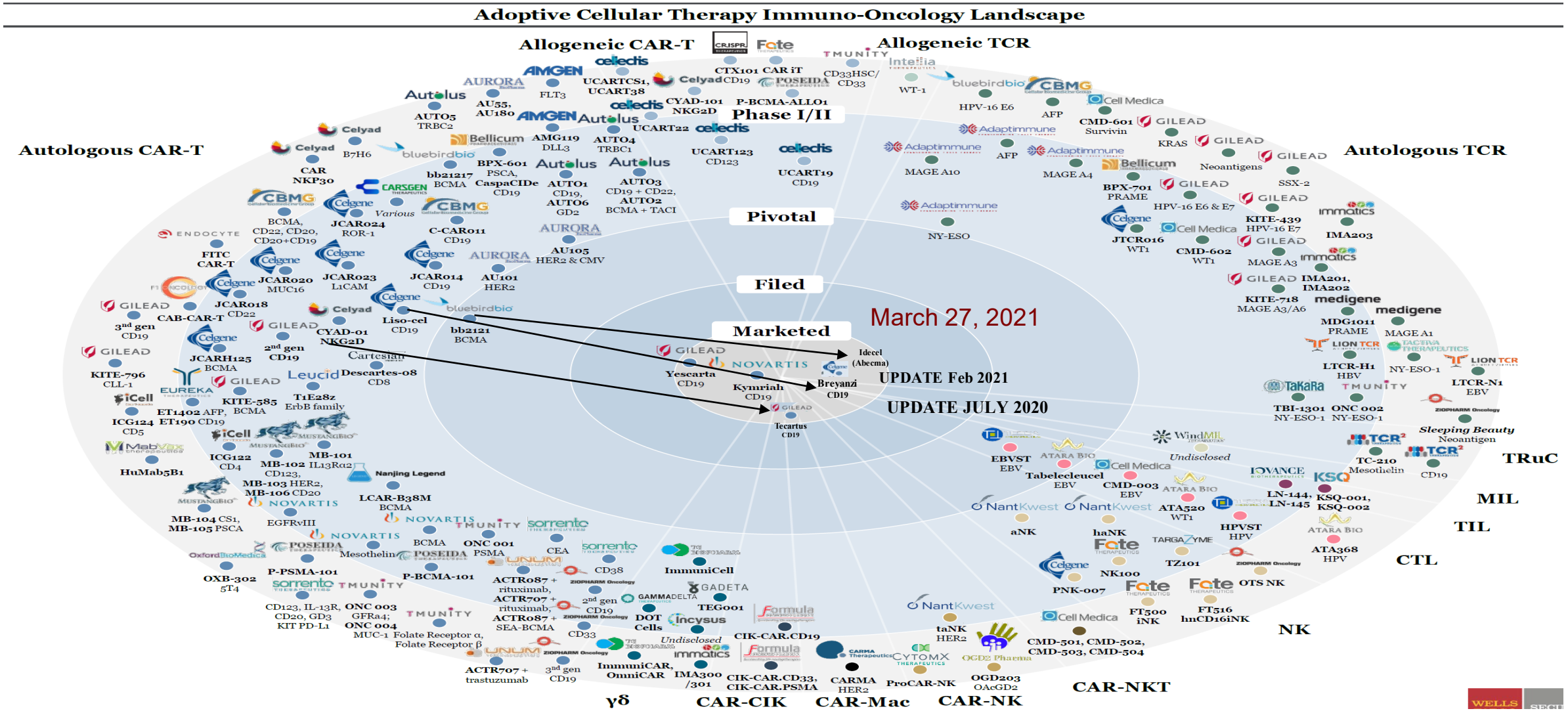
- T cell therapies
  - Gene expression
  - Autologous vs allogeneic
  - Neoantigens
  - TILs
  - Tregs
- Natural Killer cells
- Vaccines- peptide, dendritic cell,
- Checkpoint blockade (inhibitors)
- Checkpoint agonists
- Humoral immune therapy
  - Monoclonal antibodies
  - Ivlg
  - BITEs
- Cytokines

Pipeline of Cancer Immunotherapies-Commercialization



Axel Hoos, Nature Reviews Drug Discovery (2016) doi:10.1038/nrd.2015.35

Cell Therapy Landscape: 2018-2021 View



Prediction: cell and gene landscape rapid growth

- Fewer than 10 cell and gene therapies currently approved and in use, but with another **10+ expected annually in 2021 and beyond**
- 1,000+ clinical trials for cell and gene therapies underway in the U.S. (asgct.careboxhealth.com)
- 24+ conditions on the near-term pipeline and constantly changing
- Number of manufacturers in cell and gene therapy market growing exponentially including big players
- Constantly shifting market; Not all cancer

Forecast (2021-2022 Pipeline)

Blood Disorders

- Hemophilia B (gene)
- Hemophilia A (gene)
- Transfusion dependent β-thalassemia (gene)

Cancer

- Follicular lymphoma (CAR-T expanded indications)
- Multiple myeloma (CAR-T)
- Bladder cancer (gene)
- Epstein-Barr virus-associated post-transplant lymphoproliferative disease (CTL)
- Cervical cancer (TIL)
- Metastatic melanoma (TIL)
- Marginal zone lymphoma (CAR-T expanded indications)
- Diffuse large B-cell lymphoma (CAR-T)
- Acute lymphoblastic leukemia (CAR-T)
- Synovial sarcoma (TCR T-Cell)

Ocular Disorders

- Choroideremia (gene)
- Leber hereditary optic neuropathy (gene)
- Wet & dry age-related macular degeneration (gene/cell)

Metabolic Disorders

- Cerebral adrenoleukodystrophy (gene)
- Mucopolysaccharidosis type III (gene)

Neurodegenerative

- Aromatic L-amino acid decarboxylase (AADC) deficiency (gene)
- Spinal muscular atrophy (expanded indications-gene)

Skin Disorders

- Recessive dystrophic epidermolysis bullosa (gene)
- Scleroderma (gene)

Inherited Immunodeficiencies

- Wiskott-Aldrich syndrome (gene)
- Leukocyte adhesion deficiency type I (gene)

Specifically, what we see coming includes

In 2022, US could see these annualized numbers of patients (or higher) in need of services:

Category	Patients / 50 Million Lives*
Organ Transplant	4,850
Bone Marrow Transplant	3,400
Leukemia / Lymphoma (CAR-T)	23,000
Spinal Muscular Atrophy (SMA)	120
Multiple Myeloma	3,300
Hemophilia A	4,000
Bladder Cancer	13,700
Total	52,370

*US population currently estimated at 333 million

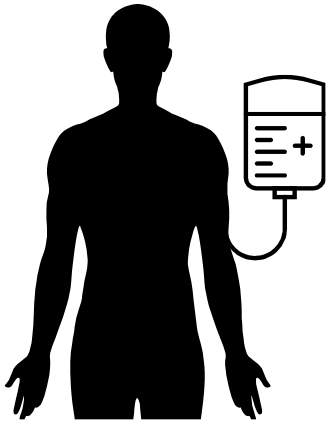
What is CAR-T?

- CAR T therapy - **chimeric antigen receptor (CAR) genetically modified T cells -** designed to recognize Tumor specific antigens (TSA) → in vivo activation and proliferation → significant and durable malignant cell immunity
- CAR T cells : **"living drug"** –can persist for long periods of time
- CAR T cells - generally autologous product from patient's own blood cells, although universal donor "off the shelf" CAR T cells emerging

