The Role of Stem Cell Transplantation in Relapsed / Refractory Hodgkin’s Lymphoma

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10th Educational Course on Lymphomas and Stem Cell Transplantation.
Nicosia, October 16th – 17th, 2014
1st Line Therapy Has Improved Long Term Outcome of Patients with Hodgkin’s Lymphoma Over Time

Sjöberg et al, Blood, 2012
SALVAGE CHEMOTHERAPY REGIMENS IN R/R HL

**Partial response data not reported.**

R/R – relapsed / refractory; HL – Hodgkin lymphoma; BEAM - carmustine, etoposide, cytarabine, melphalan; DEXA - dexamethasone; DHAP - dexamethasone, ara-C, cisplatin; GDP - gemcitabine, dexamethasone, cisplatin; GVD, gemcitabine, vinorelbine, doxil (liposomal doxorubicin); ICE - ifosfamide, carboplatin, etoposide; IEV - ifosfamide, etoposide, vinorelbine; IV - fosfamide, vinorelbine.

ASCT is the standard therapy for HL Relapsing after 1\textsuperscript{st} Line Chemotherapy

BNLI Trial
Mini-BEAM + ABMT vs Mini-BEAM

<table>
<thead>
<tr>
<th></th>
<th>N. of patients</th>
<th>TRM</th>
<th>EFS (3 yrs)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-BEAM</td>
<td>20</td>
<td>9</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Mini-BEAM + ABMT</td>
<td>20</td>
<td>5</td>
<td>53</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Linch et al, Lancet 1993
ASCT is the standard therapy for HL Relapsing after 1st Line Chemotherapy. HDR1 Trial (GHSG/EBMT)

Dexa-BEAM + ASCT vs Dexa-BEAM

Early, late and multiple relapse

- 2 x Dexa-BEAM (CR or PR)
- 2 x Dexa-BEAM
- BEAM + PBSCT

Schmitz et al, Lancet 2002
Figure 3: Freedom from treatment failure for patients with relapsed chemosensitive Hodgkin’s disease

Schmitz et al, Lancet 2002
Not all Relapsing Patients do so Well after an Autologous Stem Cell Transplantation

Predictors of poor response:
- Primary refractory disease
- Early (<12 months) relapse
- Bulky disease
- B-symptoms
- Extranodal involvement
- Advanced stage at relapse
The Impact of the Duration of First Complete Remission in the ASCT Outcome

Schmitz et al, Lancet 2002
The Impact of the Duration of First Complete Remission in the ASCT Outcome

Schmitz et al, Lancet 2002
The Impact of the Duration of First Complete Remission in the ASCT Outcome

Schmitz et al, Lancet 2002
The Impact of Disease Status Before Transplantation in the ASCT Outcome

Not All Patients with Relapse HL do Equally Well after an ASCT

Fig 3. Kaplan-Meier curves of progression-free survival in four groups of patients differentiated with an adapted prognostic score. Presence of stage IV disease, early or multiple relapse, and anemia summed up to a score ranging from 0 to 3.

Josting et al, JCO 2010
Retrospective data, 211 consecutive relapsed/refractory patients, 1993–2004

**Progression free survival**

**Overall survival**

*Jabbour et al, Cancer 2007*
PET Scan Can Also Discriminate Those Patients with Worse Outcome after ASCT

Moskowitz et al. Blood 2010
Dose Intensity of Chemotherapy in Patients with Relapsed / Refractory Hodgkin’s Lymphoma

Josting et al, JCO 2010
Inclusion criteria for tandem ASCT:

- Primary refractory patients ($n = 77$)
- First relapse with $\geq 2$ risk factors ($n = 73$)
  - Time to relapse $< 12$ mo
  - Stage III-IV at relapse
  - Relapse within irradiated areas
- Single ASCT ($n = 95$):
  - Intermediate risk patients ($0 \sim 1$ risk factors)

*Morschhauser et al. J Clin Oncol 2008*
1\textsuperscript{st} ASCT:
Cyclophosphamide
Carmustine
Etoposide
Mithoxantrone

2\textsuperscript{nd} ASCT (45 – 90 days after first ASCT):
TBI (or Bu)
Ara-C
Melphalan

