Carter BloodCare

Hospital Forum Minutes
"*Eat Cake and Celebrate!*"
April 6, 2018

Attendees:

Guests: Ryan Phillips, Methodist Charlton Medical Center; Limiaa Khalifa, Parkland; Erin Portillo, Parkland; Krista Roberts, Texas Health Arlington Memorial Hospital; Liang Shen, Texas Health Harris Methodist Fort Worth; Catrina Donnelly, Texas Health Harris Methodist Fort Worth; Tanya Robohm, Texas Health Dallas; Adam Martin, Texas Health Dallas; Patti Calcote, UT Health Tyler; Laura Gilbert, Providence Health Center; Ashley Flores, Cook Children's Medical Center; Rick Melman, BSW All Saints Medical Center; Jennifer Packard, Children's Medical Center Dallas; Roberta Murfin, Children's Medical Center Dallas; Suzanne Moore, Medical City Dallas; Monica Phillips-Bryant, Goodall-Witcher Medical Center; Dionne Cook, Temple VA; Craig Winninger, Temple VA; Kathy Spigener, Methodist Mansfield Medical Center; Mike Newhouse, Medical City Dallas; Neeta Majmudar; JPS; Monica Hammonds, Dallas VA Medical Center; Marie Becerra, JPS; Jivca Jivoinovici, Texas Health Hospital Carrollton; Ashley Tank, BSW All Saints Medical Center; Parivash Abbasalizadah; Baylor University Medical Center; Julia Blackburn, Texas Health HEB; Kathleen Cage, Texas Health Alliance; Jessica Gandy, Texas Health Southwest; Michael Martin, BSW All Saints Medical Center; Gretchen Vinson, UT North Campus Tyler; Glenda Strain, Titus Regional Medical Center; Robin Mosley, UT Health Pittsburg; Kenni Monk; UT Health Quitman; Chanel Sokol, Christus Mother Frances – Sulphur Springs; Corrie Long, Providence Health Center

Carter BloodCare: Dr. Merlyn Sayers, Vince Zost, Fernando Lerma, Rose Ongaro, Judy Thornburg, Andrea Sign, Pam Boyd, Dr. Todd Nishimoto, Linda Goelzer, Nancy Perez, Lavetta Kennedy, Sandy Wortman, Carla Beck, Josey Keep, Marla Boren, B.J. Smith, Dr. Laurie Sutor, Dr. William Crews,

<u>What's All of the Fuss with CAR T Cells? Vince Zost, SBB, MT(ASCP), Stem Cell Laboratory Manager, Carter BloodCare</u>

- ✓ Presentation handouts attached, review for comprehensive information shared.

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- Attendee questions/comments
  - Based on the information shared, a small population of T-cells are harvested and then returned– correct?
    - Yes, about 300 x 10^6 CAR T-cells are infused
  - Is the cytokine release syndrome (possible side effect) dependent on the tumor burden?
    - Yes; therefore, the earlier you start treatment the better.
  - Is this considered a first line treatment?
    - This treatment is employed once all other treatments have been unsuccessful.
  - How long does the infusion of the CAR T-cells take?
    - Generally about 5-10 minutes because of the small amount infused
  - Is the infusion given in an outpatient setting?
    - Typically it is; patients go home the same day
  - If the first round of CAR T-cells is not successful, do you proceed to try again?
    - No

Lookbacks, Recalls and Market Withdrawals, Laurie Sutor, MD, MBA, Vice President of Medical and Technical Services, Carter BloodCare

- ✓ Presentation handouts attached, review for comprehensive information shared.
  - Attendee Questions/Comments
    - Have there been any reports that Accutane has caused teratogenic effects?
      - Not to my knowledge
    - Are components destroyed once they are returned to Carter BloodCare?
      - Once the investigation is complete, and it is determined that the component must destroyed, then it will be destroyed.
    - Can anyone from the group share how you handle the patient notification for lookbacks? Sometimes we struggle with getting cooperation from the patient's ordering/attending physician to become involved and notify.
      - Risk management gets involved
      - Risk management handles
      - 3 attempts are made with the attending; then escalated to the head of the service; and finally pathologist will notify the patient or next of kin

