ASBMT Perspective: CAR T & Engineered T Cell Therapies

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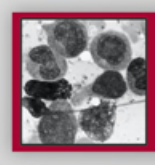
June 29, 2017
Boston



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Why the ASBMT?

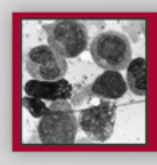
Membership with extensive cellular therapy experience:

- International professional society with over 2200 members (physicians, scientists, allied clinicians) dedicated to hematopoietic transplantation and cellular therapies.

Advancement of cellular therapies:

- Provided scientific leadership in cellular therapies for 25 years
- Co-Parent of FACT (with ISCT)
- Advocated for the reimbursement frameworks (e.g., coding)
- Partner of Registry (CIBMTR) and SCTOD
- Co-sponsor, with CIBMTR, of annual BMT Tandem Meetings
- Developed a questionnaire (ASBMT RFI) used by most payers to assess centers for network inclusion
- Partner to NMDP/Be The Match on patient access issues

And simply – this is a game changer for the field.



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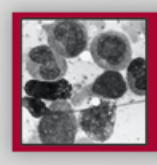
ASBMT Activities Thus Far

- **Heavily involved membership**
  - Cellular Therapy standing committee; Task Force
  - CAR T research, trials, administrative implementation
- **Assessing Value in Engineered T Cell Therapies** (May 25, 2017)
  - Forthcoming conference proceedings and manuscript (9/17)
- **Coding/reimbursement projects**
  - Interim guidance on coding
  - Assessment of needed new codes
  - Advocacy with CMS re: codes, NTAP status, DRG placement



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Future Activities

- Applications for new codes
- On-going education and advocacy
- Strategic planning re: how does CAR T fit within ASBMT?
- Potential joint session with ASCO
- Others as suggested by membership or payers

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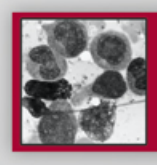
A (very) brief history of cellular therapy

- 1950s. Arnold Rich "Literally nothing of importance is known regarding the potentialities of [small lymphocytes]...one of the most humiliating and disgraceful gaps in all medical knowledge."
- 1957. E. Donnall Thomas starts transplanting bone marrow
- Early 1960s. J. F. Miller suggests thymus has immunologic function
- 1968: J.F. Miller, R.A. Good suggest that B and T cells are separate lineages of lymphocytes (also 1st successful allo-SCT for SCID)
- 1970s. Characterization of separate subsets of CD4+ and CD8+ T cells and mechanisms of antigen recognition.
- 1985. Donor derived CMV-specific T cell therapy for alloSCT (Riddell, NEJM)
- 1990. Clinical evidence that T cell depletion increases relapse rates after alloSCT.
- 1998. First evidence that human thymic function persists.
- 2011. First trials of CAR-T cells in advanced CD19+ malignancies (June, STM)
- 2017. BLAs filed by Kite and Novartis for CD19-specific CAR-T therapies.



