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بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني



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جامعة عين شمس

التوثيق الإلكتروني والميكرو فيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
على هذه الأقراص المدمجة قد أعدت دون أية تغييرات





Value of the Assessment of Interleukin 6 level in Allogenic T-cell Replete Haploidentical peripheral blood haematopoietic stem cell transplantation using post-transplant cyclophosphamide as a predictor for the occurrence of acute Graft versus Host Disease

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبِّحْ اِنَّكَ لَا تَعْلَمُ لَنَا
اِلَّا مَا عَلَّمْتَنَا اِنَّكَ اَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
ADAM.....	A disintegrin and metalloprotease
aGVHD	Acute graft-versus-host disease
AHSCT	Allogeneic hematopoietic stem cell transplant
AML.....	Acute myeloid leukemia
ANC.....	Absolute neutrophil count
ANG2.....	Angiopoetin-2
APCs.....	Antigen presenting cells
ATG	Antithymocyte globulin
AUC	Area under the curve
BM CTN	The Blood and Marrow Transplant Clinical Trials Network
BM	Bone marrow
BM.....	Bone marrow
BMT	Bone marrow transplantation
CBT.....	Cord blood transplantation
cGVHD	Chronic GVHD
CIBMTR	The Center for International Blood and Marrow Transplant Research
CML.....	Chronic Myelogenous Leukemia
CMV.....	Cytomegalovirus
CNTF.....	Ciliary neurotrophic factor
Csa.....	Cyclosporine
CXCR4.....	Chemokine receptor 4
DAMPs	Danger associated molecular pattern molecules
DLI.....	Donor lymphocyte infusion
DNA.....	Deoxyribonucleic acid
DRI	Disease risk index

List of Abbreviations Cont...

Abb.	Full term
dUCB	Double unit umbilical cord transplant
EBMT	The European Group for Blood and Marrow Transplantation
ECP	Extra corporal photo pheresis
ELISA	Enzyme-linked immunosorbent assay
FI	Full intensity
G-CSF	Granulocyte colony-stimulating factor
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GVHD	Graft-versus-host disease
HCT	Hematopoietic cell transplant
HGF	Hepatocyte Growth Factor
HL	Hodgkin lymphoma
HLA	Human leukocyte antigen
HSCT	Hematopoietic stem cell transplant
HSV	Herpes simplex virus
IBMTR	International Bone Marrow Transplantation Registry
IFN- γ	Interferon-gamma
IL-1	Interleukin-1
iNKT cells	Invariant natural killer T cells
INR	International normalized ratio
IPS	Idiopathic Pneumonia Syndrome
ISC	Immune stem cells
IV	Intravenously
JAKs	Janus kinases
LGVHR	Lymph hematopoietic graft- <i>versus</i> -host reactions

List of Abbreviations Cont...

Abb.	Full term
LIF	Leukemia inhibitory factor
MA	Myeloablative
MDSCs	Myeloid derived suppressor cells
M-MDSCs	Monocytic MDSCs
MMF	Mycophenolate mofetil
NHL	Non-Hodgkin lymphoma
NIH	National Institutes of Health
NK	Natural killer cells
NO	Nitric oxide
NRM	Non-relapse mortality
OS	Overall survival
PAMPs	Pathogenic associated molecular pattern molecules
PBSC	Peripheral blood stem cell
PBSCTs	Peripheral blood stem cells transplant
PCR	Polymerase Chain Reaction
PCV	Pneumococcal conjugate
PT	Prothrombin time
PT-Cy	Post-transplant cyclophosphamide
PTT	Partial Thromboplastin Time
REG3 α	Regenerating islet-derived 3- α
RIC	Reduced intensity Conditioning
SCID	Severe combined Immunodeficiency
SD	Sibling donors
SDF-1	Stromal cell-derived factor-1- α
sIL-2R	Soluble IL-2 receptor
sIL-7R	Soluble IL-7 receptor
SNPs	Single-nucleotide polymorphisms

List of Abbreviations Cont...

Abb.	Full term
SOS.....	Sinusoidal obstruction syndrome
ST2.....	Stimulation 2
T reg	T regulatory cells
TAC.....	Tacrolimus
TAM.....	Transplantation associated microangiopathy
TBI.....	Total body irradiation
TCZ	Tocilizumab
TMP-SMX.....	Trimethoprim-sulfamethoxazole
TNFR.....	Tumor necrotizing factor receptor
TNF- α	Tumor necrosis factor-alpha
TRM.....	Transplant-related mortality
UCB	Umbilical cord transplant
UD	Unrelated donors
UDCA	Ursodeoxycholic acid
VOD	Veno occlusive disease
VZV.....	Varicella zoster virus

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INTRODUCTION

Allogeneic hematopoietic cell transplantation (HSCT) is one of the curative therapeutic options for hematological malignancies (*Henden et al., 2015*). The host hematopoietic system is reconstituted with donor hematopoietic system and donor lymphocytes, especially T cells that have the potential to exert Graft Versus Tumor effects concurrently with graft-versus-host disease (*Mussetti et al., 2017*). Clinical data have shown that the severity of GVHD is negatively correlated with the chance of relapse (*Greco et al., 2016*). Acute GVHD is a major side effect of allogeneic HSCT.

Large number of pro inflammatory cytokines are involved in the pathophysiology of GVHD such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF- α), and interferon-gamma (IFN- γ) (*Drobyski et al., 2018*). These cytokines are elevated after allogeneic BMT and affect GVHD through either direct cytotoxic effects on host tissues or by activation of immune effector cells (*Toubai et al., 2016*). Blockade of these cytokines modulated the severity of GVHD.

IL-6 is a cytokine that have broad effects, such as maturation and activation of B cells, T cells, and macrophages (*Tvedt et al., 2017*). IL-6 has been directly implicated in many human inflammatory diseases. Blockade of IL-6 signaling with anti-IL-6R monoclonal antibody Tocilizumab, has been shown to have therapeutic effects in many human diseases, such as