Role of Pharmacist in Hematologic malignancies

Manit Sae-teaw
B.Pharm, BCOP, BCP
Grad. Dip. In Pharmacotherapy
Faculty of Pharmaceutical Science
Ubon Ratchathani University
Outline

● Cancer facts
● Hematologic malignancies review
● Pharmaceutical care in cancer
● Roles of pharmacy
● Process to develop pharmaceutical care
● Barrier to develop pharmaceutical care
● Conclusion
## Cancer facts

<table>
<thead>
<tr>
<th>No (thousands)</th>
<th>World</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>7,054,446</td>
<td>69,892</td>
</tr>
<tr>
<td>Number of new cases</td>
<td>14,090.1</td>
<td>123.8</td>
</tr>
<tr>
<td>Number of cancer death</td>
<td>8,201</td>
<td>85</td>
</tr>
<tr>
<td>Most frequent</td>
<td>Lung, Breast,</td>
<td>Lung, Breast, Liver, CRC, Cervix</td>
</tr>
<tr>
<td></td>
<td>CRC, Stomach,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prostate</td>
<td></td>
</tr>
</tbody>
</table>
## Cancer facts
### Hematologic malignancies (Thailand)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Incidence</th>
<th>Death</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>8,758</td>
<td>6,490</td>
<td>74.1</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3,951</td>
<td>2,706</td>
<td>68.5</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3,744</td>
<td>3,071</td>
<td>82.0</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>751</td>
<td>582</td>
<td>77.5</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>312</td>
<td>131</td>
<td>42.0</td>
</tr>
</tbody>
</table>

Remark: Hematologic malignancies including NHL, HD, MM and Leukemia

GLOBOCAN 2012 (IARC) Section of cancer information
## Cancer facts
### Leukemia and lymphoma

<table>
<thead>
<tr>
<th></th>
<th>World</th>
<th></th>
<th>Thailand</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>2012</td>
<td>2020</td>
<td>2012</td>
</tr>
<tr>
<td>New cases</td>
<td>803,656</td>
<td>948,942</td>
<td>8,007</td>
<td>9,015</td>
</tr>
<tr>
<td>Cancer death</td>
<td>490,560</td>
<td>584,212</td>
<td>5,908</td>
<td>6,706</td>
</tr>
</tbody>
</table>

GLOBOCAN 2012 (IARC) Section of cancer information
Leukemia

- Characterized by unregulated proliferation of blood forming cell in bone marrow
- Can be classified into
  - Acute leukemia: AML, ALL (blasts ≥ 20%)
  - Chronic leukemia: CML, CLL (indolent)
- Classification
  - World health organization classification
Leukemia

- **Acute myeloid leukemia**
  - Induction phase: Cytarabine + Anthracycline
  - Intensification/Consolidation: High dose cytarabine or Cytarabine + Anthracycline

- **Acute lymphocytic leukemia**
  - Induction phase
  - Intensification phase
  - CNS prophylaxis
  - Maintenance
Leukemia

- Chronic myeloid leukemia
  - Classified disease stage into chronic phase, accelerated phase and chronic phase
  - Goal: maintain chronic phase and symptom control
  - Tyrosine kinase inhibitor
    - Imatinib, Nilotinib, Dasatinib
- Evaluation hematologic response, cytogenetic response and molecular response
Lymphoma

- Malignancies transformation of immune cell predominantly lymphoid tissue
- Can be classified into
  - Hodgkin lymphoma: less common, good prognostic
  - Non-Hodgkin lymphoma: most common, varies prognostic
- Staging by Ann Arbor criteria
Ann Arbor Staging System for NHL

“Bulky disease” tumor mass > 10 cm in greatest diameter
“B” symptoms (weight loss > 10%, fever > 38°C or night sweats)
Lymphoma

- Hodgkin lymphoma
  - Early stage (1 and 2)
    Chemotherapy (ABVD) 4 cycles + Radiation
  - Advanced stage (3 and 4)
    Chemotherapy (ABVD) 6-8 cycle

- Non-Hodgkin lymphoma
  - Early stage (1 and 2)
    Chemotherapy (CHOP ± R) 3 cycles + Radiation
  - Advanced stage (3 and 4)
    Chemotherapy (CHOP ± R) 6-8 cycle
Why clinical pharmacist ???

- More cancer are curable or can be halted in a chronic state
  - Patients quality of life is an important outcome alongside the tumor response
- More complex drug regimen
  - Higher risk of drug-related problems

Disease-focused  \rightarrow  Patient-focused
Drug-oriented service  \rightarrow  Patient-oriented service

Pharmaceutical care

- American Society of Health-System Pharmacists (1992)
  - The mission of the pharmacist is to provide pharmaceutical care
  - Pharmaceutical care is the direct, responsible provision of medication-related care for the propose of achieving definite outcome that improve a patient’s quality of life

Ref: ASHP statement on pharmaceutical care. www.ashp.org
Oncology pharmacist

- Cytotoxic compounding and standardization of chemotherapy order forms the 1st step of pharmaceutical care

- Oncology pharmacist
  - Recommended, designs, implement, monitor, modified care plans
  - Optimize outcome of individualized cancer patient

Area involvement

- In-patient department (oncology ward)
- Out-patient
  - Outpatient clinics
  - Infusion centers
- Community pharmacy/nursing home
- Medication therapy management

