NHL

Yüksek doz Kemoterapi
Transplantasyon

Prof. Dr. Yener Koç
JACIE - EBMT / ISCT
Indications for Hematopoietic Stem Cell Transplants in the United States, 2009

Number of Transplants

- Multiple Myeloma
- NHL
- AML
- HD
- ALL
- MDS/MPD
- Aplastic Anemia
- CML
- Other Leuk
- Non-Malignant Disease
- Other Cancer

Allogeneic (Total N=7,012)
Autologous (Total N=9,778)
When do we need Auto?

- Chemosensitive relapse
- High intermediate / high risk IPI
- High grade NHL (Burkitt/LBL) in 1st CR
- ? Ki-67 (>90%)
SCT in the treatment of DLCL is more effective than conventional chemotherapy and is the recommended treatment for the following:

- 1st chemotherapy-sensitive relapse
- 1st CR in high/intermediate-high risk IPI patients
- as HDSC in intermediate-high/high risk IPI untreated patients
Additional indications for Auto-Transplantation

Burkitt NHL in 1st CR, > Stage 1

Lymphoblastic lymphoma

MCL in 1st CR
Probability of Survival after Autotransplants for Follicular Lymphoma, 1996-2004 - by Disease Status and Transplant Year -

Chemo-sensitive, 1996-99 (N=1,013)

Chemo-sensitive, 2000-04 (N=1,067)

Chemo-resistant, 1996-99 (N=122)

Chemo-resistant, 2000-04 (N=90)

P < 0.001
Probability of Survival after Autotransplants for Diffuse Large B-Cell Lymphoma, 1996-2004 - by Disease Status and Transplant Year -

- Chemo-sensitive, 1996-99 (N=1,711)
- Chemo-sensitive, 2000-04 (N=3,122)
- Chemo-resistant, 1996-99 (N=283)
- Chemo-resistant, 2000-04 (N=258)

P < 0.001
High dose sequential chemotherapy and autologous stem cell transplantation in patients with relapsed/refractory lymphoma

BASAK OYAN, YENER KOC, EVREN OZDEMIR, AYSE KARS, ALEY TURKER, OULTEN TEKUZMAN, & EMIN KANSU

Hacettepe University, Institute of Oncology, Section of Medical Oncology, Hematopoietic Stem Cell Transplantation Unit, Ankara, Turkey

Abstract

Although high-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has become the standard approach for patients with relapsed/refractory Hodgkin's disease (HD) or non-Hodgkin's lymphoma (NHL), more than 50% of patients experience relapse following ASCT. High-dose sequential chemotherapy (HDSC) can intensify the conventional salvage treatment and improve the outcomes of HD patients by maximal debulking of the tumor load with the use of non-cross resistant drugs, each at their maximal tolerated doses. We conducted a phase II study in 40 patients with relapsed/refractory HD (n = 18) and NHL (n = 22) using HDSC followed by ASCT. Only patients sensitive to salvage chemotherapy were eligible for the protocol, consisting of three phases. Phase I consisted of cyclophosphamide (4.5 g/m^2) followed by G-CSF and peripheral blood stem cell (PBSC) collection. Phase II consisted of etoposide (2.5 g/m^2). The transplant phase consisted of mitoxantrone (60 mg/m^2) and melphalan (180 mg/m^2) followed by PBSC infusion. Eleven out of nineteen patients with B-cell lymphoma received intrathecal. Prior to HDSC, 65% of patients were in complete remission (CR) and 55% were in partial remission (PR). After completion of all phases of the protocol, 35 out of 39 evaluable patients achieved CR (85%), and this was durable in 30 (75%) patients with a projected progression-free survival (PFS) rate at 4 years of 71.7%. Treatment-related mortality rate at day +100 was 2.5% (n=1). At a median follow-up of 32 months (range, 3–41), nine patients relapsed progression and eleven patients died. The estimated 4-year PFS and overall survival (OS) were 72.2% and 47.8% in HD patients and 70.5% and 69.4% in NHL patients, respectively. Factors predicting OS were response to conventional salvage therapy and stage prior to salvage therapy. When compared to patients achieving CR prior to HDSC, patients who attained CR prior to HDSC had a significantly higher probability of 4-year OS (74.4% vs 31.1%, p = 0.02). Three prognostic subgroups were identified according to the risk determined by stage prior to intravenous salvage chemotherapy—remission duration prior to salvage therapy (early relapse vs. late relapse) and response to salvage. Prognostic score was found to predict OS, PFS, and event-free survival (EFS). In conclusion, HDSC followed by ASCT is an effective salvage therapy with acceptable toxicity, allowing further consolidation of response attained by conventional salvage therapy.

