Chimeric Antigen Receptor-T (CAR-T) Cell Therapy for Relapsed/Refractory Pediatric, Adolescent and Young Adult B-ALL

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No Disclosures/COI

CAR T-Cell Education Symposium,
Pediatric Specialists of Virginia/INOVA
January 12, 2021

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Learning objectives

- Briefly review reported outcomes of CAR-T cell therapy (tisagenlecleucel)- clinical studies and real world data for pediatric, adolescent and young adult B-ALL
- Role of CAR-T cell therapy (versus other immunotherapies) for relapsed/refractory B- ALL in pediatric, adolescent and young adults
- Importance of timely referral of relapsed/refractory B-ALL patients for CAR-T cell therapy
- Role of hematopoietic cell transplant (HCT) in patients receiving CAR-T cells

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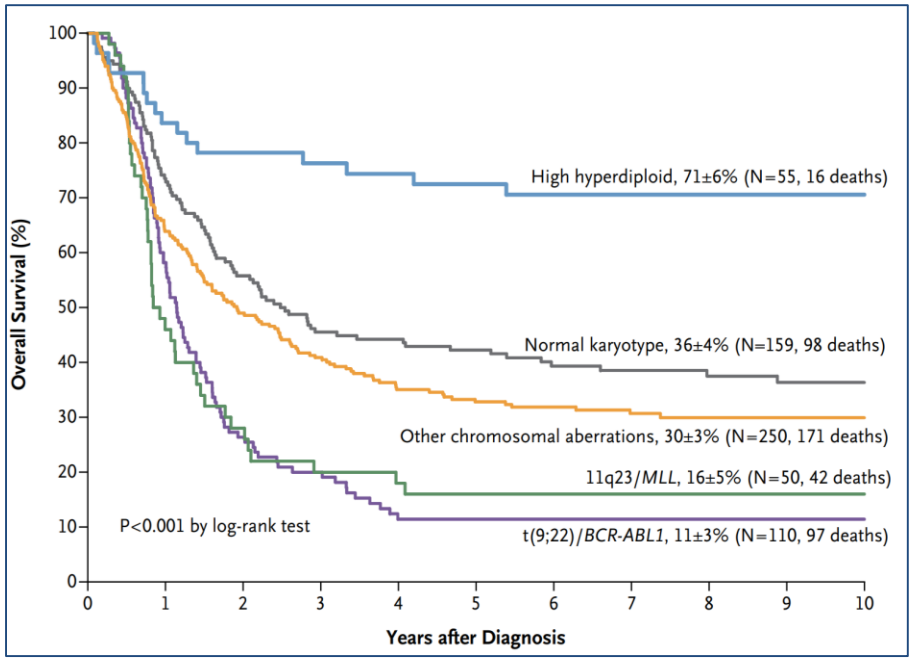
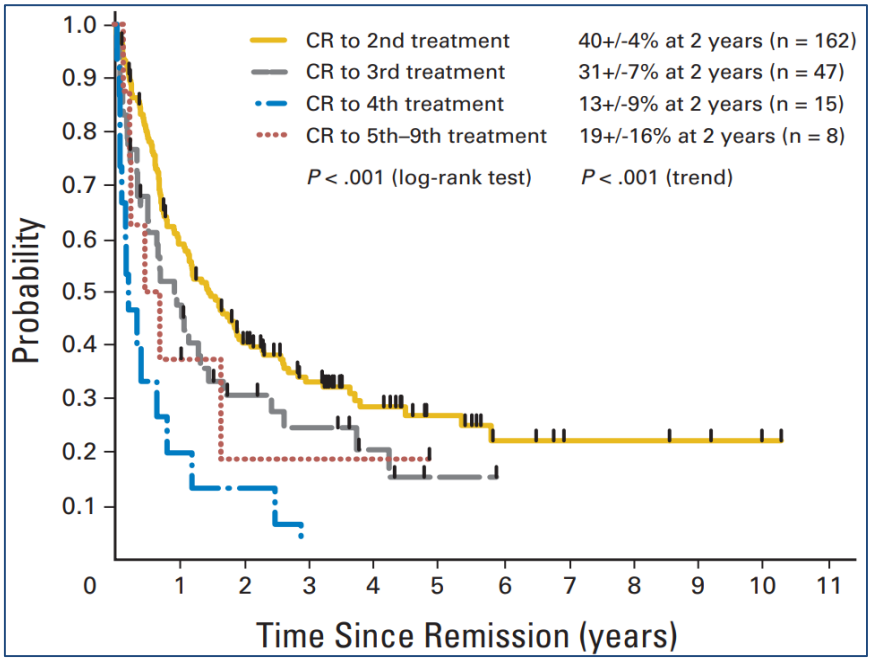
Need for better therapies for relapsed/refractory pediatric B- ALL





Schrappe *et al*, *NEJM*, 2012

Ko *et al*, *JCO*, 2010

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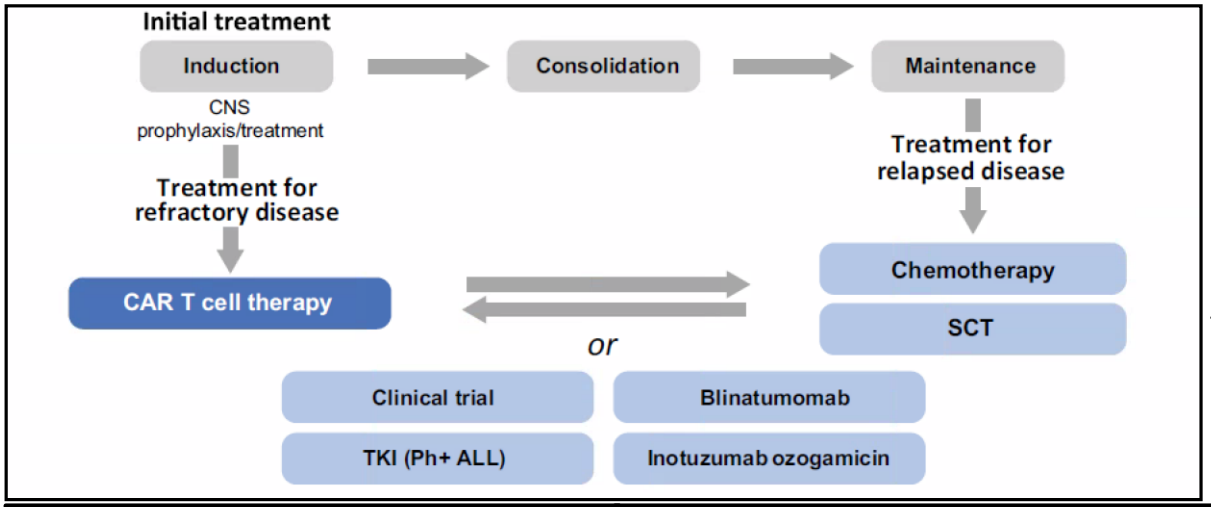
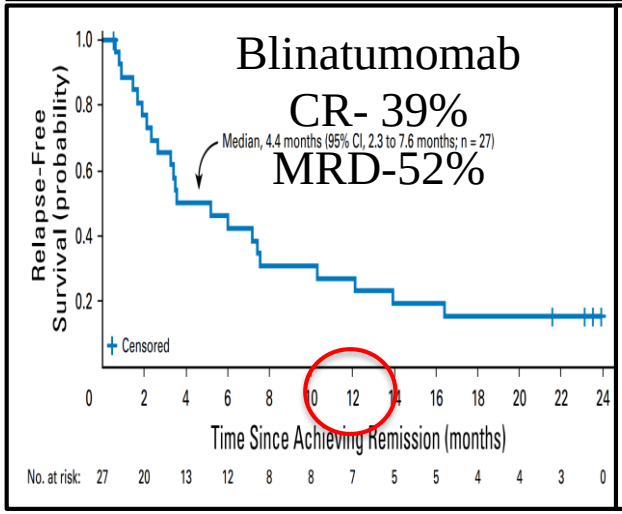
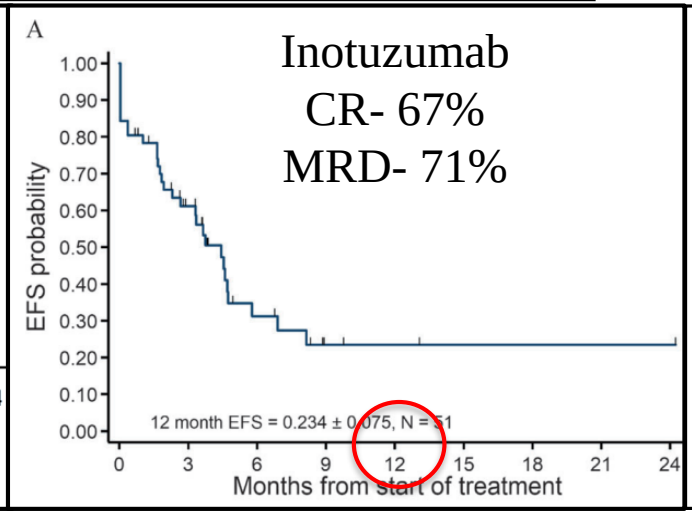
Immunotherapy for Rel/Ref B-ALL



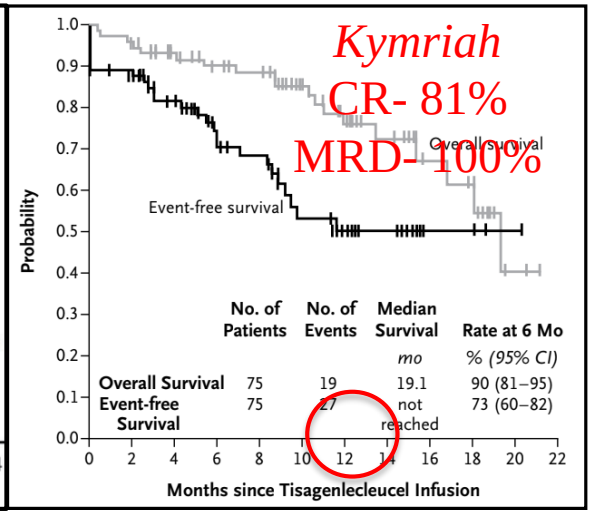
Hucks and Rheingold, *Blood Cancer Journal*, 2019



von Stackelberg *et al*, *JCO*, 2016



Bhojwani *et al*, *Leukemia*, 2019



Maude *et al*, *NEJM*, 2014

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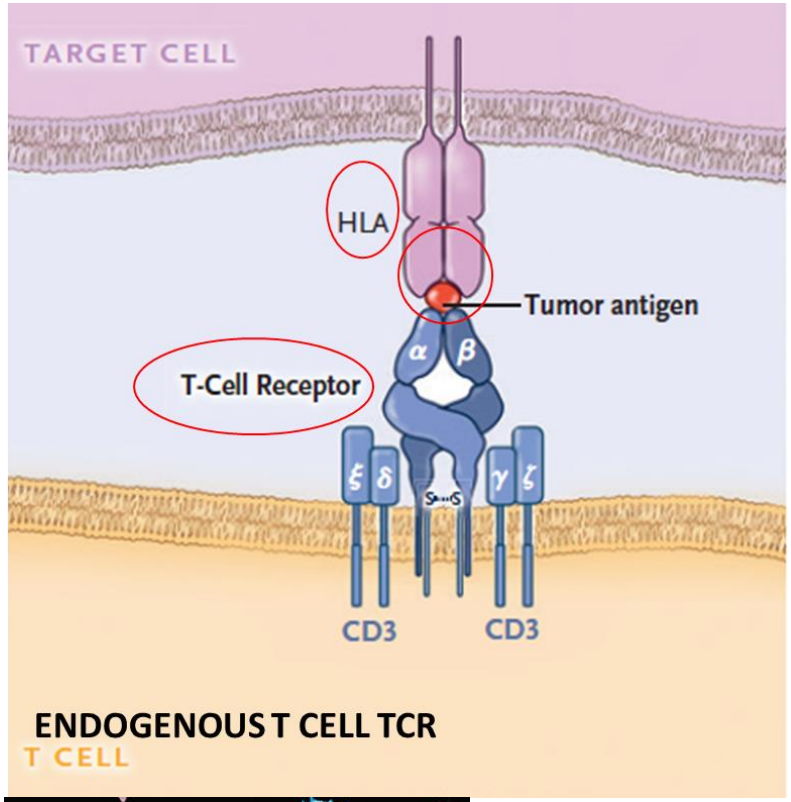
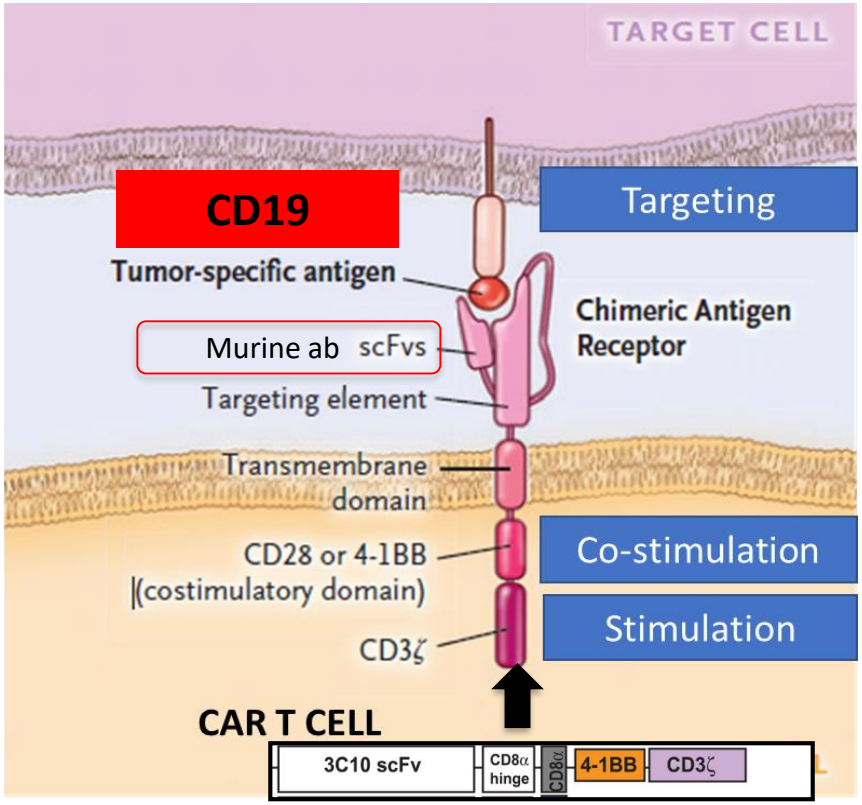
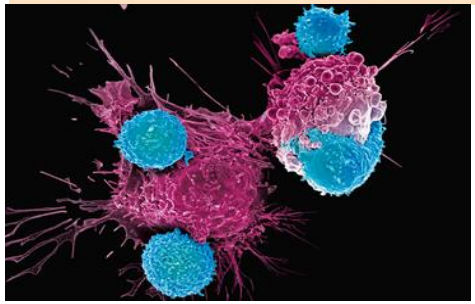
Endogenous *versus* CAR-T cells