\textit{Morschhauser et al. J Clin Oncol 2008}
RAD001: an oral mTOR-inhibitor

- Daily administration results in cont. mTOR inhibition
- Safety data from more than 3,000 cancer patients available
- Numerous phase II und III-studies in RCC, NET, Lymphoma, NSCLC, breast cancer
# HDR3i: Phase II

<table>
<thead>
<tr>
<th>Phase</th>
<th>To do</th>
<th>n</th>
<th>Duration [M]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>Ever-DHAP: 3+3 Design, dose levels 2,5; 5; 7,5; and 10 mg, DLT-Definition without hematological tox. (DHAP!)</td>
<td>12-24</td>
<td>6</td>
</tr>
<tr>
<td>Phase II</td>
<td>2x DHAP + PET-CT</td>
<td>50</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>2x Ever-DHAP + PET-CT</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>
HDR3i: Phase II Design

- 28
  - Scree ning
  - randomization

  SC-Apheresis (SC-Apheresis)

  Ever-DHAP
  Ever-DHAP

  Placebo-DHAP
  Placebo-DHAP

  PET-CT

  15

  36

  52 (~42-60)
  Follow up

  BEAM

  ?
Expression of CD30
Brentuximab Vedotin: Biology

Brentuximab vedotin antibody-drug conjugate (ADC)
- Monomethyl auristatin E (MMAE), microtubule-disrupting agent
- Protease-cleavable linker
- Anti-CD30 monoclonal antibody

1. Brentuximab vedotin binds to CD30
2. Brentuximab vedotin-CD30 complex is internalized and traffics to lysosome
3. MMAE is released
4. MMAE disrupts microtubule network
5. G2/M cell cycle arrest
6. Apoptosis

Bartlett NL et al, Poster presentation at ASCO 2010 Chicago, IL, USA (Abstract #8062)
Younes A et al, Poster presentation at ASH 2008, San Francisco, CA, USA (Abstract #1006)
Brentuximab vedotin in relapsed/refractory CD30-positive lymphomas without prior high-dose chemotherapy and SCT

- **Endpoints:** OR, CR, PD, OS, PFS, safety
- **Patients:** 16 patients with HL or sALCL from GHSG enrolled in a NPP
  - Patients had not undergone prior HDCT and SCT
  - Median age: 48.5 years (range, 24–74)
  - CD30+ rel/ref HL: n=14; relapsed ALCL: n=2
  - Clinical stage IIA: n=1; IIB: n=5; IIIA: n=2; IIIB: n=1; IVA: n=2; IVB: n=5
  - Median prior chemotherapy regimens: 3 (range, 2–6)
  - Refractory to prior chemotherapy: n=13
- **Treatment:** Brentuximab vedotin 1.8 mg/kg as a 30-minute infusion Q3wk

Rothe A, et al. ASH 2012, Atlanta, GA, USA (Abstract 2743)
Retrospective analysis: Brentuximab vedotin in relapsed/refractory CD30-positive lymphomas without prior high-dose chemotherapy and SCT

• **Safety:** Brentuximab vedotin toxicity profile was reported to be similar to previously published data (data not shown)*
  – No dose reductions required
  – No patient had to stop treatment due to toxicity

• **Response:**

<table>
<thead>
<tr>
<th>Best response, n (%)</th>
<th>All patients (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>11 (69)</td>
</tr>
<tr>
<td>CR</td>
<td>5</td>
</tr>
<tr>
<td>PR</td>
<td>6</td>
</tr>
</tbody>
</table>

  – 6 of the 11 patients with chemotherapy-refractory disease and 4 of the 4 patients with significant comorbidity achieved an OR
  – 3 of the 5 patients with PD died

Rothe A, et al. ASH 2012, Atlanta, GA, USA (Abstract 2743)
Brentuximab vedotin in relapsed/refractory CD30-positive lymphomas without prior high-dose chemotherapy and SCT

- **PFS and OS:**
  - 6 of the 16 patients proceeded to SCT after treatment with brentuximab vedotin
    - Autologous SCT: 4 pts
    - Allogeneic SCT: 2 pts
  - Median PFS, 9 months (range, 1–15)
  - 11 of the 16 patients were alive at the time of analysis; median OS had not yet been reached
  - 12-month OS: 68% (95% CI: 40, 95)
  - 12-month PFS: 22% (95% CI: 0, 48)