Keywords: High dose sequential, lymphoma, relapse, refractory, autologous

Introduction

Despite advances in therapy, 40% to 60% of patients with non-Hodgkin's lymphoma (NHL) either fail to achieve a complete remission (CR) or relapse after standard first-line therapy [1]. With conventional salvage regimens, these patients have a less than 10% chance of achieving a prolonged disease-free interval [1]. Although the majority of patients with Hodgkin's disease (HD) will be cured with initial therapy, 5–10% will not achieve a CR and 10–30% will relapse following standard therapy [2]. High dose chemotherapy (HDCT) and autologous stem cell transplantation (ASCT) is the most effective—and currently the standard approach—for patients with relapsed/refractory NHL or HD [3–5]. Still, relapse occurs in 50% or more of the patients who are autologous transplanted relapsed or refractory NHL or HD. One way to get through this problem might be intensification of salvage and conditioning regimen.

Patients had significantly different 4-year OS, PFS and DFS when divided into three subgroups according to a prognostic score (Table I). Patients with score D (n = 14) had a 4-year OS of 88.4%, compared with 38.3% in patients with score 2 and 26% in those with score 3 (Figure 1). In patients with B-cell NHL (n = 14), no significant difference in 4-year DFS was observed between patients who received rituximab (81.8%) and those who did not (48.4%).

Toxicity

Major toxicities of the HDSC protocol were grade 3–4 hematological toxicity and febrile neutropenia. Grade 3–4 thrombocytopenia and neutropenia were observed in all patients at all phases. No treatment-related mortality occurred in the first two phases and all patients achieved autologous stem cell infusion. Only one patient experienced mobilization failure and a second attempt of stem cell collection was successful after mobilization with G-CSF (10 mg/kg) for 6 days. The majority of patients experienced grade 1 mucositis, grade 2 nausea and vomiting. Only two patients developed grade 3 mucositis during phase III. Median time to neutrophil and platelet engraftment was 14 (range, 10–29) and 23 days (range, 15–21), respectively. Delay in platelet engraftment was observed in five (13%) patients. Invasive aspergillosis was documented and successfully treated in one patient. No episode of hemorrhagic cysts was observed following cyclophosphamide infusions. Five patients developed symptomatic congestive heart failure (CHF) and one patient died due to CHF. One of the patients developing CHF had diagnosis of thrombocytopenia and infection-related hemochromatosis that contributed to CHF.

One death occurred in the first 100 days after ASCT and was due to veno-occlusive disease, possibly related to history of chronic alcoholism.

High dose sequential chemotherapy in lymphoma

Late mortality after post-transplant day 100 occurred in three patients: one due to CHF, one due to secondary acute myeloblastic leukemia (AML), and one due to myelodysplasia and chronic hepatitis C infection.

Two patients with HD developed secondary malignancy. One patient, who received HDSC for relapse, died of AML 13 months after ASCT and one patient who received HDSC after third relapse, developed myelodysplasia and reactivation of hepatitis C after 36 months from ASCT and died. Both patients had been exposed to radiotherapy as a part of their first-line treatment.

Discussion

Patients with relapsed or refractory lymphoma can rarely be cured with conventional chemotherapy [1,13]. Although HDCT followed by ASCT has become the standard approach for most of these patients, approximately 40% of patients develop recurrence following ASCT. Most important variables affecting outcome in HDCT and ASCT are chemosensitivity to conventional salvage chemotherapy and the remission status before HDCT. CR having the best outcome, followed by PR and then stable disease (Fig. 14–17). This different studies have focused on investigation of an optimal salvage regimen to obtain maximum response before ASCT [16,18]. High-dose sequential chemotherapy can intensify the conventional salvage treatment and improve the outcome of ASCT by maximal debulking of the tumor load with the use of non-cross resistant drugs, each at their maximal tolerated doses. The regimen also takes the advantage of the collection of usually large amounts of PBSC after high-dose cyclophosphamide.

