Allogeneic Stem Cell Transplantation For DLBCL In The Rituximab Era

Dr Stephen Robinson
Program Director
BMT Unit
University Hospital Bristol
Overview

• Introduction: autoSCT and alloSCT for DLBCL

• Allogeneic SCT For DLBCL Relapsing after autoSCT

• Allogeneic SCT as an alternative to autoSCT in patients failing first line therapy
EBMT Registry: SCT for DLBCL 1990-2009

SCT In DLBCL
- AlloSCT uncommonly used
- Lowest ratio of allo:auto
- 0.3 alloSCT/center/year
Problems With Allogeneic SCT In DLBCL

• Toxicity
  - Immunesuppression
  - Graft versus host disease (acute and chronic)

• Limited donor availability
  - Sibling 25-30%
  - MUD 20-70%

• Cost
  - UK sibling alloSCT £60k
  - UK MUD alloSCT £80-100k
The Historical Perspective Of AutoSCT In Aggressive NHL

- Only chemosensitive patients
- "Aggressive" histology
- Small numbers
- Pre Rituximab era

(Philip et al. NEJM, 1995, 333: 1540)
What has changed in the recent era?

- The introduction of Rituximab
The Coral Study
The Impact Of First Line Rituximab On Salvage Induction

1st Line

Chemo Only

R-Chemo

CORAL Salvage

R-Salvage

Response =51%

Response =83%

“…patients who had received Rituximab had more adverse factors…”
The Coral Study
The Influence Of Prior R And Time To Relapse

Prior R and Relapse<12 months

Gisselbrecht C et al. JCO 2010;28:4184-4190
The Impact Of Rituximab?

- More patients cured with first line chemotherapy
- Fewer patients requiring salvage and SCT
- Relapsing/refractory patients inherently higher risk disease
- Results of salvage strategies may deteriorate
  - Salvage induction less effective
  - HDT consolidation less effective
What has changed in the recent era?

- The introduction of Rituximab
- Development of transplant practice
Evolution In Transplant Practice

• Improving supportive care
  – Tissue typing
  – CMV monitoring and therapy
  – Antifungal therapy
  – Prevention and treatment of GVHD

• Improving patient selection
• Expanding donor pool (VUD, cord, haplo)

• Improving transplantation technique
  – Reduced intensity conditioning
  – Donor lymphocyte infusions
  – Cord blood and haploidentical transplantation
  – Radioimmunotherapy based conditioning
Conditioning Regimens For AlloSCT In DLBCL

Non-Myeloablative

2GyTBI+Flu (Baron 2005)
Flu+Melph+CAM (Morris 2004)
Flu+Cyclo+TT (Corradini 2005)

Myeloablative

Cyclo-TBI
Flu+Cy+Bu (Glass 2009)
BEAM-CAM (Faulkner 2004)
LACE-CAM

Myelosuppression

Immune-suppression

2GyTBI (Baron 2005)
Flu+Cyclo+R (Escalon 2004)
Improving NRM Following Allo-SCT For NHL
What has changed in the recent era?

- The introduction of Rituximab
- Development of transplant practice
- Development of novel therapies
  - (Lenolidamide, Bortezomib, Ibrutinib, Ofatumumab, Inotuzomab Ozagamicin, CAL101, Everolimus, …)
Chronic Active B-Cell Receptor Signaling Activates NF-κB in ABC DLBCL

EHA 2013, PCYC-1106 de Vos et al.
Ibrutinib: Response in ABC and GCB DLBCL

Response (CR+PR), %

100
90
80
70
60
50
40
30
20
10
0

ABC DLBCL

41%
12/29

PR 24%
CR 17%

GCB DLBCL

PR 5%
1/20

P = 0.007

EHA 2013, PCYC-1106 de Vos et al.
What has changed in the recent era?

• The introduction of Rituximab

• Development of transplant practice

• Development of novel therapies
  – (Lenolidamide, Bortezomib, CAL101, Everolimus, Ibrutinib, Ofatumumab, Inotuzomab Ozagamicin…)

• Re-evaluation of salvage strategies required
What is the role of alloSCT in DLBCL in the Rituximab era?