Rothe A, et al. ASH 2012, Atlanta, GA, USA (Abstract 2743)
OUTLINE OF THE STUDY

HL ≥18 yr, refractory to first line chemotherapy or first relapse

Registration

2 cycles of BV-DHAP

PET-CT

CT / stem cell harvest

3rd cycle of BV-DHAP

SD/PD

Off Study

PR/CR

PET-CT

HDT ASCT

PET-CT

Follow up

BV: Brentuximab Vedotin
ASCT: Autologous Stem Cell Transplantation
Treatment Protocol

ESHAP

PBSC Collection

ASCT / BEAM

Brentuximav Vedotin*: 1,8 mg/Kg, 1st day of ESHAP and day +21 after 3rd ESHAP (every 21 – 28 days)

BV post-ASCT: from day +28 to +56, 3 doses every 21 days

+ Radiotherapy (Bulky disease)
A Randomized, Double-Blind Placebo-Controlled Phase 3 Trial of SGN-35 vs Placebo in High-Risk HL Patients Undergoing and ASCT (AETHERA Trial)
Take-Home Messages

- ASCT is the standard of care for the vast majority of patients with HL in first chemosensitive relapse
- Several well defined prognostic factors including PET positivity / negativity significantly change the outcome after ASCT in this population of patients
- Results of ASCT can be optimized by:
  - Use of new drugs during salvage therapy before ASCT or as maintenance therapy
- Other treatment strategies have to be developed to treat those patients:
  - With adverse prognostic features at the time of relapse
  - Relapsing after ASCT
OS from relapse after an ASCT. The experience of the LWP EBMT/GITMO

Median follow-up of survivors 50 months (75% of cases > 34 months)

39.5% (95% CI: 35-44) at 3 years

29.7% (95% CI: 25-34) at 5 years

OS from relapse after an ASCT. The experience of the LWP EBMT/GITMO

- Stage at relapse
- B symptoms at relapse
- Bulky disease at relapse
- Extranodal involvement at relapse
- Poor performance status at relapse
- Early relapse (<6 months) after one ASCT

*p<0.0001

We Have Been Able to Reduce NRM with RIC Protocols

NRM

RR 2.42 (95% CI 1.58-3.96)
\[ p<0.001 \]

RIC (n=97)

Conventional (n=93)

PFS

RR 1.38 (95% CI 0.9-1.96)
\[ p=0.07 \]

RIC (n=97)

Conventional (n=93)

Estimate of the NRM and PFS based on a COX model, adjusted by all covariates with impact on the outcomes. RR and p values from multivariate Cox model.

Sureda et al, JCO 2008
We Have Been Able to Demonstrate the Existence of a Beneficial GVL Effect

Impact of cGVHD after allo-SCT in relapse rate and PFS

Relapse or Progression (%)

Progression free survival (%)

Time after allo-SCT (months)

RR 1.89 (95% CI 1.02-3.49)  
$p=0.04$

RR 1.57 (95% CI 0.91-2.72)  
$p=0.1$

Sureda et al, JCO 2008
Allo-SCT for Hodgkin lymphoma: 1990-2009

Number of allo-SCT by year
RIC vs MAC in allo-SCT: 1990-2009

RIC or conventional conditioning by year

Conventional RIC

The European Group for Blood and Marrow Transplantation
In a Donor vs No Donor Analysis ..... RIC-Allo Achieves Better Results Than Other Strategies ..... 

The donor versus no-donor analysis had the day of relapse after autologous transplantation as the starting point.

Sarina et al, Blood 2010

EBMT
European Society for Blood and Marrow Transplantation
40th Anniversary
Saving lives since 1974
Published Series on allo-SCT in HL: Failures to a prior ASCT

<table>
<thead>
<tr>
<th>Author, year</th>
<th>N</th>
<th>Prior ASCT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peggs et al, 2005</td>
<td>49</td>
<td>44 (90)</td>
</tr>
<tr>
<td>Alvarez et al, 2006</td>
<td>40</td>
<td>29 (73)</td>
</tr>
<tr>
<td>Anderlini et al, 2008</td>
<td>58</td>
<td>48 (83)</td>
</tr>
<tr>
<td>Sureda et al, 2008</td>
<td>168</td>
<td>87 (52)</td>
</tr>
<tr>
<td>Robinson et al, 2009</td>
<td>285</td>
<td>229 (80)</td>
</tr>
<tr>
<td>Claviez et al, 2009</td>
<td>91</td>
<td>40 (44)</td>
</tr>
<tr>
<td>Devetten et al, 2009</td>
<td>143</td>
<td>89 (62)</td>
</tr>
<tr>
<td>Sureda et al, 2012</td>
<td>92</td>
<td>79 (86)</td>
</tr>
</tbody>
</table>
HDR-Allo Protocol

