Inspired by research. Driven by compassion. Inspiré par la recherche. Guidé par la compassion.

CAR-T CELLS: NEW HOPE FOR CANCER PATIENTS

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PATIENT EDUCATION FORUM

NOV 10, 2017

CANCER CELLS EVADE THE IMMUNE SYSTEM

Attack or inhibit our normal immune cells

Shielded from immune cells trying to fight them

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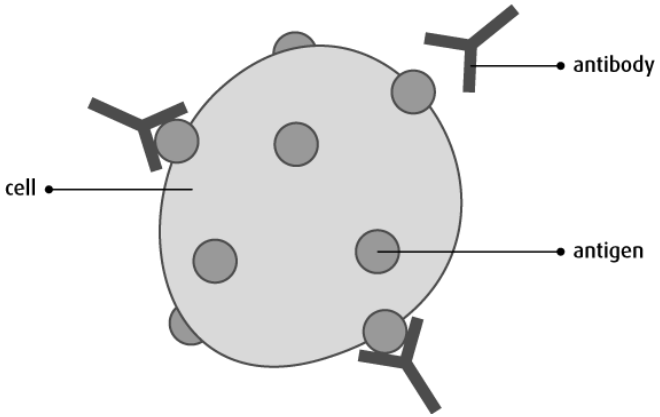
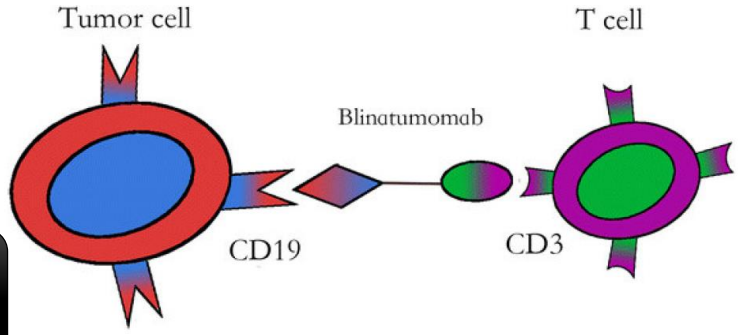
NEW CANCER THERAPIES ARE ARRIVING…

Antibodies

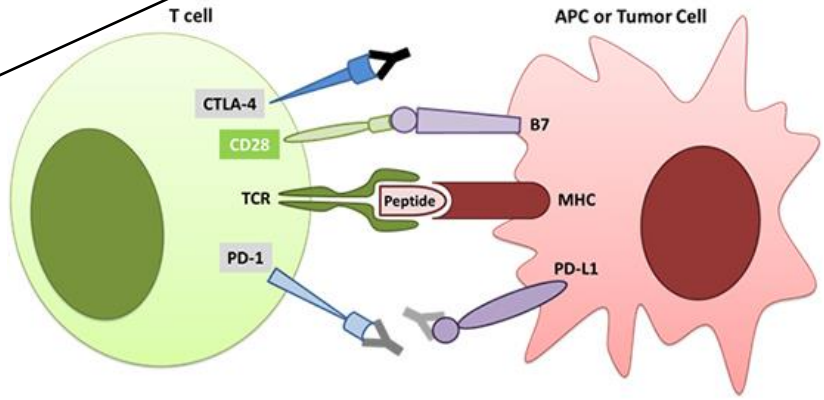


Bispecific T-cell engagers (BiTEs)



Immunotherapy

Checkpoint inhibitors



CAR-T cells

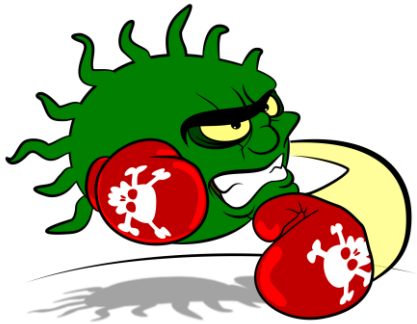
http://www.genscript.com/immune-checkpoint-inhibitors.html

Wu J, et al. J *Hematol Oncol.* 2015;8:104.

