بسم الله الرحمن الرحيم

STATE OF KUWAIT
MINISTRY OF HEALTH
AS'AD AL-HAMAD
DERMATOLOGY CENTER
AL-SABAH HOSPITAL

دولة الكويت
وزارة الصحة
مركز أسعد الحمد للأمراض الجلدية
مستشفى الصباح

CUTANEOUS T-CELL LYMPHOMA PROFORMA

Serial number: **File Number:** **Date:**

Name: **Age:** **Sex:**

Marital Status: **Nationality:** **I.D. Number:**

Address:
Tele:

Profession: **Referring Doctor:**

Diagnosis:

Previous Biopsy
No. **Date:** **Center:** **Comment:** **Reviewed:** Yes | No

Duration of Disease: **Age of Onset:**

Site of Onset:	**Face**	**Scalp**	**Extremities**	**Trunk**	**Palms**	**Soles**	**M.M.**

Sites affected:	**Face**	**Scalp**	**Extremities**	**Trunk**	**Palms**	**Soles**	**M.M.**

Progression of the disease:	**Slow**	**Rapid**	**Stationary**

Precipitating/Aggravating Factors:	**Drugs**	**Infection**	**Stress**	**Occupation**	**Hormonal**

Associated Diseases:	**Photosensitive disorders**	**Malignancy**	**DM**	**Hypertension**	**Others**

Past History	**Transfusion**	**Surgery**	**Drug allergies**	**Cancer**
	Radiation	**Chemical exposure**		**Others**

If yes specify:

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Past Treatment:

Family history

Similar disease	Cancer	Significant medical disease

Others:

Examination:

Cutaneous:

Morphology:	**Macules/patches/papules/plaques/nodules/vesicles/**
Specify:	**tumours/erythroderma/necrotic**
Extent (%):	
Sites:	
Nails:	
Scalp:	
Palms/ Soles:	
Keratoderma	

Lymph nodes	Rt	Lt	Lymph nodes	Rt	Lt
Occipital			Axillary		
Cervical			Inguinal		
Abdominal					

Lymph Nodes:

Occipital:		**Axillary:**	
Cervical:		**Inguinal:**	
Abdominal:			

Chest:

Abdomen:

Liver:		
Spleen:		
Other:		

Pelvis:

Others:

Investigations:

	Date	Findings
Blood counts		
CBC		
ESR		
Peripheral blood film		
Liver Profile:		
Kidney Profile:		
S. Biochemistry:		
Urine M/E:		
Stools M/E:		
Hepatitis screen		
HBs antigen		
HC Core Abs		
HC Abs		
HIV		
X-Ray Chest P/A view:		
Eye Examination:		
Skin biopsy:		
Histopathology:		
Immunehistochemistry:		
PCR:		
Clinical Photography:		
C. D. markers		

(flowcytometry-peripheral blood):		
sIL-2 R		
U. S. Abdomen/ Pelvis:		
C. T. Scan:		
Chest:		
Abdomen:		
Pelvis:		
Whole body Gallium Scan:		
Lymph node biopsy:		
Bone Marrow:		
MRI:		
HLA markers:		
Others:		

TNM classification:

Ia	Ib	IIa	IIb	III	IVa	IVb

EORTC classification:	
Final Diagnosis:	

Follow-up Sheet (Quarterly Assessment Sheet)

Date	Clinical Condition Skin/Systemic	Current Treatment	Response[1]	Side Effects	Compliance[2]	Skin Biopsy (details if done)	Other Significant Investigations	Remarks

[1] Response: NR= No Response; MR= Minimal Response (< 25%); PR= (25% - 50%); CR= Complete Response; S= Stable Disease; P= Progressive Disease

[2] Compliance: R= Regular; IR= Irregular

Guidelines of Care for Primary CTCL

Introduction

EORTC* define primary CTCL as non-hodgkin lymphomas presenting in the skin, with no evidence of extracutaneous disease at the time of diagnosis and within 6 months after diagnosis.

