Outcome of Cyclophosamide, Melphalan and Etoposide as a Conditioning Regimen in Autologous Bone Marrow transplantation for Relapsed Lymphomas

Thesis

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List of Abbreviations

Abbr.	Title
aa-IPI	: Age-adjusted IPI
ABVD	: Doxorubicin bleomycin vinblastine dacarbazine
ACVBP	: doxorubicin cyclophosphamide vindesine bleomycin prednisolone
ALCL	: Anaplastic large cell lymphoma
ALK	: Anaplastic lymphoma kinase
ASCT	: Autologous stem cell transplantation
B-ALL	: B-acute lymphoblastic leukemia
BEAC	: Carmustine etoposide cytarabine and cyclophosphamide)
BEACOPP	: Bleomycin etoposide doxorubicin cyclophosphamide vincristine procarbazine and prednisone
BEAM	: Carmustine etoposide cytosine-arabinoside and melphalan
BrECADD	: Brentuximab vedotin etoposide cyclophosphamide doxorubicin dacarbazine and dexamethasone
BrECAPP	: Brentuximab vedotin etoposide cyclophosphamide doxorubicin procarbazine and prednisone)
BuCy	: Busulfan and cyclophosphamide
BuCyE	: Busulfan cyclophosphamide etoposide
CBV	: Carmustine etoposide cyclophosphamide
CHOP	: Cyclophosphamide doxorubicin vincristine and prednisone
CNS	: Central Nervous System
CR II	: Complete remission
CRd	: Cyclophosphamide lenalidomide and dexamethasone
CTd	: Cyclophosphamide thalidomide and dexamethasone)
CY-TBI	: Cyclophosphamide plus total body irradiation
DFS	: Disease free survival
DHAP	: Dexamethasone cisplatin cytarabine)
DLBCL	: Diffuse large B-cell lymphoma

EFS : Event free survival
FC : Fludarabine and cyclophosphamide
FDG : 18-fluorodeoxyglucose
FFTF : Freedom from treatment failure
FL : Follicular lymphomas
FM : Fludarabine and mitoxantrone
G-CSF : Granulocyte colony-stimulating factor
Gem Bu Mel : Gemcitabine busulphan and melphalan
HBV : Hepatitis B Virus
HCV : Hepatitis C Virus
HDC : High-dose chemotherapy
HDCT : High-dose chemotherapy
HL : Hodgkin lymphoma
HLA : Human leukocyte antigen
HR : High risk
HZV : Herpes Zoster Virus
IFRT : Involved-field radiation therapy
IHD : Ischemic Heart Disease
IPI : International Prognostic Index
LB : Lymphoblastic lymphoma
LDH : Lactate dehydrogenase
MALT : Mucosal-associated lymphoid tissue
MIPI : Mantle cell International Prognostic Index
MOPP : Nitrogen mustard vincristine procarbazine and prednisone)
MZL : Marginal zone lymphoma
NB : Neuroblastoma
NHL : Non-Hodgkin lymphoma
NK : Natural Killer
NMZL : Nodal marginal zone lymphoma
NRM : Non-relapse mortality
OS : Overall survival
PAD : Bortezomib doxorubicin and dexamethasone)
PBPCs : Peripheral blood progenitor cells

PCR : Polymerase chain reaction
PET : Positron emission tomography
PFS : Progression free survival
PPI : Proton-pump inhibitor
PR : Partial remission
PTCLs : Peripheral T-cell lymphomas
RACVBP : Rituximab doxorubicin vindesine cyclophosphamide bleomycin and prednisolone
R-CNOP : Cyclophosphamide mitoxantrone vincristine and prednisone
R-DHAP : Rituximab cisplatin cytosine arabinoside and dexamethasone
REAL : Revised European American Lymphoma Classification
R-GEMOX : Rituximab gemcitabine and oxaliplatin
R-ICE : Rituximab ifosfamide carboplatin and etoposide
RIT : Radioimmunotherapy
SMZL : Splenic marginal zone lymphoma
TBI : Total body irradiation
TRM : Treatment-related mortality
Vd : Bortezomib dexamethasone
VP16/MEL : Etoposide and melphalan
VTd : Bortezomib thalidomide and dexamethasone
WHO : World Health Organization