WHAT ARE T CELLS?

- Helper T cells (CD4 +) produce chemical messages called cytokines which boost immune responses by other immune cells such as B cells and macrophages

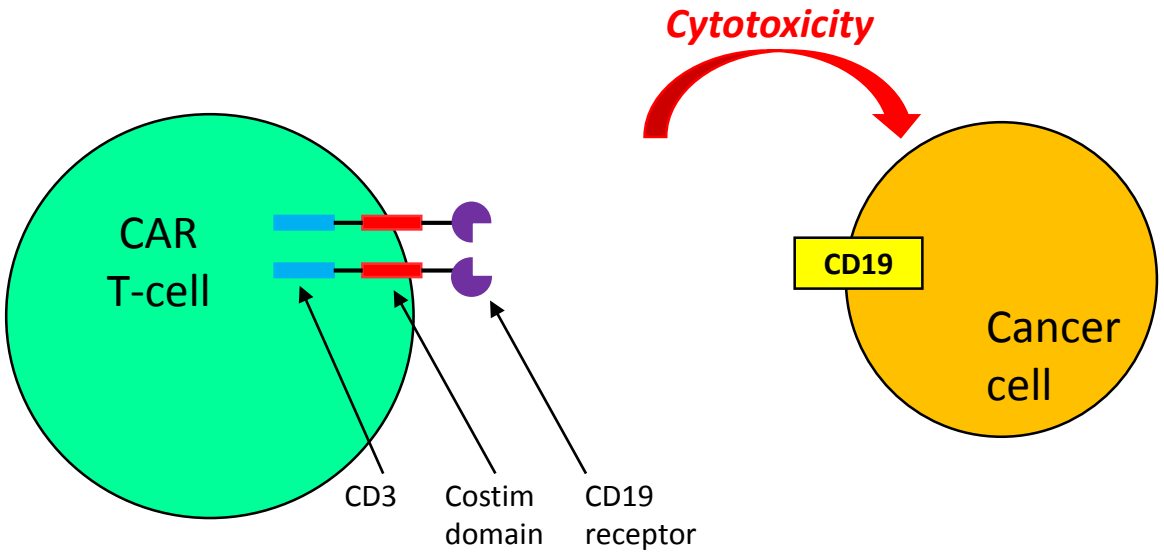
- Cytotoxic T cells (CD 8+) patrol the body checking our own cells for invaders such as viruses



http://commonconstitutionalist.com

WHAT ARE CAR-T CELLS?

- T-cells that are taken from a patient and genetically modified to target cancer cells
- This creates “super T-cells” which can target tumour specific antigens, then activate and kill the tumour cells
- CD19 is found on some leukemias and lymphomas