EORTC – The European Organization for Research and Treatment of Cancer

* This basic principle does not apply to patients with classical MF presenting with skin and peripheral lymph-node involvement and to Sezary syndrome.
* EORTC classification excludes malignant lymphomas with secondary skin involvement as well as malignant lymphomas in immunocompromised patients.

Part 1

Clinical Aapproach to the patient

I. Clinical history + examination

II. Skin Biopsy

- Histopathology**
- Immunehistochemistry
  - CD2
  - CD3
  - CD4
  - CD5
  - CD7
  - CD8
  - CD20
  - CD30
  - CD45RO
  - CD56
  - Others
- PCR

III. Diagnosis

a) Type of CTCL

(EORTC Classification):

b) Stage of CTCL

** More than one skin biopsy is indicated:

- When skin lesions of different morphology
- If the previous biopsy results are not typical
- Each patient of CTCL treated in As'ad Al-Hamad Dermatology Center should have a biopsy done in the center.

EORTC Classification of Primary Cutaneous T Cell Lymphomas

A. Indolent

1. Mycosis fungoides
2. MF + Follicular Mucinosis
3. Pagetoid reticulosis
4. $CD30^+$ Lymphoproliferative disorders
   a) Large cell CTCL
      - Anaplastic
      - Immunoblastic
      - Pleomorphic
   b) Lymphomatoid papulosis

B. Aggressive

1. Sezary syndrome
2. Large cell CTCL $CD30^-$
   - Immunoblastic
   - Pleomorphic

C. Provisional

1. Granulomatous slack skin
2. CTCL pleomorphic small/medium-sized
3. Subcutaneous panniculitis like T cell lymphoma

TNM Classification of CTCL

Classification	Description
T: (Skin)	
T0	Clinically and/or histopathologically suggestive lesions
T1	Limited plaques, patches, papules etc., <10% skin surface area involvement
T2	Skin lesions affecting >10% of the skin surface area
T3	Tumours (>1 in no)
T4	Erythroderma
N: (Lymphnodes)	
N0	No palpable lymphnodes, Pathology –ve for CTCL
N1	Palpable lymphnodes, pathology –ve for CTCL
N2	Clinically not palpable, pathology +ve for CTCL
N3	Clinically palpable, pathology +ve for CTCL
B: (Peripheral blood)	
B0	No atypical circulating lymphocytes (or <5%)
B1	+ve atypical circulating lymphocytes (>5%)
M: Visceral organs)	
M0	No visceral involvement
M1	Visceral involvement (must have pathology confirmation and organ to be specified)

Staging for cutaneous T cell lymphomas

Stage	**1A**	-	T_1	N_0	M_0
	IB	-	T_2	N_0	M_0
	IIA	-	T_{1-2}	M_1	M_0
	IIB	-	T_3	N_1	M_0
	III	-	T_4	N_{0-1}	M_0
	IVA	-	T_{1-4}	N_{2-3}	M_0
	IVB	-	T_{1-4}	N_{0-3}	M_1

IV

Investigative approach to the patients

a) If the disease is limited to skin (Patch/Plaque) and no palpable LN/Organomegaly

- CBC, ESR
- Serum biochemistry
- Urine R/M
- Stools M/E
- X-Ray chest P/A view
- Hepatitis screening (if past H/o transfusion, jaundice, etc.)
- U. S Abdomen/Pelvis

b) If palpable lymphnodes/ organomegaly, add:

- CT Scan
  - . Abdomen
  - . Chest
  - . Pelvis
- L.N. Biopsy
- Gallium scan (if indicated)

C) If abnormal cells are present in peripheral blood film or patient has tumour stage or is erythrodermic add:

- Flowcytometry
- Bone-marrow biopsy
- SIL-2 receptors***

***** Increased SIL-2 receptors levels may confer poor prognosis**

V)