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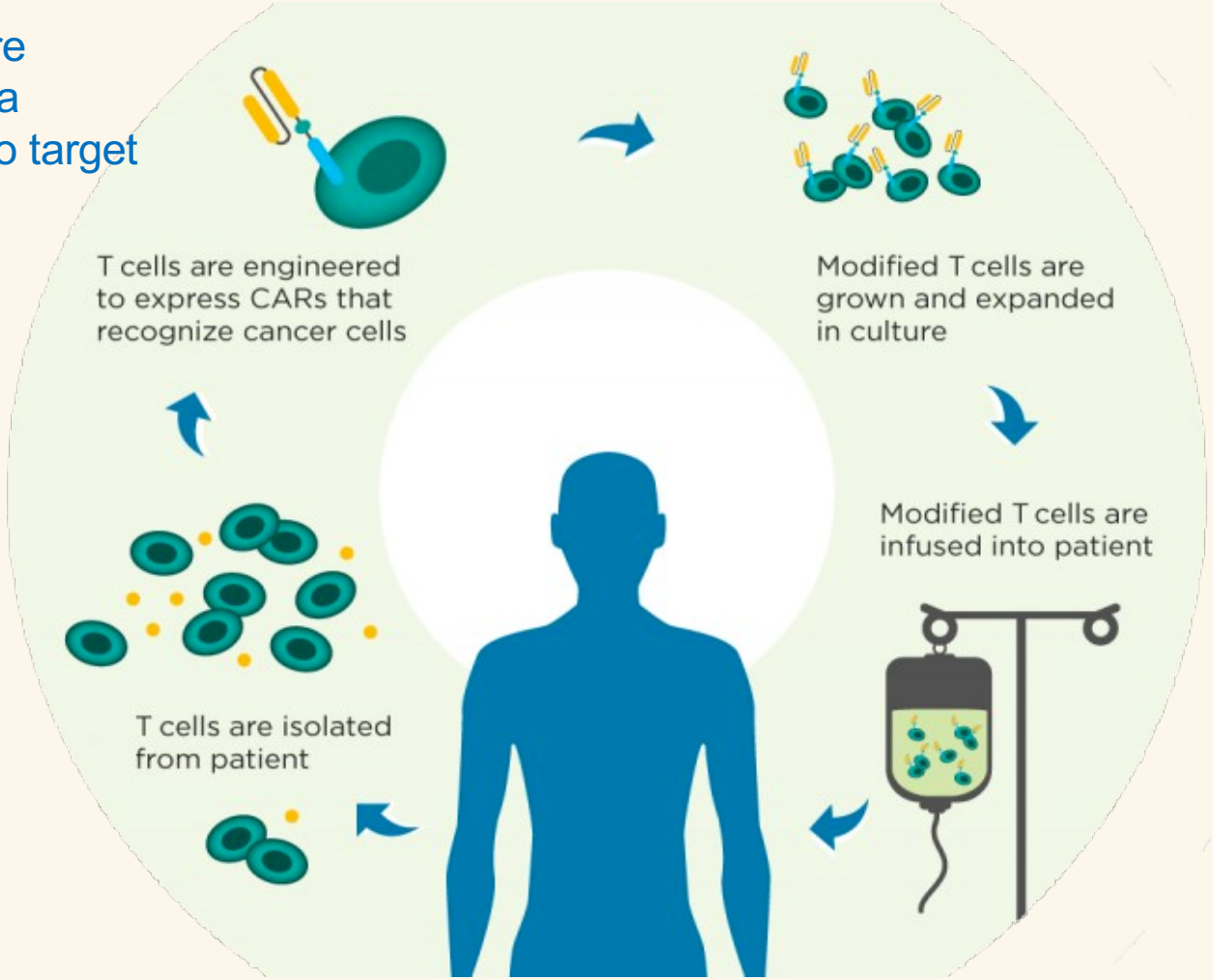
- An Immune System Trained to Recognize Cancer (NYT, Sep 2011)

- *Science* Breakthrough of the Year, 2013

- Setting the body's 'serial killers' loose on cancer (NYT, Aug 2016)

Product description – Autologous CAR T

Patient T-cells are transduced with a lentiviral vector to target CD19.



Disease Targets w/in HCT Realm

Current:	Soon-ish:	Horizon:
• Diffuse Large B-Cell Lymphoma (DLBCL) • Follicular Lymphoma • B-cell Acute Lymphoblastic Leukemia (B-ALL) • Primary Mediastinal B-cell Lymphoma (PMBCL)	• Multiple Myeloma • Non-Hodgkin Lymphoma • Mantle Cell Lymphoma	• Acute Myeloid Leukemia • Pediatric Neuroblastoma • Chronic Lymphocytic Leukemia

First FDA approvals expected Summer 2017

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Allogenic CAR T: Specific and/or Universal

Pursuing Companies

- Cellectis-Pfizer
- Kite
- Celyad
- Fate Therapeutics
- Cell Medica
- Regeneron

Early Win

MIT Technology Review

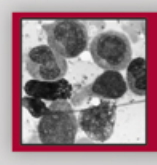
Topics+ Top S

Rewriting Life

Two Infants Treated with Universal Immune Cells Have Their Cancer Vanish

In a medical first, the children were treated with genetically engineered T-cells from another person.

by Antonio Regalado January 25, 2017



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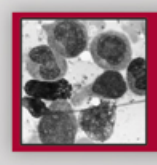
Home Brew: On-site CAR T

- Centers are beginning to manufacture their own, non-branded product on-site for selected patients
- TBD in terms of success and access beyond early trials
  - Payer authorization/reimbursement?
  - FDA approval needed?
  - Consistent manufacturing capabilities?
  - Cost – cheaper?