Pharmacist role in hematologic malignancies

- Direct patient care
- Education
- Guideline, Policies and standard
- Advocacy

Direct patient care

Provide medication management services across the care continuum

- Recommend or select most appropriate therapies

## Pharmaceutical care in cancer patients

<table>
<thead>
<tr>
<th>Drug-related needs</th>
<th>Drug-related problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Additional drug therapy</td>
</tr>
<tr>
<td></td>
<td>Unnecessary drug therapy</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Drug without indication</td>
</tr>
<tr>
<td></td>
<td>Dose too low</td>
</tr>
<tr>
<td>Safety</td>
<td>Adverse drug reaction</td>
</tr>
<tr>
<td></td>
<td>Dose too high</td>
</tr>
<tr>
<td>Adherence</td>
<td>Noncompliance</td>
</tr>
</tbody>
</table>

Pharmaceutical care in cancer patients

Direct patient care

Provide medication management services across the care continuum

- Recommend or select most appropriate therapies
- Monitor the efficacy and safety
- Prevent and manage adverse effect
- Facilitate transfers of patients and their medications (Medication reconciliation)

Education

- Provide education and consultation to the healthcare team
- Evaluation of the literature and integration of new information to practice
- Patient counseling
- Development of educational tools
- Participation in research

Strategies for establishing the Pharmacist-patient relationship (FYI)

- Introduce self to patients during encounter
- Outline for patient about encounter
- Demonstrate empathy or caring attitude
- Discuss amount time needed for encounter
- Discuss the expected outcome for encounter
- Use feedback strategies
- Ensure enough time for patient ask question
- Resolve a drug therapy problem
- Follow up with patient

Ref: Rover JP. A practice guide to pharmaceutical care. 2nd ed. 2003
Guideline, Policies and Standards

To provide policy and procedure development and support for other oncology and medication related issues

- Updating standards and policies
  - Treatment protocol
- Participate in therapeutic committees

Advocacy

- Patient: optimal and safe care
- Institution: financial responsibility
- Healthcare colleagues: education and standards
- Community: prevention and early detection

How to establish pharmaceutical care service in hematologic malignancies

Preparation process

- Selected diagnoses and procedure
- Search of scientific literature
- Appoint a development team
- Document current processes and outcomes
- Preparation tools and documents
- Educate participants

Ref: ASHP. ASHP guideline on the pharmacist’s role in the development, implementation, and assessment of critical pathways. www.ashp.org
Tools and documents

- Single/Multidisciplinary work sheet
- **Treatment protocols**
- Tools for data and outcome collection
- Patient education tools
- Multidisciplinary communication tools

Ref: ASHP. ASHP guideline on the pharmacist’s role in the development, implementation, and assessment of critical pathways. [www.ashp.org](http://www.ashp.org)
**Current status: Admit at CCU (10/12/2555)**

**General**
- **Address**
- **Name:**
- **Sex:** Male
- **Marital status:**
- **Birth Date:** Age: 73 Years old
- **Payment:**

**Diagnosis**
- **Underlying Disease:**
  - 10/12/2555: Acute subendocardial myocardial infarction
  - 31/03/2552: Sequelae of intracerebral haemorrhage
  - 30/12/2551: Sequelae of intracerebral haemorrhage
  - 12/10/2551: Sequelae of intracerebral haemorrhage

**Pharmaceutical care activity:**
- **Date:** 19/12/2555
- **P’Care Note:**
- **P’Care Activity:**
  - **Drug therapy problem**
  - **Adverse product reaction**
  - **Idiosyncrasy**
  - **Severe Side effect (อาการข้างเคียงฉุกเฉิน)**
  - **Side effect (อาการข้างเคียง)**
  - **Toxicity**
  - **Allergy/hypersensitive**
  - **Opinion not clear**
  - **Other perspective: การใช้ยา/เพิ่มผลประสิทธิภาพ**

**Lab Chemistry**
- **Date:** 11/12/2555 (08:08)
- **Lab type:**
- **Lab:** BUN
- **Normal:** 6 - 20
- **Result:**
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Electrolyte
  - **Lab:** Chloride
  - **Normal:** 98 - 107
  - **Result:** 1
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Lipid 2
  - **Lab:** Cholesterol
  - **Normal:** 1 - 200
  - **Result:** 1
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Electrolyte
  - **Lab:** CO2
  - **Normal:** 22 - 29
  - **Result:**
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** BC
  - **Lab:** Creatinine
  - **Normal:** 0.5 - 1.2
  - **Result:** 1
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Glucose
  - **Lab:** Glucose
  - **Normal:** 74 - 109
  - **Result:** 2
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Lipid 2
  - **Lab:** HDL-cholesterol
  - **Normal:** 35 - 65
  - **Result:**
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Lipid 2
  - **Lab:** LDL-cholesterol
  - **Normal:** 100 - 129
  - **Result:** 1
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Magnesium
  - **Lab:** Magnesium
  - **Normal:** 1.7 - 2.6
  - **Result:** 2
- **Date:** 11/12/2555 (08:08)
  - **Lab type:** Electrolyte
  - **Lab:** Potassium
  - **Normal:** 3.5 - 5.3
  - **Result:** 4

**Current Med IPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** ASPIRIN 81 MG

**Previous Med IPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** AUGMENTIN INJ 1.2 G - L

**Home Med**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** CPM INJ.10 MG/ML

**Med OPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** D-5-W 100 ML

**Med OPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** D-5-W 500 ML

**Med OPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** DOPAMINE INJ.250 MG/10 ML-L (H)

**Med OPD**
- **First Date:** 10/12/2555
- **Last Date:** 10/12/2555
- **Drug:** DOPAMINE INJ.250 MG/10 ML-L (H)
How to establish pharmaceutical care service in hematologic malignancies