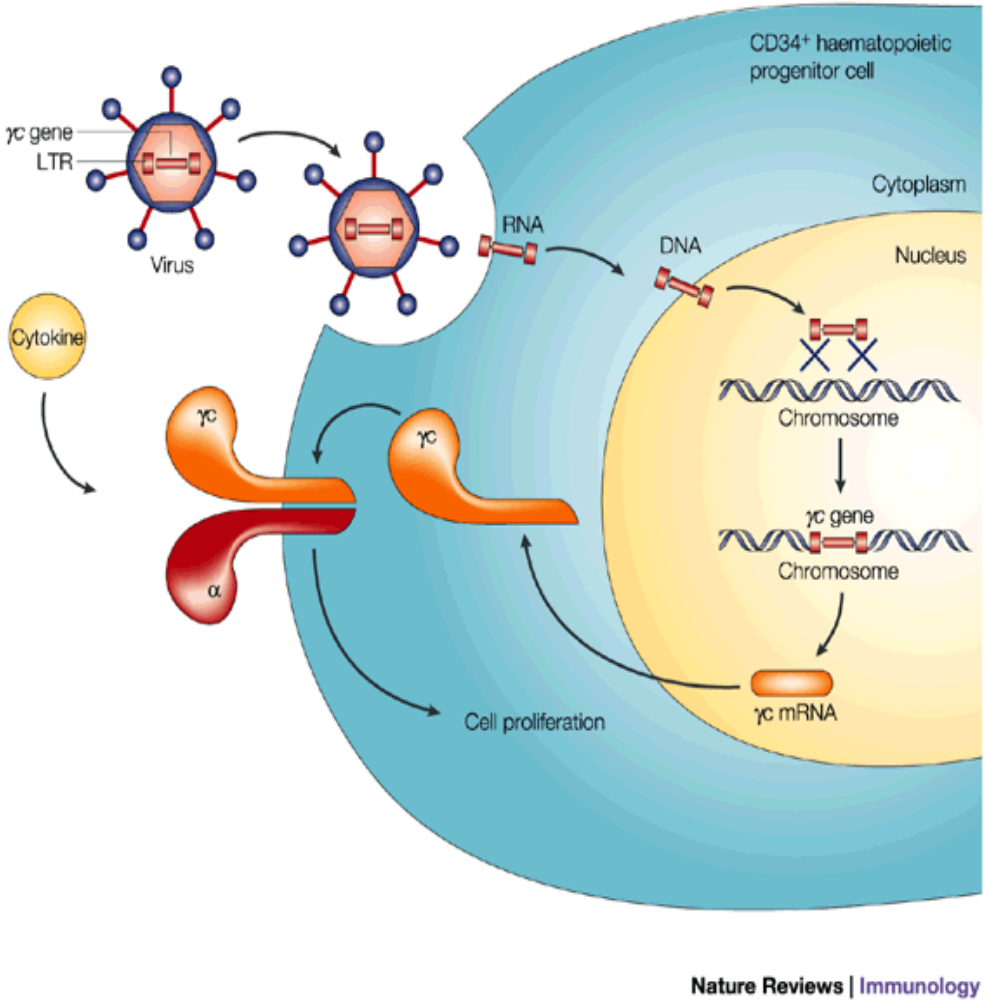


How CAR-T cells are made:

Step 1: Collect T cells from the patient

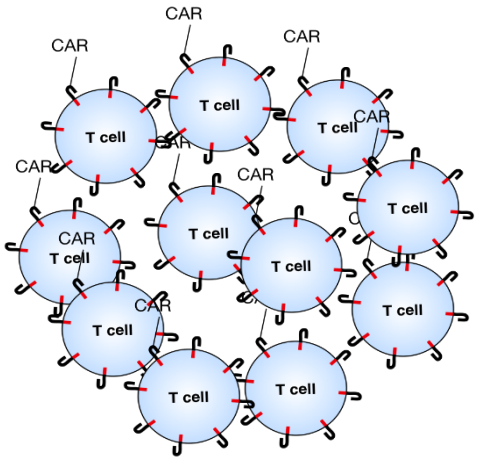
How CAR-T cells are made:

Step 2: CAR-T cell production and expansion



Anti-CD19 CAR

=



http://www.nature.com/nri/journal/v2/n8/fig_tab/nri859_F3.html

How CAR-T cells are made:

Emily's Story

- In May 2
  started a
- In Octob
- 2 weeks
  was canc
- Her fami
  weeks to
- In April 2 T cells
- Emily Wh Penn
- She had a difficult course…
- In May 2012, bone marrow showed she was in complete remission

Maude, SL et al. N Engl J Med 2014; 371:1507-1517

CLINICAL EVIDENCE FOR CAR-T CELLS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia

Shannon L. Maude, M.D., Ph.D., Noelle Frey, M.D., Pamela A. Shaw, Ph.D., Richard Aplenc, M.D., Ph.D., David M. Barrett, M.D., Ph.D., Nancy J. Bunin, M.D., Anne Chew, Ph.D., Vanessa E. Gonzalez, M.B.A., Zhaohui Zheng, M.S., Simon F. Lacey, Ph.D., Yolanda D. Mahnke, Ph.D., Jan J. Melenhorst, Ph.D., Susan R. Rheingold, M.D., Angela Shen, M.D., David T. Teachey, M.D., Bruce L. Levine, Ph.D., Carl H. June, M.D., David L. Porter, M.D., and Stephan A. Grupp, M.D., Ph.D.

