Transplant Or Not?  
The Truth About Cellular Infusions

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WHAT ARE WE GOING TO DO?

Once and for all understand the difference between a transplant, DLI, a boost and other cells patients get.

Once and for all know exactly how to fill in all the proper forms properly.

Learn some easy ways to remember the above and clues when to ask for the truth.

Goals of Blood and Marrow Transplantation

- Replace blood/bone marrow derived hematopoietic stem cells destroyed by disease or drugs used to treat disease
- Destroy malignancy
  - High-dose chemotherapy/ radiation (which also destroys blood stem cells)
  - Immune effects of donor cells

GRAFT SOURCE: Bone Marrow

- Collected in the OR
- General or spinal anesthesia
- Collect ~15 mls/kg recipient weight
- Most of what is collected is “junk”
- Harvesting Bone Marrow is Boring!!
- Moderate donor disability

GRAFT SOURCE: Blood Stem Cells

- Stem cells circulate in blood in low levels
- Stem cells can be “mobilized” from the BM:
  - by chemotherapy
  - by growth factors (GCSF, GMCSF)
  - synergy of chemotherapy followed by growth factors
  - Plerixafor / Mozobil
  - antagonist of CXCR4
- For allogeneic donors, G-CSF mobilization is the standard
- Stem cells are collected from the blood via aphaeresis as outpatients

GRAFT SOURCE: Peripheral Blood Cells vs. Bone Marrow

- Possible to collect more CD34+ve cells from blood than resting BM
- multiple “transplants”
- purging, gene therapy, other manipulations
- more rapid recovery of counts
- Cell mix is different with PBSC than resting BM
- more CD34 +ve cells
- partially committed progenitors
- more T-cells (~1 log)
- Less tumor contamination with autologous PBSC
WHAT ARE WE TALKING ABOUT?

All Hematopoietic Cells

CD34 +ve cells

True Stem Cells

Lymphocytes
  multiple sub-types
  CD3, CD4, NK

MSC

What Is In Different Products?

<table>
<thead>
<tr>
<th>Product</th>
<th>Rest BM</th>
<th>Stem BM/PB</th>
<th>CD34+Sel BM/PB</th>
<th>Phleb lymphs</th>
<th>Rest apheresis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stem Cells</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+/–</td>
</tr>
<tr>
<td>Lymphs</td>
<td>+</td>
<td>+/–</td>
<td>+</td>
<td>+/–</td>
<td>+/–</td>
</tr>
</tbody>
</table>

1. There are very small numbers of stem cells but not enough to engraft and recover blood counts.
2. Lymphocytes collected after G-CSF are different than lymphocytes collected at rest. G-CSF lymphocytes cause less GVHD and have less Graft versus tumor activity.

Answer These and You Should Know What Was Done

• Why were the cells given?
• What did they do to get the cells?
• What did they give the recipient before they gave the cells?

Form 2100

For each QO given, report the total number of cells infused. If the cells were cryopreserved, report the total after processing, but before cryopreservation. Copy the pages to regenerate form one above. Signly represents UI.

Form 2100

What About Other Cells in Q612-620 from 2100 Form

• Mesenchymal Cells
  - Research protocols; Osiris or home grown
  - Prevent / treat GVHD
  - From third person or original donor
• Dendritic Cells
  - Research protocols
  - Usually tumor or infection vaccine trials
  - Mostly auto cells occasionally donor's cells
1. Not stem cells. Cannot repopulate the bone marrow and make blood cells

Other Cells in Form 2100

• NK Cells
  - A specific type of lymphocyte
  - Expanded in the lab with cytokines like IL-2
  - Anti-tumor activity
  - May be given at the same time or after (or both) the stem cell transplant
• Fibroblasts
  - No idea why this is here! Never seen a protocol or found a paper!
1. Not stem cells. Cannot repopulate the bone marrow and make blood cells
Definition of HSCT

- Delivers CD34+ cells which include Hematopoietic Stem Cells (HSC)
- HSC are intended to restore hematopoiesis and immunity
- HSC Infusion (a transplant) is usually preceded by a preparative regimen which kills cancer and prevents rejection

However
- Boosts may not include a preparative regimen
- HSCT for Immune deficiency disease may not include a preparative regimen

But these are still transplants (HSCT).

Why Were The Cells Given?: HSCT

1. 2, 3, 6, 8, 9: all relate to failure of the original stem cells to engraft and/or repopulate the marrow
2. 4, 5: these could also be an indication for DLI
3. 6: you knew this would happen before HSCT 1. e.g. MM
4. 7: e.g. the patient had NHL and now has MDS

Why Were The Cells Given?: DLI

- Usually this is % donor CD3 in sorted or selected peripheral blood chimerism
- Usually this is after a non-myeloablative transplant

Answer These and You Should Know What Was Done

- Why were the cells given?
- What did they do to get the cells?
- What did they give the recipient before they gave the cells?
BLOOD CENTER CHIMERISM REPORT

Graft vs. Tumor Effect of DLI

Response To NST / RIC Allotransplants May Require DLI

Answer These and You Should Know What Was Done

What Did They Do To Get The Cells?