- Implementation process
  - Documents

- Assessment process
  - Evaluation according to desired outcome

- Disseminate the result of the assessment
  - Report
  - Research

Ref: ASHP. ASHP guideline on the pharmacist’s role in the development, implementation, and assessment of critical pathways. www.ashp.org
Barrier to establish pharmaceutical care in hematology malignancies

- I don’t have knowledge and skills
  - Training
  - Practice

- I don’t know pharmacist roles in this team
  - Clarify pharmacist role before initiation
  - Sight seeing another practice site
Barrier to establish pharmaceutical care in hematology malignancies

- I don’t know how to report pharmacist outcome
  - Identify team-based outcome and pharmacist outcome according to standard accreditation requirement
- Convert all outcome into financial budget (if possible)
- Documentation
Barrier to establish pharmaceutical care in hematology malignancies

- I don’t know resource to get information related to hematologic malignancies
- Make collaboration with multidisciplinary team
- Make collaboration with oncology pharmacy network
Conclusion

- Hematologic malignancies have high mortality rate (growing an incidence)
- Pharmacist move from drug-oriented to patient-oriented
- Roles of pharmacist including direct patient care, education, policies, advocacy
- Process to establish including preparation, implementation, assessment, disseminate result
Role of Pharmacist in Hematologic Stem Cell Transplantation (HSCT)

Manit Sae-teaw
B.Pharm, BCOP, BCP
Grad. Dip. In Pharmacotherapy
Faculty of Pharmaceutical Science
Ubon Ratchathani University
Objectives

- Describe the different sources of hematopoietic stem cells
- Describe bone marrow transplantation process
- Understand role of pharmacist in bone marrow transplantation process
Introduction

- HSCT is a process involves IV infusion hematopoietic stem cell from compatible donor into recipient
  - After administrative high-dose chemotherapy
  - Although standard dose chemotherapy can prolong survival but most pts are not cured
- HSCT become important modality for variety malignant and nonmalignant treatment
Donor and Histocompatibility Testing

- Autologous transplantation: patients receive their own hematopoietic stem cell
- Syngeneic transplantation: identical twin serves as the donor
- Allogeneic transplantation: genetic not identical but share some common tissue antigens
<table>
<thead>
<tr>
<th>Allogeneic Advantages</th>
<th>Autologous Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No tumor contamination</td>
<td>1. Easy identification of Stem cells</td>
</tr>
<tr>
<td>2. Graft vs. tumor effect</td>
<td>2. Less risk of infection</td>
</tr>
<tr>
<td>3. Used for bone marrow malignancies</td>
<td>3. Dose intense Rx even up to age 70</td>
</tr>
<tr>
<td></td>
<td>4. Low early treatment mortality</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Allogeneic Disadvantages</th>
<th>Autologous Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Younger pts preferred</td>
<td>1. Stem cell damage from condition chemotherapy</td>
</tr>
<tr>
<td>2. Time to find matched donor</td>
<td>2. No Graft vs tumor effect</td>
</tr>
<tr>
<td>3. GVHD &amp; infection risks</td>
<td>3. Not feasible if marrow or peripheral stem cells are cancerous</td>
</tr>
</tbody>
</table>
## Comparison of immunologic source of stem cells

<table>
<thead>
<tr>
<th>Relative risk</th>
<th>Allogeneic</th>
<th>Syngeneic</th>
<th>Autologous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>GVHD</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Others complication</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Engemann AM. ACCP/ASHP Oncology Pharmacy Preparatory Review Course 2010.
Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Indications

- Malignancies
  - Acute & chronic leukemia
  - Lymphoma
  - Multiple myeloma
  - Myelodysplasia
  - Testicular cancer
  - Pediatric tumors

- Non-malignancies
  - Genetic disorders (thalassemia, sickle cell anemia)
  - Combined immunodeficiency disorders
Indication for HSCT

- In patient with defective bone marrow, give an allogeneic stem cell infusion
- Non-bone marrow defect can give autologous stem cell infusion
- Patients with a resistant hematologic cancer may be given either an allogeneic or autologic HSCT
<table>
<thead>
<tr>
<th>Disease/Condition</th>
<th>Allogeneic</th>
<th>Autologous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute leukemia (myeloblastic; lymphoblastic)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chronic myelogenous leukemia</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Myelodysplastic syndrome</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Non Hodgkin Lymphoma</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hodgkins Disease</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Selected solid tumors (testicular ca, pediatric tumors)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Severe combined immunodeficiency</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Patient Evaluation

- Complete history and physical exam
- Complete blood count and serum chemistry
- Virology study
- Blood group and HLA typing
- Disease specific parameter
- CXR, EKG, Cardiac function, CT scan
Donor evaluation

- Complete history and physical exam
- Complete blood count and serum chemistry
- Virology study
- HLA issue
  - Matching donor and recipient based on HLA antigen
Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Hematopoietic stem cell source

Bone marrow

Cord blood

Peripheral blood
Anatomic source of stem cell

- Hematopoietic stem cells serve as “mother” cells of erythrocytes, leukocytes, platelets
- Hematopoietic stem cells are rare cell composing less than 0.01% of all bone marrow cell
- Hematopoietic stem cell are found in
  1. Bone marrow
  2. Peripheral blood
  3. Umbilical cord blood
Anatomic source of stem cell
1. Bone marrow