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ABSTRACT

Introduction: Lymphatic cancers are classified by the type of immune cells affected. There are two main types of lymphomas including Hodgkin lymphoma, an uncommon form of lymphoma that involves an abnormal type of B lymphocyte, named Reed-Sternberg cells. **Aim of the work:** The aim of retrospective study is to evaluate the outcome of cyclophosamide, melphalan and etoposide as a conditioning regimen in autologous bone marrow transplantation for relapsed lymphomas regarding: Disease free survival (DFS), overall survival (OS) and transplantation related toxicity and mortality. **Patients and Methods:** Patients with relapsed or refractory lymphomas who underwent autologous bone marrow transplantation using cyclophosamide, melphalan and etoposide as conditioning regimen in Al Sheikh Zayed specialized Hospital. Patients files reviewed regarding: Demographic data: age, sex, initial diagnosis: (NHL, HL), stage of disease after diagnosis, pre- and post -transplant evaluation including: full clinical examination, laboratory assessment (hematological assessment, liver function tests, and kidney function tests), radiological assessment (CT neck, chest, abdomen and pelvis with contrast, PET CT). **Results:** The present study shows that Overall survival at 24 months is 77% and at 60 months is 64.5%. **Conclusion:** the current study showed that Overall survival at 24 months is 77% and at 60 months is 64.5%. Also, Disease free survival at 24 months is 73% and at 60 months is 63%. **Recommendations:** Further studies with more closed follow up for longer time are needed for relapsed and refractory lymphoma patients who under autologous bone marrow transplantation using CMV regimen in conditioning. Further studies on the outcome of CMV regimen in comparison with other conditioning regimens in autologous bone marrow transplantation. Further studies with larger sample size are needed to objectively charge our study.

Key words: Lymphatic cancers, immune cells, Hodgkin lymphoma, overall survival, cyclophosamide

Introduction

Lymphoma is a type of blood cancer that occurs when lymphocytes, which are white blood cells that protect the body from infections and diseases begin behaving abnormally. Instead of dying in the normal cell life cycle, cancerous cells continue to divide into new abnormal cells, and grow out of control. Lymphoma may develop in many parts of the body, including the lymph nodes, spleen, bone marrow, blood or other organs ***(Siegel et al., 2013).***

Lymphatic cancers are classified by the type of immune cells affected.There are two main types of lymphomas including Hodgkin lymphoma, an uncommon form of lymphoma that involves an abnormal type of B lymphocyte, named Reed-Sternberg cells There are many subtypes of Hodgkin's lymphoma, typed by differences seen under the microscope - but a very high percentage of cases are classed as "classic" Hodgkin's. The other type is non-Hodgkin lymphoma, in which B-cells and T-cells are affected. Any lymphoma that does not involve Reed-Sternberg cells is classified as non-Hodgkin lymphoma ***(Goldin et al., 2009).***

The symptoms typically involve painless swelling of the lymph nodes (glands), often in the neck or armpits where these nodes are concentrated. Swelling may also occur in the

groin and abdomen, although some people do not experience any detectable swelling in any part of the body, Other symptoms that can be experienced by people with lymphoma include night sweats, fever, weight loss, loss of appetite, easy fatigue, fever, chills, and unusual itching ***(Proctor et al., 2011)***.

Lymphoma treatment includes some form of chemotherapy, radiation therapy, or a combination of the two is typically used to treat Hodgkin lymphoma. Bone marrow or stem cell transplantation may also sometimes be done under special circumstances. Most patients with Hodgkin lymphoma live long and healthy lives following successful treatment **(*Engert et al., 2010).***

Many people treated for non-Hodgkin lymphoma will receive some form of chemotherapy, radiation therapy, biologic therapy, or a combination of these. Bone marrow or stem cell transplantation may sometimes be used. Surgery may be used under special circumstances, but primarily to obtain a biopsy for diagnostic purposes ***(Bari et al., 2010).***

In some cases of lymphoma cases are treated by stem cell transplantation. This is a process that allows high-dose chemotherapy, and sometimes high-dose radiotherapy, to be given. High-dose treatment would usually cause permanent damage to the bone marrow, but the stem cell transplant

given after treatment restores damaged bone marrow. Blood cells, like all the cells of the body, grow from ‘stem cells'. The stem cells are given into your blood in a drip. From there, they find their way to your bone marrow. Once they have settled in your bone marrow these new stem cells will start to make mature blood cells again ***(Rodríguez et al., 2003).***