- Relapse post autoSCT?
- As an alternative to autoSCT in patients failing first line therapy?
Survival Post Relapse After Autologous Stem Cell Transplantation

Median OS < 1 yr

(Kewalramani et al BMT 2003)
AlloSCT For Relapsed DLBCL After AutoSCT
(van Kampen 2010)

- EBMT retrospective analysis
- 101 patients
- 37 Myeloablative 64 Reduced Intensity
- 1997-2006
- 19 Prior Rituximab
- 72 sibling/29 MUD
AlloSCT For Relapse After AutoSCT (van Kampen 2010)

- Overall Survival
- PFS

- 52% (95% CI, 42% to 63%) at 36 mo
- 42% (95% CI, 32% to 52%) at 36 mo
AlloSCT For Relapse After AutoSCT (van Kampen 2010)

RIC AlloSCT lower NRM

Outcome better if:
- chemosensitive
- late relapse
Reduced Intensity AlloSCT For DLBCL (Thomson JCO 2009)

Fludarabine/Melphalan/CAMPATH Conditioning

Prior AutoSCT
n=34
## Results Of RIC AlloSCT In DLBCL

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Prior SCT</th>
<th>NRM % (years)</th>
<th>RR</th>
<th>PFS</th>
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<tbody>
<tr>
<td>EBMT Registry 2010</td>
<td>64</td>
<td>64/64</td>
<td>20 1yr</td>
<td>3yr</td>
<td>42 3yr</td>
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<tr>
<td>Thiotepa/Cyclo/Fludara 2005</td>
<td>61</td>
<td>34/61</td>
<td>15 3yr</td>
<td>15 3yr</td>
<td>54 3yr</td>
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<tr>
<td>2Gy TBI+-/Flu 2008</td>
<td>33</td>
<td>24/33</td>
<td>25 3yr</td>
<td>25 3yr</td>
<td>35 3yr</td>
</tr>
<tr>
<td>Flu/Mel/CPATH 2010</td>
<td>48</td>
<td>34/48</td>
<td>32 4yr</td>
<td>32 4yr</td>
<td>48 4yr</td>
</tr>
<tr>
<td>French Registry 2010</td>
<td>68</td>
<td>54/68</td>
<td>23 1yr</td>
<td>23 1yr</td>
<td>44 2yr</td>
</tr>
</tbody>
</table>
AlloSCT For DLBCL Relapse After AutoSCT

- Reduced intensity alloSCT is feasible and effective
- NRM 15-25% with RICalloSCT
- Better outcome if >12 months to relapse after auto and chemosensitive
- Remaining questions
  - Reduced intensity/Intermediate intensity
  - Role of T cell depletion
- Consider sibling, VUD, cord/haploidentical
- Place relative other therapies/novel therapies?
### Stem Cell Transplantation In DLBCL

**BSBMT Current Guidelines 2013**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Autograft</th>
<th>Sibling transplant</th>
<th>MUD transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR1</td>
<td>GNR&lt;sup&gt;1&lt;/sup&gt;</td>
<td>GNR</td>
<td>GNR</td>
</tr>
<tr>
<td>PR1 (sensitive to salvage)</td>
<td>S&lt;sup&gt;2&lt;/sup&gt;</td>
<td>S&lt;sup&gt;2&lt;/sup&gt;</td>
<td>S&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>CR/PR&gt;1</td>
<td>S&lt;sup&gt;3&lt;/sup&gt;</td>
<td>CO&lt;sup&gt;4&lt;/sup&gt;</td>
<td>CO&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chemorefractory</td>
<td>GNR</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td>Relapse post autograft</td>
<td>GNR</td>
<td>S&lt;sup&gt;5&lt;/sup&gt;</td>
<td>S&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
What is the role of alloSCT in DLBCL in the current era?

• Relapse post autoSCT?

• As an alternative to autoSCT in patients failing first line therapy?
Allogeneic Stem Cell Transplant As An Alternative To Autologous Stem Cell Transplant?