June and Sadelain, *NEJM*, 2018

ELIANA Trial 2012 2020

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CD19 CAR-T cell clinical trials for B-ALL

Institution (Reference)	Patients (n)	CR-MRD n (%)	Median follow up	Overall survival	Relapse Overall (%) CD19 neg (%)	HSCT (% of CR-MRD)
MSKCC (Park et al; 2018)	Adults (53)	32 (67)	29 mo	12.9 mo (median)	16 (50) 4 (25)	16 (50)
MSKCC (Curran et al; 2019)	PAYA (24)	18 (89)	7.7 mo	-	4 (0)	15 (83)
CHOP (Maude et al; 2018)	Adults+ Pediatric (75)	61 (81)	13 mo	76% at 12 months	17 (28) 15 (88)	8 (13)
NCI (Lee et al; 2015)	Adults + Pediatric (50)	28 (56)	19 mo	-	8 (29) 5 (63)	21(75)
FHCRC (Turtle et al; 2016)	Adult (30)	26 (86)	-	-	9 (33) 2 (22)	13 (48)
Seattle Children's (Gardner et al; 2017)	Pediatric (43)	40 (93)	10 mo	66 % at 12 mo	18 (45)	11 (28)

FDA approves tisagenlecleucel for B-cell ALL and tocilizumab for cytokine release syndrome

August 30, 2017

- ***KYMRIAH* (tisagenlecleucel)**
- **First** CAR T-cell immunotherapy approved by the FDA
- Patients up to age **25** years
- B-cell precursor acute lymphoblastic leukemia (ALL) that is **refractory** or in **second or later relapse**.

Reference: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-b-cell-all-and-tocilizumab-cytokine-release-syndrome

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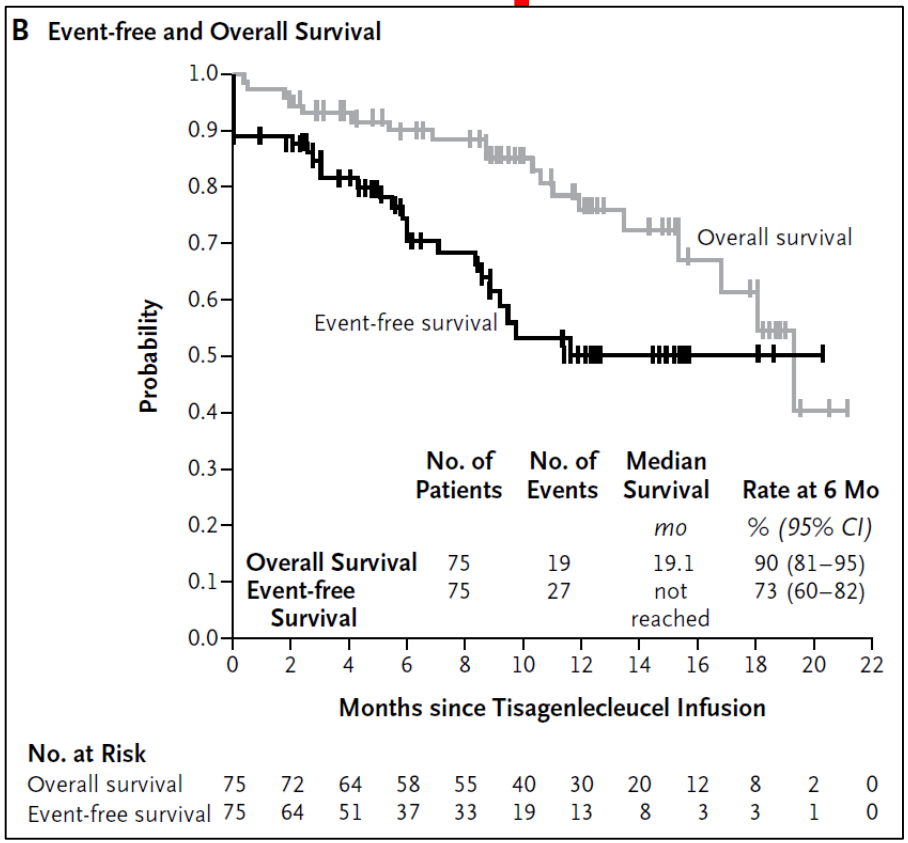
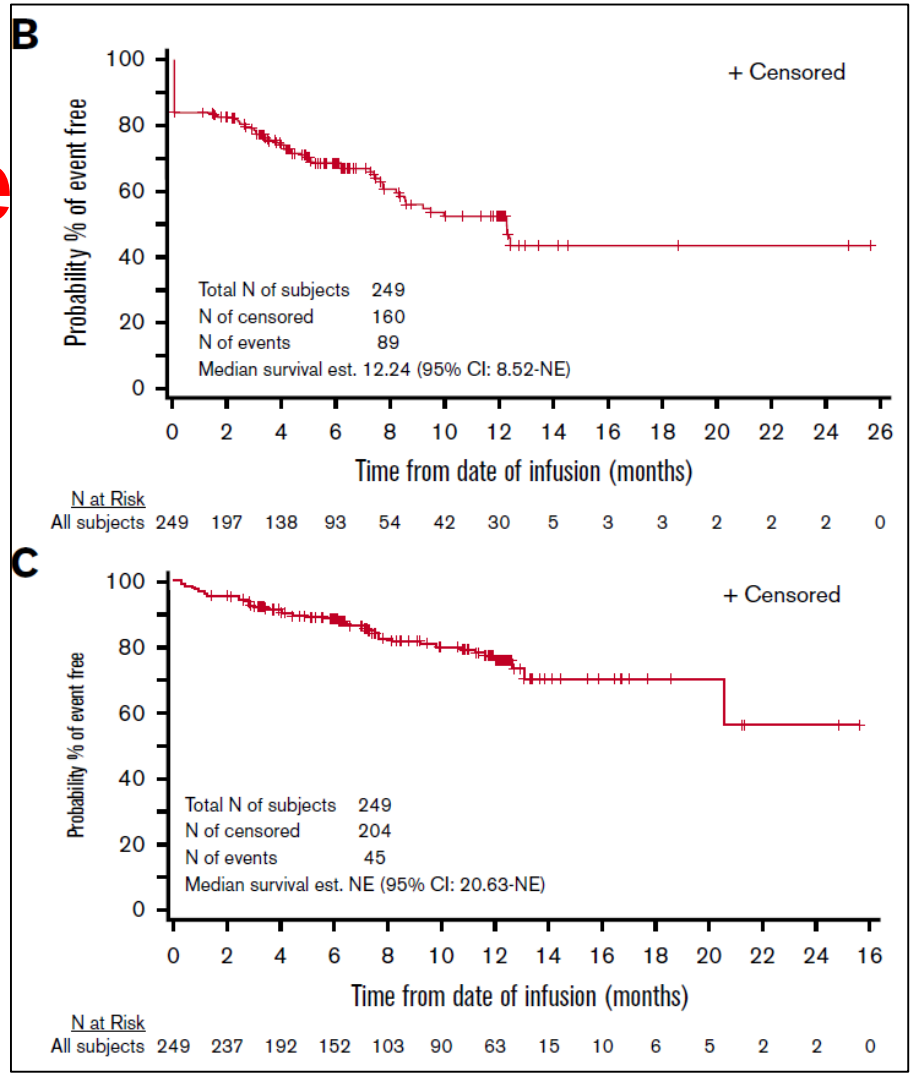
Real World CAR-T Experience



Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia

N ENGL J MED 378;5 NEJM.ORG FEBRUARY 1, 2018



Real-world evidence of tisagenlecleucel for pediatric acute lymphoblastic leukemia and non-Hodgkin lymphoma

blood advances 10 NOVEMBER 2020 • VOLUME 4, NUMBER 21

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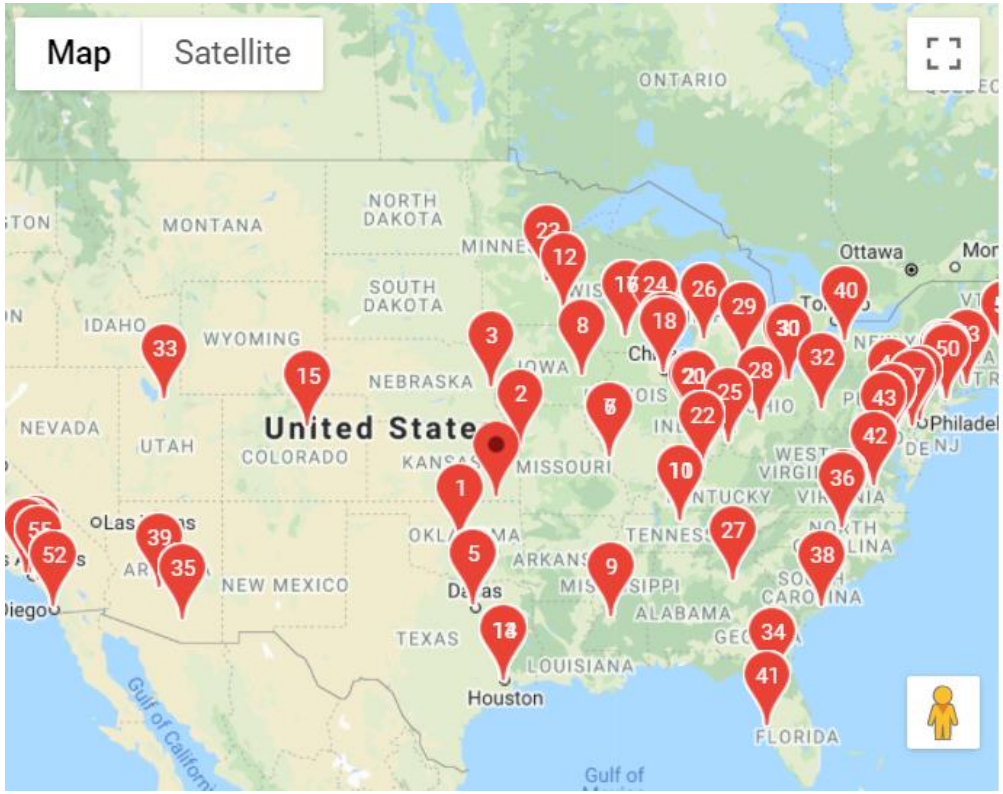
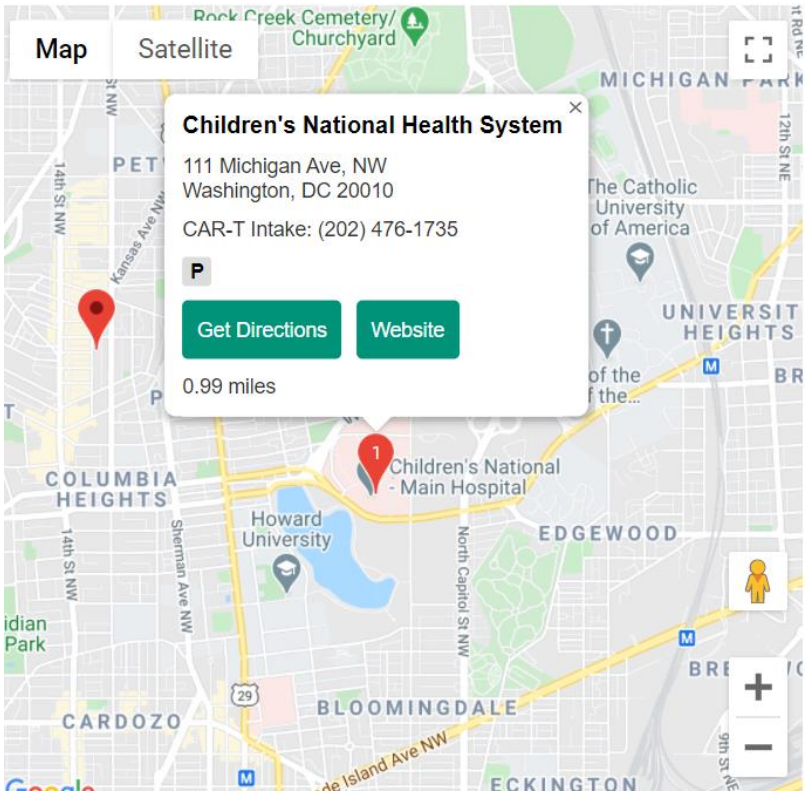
62 *Kymriah* treatment centers