CAR T-Cell Therapy: Underlying Principles

Leukapheresis

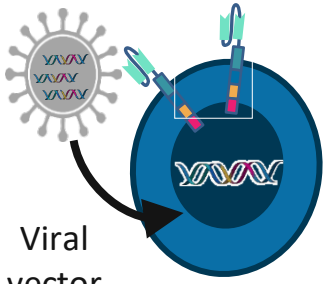
Collect patient's white blood cells

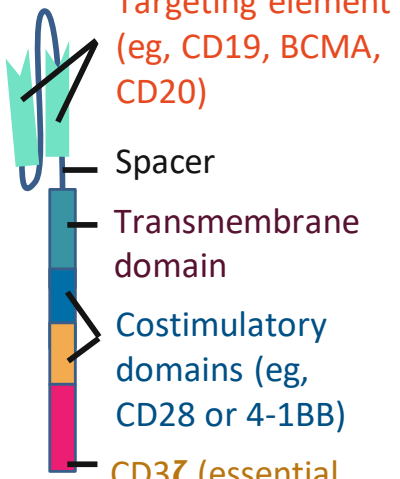


Manufacturing

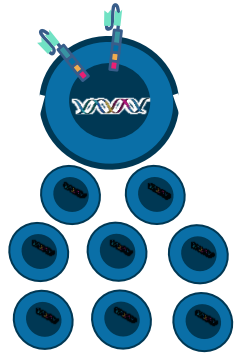
Isolate and activate T-cells

Engineer T-cells with CAR gene





Expand CAR T-cells

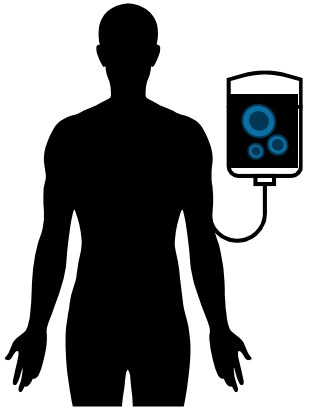


Median manufacturing time: 17-28 days

Patients undergo lymphodepleting (and possibly salvage/bridging) therapy

Infusion

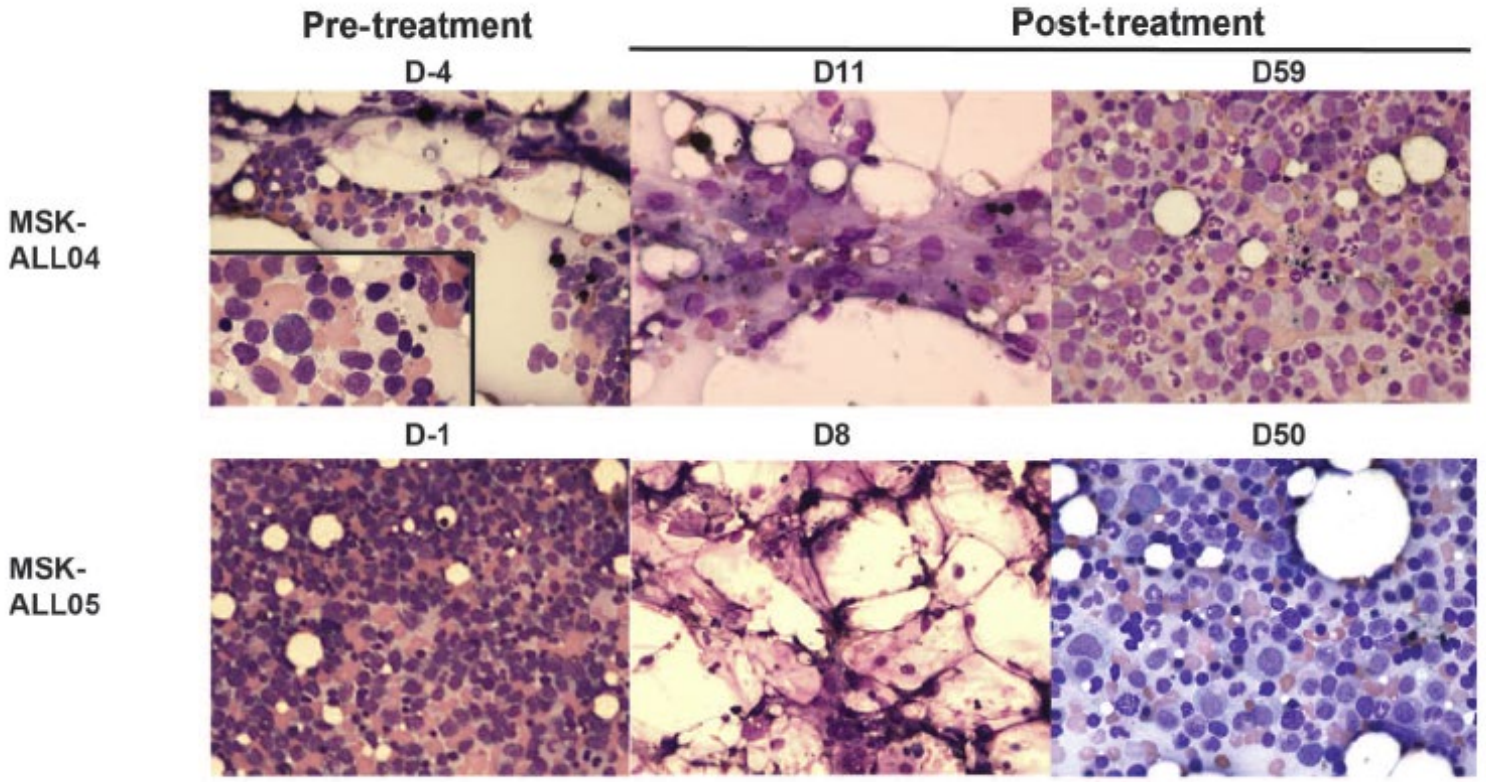
Infuse same patient with CAR T-cells



Activity

Majors. EHA 2018. Abstr PS1156. Lim. Cell. 2017;168:724. Sadelain. Nat Rev Cancer. 2003;3:35.
Brentjens. Nat Med. 2003;9:279. Park. ASH 2015. Abstr 682. Axicabtagene ciloleucel PI. Tisagenlecleucel PI.

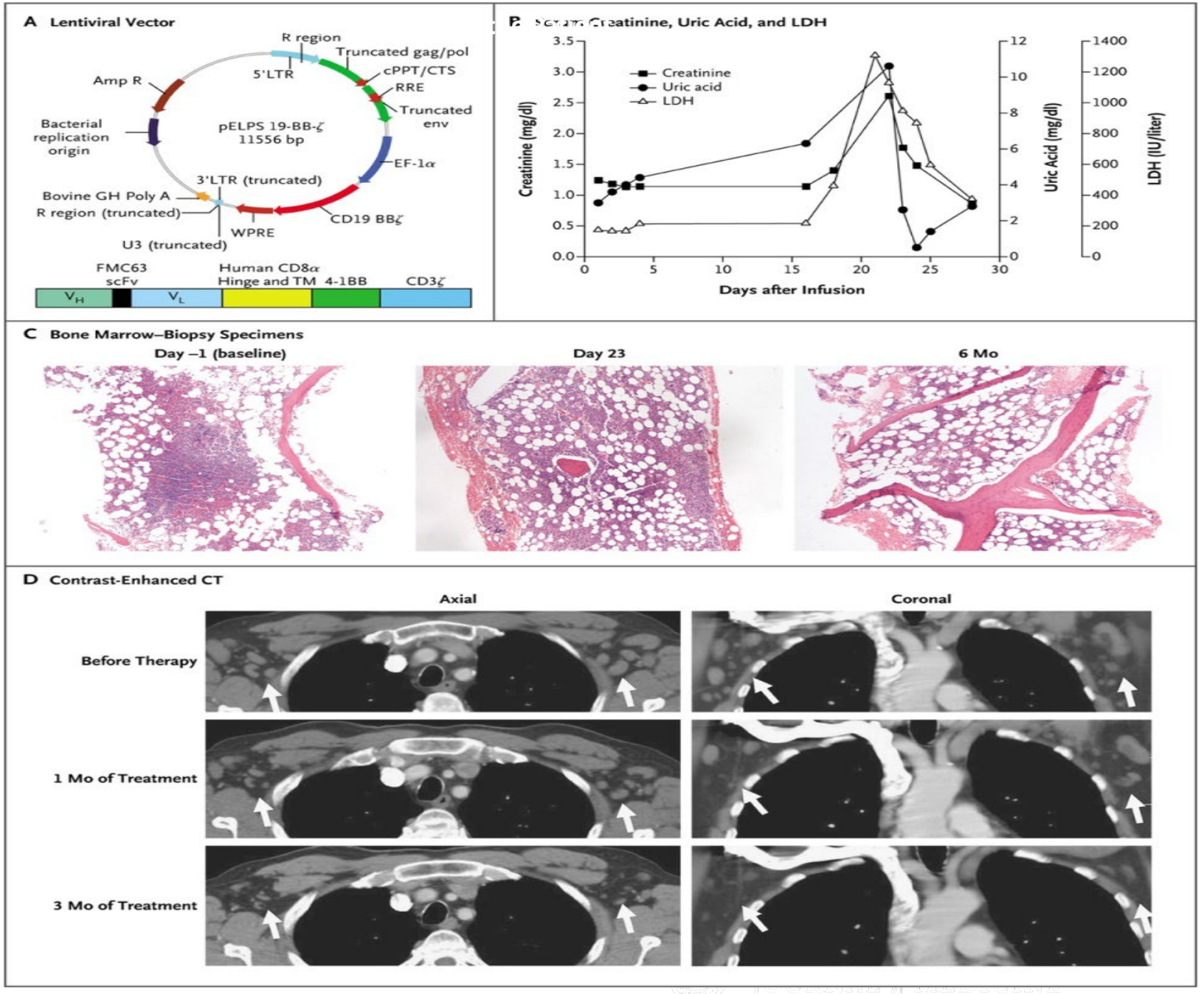
Rapid tumor elimination and recovery of normal bone marrow after 19-28z CAR T cell therapy



Sci Transl Med. 2013 Mar 20;5(177):177ra38

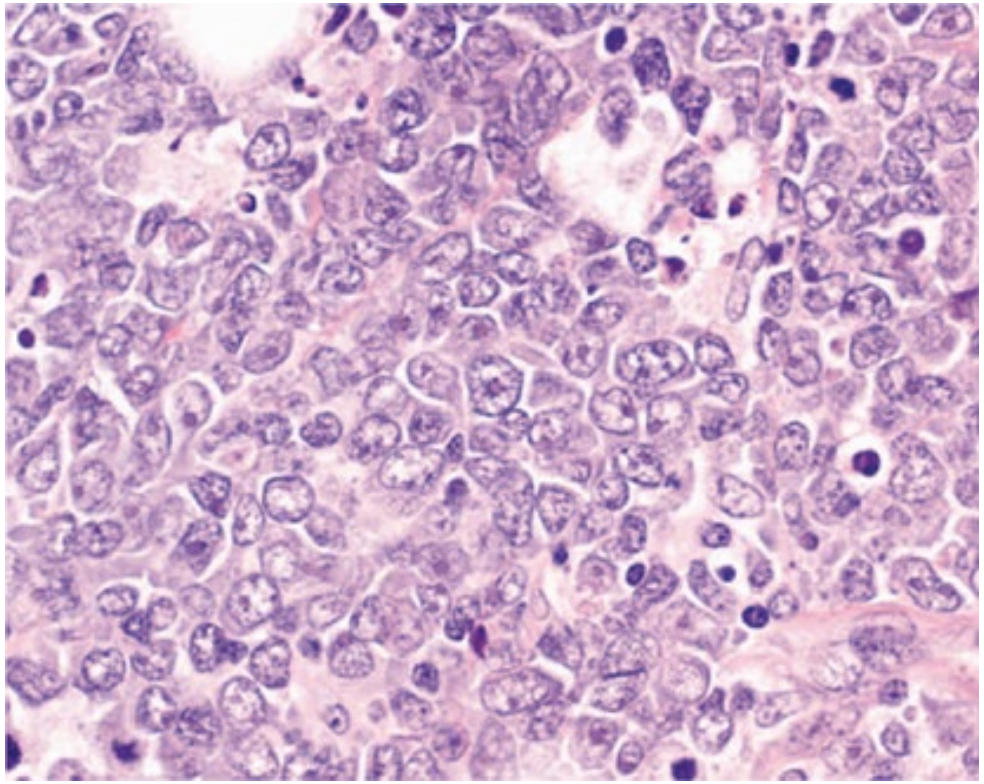
First 2 patients: Refractory CLL
Still alive and in CR, >10 yrs after single application

Decade-long leukaemia remissions with persistence of CD4 $^{+}$ CAR T cells,
Melenhorst et al, Nature. 2022 Feb;602(7897):503-509



Porter DL et al. N Engl J Med 2011;365:725-733.

CAR T vs Tx for NHL



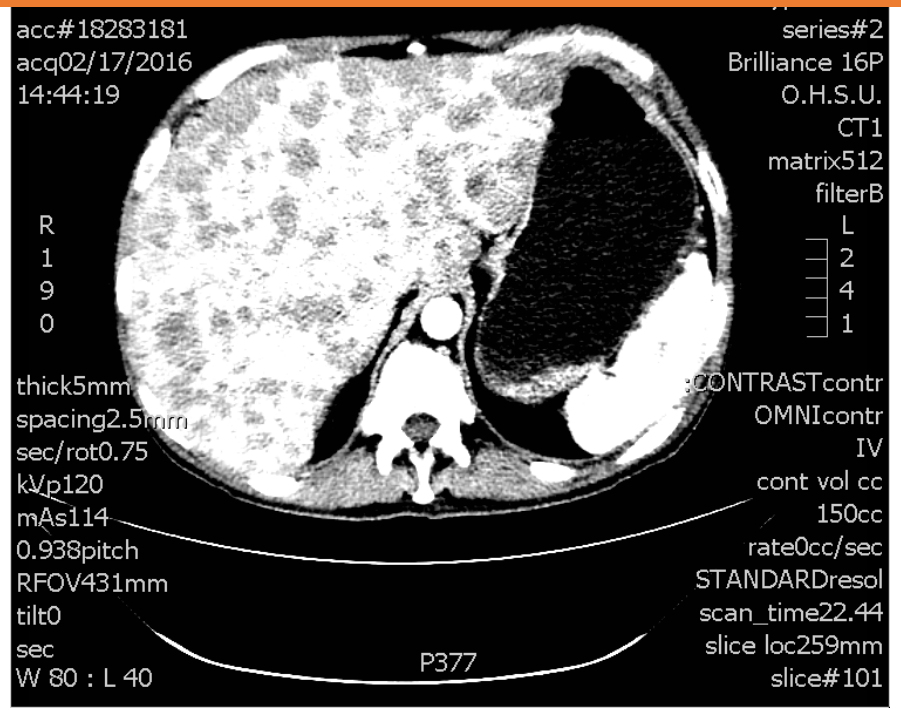
Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the ASTCT, Kanate BBMT 2020