ALLOGENEIC SCT
- Conditioning Therapy
- The GVL Effect
- Purged marrow
- No Late MDS

AUTOLOGOUS SCT
- Conditioning Therapy
- Lower toxicity
- Lower cost
Is There A Graft Versus DLBCL Effect?

• Indirect Evidence
  – Relapse rate alloSCT vs autoSCT
  – Impact of GVHD on relapse rate

• Direct Evidence
  – Impact of DLIs for relapse post alloSCT
  – Impact of withdrawal of immunesuppression
Is The Relapse Rate Following AlloSCT Lower Relative To AutoSCT?

Yes

(Peniket BMT 2003)

No

(Lazarus BBMT 2010)

Ratanatharathorn et al. Blood 1994, 84, 1050
Schimmer et al. BMT 2000, 26, 859
Impact Of GVHD On Relapse Post AlloSCT (Chopra 2002)

- Retrospective analysis
- 101 patients with NHL
  - Int/HG 38, LBL 55, BL 11, LG 7
- 18 developed cGVHD (all LBL or Int/HG)
  - Relapse Rate 0%
- 30 no cGVHD (and survived >3 months)
  - Relapse rate=35%
Clinical evidence of a graft-versus-lymphoma effect against relapsed diffuse large B-cell lymphoma after allogeneic hematopoietic stem-cell transplantation

M. R. Bishop¹*, R. M. Dean¹,², S. M. Steinberg³, J. Odom¹, S. Z. Pavletic¹, C. Chow⁴, S. Pittaluga⁵, C. Sportes¹, N. M. Hardy¹, J. Gea-Banacloche¹, A. Kolstad⁶, R. E. Gress¹ & D. H. Fowler¹

-Single institution retrospective study
-15 patients with DLBCL
-Persistent/relapsed disease post allogeneic stem cell transplant
-Treatment with withdrawal of immunesuppression+/-DLI+/-chemo
Clinical evidence of a graft-versus-lymphoma effect against relapsed diffuse large B-cell lymphoma after allogeneic hematopoietic stem-cell transplantation

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>Sex</th>
<th>Time from Dx to RIST (months)</th>
<th>Number of prior Tx</th>
<th>Prior auto HSCT</th>
<th>Disease status at study entry</th>
<th>IPI score at study entry</th>
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<tr>
<td>1</td>
<td>33</td>
<td>F</td>
<td>10</td>
<td>2</td>
<td>No</td>
<td>Primary refractory</td>
<td>2</td>
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<tr>
<td>2</td>
<td>34</td>
<td>F</td>
<td>11</td>
<td>3</td>
<td>No</td>
<td>Primary refractory</td>
<td>0</td>
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<tr>
<td>3</td>
<td>61</td>
<td>F</td>
<td>16</td>
<td>3</td>
<td>Yes</td>
<td>Refractory relapse</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>F</td>
<td>9</td>
<td>3</td>
<td>No</td>
<td>Primary refractory</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>F</td>
<td>18</td>
<td>2</td>
<td>No</td>
<td>Sensitive relapse</td>
<td>1</td>
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<tr>
<td>6</td>
<td>45</td>
<td>M</td>
<td>18</td>
<td>3</td>
<td>Yes</td>
<td>Refractory relapse</td>
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<tr>
<td>7</td>
<td>31</td>
<td>F</td>
<td>16</td>
<td>3</td>
<td>Yes</td>
<td>Sensitive relapse</td>
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<tr>
<td>8</td>
<td>54</td>
<td>F</td>
<td>126</td>
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<td>No</td>
<td>Sensitive relapse</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>32</td>
<td>M</td>
<td>14</td>
<td>4</td>
<td>Yes</td>
<td>Primary refractory</td>
<td>2</td>
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<tr>
<td>10</td>
<td>58</td>
<td>F</td>
<td>10</td>
<td>6</td>
<td>Yes</td>
<td>Primary refractory</td>
<td>2</td>
</tr>
<tr>
<td>11</td>
<td>39</td>
<td>M</td>
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<td>2</td>
<td>No</td>
<td>Primary refractory</td>
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<tr>
<td>12</td>
<td>50</td>
<td>M</td>
<td>60</td>
<td>6</td>
<td>Yes</td>
<td>Refractory relapse</td>
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<tr>
<td>13</td>
<td>43</td>
<td>M</td>
<td>15</td>
<td>3</td>
<td>Yes</td>
<td>Sensitive relapse</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>49</td>
<td>M</td>
<td>43</td>
<td>5</td>
<td>No</td>
<td>Refractory relapse</td>
<td>2</td>
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<tr>
<td>15</td>
<td>41</td>
<td>M</td>
<td>71</td>
<td>9</td>
<td>Yes</td>
<td>Refractory relapse</td>
<td>4</td>
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8/15  11/15
Withdrawal of Immunesuppression
Clinical evidence of a graft-versus-lymphoma effect against relapsed diffuse large B-cell lymphoma after allogeneic hematopoietic stem-cell transplantation