- Obtained by multiple aspirations from anterior and posterior iliac crests
  - The donor is under general anesthesia
- Procedure take ~ 1hr (200-1500 ml yield)
- In alloHSCT the marrow stem cell given to recipient 12-24 hr after harvest
- In autoHSCT the marrow is frozen and store until needed
- Donor experience local soreness a few days
  - Life threatening complication <0.3%
Anatomic source of stem cell
2. Peripheral blood (PBSCs)

- Collected by procedure called leukopheresis (or apheresis)
- The number of hematopoietic stem cell in peripheral blood normally is too low
  - Mobilization techniques are required
- Mobilization techniques method
  - Administration chemotherapy
  - Administration recombinant hematopoietic growth factor (G-CSF, GM-CSF)
Anatomic source of stem cell

2. Peripheral blood (PBSCs)

### Autologous mobilization regimen (FYI)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose/Units</th>
<th>Day(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTX +</strong></td>
<td>4 g/m²</td>
<td>Day 1</td>
</tr>
<tr>
<td><strong>G-CSF or GM-CSF</strong></td>
<td>5-16 mcg/kg/day</td>
<td>Day 2-Leukopheresis</td>
</tr>
<tr>
<td><strong>Leukopheresis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Paclitaxel +</strong></td>
<td>250 mg/m²</td>
<td>Day 1 (Pre CTX)</td>
</tr>
<tr>
<td><strong>CTX +</strong></td>
<td>3 g/m²</td>
<td>Day 1</td>
</tr>
<tr>
<td><strong>G-CSF</strong></td>
<td>5 mcg/kg/day</td>
<td>Day 2-Leukopheresis</td>
</tr>
<tr>
<td><strong>G-CSF</strong></td>
<td>10 mcg/kg/day</td>
<td>Day 1-Leukopheresis</td>
</tr>
<tr>
<td><strong>CTX +</strong></td>
<td>4 g/m²</td>
<td>Day 1</td>
</tr>
<tr>
<td><strong>Etoposide</strong></td>
<td>200 mg/m²</td>
<td>Day 1-3</td>
</tr>
<tr>
<td><strong>G-CSF</strong></td>
<td>5 mcg/kg/day</td>
<td>Day 4-Leukopheresis</td>
</tr>
<tr>
<td><strong>CTX</strong></td>
<td>4 g/m²</td>
<td>Day 1-2</td>
</tr>
<tr>
<td><strong>Pegfilgrastim</strong></td>
<td>6-12 mg</td>
<td>Day 4</td>
</tr>
</tbody>
</table>
Anatomic source of stem cell
2. Peripheral blood (PBSCs)

- Plerixafor (AMD3100 or Mozobil®)
  - in combination with filgrastim to Enhance mobilisation of CD34+ cells in patients with multiple myeloma and NHL
- For autologous transplants
- MOA: specifically and reversibly inhibits binding of SDF-1 (stroma cell-derived factor - 1) to CXCR4
- Dose adjustments for CrCL < 50mL/min (0.24 vs 0.16 mg/kg/day)
Mozobil® (Plerixafor injection)

<table>
<thead>
<tr>
<th>Day</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>G-CSF</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Mozobil</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Apheresis</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
</tbody>
</table>

- Administer G-CSF (10 mcg/kg/day) each morning for 4 day prior to 1st evening dose of Mozobil and each morning of apheresis
- Administer Mozobil (0.24 mg/kg) approximate 11 hr prior to initiate apheresis
  - Can be administer up to 4 consecutive days
Anatomic source of stem cell
2. Peripheral blood (PBSCs)

Advantages

- More rapid hematopoietic engraftment
  - Neutrophil 12-21 day (BM) vs 9-14 day (PB)
  - Platelet 18-32 day (BM) vs 11-21 day (PB)

- Donor does not experience the discomfort associated with marrow aspirations

- Less likely to be contaminated with malignant cell compare with bone marrow

- Provide Graft versus tumor effect
  - From mononuclear cell (NK cell, T lymphocyte)
Anatomic source of stem cell
2. Peripheral blood (PBSCs)

Disadvantages

- Increase risk of GVHD (T lymphocyte)
- AlloHSCT concern about safety and ethic administering G-CSF to donor
Anatomic source of stem cell
3. Umbilical cord blood

- Stem cells are collected from placental blood
  - No risk to mother and baby
  - Very low risk of transmissible infectious disease
- A source of stem cell who does not have HLA-matched sibling donor
  - Lower immunogenicity leading to lower risk of GVHD
- Frozen in small volumes, DMSO minimized
Anatomic source of stem cell
3. Umbilical cord blood

Disadvantages

- Low number of stem cells in cord units may be inadequate for adults
- Increased length of stay in hospital and greater transfusion needs due to longer time to engraftment (costs increase)
- Lack of donor lymphocyte infusions for immunotherapy following loss of donor chimerism
- Lack of experience and long term outcomes
Adequate stem cell collection

Bone marrow stem cell
● TWC : 3-5 x 10^8 cell/kg of recipients
● CD34+ : 3-5 x 10^6 cell/kg of recipients

Peripheral blood stem cell
● TWC : 3-5 x 10^7 cell/kg of recipients
● CD34+ : 3-5 x 10^5 cell/kg of recipients
Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Approaches to eradicate malignant cells

- Myeloablative conditioning regimens
- Reduced intensity conditioning regimen
  - Non-myeloablative conditioning regimen
Myeloablative conditioning regimens