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Case Study 1; Fernando Lerma, SBB(ASCP), Reference and Transfusion Services, Carter BloodCare

- ✓ Presentation handouts provided.
  - Attendee Questions/Comments
    - How much bench time was involved to complete the work-up?
      - Approximately 24 hours; the long range amplification molecular genotype took a year to get results
    - How much patient sample was needed to complete the work-up?
      - 2 EDTA samples
    - Does this patient have siblings that could be typed and be possible directed donors?
      - Unsure

AABB Standards, 31st edition changes, Sandy Wortman, SBB, MT(ASCP), Director of Reference and Transfusion Laboratory Services, Carter BloodCare

- ✓ Presentation handouts provided.
  Plan to implement a process to meet the standard by June 4, 2018. This may require you, the client, to provide a sample collected at a separate phlebotomy (applies only to patient's with no history) if electronic positive patient identification or another validated process to reduce the risk of misidentification is not employed at your facility.
  - Attendee Questions/Comments
    - If a second sample is needed for the confirmatory blood type, will there be a charge?
      - No
    - Can you accept our previous history?
      - Not approved currently
    - Can you add a question on the requisition to determine if electronic PPID or another process was used to collect the sample?
      - Good suggestion and will evaluate
    - How is the group handling the Notes section of the CAP standard TRM.40670?

      TRM.40670 ABO Group and Rh(D) Type Verification Phase II - The recipient's ABO group and Rh(D) type has been verified by repeat testing of the same sample, a different sample, or agreement with a historical type in the laboratory's records.
      NOTE: Repeat testing of the same sample may be inadequate unless the sample has been drawn

using a mechanical barrier system or digital bedside patient identification system. For laboratories that employ computer crossmatching, serologic crossmatch techniques must be employed when ABO typing discrepancies are present (e.g. mixed field reactivity, missing serum reactivity, apparent change in blood type post hematopoietic stem cell transplant).
Evidence of Compliance: ✓ Written procedure defining method for verification of ABO AND ✓ Work records of test results and/or search of records verifying ABO type

- One client stated that their blood bank system indicates when one of those situations occurs that is described in the notes; therefore, alerting staff that an electronic crossmatch is not acceptable and/or needs further review prior to performing an electronic crossmatch.

Client Resources, Hospital Relations, Carter BloodCare

- ✓ Presentation handouts provided.
- Follow us on LinkedIn at **https://www.linkedin.com/company/specialtyservicesatcarterbloodcare/**
- Please RSVP as soon as possible for the BCA IRL Conference because we are limited to 15 attendees.

  - Carter BloodCare to implement extended apheresis platelet expiration up to 7 days. We are hopeful that this can help meet patient needs while decreasing component outdate.
    - There is no additional cost to you at this time.
    - New ISBT product codes to be shared
    - Tentative implementation date is mid-August 2018.

A most sincere thank you to the presenters – this program exists because of your generosity to share your knowledge and experiences with the group.

And of course, thank you to all the attendees!

AABB Standards 31st Edition

Sandy Wortman, SBB,MT(ASCP)

Director of Reference and Transfusion Laboratory Services

AABB Standards 31st Edition

- Effective April 1, 2018
- Standard 5.1.8A Transportation requirements for platelets
- Standard 5.15.1 Use of Low-titer Group O Whole Blood
- Standard 5.14.5 “Two-sample requirement” for ABO confirmation
- Standard 7.3 Classifying adverse events

5.1.8A Requirements for Storage, Transportation, and Expiration

Platelets: Transportation

Maximum time without agitation: 30 hours

Standard 5.15.1

Recipients shall receive ABO group-compatible Red Blood Cell components, ABO group-specific Whole Blood, or low-titer group O Whole Blood (for non-group-O recipients or for recipients whose ABO group is unknown).

Standards 5.15.4, 5.27.1, and 5.27.1.1 apply

Standard 7.3

The BB/TS shall use nationally recognized classifications for donor and patient adverse events.

The medical director shall participate in the development of protocols used by the staff to identify, evaluate, and report adverse events.

