ALLOGENEIC STEM CELL TRANSPLANTATION @ ASH 2015

TESSA KERRE
POST ASH MEETING 8-1-2-016
Selection ‘bias’

- Prospective randomized controlled trials
  - Oral > poster
- Belgian presenters/authors
  - Mauricette Michallet
Indications

Donor

Conditioning

Microbioma

aGVHD
cGVHD

Complications

Post-SCT strategies

Relapse

score

Immunotherapy
INDICATIONS

- AML
- Multiple myeloma
Indications: AML

Abstract #4364 (X Poire et al): allo sct for elderly pts with int risk AML and flt3-itd (a study of alwp of ebmt)

- **QUESTION**: pts ≥ 60y with IRC-AML and FLT3-ITD: indication for allo SCT
- **STUDY**:
  - Retrospective (EBMT registry)
  - Inclusion: de novo acute myeloid leukemia (AML), IRC-AML and FLT3-ITD, MRD or MUD (9/10 or 10/10), SCT January 2000 - July 2014 (N=205)
- **RESULTS**:

![Graphs showing LFS and OS with percentage values](image-url)
Indications: AML

Abstract #4364 (X Poire et al): allo sct for elderly pts with int risk AML and FLT3-ITD (a study of alwp of ebmt)

• CONCLUSIONS:
  – Allogeneic SCT in elderly (≥ 60 up to 75 year-old) patients with IRC-AML and FLT3-ITD: good treatment strategy if performed in CR1
  – independently of age
  – somewhat inferior outcome in transplants from unrelated donors.
Indications: multiple myeloma

Abstract #4373 (J. Perez-Simon et al): allo sct as first line rescue for relapse of MM after 1st line containing auto SCT

- **AIM:** outcome of pts with MM after allo SCT as treatment for relapse after 1st line treatment containing auto SCT

- **STUDY:**
  - retrospective analysis (EBMT registry)
  - Inclusion: pts with MM, relapse within first year after 1st line treatment (including autoSCT), treated with allo SCT. SCT 1991-2014 (N=573).
  - Conditioning: MAC (N=102), RIC (N=284), NMA (N=120), tandem auto-allo (N=67).
Indications: multiple myeloma

Abstract #4373 (J. Perez-Simon et al): allo sct as first line rescue for relapse of MM after auto SCT

• RESULTS
Indications: multiple myeloma

Abstract #4355 (M shippton et al): Seattle ric regimen for MM

• **QUESTION**: evaluate safety, tolerability and efficacy of RIC-SCT in MM, in CR after auto-SCT.

• **STUDY**
  - **Retrospective**, multi-center study
  - Inclusion: MM, CR after auto SCT (N=42)
  - Conditioning: RIC Seattle regimen (30 mg/m² fludarabine and 2 Gy TBI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
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<tbody>
<tr>
<td>Median β₂-microglobulin at diagnosis, mg/L (range)</td>
<td>3.1 (1.5-18.0)</td>
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<td>Median albumin at diagnosis, g/L (range)</td>
<td>40.5 (21.0-49.0)</td>
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<td>Median age at RIC in years (range)</td>
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<td>Median time from diagnosis to RIC in months (range)</td>
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<td>Time when RIC administered (%)</td>
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<td>First remission</td>
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<td>Remission status at RIC (%)</td>
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<td>13 (38.2)</td>
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<td>2 (5.9)</td>
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</table>

**Table 1: Baseline patient characteristics**
Indications: multiple myeloma
Abstract #4355 (M shipton et al): seattle ric regimen for MM

• RESULTS
  – TRM @D100: 2.4%, TRM @1y: 9.5%
  – cGVHD: 82%
  – Association between GVHD and enhanced disease control
  – Relapse @2y 50%, salvage treatment with DLI/IMIDs
  – Potentiated response to lenalidomide (despite previous treatment with IMIDs in majority of pts)
  – OS@2y 70%
DONOR CHOICE