- Goal: To kill as many malignant as possible
  - AlloHSCT: prevent graft rejection
- Usually include anticancer drugs given at very high dose
  - Associated with severe BM suppression
  - Cyclophosphamide is commonly used
  - Other anticancer drugs may be added in some type of cancer
- Total-body irradiation (TBI) is used for eradicate malignant cell located in inaccessible area via CMT
Myeloablative conditioning regimens for Leukemia

- Most leukemia pts undergoing alloHSCT receive
  - Cyclophosphamide and TBI (CyTBI)
  - Busulfan and Cyclophosphamide (BuCy)
- TBI can be given as single dose or fractioned
  - No longer use: Acute and Chronic toxicity, Need specialized equipment, not superior than CMT
- Busulfan IV reduce variability of systemic exposure (correlate with outcome)
# Myeloablative conditioning regimens
## Leukemia (FYI)

<table>
<thead>
<tr>
<th>Preoperative regimen</th>
<th>Regimen</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>CyTBI (gold standard) Cyclophosphamide + Total body irradiation (total dose = 1200 cGy)</td>
<td>60 mg/kg/d IV q24h x 2d fractionated daily (ex. = 200 cGy bid x 3d)</td>
<td>-5, -4 -3, -2, -1</td>
</tr>
<tr>
<td>BuCy (gold standard) Busulphan PO (IV) + Cyclophosphamide</td>
<td>1mg/kg/dose PO (0.8mg/kg/dose IV) q6h x4d 50mg/kg/d IV q24h x 4d</td>
<td>-9, -8, -7, -6 -5, -4, -3, -2</td>
</tr>
</tbody>
</table>
Myeloablative conditioning regimens
Lymphoma

- TBI usually not included in conditioning regimen because
  - Many lymphoma pts receive prior radiotherapy
  - Delivers as much radiation to normal organ than tumor cell (Anti-CD20-radiolabeled monoclonal antibodies: \(^{131}\text{I}-\text{tositumomab}\))

- Regimen used in AutoHSCT: include
  - Alkylating agent (Cyclophosphamide, Melphalan)
  - Carmustine
  - Etoposide
# Myeloablative conditioning regimens

## Lymphoma (FYI)

<table>
<thead>
<tr>
<th>Preoperative regimen</th>
<th>Regimen</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CBV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>1800 mg/m² IV Q24H</td>
<td>-6, -5, -4, -3</td>
</tr>
<tr>
<td>BCNU</td>
<td>450 mg/m²</td>
<td>-3</td>
</tr>
<tr>
<td>Etoposide</td>
<td>500 mg/m² IV Q24H</td>
<td>-6, -5, -4, -3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BEAC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCNU</td>
<td>300 mg/m² IV</td>
<td>-7</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100 mg/m² Q12H x 8 doses</td>
<td>-6, -5, -4, -3</td>
</tr>
<tr>
<td>Ara-C</td>
<td>100 mg/m² Q12H x 8 doses</td>
<td>-6, -5, -4, -3</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>35 mg/kg/day IV</td>
<td>-6, -5, -4, -3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BEAM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCNU</td>
<td>300 mg/m² IV</td>
<td>-6</td>
</tr>
<tr>
<td>Etoposide</td>
<td>200 mg/m² Q12H</td>
<td>-5, -4, -3, -2</td>
</tr>
<tr>
<td>Ara-C</td>
<td>200 mg/m² Q24H</td>
<td>-5, -4, -3, -2</td>
</tr>
<tr>
<td>Melphalan</td>
<td>140 mg/kg/day IV</td>
<td>-1</td>
</tr>
</tbody>
</table>
Reduced intensity conditioning regimens (RIC)

- Goal: Suppress immune system prevent graft rejection
- RIC used synonymous “nonmyeloablative”
- Rational of RIC based on assumption that most of tumor cell kill in AlloHSCT as result of Graft-Versus-Tumor effect (GVT)
- The major advantage is potential curative to pts would not be considered HSCT because high risk for complication
- Most of regimen include fludarabine combined with TBI or Alkylating agent
## Reduced intensity conditioning regimen (FYI)

<table>
<thead>
<tr>
<th>Preoperative regimen</th>
<th>Regimen</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>60 mg/kg IV Q24H</td>
<td>-7, -6</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>25 mg/m² IV Q24H</td>
<td>-5 to -1</td>
</tr>
<tr>
<td></td>
<td>25-30 mg/m² IV Q24H</td>
<td>-6 to -2</td>
</tr>
<tr>
<td></td>
<td>100-180 mg/m² IV Q24H</td>
<td>-2</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>30 mg/m² IV Q24H</td>
<td>-10 to -5</td>
</tr>
<tr>
<td>Melphalan</td>
<td>1 mg/kg/dose PO Q6H x 8 doses</td>
<td>-6, -5</td>
</tr>
<tr>
<td>ATG (horse)</td>
<td>10 mg/kg/day IV Q24H</td>
<td>-4 to -1</td>
</tr>
</tbody>
</table>
Reduced intensity conditioning regimen (RIC)

- Some RIC are not completely myeloablative
  - Host hematopoietic can persist lead to mixed chimerism
  - Increase risk of graft rejection, GVHD, relapse
  - Monitoring donor chimerism posttransplant may allow to prevent graft rejection or relapse
- Donor lymphocyte infusion (DLI) can be administered to enhance GVT
Reduced intensity conditioning regimen (RIC)

Hematologic stem cell transplantation process

- Initial consult to establish appropriateness
  BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Immunosuppression

For AlloHSCT

- Prevention of rejection
  - Achieved immunosuppressive of conditioning regimen
  - Required to eradicated host immune system