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5.14.5 Pre-transfusion Testing for Allogeneic Transfusion

There shall be two determinations of the recipient's ABO group as specified in Standard

5.14.1. The first determination shall be performed on a current sample, and the second determination by one of the following methods:

1) Testing a second current sample.

2) Comparison with previous records.

3) Retesting the same sample if patient identification was verified using an electronic identification system or another process validated to reduce the risk of misidentification.

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Questionnaire Summary

63 facilities responded

1. **Does your facility employ an electronic patient identification system?**
   - 31 facilities (49%) employ an electronic patient identification system.
   - 32 facilities (51%) do not employ an electronic patient identification system.

2. **a. Does your facility have a process for patient identification which has been validated to reduce the risk of misidentification?**
   - 50 of the 63 facilities (95%) have a process to reduce the risk of misidentification.

   b. If so, would your facility be able to show documented proof this process has been validated?
   - 28 of the 50 (56%) facilities indicated YES

3. **If the answers to the first two questions are No, is it possible to validate your PID process in the next two months?**
   Of the 22 facilities that did not indicate YES to showing validation proof,
   - 5 facilities stated Yes.
   - 5 facilities stated No.
   - All other respondents indicated N/A.

4. **Does your facility have access to another patient sample drawn at a separate phlebotomy to send with the blood bank sample?**
   - 36 facilities (57%) indicated Yes.
   - 20 facilities (31%) stated Sometimes.
   - 7 facilities (11%) indicated No.

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Case Study 1

Presented by: Fernando Lerma, SBB(ASCP)

Reference and Transfusion Services

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Patient History

- **46 year old African American Male**
- **Diagnosis: Hypertension/ Hyperkalemia**
- **Submitted sample to the hospital transfusion service for type, screen and crossmatching of 2 RBC units.**
  - Patient has not been transfused in the last three months.
- **Sample was sent to the IRL by the hospital for antibody identification studies**

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Patient History - IRL

- **No previous record on file**
- **Hospital initial testing reported to IRL:**
  - B Positive
  - Antibody screen: 3+ reactive with all three antibody detection screening cells
- **Carter BloodCare IRL initial testing:**
  - DAT: Negative using a tube technique (Polyspecific)
  - Antibody screen: Panaggulination with all three antibody detection screening cells

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IRL - Initial Antibody Detection Testing

D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Gel IAT
+	+	0	0	+	0	+	0	+	+	+	+	+	0	0	+	**3+**
+	0	+	+	0	+	0	+	0	0	0	+	0	+	+	+	**3+**
0	0	0	+	+	0	+	0	+	+	0	+	+	0	+	0	**3+**

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IRL Initial Antibody ID – Gel Panel

	D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Gel IAT
1	+	+	0	0	+	0	+	0	+	+	0	+	0	+	0	+	**3+**
2	+	+	0	0	+	0	+	+	+	+	+	+	+	0	+	+	**3+**
3	+	0	+	+	0	+	0	+	+	+	0	+	0	+	0	+	**3+**
4	+	0	0	+	+	+	+	+	0	0	0	+	0	0	+	0	**3+**
5	0	+	0	+	+	+	+	+	+	0	0	+	0	+	0	+	**3+**
6	0	0	+	+	+	+	+	+	+	+	0	+	+	0	0	+	**3+**
7	0	0	0	+	+	+	+	0	+	+	+	+	0	+	+	0	**3+**
8	0	0	0	+	+	0	+	0	+	+	0	+	0	+	0	+	**3+**
9	0	0	0	+	+	+	0	+	0	+	0	+	+	+	+	0	**3+**
10	0	0	0	+	+	+	0	+	+	+	0	+	+	0	+	0	**3+**
AC																	**0**

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What type of antibody do you suspect?

a) Warm Autoantibody (WAIHA)

b) Cold Autoantibodies

c) High prevalence antibody

d) Need more information

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What would you do next?

a) Antibody titer

b) Call for more patient information & send out for molecular testing

c) Phenotype & Enzyme Treatments

d) Run more panel cells

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IRL Antibody Identification Studies