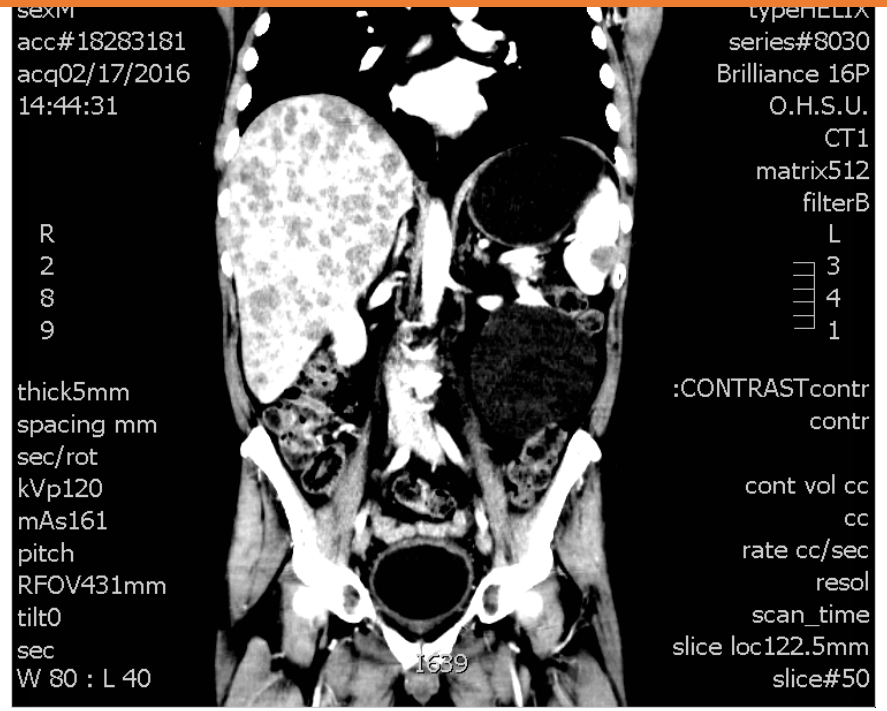
CAR-T therapy	Diffuse large B cell lymphoma/primary mediastinal B cell lymphoma- adult	
	Primary refractory, resistant (after 2 lines of therapy)	S
	First relapse, resistant	S
	Beyond second relapse	S
	Relapse after autologous transplant	S
CAR-T therapy	High-grade B cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements	
	Primary refractory, resistant (after 2 lines of therapy)	S
	First relapse, resistant	S
	Beyond second relapse	S
	Relapse after autologous transplant	S

Diffuse large B cell lymphoma	Allo	Auto
CR1 (PET negative)	N	N
Primary refractory, sensitive	S	S
Primary refractory, resistant	S	N
First relapse, sensitive	S	S
First relapse, resistant	S	N
Second or greater relapse	S	S
Relapse after autoHCT	S	N
High-grade B cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements		
CR1 (PET negative)	N	C
Primary refractory, sensitive	R	C
Primary refractory, resistant	R	N
First relapse, sensitive	R	C
First relapse, resistant	R	N
Second or greater relapse	R	C
Relapse after autoHCT	R	N

Standard of care (S); Standard of care, clinical evidence available (C);
Standard of care, rare indication (R); Developmental (D); Not generally recommended (N).

OHSU Pt: Relapsed, refractory DLBCL

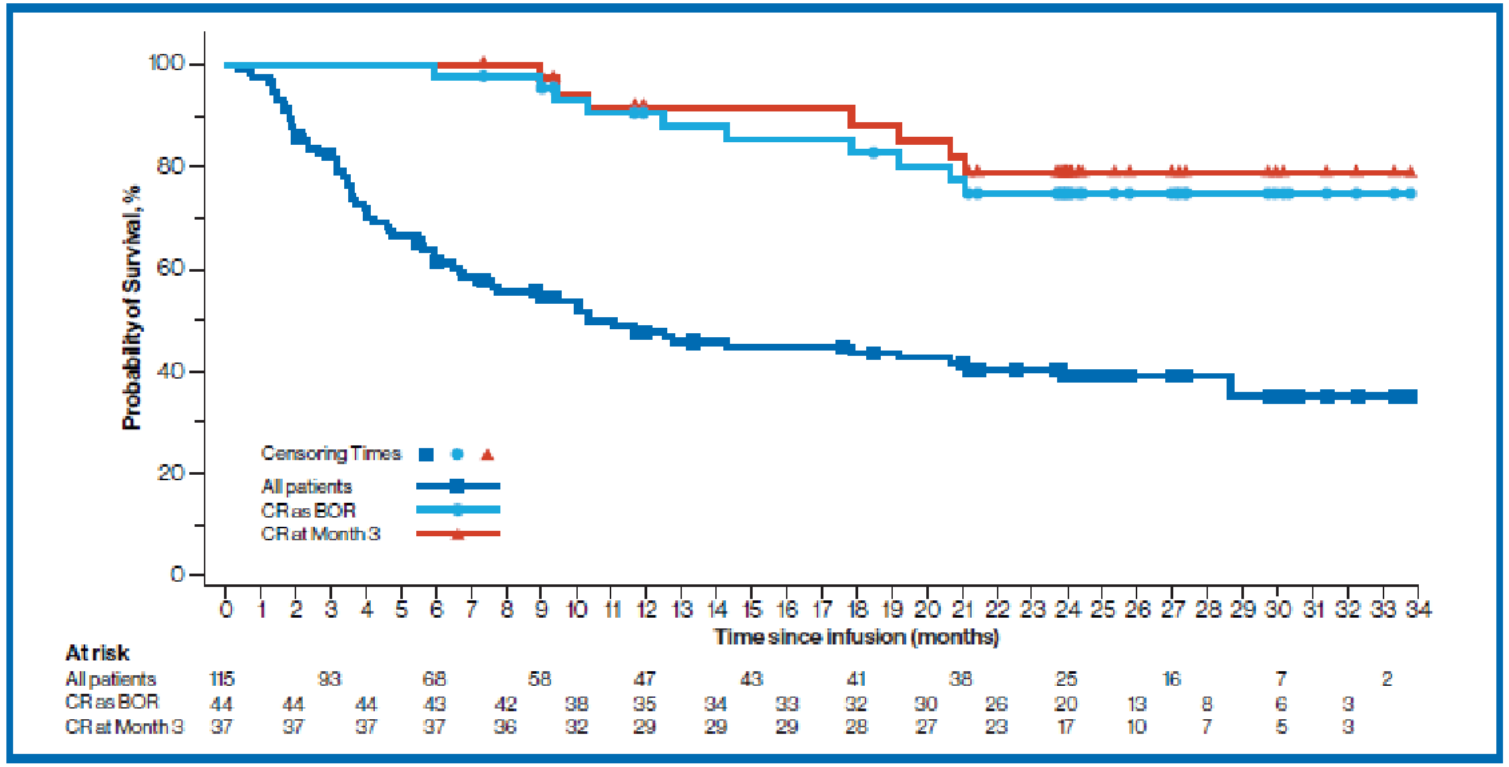




JULIET: Median Overall Survival

Median OS not reached (95% CI, 21 months-NE) in patients in CR

Figure 3. Overall Survival for Patients in CR and All Patients in the Full Cohort.

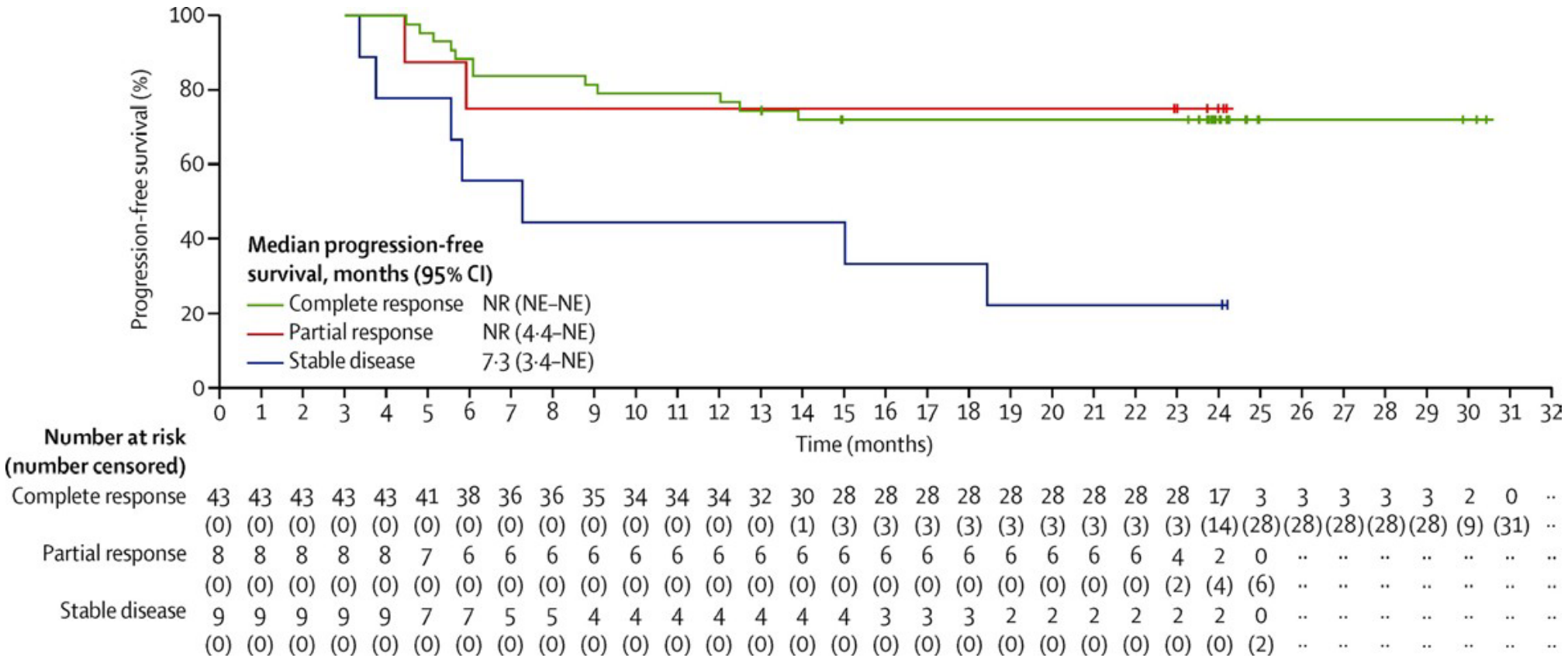


- No patients proceeded to allogeneic SCT or auto-SCT while in remission

Auto-SCT, autologous stem cell transplant; CI, confidence interval; CR, complete response; NE, not evaluable; OS, overall survival; SCT, stem cell transplant.
Median OS in CR patients: not reached (95% CI, 21 months-NE).