• MRD vs MUD
• Alternative donor: CB – MMUD – Haplo
• Age of the donor
Donor choice: MRD vs MUD

Abstract #4380 (c yam et al): unrelated donors are associated with improved RFS compared to related donors in pts with MDS undergoing RIC allo SCT

• AIM: Determine optimal donor for pts with MDS (older MRD, younger MUD)
• STUDY:
  – Retrospective Multi-variable analysis
  – Conditioning Flu/Bu

<table>
<thead>
<tr>
<th>Donor Type</th>
<th>Median Recipient Age at Transplant – yrs (range)</th>
<th>Median Donor Age at Transplant – yrs (range)</th>
<th>Median Time from Diagnosis to Transplant – mths (range)</th>
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<tbody>
<tr>
<td>Unrelated donor</td>
<td>64 (50-72)</td>
<td>60 (52-70)</td>
<td>14.9 (5.0-135.8)</td>
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<tr>
<td>Related donor</td>
<td>32 (19-53)</td>
<td>60.5 (42-72)</td>
<td>9.2 (4.5-98.6)</td>
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<table>
<thead>
<tr>
<th>IPSS Score at Diagnosis</th>
<th>Related donor (n=19)</th>
<th>Unrelated donor (n=38)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Low/Int-1 – no. (%)</td>
<td>12 (35)</td>
<td>8 (42)</td>
<td>1.00</td>
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<tr>
<td>Int-2/High – no. (%)</td>
<td>15 (44)</td>
<td>9 (47)</td>
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<tr>
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<table>
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<tr>
<th>WHO Classification at Diagnosis</th>
<th>Related donor (n=19)</th>
<th>Unrelated donor (n=38)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>RAEB1/2 – no. (%)</td>
<td>14 (44)</td>
<td>10 (33)</td>
<td>0.18</td>
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<tr>
<td>Other – no. (%)</td>
<td>18 (53)</td>
<td>9 (47)</td>
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<tr>
<td>Unknown – no. (%)</td>
<td>2 (6)</td>
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<thead>
<tr>
<th>WHO Classification at Transplant</th>
<th>Related donor (n=19)</th>
<th>Unrelated donor (n=38)</th>
<th>p value</th>
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<tbody>
<tr>
<td>RAEB1/2 – no. (%)</td>
<td>6 (18)</td>
<td>4 (21)</td>
<td>0.72</td>
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<tr>
<td>Other – no. (%)</td>
<td>25 (77)</td>
<td>13 (68)</td>
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<tr>
<td>Unknown – no. (%)</td>
<td>2 (6)</td>
<td>2 (11)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.
Baseline characteristics of patients and donors
Donor choice: MRD vs MUD

Abstract #4380 (c yam et al): unrelated donors are associated with improved RFS compared to related donors in Pts with MDS undergoing RIC allo SCT

• RESULTS:
DONOR CHOICE: ALTERNATIVE DONORS
C. ANASETTI: EDUCATIONAL

• Barriers to full success of alternative donors
  – GVHD
  – Graft failure
  – Immune deficiency
  – Relapse
DONOR CHOICE: ALTERNATIVE DONORS
C. ANASETTI: EDUCATIONAL