- Panagglutination is observed, in order to facilitate the antibody identification as fast as possible, the following is recommended:
  - Full phenotype of patients cells for common antigens
  - Cell treatments (i.e. Ficin, 0.2M DTT, Trypsin)
  - Extended phenotype of patients cells, as deemed necessary (i.e. high prevalence antigens)
- When

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IRL Patient Serological Phenotype

C	E	c	e	Interp
0/0	0/0	4+	NT	R_0R_0

M	N	S	s	K	Fy^a	Fy^b	Jk^a	Jk^b	P_1	6% Alb
3+	0	0	4+	0	0√	0√	3+	0	3+	0√

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IRL ENZYME SELECTED CELL PANEL

	D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Gel IAT	Ficin Gel IAT
1	+	+	0	0	+	0	+	0	+	+	0	+	0	+	0	+	3+	0
2	+	+	0	0	+	0	+	+	+	+	+	+	0	+	+	+	3+	0
3	+	0	+	+	0	+	0	+	+	+	0	+	0	+	0	+	3+	0
4*	+	0	0	+	+	+	+	0	+	0	0	+	0	0	+	0	3+	0
5	0	+	0	+	+	+	+	+	+	0	0	+	0	+	0	+	3+	0
6	0	0	+	+	+	+	+	+	+	+	0	+	+	0	0	+	3+	0
7	0	0	0	+	+	+	+	0	+	+	+	+	0	+	+	0	3+	0
8	0	0	0	+	+	0	+	0	+	+	0	+	0	+	0	+	3+	0
9	0	0	0	+	+	+	0	+	0	+	0	+	+	+	+	0	3+	0
10	0	0	0	+	+	+	0	+	+	+	0	+	+	0	+	0	3+	0
AC	+	0	+	+	+	+	+	0	+	+	0	+	0	0	+	+	0	0

*Phenotypically Similar Cell

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IRL ENZYME SELECTED CELL PANEL

	D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b	0.2 M DTT (Gel)
1	+	+	0	0	+	0	+	0	+	+	+	+	0	+	0	+	2+
2	+	0	+	+	0	+	0	+	0	+	0	+	0	+	+	0	2+
3	0	0	0	+	+	0	+	0	+	+	0	+	+	0	0	+	2+
4	+	0	0	+	+	0	+	0	0	+	0	+	0	0	+	0	2+

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What high prevalence AB do you test for?

a) Knops System (i.e. Kn, McC, Sl^a, Yk^a)

b) Chido/Rogers System (i.e. Ch, Rg), and/or Gerbich (Ge:2, Ge:4), and/or En^aFS

c) Duffy System (i.e. Fy3, Fy5)

d) Dombrock System (i.e. Do, Hy, Jo^a)

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IRL ABID Studies: Cell Treatments

- **Conclusion of Cell Treatments:**
  - Antibody is Ficin sensitive
  - Antibody is 0.2M DTT resistant
- **Blood group systems that follow this pattern:**
  - Chido / Rogers
  - Gerbich
  - Cartwright (variable in Ficin)
  - En^{a}FS

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IRL Extended Phenotyping

Rare Cells Tested

Ch	Rg	Yt(a)	Ge:2	En^{a}FS
2+	2+	2+	2+	2+

Hummmmmm?????

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How should you proceed when enzyme treatments and antigen typing do not yield clues to assign specificity?

a) Run more panel cells

b) Reflex the sample for molecular testing

c) Result out as an unidentified antibody to high prevalence antigen

d) Go on coffee break and pray the next shift comes in soon so you can pass it off

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IRL Antibody Identification Studies

- Running additional panel cells and a molecular genotype should aid in the process of identification (sample was reflexed for molecular testing)
- On occasions, some antibodies will not follow text book examples and therefore we must look outside the box
- Panel cells negative for antigens that are more common in people of African decent were selected as a means of narrowing down on a blood group system