- Prevention GVHD
  - Achieved with long-term immunosuppressant
  - Initiated prior to infusion stem cell until > 6 mo of HSCT or resolve GVHD
  - Required to suppress donor immune
## Immunosuppression
### Therapeutic drug monitoring

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Drug concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine</td>
<td>150-450 ng/mL (&lt;200-300 ng/mL related to GVHD)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>5-20 ng/mL</td>
</tr>
<tr>
<td></td>
<td>5-10 ng/mL (if sirolimus combine)</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>3-12 ng/mL</td>
</tr>
<tr>
<td>Micophenolate</td>
<td>Level has not been established</td>
</tr>
</tbody>
</table>
Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Infusion of stem cell

- Day of infusion of stem cell referred as day 0
- May be infusion of
  - Fresh: AlloHSCT
  - Thawed: cryopreserved AlloHSCT or AutoHSCT
- Infused via central line
  - Thawed stem cell must be infused rapidly due to viability post thawing
  - Benedryl® 25 mg IV is typically given
- Cryopreserved may be associated with DMSO toxicity
  - Nausea, Bradycardia, Garlic-like odor
  - Separate to over several days to avoid toxicity
Engraftment

- Engraftment indication
  - Sustained ANC > 0.5 x 10^9 cells/L
  - Platelet count > 20 x 10^9 cells/L
  - Sustained for 3 consecutive day

- Time to neutrophil engraftment (Median)
  - With BMSC : 12-21 days
  - With PBSC : 9-14 days
  - With UCB : 21-28 days

- Time to platelet recovery (Median)
  - With BMSC : 18-32 days
  - With PBSC : 11-21 days
  - With UCB : 35-45 days
Engraftment

Evidence
- DNA analysis
- Donor sex chromosome
- Donor blood group

Thalassemia patient
- Normal Hb, Hct, Reticulocyte count
- Donor hemoglobin typing

Malignancy patients
- No evidence of previous malignancy
Engraftment
Role of Hematopoietic growth factors

- **AutoHSCT**: usually give hematopoietic growth factors
  - Usual dose: GM-CSF 250 mcg/m2/day, G-CSF 5-10 mcg/kg/day
  - Beginning on the day of or day after infusion of stem cells and continued until neutrophil recovery

- **AlloHSCT**: not considered standard of care
  - Growth factors can modify T-cell and dendritic cell function associated with acute GVHD

Hematologic stem cell transplantation process

- Initial consult to established appropriateness BMT/HSCT
- Patient evaluation
- Donor evaluation
- Collection stem cells
- Conditioning regimen
- Immunosuppressant
- Infusion of stem cell
- Monitoring and management complication
Prevent and Treatment complications

- Chemotherapy side effects
  (dose limiting nonhematologic toxicity)
- Graft-Versus-Host-Disease
  - Acute GVHD
  - Chronic GVHD
- Infections
### Dose limiting Nonhematologic toxicity

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiotoxicity</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Busulphan, Etoposide, Melphalan, Total body irradiation</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>Busulphan, Carmustine</td>
</tr>
<tr>
<td>Mucositis</td>
<td>Etoposide, Melphalan</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>Carboplatin, Iphosphamide, Thiotepa</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>Fludarabine, Iphosphamide, Thiotepa</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Busulphan, Carmustine, Total body irradiation</td>
</tr>
</tbody>
</table>
Graft-Versus-Host-Disease (GVHD)

- Billingham criteria
  - Graft must contain immunocompetent cells
  - Host must possess transplantation alloantigens that are lacking in the donor graft such that host appears foreign to the graft and thus is capable of stimulating it antigenically
  - Host must be incapable of mounting an effective immunological reaction against graft, at least for sufficient time for the latter to manifest its immunological capabilities
Comparison of immunologic source of stem cells

<table>
<thead>
<tr>
<th>Relative risk</th>
<th>Allogeneic</th>
<th>Syngeneic</th>
<th>Autologous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>GVHD</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other complication</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Engemann AM. ACCP/ASHP Oncology Pharmacy Preparatory Review Course 2010.
Graft-Versus-Host-Disease (GVHD)

- GVHD cause by donor T cell reacting against host antigens presented by antigen-presenting cell
- Type of GVHD
  - Acute GVHD: Classic, Persistent, Recurrent, Late onset
  - Chronic GVHD: Classic, Quiescent/interrupted, de novo, overlap syndrome
Acute Graft-Versus-Host-Disease

- Usually presents prior to day 100 posttransplant (Classic acute GVHD)
- Can persist after day 100 (Persistent, Recurrent, Late-onset) result of
  - Immunosuppressive withdrawal
  - Relapse or persistent malignancy
  - Administration DLI or RIC regimen
- Incidence
  - Moderate to severe (grade II-IV) 10-80%
  - Mortality 10-20% of acute GVHD pts
Acute Graft-Versus-Host-Disease

Manifestation

- **Skin**: Maculopapular rash, Erythematous rash
  - Face, ear, palms, soles, upper trunk
  - Dx Skin Bx (lymphocytic infiltrates, eosinophil bodies)
- **Liver**: cholestatic jaundice
  - Dx Liver Bx (often not done > Low platelet count)
- **GI tract**: Secretory, watery, diarrhea
  - Dx Gut Bx (crypt cell degeneration)
Acute Graft-Versus-Host-Disease