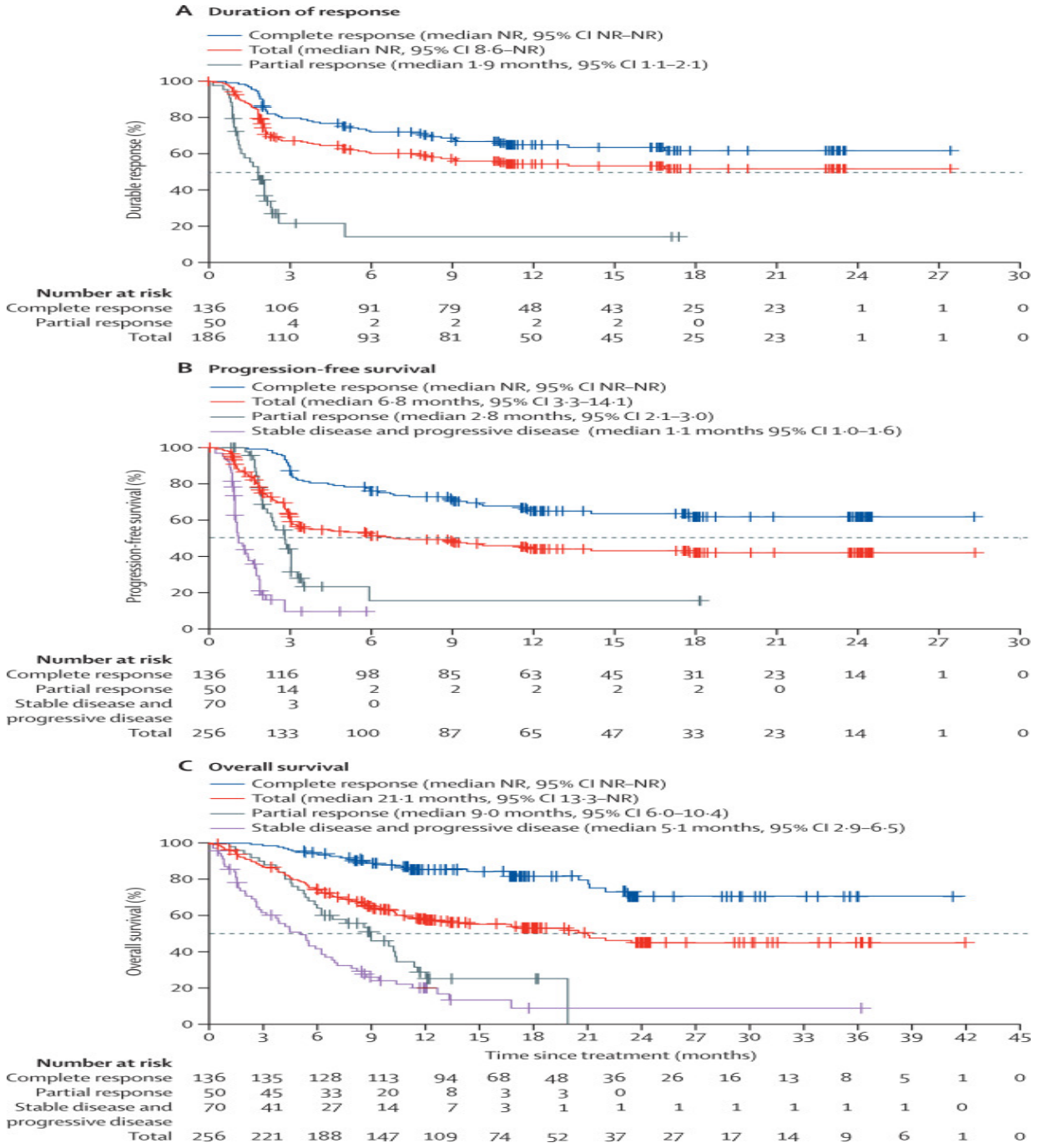
ZUMA-1: Axicabtagene Ciloleucel in r/r DLBCL

Response Duration by Best Objective Response (ZUMA-1)



Locke et al, Lancet Onc, 2019

Transform study, Lisocabtagene, Abramson et al, Lancet 2020



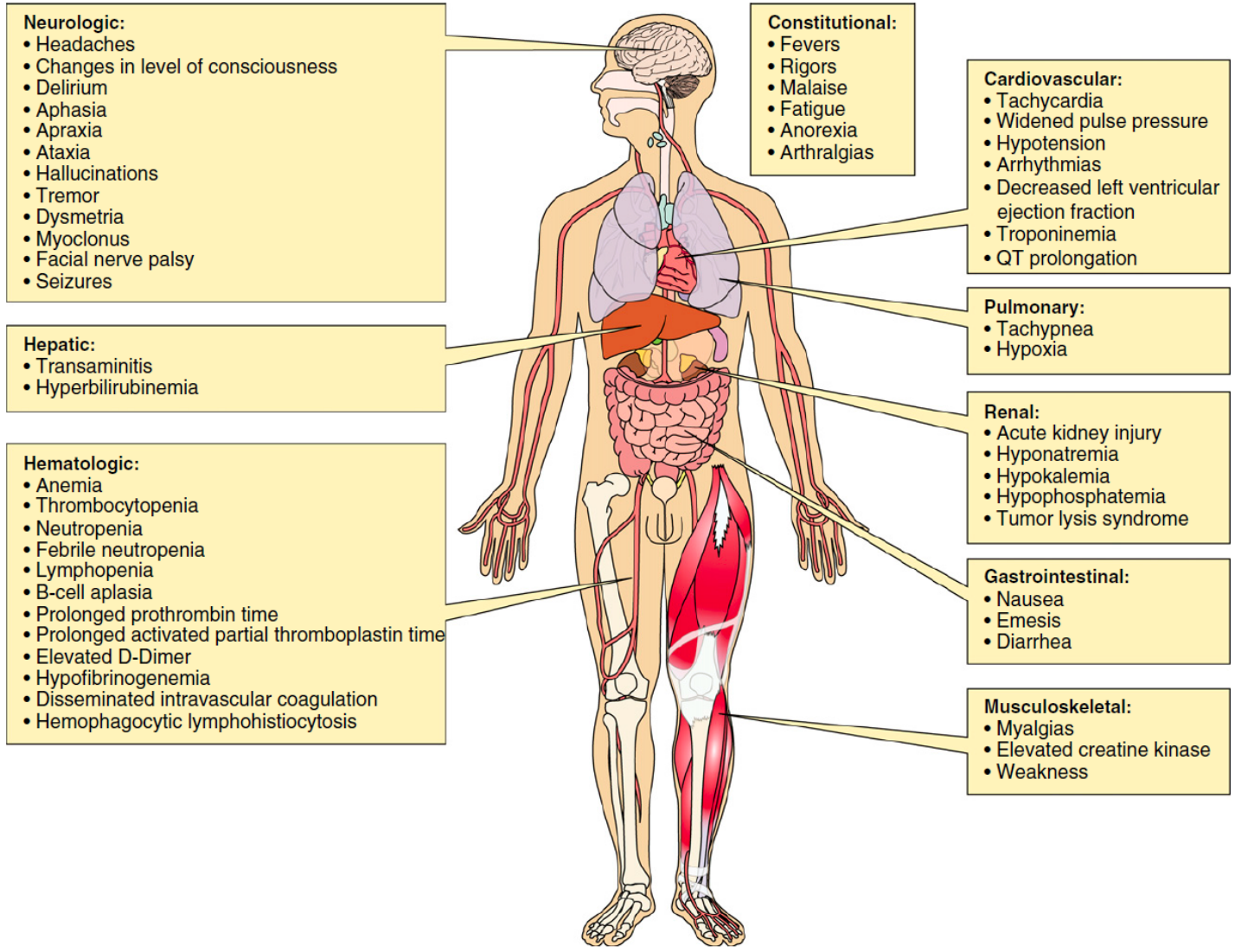
Potential Baseline Predictors of Efficacy

Clinical Trials and Real-World Evidence

- **LDH**
- **Tumor burden**
- **CRP, ferritin, and serum cytokines**
- ECOG PS and disease state
- Bridging vs no bridging chemotherapy
- Baseline platelet levels
- Baseline ALC

ALC, absolute lymphocyte count; CRP, C-reative protein; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase.

Adverse Events of Special Interest
CRS and Neurological Events after CAR-T Cells



Brudno JN, Kochenderfer JN. Blood. 2016;127(26):3321-3330.

Risk Factors for Severity of CRS and Neurological Events

Risk Factors	Comments
Tumor burden	Higher activation and proliferation of CAR T cells is observed with high tumor burden leading to an exaggerated inflammatory response and higher toxicity (4, 5, 9, 13, 16).
Cell dosing	A higher dose of cells can lead to increased cytokine release and therefore greater toxicities once these cells are activated (18, 24).
Comorbidities	Higher number of comorbidities has been associated with increased risk and severity of CRS (17).
Age	Although there are no definitive studies, older patients may have a lower tolerance to CRS and neurotoxicity (4, 17).
Chemotherapy regimen	The chemotherapy regimen prior to cell infusion is important to ensure replication and survival of CAR T cells. A regimen that leads to severe immunosuppression and therefore an exaggerated proliferation of CAR T cells can result in increased toxicity (9, 18, 24).
Timing of onset of symptoms	Early onset of symptoms is associated with worse toxicity and should lead to more aggressive monitoring and treatment (5, 24).
Cell product	Variabilities of the cell construct between protocols can potentially have an effect on cell proliferation and activity. Some factors include the costimulatory domain used, vector used, time in culture, and type of culture (9).

CAR = chimeric antigen receptor, CRS = cytokine release syndrome.

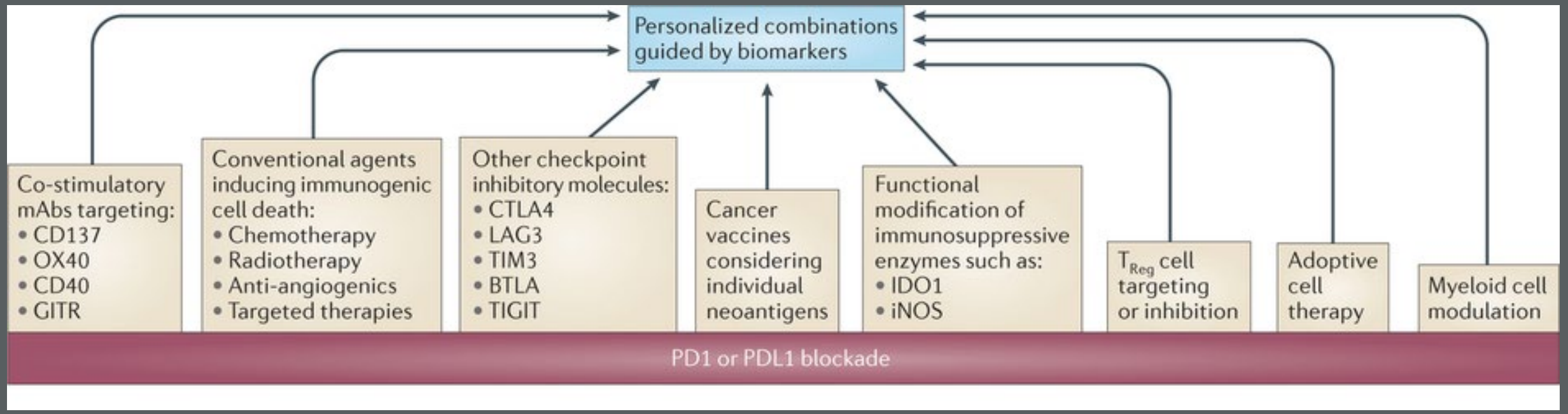
Gutierrez, et al. Crit Care Med. 2018;46:1402-1410.

ASTCT CRS Consensus Grading, Lee et al, BBMT 2019

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

Low-flow nasal cannula is defined as oxygen delivered at ≤ 6 liters/minute.
Low flow also includes blow-by oxygen delivery, sometimes used in pediatrics.
High-flow nasal cannula is defined as oxygen delivered at > 6 liters/minute.