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Additional panel cells

	D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b		Gel IAT
1	+	+	0	0	+	0	+	0	+	+	0	+	0	+	0	+	Cr(a-)	3+
2	+	0	0	+	+	0	+	+	+	+	+	+	0	0	+	+	Hy-	3+
3	+	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	U-	**0**
4	+	0	0	0	0	+	+	0	+	0	0	+	0	0	+	0	-D-	3+
5	+	+	0	+	+	+	+	+	+	0	0	+	0	+	0	+	At(a-)	3+

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IRL ABID Studies: Additional Testing

- **Additional U negative, U variants and hybrids were run to verify specificity**

	D	C	E	c	e	M	N	S	s	P_1	K	k	Fy^a	Fy^b	Jk^a	Jk^b		Gel IAT
1	+	+	0	+	+	0	+	0	0	+	+	+	+	0	0	+	U-	0
2	+	0	0	+	0	+	0	0	0	0	0	+	0	+	+	+	U-	0
3	0	0	0	+	+	0	+	0	+	+	0	+	+	0	+	0	Dantu + U-	0
4	+	0	0	+	+	+	+	0	0	0	0	+	0	0	0	+	U variant	0
Pt	+	0	0	+	+	+	0	**0**	+	+	0		0	0	+	0		

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What is the most likely explanation for this discordant antigen plus its corresponding antibody?

a) Patient is demonstrating an Auto-anti-U antibody

b) Patient has an altered allele in the GYPB gene with an anti-U "like" antibody

c) Patient was mistyped for the little s antigen

d) Patient has a GATA box mutation that is affecting the little s antigen

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Troubleshooting

- We know this is not an auto-anti-U since the patient autocontrol is negative
- Repeat testing using multiple sources of anti-s and unlicensed anti-U were used to troubleshoot the anomaly
- Patient cells were also tested against a single source of anti-Dantu to rule in the presence of an altered allele

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Troubleshooting

s	s	U	U	U	Dantu
Imm	ALBA	N-9	T-3	U13	V14
4+	3+	2+	4+	2+	0

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R&T Molecular Testing Lab Report

- **Molecular genotyping report supported the serologic phenotype results:**

RHCE*ce								
C	E	c	e	CW	V	hr^S	VS	hr^B
0	0	+	+	0	0	+	0	+

KEL*k_KPB_JSB					
K	k	Kp^a	Kp^b	Js^a	Js^b
0	+	0	+	0	+

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R&T Molecular Testing Lab Report

- **Also revealed a GATA box mutation:**

JK*A	
Jk^a	Jk^b
+	0

FY*B_ GATA	
Fy^a	**Fy^b**
0	**0**

DI*B	
Di^a	Di^b
0	+

CO*A	
Co^a	Co^b
+	0

GYPA*M, GYPB*s					
M	N	S	s	U	Mi^a
+	0	0	+	+	0

DO*A, DO*A_JO			
Do^a	Do^b	Hy	Jo^a
+	0	+	+

YT*A	
Yt^a	Yt^b
+	0

LU*B	
Lu^a	Lu^b
0	+

IRL's Transfusion Recommendations

- **Transfusion recommendations:**
  - Avoid transfusion, if possible
  - Leukocyte reduced red blood cells that are S-s-U- or U variant

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IRL's Transfusion recommendations

- At this point we know we have an anti-U "like" antibody, however the serology and molecular are incongruent with the antibody the patient developed
- In an attempt to determine an explanation for the anti-U "like" specificity in the presence of a normal little s antigen, the sample was sent out for DNA sequencing of GYPB

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Genotype for Glycophorin B

- Long range amplification of GYPB exon 2 to 6
- Exons1,2, pseudo exon 3 and 6: No changes from conventional
- Exon 4: 143C/C (48Thr); GYPB*s/s
- Exon 5: 251C/C (84Thr); known variable polymorphism; not previously reported to alter antigen expression

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Interpretations / Conclusions

The GYPBc.251G>C (Ser84Thr) change has not previously been reported to alter the protein; however based on the anti-U "like" antibody in the patients plasma it is possible this change encodes an altered or partial s antigen with both anti-S and anti-s antibodies in the plasma

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IRL's Final Conclusions

- **Additional plasma studies confirm the presence Anti-S and anti-s, hence the sensitivity to Ficin**

- **Moral of the story:**
  - Both serology and molecular testing are tools that aid in the process of identification
  - Think outside the box!
  - Antibodies don't read the books

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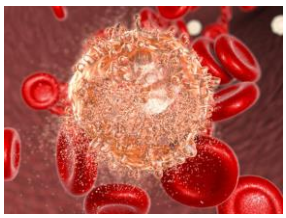
QUESTIONS???