<table>
<thead>
<tr>
<th>Day +28 response</th>
<th>Day +100 response</th>
<th>Intervention</th>
<th>Response to intervention</th>
<th>GVHD*</th>
<th>Current status (m)</th>
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<tbody>
<tr>
<td>1 SD</td>
<td>PD</td>
<td>WOI</td>
<td>PD</td>
<td>Y (acute + chronic)</td>
<td>PD/died (4)</td>
</tr>
<tr>
<td>2 SD</td>
<td>PR</td>
<td>WOI</td>
<td>CR</td>
<td>Y (acute + chronic)</td>
<td>CR/died sepsis (80)</td>
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<tr>
<td>3 PR</td>
<td>PD (+40)</td>
<td>WOI</td>
<td>PD</td>
<td>Y (acute)</td>
<td>PD/died (2.5)</td>
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<tr>
<td>4 PR</td>
<td>PD</td>
<td>WOI</td>
<td>PR</td>
<td>Y (acute)</td>
<td>PD/died (6)</td>
</tr>
<tr>
<td>5 CRu</td>
<td>CR→PD (+157)</td>
<td>DLI</td>
<td>CR</td>
<td>N</td>
<td>CR/alive (83+) *</td>
</tr>
<tr>
<td>6 PR</td>
<td>PD</td>
<td>WOI, Chemo + DLI</td>
<td>CR</td>
<td>N</td>
<td>CR/alive (76+) *</td>
</tr>
<tr>
<td>7 CRu</td>
<td>CRu→PD (+169)</td>
<td>Chemo + DLI</td>
<td>CR</td>
<td>Y (chronic)</td>
<td>CR/alive (74+) *</td>
</tr>
<tr>
<td>8 PR</td>
<td>PR</td>
<td>WOI</td>
<td>PD</td>
<td>Y (chronic)</td>
<td>PD/died sepsis (11)</td>
</tr>
<tr>
<td>9 CR</td>
<td>PD</td>
<td>WOI, DLI, Chemo + DLI</td>
<td>SD</td>
<td>N</td>
<td>PD/died (21)</td>
</tr>
<tr>
<td>10 SD</td>
<td>PD</td>
<td>WOI</td>
<td>PD</td>
<td>N</td>
<td>PD/died (5.5)</td>
</tr>
<tr>
<td>11 PR</td>
<td>PD</td>
<td>WOI</td>
<td>CR</td>
<td>N</td>
<td>PD/died (26)</td>
</tr>
<tr>
<td>12 PR</td>
<td>PR</td>
<td>WOI</td>
<td>CR</td>
<td>N</td>
<td>CR/alive (63+) *</td>
</tr>
<tr>
<td>13 PR</td>
<td>PR</td>
<td>WOI</td>
<td>CR</td>
<td>Y (chronic)</td>
<td>CR/alive (42+) *</td>
</tr>
<tr>
<td>14 PR</td>
<td>PD</td>
<td>WOI</td>
<td>CR</td>
<td>Y (chronic)</td>
<td>CR/alive (44+) *</td>
</tr>
<tr>
<td>15 SD</td>
<td>PR</td>
<td>WOI, DLI, Chemo + DLI</td>
<td>SD</td>
<td>Y (acute + chronic)</td>
<td>PD/died (12)</td>
</tr>
</tbody>
</table>

