What’s a Transplant?
What’s not?

How to report the difference?

Daniel Weisdorf MD
University of Minnesota

Anti-cancer effects of
BMT or PBSCT [HSCT]

Kill the cancer
Save the patient
Restore immunocompetence

Prevent Infection
Prevent cancer recurrence {GVL}

Blood and Marrow Transplantation

Radiation/Chemotherapy to kill the cancer

Support until recovery

Stem cells to Restore marrow & immune defense
Blood and Marrow Transplantation

Radiation/Chemotherapy to kill the cancer

Support until recovery

Stem cells to Restore marrow & immune defense

Organ injury, Low blood counts

Replace blood/marrow, Fight infections, Attack residual cancer

Dose Intensity for BMT

Marrow suppression

Need growth factors

Need Stem cells

Non-hematologic toxicity

Barriers to Transplant Success

Regimen toxicity

Engraftment

GVHD

Relapse
Conventional High dose Transplantion

**Chemo-radiotherapy**

- Mucositis
- Pneumonitis
- VOD

**Regimen toxicity**

- Engraftment
- GVHD
- Relapse

**Toxicity**

**Engraftment**

**GVHD**

**Relapse**

---

**Conventional High dose Transplantion**

**HLA matching**

- Cell dose
- Cell source {BM, PBPC, UCB}

**Prophylaxis** {T-depletion; drugs}

**Prolonged Immunodeficiency**

**Infections**

**Bleeding**

**Transfusions**

**Regimen toxicity**

- Engraftment
- GVHD
- Relapse

---

**Conventional High dose Transplantion**

**HLA matching**

- Cell dose
- Cell source {BM, PBPC, UCB}

**Prophylaxis** {T-depletion; drugs}

**Prolonged Immunodeficiency**

**Infections**

**Bleeding**

**Transfusions**

**Regimen toxicity**

- Engraftment
- GVHD
- Relapse

---
Conventional High dose Transplantion

Disease status
Conditioning
Graft vs tumor

Regimen toxicity
Engraftment
GVHD
Relapse

Blood and Marrow Transplantation

Donor -- Allogeneic Graft

Support until recovery

Stem cells to Restore marrow & immune defense

Blood and Marrow Transplantation

Patient as donor -- Autologous
Collect & freeze cells

Support until recovery

Stem cells to Restore marrow & immune defense
The Therapeutic Conflict

Cancer ——— To toxicity

Patient Safety & Cure

---

High dose Conditioning Regimen

• Kill cancer cells
• Suppress host immunity
  --- > promote engraftment
• Undesired tissue toxicity
• Undesired enhancement of GVHD

---

The Therapeutic Conflict

Cancer ——— To toxicity

Patient Safety & Cure
Dose-intensity may prevent relapse and cure resistant cancer
AML, Myelodysplastic syndrome
ALL
CML
NHL
Hodgkins Disease
Myeloma
Some solid tumors (ovarian, testis, brain, breast)
Non-myeloablative Reduced Intensity Transplants
“Mini-transplants”
- Reduced intensity immune suppression
- Establish the donor graft
- Immune attack on the cancer

Suitable for older or sicker patients

Particularly promising for immuno-sensitive tumors
- Follicular NHL; CLL; CML;
- ? Myeloma; Hodgkins; Renal cell CA

Enhance Immune attack with Donor Cell Infusions
Blood/Marrow Transplantation + Donor Cell Infusions

- Stem cells to Restore marrow & immune defense
- Donor -- Allogeneic Graft
- Donor lymphoid cells to Boost immune defense & Fight cancer
- Support until recovery

Non-Ablative Transplants for Cancer

- Stem cells are Restorative
- Conditioning designed for Therapeutic Index
- Not for leukemia
Non-myeloablative BMT

Lower intensity conditioning
Immunosuppressive to support engraftment
Not intended to eradicate cancer

Allow graft to strengthen; over time

Enhance GVL
Limited duration GVHD prophylaxis
Donor Lymphocyte infusions

Lesser Regimen toxicity
Engraftment
GVHD
Relapse

Regimen toxicity develops over time
Engraftment
GVHD
Relapse
So

What’s a transplant?

What’s a Donor Cell Infusion?

& How do I report it?
**Definitions**

Hematopoietic Stem Cell Transplant (HSCT)

Delivers CD34+ cells which include Stem Cells

HSC are intended to restore hematopoiesis and immunity

HSC Infusion {a transplant} is usually preceded by a Conditioning regimen which kills cancer and prevents rejection

However

- Boost may not have conditioning
- HSCT for Immune deficiency disease may not have conditioning

But these are still transplants (HSCT).