What's All of the Fuss with CAR T Cells?



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Is It the Therapy of the Future?

Most common diseases treated by BMT include:

- **Leukemia**
- **Anemia like severe aplastic anemia and Fanconi's**
- **Lymphoma**
- **Multiple Myeloma**
- **Inherited immune deficiencies like SCID and WAS**
- **Some solid tumor cancers like NBL and testicular cancer**
- **Hemoglobinopathies**
- **Inherited metabolic disorders like Hurler's**

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Other Stem Cells for Usages

Some other types of stem cells (SC) or treatments being studied:

- **Limbal SC for corneal regeneration**
- **Mesenchymal SC for bone or cartilage regeneration**
- **Pancreatic SC for diabetes**
- **Glial SC for spinal cord injuries**
- **Human embryonic SC for Parkinson's**

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Failure of the Immune System

- T cells fail to recognize the leukemic or lymphoma cells.
- Allografts in the BMT setting use someone else's T cells to fight the cancer. GVHD becomes a major issue though.
- Now, the thought is to use the patient's own T cells and teach them to be better defenders. It's their own cells so no GVHD.

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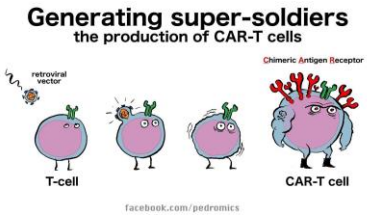
The Latest and Greatest (So Far)

- The latest autologous cellular therapy in the news is CAR (chimeric antigen receptor) T cell therapy.



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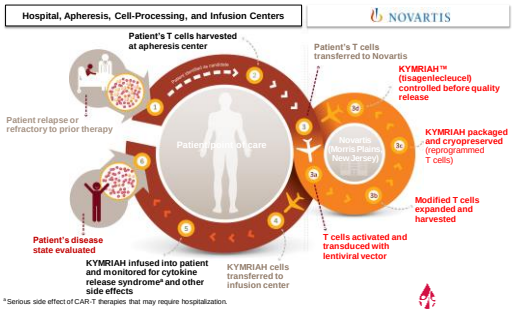
The Novartis CAR-T Therapy Process



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Seeing Quick Approvals From the FDA

Regulations and acts changes in the past decades have sped the process along:
- ✓ 1992 Accelerated Approval regulations
- ✓ 2012 FDA Safety Innovations Act (FDASIA)
- ✓ 2016 21st Century Cures Act

These led to processes like Fast Track, Breakthrough Therapies, Accelerated Approvals, and Priority Review.

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The Promise Being Seen with CAR T

Effectiveness of the CAR T cell therapies has been outstanding.

Novartis' ELIANA Global Phase 2 Trial showed 83% of patients who received their product achieved remission with 75% of the responders still in remission at 6 months.

KITE's ZUMA-1 Trial showed 71% of patients treated responded to therapy including 51% who had no detectable cancer remaining.

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New FDA Approved Cell Therapies

2 recently FDA approved therapies – Novartis' Kymriah™ for B cell ALL on 8/30/2017 and KITE's Yescarta™ for Large B cell Lymphoma on 10/18/2017. Both target the cell marker CD19 on B cell populations.