Fludarabine: 30, 30, 30, 30, 30, 70, 70
Melphalan: 70, 70, 8, 7, 6, 5, 4, 3, 2, 1, 0, +1, +2, +3, +4, +5, +6

ATG (URD) 15, 15, 15
PBSCs

Mtx 10 mg/m²

CsA

Sureda et al. Haematologica 2012
Non-relapse mortality

CI NRM (%)

Time after RIC-allo (months)

8% at 100 days
15% at 1 yr
17% at 2 yr
19% at 3 yr

Sureda et al. Haematologica 2012
Relapse Incidence in Chemosensitive Patients

Sureda et al. Haematologica 2012
Impact of cGVHD on Relapse Incidence

Sureda et al. Haematologica 2012
PFS and OS after RIC-Allo in Chemosensitive Patients (n = 50)

Sureda et al. Haematologica 2012
DLIs Modulate Relapse Risk in Mixed Chimeras and Induce Durable Responses in Relapsed Patients Treated with a T-Cell Depleted RIC

Peggs et al, JCO 2011
# Published Series on allo-SCT in HL. Relapse Rates after Transplant

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Relapse Rate</th>
<th>Impact of disease status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvarez et al, 2006</td>
<td>47% (3 yrs)</td>
<td>2.5 (1.2 – 5.6), p = 0.01</td>
</tr>
<tr>
<td>Anderlini et al, 2008</td>
<td>55% (2 yrs)</td>
<td>2.9 (0.9 – 8.8), p = 0.05</td>
</tr>
<tr>
<td>Sureda et al, 2008</td>
<td>27% vs 46% (1 yr) 30% vs 57% (3 yrs) 32% vs 58% (5 yrs)</td>
<td>1.51 (0.95 – 2.39), p = 0.08</td>
</tr>
<tr>
<td>Robinson et al, 2009</td>
<td>41% (1 yr), 53% (3 yrs), 59% (5 yrs)</td>
<td>2.1 (1.5 – 2.9), p &lt; 0.001</td>
</tr>
<tr>
<td>Claviez et al, 2009</td>
<td>36% (3 yrs), 44% (5 yrs)</td>
<td>2.1 (1.0 – 4.4), p = 0.04</td>
</tr>
<tr>
<td>Devetten et al, 2009</td>
<td>40% (1 yr), 47% (2 yrs)</td>
<td>----</td>
</tr>
<tr>
<td>Sureda et al, 2012</td>
<td>37% (1 yr), 49% (2 yrs), 59% (3 yrs)</td>
<td>2 (1.6 – 3), p = 0.01</td>
</tr>
</tbody>
</table>
Allo-SCT in children and adolescents with recurrent HL

The type of conditioning had no impact on NRM. RIC regimens were associated with an increased risk of progression, with a lower PFS.

Claviez et al. Blood 2009
NRM and RR after allo-SCT According to the Intensity of the Conditioning Regimen

![Graph showing cumulative incidence of relapse and non-relapse mortality](image)

- **Relapse**
  - RIC
  - Not RIC
  - \( p = 0.051 \)

- **Non-relapse mortality**
  - RIC
  - Not RIC
  - \( p = 0.772 \)

*Fig 1. Nonrelapse mortality after allogeneic stem-cell transplantation (alloSCT) for Hodgkin’s lymphoma according to the type of conditioning regimen, based on a Cox model. The curves represent an estimate of the probability of nonrelapse mortality adjusted by chemotherapy sensitivity of the disease at stem-cell transplantation, a previously failed autologous stem-cell transplantation, and age of the patient at alloSCT. Relative risk (RR) and P-values are from multivariate Cox models. RIC, reduced-intensity conditioning.*
NRM and RR after allo-SCT According to Disease Status at allo-SCT

Genadieva et al, EBMT 2014
EFS after allo-SCT According to the Intensity of the Conditioning Regimen