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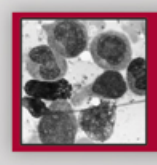
Ok, but what is it??

Differing Perspectives:

- Cellular Therapy – similar to HCT:
  - Very similar components – apheresis, cell manipulation, infusion, monitoring for post-infusion symptoms, specialized teams and beds
  - But, purposes differ – immune reconstitution (primary) vs. antineoplastic
- Biologic (aka Drug):
  - Early indications from FDA and CMS are that they are thinking of this as a 'personalized biologic' – similar to Dendreon
  - Pharmaceutical vs. medical benefit?
- Hybrid Vigor?
  - Specialized care episode with personalized product



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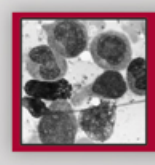
Access Concerns: Medicare & Medicaid

- CMS:
  - Primary payer for DBLCL
  - Will not be a separate MS-DRG for at least 2 years
  - Will not be coded/paid as an Auto HCT – likely general lymphoma stays ($10-35k)
  - Unclear whether will qualify for New Tech Add-on Payment
  - Potential for coverage limitations or CED?
- Medicaid
  - Significant payer for B-ALL
  - All state decisions – no uniform adoption
  - Frequently difficult to get clearance to travel out of state
  - Removal of Essential Health Benefits and/or implementation of per person caps will make CAR T very difficult for Peds patients to access



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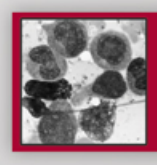
Access Concerns: Cost & Coding

- Cost predictions: $250k+ for just the product
  - Hospital stay = 5-7 days if uncomplicated
  - Complications = 15+ days, multiple rounds of Tocilizumab ($20k/per), ICU
  - The CAR T care episode will be bookended by other expensive care
- Variations in apheresis models – i.e. bill separately from rest of episode vs. include
  - Increase in cost/billing for leukapheresis?
- Currently, the patient travels to the future site of infusion for apheresis vs. use of a local site
  - Will incur additional travel and lodging costs for the additional visits
- CMS just approved new ICD-10-PCS code for CAR T; goes into effect October 1, 2017
  - No other good CPT or ICD-10 codes exist.
  - Will be 2020 before appropriate new CPT codes can be finalized