- Limitations in comparing outcomes of SCT from different HSC sources

<table>
<thead>
<tr>
<th></th>
<th>Unrelated adult MMUD</th>
<th>Unrelated cord</th>
<th>Related haplo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age</td>
<td>Children (Children)</td>
<td>Children (Children)</td>
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<td>Adults (Adults)</td>
<td>Adults (Adults)</td>
<td>Adults (Adults)</td>
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<td>Conditioning</td>
<td>Non-myeloablative (Non-)</td>
<td>Non-myeloablative</td>
<td>Non-myeloablative (Non-)</td>
</tr>
<tr>
<td></td>
<td>Myeloablative (Myeloablative)</td>
<td>Myeloablative (Myeloablative)</td>
<td>Myeloablative (Myeloablative)</td>
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<td>GVHD prophylaxis</td>
<td>ATG (ATG)</td>
<td>Cy/MMF (Cy/MMF)</td>
<td>Post SCT CY (Post SCT CY)</td>
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<td></td>
<td>Tac/MTX (Tac/MTX)</td>
<td></td>
<td>Tac/MMF (Tac/MMF)</td>
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<td>Comparisons</td>
<td>Retrospective (Retrospective)</td>
<td>Retrospective (Retrospective)</td>
<td>Retrospective (Retrospective)</td>
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</tbody>
</table>
## DONOR CHOICE: ALTERNATIVE DONORS
### C. ANASETTI: EDUCATIONAL

- Pros and cons of HLA-disparate related, unrelated donors or cord units

<table>
<thead>
<tr>
<th></th>
<th>Unrelated adult MMUD</th>
<th>Unrelated cord</th>
<th>Related haplo</th>
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</thead>
<tbody>
<tr>
<td>HLA disparity</td>
<td>Best</td>
<td>Intermediate</td>
<td>Worst</td>
</tr>
<tr>
<td>KIRs, CCR5, others</td>
<td>Best</td>
<td>Intermediate</td>
<td>Worst</td>
</tr>
<tr>
<td>Cell #/graft</td>
<td>Better</td>
<td>Worst</td>
<td>Better</td>
</tr>
<tr>
<td>Immune reconstitution</td>
<td>Better</td>
<td>Worse</td>
<td>Better</td>
</tr>
<tr>
<td>Cost</td>
<td>Intermediate</td>
<td>Worst</td>
<td>Best</td>
</tr>
<tr>
<td>Procurement time</td>
<td>Worst</td>
<td>Intermediate</td>
<td>Best</td>
</tr>
<tr>
<td>GVHD pathogenenicity</td>
<td>Worse</td>
<td>Better</td>
<td>Worse</td>
</tr>
<tr>
<td>Infectious transfer potential</td>
<td>Worse</td>
<td>Best</td>
<td>Worse</td>
</tr>
</tbody>
</table>
Donor choice: alternative donors
C. Anasetti: educational

1st choice = prospective clinical trials!

- Time critical?
  - yes: HAPLO
  - no: Cost limiting?
    - no: Recipient CMV?
      - neg: Adequate CB dose?
        - yes: CB (1-2)
        - no: unavailable
      - pos: 7/8 MMUD
        - KIR optimal
        - CMV match
        - ABO match

HLA antibodies must be negative against any graft!
Donor choice: alternative donors
C. Anasetti: educational

• Ongoing trial: BMT CTN Protocol 1101

Patient age 18-70
Acute leukemia or lymphoma
Adequate organ function and performance

Double CB and Haplo donor BOTH AVAILABLE
No donor-specific anti-HLA antibodies circulating

Randomization
Stratified by transplant center

Double CB
Haplo (BM)
Donor choice: alternative donors

Abstract #0152 (S gaballa et al): phase II clinical trial using PT CY for prevention of GVHD in haplo and MMUD SCT

• **AIM:** comparison haplo vs 9/10 MMUD

• **STUDY:**
  
  – **Prospective non-randomized** phase 2 clinical trial with two parallel arms, HAPLO (n=60) and 9/10 MUD (n=46) transplants
  
  – Inclusion: pts with advanced hematologic malignancies or aplastic anemia who lacked a MRD and 10/10 MUD.
  
