Chemotherapy Induced Cognitive and Executive Impairment in Hematological Malignancies

Thesis

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Mohamed Gamal Mohamed Kotb

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List of Abbreviations

Abb.	Full term
5-FU	*5-fluorouracil*
ALL	*Acute lymphoblastic leukemia*
AML	*Acute myelogenous leukemia*
ANCs	*Absolute neutrophil counts*
APL	*Acute promyelocytic leukemia*
ATRA	*All-trans retinoic acid*
BMT	*Bone marrow transplantation*
CALGB	*Cancer And Leukemia Group B*
CBC	*Complete blood count*
CICI	*Chemotherapy induced cognitive impairment*
CINV	*Chemotherapy induced nausea and vomiting*
CIPN	*Chemotherapy induced peripheral neuropathy*
CLL	*Chronic lymphocytic leukemia*
CML	*Chronic myelocytic leukemia*
CNS	*Central nervous system*
CR	*Complete remission*
CSF	*Cerebrospinal fluid*
CT	*Computed tomography*
CTX	*Chemotherapy*
DIC	*Disseminated intravascular coagulation*
EBV	*Epstein-Barr virus*
ECOG	*Eastern Cooperative Oncology Group*
EPO	*Erythropoietin*
ESR	*Erythrocyte sedimentation rate*
FDA	*Food and Drug Administration*
FDG-PET	*Fluorodeoxyglucose-positron emission tomography*
FISH	*Fluorescence in situ hybridization*
GI	*Gastrointestinal*

List of Abbreviations (Cont...)

Abb.	Full term
HBV	*Hepatitis B virus*
HCT	*Hematopoietic stem cell transplantation*
HCV	*Hepatitis C virus*
HIV	*Human immunodeficiency virus*
HL	*Hodgkin's Lymphoma*
HLA	*Human leukocyte antigen*
IL	*Interleukin*
LBCL	*Large B cell lymphoma*
LDH	*Lactate dehydrogenase enzyme*
MCHL	*Mixed-cellularity Hodgkin's lymphoma*
MDS	*Myelodysplastic syndrome*
MM	*Multiple myeloma*
MRD	*Minimal residual disease*
MRI	*Magnetic resonance imaging*
MUGA	*Multiple gated acquisition*
MZL	*Marginal zone lymphoma*
NCCN	*National Comprehensive Cancer Network*
NHL	*Non-Hodgkin's Lymphoma*
NHL	*Non-Hodgkin's lymphoma*
NLPHL	*Nodular lymphocyte predominant Hodgkin's disease*
NSHL	*Non sclerosing Hodgkin's lymphoma*
OS	*Overall survival*
PCR	*Polymerase chain reaction*
PET	*Positron Emission Tomography*
Ph	*Philadelphia*
RT-PCR	*Reverse transcriptase polymerase chain reaction*

List of Abbreviations (Cont...)

Abb.	Full term

S1P.....*Sphingosine-1-phosphate*
SLE.....*Systemic lupus erythematosus*
SLL.....*Small lymphocytic lymphoma*
SWOG.....*Southwest Oncology Group*
THRLBCL.....*T-cell histiocyte-rich large B-cell lymphoma*
TKIs.....*Tyrosine kinase inhibitors*
TNF.....*Tumor necrosis factor*
TTF.....*Time to treatment failure*
WBC.....*White blood cell count*
WHO.....*World Health Organization*

INTRODUCTION

In 2015, an estimated 162, 000 new cases of hematological malignancies were diagnosed (approximately 10% of all cancer diagnoses) and over 1·8 million haematological cancer survivors live in the United States ***(Howlader et al., 2014).***

Improved diagnosis and treatment have markedly increased survival for many patients with haematological malignancies. Based on the most recent literature, current 5-year survival rates are as follows: all leukaemia 60.3%, Hodgkin lymphoma (HL) 87.7% and non-HL (NHL) 71.4% ***(Howlader et al., 2014).***

Nearly all leukaemias and 69% of NHL are treated with chemotherapeutic agents ***(Rossi et al., 2015).***

Treatment-related side effects, including cognitive impairment, can decrease treatment compliance and ultimately impact quality of life; however, a deep understanding of the etiology of these cognitive problems as a consequence of disease and/or treatment in hematological malignancies is still in its infancy ***(Wefel et al., 2004).***

Chemotherapy-induced cognitive impairment (CICI) is a collection of problems in memory, attention, concentration and executive functions that is associated with chemotherapy treatments in cancer patients. These problems can range from

subtle to severe and last for months or years after treatment ***(Bradley et al., 2005).***

CRCI affects an estimated 10 million cancer survivors in the United States. Based on data from all types of cancers, up to 30% of survivors experience cognitive impairment prior to therapy, 80% during therapy, and up to 35% may live with CRCI up to 20 years after treatment ***(Koppelmans et al., 2012).***

Decreased cognitive function is associated with poorer quality of life, inability to achieve work and educational goals, inability to drive or read, and decreased social connectedness ***(Reid-Arndt et al., 2010).***

To date, the CICI literature is dominated by breast cancer and other solid tumours. Haematological malignancies are usually systemic, and often treated with chemotherapeutic agents that have been implicated in CICI in solid tumours. The growing literature in this area suggests that cognition is an important predictor of survival in patients with haematological malignancies and therefore, understanding factors that lead to CICI in haematological malignancies warrants attention ***(Dubruille et al., 2015)***.

Research on cognitive function in most types of haematological malignancies is limited. However, studies of cognitive function in paediatric acute lymphoblastic leukaemia (ALL), indicate that cognitive impairment can persist for years

after completion of treatment. Clearly, a subset of hematological malignancy survivors experience CICI ***(Elisabeth et al., 2009)***.

A study done 2005 on Acute Myeloid Leukemia (AML) and Myelodysplastic syndrome (MDS) patients had revealed Decline on motor function, psychomotor speed, memory, executive function post chemotherapy ***(Meyers et al., 2005).***

Another study done at 2012 on Hodgkin lymphoma patients revealed worse than controls on attention, memory, executive function, processing speed post chemotherapy ***(Krull et al., 2012).***