The public sector role in funding CAR T technologies

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T-cells and receptors

- T-cells are types of immune cells (aka: “white blood cells” or lymphocytes)
- Receptor are molecules that bind to and receive chemical signals
Chimeric Antigen Receptor T-cell (CAR T) Therapy

(Lim and June, 2017)
CAR T manufacturing and Treatment

Hartmann et al, 2017

CRISPR
Cell manipulation core facility

(Wikipedia, 2017)

(Milteny, 2017)
Dr. Stephan A. Grupp presented "CD 19 CAR T Cells in Leukemia" at the 2017 BMT Tandem Meetings
Types of CAR T-cell Therapy

- 133 clinical trials targeting hematological malignancies:
  - 56 ongoing CD19
    - ALL- 2017, new: 5,970, deaths:1,440
    - CLL
    - NHL
- 78 solid tumors
  - Prostate cancer, Neuroblastoma, Glioma
- Difficulties:
  - Proper T-cell infusion of Solid tumors
  - Internal environment of tumor can be immunosuppressive
CAR T and Public sector funding

- NIH Reporter database --> “chimeric antigen receptor”:
  - The records go back to 1993.
  - 356 project
  - 72 different institutions
  - 100 PIs.
  - Total NIH funding was $204, 288, 340

- Clinical Trials
  - Only 20% of CAR T cell trials are sponsored by pharmaceutical industry (Hartmann et al. EMBO-MM, Aug 2017).
  - 91% of CAR T trials have an academic sponsor (DeWilde et al. International society for cellular therapy, March 2017).
Kite Pharma and NCI CAR T technology

- Kite Pharma Relies heavily on NCI CAR T research.
  - 3 CRADAs, 6 Exclusive license Agreements
  - 2012- NCI conducts research into various different types of TCR therapies, and Kite pays the NIH $3 million annually.
  - Jan 2016-clinical evaluations on KTE-C19, costing $2.5 million

- Dr. Steven A. Rosenberg a PI with a long career at NCI and pioneer in immunotherapy as a "Special Advisor" to Kite

- Kite reported spending $317 million in R&D from 2012 to June 30, 201

- Kite is selling the company for $11.9 billion Gilead
Novartis/ UPenn-Kymriah (tisagenlecleucel, CTL019)

2011- Dr. Carl June from UPenn has been working on T-cell for many years and in 2011 published an important paper using an anti-CD19 CAR T-cell therapy in CLL

2012- Novartis and UPenn deal
- $20 million towards a research center
- Novartis gets exclusive worldwide rights to all CARs developed through the collaboration and to CART 19, which is already in the clinic

- NIH- grants to Dr. Carl June:
  $30,335,306 of funding from the NIH for 39 projects relating to CAR T between 1993 and 2016.
  (Dr. June received $16,330,088, 1993 to 2011)

- August 2017, FDA approval the first CAR T-cell therapy
  - Pediatric and young adult (under 25) patients with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
  - $475,000 for one-time treatment (100% reimbursements if no response after 1 month)
CD19 CAR CTL019 in relapsed/refractory pediatric ALL: 93% complete response rate

Results presented at ASH 2015

- CR in 55 of 59 patients (93%) at 1 month; median follow-up of 12 months
- 6 patients went to subsequent transplant, 1 to DLI
- 12 month OS: 79% (95% CI: 69, 91)

- Relapse-free survival (RFS)
  - 6 month RFS: 76% (95% CI: 65, 89)
  - 12 month RFS: 55% (95% CI: 42, 73)

- No relapses past 1 year
- 18 patients in remission beyond 1 year, 13 without further therapy

- Humanized CTL119 – 22/22 CR in same population, early F/U
Thank you.
Adverse reaction

Cytokine release syndrome

Neurologic toxicities

B-cell aplasia
Current CART in clinical trial

- As of 2016,
  - 133 hematological
  - 78 solid tumors

Response is pretty good in ALL. The remission rates for ALL varies across clinical trials ranging from 11% to 50% (for 5 trials).
Tisagenlecleucel (CTL 019)

Fda approved

Phase 2 Eliana study

Kymria
What is a cart

Nomenclature- 1st gen, 2nd gen...

How it’s done (how to get it into the cells)

Risks- crs

General clinical trials (hema vs solid pro/ cons).

Shedding light on Novartis clinical data,

Future of CarT, how to decide?