  – Conditioning: MEL – thiotepa (if unavailable 2 Gy TBI) – fludarabine. If CD20-positive lymphoma: addition of rituximab (375 mg/m²)
  
  – GVHD prophylaxis: PTCy – MMF - tacrolimus
  
  – HSC source: unmodified bone marrow
Donor choice: alternative donors

Abstract #0152 (S gaballa et al): phase II clinical trial using PT CY for prevention of GVHD in haplo and MMUD SCT

- RESULTS

![Graph A: Haploidentical](image)

- OS
- PFS

![Graph B: 9/10 MUD](image)

- OS
- PFS
Donor: alternative donors - age of the donor

Abstract #0154 (S Seo et al): the impact of donor age on outcome after unrelated BMT: comparison with unrelated CB SCT

- **AIM**: comparison of unrelated donors (8/8, 7/8 and CB)

- **STUDY**:
  - **Retrospective** cohort study (registry JapanSHCT)
  - Inclusion: adult patients, $\geq 16$ y, with AML, MDS, ALL, or CML, 1st SCT 2000-2010 (N=6035)
  - Donors:
    - UBMT from 8/8 HLA-matched or 7/8 HLA-matched for HLA-A, -B, -C, and -DRB1 allele-level donor (N=3304)
    - single-unit UCBT from maximum 2-antigen (HLA-A, -B, -DR antigen-level) mismatched donor (N=2731)
Donor: age of the donor

Abstract #0154 (S Seo et al): the impact of donor age on outcome after unrelated BMT: comparison with unrelated CB SCT

• RESULTS

![Graph showing overall survival by donor types in standard risk group](image-url)
Donor: age of the donor

Abstract #0154 (S Seo et al): the impact of donor age on outcome after unrelated BMT: comparison with unrelated CB SCT

• CONCLUSIONS

• Worse outcome of HSCT recipients with older donor (≥40 years) compared with recipients of younger donor, esp in the standard risk group or HLA-mismatched donors

• Possible reason: higher incidence of aGVHD grade II-IV.

• If no 8/8 matched younger donor is available, viable options are:
  – a 7/8 matched younger donor
  – an 8/8 matched older donor
  – a (single) UCBT
Donor: age of the donor

Abstract #0151 (M showel et al): related NMA haplo SCT with PT Cy for AML: donor age impacts outcome

- **AIM**: impact of donor age in haplo SCT

- **STUDY**:
  - **Retrospective** review
  - Inclusion: all adult patients at Johns Hopkins, mini-haplo BMT for AML (January 2003 - February 2013) (N=93)
  - Conditioning with Cy - fludarabine - 200 cGy TBI; GVHD prophylaxis PTCy/MMF/tacrolimus.

- **RESULTS**

  ![OS and PFS of entire cohort](image1)
  ![OS according to age of the donor](image2)
Donor: age of the donor

Abstract #0151 (M showel et al): related NMA haplo SCT with PT Cy for AML: donor age impacts outcome

At Hopkins: no more age limits for patients, but considering age limits for donors: can’t change patient age, but can change donor age.

Be nice to your grandchildren this holiday season
50% of them are haploidentical to you...
CONDITIONING

• RIC vs MAC
  – In CB SCT for acute leukemia (AML/ALL)
  – In AML/MDS
• TMLI based conditioning for R/R AML/ALL
• RIC allo SCT: optimal conditioning regimen
  – Flu-Bu vs Flu-Mel
  – Flu-Bu vs Flu/TBI (400 cGy)
• The perfect allo SCT
Conditioning: RIC vs MAC in CB SCT

Abstract #0155 (F Baron et al): RIC vs MAC for unrelated CB SCT in adults with AL (Eurocord – EBMT)

• **AIM:** comparison RIC vs MAC in unrelated CB SCT for AL
• **STUDY:**
  – Retrospective (EBMT registry, EUROCORD)
  – Inclusion: adults, ≥ 18y, primary AL (AML/ALL), 1st single or double CB SCT (N=1352, RIC (N=518), MAC (N=834))
Conditioning: RIC vs MAC in CB SCT

Abstract #0155 (F Baron et al): RIC vs MAC for unrelated CB SCT in adults with AL (Eurocord – EBMT)