Final Diagnosis	

Part II

Treatment protocol of patients with CTCL

A. Treatment modalities used for CTCL

a) Topical:

1. Steroids (Potent)*
2. Mechlorethamine (HN2)
3. Carmustine (BCNU)
4. Bexarotene

b) Photochemotherapy/Phototherapy:

1. PUVA*
2. UVB*
3. Narrowband UVB (TL01)*
4. UVA1

c) Systemic:

1. Retinoids
   - Acitretin*
   - Isotretinoin*
   - Targretin ™ (Bexarotene)
2. Interferon Alpha*
3. Methotrexate*
4. Cyclophosphamide*
5. Cyclosporine*
6. Vinca alkaloids*
7. Corticosteroids*
8. Alkylating agents*
9. Topoisomerase – II inhibitors
10. Adenosine analogues (2 – deoxycoformycin, fluadarabine, and 2-chlorodeoxyadenosive)

d) Extracorporeal Photopheresis

e) Radiotherapy

1. Local*
2. Total body electron beam radiation therapy (EBT)*

f) Experimental

1. Fusion toxin (IL-2 Fusion toxin)
2. Monoclonal Abs

3. Interleukin (IL-2)
4. Bone-marrow transplant

g) Combination Therapies

1. Re-PUVA*
2. Re-interferons*
3. PUVA – Interferon alpha*
4. PUVA + EBT*
5. PUVA + Topical chemotherapy
6. PUVA + Systemic chemotherapy*
7. Multiagent chemotherapy*
8. Others

♦ **Treatment approach is individualized to each patient.**
♦ **Treatment to be planned in collaboration with oncologist in Kuwait Cancer Center (KCC)**

*** Treatment is available in Kuwait**

B. Treatment Approach to a patient

1. Mycosis fungoides:

a) Stage 1 – IIa

-Topical steroids*
-UVB/Narrow band UVB (TL01)*
-PUVA*
-Carmustine
-Mechlorethamine
-Retinoids*
-Interferons alpha* (KCC/Dermatology)
-Methotrexate*
-Total skin electron beam radiations (EBT)* (In KCC)
-Combinations*

(For limited patches/plaques (1-3 lesions) local radiotherapy is indicated)

b) Stage II_b & IV

Chemotherapy* (KCC)
Combination therapies*

a) Stage III

- Methotrexate*
- EBT* (KCC)
- Interferon alpha*
- Extracorporeal photopheresis

- Chemotherapy*

2. MF – Associated follicular Mucinosis:

- Long duration of PUVA* / Mechlorethamine
- EBT* (KCC)

3. Pagetoid Reticulosis:

- Radiotherapy (local)* (KCC)
- Surgical excision* (KCC)

4. $CD30^+$ cutaneous Large T-cell Lymphoma

a) Solitary or localized lesions – Radiotherapy* (KCC)
b) Generalized skin lesions – Multiagent chemotherapy* (KCC)

5. Lymphomatoid papulosis

- PUVA*
- Topical chemotherapy*
- Low dose methotrexate*

6. Sezary Syndrome

- Methotrexate*
- Chlorambycil + prednisolone* (KCC)
- Extracorporeal photopheresis
- EBT* (KCC)
- Combinations* (KCC + Dermatology)

7. $CD30^-$ Cutaneous large T-cell lymphoma

a. Solitary/Localized lesions – Radiotherapy* (KCC)
b. Multiple lesions – wide spread disease
Multiagent chemotherapy* (KCC)

8. Granulomatous slack skin

- Radiotherapy* (KCC)
- Surgical excision* (KCC)

9. Pleomorphic small/medium – sized CTCL

a) Localized disease – Radiotherapy* (KCC)
b) Generalized disease
- Cyclophosphamide* (KCC + Dermatology)
- Interferon alpha* KCC + Dermatology)

10. Subcutaneous panniculitis like T-cell lymphoma

Multiagent Chemotherapy* (KCC)

Part III.