What Did They Do?

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Graft vs. Tumor Effect of DLI

Response To NST / RIC Allotransplants May Require DLI

Answer These and You Should Know What Was Done

What Did They Do To Get The Cells?

What Did They Do?

What Did They Do To Get The Cells?

This does not always distinguish SCT from DLI

Pre-Collection Therapy

- Bone marrow harvest
- Ordered a Cord Blood Unit
- G-CSF mobilization of the donor
- CD34 selected the BM or PB cells
  - Positive fraction includes the stem cells
  - Negative fraction includes the lymphocytes
- How to handle back up auto cells given to failed NST? This DOES NOT require a new transplant report.
What Did They Do To Get The Cells?

- 593. Probably an HSCT but I can't promise
- 594. No stem cells so has to be a DLI
- 595. No stem cells so has to be a DLI
- 596. Depends. Need more info. See # 604-611
- 598. Too few stem cells so has to be a DCI

What Did The Give The Recipient Before The Cells?

- SALVAGE therapy (chemo, XRT, antibodies) can be given to control relapsed disease
- CONDITIONING therapy is given to facilitate engraftment of the stem cell containing graft
- Many of the therapies may be used for either...

Not Conditioning Regimen Drugs or Combinations

- Rituximab (Rituxin)
- CHOP
- 7+3 (cytarabine + either idarubicin or daunorubicin)
- mylotarg
- thalidomide
- steroids
- decitabine or azacitadine
- Hydroxyurea

Sometimes It Depends: So You Have To Ask!
More Confusing Examples

Not Conditioning
- CHOP
- ESHAP
- DHAP

Could Be Conditioning
- FCR
- ICE
- Cyclophosphamide
- Radiation

Why Were The Cells Given?: DLI

Why Were The Cells Given?: DLI

Data Collection Requirements

Subsequent HSCTs and the Infusion form

DCI Infusion data

Product was collected under SCTOD
- Any allogeic transplant
- Related HSCT where the recipient and/or donor donated research samples for the NMDP repository
- Recipient was selected for comprehensive report forms

DCI infusion data is reported on the follow-up forms
- Post-TED
- Form 2100 - 100 day follow-up form
- Form 2200 - 6 month to 2 year follow-up
- Form 2300 - > 2 year follow-up
• Let's look at the Forms Now

Examples of more than one graft source
1. Double cord (e.g. BMT CTN trial #)
2. Cord + haploidentical family member
3. PBSC + NK cells (experimental protocol)

We Used To Think This Was Crazy Talk

WHAT IS A BOOST?

• Additional cells given to facilitate hematopoietic recovery
• No additional conditioning
• Generally uses cells previously stored
• Autologous – does not require second transplant form
• Allogeneic – does require a second transplant form

YES means this was a transplant!
NO could still be a transplant
e.g. a “boost”
e.g. SCT for immune deficiency
Pre-TED

Box A

GVHD PROPHYLAXIS (ALLO ONLY)

Was GVHD prophylaxis planned/given?  
☐ Yes  ☐ No

(Check all that apply)

Not helpful really.
YES could apply to both HSCT and DLI.
NO more likely a non-HSCT DCI

Pre-TED 080409-r2

Post-TED

HSCT FOR NON-MALIGNANT DISEASE ONLY

If given in this period?
☐ Yes, also complete "DCI" section on pg 2; starting at Q.110
☐ No, started only pg 1

Post-TED-081009-r2

FORM 2100

PRE-TED

 Box B  POST-HSCT DISEASE THERAPY PLANNED AS OF DAY 8

Is this TDCI part of a planned multiple (sequential) transplant (Tx)?
☐ Yes  ☐ No

Is additional post-HSCT therapy planned?
☐ Yes  ☐ No

(DCC Optional for non-U.S. centers)

NOW Cellular Therapy (e.g., DCI, DLI)

Hmm? As Bill Clinton might say
It depends on what the definition of "planned" is...

Pre-TED 080409-r2

FORM 2100

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☐ Yes, also complete "DCI" section on pg 2; starting at Q.110
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Post-TED-081009-r2

FORM 2100

RE #94 and #95. Important to understand the details.
E.g. "Planned to give if disease present" at day 100 evaluation is NOT "planned"

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FORM 2100

Filter/cell number

DCC Information (e.g., Velandol, I.)

This section contains information on DCI (question 7) answered "yes" from any donor source (unrelated peripheral blood stem cell donor, cord blood, etc.)

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In The DLI Section of Form 2100

Some answers will raise red flags of inquiry for you.

604. Ask the MD why they gave growth factors to mobilize DLI. Is this really a boost (no conditioning) or a transplant (conditioning)?

610. This could be AMD3100 (Plerixafor), Stem Cell Factor.

This Information Is In The Processing Lab For Each Product Given

For each 500 given, count the total number of cells (CD34) and the total number of progenitor cells. These results are reported to the lab after processing.

Questions