

Results of Cladribine in Hairy Cell Leukemia:
Nasser Institute Experience.

Thesis

Submitted for Partial Fulfillment of
Master Degree in Clinical Hematology

By

Haitham Elsayd Sherif

M.B, B.Ch

Supervised By

Dr. Hoda Ahmed GadAllah

Professor of Internal Medicine and Clinical Hematology
Faculty of Medicine, Ain Shams University

Dr. Mohammed Mahmoud Mousa

Assistant Professor. Of Internal Medicine and Clinical Hematology
Faculty of Medicine, Ain Shams University

DR. Raafat Mohamed Abd El-Fattah

Consultant of medical oncology, National Cancer Institute
Cairo University

Faculty of Medicine
Ain Shams University

2015

List of Contents

	<u>Page</u>
List of abbreviations.....	I
List of tables	II
List of figures	III
Introduction & aim of the study	1
Review of Literature:	
I- Hairy Cell Leukemia.....	4
II-Clinical features of Hairy cell leukemia.....	15
III- Diagnosis of hairy cell leukemia.....	27
IV- Differential Diagnosis.....	42
V- Treatment of Hairy Cell Leukemia.....	46
VII- Immunotherapeutic approaches.....	60
Patients and Methods.....	70
Results.....	75
Discussion	83
Summary	89
References	91
Arabic Summary	

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

لَوْ قَدْ رَبَّ
زِدْنِي عِلْمًا

سورة طه
الآية (١١٤)

صَدَقَ اللَّهُ الْعَظِيمُ

Acknowledgment

*Thanks first and last to **GOD** almighty for helping me to proceed and complete this work.*

*I am deeply grateful to **Dr. Hoda Ahmed Gad Allah**, professor of Internal Medicine and clinical hematology, Faculty of Medicine, Ain Shams University, for her kind supervision, and remarkable advice throughout the process of this work.*

*Extended thanks and appreciation to **Dr. Mohamed Mousa** Internal Medicine and clinical hematology Ain Shams University and **Dr. Raafat Abd El Fatah** Consultant of Medical Oncology, National Cancer Institute, Cairo University, for their generous assistance and full support of this work.*

*Finally , I express my sincere thanks to **all my professors , Colleagues and the Personnels** in the Hematology department at Naser Institute .*

List of Abbreviations

2-cdA	2-Chlorodeoxyadenosine
ADA	Adenosine deaminase
BM	Bone marrow
BMA	Bone marrow aspiration
BMB	Bone marrow biopsy
B-PLL	B-prolymphocytic leukemia
CD	Cluster of differentiation
CLL	Chronic lymphocytic leukemia
CNS	Central nervous system
CR	Complete remission
dADP	Deoxyadenosine Diphosphate
dAMP	Deoxyadenosine Monophosphate
dATP	Deoxyadenosine Triphosphate
dCF	2-Deoxycoformycin
DCs	Dendritic cells
EBV	Ebstein Bar virus
F-ara-A	Fludarabine
FC	Flow cytometry
H&E	Haematoxylin and eosin
HC	Hairy cell
HCL	Hairy cell leukemia
IFN-α	Interferon alpha
LGL	Large granular lymphocytic
NR	NO response
PCR	Polymerase chain reaction
PLL	prolymphocytic leukemia
PR	partial remission
RES	Reticuloendothelial system
RLC	Ribosomal-lamella complex
SEM	Scanning electron microscopy
SI	Splenic irradiation
SIg	Surface immunoglobulin
SLVL	splenic lymphoma with villous lymphocytes
TEM	Transmission electron microscopy
TPA	Tetradecanoyl-phorbol-13-acetate
TRAP	Tartrate-resistant acid phosphatase
WBC	White blood cells