• RESULTS

<table>
<thead>
<tr>
<th></th>
<th>RIC</th>
<th>MAC</th>
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<tbody>
<tr>
<td>Relapse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.0001</td>
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<tr>
<td>NRM</td>
<td></td>
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<tr>
<td>P</td>
<td>=0.58</td>
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</tr>
<tr>
<td>PFS</td>
<td></td>
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<tr>
<td>OS</td>
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<tr>
<td>P</td>
<td>=0.012</td>
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</table>
Conditioning: RIC vs MAC in CB SCT

Abstract #0155 (F Baron et al): RIC vs MAC for unrelated CB SCT in adults with AL (Eurocord – EBMT)

• **RESULTS**: in comparison to MAC, RIC regimens:

**AML:**
- ↑ aGVHD
- ≈ cGVHD
- ↑ Relapse
- Trend ↓ NRM
- ≈ LFS
- ≈ OS

**ALL:**
- ≈ aGVHD
- ↓ cGVHD
- ↑ Relapse
- ↓ NRM
- ≈ LFS
- ≈ OS
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

- **AIM**: comparison RIC vs MAC in allo SCT for MDS/AML
- **STUDY**:
  - Prospective, phase III, randomized, multi-center
  - Inclusion: MDS (N=54) or AML (N=218)
  - Goal: 365 pts: accrual stopped because of presumed benefit of MAC

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<thead>
<tr>
<th>Condition</th>
<th>RIC Regimens</th>
<th>MAC Regimens</th>
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<td>Flu/Bu2</td>
<td>Flu/Mel</td>
<td>Flu/Bu4</td>
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<td>Flu/Mel</td>
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<td>Bu4/Cy</td>
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<tr>
<td></td>
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<td>Cy/TBI</td>
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18 Month Overall Survival

**Randomization**

- MDS/AML< 5% blasts
- 18-65 years
- PB/BM
- HCT-CI ≤ 4
- (-) CNS
- MRD/MUD (7/8)
- (-) circ. blasts

**GVHD**

Prophylaxis per Institutional guidelines: T-replete, post-transplant Cy excluded
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

• RESULTS

• OS

P=0.07 (18 month pointwise)
9.7% difference (95% CI: -0.9%, 20.3%) MAC vs. RIC

OS

RIC 67.7%
MAC 77.4%

Survival Probability

0.0 0.2 0.4 0.6 0.8 1.0

0 3 6 9 12 15 18

Months

RIC 137 129 117 102 96 89 82
MAC 135 130 126 114 109 99 89
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

- RESULTS
- OS

Survival Probability

MDS (N=54)  
P=0.71 (18 month pointwise)

AML (N=218)  
P=0.027 (18 month pointwise)
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

**RESULTS**

- **LFS**

### Survival Probability

<table>
<thead>
<tr>
<th>Months</th>
<th>MAC 135</th>
<th>125</th>
<th>115</th>
<th>105</th>
<th>99</th>
<th>86</th>
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<tr>
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<td>135</td>
<td>125</td>
<td>115</td>
<td>105</td>
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<tr>
<td>RIC</td>
<td>137</td>
<td>104</td>
<td>78</td>
<td>70</td>
<td>68</td>
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</tr>
</tbody>
</table>

**P < 0.01 (18 month pointwise)**

- Difference of MAC and RIC, 20.4% (95% CI: 8.8%, 31.9%)
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

- **RESULTS**
- **MAC:**
  - ↑ aGVHD II-IV (D100)
  - = aGVHD III-IV (D100)
  - ↑ cGVHD (18M)

P=0.02 (18 month pointwise)
Conditioning: RIC vs MAC in MDS/AML

Abstract #LBA-8 (Bart Scott et al): Results of a Phase III Randomized, Multi-Center Study of Allo SCT after High Versus Reduced Intensity Conditioning in Patients with MDS or AML (BMT CTN 0901)