This study, patients chemosensitive to salvage regimen were eligible for HDSC/ASCT, since many studies have shown that this group of patients has

Figure 1. Estimated (a) overall survival (OS) and (b) progression-free survival (PFS) according to prognostic score.
Median overall survival = 47 months

MCL

Auto SCT w/o purging
AutoSCT with purging

HR 0.36 (0.18-0.90); p 0.027
Mantle Cell Lymphoma: Decision Making for Transplant

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Medical Park Hospital, Antalya and Ankara University Medical School, Ankara Turkey

1. Introduction
1.1 Definition and clinical characteristics
Mantle Cell Lymphoma (MCL) is a relatively rare type of mature B-cell lymphoma that comprises 5% of Non-Hodgkin’s Lymphomas (NHL) [1-3]. MCL was added to the Revised European-American Lymphoma classification in 1994. Having both indolent and incurable features associated with aggressive clinical course, MCL is most frequently seen in 6th decade of life, with male dominance 3 to 4:1. Malignant origin of MCL cells appear to derive from an antigen-naive pregerminal center cell [4-5].

1. B-cell neoplasms
1.1 Precursor B-cell
1.2 Mature B-cell
   - Chronic lymphocytic leukemia/small lymphocytic lymphoma
   - Lymphoplasmacytic lymphoma
   - Splenic marginal zone lymphoma
   - Extranodal marginal zone B-cell lymphoma of MALT
   - Nodal marginal zone B-cell lymphoma
   - Follicular lymphoma
   - Mantle cell lymphoma
   - Diffuse large B-cell lymphoma
   - Mediastinal (thymic) large B-cell lymphoma
   - Intravascular large B-cell lymphoma
   - Primary effusion lymphoma
   - Burkitt’s lymphoma/leukemia
1.3 B-cell proliferations of uncertain malignant potential
2. T-Cell and NK-Cell neoplasms

| Table 1. World Health Organization Classification of Lymphomas [1]. |
When do we need Allo?

Relapsed Refractory NHL
DHAP – BEAM - AUTO

Original article

High-dose sequential chemotherapy followed by autologous stem cell transplantation in relapsed and refractory aggressive non-Hodgkin’s lymphoma: results of a multicenter phase II study

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Received 8 October 2004; revised 17 March 2005; accepted 18 March 2005

Background: Combination chemotherapy can cure patients with non-Hodgkin’s lymphoma (NHL), but those who suffer treatment failure or relapse still have a poor prognosis. High-dose chemotherapy (HDCT) with autologous stem cell transplantation (ASCT) can improve the outcome of these patients. We evaluated an intensified high-dose sequential chemotherapy program with a final myeloablative course.

Patients and methods: Inclusion criteria were age 18–65 years, histologically proven primary progressive or relapsed aggressive NHL and eligibility for HDCT. The therapy consists of two cycles DHAP: daunorubicin 40 mg (day 1–4), high-dose cytarabine 2 g/m2 (day 2), cisplatin 100 mg/m2 (day 5); patients with partial (PR) or complete remission (CR) received cyclophosphamide 4 g/m2 (day 17), followed by peripheral blood stem cell (PBSC) harvest; methotrexate 8 g/m2 (day 1) plus vinorelbine 1.4 mg/m2 (day 51); and etoposide 500 mg/m2 (day 58–62). The final myeloablative course was BEAM: cytarabine 200 mg/m2 (day 81–84), etoposide 150 mg/m2 (day 81–84), melphalan 140 mg/m2 (day 80), carmustine 500 mg/m2 (day 80) followed by PBSC.

Results: Fifty-seven patients (median age 45 years, range 24–65) were enrolled: 23 (40%) patients were refractory to primary therapy and 34 (60%) patients had relapsed NHL. The response rate (RR) after 2 cycles of DHAP was 72% (95% CI, 65%–79%) and at the final evaluation (100 days post-transplantation) 45% (33% CR, 11% PR). Toxicity was tolerable. Median follow-up was 24 months (range 6–76 months). Freedom from second failure (FF2F) and overall survival (OS) at 2 years were 25% and 47% for all patients. OS2F at 2 years for patients with relapse and for patients refractory to primary therapy were 31% and 9% (P=0.005), respectively. OS of 2 years for patients with relapse and for patients refractory to primary therapy were 58% and 24% (P=0.004), respectively.

Conclusions: We conclude that this regimen is feasible, tolerable and effective in patients with relapsed NHL. In contrast, the results in patients with progressive disease are unsatisfactory. This program is currently being modified by addition of rituximab for patients with relapsed aggressive NHL.