List of Tables

	<u>Page</u>
Table 1: Diagnostic features	- 5 -
Table 2: Opportunistic infections	- 19 -
Table 3: Unusual clinical manifestations	- 20 -
Table 4: Auto (immune) associations.....	- 24 -
Table 5: Unusual clinical manifestations.....	- 25 -
Table 6: Hairy cell morphology	- 31 -
Table 7: Bone marrow pathology	- 34 -
Table 8: Hairy cell scoring system	- 36 -
Table 9: Immunophenotypic Profile.....	- 36 -
Table 10: Splenic pathology	- 37 -
Table 11: Pathophysiologic Correlates of Gene Expression Profiling Signature.....	- 40 -
Table 12: Differential diagnosis of HCL immunophenotype	- 42 -
Table 13: Comparison of various intravenous application regimens of cladribine ..	- 55 -
Table 14: NCI Criteria of response in HCL	- 74 -
Table 15: Patient characteristics	- 76 -
Table 16: Sex distribution of the studied subjects.	- 77 -
Table 17: The mean TLC, hemoglobin and platelet counts	- 77 -
Table 18: Initial BM HC.....	- 79 -
Table 19: Initial TRAP	- 79 -
Table 20: CD103_initial	- 79 -
Table 21: CD25_initial	- 80 -
Table 22: Post –treatment evaluation for the 33 patients	- 83 -
Table 23: Response evaluation at Last FU	- 83 -
Table 24: OS_status.....	- 84 -
Table 25: PFS status	- 84 -

List of Figures

	<u>Page</u>
Figure 1: Significance of Immunoglobulin gene analysis in Hairy Cell Leukemia... -	31
Figure 2: Hairy cell from the PB (transmission electron microscopy)	31 -
Figure 3: Bone marrow in hairy cell leukemia	33 -
Figure4: Survival function.	84 -

ABSTRACT

Purpose

The aim of this study is *to evaluate the Results of Cladribine in Patients With Hairy Cell Leukemia, Nasser Institute Experience.*

Patients & Methods

Thirty three patients with hairy cell leukemia received a single dose of cladribine at a dose of 0.09 mg / kg /day for seven days by continuous I.V. route.

Results

Follow up at three years revealed CR in 96.6% of patients. Cladribine therapy was tolerable with mild to moderate side effects, mainly in the form of neutropenic fever grade II , GIT toxicity and HZV skin infection .

Conclusion

Cladribine was found to be a well-tolerated therapy with acceptable side effects .The disease free and overall survival was as high as 96.6% .However more cases and longer follow up are needed to reach a firm conclusions.

Key words

Hairy cell leukemia , Cladribine therapy

INTRODUCTION

Hairy cell leukaemia (HCL) is an uncommon B-cell lymphoproliferative disorder affecting adults. HCL was first reported as a distinct disease in 1958. The prevalence has been estimated at 2% of all forms of leukaemia and, of patients affected by lymphoproliferative diseases which comprise mature B or T cells, HCL accounts for 8% of cases. HCL is 6–10 times more rare than chronic lymphocytic leukaemia (CLL) Interest in HCL has evolved in parallel with the development of useful therapeutic agents: interferon alpha and pentostatin in the 1980s and cladribine in the 1990s. **(Grever. 2010)** HCL affects middle-aged men more commonly than women; the male: female ratio being 4.5:1 with a median age at onset of 50 years **(Harris et al., 2008)**.

Patients may be asymptomatic and the disease is identified because a full blood count is taken for an unrelated reason. Other patients present with symptoms of cytopenia, particularly infections. The most common laboratory finding is cytopenia, usually affecting two or three lineages; monocytopenia is a consistent feature. Leucocyte counts tend to be low (usually less than $5 \times 10^9/l$ and very rarely over $10 \times 10^9/l$), except in the HCL- variant where the count is typically higher and monocytopenia is not a feature, Hairy cells are often seen in peripheral blood films but their proportion is variable. Splenomegaly is a common finding. Demonstration of TRAP by cytochemistry has been shown to be a useful test for HCL in the past but the availability of monoclonal antibodies reactive with TRAP, which can be used successfully in bone marrow trephine sections, has largely obviated the need for the cytochemical test. The HCL panel