• CONCLUSIONS
  • Incidence of aGVHD and cGVHD: higher after MAC
  • No significant difference in OS (p=0.07), but a significant difference in LFS, and for AML
  • MAC remains treatment of choice in AML/MDS
  • Future directions
    – Less toxic MAC regimens
    – In pts who require RIC: effective post SCT maintenance to improve disease control
Conditioning: TMLI

Abstract #0735 (A. Shein et al): phase 1 trial of TMLI based conditioning of allo SCT for acute leukemia

• STUDY: R/R AML/ALL; TMLI (5d) - VP16 - CY (N=51)
• TMLI dose escalation
  – Min 1200 cGy (8 fractions of 150 cGy, 2x/d)
  – Dose increase in increments of 150 cGy until:
    – 1500 cGy (10 fractions of 150 cGy, 2x/d)
    – Dose increase in increments of 100 cGy until
      – Max 2000 cGy (10 fractions of 200 cGy, 2x/d)
• HSC source: BM (N=3) or PBSC (N=48)
• Sir/tac for GVHD prophylaxis
Conditioning: TMLI

Abstract #0735 (A. Shein et al): phase 1 trial of TMLI based conditioning of allo SCT for acute leukemia

**STUDY:**

![Dose Distribution of Patient Treated at 2000 cGy]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (range) or N</th>
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<tbody>
<tr>
<td>Age at transplant (yrs)</td>
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<td>Disease diagnosis</td>
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<td>AML</td>
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<tr>
<td>ALL Ph−</td>
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<td>Biphenotypic</td>
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<tr>
<td>Undifferentiated</td>
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<tr>
<td>Disease status at HSCT</td>
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<td>1 RL</td>
<td>3</td>
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<tr>
<td>2 RL</td>
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<td>IF</td>
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<td>Cytogenetic risk (SWOG criteria)</td>
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</tr>
<tr>
<td>KPS at HSCT</td>
<td>80 (60–100)</td>
</tr>
<tr>
<td>Donor source</td>
<td></td>
</tr>
<tr>
<td>Sibling</td>
<td>25</td>
</tr>
<tr>
<td>HLA matched unrelated</td>
<td>21</td>
</tr>
<tr>
<td>Mismatched (1 allele) unrelated</td>
<td></td>
</tr>
<tr>
<td>WBC at HSCT</td>
<td>1.4 (0.1–14.9)</td>
</tr>
<tr>
<td>% Blasts in blood at transplant*</td>
<td>4 (0–93)</td>
</tr>
<tr>
<td>% Blasts in marrow at transplant*</td>
<td>52 (8–98)</td>
</tr>
<tr>
<td>Extramedullary disease at time of HSCT</td>
<td>11</td>
</tr>
</tbody>
</table>

*Excludes patients with solely extramedullary disease, n=4*
Conditioning: TMLI
Abstract #0735 (A. Shein et al): phase 1 trial of TMLI based conditioning of allo SCT for acute leukemia

• RESULTS AND CONCLUSIONS:
• OS @1y: 55%, PFS@1y: 40%, R/PD@1y: 52%
• Regimen 2000 cGy TMLI – VP16 - CY is safe in the studied context
• No increased incidence of aGVHD (overall 55%, grades III-IV 14%)
• NRM @D100 <5%, NRM @1y 8%

• A phase II trial (single arm, 2y PFS endpoint) is ongoing
Conditioning: FLU/BU vs FLU/MEL
Abstract #0736 (A. Alhateeb) Flu/Bu is associated with increased relapse risk compared to FLU/MEL in RIC allo SCT

• BACKGROUND: 2 retrospective trials showed that FLU/BU (compared to FLU/MEL) has:
  – Higher cumulative incidence of relapse
  – Lower NRM, lower aGVHD
  – References
    • Baron et al, Cancer 2015 (AML, N=394)
    • Shimoni et al, Leukemia, 2007 (hem mal, N=151)

• STUDY:
  – Retrospective, single center
  – Inclusion: AML/MDS, BU IV, AUC dose adjustment (N=134)
Conditioning: FLU/BU vs FLU/MEL