N Engl J Med 2014; 371:1507-1517

TABLE 1

- Patients with relapsed or refractory CD19+ malignancies who were ineligible for allo SCT or who relapsed after a prior allo SCT were eligible
- Majority of patients enrolled were under age 22
- Majority of patients had detectable disease at time of enrollment

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Pediatric Cohort (N=25)	Adult Cohort (N=5)	Total (N=30)
Sex — no. (%)			
Female	11 (44)	1 (20)	12 (40)
Male	14 (56)	4 (80)	18 (60)
Age at infusion — yr			
Median	11	47	14
Range	5–22	26–60	5–60
Allogeneic transplantation — no. (%)	18 (72)	0	18 (60)
Primary refractory disease — no. (%)	0	3 (60)	3 (10)
Relapse — no. (%)			
1	3 (12)	2 (40)	5 (17)
≥2	22 (88)		22 (73)
Baseline burden of acute lymphoblastic leukemia — no. (%)			
Presence of detectable disease†	20 (80)	4 (80)	24 (80)
Morphologic remission‡		1 (20)	1 (3)
Absence of minimal residual disease	5 (20)		5 (17)

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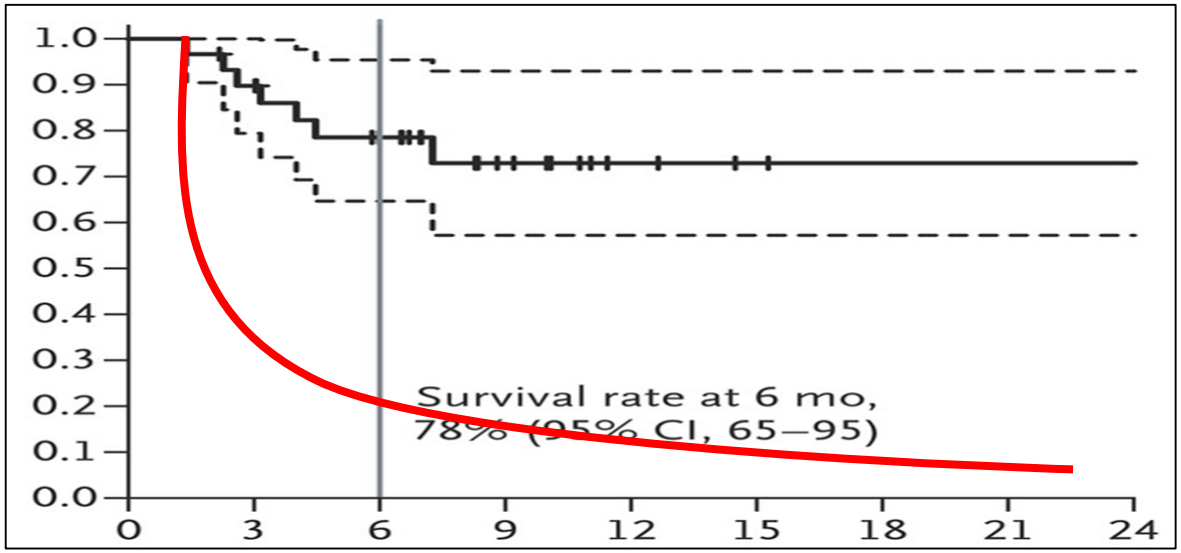
RESULTS - SAFETY

- 30 children and adults received CTL019

- 13 patients had neurologic toxic effects
  - ranged from delirium during the period of high temperatures to global encephalopathy with one or more of the following: aphasia, confusion, delirium, and hallucinations