Annals of Oncology

9/15 CR/PR
6/15 Alive
Impact Of DLIs On Relapse Of DLBCL Post AlloSCT (Thomson JCO 2009)

- 4 patients primary DLBCL
  - ¾ developed grade III/IV GVHD
  - All patients died of relapse within 5 months

- 6 patients transformed FL
  - 3 died of relapse within 16/12
  - 3 responded to DLIs alone
Is There A Graft Versus DLBCL Effect?

- Evidence inconsistent
- Difficult to quantify magnitude of effect
- Why?
  - There is no GV DLBCL response
    - Tumour escape mechanisms?
  - There is a GV DLBCL response but…..
    - GVL response inadequate in rapidly growing tumours
    - Available data insufficiently powered to show effect
    - Unidentified bias in retrospective registry studies
Purging vs The GVL Effect (Bierman JCO 2003) 
(WF Intermediate Grade NHL, n=1848) 

Reduction of relapse rate post alloSCT is due to the provision of a purged graft?

<table>
<thead>
<tr>
<th></th>
<th>Syngeneic AutoSCT</th>
<th>Syngeneic AlloSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RR</strong></td>
<td>29%</td>
<td>29%</td>
</tr>
<tr>
<td><strong>55%</strong></td>
<td></td>
<td>25%</td>
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</table>
Risk of Secondary Cancers Following Autologous Stem Cell Transplant (Brown 2005)
Allogeneic Stem Cell Transplant As An Alternative To Autologous Stem Cell Transplant?

Allogeneic SCT Conditioning Therapy
The GVL Effect
Purged marrow
No Late MDS

Autologous SCT Conditioning Therapy
Lower toxicity
Lower cost
Stem Cell Transplantation For Diffuse Large B Cell Lymphoma In The Rituximab Era.

Stephen P Robinson, Ariane Boumendil, Herve Finel, Roberto Foa, Irit Avivi, Catherine Thieblemont, Charles Craddock, Maria Gilleece, Stig Lenhoff, Kim Orchard, Urs Schanz, Jan Cornelissen, Harry Schouten, Peter Dreger
On Behalf Of The Lymphoma Working Party Of The EBMT
Objectives:
- To assess the outcome of SCT for DLBCL failing first line therapy in the last decade

Methods
- Retrospective study, SCT 2002-2010
- Relapsed/refractory DLBCL
- First transplant
  - AutoSCT or alloSCT (RIC and MA)
The Outcome Of Autologous SCT and Allogeneic SCT When Performed As A First Transplant For Chemosensitive Relapsed DLBCL

<table>
<thead>
<tr>
<th></th>
<th>AutoSCT</th>
<th>MAC AlloSCT</th>
<th>RIC AlloSCT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>2652</td>
<td>54</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Age, median (Q3-Q4)</td>
<td>52 (43-59)</td>
<td>44 (36-51)</td>
<td>54 (46-57)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male/Female</td>
<td>58/42</td>
<td>53/47</td>
<td>62/38</td>
<td>0.66</td>
</tr>
<tr>
<td>Diagnosis-SCT, median (Q3-Q4)</td>
<td>23.3 (43-59)</td>
<td>18.5 (36-51)</td>
<td>23.7 (46-57)</td>
<td>0.097</td>
</tr>
<tr>
<td>Diagnosis-SCT &lt; 1 year %</td>
<td>21.9</td>
<td>31.5</td>
<td>32.8</td>
<td>0.033</td>
</tr>
</tbody>
</table>

(Robinson ASH 2012)
Chemosensitive Relapse: Disease Free Survival

- DFS Auto: 46% 4yrs
- DFS MACallo: 37% 4yrs
- DFS RICallo: 37% 4yrs

Adverse Risk Factors For DFS:
- Male Sex
- Diag-SCT<1yr
- MACallo SCT

(Robinson ASH 2012)
Chemosensitive Relapse: Overall Survival

Adverse Risk Factors For OS:
- Age>50
- Diag-SCT<1yr
- MACallo SCT

(Robinson ASH 2012)
Conclusions From This Study

• Retrospective study

• Why were patients selected for an alloSCT in place of an autoSCT?