Follow-up Protocol

Clinical Assessment

- Baseline
- Two week after starting the treatment*
- Quarterly**

*At two weeks patient to be monitored for compliance of treatment, tolerance of treatment
and the side effects related to the treatment.

**Quarterly to be assessed for clinical condition, response to the treatment, treatment compliance, and side effects of treatment.

P.S. Assessment at any time when new suspicious lesions appear or other factors related to
treatment/patients

Clinical Assessment of Response

A. Complete Response (CR): -
Disappearance of all clinical evidence of disease

B. Partial Response (PR):-
A 50% or more decrease in extent or severity of disease

C. Minimal Response (MR):-
Less than 50% decrease in extent or severity of disease

D. Stable Disease (SD):-
Less than 25% decrease in disease or no response

E. Progressive Disease (PD):-
More than 25% increase in extent or severity of disease

Treatment Failure

a) Inadequate response***
b) Intolerable side effects or toxicities

c) Disease progression
d) Patient's withdrawal for any reason

Discontinuation of the treatment due to the above reasons:

*** For evaluation of inadequate response the patient needs to continue the recommended treatment regularly for a period of 3-12 months (depending upon the treatment modality type and extent of the disease) and patient needs to be evaluated for alternative treatment approach. Time to treatment failure (TTF) is time from start of treatment until abandonment of therapy or changing / addition of another specific therapy.

Follow-up Investigations

Need to be tailored depending upon the choice of therapy used and clinical status of the patient.

Discontinuation of Treatment

Can be considered when the patient has the complete response. Minimum of two involved dermatologist should examine the patient independently and jointly agree on the decision.

Follow-up After Discontinuation of Treatment

Monthly	x	6 Months
Quarterly	x	1 year
Biannually	x	3 years
Annually	x	4 – 5 years

Follow-up whenever patient has a new relapse, suspicious lesions irrespective of the time.

Time to relapse (TTR) : Synonymous with freedom from relapse (FFR), disease-free survival (DFS), and duration of complete response (CR), requires first that CR has initially been achieved.

Follow-up Biopsy

Indicated when –

a) While on the treatment Patient develops new lesions of different morphology than
   Before starting the disease; or when a transformation is suspected.
b) Before stopping the treatment■
c) A new relapse after stopping the treatment

■ The issue is debatable, needs to be tailored according to a given patient

Immunophenotypes of the neoplastic lymphocytes in primary CTCL

CTCL TYPE	CD3	CD45RO	CD4	CD8	Loss of some Pan T-Antigens (CD_2,CD_3, CD_5, CD_7)	CD30	CD56	CD20
Mycosis Fungoides	+	+	a) + b) -*	a) – b) +*	+	+/- ♦	-	-
MF + follicular mucinosis	+	+	c) + d) -*	c) – d) +*	+	+/- ♦	-	-
Pagetoid reticulosis	+	+	a) + b) -*	a) - b) +*	+	+/-	-	-
$CD30^{(+)}$ large cell type	+	+	a) + b) -*	a) - b) +*	+	+ EMA^-; $CD15^-$	-	-
Lymphamatoid papulosis **-A & C type** **-B type**	+ +	+ +	+/- +	- -	+/- +/-	+(EMA^-; $CD15^-$)	- -	- -
Sezary syndrome	+	+	+	-	+	-	-	-
$CD30^{(-)}$ large cell type	+	+	+	-	+	-	-	-
Granulomatous slack skin	+	+	+	-	+	-	-	-
Plemporphic small/medium sized	+	+	+	a) – b) +*	+	-	-	-
Subcutaneous panniculitis like	+	+	a) + b) -*	a) – b) +*	+	-	-	-

* Some cases may have this expression

♦ $CD8^+$ (suppressor T cells) type of MF may have more aggressive course than $CD4^+$ type. In advanced stages of MF progression to $CD30^+$ or $CD30^-$ large T cell lymphoma may be observed and is often associated with aggressive clinical course.