Children's National Hospital is the only *Kymriah* treatment center for pediatric, adolescent and young adults in Washington D.C

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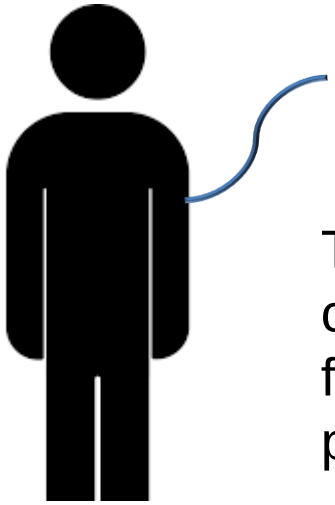
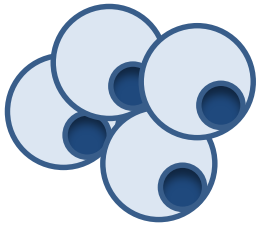
Delivery of CAR-T therapy

Lymphodepletion and infusion of CAR-T cells

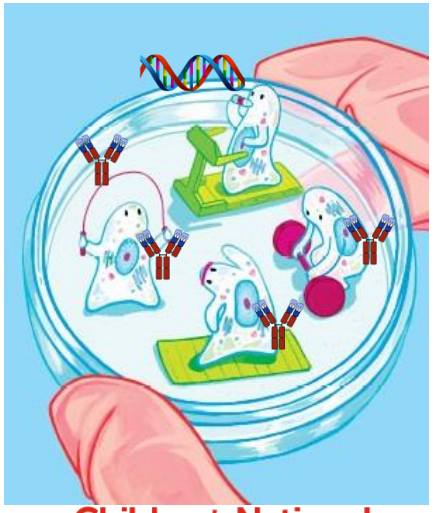


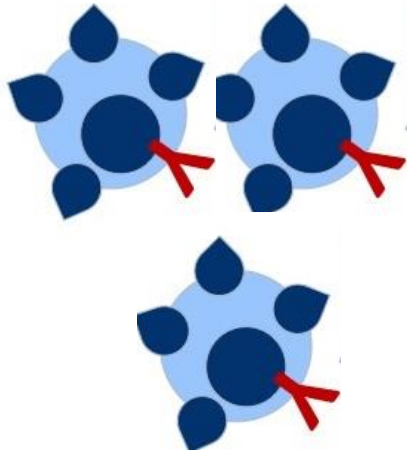


T cells collected from patient

Shipped to the manufacturer

T cells activated and gene modified to insert CAR



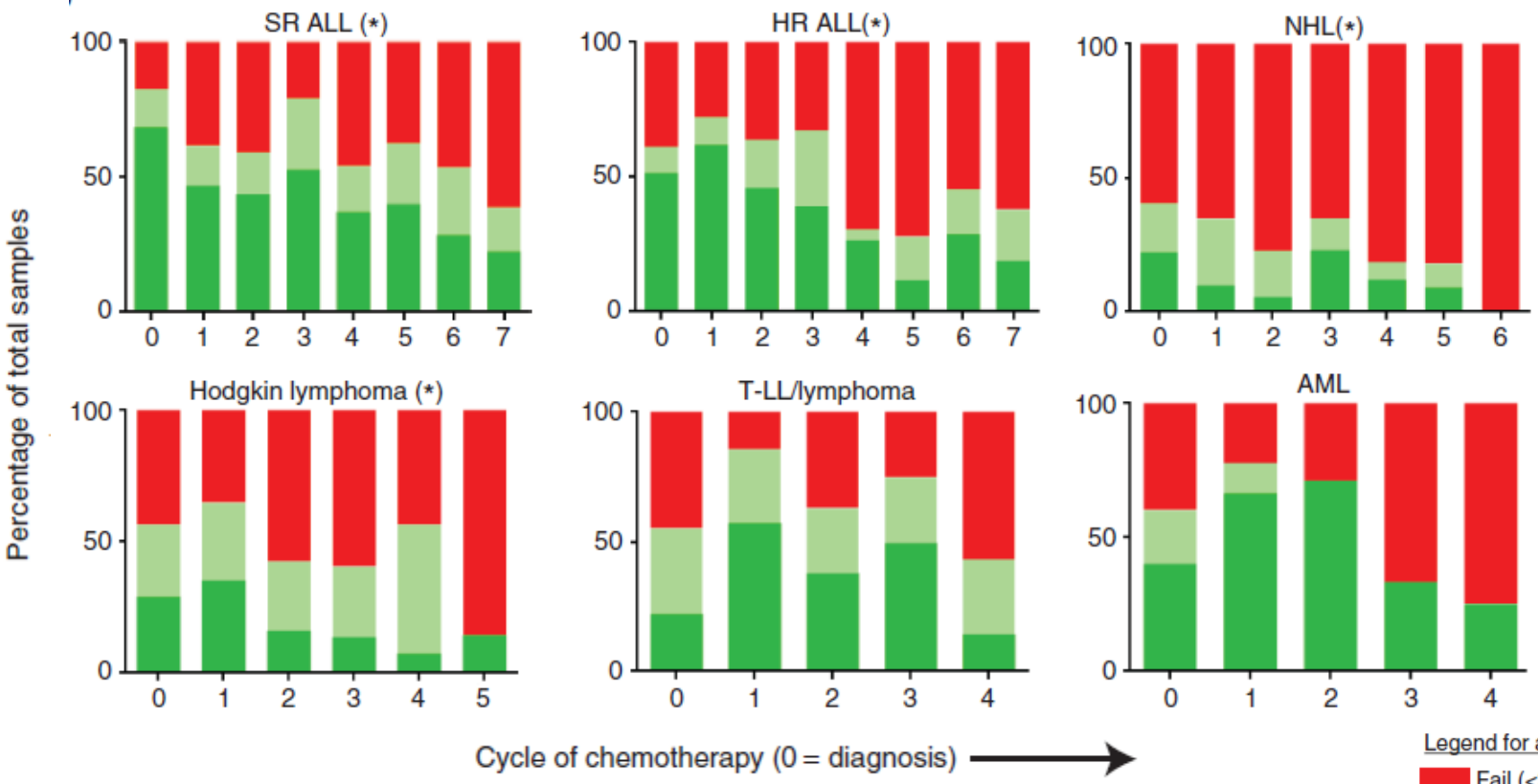


CAR-T cells expanded

CAR-T shipped to treating facility

Naïve T-cell Deficits at Diagnosis and after Chemotherapy Impair Cell Therapy Potential in Pediatric Cancers

Rajat K. Das[1], Lauren Vernau[1], Stephan A. Grupp[1,2], and David M. Barrett[1]



SIGNIFICANCE: Cumulative chemotherapy cycles deplete naïve T cells in many pediatric cancer regimens, reducing expansion potential associated with successful adoptive cellular therapies. Naïve T-cell deficits can be seen at diagnosis as well, implying immune deficits that exist prior to chemotherapy, which may also affect the development of immune-based therapies.

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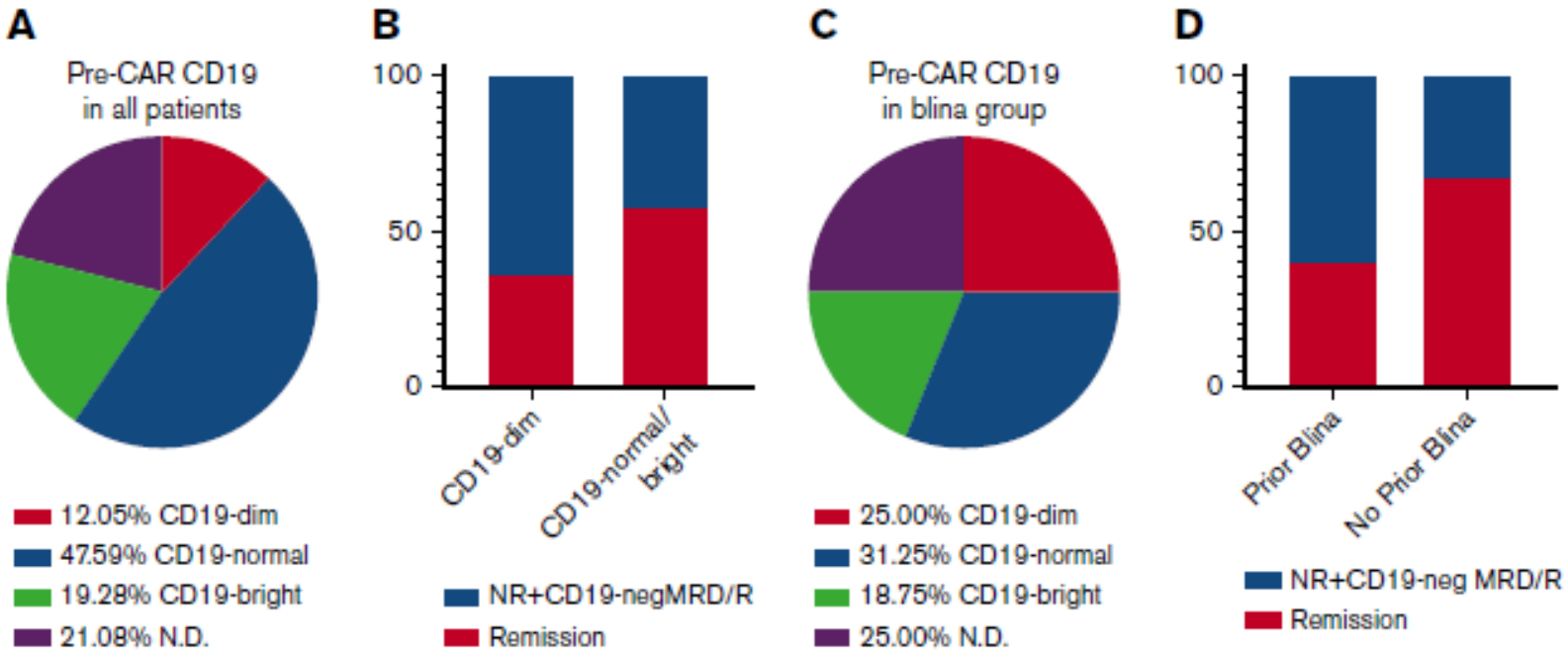
CAR T-cell therapy is effective for CD19-dim B-lymphoblastic leukemia but is impacted by prior blinatumomab therapy

Vinodh Pillai,[1] Kavitha Muralidharan,[2] Wenzhao Meng,[1] Asen Bagashev,[1] Derek A. Oldridge,[1] Jaclyn Rosenthal,[2] John Van Arnam,[1] Jos J. Melenhorst,[1] Diwakar Mohan,[3] Amanda M. DiNofia,[4] Minjie Luo,[1] Sindhu Cherian,[5] Jonathan R. Fromm,[5] Gerald Wertheim,[1] Andrei Thomas-Tikhonenko,[1] Michele Paessler,[1] Carl H. June,[1] Eline T. Luning Prak,[1] Vijay G. Bhoj,[1] Stephan A. Grupp,[4] Shannon L. Maude,[4,*] and Susan R. Rheingold[4,*]

blood advances 26 NOVEMBER 2019 · VOLUME 3, NUMBER 22



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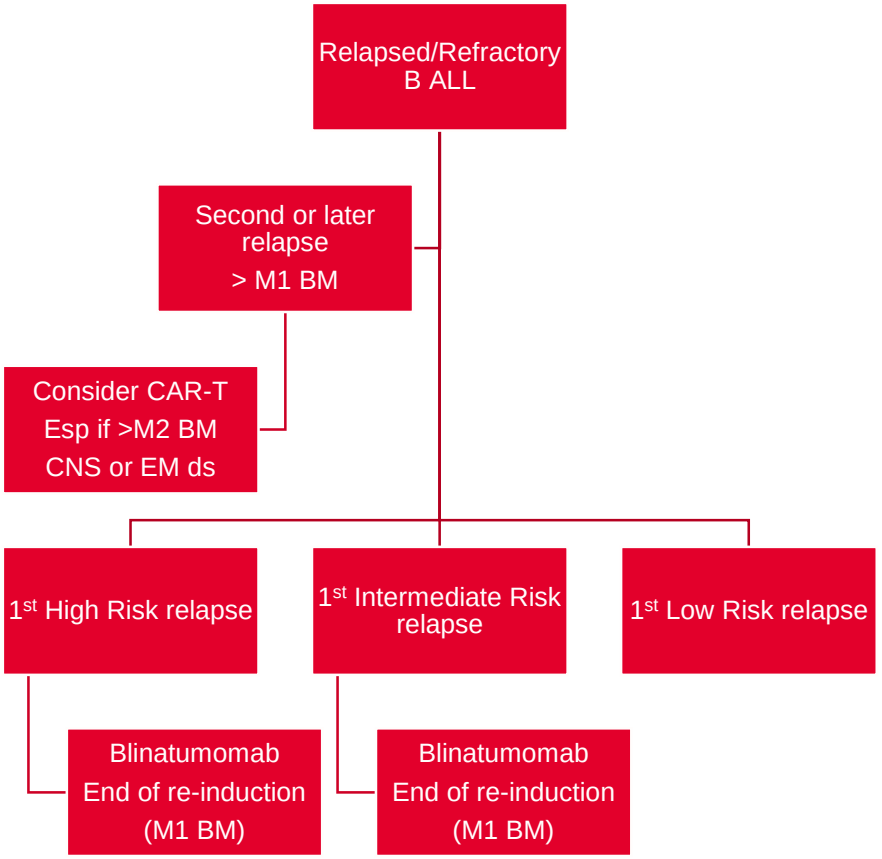
Immunotherapies for Rel/Ref B-ALL