• PFS and OS in RICalloSCT and autoSCT cohorts were similar
Is there any role for allogeneic SCT in place of autoSCT?

• Failure to collect autologous stem cells

• In patients predicted to be at high risk of failing an autoSCT?
Prognostic Factors Predicting Outcome Of Autologous Stem Cell Transplantation

150 patients with chemosensitive DLBCL

Second line age adjusted IPI (sAAIPI)

Factors: High LDH, Stage 3 or 4, Poor performance status

Low risk: 0 factors
Int. risk: 1 factor
High risk: 2 or 3 factors

Prognostic Factors Predicting Outcome Of Autologous Stem Cell Transplantation

Prognostic value of PET status pre-auto transplant for aggressive lymphoma: PFS

Who Should Be Considered For An AlloSCT Rather Than An Auto Transplant?

- DLBCL Failing R-Chemo AutoSCT REMAINS the standard therapy

- However high risk of failure in some patients:-
  - High sAAIPI Score
  - Time to relapse <12 Months
  - PET+ve post salvage
  - Myc+?
  - ABC subtype?
  - “Double Hit” lymphomas

- Clinical studies required to assess efficacy of alloSCT in this setting
AlloSCT As Alternative To AutoSCT For Salvage

• Conditioning Regimen
  – Myeloablative?
  – Intermediate Intensity?
  – Reduced intensity?

• Donor
  – Sib/MUD/Cord/haploidentical

• T Cell Depletion?
Does Conditioning Regimen Intensity Matter?

![Graphs showing probability of PFS and NRM & Progression/Relapse over years for different conditioning regimens.](Bacher U et al. Blood 2012;120:4256-4262)
Cord Blood AlloSCT In Lymphoma
(Rodrigues JCO 2009)

A

Progression-Free Survival (%)

0 3 6 9 12 15 18 21 24

Time (months)

Mantle Cell
Indolent NHL
Hodgkins
Aggressive NHL

75%
60%
30%
29%
BEAM-CAMPATH AlloSCT For DLBCL and PTCL

- **n**: 46
- **Median age**: 43 (17-59)
- **DLBCL**: 31
- **TCL**: 15
- **Prior auto**: 5

**Median Prior Lines**: 2.5 (1-5)
- **Chemosensitive**: 34
- **Chemrefractory**: 11
- **Sib/UD**: 32/14

**NRM 11% at 3yrs**

**NRM Sibling**: 3% at 3yrs
**NRM VUD**: 30% at 3yrs

(Robinson ASH 2012)
BEAM-CAMPATH AlloSCT For DLBCL and PTCL

PFS 36% at 5 years

OS 42% at 5 years

(Robinson ASH 2012)
## Stem Cell Transplantation In DLBCL
Current BSBMT Guidelines

<table>
<thead>
<tr>
<th></th>
<th>Autograft</th>
<th>Sibling transplant</th>
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</tr>
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<tbody>
<tr>
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<td>S&lt;sup&gt;2&lt;/sup&gt;</td>
<td>S&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>CR/PR&gt;1</td>
<td>S&lt;sup&gt;3&lt;/sup&gt;</td>
<td>CO&lt;sup&gt;4&lt;/sup&gt;</td>
<td>CO&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chemorefractory</td>
<td>GNR</td>
<td>D</td>
<td>D</td>
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<tr>
<td>Relapse post autograft</td>
<td>GNR</td>
<td>S&lt;sup&gt;5&lt;/sup&gt;</td>
<td>S&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Summary

Relapsed/refractory DLBCL

Salvage Induction? +/- novel agents

CR/PR

<PR

Low Risk

-PET post salvage
-Time to relapse
-SaalPI
-ABC/myc+/DH?

High Risk

AutoSCT

AutoSCT

AlloSCT

Novel Agents
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