Key words: high-dose chemotherapy, non-Hodgkin’s lymphoma, relapse

Introduction

Patients with aggressive non-Hodgkin’s lymphoma (NHL) treated at first diagnosis with polychemotherapy alone or combined chemotherapy can achieve high response rates [1–7]. However, patients with relapsed or progressive disease still have a poor prognosis. High-dose chemotherapy (HDCT) followed by autologous stem cell transplantation (ASCT) is the treatment of choice for these patients [8–16]. The most compelling evidence for the superiority of HDCT compared with conventional-dose salvage therapy in relapsed and progressive NHL is based on the randomized “Parma trial” [15]. In this study, all patients received two cycles of conventional chemotherapy. The responders were randomized to receive...
Why do we need Allo?

Clean graft ...

GVL !...

Elimination of HSC damage (secondary leukemia)
Auto versus Allo?

Randomized trial

Disease progression, favors allogeneic: 69% vs 20%  
$p = 0.001$

Chemoresistant disease

auto vs allo: 87% vs 19%  
$p = 0.008$

Ratanatharathorn V, Blood 1994;84:1050
Benefit of Allo-HSCT: GVL effect

Existence of a GvL effect: ability of DLI and withdrawal of immunosuppression to lead to durable remission

van Besien KW, Giralt SA BMT 1997;19:977

Allo-HSCT for MCL
Patients achieved remission in conjunction with GvHD

Patients converted from PCR-positive to PCR-negative over time following Allo-HSCT, supporting an active role of GvL

Allo-HSCT reports in HL < 2000

50 % TRM

Myeloablative

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient number</th>
<th>TRM</th>
<th>Relapse</th>
<th>DFS/PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBMTR[52]</td>
<td>100</td>
<td>61% (3 years)</td>
<td>65% (3 years)</td>
<td>15% (3 years)</td>
</tr>
<tr>
<td>EBMT [54]</td>
<td>45</td>
<td>48%</td>
<td>61%</td>
<td>15% (4 years)</td>
</tr>
<tr>
<td>Seattle [53]</td>
<td>53</td>
<td>58%</td>
<td>48%</td>
<td>22% (5 years)</td>
</tr>
</tbody>
</table>

Gajewski JL, JCO 1996;14:572
Milpied N, JCO 1996;14:1291
Anderson JE, JCO 1993;11:2342
Transplantation for aggressive NHL

Given the high TRM, allografting has been restricted to patients with:

- Refractory or multiply-relapsed disease

Dhedin N, Br J Haematol 1999;107:154
Mitterbauer M, Leukemia 2001;15:635
Soiffer RJ, BMT 1998; 21:1177
van Besien K, BBMT 1997;3:150
MDACC experience < 2000

Myeloablative Allo in Aggressive NHL

High response rate (79%)

Extremely high mortality rate (77%)

Median survival : 118 days

Causes of death

- Recurrent/Progressive disease (23%),
- Fatal infections (21%)
- Grade IV acute GvHD (11%)
- Extensive chronic GvHD(9%)

1 yr DFS : 23%

20% remain alive without disease (median F/U 2.6 yr)

van Besien K, BBMT 1997;3:150
Allografting in LG-NHL < 2000

IBMTR, n = 113

DFS at 3 years : 49%
Recurrence rate : 16%
Non-relapse mortality : 40%

Factors associated with a better survival :
- Age < 40 yr, better performance status
- Chemosensitive disease
- Use of TBI

Van Besien K, Blood 1998;92:1832
Allo-transplant Risks in Lymphoma

“heavily pre-treated”

and

multidrug-resistant

prolonged 1st line & salvage
Allo-transplant Risks in Lymphoma

2\textsuperscript{nd} transplant

(after autotransplant)
Allo-transplant Risks in Lymphoma

relatively lower sensitivity to GVT

HL / NHL - lymphoblastic & intermediate grade
Allo-transplant Risks in Lymphoma

impaired T-cell immunity

pre & post-transplant infections

aspergillus, PTLD, toxo
Causes of Death after Transplants 2008-2009

**Unrelated Donor**
- Primary Disease (33%)
- GVHD (15%)
- Other (29%)
- Organ Failure (6%)
- Infection (16%)
- New Malignancy (1%)