Genadieva et al, EBMT 2014
EFS after allo-SCT According to Disease Status at allo-SCT

Genadieva et al, EBMT 2014
OS after allo-SCT According to the Intensity of the Conditioning Regimen

Genadieva et al, EBMT 2014
### RETROSPECTIVE ANALYSIS: PATIENTS WITH R/R HL WHO RECEIVED REDUCED INTENSITY ALLO-SCT POST BRENTUXIMAB VEDOTIN

Retrospective analysis of 19 patients*

#### Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>N=19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>31 (23–55)</td>
</tr>
<tr>
<td>Prior chemotherapy regimens, median (range)</td>
<td>5 (3–8)</td>
</tr>
<tr>
<td>Prior ASCT, n</td>
<td>18/19</td>
</tr>
<tr>
<td>Prior XRT, n</td>
<td>10/19</td>
</tr>
<tr>
<td>Best response to brentuximab vedotin, %</td>
<td>CR: 42%; PR: 42%; SD: 11%; PD: 5%</td>
</tr>
<tr>
<td>Number cycles of brentuximab vedotin, median (range)</td>
<td>8 (2-16)</td>
</tr>
<tr>
<td>Disease status at time of allo-SCT</td>
<td>CR: 37%; PR: 37%; SD: 11%; PD: 16%</td>
</tr>
</tbody>
</table>

* Treated at City of Hope or Seattle Cancer Care Alliance/Fred Hutchinson Cancer Center

R/R – relapsed/refractory; HL – Hodgkin lymphoma; Allo-SCT – allogeneic stem cell transplantation; ASCT – autologous stem cell transplantation; CR – complete response; PR – partial response; SD – stable disease; PD – progressive disease; XRT - radiotherapy

Chen R et al. Oral presentation at ICML 2013, Lugano, Switzerland (Abstract #140).
## Transplant-related outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N=19</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Engraftment</strong></td>
<td></td>
</tr>
<tr>
<td>Days to ANC ≥ 0.5 x 10⁹/L</td>
<td>14 (range: 0 – 21)</td>
</tr>
<tr>
<td>Days to platelets &gt; 20,000</td>
<td>14 (range: 0 – 21)</td>
</tr>
<tr>
<td>% Chimerism</td>
<td>&gt; 99% (Day 30 – 209)</td>
</tr>
<tr>
<td><strong>Acute GVHD, %</strong></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>26.3</td>
</tr>
<tr>
<td>II</td>
<td>5.3</td>
</tr>
<tr>
<td><strong>Chronic GVHD, %</strong></td>
<td></td>
</tr>
<tr>
<td>Limited</td>
<td>73.7</td>
</tr>
<tr>
<td>Extensive</td>
<td>68.4</td>
</tr>
<tr>
<td><strong>Infectious disease, %</strong></td>
<td></td>
</tr>
<tr>
<td>EBV reactivation</td>
<td>0</td>
</tr>
<tr>
<td>CMV reactivation</td>
<td>10.5</td>
</tr>
<tr>
<td>Clinical zoster</td>
<td>15.8</td>
</tr>
</tbody>
</table>

R/R – relapsed/refractory; HL – Hodgkin lymphoma; Allo-SCT – allogeneic stem cell transplantation; ANC - absolute neutrophil count; GVHD - Graft vs. host disease; EBV - Epstein-Barr virus; CMV - cytomegalovirus

Chen R et al. Oral presentation at ICML 2013, Lugano, Switzerland (Abstract #140).
## RETROSPECTIVE ANALYSIS: PATIENTS WITH R/R HL WHO RECEIVED REDUCED INTENSITY ALLO-SCT POST BRENTOXIMAB VEDOTIN

### Clinical outcomes

<table>
<thead>
<tr>
<th></th>
<th>N=19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up, months</td>
<td>25.6</td>
</tr>
<tr>
<td>2 - year OS, %</td>
<td>79.3 (CI: 56.0, 91.1)</td>
</tr>
<tr>
<td>2 - year PFS, %</td>
<td>59.3 (CI: 43.9, 71.7)</td>
</tr>
<tr>
<td>2 – year PFS in CR patients, %</td>
<td>71.4 (CI: 40.3, 88.3)</td>
</tr>
<tr>
<td>2 - year PFS in non-CR patients, %</td>
<td>54.6 (CI: 37.5, 68.9)</td>
</tr>
</tbody>
</table>

R/R – relapsed/refractory; HL – Hodgkin lymphoma; Allo-SCT – allogeneic stem cell transplantation; OS – overall survival; PFS – progression free survival; CR – complete response.