- 22 patients had a severe flu-like illness called cytokine release syndrome, none of whom died from this

RESULTS - OUTCOMES



- Complete remission was achieved in 27 patients (90%)
- 6-month event-free survival rate was 67%
- 6-month overall survival rate was 78%

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FDA announces first US gene therapy approval for cancer treatment

By Michael Nedelman, CNN

Updated 1:07 PM ET, Wed August 30, 2017

Source: CNN

New cancer drug heading for US approval 03:47

Story highlights

Kymriah works by genetically modifying a patient's own cells so they can attack the cancer

(CNN) — The US Food and Drug Administration approved a new leukemia treatment, which the agency considers the first gene therapy it has cleared to hit the market in the United States.

More from CNN


'Be quiet! It's him!' Survivors say shooter walked pew by pew...


Former Phillies, Blue Jays Pitcher Roy Halladay Dies in Plane...

CAR-T CELLS IN CLL AND NON-HODGKIN'S LYMPHOMA

UPenn	Lentivirus	4-1BB	CLL (n =		Median OS: 29 months
			CLL (n = 35)	Investigator's choice	ORR: 19/40
			B-NHL (n = 24)	Investigator's choice	ORR: 15/22 PFS: 62% at 11.7 months

Abstract 56 from FHCRC:

18 pts (median age 60) with CLL

- 3 failed allo, all ref to FR–containing regimen
- 11 were ibrutinib-ref, 3 were ibrutinib-intolerant, and 4 were ref to venetoclax
- 11 pts had 17p deletion
- 5 had grade 2 CRS, 3 had grade 3, and 1 had grade 4 CRS
- ORR was 76% (8 PR and 5 CR)
- No pt in CR has relapsed or died with a median follow-up of 8.4 months

Late-breaking Abstract (ZUMA-1; NCI)

- FluCy conditioning
- Pts with DLBCL who received a prior anti-CD20 and an anthracycline-containing regimen.
- 111 pts from 22 institutions were enrolled and leukapheresed, and 101 pts received KTE-C19
- 93 patients had data available at time of presentation
- ORR of 76%, with 47% CRs and 29% PRs.
- 92% of responses occurred within the 1st mo, and 39% of pts had ongoing responses (CR in 33%) at 3 mos.
- Grade ≥3 CRS and neurologic events occurred in 20% and 29%

Geyer MB, Brentjens RJ. Review. Cytotherapy. 2016 Aug 31. PubMed PMID: 27592405.

CAR-T CELLS IN PATIENTS WHO FAIL IBRUTINIB

- Phase I/II study for the safety and feasibility of anti-CD19 CAR-T cell therapy in patients with CLL who had previously received ibrutinib

- 24 patients with CLL received chemotherapy and CAR-T cells at one of 3 dose levels (2×10^5, 2×10^6, or 2×10^7/kg)

- 19 patients had progressed on ibrutinib and 3 were ibrutinib intolerant
- 6 patients did not respond to venetoclax
- 23 had a complex karyotype and/or 17p deletion

- 4 weeks after CAR-T cell infusion:
  - Overall response rate was 71% (17 of 24 patients)
  - 21 patients (83%) developed cytokine release syndrome
  - 8 patients (33%) developed neurotoxicity, which was reversible in all but one patient with a fatal outcome