**HLA-identical Sibling**
- Primary Disease (47%)
- GVHD (14%)
- Other (21%)
- Infection (12%)
- Organ Failure (4%)
- New Malignancy (1%)
Risklerin azaltılması

- Konsey Toplantıları
- Tedavi Öncesi Hazırlık Toplantıları
- Koordinasyon
- Kalite-Kontrol
- Akreditasyon çalışmalarları
Transplanta Hazırlık
Alıcı ile ilgili Faktörler / Transplant Konseyi

✓ Transplant öncesi yeniden evrelendirme

✓ Non-hematolojik toksisite yaratan ajanların kümulatif dozlarının değerlendirilmesi
  CDDP, Bleo, Antrasiklin, RT

✓ Var olan veya geçirilmiş kronik infeksiyonların belirlenmesi
  Aspergillus, Tbc, HIV

✓ Ko-morbid problemler ve allerjilerin tespiti
  b-laktam, TMP-SMZ

✓ Uygun hazırlayıcı rejinin seçilmesi
  EKO, SFT, DLCO, CLCr
Intensity of preparative regimens

Immunosuppression

- Haplo/T-cell dep
- MUD
- Matched sibling

Genetic disparity

Myelosuppression

Aggressiveness of malignancy

- CLL/LGL
- CML
- MM
- LCL
- AML

Standard dose chemotherapy w/o BMT

- Flag-Ida
- FC
- PFA

Needs BMT

- FM
- BEAM
- Bu8/F/ATG

Maximally tolerated high dose

- TBI/Cy
- TBI/F/TT
- Bu16/Cy

- Bu16/Cy
- Cy/TBI
Non-Myeloablative Rejim

Preparative regimen

HSCT

DLI

Recipient

Mixed Chimera

Full Chimera
Non-myeloablatif Hazırlayıcı Rejim

- MMF 15 mg/kg PO bid
- CSA 2,5 mg/kg IV +30 +60 +100
  - CsA orale geçilir 5 mg/kg bid
  - Donör G-CSF
- Fludarabine 25 mg/m²
  - -3 => +1
  - -6 -5 -4 -3 -2 -1 0
  - CD34+ cells/kg
- PBSC 8-12x10⁶
- TBI 2 - 4 Gy
  - +14 - 21 +30 +60 +100
  - CSA 2,5 mg/kg IV
  - MMF 15 mg/kg PO bid
- Kimerizm 50% donor
- DCI Tüber hastalar
  - 1 x 10⁷ CD3+hücre/kg
- DCI GVHD olmayan tüm hastalara
  - 0.1-4 x 10⁷ CD3+hücre/kg
- TRM 0 %
- n = 40
- +100. gün
- EBMT CIC-919, CIBMTR 11080
RIC Hazırlayıcı Rejim

**Fludarabine**

-6 -5 -4 -3 -2 -1 0

25 mg/m²

BU

≤ 8 mg/kg IV

-3 => +1

Donör G-CSF

**PBSC**

6-8x10⁶ CD34+ cells/kg

**CsA orale geçilir**

5 mg/kg bid

**CSA**

2.5 mg/kg IV

+14 - 21

+30 +60 +100

**MMF**

15 mg/kg PO bid

**PBSC**

6-8x10⁶ CD34+ cells/kg

TRM 4 %
n = 49

+100. gün, Full matched sibling

EBMT CIC-919, CIBMTR 11080
Myeloablatif Hazırlayıcı Rejim

Fludarabine
-6  -5  -4  -3  -2  -1  0
25 mg/m²
BU
> 8 mg/kg IV

MMF
15 mg/kg PO bid

PBSC
6-8x10⁶ CD34+ cells/kg

CSA
2,5 mg/kg IV
+14 - 21
+30
+60
+100

CsA orale geçilir
5 mg/kg bid

Donör G-CSF

TRM 9 %
n = 21
+100. gün
EBMT CIC-919, CIBMTR 11080

Kimerizm
>90% donör

DCI
Nadiren Rejeksiyon olursa
1 x 10⁷ CD3+
 hücre/kg

Cevap değerlendirmesi
Hangi Yaşa Kadar?