NOW APPROVED
YESCARTA™
(axicabtagene ciloleucel)

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The Difficulties Involved in CAR T Cell Production

- **With the cells being autologous, they can come from extremely sick patients like the ones for B cell ALL.**
- **They are relapsed and not getting back into remission.**
- **Scheduling for these patients is on short notice and move day to day. The patient has to meet minimum counts for ALC and CD3.**
- **It requires good teamwork and communication between the clinical staff, the apheresis staff, the cell processing staff and the manufacturer.**
- **The turnarounds are very time sensitive and somewhat time consuming with the paperwork and data entry involved.**
- **The process is minimized by following cGMP.**
- **It still takes approximately a month to get the cells back to the patient and they may not have that much time.**

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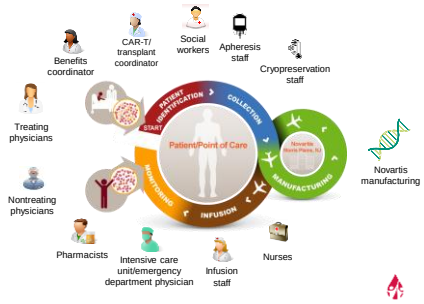
KYMRIAH™ Therapy Involves Many Roles



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The Bad That Comes With The Good

- **These outstanding results do not come without risks that the patient and families are made very aware of.**
- **As the CAR T cells fight the cancer cells and destroy them, it could lead to Cytokine Release Syndrome (CRS) and neurological toxicities. The infusion is only performed at centers where the manufacturers are satisfied that the medial staff can manage these side effects of the treatment.**
- **Symptoms include not are not limited to:**

Fever, hypotension, tachycardia, hypoxia, chills cardiac arrhythmias, cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS)

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Substantial Costs Involved

- Besides the time required to produce the CAR T cells, another potential roadblock to the patient receiving treatment is the massive cost for the FDA approved products.
- Kymriah™ is $475,000
- Yescarta™ is $373,000

Carter BloodCare

Evolution of CAR T Cell Production

- The next step in CAR T development is the use of an additional co-stimulatory motif with the CAR's to assist in better targeting of the cancer cells plus to assist destruction of the cancer cells when they start to become resistant and hide from the therapy by losing the antigen to which the CAR is targeted or up-regulation of inhibitory ligands.
- Another step would be an allogeneic off the shelf cell therapy. The cells would need to be made blind to HLA to prevent GVHD. There is a study that looks to create an off the shelf product using cord blood NK cells to make CAR NKs.

Carter BloodCare

Hospital Forum Luncheon

Agenda

Topics:

Cell Therapy, What is CAR-T?, Vince Zost, SBB, MT(ASCP), Stem Cell Laboratory Manager, Carter BloodCare

Lookbacks, Recalls, Quarantines, and Market Withdrawals, Laurie J Sutor, MD, MBA, Vice President of Medical and Technical Services, Carter BloodCare

Case Study, Fernando Lerma, SBB(ASCP), Reference and Transfusion Services, Carter BloodCare

AABB Standards, 31st Edition Changes, Sandy Wortman, SBB, MT(ASCP), Director of Reference and Transfusion Laboratory Services, Carter BloodCare

Client Resources, Hospital Relations, Carter BloodCare

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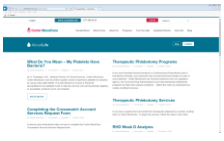
Client Resources

- Local customer care representatives/consultation services
- Videos and Blog – How to and FAQ
- Mock inspections for transfusion service accreditation readiness
- Medical Director led in-services
- Best practices questionnaires
- Known samples for competency and validation
- iWeBB Historical Antigen results
- Pipette Calibration
- Thermometer Standardization & Digital Timer QC services
- Educational Opportunities – Blood Bank Refresher, Hospital Forums, Molecular Symposium, and SBB observations

Videos and Blog

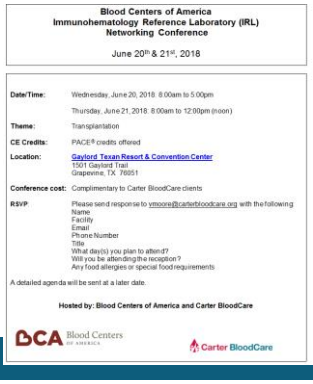
YouTube

BLOG



LinkedIn

Education Opportunities



Blood Centers of America
Immunohematology Reference Laboratory (IRL)
Networking Conference

June 20th & 21st, 2018

Date/Time: Wednesday, June 20, 2018 8:00am to 5:00pm
Thursday, June 21, 2018 8:00am to 12:00pm (noon)

Theme: Transplantation

CE Credits: PACE® credits offered

Location: Gaylord Texan Resort & Convention Center
1501 Gaylord Trail
Grapevine, TX 76051

Conference cost: Complimentary to Carter BloodCare clients

RSVP: Please send response to vmoore@carterbloodcare.org with the following:
Name
Facility
Email
Phone Number
Title
What day(s) you plan to attend?
Will you be attending the reception?
Any food allergies or special food requirements

A detailed agenda will be sent at a later date.