Chen R et al. Oral presentation at ICML 2013, Lugano, Switzerland (Abstract #140).
Impact of the Administration of Brentuximab Vedotin pre-allo-SCT in Peri-transplant Toxicity and Long Term Outcome

- N = 21 HL pre-treated with BV before allo-SCT (2009 – 2012)
- N = 23 HL not pre-treated with BV before allo-SCT (2003 – 2012)
- Conditioning regimen: Flu-Mel based
- BV pre-treated group:
  - More likely to be in CR before allo-SCT (p = 0.04)
  - Better co-morbidity index (0 vs 2, p = 0.03)
  - Less grades III-IV Bearman toxicities during allo-SCT (0 vs 7, p = 0.015)
- Median follow up:
  - No BV: 70.2 mo
  - BV: 23.3 mo

Chen et al. ASH 2013
**Impact of the Administration of Brentuximab Vedotin Pre-allo-SCT in Peri-transplant Toxicity and Long Term Outcome**

<table>
<thead>
<tr>
<th></th>
<th>BV (n = 21)</th>
<th>No BV (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-yr PFS</td>
<td>51.8%</td>
<td>26.1%</td>
</tr>
<tr>
<td>2-yr RR / Progression</td>
<td>28.9%</td>
<td>56.5%</td>
</tr>
<tr>
<td>2-yr OS</td>
<td>66.6%</td>
<td>56.5%</td>
</tr>
<tr>
<td>NRM (100 days and 1 yr)</td>
<td>0% / 11.8%</td>
<td>4.3% / 17.4%</td>
</tr>
<tr>
<td>aGVHD</td>
<td>33%</td>
<td>56.5%</td>
</tr>
<tr>
<td>cGVHD</td>
<td>76%</td>
<td>78.3%</td>
</tr>
</tbody>
</table>

Chen et al. ASH 2013
**Brentuximab Vedotin in Rel/Ref HL prior to RIC allo-HCT**

**2-year PFS:**
- SGN-35 = 52%
- No SGN-35 = 26%

**2-year OS:**
- SGN-35 = 67%
- SGN-35 = 57%

Chen R et al. ASH 2013, New Orleans, LA, USA (Abstract 3374)
Brentuximab Vedotin in Rel/Ref HL prior to RIC allo-HCT

2-year probability of relapse:
- SGN-35 = 29%
- No SGN-35 = 57%

Chen R et al. ASH 2013, New Orleans, LA, USA (Abstract 3374)
Response-adjusted transplantation strategy

N = 28
Age [median (range)]: 32 (18 – 66)

Primary refractory disease: 11 pts
Early relapses: 5 pts
Late Relapses: 12 pts

ABVD as initial therapy: 24 pts
ESHAP as first salvage therapy: 24 pts

ASH 2011: Thomson & Peggs
**PAIReD trial:**

**Hodgkin lymphoma: primary resistant or first relapse**

- Tissue type patient and siblings. Initiate UD search as appropriate
- 2 cycles of salvage chemotherapy
- PET-CT (centrally reported)

- **CR**
  - *<CR, non-progressive*:
    - Further line of salvage permissable
    - Non-progressive (incl. CR) → Not suitable for study
    - Progressive disease
  - Not suitable for study

- **Progressive disease**
  - Further line of salvage permissable
  - Not suitable for study

- **Suitable donor?**
  - Yes: BEAM-C allograft
  - No: Not suitable for study
Unmanipulated haploidentical bone marrow transplantation following non myeloablative conditioning and post-transplantation cyclophosphamide for advanced Hodgkin’s Lymphoma.


Bone Marrow Transplant 2013, in press
Take-Home Messages

- In the absence of prospective clinical trials, allo-SCT is an effective salvage therapy for patients relapsing after an ASCT
- Non-relapse mortality is not a significant issue nowadays. Major efforts should be dedicated to decrease the relapse rate after allo-SCT
- The role of allo-SCT in earlier stages of the disease and in the era of “new drugs” needs to be assessed