Tarama testleri ve klinik değerlendirmeyi geçmek şartı ile;

- Non-myeloablatatif: ≥ 70 yaş
- RIC: < 70 yaş
- Myeloablatif: < 60 yaş
- Akraba dışi myeloablatif: < 55 yaş
Follicular Lymphoma
HLA-identical Sibling

2000-2009

Probabilty of Survival, %

Years

Sensitive (N=698)
Resistant (N=144)
Diffuse Large B-Cell Lymphoma

Probability of Survival, %

2000-2009

Sensitive (N=383)

Resistant (N=124)
Mantle Cell Lymphoma

Probability of Survival, %

- Sibling donor (N=498)
- Unrelated donor (N=325)
- Autologous (N=2,574)

Years

P < 0.0001
Tam uyumlu verici yok ise?

Haploidentical Transplantation
1980s: worse survival with ↑ mismatch

AML CR1, CML CP, ALL CR 1 or 2

Haploidentical Transplantation

Figure 1. Treatment schema for nonmyeloablative conditioning and HLA-haploidentical bone marrow transplantation. From ref. 11.
Post-transplantation Cy (Hopkins)
No worse GVHD with ↑ HLA mismatch

- Cumulative incidence of acute GVHD (%)
- Days after transplantation

- 0-2 Ag MM
- 3-4 Ag MM

$P = .68$
Mini-haploBMT for lymphoma

![Graph showing event-free survival over days after transplantation for different lymphoma types.](image)

- **Hodgkin lymphoma** (n=22)
- **Mantle cell lymphoma** (n=10)
- **Non-Hodgkin lymphoma** (n=50)
Survival benefit of Class I mismatching

HVG direction

- 2-3 mismatches
- 0-1 mismatch

EFS (%)

HR 0.45, p = 0.001

Overall Survival (%)

HR = 0.41, p = 0.0003
Hopkins Relapse Data

A. HLA-DR antigen mismatch in GVH direction
   - Relapse: no mismatch
   - Relapse: + mismatch
   - Non-relapse mortality (p=0.8)

B. HLA Class I allele mismatch in GVH direction
   - Relapse: 0-1 mismatch
   - 2-3 mismatches
   - Non-relapse mortality (p=0.7)

TRM % 20
Haploidentik Myeloablatif Hazırlayıcı Rejim

Fludarabine 25 mg/m²
-6 -5 -4 -3 -2 -1 0
BU 9,6 mg/kg IV
-6 -5
CTX 14.5 mg/kg

PBSC 12x10⁶ CD34+ cells/kg

CSA 2,5 mg/kg IV
+14 - 21 +30 +60 +100

MMF 15 mg/kg PO bid

Kimerizm >90% donör

DCI Rejeksiyon < %10

TRM 19 %
n = 60
+100. gün
EBMT CIC-919, CIBMTR 11080

Koc Y, 2010-2012
## Transplant activity for Lymphoma
### 2000 - 2012

<table>
<thead>
<tr>
<th>Total # of transplants: 615</th>
<th>(195,105,315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma: 232 transplants</td>
<td>(37%)</td>
</tr>
<tr>
<td>Auto n = 186</td>
<td>(80%)</td>
</tr>
<tr>
<td>Allo n = 46</td>
<td>(20%)</td>
</tr>
<tr>
<td>identical sibling</td>
<td>25</td>
</tr>
<tr>
<td>mismatched</td>
<td>9</td>
</tr>
<tr>
<td>haploidentic</td>
<td>7</td>
</tr>
<tr>
<td>MUD</td>
<td>4</td>
</tr>
<tr>
<td>Cord Blood</td>
<td>1</td>
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Transplant activity for NHL
2000 - 2012

Total # of transplants for lymphoma: 232

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>NHL</td>
<td>148</td>
<td>64%</td>
</tr>
<tr>
<td>Auto n</td>
<td>123</td>
<td>83%</td>
</tr>
<tr>
<td>Allo n</td>
<td>25</td>
<td>17%</td>
</tr>
<tr>
<td>identical sibling</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>mismatched</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>haploidentic</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>MUD</td>
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Transplant activity for NHL
2009 - 2012

Total # of transplants for lymphoma : 97

<table>
<thead>
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<th>Type</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
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<td>60</td>
<td>62%</td>
</tr>
<tr>
<td>Auto</td>
<td>44</td>
<td>73%</td>
</tr>
<tr>
<td>Allo</td>
<td>16</td>
<td>27%</td>
</tr>
<tr>
<td>identical</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>mismatched</td>
<td>7</td>
<td>(1 mm: 4, haplo: 3)</td>
</tr>
<tr>
<td>MUD</td>
<td>1</td>
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# Post-Transplant Survival

