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Faculty of Medicine
Department of Internal Medicine

Ain Shams University

Outcome of Allogeneic Hemopoietic Stem Cell Transplantation in Patients with Lymphoma

Thesis

Submitted for Partial Fulfilment of Master Degree in **Haematology**

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Aya Abdelhakim Awad Ibrahim

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List of Abbreviations

Abb.	Full term
ABC	*Activated B cell*
ALCL	*Anaplastic large cell lymphoma*
ALK	*Anaplastic lymphoma kinase*
ALL	*Acute lymphoblastic leukemia/lymphoma*
BCL2	*B cell leukemia/lymphoma 2*
BCL6	*B cell lymphoma 6*
BR	*Bendamustine plus rituximab*
Btk	*Btk*
BV	*Brentuximab vedotin*
CAR	*Chimeric antigen receptor*
Cdk	*Cyclin-dependent kinases*
cHL	*Classic HL*
CLL	*Chronic lymphocytic leukemia*
CR	*Complete response*
CRS	*Cytokine release syndrome*
CT	*Computed tomography*
CTCL	*Cutaneous T-cell lymphoma*
CTCL	*Cutaneous T-cell lymphomas*
DLBCL	*Diffuse large B cell lymphoma*
DLI	*Donor lymphocyte infusion*
EBV	*Epstein-Barr virus*
EORTC	*European Organization for the Research and Treatment of Cancer*
ESR	*Erythrocyte sedimentation rate*
FDA	*Food and Drug Administration*
FDG	*Fluorodeoxyglucose*
FISH	*Fluorescence in situ hybridization*
FL	*Follicular lymphoma*
GCB	*Germinal center B cell*
GEP	*Gene expression profiling*
GHSG	*German Hodgkin Study Group*

List of Abbreviations **cont...**

Abb.	Full term
GI	*Gastrointestinal*
HDAC	*Histone deacetylase*
HL	*Hodgkin lymphomas*
HMTs	*Histone methylstransfer-ferares*
HSCI	*Hematopoietic stem cell infusion*
HSCT CI	*HSCT Comorbidity Index*
HSCT	*Hematopoietic stem cell transplantation*
Ig	*Immunoglobulin*
IHC	*Isimmunohistochemistry*
IMT	*Inflammatory myofibroblastic tumor*
IPS	*International prognostic score*
LDCHL	*Lymphocyte depleted cHL*
LDH	*Lactate dehydrogenase*
LMP	*Latent membrane protein*
LRCHL	*Lymphocyte rich cHL*
MCCHL	*Mixed cellularity cHL*
MCL	*Mantle cell lymphoma*
MF	*Mycosis fungoides*
MSD	*Matched sibling donor*
NCCN	*National Comprehensive Cancer Network*
NHL	*Non-Hodgkin lymphoma*
NLPHL	*Nodular lymphocyte predominant HL*
NMDP	*National Marrow Donor Program*
NRM	*Nonrelapse mortality*
NSCHL	*Nodular sclerosis cHL*
OS	*Overall survival*
PAM	*Pre-transplantation Assessment of Mortality*
PCR	*Polymerase chain reaction*
PET	*Positron emission tomography*
PFS	*Progression-free survival*

List of Abbreviations **cont...**

Abb.	Full term

PI3K.....Phosphatidyl-inositole3 kynase
PKC .....Protein kinase C
PLD.....Pegylated Liposomal Doxorubicin
PNP .....Purine nucleoside phophoryalse inhibitor
PR .....Partial response
REMS .....Risk evaluation and mitigation strategy
RIC.....Reduced-intensity conditioning
RON.....Recepteur d'Origine Nantais
RS .....Reed-Sternberg
RT .....Radiation therapy
SLL .....Small lymphocytic lymphoma
SS.....Sezary Syndrome
TdT .....Terminal deoxynucleotidyl transferase
T-PLL .....T-prolymphocytic leukemia
WHO.....World Health Organization

Abstract

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is increasingly used in patients with lymphoma who experience disease relapse after autologous hematopoietic stem cell transplantation (auto-HSCT) because the allograft is tumor free and may induce a graft-versus-tumor effect.

Aim and objectives: Assess the clinical outcome in Egyptian patients diagnosed with lymphomas subjected to hemopoietic allogeneic stem cell transplantation from Human Leukocyte Antigen identical sibling donors.

Subjects and methods: This is A Retrospective study, carried out on 35 patients, at Bone Marrow Transplantation Unit at Nasser Institute Hospital, from May 1997 to August 2018.

Results: There was significant difference between the AGVHD/2–4 yes and no groups as regard MMF, STD, CMV, Mortality, HCV Ab and HCV PCR.

Conclusion: There was significant difference between patients who had the allogenic transplantation who relapse after the autologous transplantation

Keywords: Allogeneic Stem Cell Transplantation, Lymphoma, Haemodialysis, Autologous Stem Cell Transplantation.

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is now established as a standard therapeutic modality for a variety of malignant and non-malignant diseases. The first successful allogeneic HSCT was done with bone marrow (BM) as the source of hematopoietic stem cells in 1968 ***(Cheuk et al., 2013).***

Nowadays transplant physicians are faced with 3 viable choices of stem cells for allogeneic HSCT, namely Bone Marrow, Peripheral Blood Stem Cells and Cord Blood and clinicians have to face the challenges of selecting the optimal stem cell source. Although all 3 sources of stem cells are capable of reconstituting the hematopoietic system in recipient after transplant, they have many inherent differences in cellular constituents and biological and immunological properties ***(Cheuk et al., 2013).***

Important difference among the sources of stem cell is the amount of mature T cells present. PBSC usually contains a lot more mature T cells compared to BM, which in turn contains more T cells compared to CB, and this partly explains the differences in the risk of graft rejection and graft-versus-host disease (GVHD). Depletion of T cells is associated with increased risk of graft rejection and disease relapse, but lower risk of GVHD ***(Switzer et al., 2013).***

G-CSF-mobilized PBSC are increasingly used instead of BM cells for allogeneic transplantation because they provide faster engraftment and better survival in recipients with poor-risk disease ***(Group SCTC 2005).*** One of the main reasons for preferring PSC worldwide is the important advantages provided by this method to the donor. These advantages are avoidance of anesthesia, lack of the need for hospitalization or blood transfusion, and very low serious adverse event risk ***(Itır Sirinoglu Demiriz et al., 2012).***

Most of the randomized controlled trials (RCTs) comparing matched related donor BM and PBSC transplantation for patients with hematological malignancies found no significant differences between the two stem cell source in important outcomes including overall survival, disease-free survival, transplant-related mortality, relapse, acute GVHD and chronic GVHD ***(Warren et al., 2000).*** However, all trials showed significantly faster neutrophil engraftment in PBSC transplants, and all but one trial showed significantly faster platelet engraftment in PBSC transplants, which may result in earlier hospital discharge for PBSC recipients and lower cost for PBSC transplantation. Lymphocyte recovery was also found to be better in the PBSC group in one trial ***(Powles et al., 2000).***

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of hematologic malignancies with varied aggressiveness and many therapeutic options. An estimated 66,360 new cases