Only 30-40% CR with MRD neg response in patients with M2/M3 BM disease burden (RIALTO study)



<u>CAR-T *versus* Ab based immunotherapy</u>

Factors to consider:

- Insurance approval
- EOI disease burden
- Prior HCT
- Performance score
- Suitable donor
- EM/CNS disease
- HR Cytogenetics

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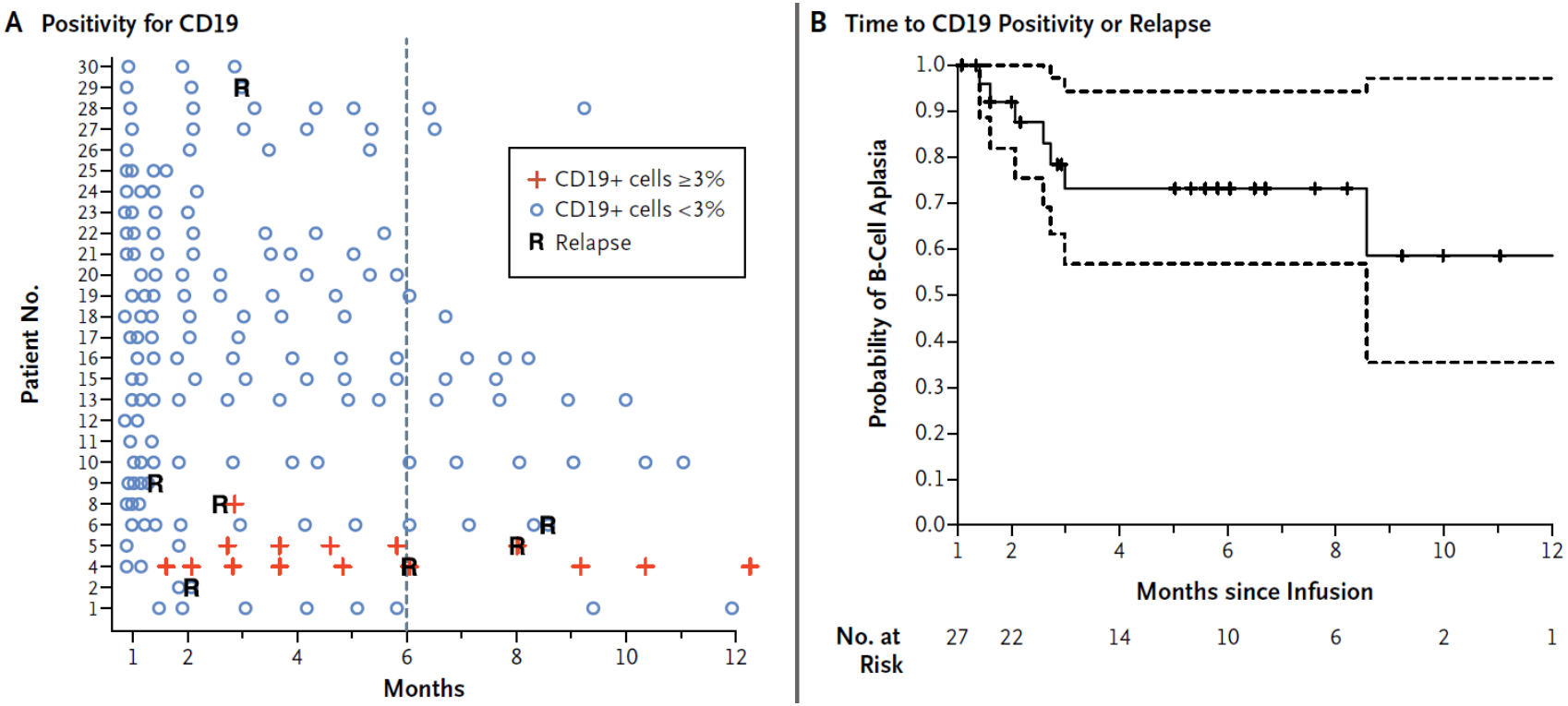
Importance of persistent B-cell aplasia



Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia

N ENGL J MED 371;16 NEJM.ORG OCTOBER 16, 2014

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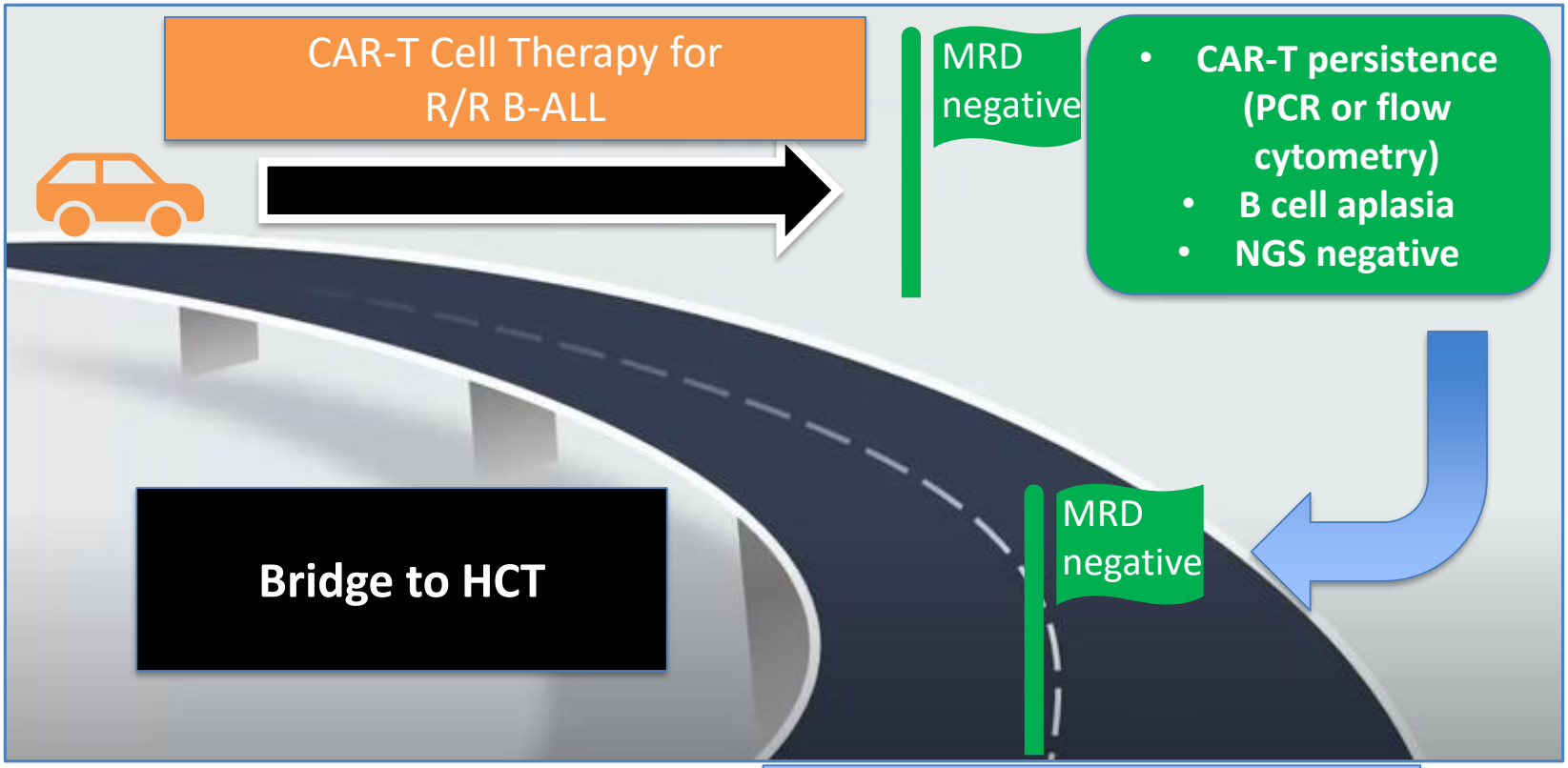
CAR-T therapy: transplant or no transplant



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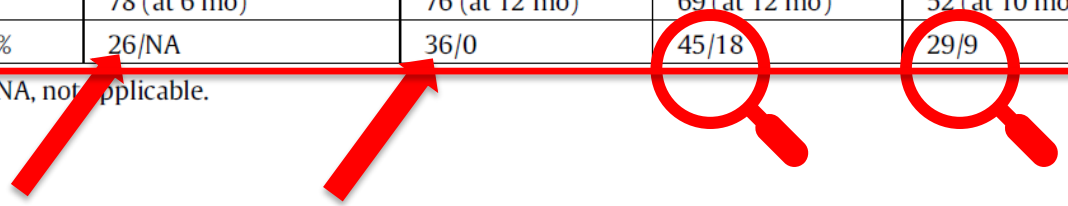
Major clinical trials in pediatric and young adult B-ALL patients

Summary of Major Results from Selected Clinical Trials Using Anti-CD19 CAR T Cells in Pediatric and Young Adult B-ALL Patients

Parameter	Maude et al (UPenn/CHOP) [19]	Maude et al (ELIANA) [22]	Gardner et al (Seattle) [41]	Lee et al (POB/NCI) [43-45]	Curran et al (MSKCC) [47]
Costimulatory domain	4-1BB	4-1BB	4-1BB	CD28	CD28
Treated patients, n	30 (5 adults)	75	45	53	25
Previous allo-HCT, %	60	61	62	35	20
CR, %	90	81	93	61	75
MRD-negative CR, %	78	81	93	53	67
Post-allo-HCT in CR, %	10	14	28	75	83
EFS/LFS rate, %	67 (at 6 mo)	50 (at 12 mo)	51 (at 12 mo)	49 (at 18 mo)	NA
OS rate, %	78 (at 6 mo)	76 (at 12 mo)	69 (at 12 mo)	52 (at 10 mo)	NA
Relapse after CR, overall/after allo-HCT, %	26/NA	36/0	45/18	29/9	33/27

POB indicates Pediatric Oncology Branch; NA, not applicable.