**NHL** 2009 - 2012

Total # of transplants for lymphoma: 97

<table>
<thead>
<tr>
<th>Type</th>
<th>n</th>
<th>OS at 4 yr</th>
</tr>
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<tbody>
<tr>
<td>NHL</td>
<td>60</td>
<td>50 %</td>
</tr>
<tr>
<td>Auto</td>
<td>44</td>
<td>57 %</td>
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<tr>
<td></td>
<td></td>
<td>standard risk n=25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>high risk n=19</td>
</tr>
<tr>
<td>Allo</td>
<td>16</td>
<td>42 %</td>
</tr>
<tr>
<td>Type</td>
<td>Percentage</td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td>identical sibling</td>
<td>% 4</td>
<td></td>
</tr>
<tr>
<td>mismatched sibling / MUD</td>
<td>% 13</td>
<td></td>
</tr>
<tr>
<td>haploidentic</td>
<td>% 19</td>
<td></td>
</tr>
</tbody>
</table>
Relaps / Refrakter HL

Otolog

Refraktor

Full match Allo

4. ayda relaps

Haploidentik

CR
Relaps / Refrakter HL

Salvage

Refrakter
Relaps / Refrakter HL

Salvage:
- Refrakter
- Otolog
- PR
- XRT
- CR
- Allo
Relaps / Refrakter HL

Salvage
- Refrakter
  - Otolog
    - PR
    - XRT
      - CR
      - Allo
RIC - Allojenik Transplant Lenfoma

\[ n = 24 \]

2. Transplant : \[ n = 17 \]

3. Transplant : \[ n = 2 \]

Haploidentik : \[ n = 4 \]

Koc Y, 2012
Allojenik Transplant
Lenfoma

TRM %4  0-100. gün
n=1/24
1 rejeksiyon

Koc Y, 2012
Allojenik Transplant
Lenfoma

Kaplan-Meier Cum. Survival Plot for Survival (months)
Censor Variable: Censor-OS
Grouping Variable: Allo Donor Type

HLA identical
% 71

HLA mismatched
% 37

n = 12
n = 12

p = 0.01

Koc Y, 2012
Lenfoma Allo-Transplant
Ne zaman yapılmalıdır?

- Otolog sonrası relapslarda (HL, MCL, LG-NHL)
- Otolog ilik nakli endikasyonu var ve yapılamıyor ise
- 20-45 yaşta küratif amaç ile (MCL, LG-NHL)
- Kemosensitif relapslarda, CR elde edilebilir ise (HG-NHL)
- Relaps MCL, Relaps Burkitt ve LBL
Lenfoma Allo-Transplant Prensipleri

Pre-transplant tam remisyon sağlanmalı

- Gerekirse salvage olarak Otolog transplant yapılmalıdır
- Otolog sonrası rezidüel hastalık RT ile muamele edilmeli
- PET-CT negatifliği sağlanmalıdır

Seattle verilerinde PR ile transplanta girenlerde uzun süreli yaşam gözlenmedi
Lenfoma Allo-Transplant Prensipleri

Transplant öncesi tedavilerde kalıcı toksisiteli rejimlerden kaçınılmalı:

- CHOP uzatılmamalı, 2 kür sonra PET
- Salvage rejimlerde cisplatin ve antrasiklinden kaçınılmalı
- Pelvik - kardiyak RT den kaçınılmalı
Lenfoma Allo-Transplant Prensipleri

- TRM yi azaltmak için
- Rejeksiyon riskini azaltmak için
- DCI ihtiyacını azaltmak için
- Anti-tümör etki için

Myeloablatif / yoğunluğu azaltılmış hazırlayıcı rejim tercih edilmeli (Flu + IV-BU 8-9.6 mg/kg)
Lenfoma Allo-Transplant Prensipleri

- GVT etkisini artırmak için
- Erken GVT başlaması için
- Relaps riskini azaltmak için
- Uzun süreli ve kalıcı Anti-tümör etki için

Tam uyumlu olmayan veya haploidentik donör seçilmeli

PET ile rekurens takibi → Kemoterapi → DLI → IFN
Lenfoma Allo-Transplant Prensipleri

- Standart bir yaklaşım olmadığı için

Bireysel değerlendirme yapılarak konsey kararında komorbidite ve riskler tartışılarak hastaya teklif edilmeli
Teşekkürler...