Abstract #0736 (A. Alhateeb): Flu/Bu is associated with increased relapse risk compared to FLU/MEL in RIC allo SCT

- RESULTS: Flu/BU associated with higher relapse rate, = NRM, = OS
Conditioning: FLU/BU vs FLU/TBI


- Retrospective analysis
- AML/MDS
- N=71
  - FLU/TBI (N=38)
  - FLU/BU (N=33)

<table>
<thead>
<tr>
<th>Variable</th>
<th>FluTBI N (%)</th>
<th>BuFlu N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell complete donor chimerism</td>
<td>29 (78)</td>
<td>26 (81)</td>
<td>0.83</td>
</tr>
<tr>
<td>Graft failure/rejection</td>
<td>3 (8)</td>
<td>3 (9)</td>
<td>0.87</td>
</tr>
<tr>
<td>Grade II–IV acute GvHD</td>
<td>13 (34)</td>
<td>17 (52)</td>
<td>0.24</td>
</tr>
<tr>
<td>Grade III–IV acute GvHD</td>
<td>3 (8)</td>
<td>6 (18)</td>
<td>0.21</td>
</tr>
<tr>
<td>Any Chronic GvHD</td>
<td>16 (42)</td>
<td>14 (42)</td>
<td>0.91</td>
</tr>
<tr>
<td>Extensive chronic GvHD</td>
<td>8 (21)</td>
<td>13 (39)</td>
<td>0.06</td>
</tr>
<tr>
<td>CMV reactivation</td>
<td>12 (32)</td>
<td>13 (39)</td>
<td>0.66</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>0.83</td>
</tr>
<tr>
<td>Relapse (2–years)</td>
<td>20 (53)</td>
<td>17 (52)</td>
<td>0.96</td>
</tr>
<tr>
<td>100 day mortality</td>
<td>13 (95% CI 6–29)</td>
<td>9 (95% CI 3–26)</td>
<td>0.59</td>
</tr>
<tr>
<td>Non-relapse mortality (2–years)</td>
<td>29 (95% CI 15–44)</td>
<td>29 (95% CI 14–45)</td>
<td>0.56</td>
</tr>
<tr>
<td>Relapse mortality (2–years)</td>
<td>34 (95% CI 20–49)</td>
<td>36 (95% CI 20–53)</td>
<td>0.86</td>
</tr>
<tr>
<td>Overall survival (2–years)</td>
<td>37 (95% CI 22–52)</td>
<td>35 (95% CI 19–51)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Patient outcomes
Conditioning: FLU/BU vs FLU/TBI


• RESULTS
The perfect Allo SCT

Abstract #4324 (M. Michallet et al): the perfect combination of conditioning regimen, disease stage and type of HSC donor

- **Retrospective** analysis, 1 centre (N=542), SCT 2006-2014 (single center – CH Lyon)
- Preview of outcome, depending on remission status @SCT, conditioning, type of HSC donor
- Superiority for MAC for disease in CR with MRD/MUD
GVHD

- **Prevention of aGVHD**
  - IV azacitidine early post SCT 45 mg/m² in phase 1 (n=16) (abstract #1935)
  - Ex vivo modulation of donor T cells (abstract #1884) by combination of small molecule modulators (FT1050, FT4145) that promote the activation of genes implicated in cell cycle, immune tolerance and anti-viral properties of T cells, as well as in the survival, proliferation and engraftment potential of CD34+ cells (in vitro on human cells and in mouse model)
  - Addition of MMF to tacrolimus/MTX in RIC (abstract # 3144); retrospective analysis (N=294): no increase in NRM or relapse rate after addition of MMF, no decrease in aGVHD or cGVHD → addition of MMF not recommended
  - Carfilzomib (abstract #1907) addition to tac/MTX as IS regimen in SCT after conditioning with FLU/MEL or FLU/BU. Phase 1, single arm; safe/tolerable (N=10).
GVHD