Reference: Bouziana and Bouzianas, 2020, BBMT, e183-e191

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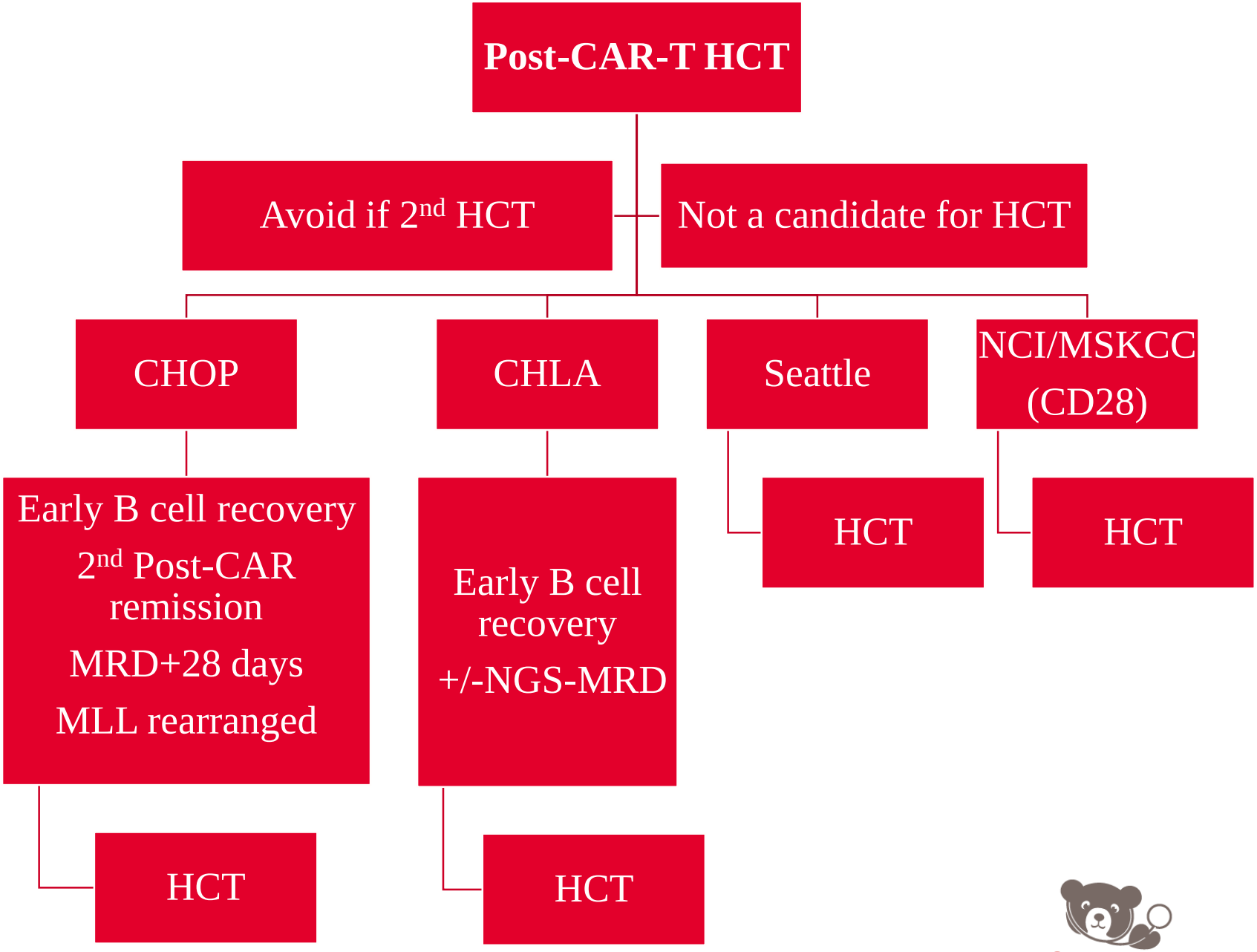

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CAR-T cell related toxicities

MOST COMMON ADVERSE EVENTS
Cytokine Release Syndrome (CRS) (~80%)
INFECTIONS (~40%)
Immune Effector Cells Associated Neurotoxicity (ICANS) (~40%)
FEBRILE NEUTROPENIA
PERSISTENT CYTOPENIA (~40%)
TLS (~10%)
HLH (~5%)
DIC (rare)

High Pre-CAR-T disease burden associated with higher rates of toxicities

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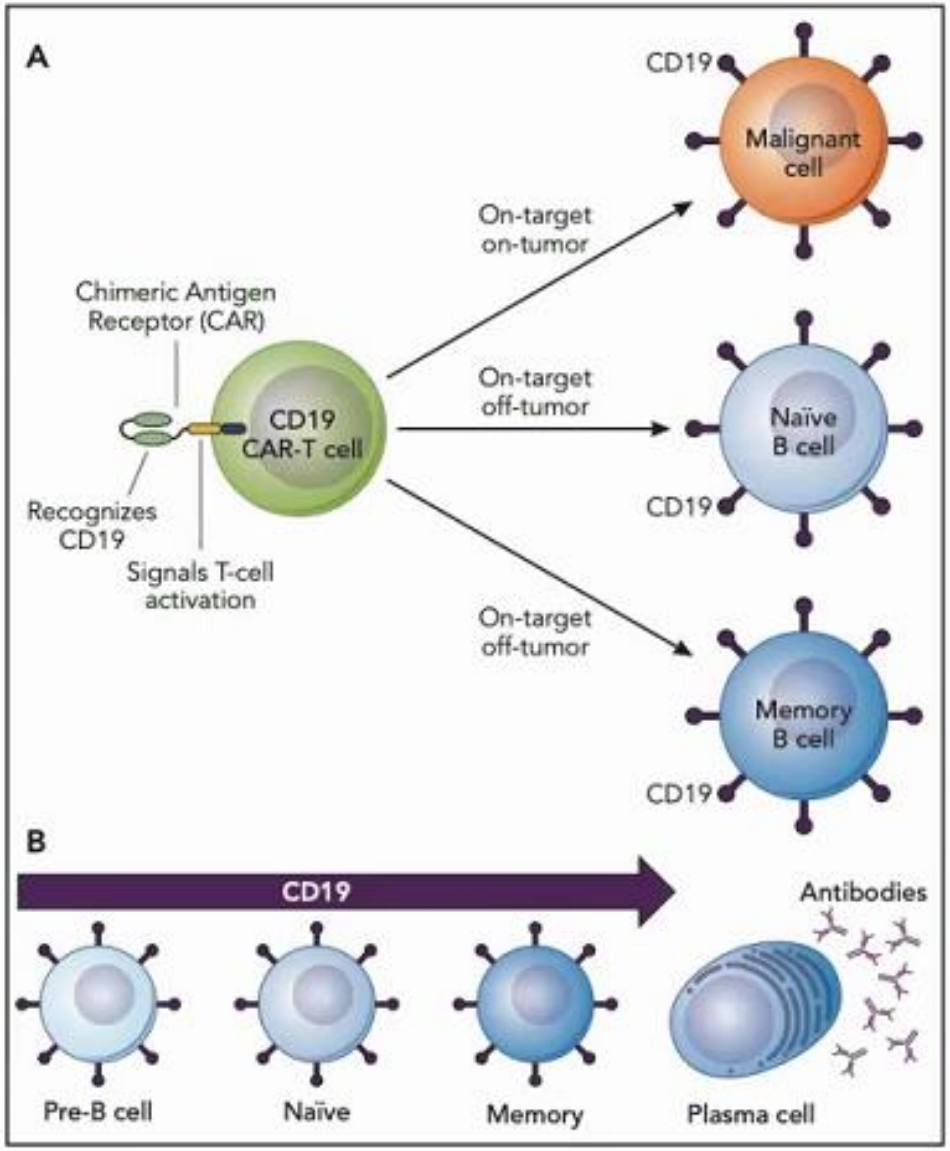
Targeting of CD19 on B-Cells



Hill and Seo, *Blood*, 2020

Post-CAR-T B-cell aplasia and need for IVIG

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A collaborative approach at CNH

Catherine Bollard, MD

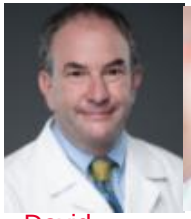
Patrick Hanley, PhD

Immunotherapies for HR hematologic malignancies in pediatric adolescent and young adults

CELLULAR IMMUNOTHERAPIES

ANTIBODY BASED IMMUNOTHERAPIES

BMT/Cellular Therapy



David Jacobsohn

Anne Angiolillo

Hema Dave

Leukemia/ Lymphoma

HCT

Genetically modified CT

Commercial CAR-T

Experimental CAR-T cells

PLAT studies

(PLAT-05, 06, 07)

Non-genetically modified CT

RESOLVE (AML)

SUSTAIN (Lymphoma)

Blinatumomab

Inotuzumab

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Multidisciplinary CAR-T Team

Meetings

<u>Weekly :</u>

CAR-T/BMT/HR Hematologic Malignancy Meetings

CAR-T BMT Meeting

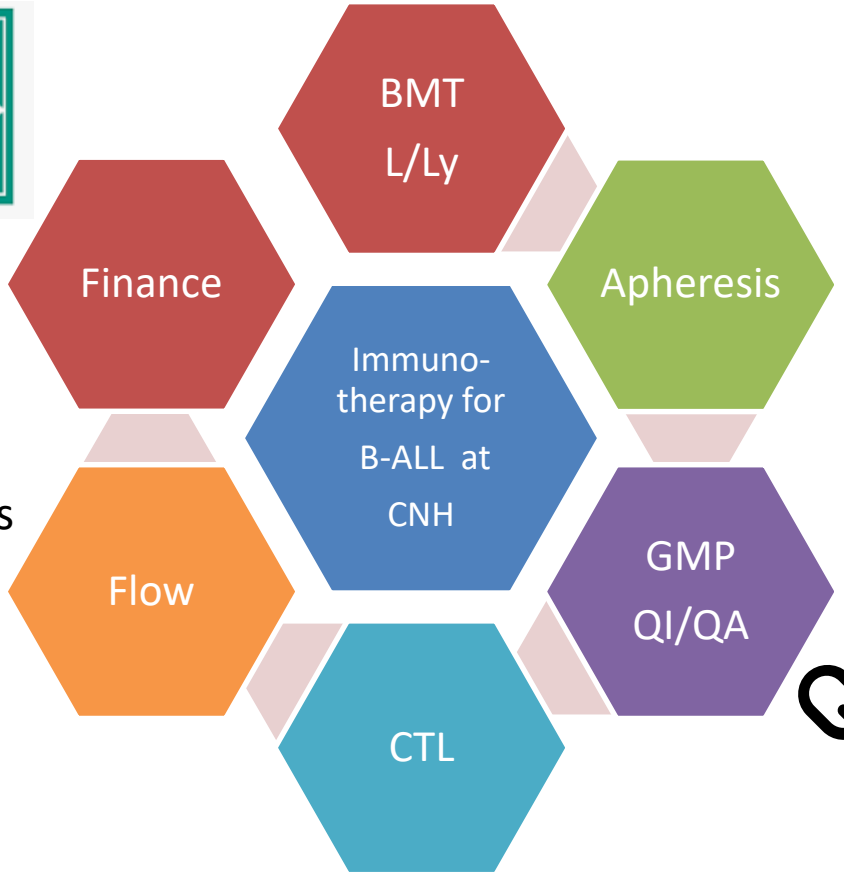
<u>Every 3-6 months:</u>

Educational symposium

<u>Yearly</u>

Audit

REMS Training



KYMRIAH Treatment Center

Nursing/Coordinators
PICU
Neurology
Pharmacy
IT Support/EMR
Data coordinators

Pharmaceutical companies

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Workflow

Importance of early referral (Screening and eligibility, optimal T cell collection)

Assessment for CAR-T therapy (prior Rx, disease burden, patient weight)

Review of "washout period"

Insurance approval for leukapheresis and CAR-T therapy

Coordination of leukapheresis/line placement

Shipment of leukapheresed cells to Novartis

Within 4-5 weeks of leukapheresis

2 months From CAR-T infusion

Patient at CNH or Referring Hospital → Primary Leukemia Team → Primary BMT Team → Leukapheresis → Bridging Chemo → CAR-T cell infusion → HCT or NO HCT → Leukemia team if NO HCT

Within 24 hrs

Within 7-14 days

202-476-1735 or
CART@childrensnational.org
for CAR-T referral

Admit to BMT
-LD chemo
-Management of toxicities

Optimal bridging therapy
- Less toxicity
- ? Avoid Blina or Ino

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CAR-T SOP

- Appendix 1: Workflow
- Appendix 2: Kymriah new patient (End to end) form and process
- Appendix 3: Pre-apheresis workup checklist
- Appendix 4: Bridging chemotherapy
- Appendix 5: Pre-Infusion checklist
- Appendix 6: Post-CAR-T infusion outpatient follow up
- Appendix 7: Outpatient/ER triage and management of CAR-T patients
- Appendix 8: Diagnosis and management of CRS and ICANS (Pocketbook)

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CAR-T Roadmap

Mon	Tue	Wed	Thurs	Fri	Sat	Sun
Pre- infusion checklist			D-8 H & P, Workup as per Pre-CAR T workup guidelines	D-7 Admission Neurology assessment and	D-6 Fludarabine (Flu) +Cyclophosphamide (Cy)	D-5 Flu+Cy
D-4 Flu	D-3 Flu	D-2 Rest day	D-1 Rest day Start Levetiracetam	D 0 (8/30/19) CAR T infusion	D+1 Uneventful	D+2 (9/1/19)
D+3	D+4	D+5	D+6	D+7	D+8	D+9

CRS → ICU Admission for Gr 2 or Higher CRS/ICANS → Neurotoxicity

AVOID STEROIDS!!!