How to improve on outcomes? Potential trial candidates



There is an internal message: CAR T does not cure all!!!!!

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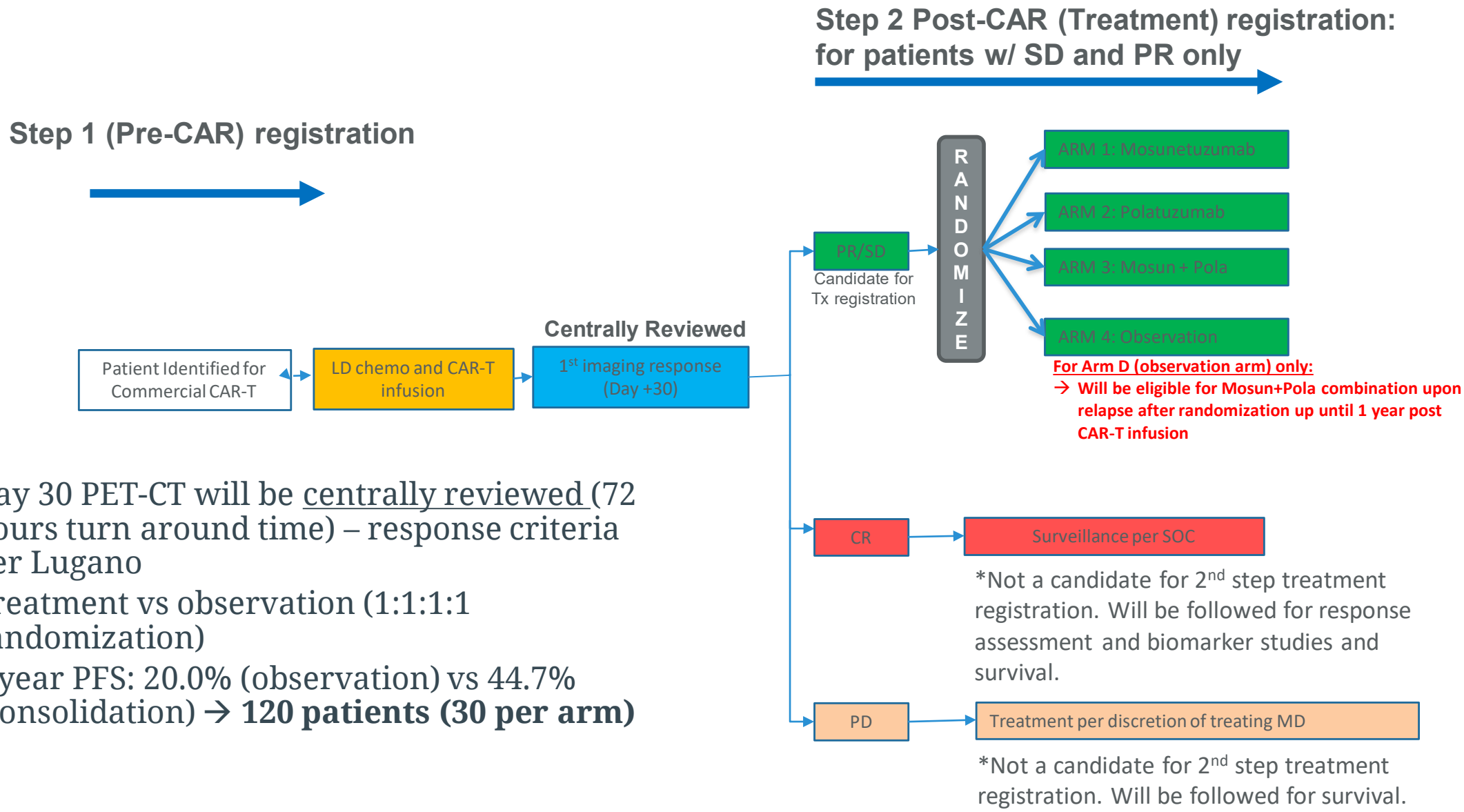
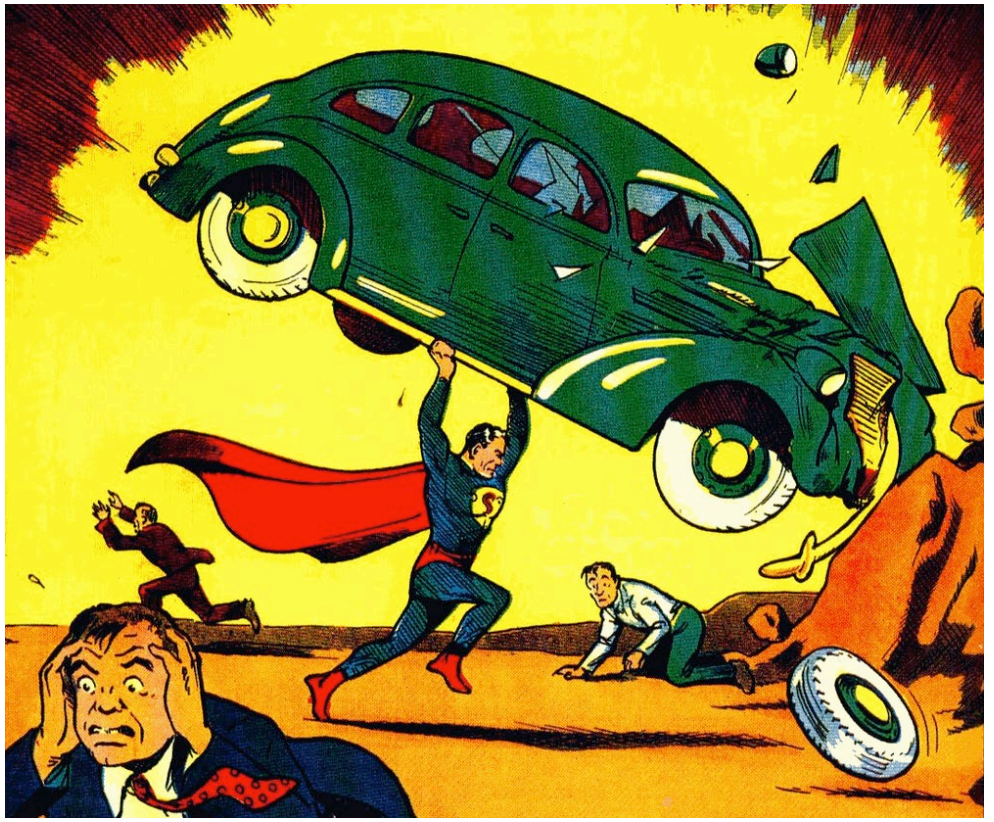
SWOG 2114: A Randomized Phase II trial of Consolidation Therapy following CD19 CAR T-cell Treatment for Relapsed/Refractory Large B-cell Lymphoma or Grade IIIB Follicular Lymphoma



- Day 30 PET-CT will be centrally reviewed (72 hours turn around time) – response criteria per Lugano
- Treatment vs observation (1:1:1:1 randomization)
- 1 year PFS: 20.0% (observation) vs 44.7% (consolidation) → **120 patients (30 per arm)**

Progress continues on CAR-T cell therapy



Approved CAR- T Products & Indications

- R/R DLBCL- 3rd line- Tisagenlecleucel, Axicabtagene, Lisocabtagene
- R/R Follicular Lymphoma- 3rd line Axicabtagene
- Mantle cell lymphoma- Brexucabtagene
- Pediatric/young adult- ≥ 2nd line- Tisagenlecleucel
- Adult ALL- Brexucabtagene
- Myeloma- Beyond 4th line- Idecabtagene, Ciltacabtagene

Anticipated 2022:

R/R – 2nd line- Axicabtagene, Lisocabtagene

R/R Follicular Lymphoma- Tisagenlecleucel

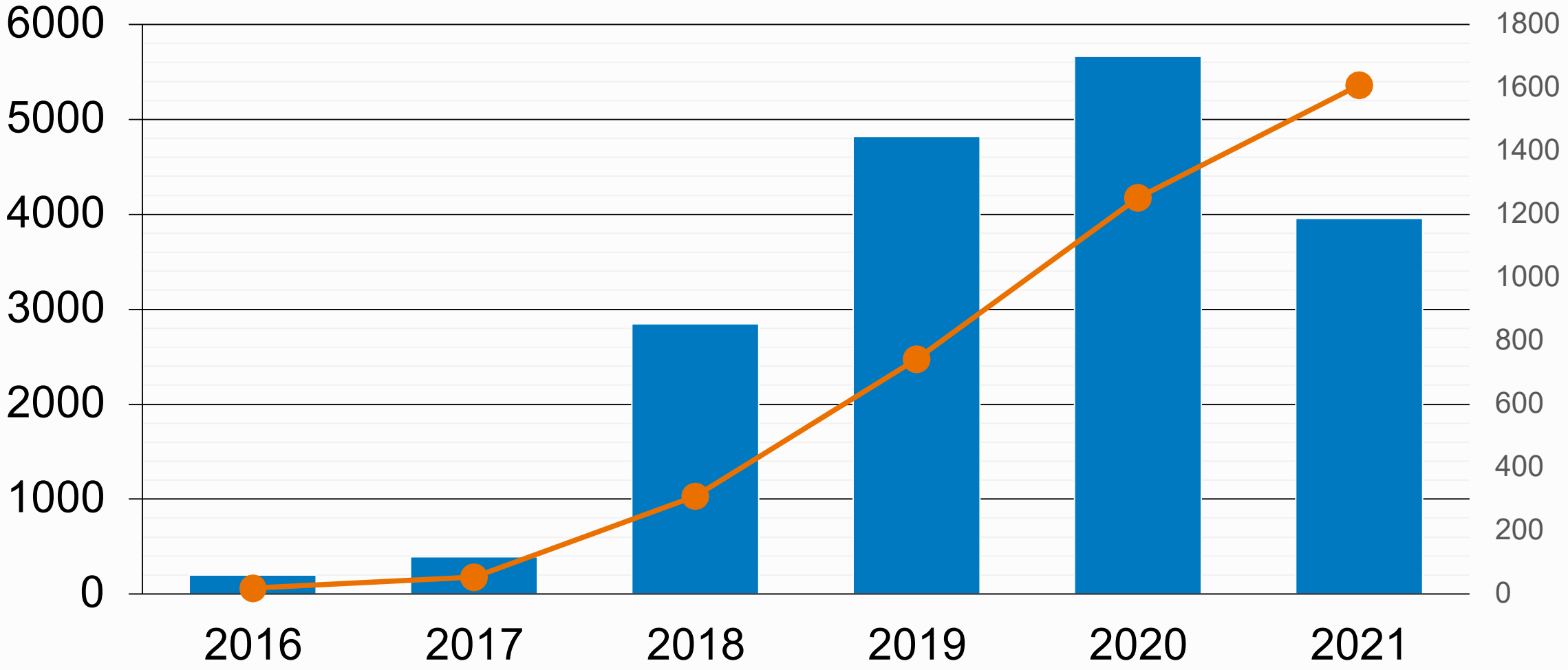
Anticipated 2023- TIL for Advanced Melanoma- Lifileucil