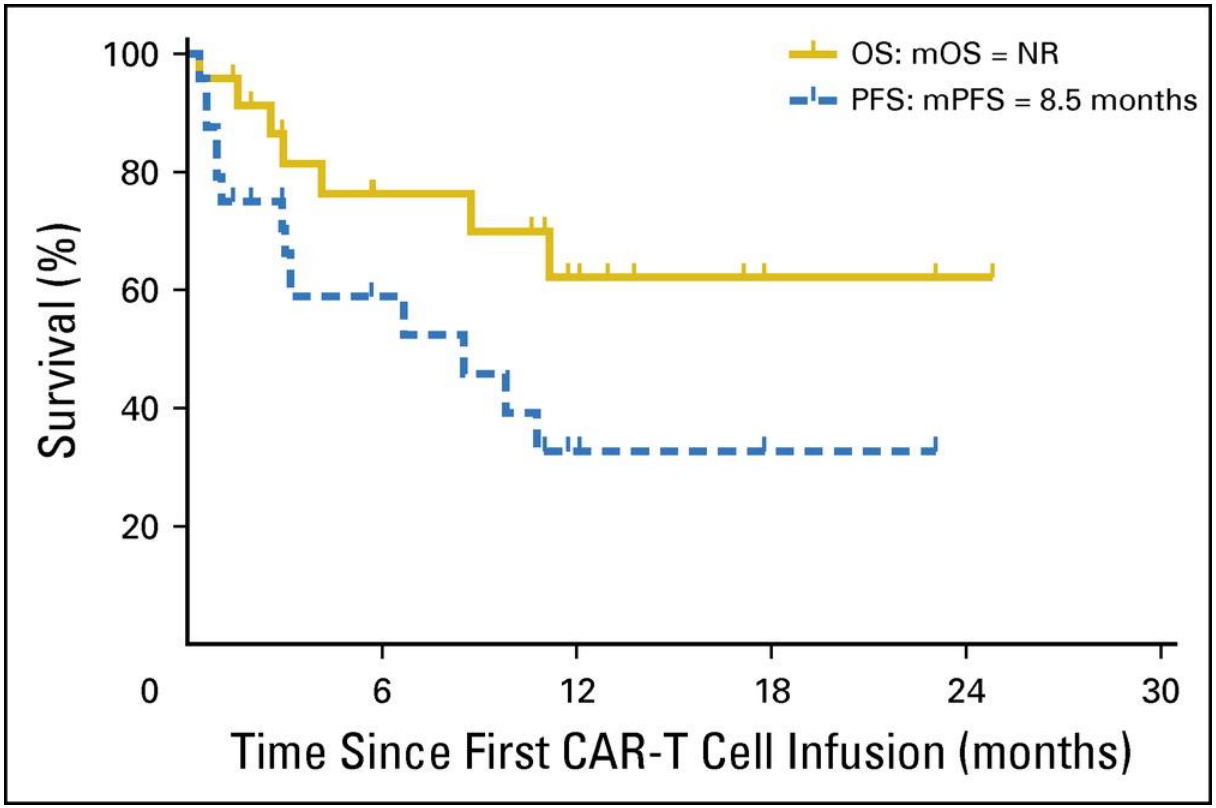


Fig A1. Progression-free survival (PFS) and overall survival (OS) for all patients with CLL.
CAR-T, chimeric antigen receptor-modified T; mOS, median OS; mPFS, median PFS; NR, not reached.