- **New treatments for steroid refractory aGVHD** (mortality 70%, CR rate 2\textsuperscript{nd} line agents 32%, no agent superior)
  - Brentuximab vedotin for steroid refractory aGVHD (abstract #1930): phase 1 (N=24), maximum tolerated dose was set at 0.8 mg/kg IV/2weeks for 4 doses; encouraging activity
  - ECP (abstract #1944) for severe steroid refractory aGVHD, grade III, 53% gut stage 3-4; 5y OS 45%, 60% in DLI group
  - (Grade III-IV) Basiliximab (anti-IL-2R) + etanercept (anti-TNF\(_\alpha\)) (abstract #3130): phase 2, multicenter, non-randomized, N=41; response >90%, OS@5y 55%

- **New treatments for cGVHD**
  - Ruxolitinib (abstract #1938, N=16, early response, steroid sparing) and Pacritinib (Jak2 inhibitor) in mice (abstract #1874): less cGVHD, through iTregs
  - Combination B cell depletion (Rituximab) and TKI (abstract #1939) (N=26, 16 finished, 3 severe side effects): 60% PR, significant decrease in affected BSA
GVHD

Abstract #3151 (H. Schoemans et al): EBMT iGVHD APP, a computer/web-based algorithm-driven application to help physicians correctly diagnose and score severity of acute and chronic GVHD (CQWP of EBMT).

• Evaluation of EBMT GVHD App
• high scores for user experience and satisfaction
• improved significantly the accuracy to diagnose and score severity of GVHD, compared to their practice with standard tools.
• Testing of v2.0 is underway
• A larger study with a subsequent v3.0 is warranted in real life setting
GVL VS GVHD

MONTY PYTHON
and the Holy Grail
• Strategies for GVHD suppression
• Clinical strategies to enhance immune regulatory mechanisms
• Adoptive therapy post SCT to enhance GVL
• Control of alloreactive T cell proliferation and trafficking suppresses GVHD pathophysiology
• Several strategies to control GVHD and separate from GVL reactions following SCT appear promising
• Randomized trials with minimum 2 year follow-up are critical
GVL-GVHD
Abstract #65 (L. Curtis et al): randomized trial comparing 2 IS regimens in RIC, MUD

• AIM: comparing 2 IS regimens in RIC, MUD
• STUDY:
  – Prospective, Phase 2, randomized trial (N=81)
  – Arm A (AC) = Alemtuzumab 100 mg (20 mg/d x5d) + Cyclosporin
  – Arm B (TMS) = Tacrolimus + Sirolimus + MTX

<table>
<thead>
<tr>
<th></th>
<th>AC (N=42)</th>
<th>TMS (N=39)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe cGVHD</td>
<td>5%</td>
<td>31%</td>
<td>0.0007</td>
</tr>
<tr>
<td>Relapse</td>
<td>51%</td>
<td>21%</td>
<td>0.0062</td>
</tr>
<tr>
<td>Survival at 3 years</td>
<td>42%</td>
<td>58%</td>
<td>0.2</td>
</tr>
</tbody>
</table>
SHIFT SCT → T cell therapy
Role of immunotherapy
S. Pavletic: scientific session: Harnessing T cells

Pre SCT cytoreduction (“bridge”) → MRD directed or post relapse therapy

Day 0

Self-standing (no SCT)
Autologous SCT

[Box] Autologous T cells (CAR/TCR)
[Box] Allogeneic T cells (CAR/TCR)

- Allogeneic HSC infusion
- Direct graft augmentation

- Combinations
  - Antibodies
  - Tumor vaccines
  - Checkpoint inhibitors
  - Immune modulators
  - NK cells
  - Cytokines
  - Conventional therapies
QUESTIONS?

ANY QUESTIONS DO YOU HAVE?

ALLOGENEIC STEM CELL TRANSPLANTATION

#C3PO
#STORMTROOPER
#BB8