Open/ Pending Clinical Trials with Cell Therapy

- Universal donor CD19 CAR T for DLBCL & ALL- CRSPR
- Universal donor CD19 NK-CAR T for NHL, CLL, ALL- Fate
- Autologous Dual Targeted CD19/CD20 for DLBCL- Miltenyi
- Autologous CAR T for BCMA+ Myeloma
- Autologous ROR1 CAR-T for advanced solid tumor malignancies expressing ROR-1
- Autologous GD2 CAR-T for osteosarcoma
- Allogeneic CART for advanced ovarian cancer
- Universal donor NK cells for R/R lymphoma (including CAR T failure)
- Autologous HLA A2.01 restricted, WT1 peptide specific T cells for AML
- HLA restricted, EBV specific donor T cells for EBV+ PTLD
- HLA restricted, NY ESO specific autologous T cells for Synovial Cell Sarcoma
- HLA restricted, NY ESO specific autologous T cells for overexpressed NY ESO in advanced Ca
- Autologous TIL for R/R NSCLC
- Autologous TIL for advanced malignancies
- HLA restricted, Virus Specific T cells for BK Cystitis and RSV/Parainfluenza/ Influenza Resp virus infections
- Her2/Neu-Macrophage CAR for overexpressed HER2/Neu malignancies
- HPV peptide loaded RBC + poly IC as systemic tumor vaccine for HPV+ malignancies
- Genetically engineered, immune activating RBC (sIL15+ 41BB+) for recurrent RCC, NSCLC

Number of CAR T cell infusions: 2016-2021 (5,364 patients and 5,625 infusions)

CIDR
CELLULAR IMMUNOTHERAPY DATA RESOURCE



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Cumulative

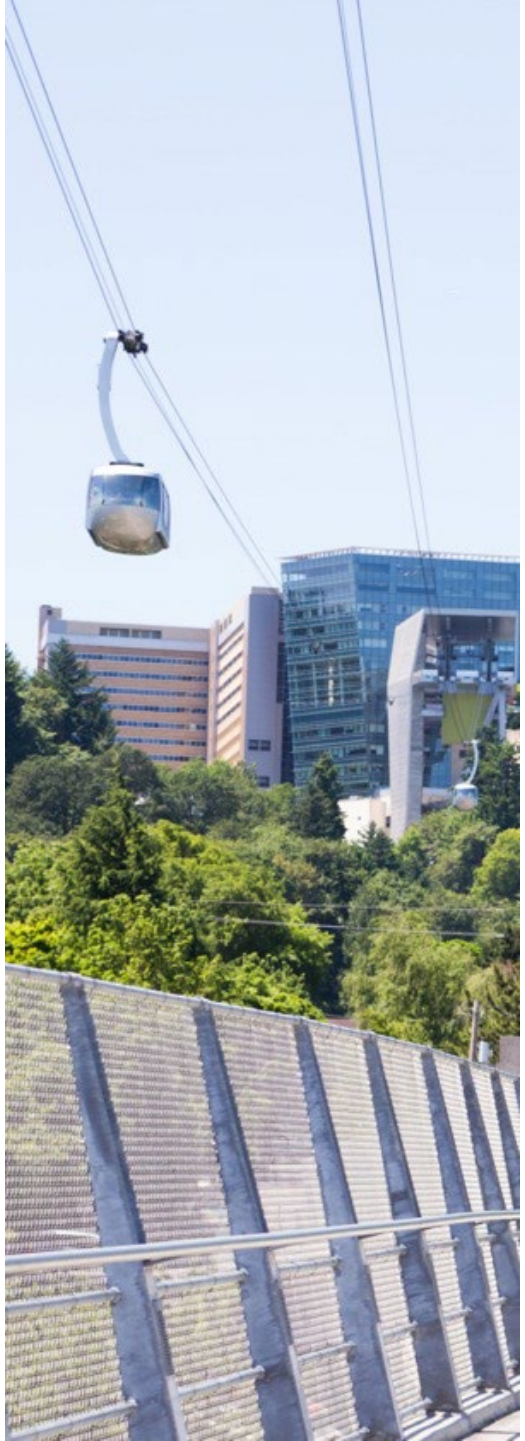
Data Incomplete for 2020 & 2021

Can we deliver cell therapy everywhere?

Where do we begin? At the beginning, of course
Cell Therapy Program Management

Patient Readiness / Logistics

- Referral
- Eligibility evaluation
  - Path review critical
- Clinical Trial Considerations
- Payer authorization support
- Leukapheresis
- Manufacturing time
- Bridging chemotherapy
- Infusion
- Short and long term management



Program Implementation

- Certification
- Preparation
  - Stakeholders
  - Training
  - Documentation
  - Management guidelines

FACT/JACIE

- Primary objective of standards - promote quality medical and laboratory practice
- FACT -standards specific to the use of Hematopoietic Cell Therapy & Immune Effector Cells (IEC).
  - Specify clinical and quality infrastructure
    - Purpose: facilitate safe administration of IECs
    - Formalize monitoring and reporting of outcomes
- Option for IEC therapy only – IEC standards manual
- For both HSCT and IEC therapies –
  - Product Collection, Processing, and Administration standards

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Unanticipated Challenges

- Need for expanded access protocols
  - Access to manufactured commercial products that do not meet release criteria
  - Requires IRB/regulatory approval for use
- Patient scheduling with short notice:
  - Apheresis unit
  - Outpatient infusion room
- On-going training for nurses and physicians – due to turnover
- Different processes for commercial products and clinical trial products
- Payment for services
- Medicare reimbursement

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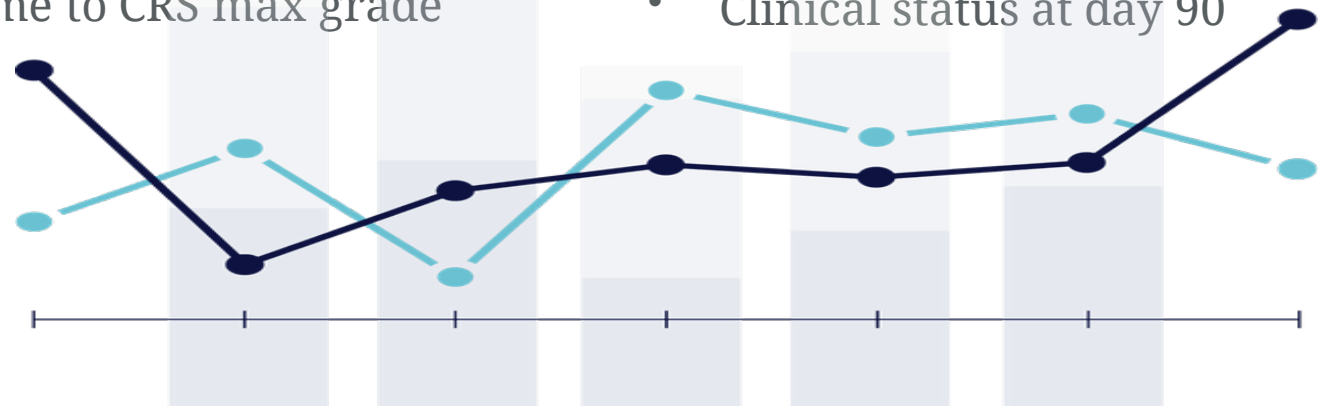
Outcomes Dashboard Metrics

- Infusion date
- Status (A/D)
- 30 day survival
- 100 day survival
- Diagnosis and Histology
- Discharge date
  (if inpatient for infusion)
- LOS (if inpatient for infusion)
- CRS max grade
- Time to CRS max grade
- Number of doses of Tocilizumab
- ICANS max grade
- Time to ICANS max grade
- Days to readmission post discharge
  (if inpatient for infusion)
- Number inpatient days within 30 days
- Number of inpatient days within 100 days
- Number of ICU days
- Clinical status at day 90



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Growth of Cell Therapy being Addressed at National/ International Level

- Access to care
- Cost of care
- Logistics of care

Launch of a Commercial Cell Therapy Product at a Clinical Site is a Complex Process

Commercial Partner/Manufacturer

- Standard Operating Procedures
- Clinical standards for toxicity management
- Initiation and auditing of a REMS program
- Adverse event and data reporting under REMS
- Implementation of Product Application (IT)

Internal

- Buy in from Center Leadership
- Submission to Pharmacy & Therapeutics
- Financial Due Diligence
- EMR record order sets/ treatment plans
- Informed Consents
- Cell Therapy Coordinator Training and Resources
- Patient education and wallet card workflow
- Payor Strategies
- Education of consulting services and ancillary staff

This process can take 3-9 months with countless hours of effort

ASTCT

Specific Start-up Qualification and Tasks

Apheresis

Machine Operation
COC/COI
QC Syste m

FACT
NMDP
AABB

2 vs 3 BVs
+/- Plasma addition

Company-specific Portal

Cell Processing

15-20 SOPs
PMs on Equipment
LN storage monitors
COC/COI
Packing and
C n
Sterile Technique
Vials/Syringes vs Bags
+/- Dosing

FACT
NMDP

Company-specific Portal

Pharmacy

Drug Logs
Toci Stock
Toci Delivery Time

Contracting

Nursing

LD Ch usion
Ce on
Infusion Reaction Management
Syringes vs Bags

FACT
JC

ASTCT

Defining resource utilization:

Table 1. Patient Characteristics

Characteristic	n (%)
Total, n	236
Age, median (range), y	62.5 (19–82)
Female sex	91 (38.6)
White race[a]	218 (92.4)
Relationship status	
Married/Life partner	163 (69.1)
Single	40 (17.0)
Divorced/Legally separated	13 (5.5)
Widowed	13 (5.5)
Unknown	7 (3.0)
CAR T-cell product	
Axicabtagene ciloleucel	183 (77.5)
Tisagenlecleucel	36 (15.3)
Axicabtagene ciloleucel combined with immunotherapy	9 (3.8)
KTE-X19	7 (3.0)
Lisocabtagene maraleucel	1 (0.4)
Lymphoma subtype	
DLBCL/Grade 3B follicular lymphoma	107 (45.3)
Indolent lymphoma transformed to DLBCL[b]	40 (17.0)
HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements	40 (17.0)
Follicular lymphoma	22 (9.3)
Primary mediastinal large B-cell lymphoma	12 (5.1)
Other	15 (6.4)

Table 1. Patient Characteristics (cont.)

Characteristic	n (%)
ECOG performance status	
0–1	194 (82.2)
2–4	38 (16.1)
Unknown	4 (1.7)
Received bridging therapy	93 (39.4)
Prior lines of therapy, median (range)	3 (0–10)
Prior autologous stem cell transplant	65 (27.5)
Days from relapse to CAR T-cell therapy, median (range)[c]	58 (11–391)
Toxicity and response	
Cytokine release syndrome (any grade)	183 (77.5)
ICANS (any grade)	126 (53.4)
Received tocilizumab	120 (50.9)
Received corticosteroids	107 (45.3)
Overall response	201 (85.2)
Complete response	152 (64.4)
Survival	184
Alive 1 year after CAR T-cell therapy[d]	116 (63.0)

Table 2. Healthcare Utilization Among CAR T-Cell Therapy Patients (n=236)

Outcome	n (%)
Length of stay for CAR T-cell hospitalization, median (range), d	15 (7–91)
ICU admission during admission for CAR T-cell therapy	30 (12.7)
Any ICU admission within 3 mo of CAR T-cell infusion[a]	36 (15.5)
Any hospital readmission within 3 mo of CAR T-cell infusion[b]	65 (28.1)
Number of hospital readmissions within 3 mo of CAR T-cell infusion among those rehospitalized, median (range)	1 (1–4)
Days from discharge to first readmission, median (range) (n=65 readmissions)	18 (1–91)
Reason for first hospital readmission (n=64 readmissions)	
Symptoms	22 (34.4)
Noncancer medical condition	10 (15.6)
Cancer progression	8 (12.5)
Infections	6 (9.4)
Febrile neutropenia	5 (7.8)
Neurotoxicity	5 (7.8)
Cytokine release syndrome	2 (3.1)
Other	6 (9.4)

ACCELLERATE FORUM

Johnson PC et al JNCCN 2020.