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CYTOKINE RELEASE SYNDROME (CRS)

American Society for Transplantation and Cellular Therapy (ASTCT) CRS Consensus Grading and Guidelines for Management

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
[5]Fever	Temperature ≥ 38.0° C	Temperature ≥ 38.0° C	Temperature ≥ 38.0° C	Temperature ≥ 38.0° C
			With	
[6]Hypotension	None	• Responds to fluid bolus • Not requiring vasopressor	Requiring a single vasopressor	Requiring multiple vasopressors
			And/Or	
Hypoxia	None	• Requiring oxygen- [H]low-flow nasal cannula (≤4L/min)	Requiring oxygen- [H]high-flow nasal cannula (>4L/min), facemask, non-rebreather mask, or Venturi mask	Requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)
Intervention	• Observe in person • Call RRT • Admit for observation (if outpatient) • Supportive care -Labs: CBC with diff, CMP, Mg, Phos, urinalysis, blood cultures, PT/aPTT, fibrinogen -Evaluate need for urine culture, respiratory virus PCR, chest radiograph -Acetaminophen prn -Antibiotics IV	• Call RRT for PICU transfer • Supportive care per Grade 1 • Provide supplemental oxygen • NS bolus up to max of 20ml/kg • Maintenance IVF • Consider blood products/ colloids • Give Tocilizumab: -Patient wt <30 kg: 12mg/kg X 1 -Patient wt ≥30 kg: 8mg/kg X 1, max 800mg/dose • Persistent fever 8 hrs after Tocilizumab: Repeat Tocilizumab every 8 hrs x 2 (max 3 doses within 24 hr period)	• Call RRT for PICU transfer • Supportive care per previous grades • O2 support with high flow • Start/continue Tocilizumab • Start vasopressors as needed • Start Dexamethasone (0.5mg/kg, max 10mg/dose) IV Q6 hrs; May increase to max 20mg/dose, if refractory CRS	• Call RRT for PICU transfer • Supportive care per previous grades • Respiratory and Vasopressors as needed • FFP, cryoprecipitate or fibrinogen as needed to correct coagulopathy • Start/continue Tocilizumab • Start/continue Dexamethasone • If no improvement with Dexamethasone in 24 hrs, consider high dose Methylprednisolone (20-30mg/kg with max 1gm daily for 3 days followed by rapid taper if response)

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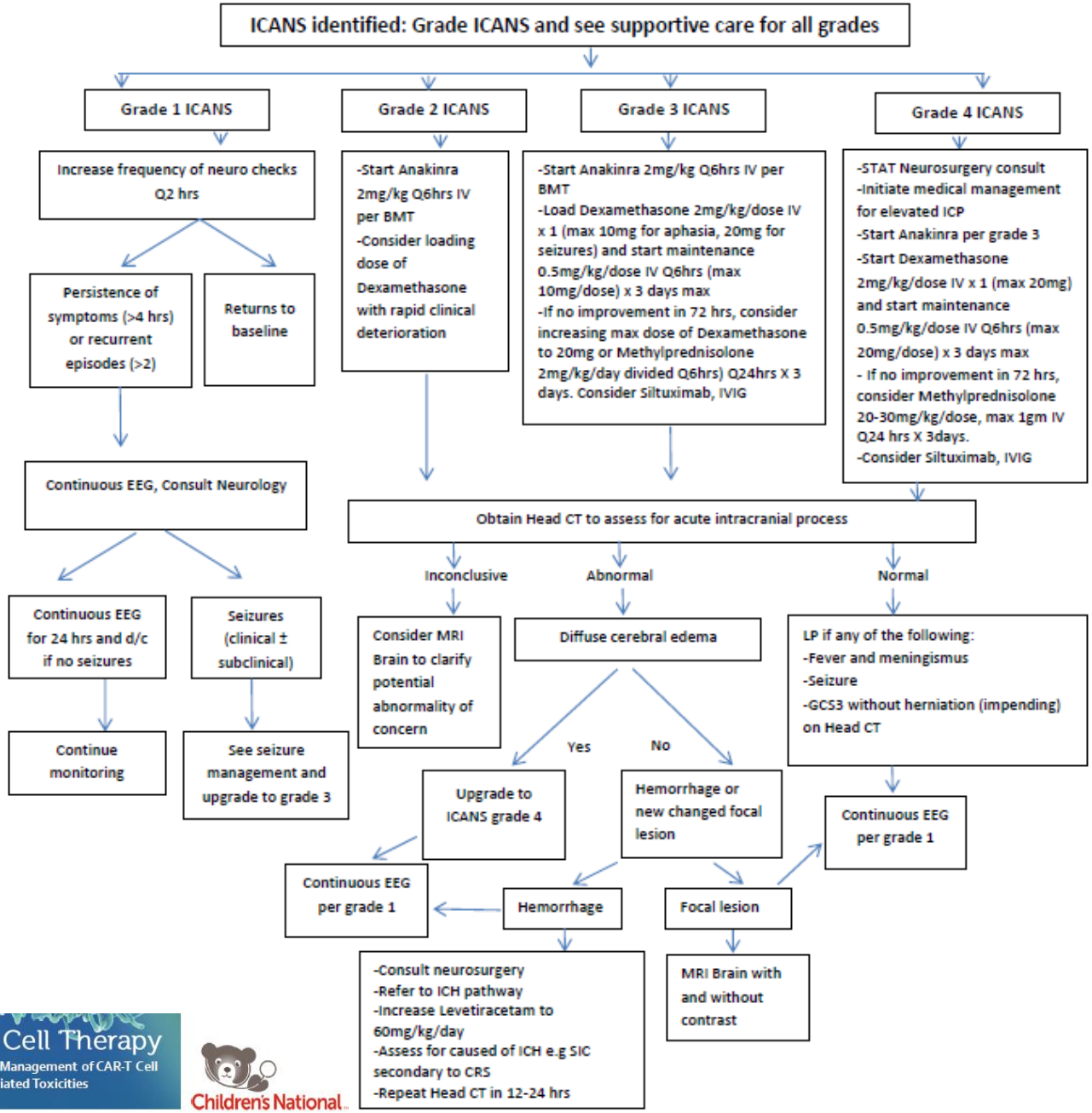

CAR-T Cell Therapy
Guidelines for Management of CAR-T Cell Therapy Associated Toxicities

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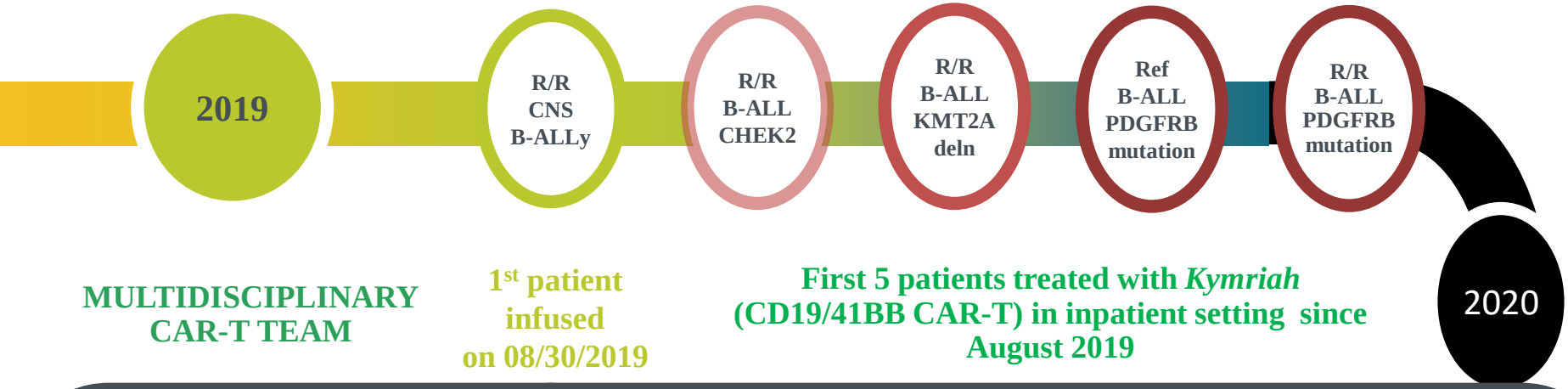
CAR-T milestones: CNH



MULTIDISCIPLINARY CAR-T TEAM

1st patient infused on 08/30/2019

First 5 patients treated with *Kymriah* (CD19/41BB CAR-T) in inpatient setting since August 2019

Driving the CAR to the Bone Marrow Transplant Program

Hema Dave[1,2] · Lauren Jerkins[1,2] · Patrick J Hanley[1] · Catherine M Bollard[1,2] · David Jacobsohn[1,2,3]

Current Hematologic Malignancy Reports (2019) 14:561–569

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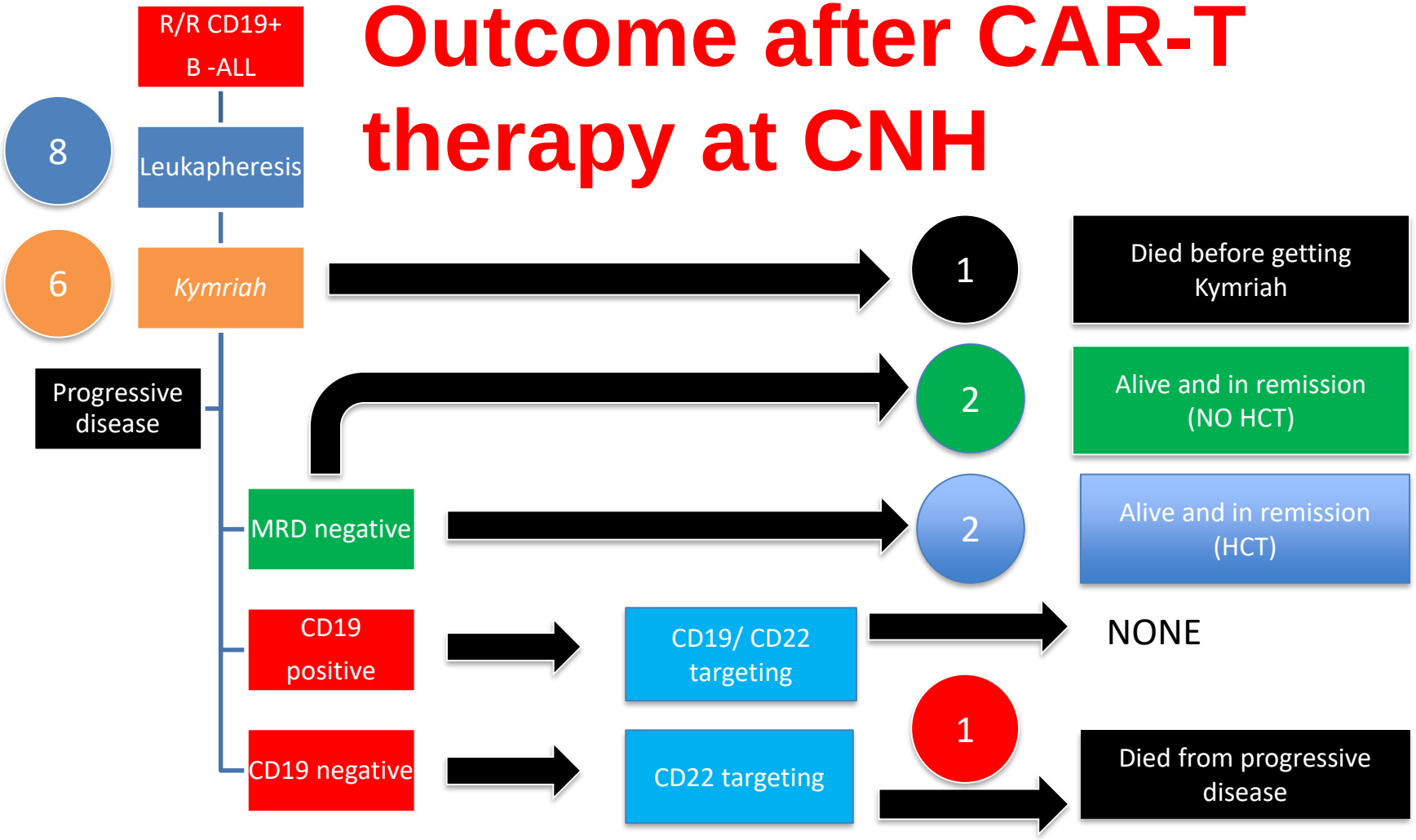
Outcome after CAR-T therapy at CNH



6th Kymriah infusion in January 2021

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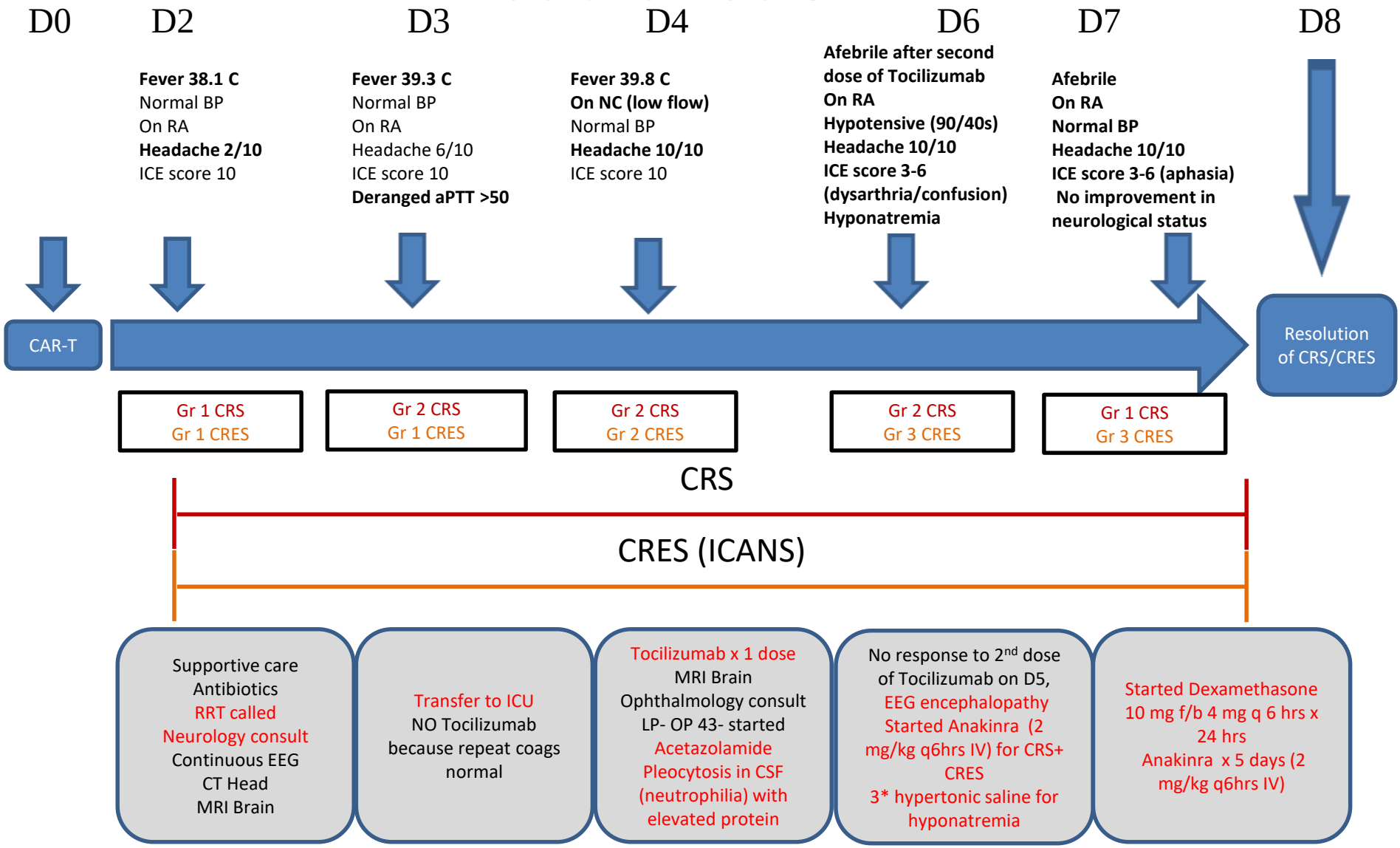
Patient 1 at CNH



