Conditioning regimens

- **Immunoablation**
  - CyTBI
  - BuCy

- **Myeloablation (Cytoreduction)**
  - FluMel
  - FluBu
  - BEAM
  - FluCy
  - FluTBI
  - TBI

RIC ➔ MAST

- CyTBI
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Conditioning regimens

- Immunoablation
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- Myeloablation (Cytoreduction)
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- FluMel
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Myeloablation (Cytoreduction)
Conditioning regimens

- Immunoablation
- Myeloablation (Cytoreduction)

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- BEAM

- MAST
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1. Aggressiveness of malignancy
2. Degree of GVM
3. Disease status (chemosensitive vs refractory)
4. Age / comorbidities*
<table>
<thead>
<tr>
<th>Conditioning / neutropenic</th>
<th>1-3 / 6mths</th>
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<tbody>
<tr>
<td><strong>Treatment-related toxicity</strong></td>
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GVHD 1

- What is GVHD?
  - Donor immune reaction against recipient’s tissues
- Main clinical challenge in allogeneic SCT
  - Major cause of both short and long-term morbidity and mortality post-transplantation
  - Direct effects
  - Indirectly 2nd complications of (immunosuppressive) therapy
GVHD 2

- Divided into acute vs chronic
- Acute GVHD
  - Donor T-cells reacting against host allo-antigens
  - “Graft rejects host”
  - Inflammatory dermatitis, enterocolitis and/or hepatitis
  - Moderate-severe acute GVHD
    - 50-70% response rate
    - 50% OS
GVHD 3

- Therapy improving
- Improved survival wrt historical outcomes
- Combination ATG + etanercept + tacrolimus

_BMT 2006; 37: 1143_
Chronic GVHD

- Abnormal maturation of donor immune system in new host
- Pleiotropic syndrome characterized by oral and ocular sicca in association with fibrotic and / or autoimmune manifestations and immunodeficiency
- Therapy based around prolonged high dose prednisolone +/- other IS drugs

Prognosis:
- Extensive stage 5yr OS 50-70%
Donor source

- Historically VUD associated with significantly increased morbidity and mortality compared with matched sibling donor
- Now survival outcomes equivalent with VUD and sibling donors
  - Better matching techniques reduce GVHD rates in VUD transplants
    - High resolution (gene) matching across 10 (not 6) HLA loci
    - HLA-A, B, C, DRB1 and DQ
  - Improvement in supportive care associated with reduced mortality
    - Pre-emptive monitoring / therapy of CMV
    - Improved fungal prophylaxis / therapy
    - Improved therapy of GVHD
Allogeneic SCT - immune reconstitution

- Defects in T and B-cell function persist for yrs post-SCT and are exacerbated by presence of chronic GVHD
  - Depressed CD4 T-cell numbers
    - Associated with
      - Functional defects in T-cell responses to mitogens
      - Increased susceptibility to viral infections
  - Absolute B-cell numbers recover by 1-2 months, but Ig levels and functional B-cell deficits take longer
    - IgG 6-9mths; IgM 9-12mths; IgA 2-3yrs
    - Reduced capacity to make specific Abs to specific antigens
    - Reduced capacity to class switch Ab production (IgM to IgG)
    - Increased risk of infection from encapsulated bacteria for months to years
Allogeneic SCT - vaccinations

- Start vaccinations at 12mths **and** off systemic IS
  - Inactivated polio vaccine (eIPV)
  - Adult tetanus/diphtheria toxoid (ADT)
  - Hepatitis B vaccination
  - Pneumococcal vaccine
  - Haemophilus Influenza Type B Vaccine

- 2 years post transplant
  - Measles, mumps, rubella (MMR - live attenuated vaccine) **ONLY** if no chronic GVHD and **no IS**

- Annually every April
  - Influenza vaccine

- Vaccinations **NOT** recommended and / or **contraindicated**
  - Meningococcal vaccine - only consider if risk of meningococcal disease felt to be significantly increased
  - Pertussis vaccine – not recommended
  - BCG vaccination - contraindicated
Confused??
Risks of SCT

Risks of underlying disease
Indications of SCT

- Response rate / curability without SCT?
  - Outcomes at relapse

- Response rate / curability with SCT?
  - Predicted overall survival (OS)
  - Predicted progression free survival (PFS)
  - Predicted event-free survival (EFS)

- Individual QOL issues
Indications of SCT

- **Leukaemia**
  - Chemotherapy vs allogeneic SCT
  - Extremely limited / no role autologous SCT
    - Outcomes no different wrt chemotherapy alone

- **Lympho-proliferative disorders**
  - Chemotherapy vs autologous SCT
  - Role for allogeneic SCT generally only after relapse post-autologous SCT due to
    - Prognosis of underlying disorder
    - Toxicity of allogeneic SCT
Acute myeloid leukaemia (AML)

- Outcome with standard chemotherapy related to:
  - Cytogenetics:
    - Good, intermediate, poor (Intergroup; SWOG; MRC)
  - Molecular characteristics
    - FLT-3, NPM1
  - Age > vs <55-60yrs
  - De novo vs secondary
    - Post chemotherapy
    - Transformed prior BM disorder (MDS, MPD)
  - Chemosensitive vs refractory
  - CR1 vs beyond 1st remission
# AML - cytogenetics

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CG: t(15;17); inv(16), t(8;21) without del(9) or complex

NO SCT in CR1
# AML - cytogenetics

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complex (>= 3 changes), -5 / del (5q), -7 / del (7q), inv (3q), 11q, 20q, 21q, 17p, del (9q), t (6;9), t (9;22)

Allo SCT in CR1 (sibling or VUD)
OS, poor risk <60yrs de novo AML RBWH 2001-2004, SCT in CR1 vs not
# AML - cytogenetics

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+8, -Y, +6, del (12p), normal
# AML - molecular

## Normal cytogenetics

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<td>FLT3 (regardless of NPM1 status)</td>
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<td>Poor</td>
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NEJM 2008; 358: 3509
# AML - molecular

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<td>Sibling or VUD Allo</td>
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AML - other

- Clinical factors associated with poor outcome irrespective of CG / molecular markers
  - Age >55-60yrs
  - Refractory AML
  - 2nd AML
  - Relapsed AML
- Allo SCT (Sibling or VUD)
OS, de novo AML >60yrs, RBWH 2000-2004 by cytogenetic risk (n=32)

(median OS ~10mths)
OS – AML allo SCT RBWH 2000-2007 (n=157)

Median OS: 7.18 Years
2YR OS: 61%
5YR OS: 55%

<60 (n=135)
>60 (n=22)
AML allo SCT RBWH 2000-2007

5 YR TRM: 24.5%

5YR Rel Risk: 31.5%