CAR T Cell Toxicities in the real world

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- Overall rates of toxicities in the real world are comparable to clinical trials.
- Toxicity rates vary by product (construct), by indication, age and other factors.
  - Improvement in management → reduction in higher grade CRS among patients with lymphoma.
- Toxicities are correlated with each other and impact overall patient outcomes.

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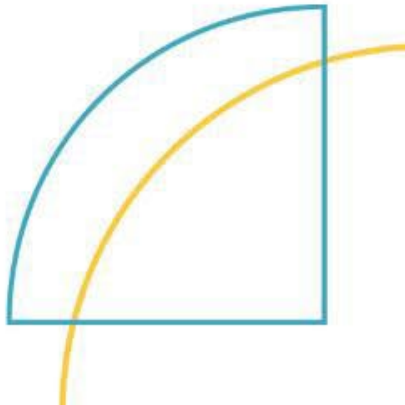
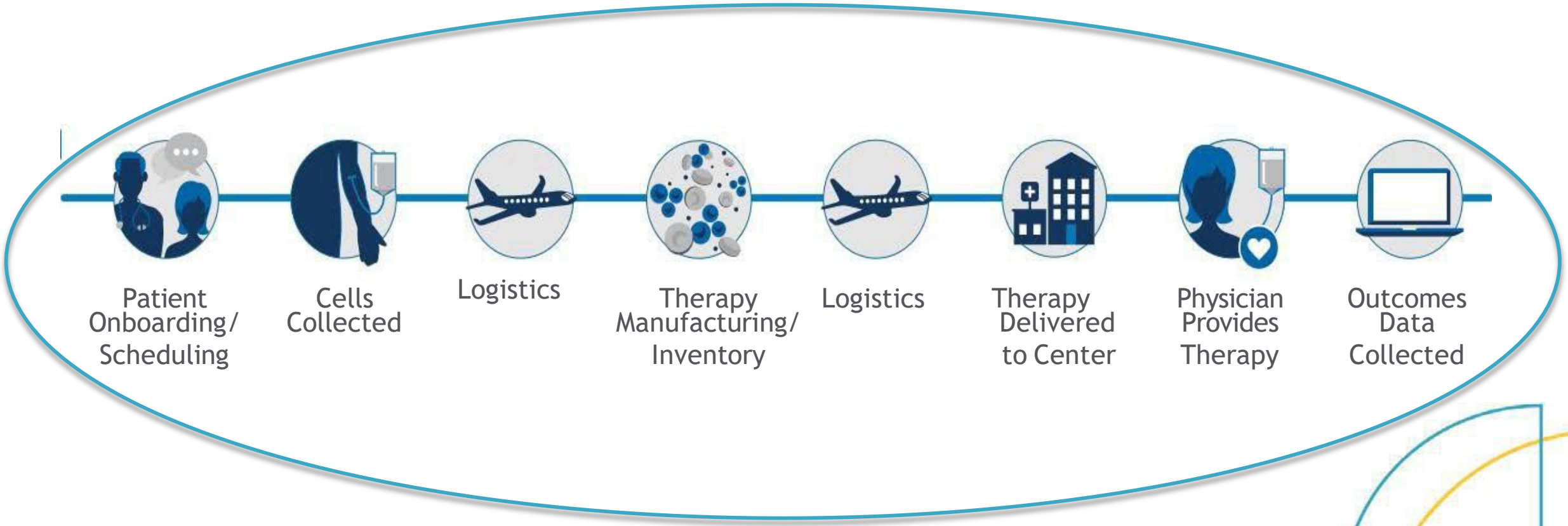
Requirements for community treatment:

- Sufficient logistical coordination for delivery of complex care (or not).
- Sufficient resources to support patient care.
  - What happens when things go awry?
- Sufficient staffing for regulatory commitments.
- Sufficient patient volume to warrant investment and maintenance of the above components.



A need for efficiencies and standardization across the cell therapy workflow –

Order management platform technology



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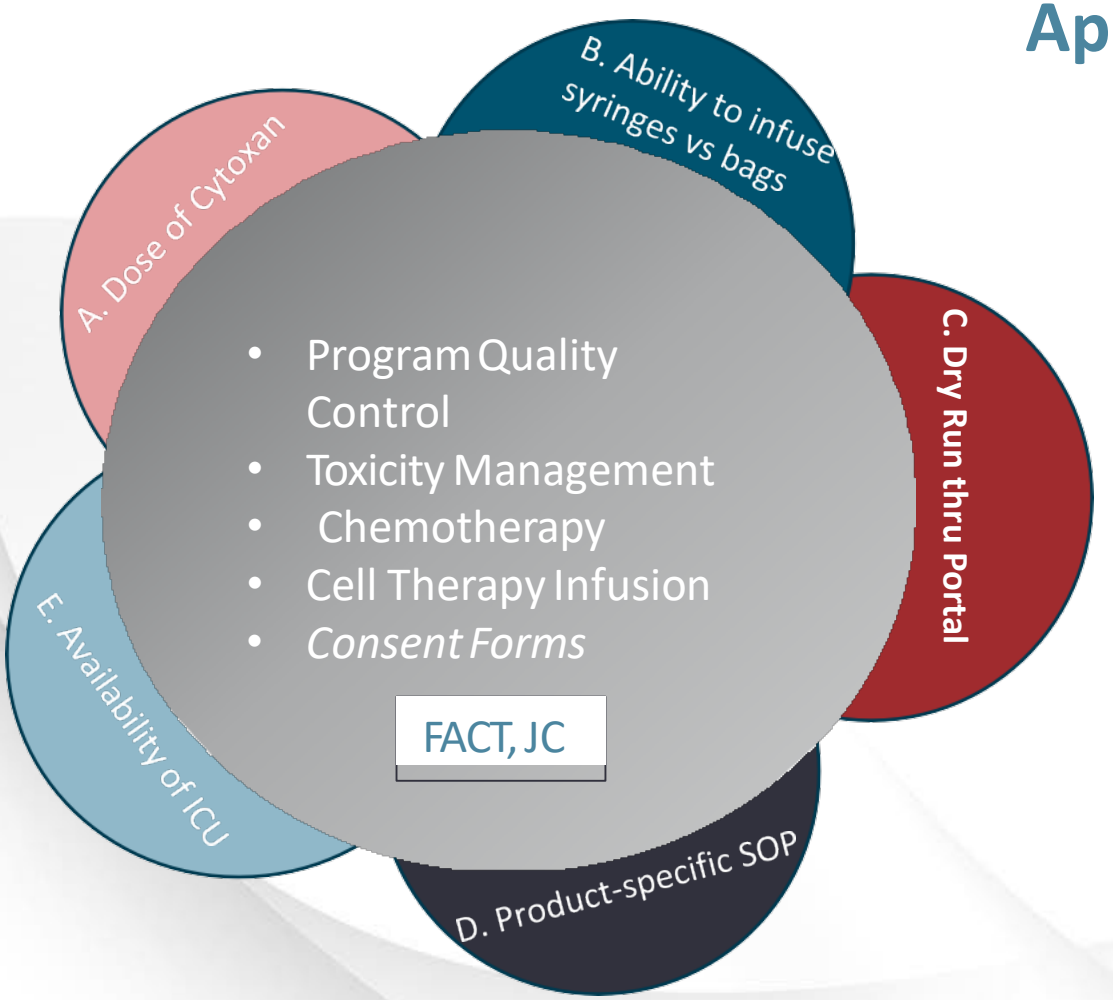
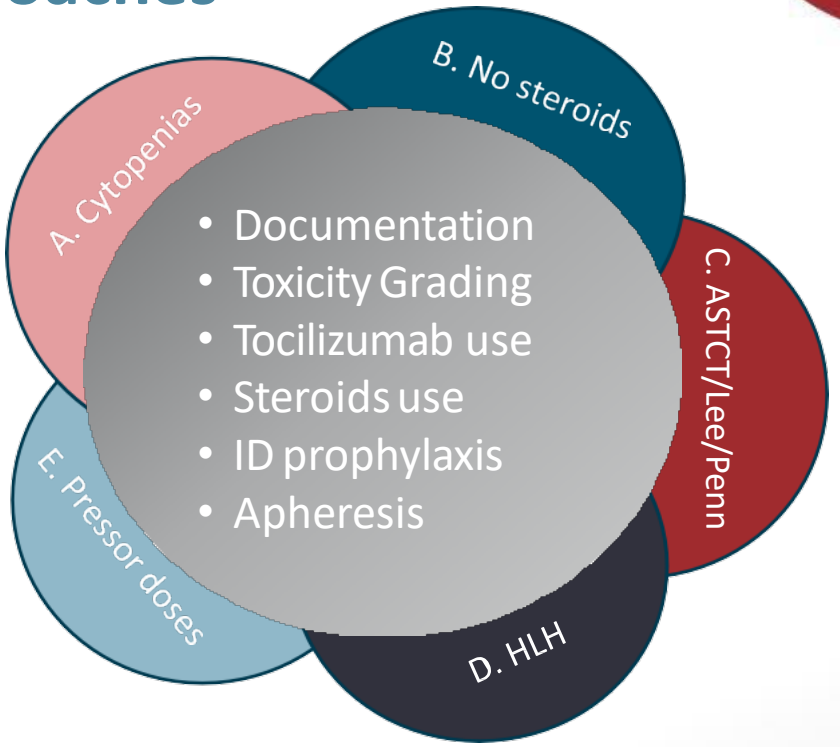
Program Onboarding



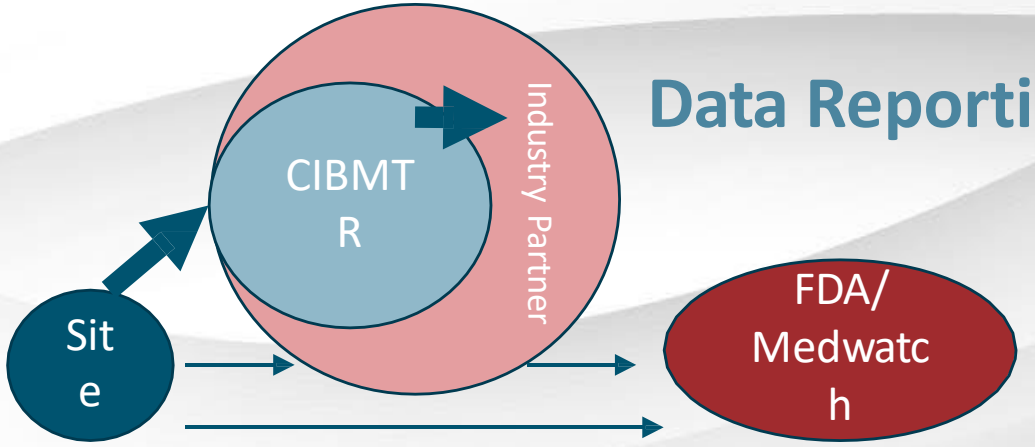
Tension between what industry partner feels they need to individually confirm vs what already exists and has been verified.