- Fever ≥ 38 C is a defining criteria for CRS
- Headache: non-specific symptom seen in CRS and/or ICANS. It is not a diagnostic criteria for either of CRS/ICANS.
- Organ toxicities graded as per CTACAE version 5.0 but not diagnostic of CRS/ICANS
- CRP/Pro-inflammatory panel/organ function labs not diagnostic of CRS

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CAR-T for R/R CD19 +B-ALL

Teenage male
Relapsed/refractory
CD19+ B ALL

Relapsed B ALL → **2nd relapse in Feb 2020 ; CNS positive; MLL rearranged; CD19 positive B ALL**

TACL Protocol 2012-002 → **Liposomal Vcr + Erwinia Asp+ Dexamethasone**

Refractory → **BM on 3/30/20- 10% blast- Leukapheresis for potential need for CAR-T cell therapy– Collect and Hold, ALC >500/mcL; CD3+ >150/mcL; neg for HIV/HepB/HepC**

Blinatumomab → **Significant increase in leukemia burden on therapy- developed TLS ; CD19- moderate-dim**

Refractory → **Leukapheresed mononuclear cells shipped to Novartis on 4/24/20; started "bridging chemotherapy"**

Kymriah (finished commercial CAR-T product) received on 5/21520

Escalating Mtx+Vcr

Admitted on 5/22/20 for lymphodepleting chemotherapy → **Flu + Cy; Baseline Neurological exam**

Infusion on 5/29/20 → **REMS refresher/ Education of HCPs**

? CRS
? ICANS
? TLS → High risk for CRS- Pre-CAR-T -53% leukemia burden in BM. 2 doses of Tocilizumab on standby

Discharge D+14
Follow up in BMT clinic → **Recovered with blasts**

Died of progressive disease

Avoid steroids!!!
Ensure adequate washout period
No active infections/inflammation/ uncontrolled leukemia

Developed CRS Gr2, ICANS Gr3- responded to Tocilizumab →Anakinra+ Dexamathasone

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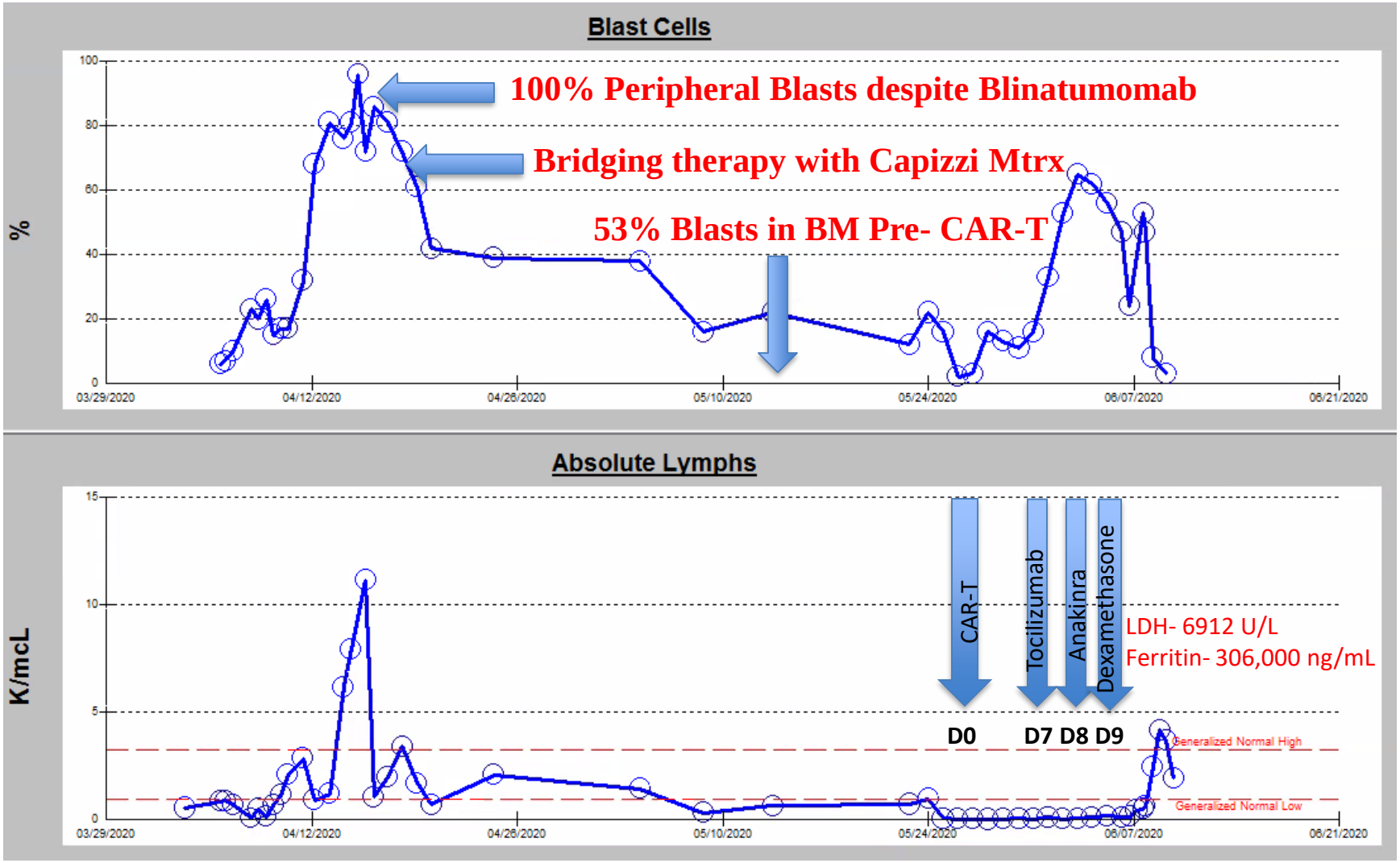
CAR-T cell and blast kinetics



CAR- T Expansion and Fall in Blast Count

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Post CAR-T therapy care

Post CAR -T Therapy	Recommendations/Comments
Discharge	D+14 if ANC >200/mcL x 2 and rising
Education	Educate caregivers about vital sign monitoring Educate caregivers to log daily ICANS questionnaire Contingency plan for fever/Kymriah “wrist bands” and wallet cards
Clinic follow up	Till D+60 or BMT which ever is later
Supportive care	Consider G-CSF for prolonged neutropenia (after D+14)
Infection prophylaxis	Prophylaxis with antibacterial, antivirals, antifungal, PJP
IVIG	Monthly monitoring of IgG. IVIG for IgG <400mg/dl
Lymphocyte subsets	Monitoring of B cell aplasia. Recovery of CD19+ cells- may be a sign of relapse
HCT	Indications for HCT post-CAR-T rapidly evolving

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Challenges

- **Toxicities**: **CRS/ICANS/HLH like/Infections (80-90%)**
- Strategies to mitigate toxicities- REMS
- More proactive use of tocilizumab, steroids and steroid sparing agents like anakinra
- Need for IgG supplementation
- **Relapses after CAR-T therapy (30-50% at 1 year)**
- Lack of persistence of CAR-T cells (CD19 pos)-CAR-T cell exhaustion- transplant as a consolidative therapy
- Immune escape (CD19 neg) (7-60%)
- **Refractory to CAR-T cell therapy (10-20%)**
- **Financial toxicity- $475,000 for *Kymriah***

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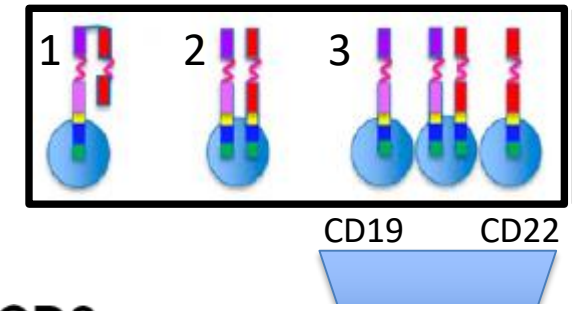
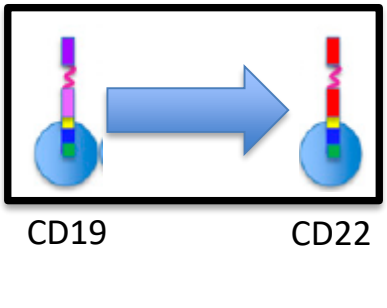
Dual antigen targeting

Simultaneous targeting

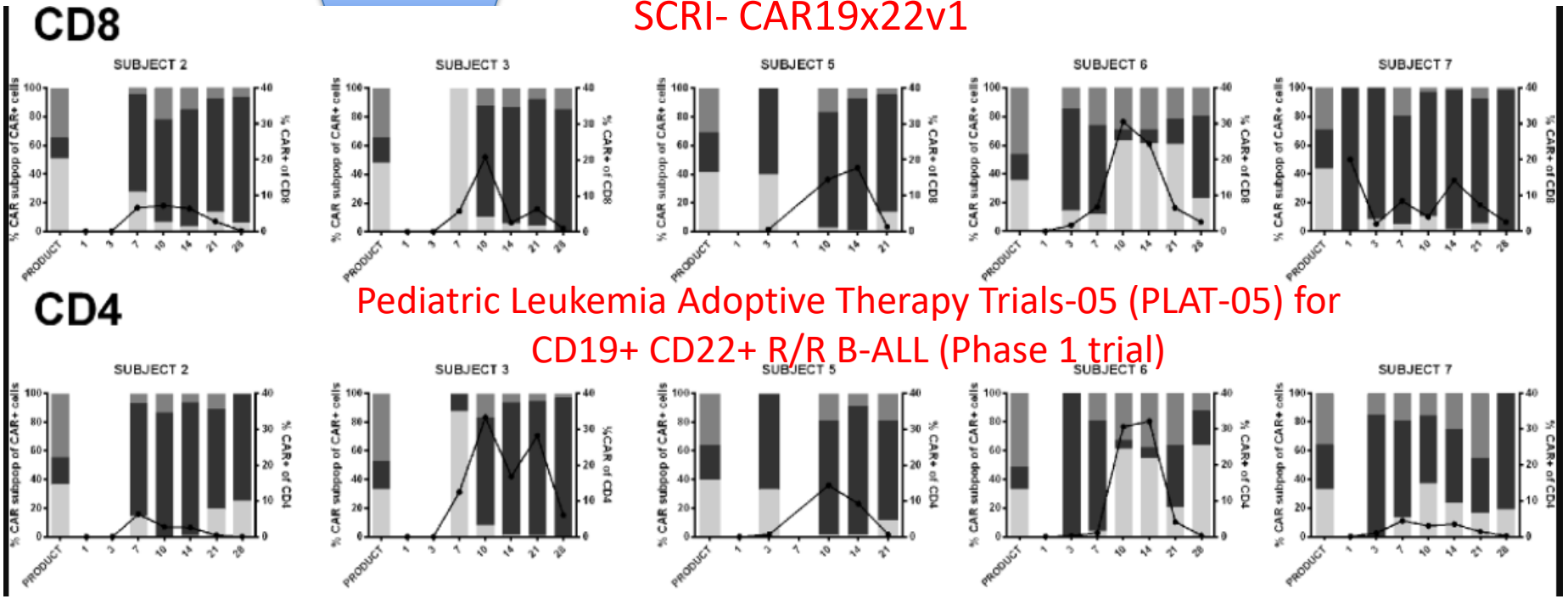


1.Bivalent (in series)
2.Bi-cistronic (in parallel)
3.Combined product

Sequential targeting



SCRI- CAR19x22v1



Pediatric Leukemia Adoptive Therapy Trials-05 (PLAT-05) for CD19+ CD22+ R/R B-ALL (Phase 1 trial)

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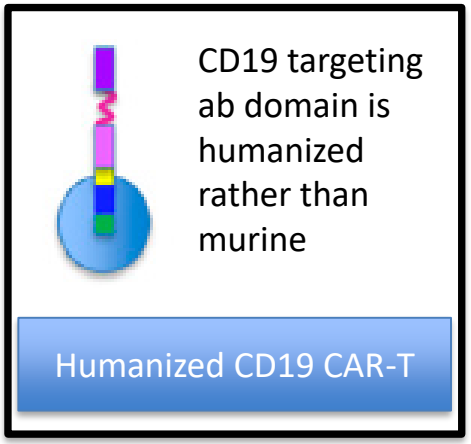
Expanding the portfolio of CAR-T therapy

1st study of humanized anti-CD19 CAR T cells at CHOP CTL119 induced
CR in 100% CAR T cell naïve patients
(12-mo RFS of 82%).
In the retreatment setting, 56% of patients with prior murine CD19 CAR T cells achieved CR.
Blood (2017) 130 (Supplement 1): 1319.