**Definition of DCI**

Donor Cell Infusion

Contains specific blood cells

- Lymphocytes (DLI)

Infused to

- Enhance graft vs. tumor reactions
- or graft vs. viral infections [EBV]

Usually *not preceded* by Conditioning regimen
**Commonly Used Conditioning Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>HLA-ident sib BMT</th>
<th>Unrelated Donor BMT</th>
<th>Auto-transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBI</td>
<td>52%</td>
<td>85%</td>
<td>25%</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>87%</td>
<td>91%</td>
<td>85%</td>
</tr>
<tr>
<td>Busulfan</td>
<td>48%</td>
<td>17%</td>
<td>10%</td>
</tr>
<tr>
<td>Etoposide</td>
<td>24%</td>
<td>19%</td>
<td>73%</td>
</tr>
<tr>
<td>Ara-C</td>
<td>5%</td>
<td>10%</td>
<td>25%</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>4%</td>
<td>14%</td>
<td>8%</td>
</tr>
<tr>
<td>Platinum*</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>7%</td>
</tr>
<tr>
<td>Nitrosourea**</td>
<td>1%</td>
<td>&lt;1%</td>
<td>53%</td>
</tr>
</tbody>
</table>

* cis-Platinum / carboplatin  ** BCNU / CCNU

**Commonly Used High-dose Conditioning Regimens for HSCT**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Major non-heme toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cy + TBI</td>
<td>Mucositis, VOD</td>
</tr>
<tr>
<td>Etoposide (VP16) + TBI</td>
<td>Mucositis</td>
</tr>
<tr>
<td>Cy + cisplatin + Carmustine (BCNU)</td>
<td>Pulmonary, VOD</td>
</tr>
<tr>
<td>Cy + carboplatin + Thiotepa</td>
<td>Mucositis</td>
</tr>
<tr>
<td>Bu + Cy</td>
<td>VOD, mucositis</td>
</tr>
<tr>
<td>Cy + VP16 + BCNU (CBV)</td>
<td>VOD, mucositis</td>
</tr>
<tr>
<td>Ifosfamide + carboplatin + VP16 (ICE)</td>
<td>Renal, mucositis</td>
</tr>
</tbody>
</table>

**Each Procedure has a Specific Purpose**

**TRANSPLANT (HSCT)**
- Provide stem cell replacement
  - hematopoiesis
  - immune reconstitution
- Graft versus tumor effect

**DCI**
- Prevent or treat disease relapse (or infection)
- Graft versus tumor effect
Drugs which might Precede DCI but not used as Conditioning Regimen Drugs

- Rituximab (Rituxan)
- CHOP
- 7+3 (AraC + Idarubicin or daunorubicin)
- mylotarg
- steroids

Indications for DCI

Prevention of Relapse
- Planned with Reduced intensity HCT
Treatment of relapse  CML, AML
Enhance engraftment
- Incomplete donor cell chimerism
Treatment of post transplant malignancy
- PTLD (Lymphoma)
Treatment of Viral Infections  EBV

Complications Post DCI

- Marrow Aplasia
- GVHD: acute and chronic
- Infusion reactions
- Infections
Complications Post DCI

- Marrow Aplasia
  Donor cells attack marrow
- GVHD: acute and chronic
- Infusion reactions
- Infections

Complications Post DCI

- Marrow Aplasia
- GVHD: acute and chronic
  New infusion on non-tolerant T cells
  Sometimes later or slower
- Infusion reactions
- Infections

Complications Post DCI

- Marrow Aplasia
- GVHD: acute and chronic
- Infusion reactions
- Infections
Complications Post DCI

- Marrow Aplasia
- GVHD: acute and chronic
- Infusion reactions
- Infections
  Mostly with GVHD

Graft & Cell Sources

<table>
<thead>
<tr>
<th>HSCT</th>
<th>DCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Marrow</td>
<td>Peripheral Blood</td>
</tr>
<tr>
<td>Peripheral Blood</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>Cord Blood</td>
<td></td>
</tr>
</tbody>
</table>

*Graft Manipulation*

Selection of desired cell types
Depletion of unwanted elements
*RBC, plasma, other cells*

& Now those Report Forms?
### HSCT Needs Preceding Conditioning

**Pre-HSCT Preparative Regimen (Conditioning)**

1.6. Height at initiation of pre-HSCT preparative regimen:
   - [ ] 1 inch
   - [ ] 2 inches

1.7. Actual weight at initiation of pre-HSCT preparative regimen:
   - [ ] 1 oz
   - [ ] 2 oz

1.8. Desired body weight used for pre-HSCT preparative regimen:
   - [ ] 1 lb
   - [ ] 2 lb

---

**Remember:** Boosts and rare HSCT (Immune deficiencies) get no conditioning—Still reported as HSCT

---

### Radiation??

194. Was radiation performed as part of the pre-HSCT preparative regimen, or given within 14 days of preparative regimen?