Clinical Management Approaches

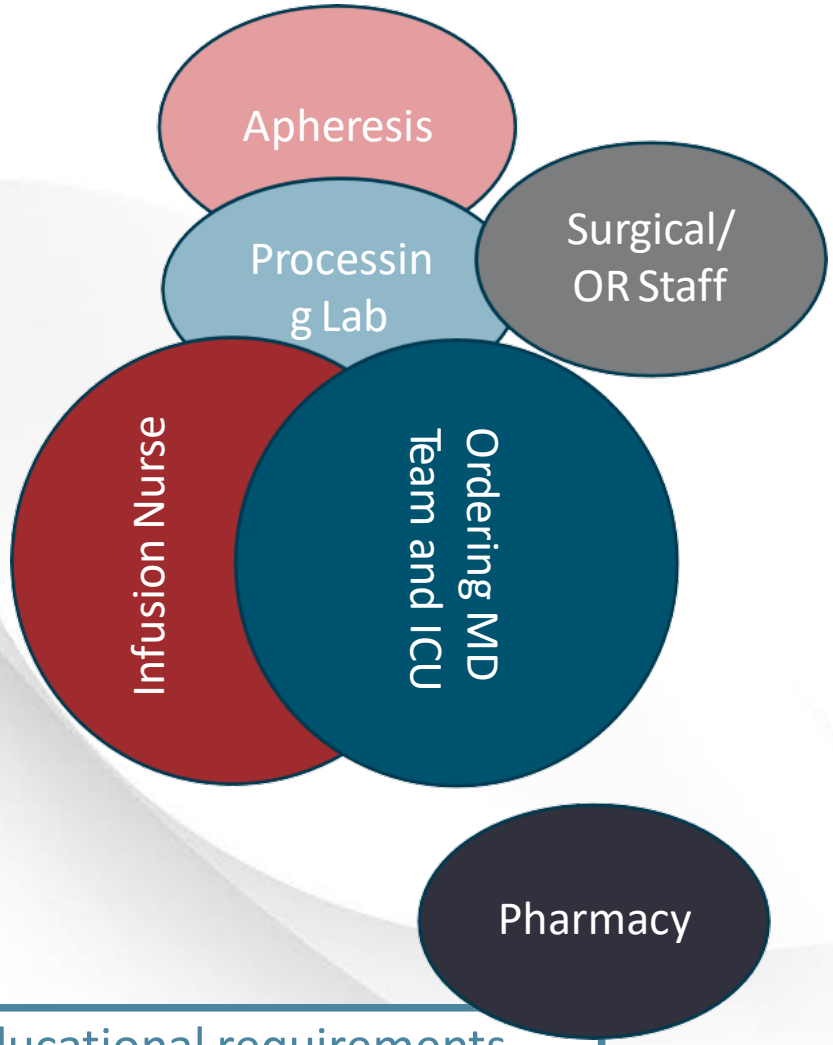


Tension between REMS guidelines and Apheresis Manual vs institutional standards

Data Reporting



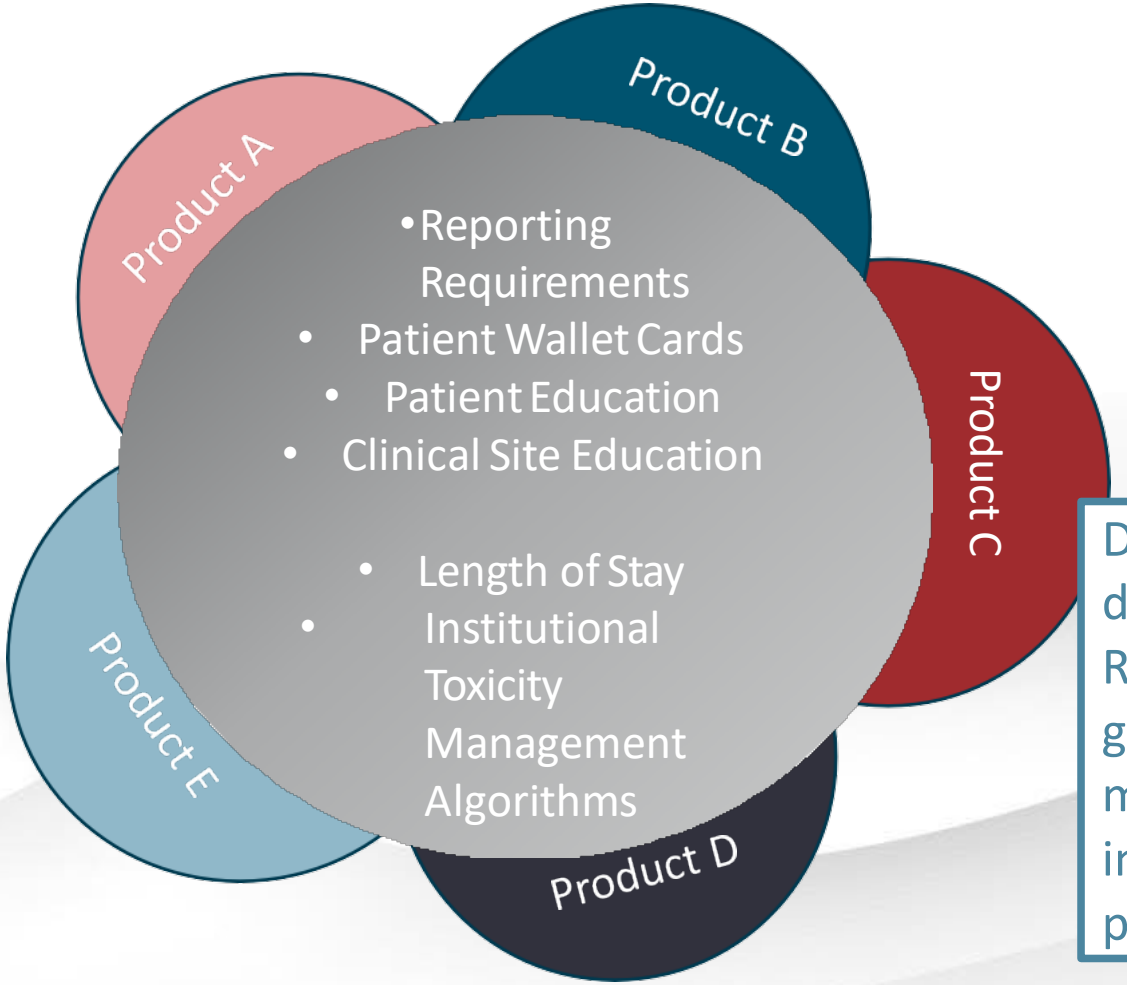
General Education



Educational requirements differ by group/sub-specialty

REMS – Prescribe Dispense Administer

Lack of clarity in who this means



Do differences in REMS guidelines for management impact site practice?

Collaboration needs to maximize community care

- Identification of partners
- Shared care models
- Flow models
- How to get a patient to OHSU: intake center or CALL ME
- How to get a patient home: pt education, recommended mgmt. of long term issues, FDA requirements of 15yr follow-up, CALL ME

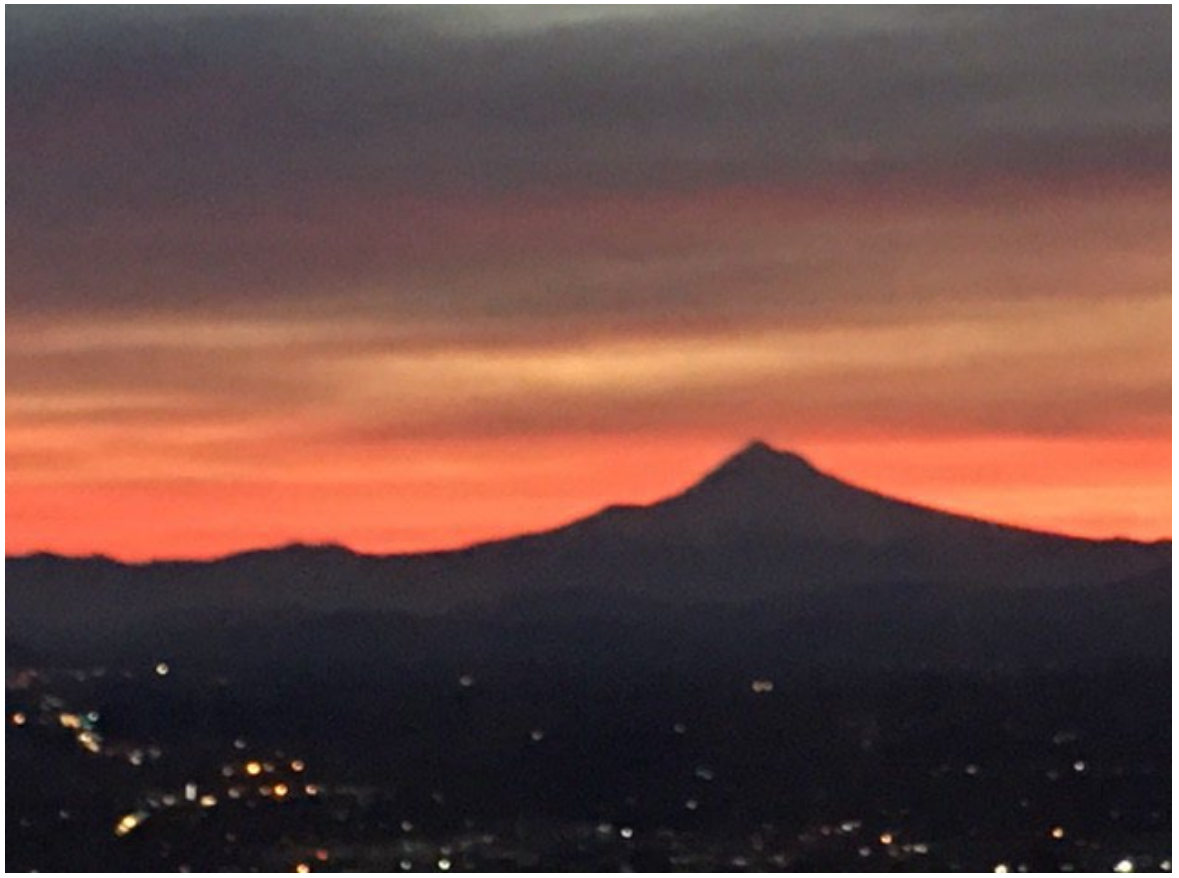
- HOW TO CALL ME: CELL is 503-805-1965

National CAR-T Landscape

- Clintrials.Gov- >1000 trials planned, ongoing, completed
- Disease targets:
  - Lymphoma- NHL and HD; MM; Neuroblastoma; ALL; CLL; Mesothelioma; Ovarian ca; Pancreatic ca; AML; Glioblastoma; Prostate ca; HCC: MUC 1+ Lung CA & triple (-) Breast Ca; Colorectal Ca; H/N Ca; SLE; other autoimmune disease
  - Targets include Her2/Neu, mesothelin, EGFRvIII, GD2 ganglioside
  - CD19/CD22 bispecific CAR-T (generated by bicistronic insertion)
  - CD19/CD20 bispecific CAR-T
  - Multi-CAR T trials
  - CAR-T with checkpoint inhibitors

CAR T & Transplant: the work evolves

Thanks to all for joining; Here to help!!!



Dawn over Mt Hood near Portland, OR