Prevention
- Donor selection based on MHC match
- Reduce intensity conditioning regimen
- Modulate T cells by reducing
  - T cells number, activation, proliferation
  - Immunosuppressants
- Block inflammatory cytokine
  - TNF-α inhibitors
  - IL-1 receptor antagonist
Acute Graft-Versus-Host-Disease

Treatment

● **1st line**: Corticosteroids
  ● Prednisolone or MP: 2 mg/kg/day (range 1-10)
  ● Recent publication suggest 1 mg/kg/day for Grade I-II GVHD
  ● Short taper over 1-3 mo depend on response

● **2nd line**: varies
  ● Cyclosporine or Tacrolimus (If not in prophylaxis regimen)
  ● ATG, MMF, Monoclonal ab (Infliximab)

● Investigation

ATG = Antithymocyte globulin, MMF = Mycophenolate mofetil
Acute Graft-Versus-Host-Disease

Specific agent for Gastrointestinal GvHD

- Prednisolone 1-2 mg/kg/day for 10 days +
- Beclomethasone 6 mg PO daily for 50 days
- Multicentered RCT, Phase III, n= 62 On an ITT assessment time to GvHD treatment failure was longer in beclomethasone cohort
- Fewer deaths were reported in beclomethasone cohort

Chronic Graft-Versus-Host-Disease

- Occur after 100 days post alloHSCT
  - Range 2 months to 2 years
  - May be present before day 100 (New diagnostic criteria)
- Chronic GVHD w/o Characteristic of acute GVHD (classic chronic GVHD)
  - Quiescent: occur after resolution acute GVHD
  - De novo: no prior GVHD
  - Overlapping syndrome: both acute and chronic GVHD occur simultaneously
Chronic Graft-Versus-Host-Disease

Risk factors (Established)
- Prior acute GVHD
- Increasing age of recipient
- Donor leukocyte infusion (DLI)
- Mismatched or Unrelated donor
- CML or Aplastic anemia
- Female donor to male pts
- PBSC
- T cell replete graft

Risk factor (Controversial)
- CMV seropositive
- CMV reactivation
- Splenectomy
- Ethnic diversity between donor and patients
- UCB (Lower incidence)
- Steroid in acute GVHD prophylaxis
- High CD34+ cell count
- Lack of MTX in acute GVHD prophylaxis
Ocular sicca
Oral ulcers
Nail dystrophy
Skin sclerosis
Deep sclerosis
Bronchiolitis obliterans
Loss of bile ducts
Fasciitis
Skin ulcers

Spectrum of manifestations in chronic GvHD

Infections
Disability
Quality of life
Endocrine
Metabolism
Nutrition
Pain
Chronic Graft-Versus-Host-Disease

Diagnosis cGVHD require

1. Distinction from acute GVHD
2. Presence at least
   - 1 diagnostic clinical sign of cGVHD
   - 1 distinction manifestation confirmed by biopsy or other relevant test
3. Exclusion of other possible diagnoses
Chronic Graft-Versus-Host-Disease

NIH Consensus Development Project

- Clinical scoring system: 0-3
- Grade each organ system and considers the impact of cGVHD on patient’s functional status

- Component of scoring system:
  - Evaluation/scoring of severity of each organ/site
  - Consideration of number of organs involved
## Categories of cGVHD

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involves only 1 or 2 organs/sites (except lung) with no clinically significant functional impairment (maximum score of 1 in all affected organs/sites)</td>
<td>Involves at least 1 organ/site with clinically significant but no major disability (maximum score of 2 in any affected organ/site) OR 3 or more organs/sites with no clinical significant functional impairment (maximum score of 1 in all affected organs or sites)</td>
<td>Indicates major disabilitiy caused by cGvHD- score of 3 in any organ or site. A lung score of 2 or greater will also be considered severe cGvHD</td>
</tr>
</tbody>
</table>
Chronic Graft-Versus-Host-Disease

Treatment

- Indication for treatment (Systematic therapy)
  - Chronic GVHD involves at least 3 organs or
  - With a score 2 Greater in any one organ

- Treatment option include
  - Alternate day prednisolone (1 mg/kg/day)
  - Prednisolone every other day with cyclosporine every other day (6 mg/kg PO bid)
  - Photophoresis has demonstrated efficacy for skin, liver, eye, lung (PUVA)
  - Rituximab (Small series published) 

---

Chronic Graft-Versus-Host-Disease

Supportive care essential

- Infection prophylaxis: (PCP, encapsulated organism)
  - Continuous TMP/SMX or
  - Daily Penicillin with twice weekly TMP/SMX

- Skin:
  - Avoidance sun exposure
  - Intact skin: topical emollient, steroid, antipruritic
  - Erosion/ulceration: culture, antibacterial, dressing
Infection

- American Society for Blood and Marrow Transplantation (ASBMT) clinical practice guidelines for preventing opportunistic infections in patients following HSCT

- Types of infections based upon time elapsed since HSCT
  - Pre-engraftment: <15-45 days
  - Immediate post-engraftment: 30-100 days
  - Late post-engraftment: >100 days
Phase I: pre-engraftment

Graft-versus-host-disease: acute

- Neutropenia, barrier breakdown (mucositis, central venous access devices)

Phase II: post-engraftment

- Impaired cellular and humoral immunity; NK cells recover first, CD8 T cell numbers increasing but restricted T cell repertoire

Phase III: late phase

- Impaired cellular and humoral immunity; B cell & CD4 T cell numbers recover slowly and repertoire diversifies