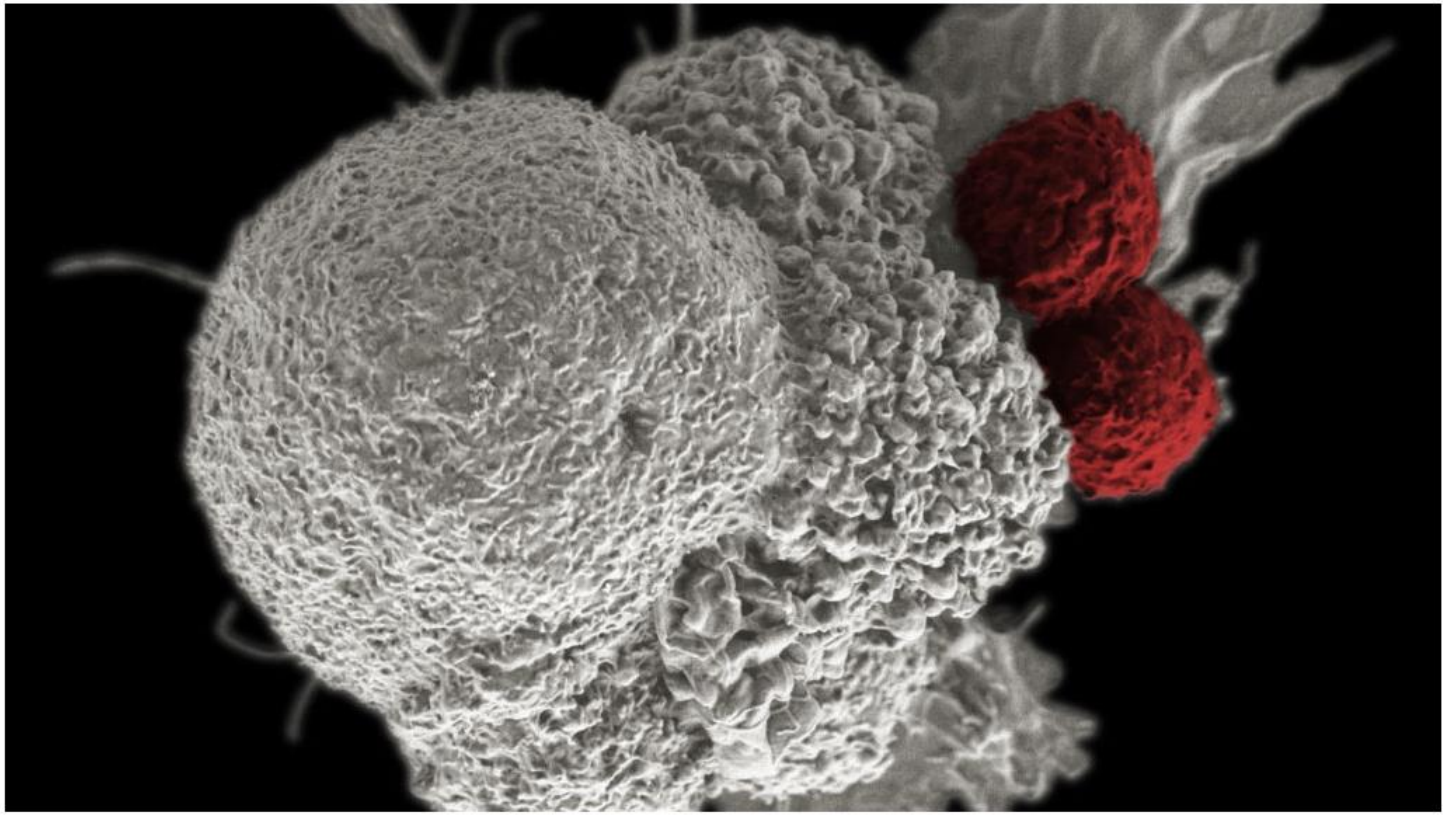
Published in: Cameron J. Turtle; Kevin A. Hay; Laïla-Aïcha Hanafi; Daniel Li; Sindhu Cherian; Xueyan Chen; Brent Wood; Arletta Lozanski; John C. Byrd; Shelly Heimfeld; Stanley R. Riddell; David G. Maloney; *JCO* **2017,** 35, 3010-3020.
DOI: 10.1200/JCO.2017.72.8519

BIOTECH

STAT+

FDA approves a game-changing treatment for blood cancer

By DAMIAN GARDE @damiangarde / OCTOBER 18, 2017



NIH

The Food and Drug Administration on Wednesday approved a promising new treatment for a particularly deadly form of cancer, bringing hope to desperate patients while rekindling a global

GAPS IN THE CURRENT DATA

Number of patients not meeting enrollment remains unclear

- Number of CD19 negative relapses and who will relapse?
- How many patients did not meet enrollment criteria?
- Number of patients tested for CAR-T who failed manufacturing?