PLAT-06

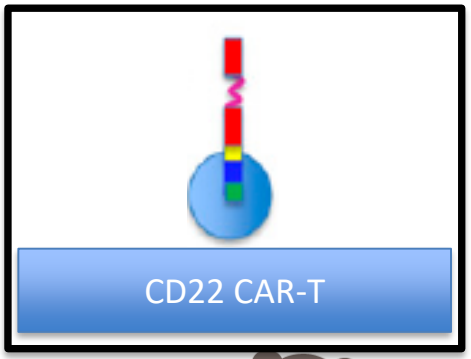


CD19+ Leukemia and Lymphoma
1-30 years

CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy

nature medicine
VOLUME 24 | NUMBER 1 | JANUARY 2018
National Institutes of Health (NIH), Bethesda, Maryland, USA.

PLAT-07



CD22+ Leukemia and Lymphoma
Up to 30 years

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Future of CAR-T therapy at CNH

Open CAR-T Cell Clinical Trials at CNH		
Trial/Sponsor	**Indication**	**Principal Investigator**
PLAT-05 (CureWorks)	Anti-CD19-22 CAR T cell for Rel/Ref B-ALL/Ly Age: 1-27 y	Anant Vatsayan
PLAT-06 (CureWorks)	Humanized Anti- CD19 CAR T for Rel/Ref B-ALL Age: 1-27 y	Anant Vatsayan
Cassiopeia (COG AALL1721)	HR MRD+ CD19+ B ALL at EOC	Anne Angiolillo (Under IRB review)
BIANCA (Novartis)	CD19+ Relapsed NHL Age: <18 years	Hema Dave (Under IRB review)
Bio-banking	Prospectively banking PB/BM and CSF samples	Hema Dave/Cath Bollard

PLAT 07 (CD22 CAR-T) coming in Fall 2020!

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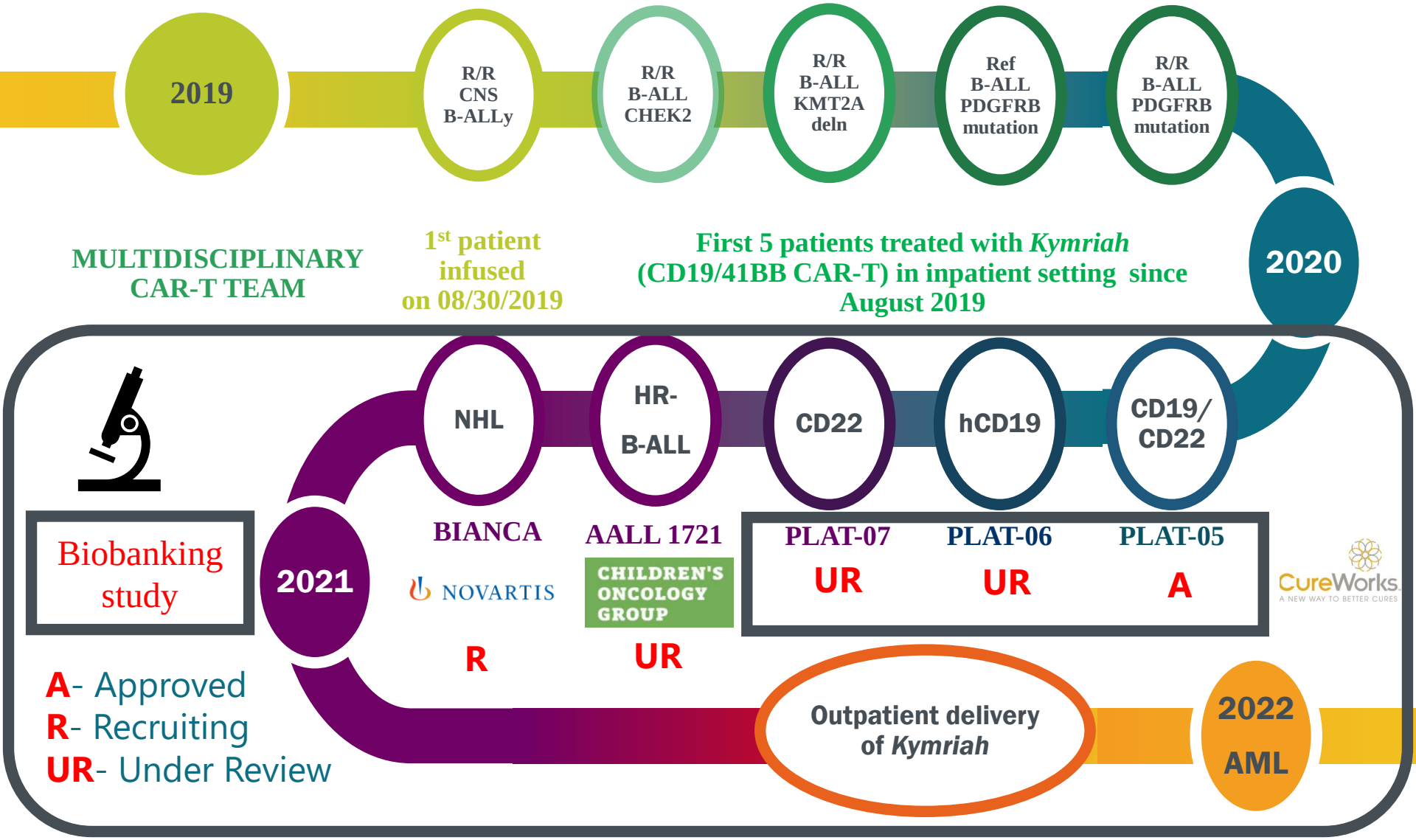
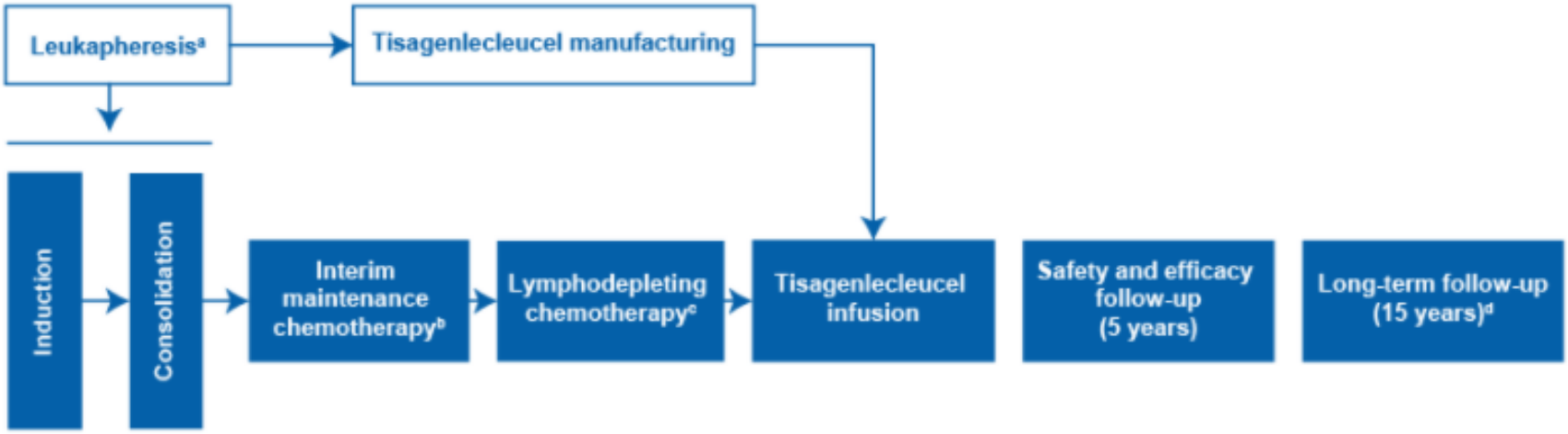
CAR-T milestones: CNH



Cassiopeia (AALL1721)

- A phase II single arm, open label, multicenter study to determine safety and efficacy of tisgenlecleucel as a first line therapy for high risk pediatric and young adults (1-25 years) with CD19+ B-ALL who are MRD (>0.01%) positive at end of consolidation

STUDY DESIGN



[a]Leukapheresis can be performed at end of induction or end of consolidation.
[b]Tisagenlecleucel can be given as soon as product is available and before completion of interim maintenance, if applicable.
[c]Lymphodepleting chemotherapy is to be completed 2 to 14 days prior to tisagenlecleucel infusion.
[d]Long-term safety follow-up as per health authority guidance conducted under a separate long-term follow-up protocol (NCT02445222).

Primary endpoint: 5 year DFS

https://www.clinicaltrials.gov/ct2/show/NCT03876769
https://www.virtualcongress.novartis.com/eha25/b-cell-malignancies/

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Unanswered questions

- **Early risk stratification** and **patient selection** (range of burden of disease, type of disease, EM/CNS disease, pre-HCT)
- **Optimal time of leukapheresis**
- **Upfront use** of CAR-T cells
- **Optimal bridging to CAR-T** therapy (CD19 or CD22 targeting immunotherapy prior to CAR-T and as an alternative)
- **Optimal lymphodepleting chemotherapy**
- **Deep remission** (utility of NGS-long-term disease surveillance)
- **Durability of remission** (type of CAR-T and its persistence; duration of B-cell aplasia, molecular MRD, and role of HCT)
- **Mechanisms of failure** of CAR-T cells
- **Mechanisms of toxicity** of CAR-T cells
- **Best strategy** which is **financially viable** in the long run

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Research database and guidelines development

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

CIDR
CELLULAR IMMUNOTHERAPY DATA RESOURCE

Pediatric Real World CAR Consortium
PRWCC

Other administrative databases looking at Quality and Cost Outcomes of different institutions for benchmarking against peers, reduce variations, expedite data collection

Building a CAR Garage: Preparing for the Delivery of Commercial CAR T Cell Products at Memorial Sloan Kettering Cancer Center

Karlo Perica [1], Kevin J. Curran [2,3], Renier J. Brentjens [1,3], Sergio A. Giralt [3,4,*]

[1] Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York
[2] Pediatric Bone Marrow Transplant Service, Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, New York

Guideline

ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells

Daniel W. Lee[1,#], Bianca D. Santomasso[2,#], Frederick L. Locke[3], Armin Ghobadi[4],

Chimeric antigen receptor T-cell therapy — assessment and management of toxicities

Sattva S. Neelapu[1], Sudhakar Tummala[2], Partow Kebriaei[5], William Wierda[6], Cristina Gutierrez[5], Frederick L. Locke[6], Krishna V. Komanduri[7], Yi Lin[8], Nitin Jain[4], Naval Daver[4], Jason Westin[1], Alison M. Gulbis[9], Monica E. Loghin[2], John F. de Groot[2], Sherry Adkins[1], Suzanne E. Davis[10], Katayoun Rezvani[5], Patrick Hwu[10], Elizabeth J. Shpall[5]

How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies

Joshua A. Hill[1-4] and Susan K. Seo[5,6]

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Summary

- Early referral of relapsed/refractory ALL patient for potential need for CAR-T therapy
- NGS should be sent at diagnosis of relapse/ refractory B-ALL
- Very high disease burden and late leukapheresis compromises the T cell yield (qualitative and quantitative) for CAR-T production
- Pre-CAR-T use of Blina or Inotuzumab may negatively impact the efficacy of CAR-T cells
- Bridging chemo should be less toxic with the goal of decreasing disease burden
- Early B-cell recovery is a surrogate marker for impending post-CAR-T relapse
- Post CAR-T consolidation with HCT is recommended if patient is a good candidate for HCT

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Pediatric Specialists of Virginia

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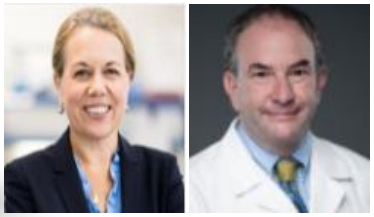
CureWorks
A NEW WAY TO BETTER CURES

Thank you to our patients!

Referring/ Collaborating physicians

BMT

Leukemia/Lymphoma



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