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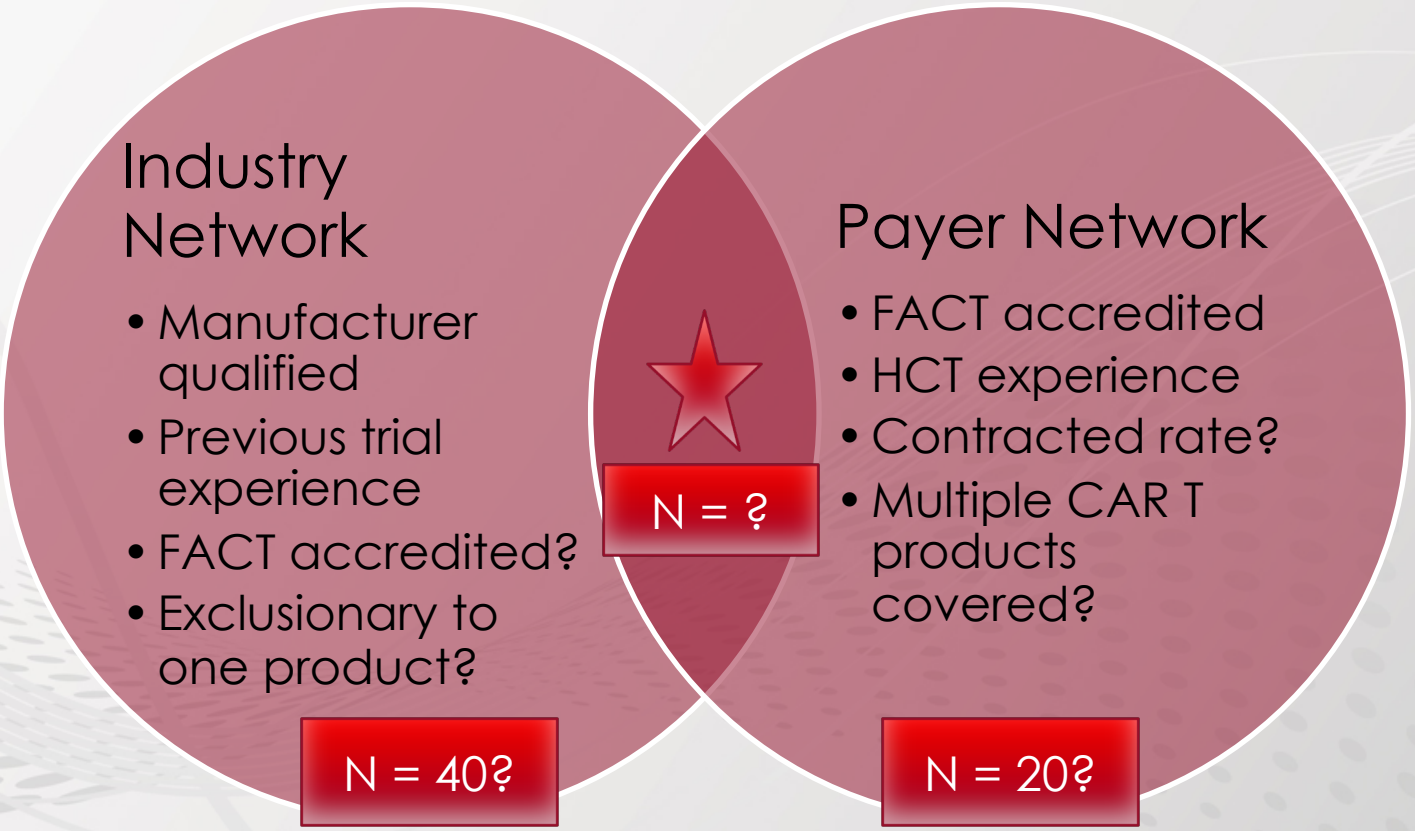
Access Concerns: Limited Facilities



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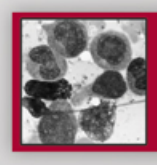
Data Dilemma: Outside of CIBMTR?

- Manufacturers are not currently required to report to CIBMTR
  - Some companies are in discussion to contract for that purpose
  - CIBMTR launched cell therapy reporting in 2016
- Extended analyses for purposes of long-term health outcomes, health services research, cost effectiveness or patient-reported outcomes will need a global data view, not short-term product-specific information
- Payers have the most leverage here – could require reporting

Beyond CAR T: Choose your own adventure?

HCT	CAR T	HCT + CAR T
• Cord blood expansion • Cord blood universal bridging • GVHD-focused "add-backs" and suicide switches • Universal donor • 'Any' donor products • Haplo donors	• Auto • Allo • Last line vs. first line? • New indications?	• Sequencing? • Certain patient subsets?

- **Innovation across all platforms at once will be difficult to decipher into best practices, guidelines and coverage policies.**
- **<u>Key concern: Tracking and integration of data</u>**



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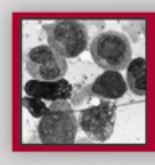
Summary

- CAR T is an extremely exciting technology that carries significant clinical risk and high cost
- Until complications like CRS and Neurotoxicities can be routinely predicted and managed, CAR T should take place in specialized facilities
- ASBMT feels that FACT Accreditation and reporting to CIBMTR will be very important for long-term learning and safety
- Payer-Provider learning partnerships would very beneficial to all as the use of the technology grows



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Questions/Discussion

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