HIGH ENGRAFTMENT RATES FOLLOWING SECOND ALLOGENEIC TRANSPLANTS FOR GRAFT FAILURE RESULT IN GOOD OUTCOMES

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On behalf of the British Society of Blood and Marrow Transplantation
Introduction

• Graft failure is a highly unsatisfactory outcome of allogeneic transplantation
• Conventionally described as primary or secondary, depending on temporal relation to transplant
• Multiple mechanisms underlying graft failure have been proposed
• Outcomes have historically been dismal
  • Schriber et al (BBMT 2010) 11% 1yr OS following second allograft for primary graft failure (n=120)
• However, publications are otherwise limited, generally small single-centre studies
Objectives and methods

• Assess patient outcomes following second allograft for graft failure, and identify factors influencing:
  • Engraftment
  • Overall survival
• Aim of the study not to investigate incidence/risk factors for graft failure
• 130 UK patients, identified from ProMISe data registry 2000-2010 (interim analysis)
• Transplant centres approached to provide follow-up data for all subjects
Results

- Mean time between transplants 173 days (8-4102d)
- Median age 9 years (4 months – 69 years)
- 40% adults (>18)
- 39/130 primary graft failure
- 47% malignant
- 68% re-conditioned for second allograft
  - Majority (69% of conditioned) used serotherapy (Alemtuzumab or ATG)
  - 30% MA, 38% RIC (compared to 56%, 43% at first allo)
<table>
<thead>
<tr>
<th>Disease</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>AML</td>
<td>17 (13%)</td>
</tr>
<tr>
<td>Biphenotypic</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Secondary</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>MDS/MPN</td>
<td>13 (9%)</td>
</tr>
<tr>
<td>CLL</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>CML</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Histiocytic disorders</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>BM failure</td>
<td>12 (9%)</td>
</tr>
<tr>
<td>Haemoglobinopathy</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>10 (7%)</td>
</tr>
<tr>
<td>Inherited disorder</td>
<td>53 (40%)</td>
</tr>
</tbody>
</table>
Results

- Sibling
- Mismatched sib / other relation
- VUD

Donor

- First allograft
- Second allograft
Results

Route of Donation

- Bone marrow
- PBSC
- Both
- Cord

First allograft
Second allograft
Results

74% for Same donor
26% for Different donor
Results – different donor

- Sibling to different sibling: 26%
- Sibling to VUD: 12%
- VUD to sibling: 6%
- VUD to different VUD: 56%
Engraftment

- Engraftment in 88% of patients following second allograft
- Factors associated with engraftment failure post 2\textsuperscript{nd} allograft
  - Primary graft failure, \(p=0.038\)
  - Older age (>18y), \(p=0.003\)
  - Male recipient, \(p=0.025\)
  - Reduced intensity conditioning, \(p=0.031\)
  - Use of different donor, \(p=0.026\)

- No effect of
  - Stem cell source
  - Time between transplants (</>90 days)
  - TNC/CD34+ infused
  - Use of serotherapy
Overall survival after second allograft for graft failure

OS 59% @ 10y
Progression free survival after second allograft for graft failure

PFS 53% @ 10y
Overall survival after second allograft for graft failure by failure type

45 vs 67% @ 5y

Primary graft failure N=39
Other graft failure N=91 P=0.042
Overall survival after second allograft for graft failure by age at transplant

- Paediatric N=81
- Adult N=49 P=0.0001

74% vs 37% @ 5y
Progression free survival after second allograft for graft failure by age at transplant

- Paediatric N=81
- Adult N=49 P=0.0001

71% vs 28% @ 5y
Overall survival after second allograft for graft failure by diagnosis

- Non-malignant N=69
- Malignant N=61, P=0.0001

78% vs 40% @ 5y
Overall survival after second allograft for graft failure by time between transplants

65% vs 47% @ 5y
Other factors in univariate analysis

- None of the following were found to have significant impact on OS or PFS
  - Route of donation (BM vs PBSC vs Cord)
  - Donor type (Sib vs other relative vs VUD)
  - Same donor or different donor
  - TNC/CD34+ dose
  - Use of serotherapy
## Multivariate analysis - Engraftment

<table>
<thead>
<tr>
<th>Multivariate</th>
<th>HR for engraftment</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary graft failure</td>
<td>2.19</td>
<td>0.245</td>
</tr>
<tr>
<td>Sex (Male )</td>
<td>2.11</td>
<td>0.389</td>
</tr>
<tr>
<td>Conditioning (None v. RIC v. MA)</td>
<td>1.90</td>
<td>0.237</td>
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<tr>
<td>Non malignant v. malignant</td>
<td>1.53</td>
<td>0.703</td>
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<tr>
<td>Age (paediatric v. adult)</td>
<td>7.31</td>
<td>0.063</td>
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<tr>
<td>Same donor</td>
<td>8.99</td>
<td>0.010</td>
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</tbody>
</table>
## Multivariate analysis – OS/PFS

<table>
<thead>
<tr>
<th></th>
<th>HR for mortality</th>
<th>P value</th>
<th>HR for progression free survival</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary graft failure vs other</td>
<td>1.22</td>
<td>0.525</td>
<td>1.45</td>
<td>0.538</td>
</tr>
<tr>
<td>Age (adult v. paediatric)</td>
<td>1.46</td>
<td>0.298</td>
<td>2.59</td>
<td>0.013</td>
</tr>
<tr>
<td>Time between transplants &lt;90d</td>
<td>1.43</td>
<td>0.224</td>
<td>1.22</td>
<td>0.468</td>
</tr>
<tr>
<td>Malignant</td>
<td>2.53</td>
<td><strong>0.018</strong></td>
<td>1.46</td>
<td>0.325</td>
</tr>
</tbody>
</table>
Conclusions

• Encouraging results
• Successful engraftment and long-term survival possible following a second allograft for graft failure
• Outcomes superior in children and those with non-malignant disease
• However, over a third of adult patients and those with malignant disease can also achieve long-term survival
ANY QUESTIONS?