**Bacterial**
- Gram negative bacilli
- Gram positive organisms
- Gastrointestinal *streptococci* species

**Viral**
- Herpes simplex virus
- Respiratory and enteric viruses (Seasonal/intermittent)
- Cytomegalovirus
- Varicella zoster virus
- Other viruses eg. HHV
- EBV PTLD

**Fungal**
- *Aspergillus* species
- *Candida* species
- *Aspergillus* species
- *Pneumocystis*

Day 0-10

Day 10-45

Day 100

Day 365 and beyond
Prophylaxis
Bacterial

- Gram-negative: strong consider FQ in pt with anticipated neutropenic > 7 days
  - 1st line: Levofloxacin 500 mg OD (Bl), Ciprofloxacin 500 mg BD (BII)
  - Alternative: Azithromycin 250 mg OD (CIII)
  - Duration: stem cell infusion until neutropenic recovery
- Decontamination with metronidazole not recommended

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Fungal

Yeast (Candida species)

- **AlloHSCT**: Fluconazole 400 mg/day
- **AutoHSCT**: use only in
  - Pts with hematologic malignancies
  - Prolonged neutropenia
  - Received Fludarabine or Cladrabine pre-transplant
- **Alternative**: Itraconazole, Voriconazole, Posaconazole, Micafungin
- **Duration**
  - Allo: +75 days
  - Auto: Engraftment or 7 days after ANC > 1000 cells/mm^3

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Fungal

Molds

● Prophylaxis in pts with
  ● Prolong neutropenia
  ● GVHD

● Recommended
  ● Micafungin 50 mg IV OD (BI)
  ● Posaconazole 200 mg PO 3 times/day (BI)

● Alternative : Voriconazole (BII)
  ● Adults >40 kg: 4 mg/kg twice daily i.v. or 200 mg twice daily orally
  ● Pediatrics:
    ● ≥ 20 kg: 100 mg twice daily i.v. or orally
    ● < 20 kg: 50 mg twice daily i.v. or orally

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Pneumocystis carinii pneumonia

- All AlloHSCT
- AutoHSCT: use only in
  - Pts with hematologic malignancies
  -Received Fludarabine or Cladrabine pre-transplant
- Recommended
  - TMP/SMX DS 3 times/week
  - TMP/SMX SS QD
- Alternative
  - Dapsone 50 mg PO BID or 100 mg PO QD
  - Aerosolized pentamidine 300 mg q 3-4 weeks
- Duration: From engraftment at least 6 months HSCT
  - TMP/SMX may affect bone marrow cells engraftment

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Viral

Herpes Simplex Virus

- All HSV-seropositive HSCT
- Recommended
  - Acyclovir (200 mg PO TID or 250 mg/m²/dose IV Q12H)
- Alternative: Valacyclovir
- Duration: Beginning of conditioning regimen until engraftment or mucositis resolves

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Viral

Varicella Zoster Prophylaxis

- AlloHSCT or AutoHSCT
- Recommended
  - Acyclovir 800 mg PO BID
  - Valacyclovir 500 mg PO QD/BID
- Duration: Beginning of conditioning regimen until
  - 1 year after AlloHSCT or AutoHSCT
  - 6 months after discontinue immunosuppressant

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Prophylaxis
Viral

Influenza A and B

- Lifelong annual seasonal influenza vaccination
  - Start before HSCT and restart 6 mo after HSCT
- Prophylaxis during outbreak influenza
  - Rimantadine 100 mg PO BID
- Consideration given neuraminidase inh (oseltamivir) if pts have symptoms during outbreak

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Vaccination of HCT recipient

- Antibody titers to vaccine-preventable diseases decline after stem cell transplantation
- Naïve T cell capable of responding to antigen at 6-12 months posttransplant
  - Inactivated vaccine: 6 months
  - Live-attenuated vaccine: > 2 years
- Chronic GVHD also need vaccination
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
<th>Initial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal</td>
<td>Preferred conjugated vaccine (7 strains) &gt; polysaccharide (23 strains)</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Diphtheria-tetanus</td>
<td>Preferred Full dose (DT) &gt; Reduced dose (Td) DT not approved for &gt; 7 yo</td>
<td>6-12 months</td>
</tr>
<tr>
<td>Pertussive</td>
<td>Recommended use acellular &gt; whole cell Tdap is available</td>
<td>6-12 months</td>
</tr>
</tbody>
</table>

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
<th>Initial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polio</td>
<td>Inactivated polio vaccine (IPV)</td>
<td>6-12 months</td>
</tr>
<tr>
<td>Influenza</td>
<td>Inactivated vaccine (seasonal vaccine)</td>
<td>4-6 months</td>
</tr>
<tr>
<td>Hib</td>
<td>Hib conjugated vaccine</td>
<td>6-12 months</td>
</tr>
<tr>
<td>Varicella</td>
<td>Preferred Chickenpox (Varivax : Low viral titier) &gt; Shingles (Zostavax)</td>
<td>&gt;24 months</td>
</tr>
<tr>
<td>MMR</td>
<td>Live-attenuated vaccine</td>
<td>&gt;24 months</td>
</tr>
</tbody>
</table>

ASBMT. Biol Blood Marrow Transplant 2009;15:1143-1238
Pharmacist roles
Bone marrow transplantation

- Provide medication information about
  - Conditioning regimens selection based on patient risk factors
- Administration and Compatibility
- Preventions transplantation related complication
  - Prophylaxis antibiotics selection
  - Prophylaxis Immunosuppressants
- Calculate chemotherapy dose for individual patient
- Monitor medication efficacy and side effects
- Treatment transplant related complications
- Patient educations
Thank you for your attention