195. What was the radiation field?

### Chemotherapy

231. Were drugs given for pre-HSCT preparative regimen?

   - [ ] yes

   **Continue with drug list on the following pages**

---

### First or subsequent HSCT??

**First or subsequent HSCT (only if a subsequent HSCT planned as part of the overall treatment plan that is a reference to pre-HSCT disease assessment)?**

- [ ] Yes
- [ ] No

**How did the first HSCT for the regimen?**

1. Not applicable; only if a subsequent HSCT planned
2. Intensive conditioning HSCT planned
3. Reduced intensity HSCT planned

---

16
HSCT source: Reason for HSCT

- What was the HSCT source for the last HSCT?
  - autologous
  - allogeneic, unrelated donor
  - syngeneic / allogeneic related donor

- Reason for current HSCT:
  - no hematopoietic recovery
  - partial hematopoietic recovery
  - graft failure / rejection

Report of 2nd HSCT within 100 days

1. Did recipient receive a subsequent HSCT (bone marrow, mobilized peripheral blood stem cells, cord blood) prior to day 100 after the HSCT for which this form is being completed? [O]

DCI from same or different donor?

2. Has the recipient received a DCI from the original donor? [O]
   - yes
   - no

   Complete DCI information questions 560-679.

Second HSCT: What’s the reason?

- Subsequent HSCT: [ ]
  - Complete this section if the recipient received a subsequent HSCT (Question 5, answered “yes”); complete is not performed with the DCI section in Question 566.
  - Date of subsequent HSCT: [ ]

575. What was the indication for subsequent HSCT?

Subsequent autologous HSCTs performed for engraftment reasons (options 1-3) do not require separate report forms to be completed. All other subsequent HSCTs will require a separate follow-up report form completed for each indication.

- no hematopoietic recovery
- partial hematopoietic recovery
- graft failure / rejection following initial hematopoietic recovery
- persistent primary disease
- recurrence primary disease
- planned second HSCT, per protocol
- new malignancy: Complete the section on New Malignancy (q)
  - status, initial chemistry
  - initial chemotherapy

- other: [ ] Specify [ ]
**HSCT source?**

- HSCT source-related (CBMT)
- HSCT source-unrelated

**Donor Cellular Infusion (DCI) Information**

560. Date the first DCI was given:

561. Specify the number of cell infusions given within 28 days of the first DCI:

562. Was the DCI infusion performed in a different institution?

Several DCI within 28 days reported together;

Beyond 28 days; report separately

**Reason for DCI: Was it planned pre-HSCT?**

- Treatment for persistent or progressive disease
- Treatment for chimeric state (repopulation, chimerism)
- Treatment for GVHD
- Reinfusion
- Stable donor chimerism
- Use of (decreased) donor T-cell chimerism
- Other

595. Specify indication for DCI:

596. Indication for DCI (planned or unplanned)

597. Specify indication for HSCT protocol

598. Specify the indication of disease detection before report the first date of disease was detected if it's not detected prior to HSCT (question 598)

599. Was chemotherapy used to attempt to induce remission:

600. Date chemotherapy began:

601. Date chemotherapy ended:

602. Date documented (placenta chemotherapy testing on page 6 or 7)
DCI: same or different donor? Primed?

Specify DCI source:
601. □ yes □ no - collected at the time of PBSC mobilization and collection
602. □ yes □ no - negative fraction of CD34 selected PBSC
603. □ yes □ no - negative fraction of CD34 selected bone marrow
604. □ yes □ no - apheresis at a different time than collection of PBSC used for allogeneic HSCT

605. Date of apheresis:
606. □ yes □ no - isolated from a unit(s) of whole blood
607. Specify number of units:

608. Were the donor cells collected by leukapheresis?

612. Did the donor receive treatment to enhance cell collection prior to donation?

DCI cell content

For each DCI given, report the total number of cells infused:

620. CD3+ cells:
621. CD4+ cells:
622. CD8+ cells:
623. CD4/C8+ cells:
624. NK cells:
625. Nucleolated cells:
626. Mesenchymal cells:

633. Were the cells manipulated prior to infusion?

Specify all methods used to manipulate the cells:

DCI Processing

Specify antibodies used during graft manipulation:

664. □ yes □ no - anti CD3
665. □ yes □ no - anti CD2
666. □ yes □ no - anti CD8
667. □ yes □ no - anti CD4
668. □ yes □ no - anti CD5
669. □ yes □ no - anti CD6
670. □ yes □ no - anti TCR alpha/beta (T10-09)
671. □ yes □ no - OKT3
672. □ yes □ no - other CD3

Specify antibodies:
673. □ yes □ no

674. □ yes □ no - anti CD52
675. □ yes □ no - anti CD10
676. □ yes □ no - anti CD19
677. □ yes □ no - anti CD20
Time for Questions