Hosted by: Blood Centers of America and Carter BloodCare

BCA Blood Centers of America | Carter BloodCare

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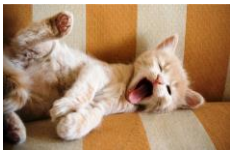
Lookbacks, Recalls and Market Withdrawals

Laurie J Sutor, MD, MBA
Vice President of Medical and Technical Services

Overview

- Introduction
- Quarantines
- Market withdrawals vs Recalls
- Lookbacks



Why This Topic?

- Lots of confusion
- Misuse of word “lookback”
- Some actions are mandatory, some are optional

Quarantines

- Preliminary notification
- Investigation is ongoing
- Gets the in-date component off the shelf
- The blood center usually pulls these back to the center
- May ultimately be determined that the component may be safe to use
- If there is a real issue, a second notification will be forthcoming

Quarantine Examples

- Donor has tested anti-HIV reactive
- Confirmation testing is pending
- Any in-date components from the donor's prior donations are quarantined until further testing is received

- A pool of platelets tests positive by Verax for presumed bacteria
- Co-components are quarantined until the work-up is finished. If no contaminant is identified the co-components may be released.

Quarantine Action for Hospitals

- Quarantine and return in date components
- Wait for further information about investigation
- Recipient notification is up to the hospital's discretion

Market Withdrawals v. Recalls

- **Similar, but recalls are of higher severity**
- **Both reflect deviations from procedure**
- **Either may be an FDA reportable event**
- **The safety, purity or potency of the blood component may be affected**
- **Recalls are considered to be violation of the FDA laws and are those deviations for which the agency might initiate legal action under 21 CFR part 7.**

Recall Classifications

Classification indicates the relative degree of the health hazard of the product being recalled

- **Class III -- least hazardous**
- **Class II – moderate level**
- **Class I – "a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death."**

Examples of Deviations

- **Post-donation information ("accidents"):**
  - Donor calls back 3 days after donation to tell the blood center that they have used IV drugs but failed to reveal that in the initial interview
  - Donor donates a second unit 3 months later and gives a history of Accutane use for the last year that they did not disclose at the time of the first unit donated.
- **Errors:**
  - Staff person fails to quarantine a unit with an incomplete questionnaire discovered at card audit – high risk question not asked.
  - ABO mistype on label (caught at retype at hospital)

Action of Hospital

- When notification is received, hospital should have a protocol or process to review recalls and withdrawals to determine their severity and whether to notify recipients or their physicians.
- Some facilities have a group decision (Transfusion Committee, ethics committee, medical staff committee etc) decide on the first instance and have a "standing order" for similar events. Others have pathologist or other doctor decide for most.
- Some are determined by some facilities to be non-actionable: e.g. CJD risk, malarial travel in donors.

Lookback

- Strictly defined in Code of Federal Regulations
- Blood centers and transfusing facilities are mandated to act within certain time limits
- Recipients must be notified within 12 weeks
- HIV: 21 CFR 610.46
- HCV: 21 CFR 610.47
- Chagas disease antibody: FDA guidance document

Lookback

- Lookback usually occurs when a donor previously gave and units were transfused, and now the donor has returned and tested positive.
- For lookback to occur, generally the initial screening is confirmed with a secondary test (although sometimes this does not occur -- if confirmation is not available, lookback must sometimes proceed anyway).
- Usually a quarantine notice was sent first for the initial screening test positive for in date components, but lookback often goes back further (one year prior to the last negative test result)