Number of patients not able to receive CAR-T remains unclear

- How many progress or died before receiving CAR-T cells?
- Time from enrollment to manufacturing to administration?

Now with FDA approval, there are more unanswered questions

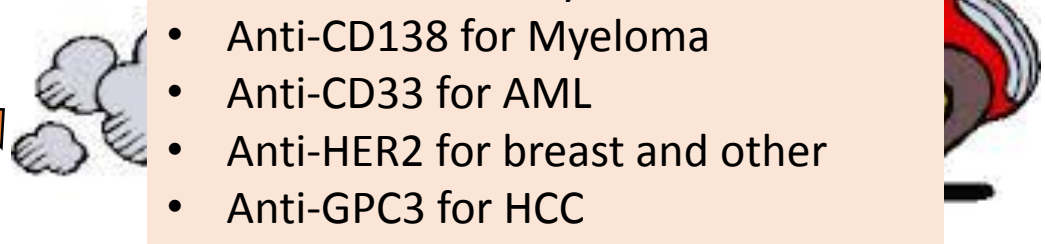
- Is there a priority setting in the wait list for CAR-T cells?
- What happens to the product if never infused?
- Are there any manufacturing concerns (ie. purity of T cells)?
- How do we predict and plan for CAR-T cell complications?

FUTURE OF CAR-T CELLS

Change the DRIVER:
- New vectors
- New viruses

Add BRAKES:
- Suicide gene inserts

Current CAR-T cell trials:
- Anti-CD22 for ALL and Lymphoma
- Anti-CD30 for Lymphoma
- Anti-BCMA for Myeloma
- Anti-CD138 for Myeloma
- Anti-CD33 for AML
- Anti-HER2 for breast and other
- Anti-GPC3 for HCC
- Anti-Eph2 for malignant glioma



Improve TOXICITY:
- Treatment of CRS/neurotox
- Predictors of CRS

Change the ROAD:
- New antigens
- New tumours

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CAN WE GET CAR-T CELLS IN CANADA?

- We are still waiting for the roll-out after FDA approval

- KiTE/Gilead **FDA approved** for large cell lymphomas who have failed at least 2 lines of treatment:
  - Diffuse large B-cell lymphoma (DLBCL)
  - Primary mediastinal large B-cell lymphoma (PMBCL)
  - High-grade B-cell lymphoma
  - DLBCL arising from follicular lymphoma

- Novartis **FDA approved** for patients up to age 25 with relapsed or refractory ALL

- Ontario is working to create a plan for patients to get CAR-T cells at Canadian centers or to go to the USA until we have the resources in place

Building the Capacity to make CAR-T cells in Canada

WHY BRING THIS TO CANADA?

- **Fast-paced growth of CAR-T cell therapies, but this technology is still missing in Canada**

- **Most patients in Canada cannot currently access CAR-T cell clinical trials**
  - Very few American trials have opened in Canada, with very limited spots
  - Cost is a minimum of **$500,000 USD** to get CAR-T cells

- **Steps to create a CAR-T cell platform in Canada:**
  1) Patients need access to clinical grade CAR-T cells for relapsed or refractory CD19+ B-cell malignancies

  2) Create a ***Canadian clinical and research platform*** to build on the current CAR-T landscape creating innovative basic science and clinical studies for Canadian patients

GOALS OF THESE INITIATIVES

1) *Our #1 priority is access to anti-CD19 CAR-T cell therapy for our patients in Canada*

2) *Hopefully create a precedent in how to build a national cellular immunotherapy program*

3) *Create a research platform for new and innovative approaches to CAR-T cell therapy*

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BioCanRx
Biotherapeutics for Cancer Treatment
Biothérapies pour le traitement du cancer

HOW CAN YOU GET INVOLVED?

- We want to learn from the patient perspective what we should and shouldn't do

- If you have had leukemia or lymphoma and would like to get involved, please contact:

Sarah Asad, Research Assistant

sasad@ohri.ca

613-737-8899 ext. 73813

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