Cutaneous T-cell Lymphoma: Current and New Treatment Strategies

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July 27, 2019
## Conflicts of Interest

| Research Support/P.I. | Miragen, Seattle Genetics, Rhizen, Elorac, Galderma |

Off label use of medications
Outline

• Cutaneous T-cell lymphoma overview

• Current management guidelines

• What’s new in T-cell cutaneous lymphoma
  • New treatment targets
  • Diagnostic accuracy (reactive vs malignant)
<table>
<thead>
<tr>
<th>Cutaneous T-cell and NK-cell lymphomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycosis fungoides</td>
</tr>
<tr>
<td>MF variants and subtypes</td>
</tr>
<tr>
<td>Folliculotropic MF</td>
</tr>
<tr>
<td>Pagetoid reticulosis</td>
</tr>
<tr>
<td>Granulomatous slack skin</td>
</tr>
<tr>
<td>Sézary syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adult T-cell leukemia/lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary cutaneous CD30^+ lymphoproliferative disorders</td>
</tr>
<tr>
<td>Primary cutaneous anaplastic large cell lymphoma</td>
</tr>
<tr>
<td>Lymphomatoid papulosis</td>
</tr>
<tr>
<td>Subcutaneous panniculitis-like T-cell lymphoma*</td>
</tr>
<tr>
<td>Extranodal NKT-cell lymphoma, nasal type</td>
</tr>
<tr>
<td>Primary cutaneous peripheral T-cell lymphoma, unspecified</td>
</tr>
<tr>
<td>Primary cutaneous aggressive epidermotropic CD8^+ T-cell lymphoma (provisional)</td>
</tr>
<tr>
<td>Cutaneous γδ T-cell lymphoma (provisional)</td>
</tr>
<tr>
<td>Primary cutaneous CD4^+ small/medium-sized pleomorphic T-cell lymphoma (provisional)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cutaneous B-cell lymphomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary cutaneous marginal zone B-cell lymphoma</td>
</tr>
<tr>
<td>Primary cutaneous follicle center lymphoma</td>
</tr>
<tr>
<td>Primary cutaneous diffuse large B-cell lymphoma, leg type</td>
</tr>
<tr>
<td>Primary cutaneous diffuse large B-cell lymphoma, other</td>
</tr>
<tr>
<td>Intravascular large B-cell lymphoma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Precursor hematologic neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4^+/CD56^+ hematodermic neoplasm (blastic NK-cell lymphoma)†</td>
</tr>
</tbody>
</table>
## Indolent vs Aggressive

<table>
<thead>
<tr>
<th>INDOLENT</th>
<th>AGGRESSIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycosis Fungoides</td>
<td>Sézary Syndrome</td>
</tr>
<tr>
<td>Folliculotropic MF</td>
<td>Primary cutaneous NK/T cell lymphoma, nasal-type</td>
</tr>
<tr>
<td>Pagetoid Reticulosis</td>
<td>Primary cutaneous aggressive CD8+ T-cell lymphoma</td>
</tr>
<tr>
<td>Granulomatous Slack Skin</td>
<td>Primary cutaneous γ/δ T cell lymphoma</td>
</tr>
<tr>
<td>Primary cutaneous anaplastic large cell lymphoma (ALCL)</td>
<td>Primary cutaneous peripheral T-cell lymphoma, unspecified</td>
</tr>
<tr>
<td>Lymphomatoid papulos (LyP)**</td>
<td>Mycosis Fungoides with large cell transformation</td>
</tr>
<tr>
<td>Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoproliferative disorder</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Panniculitis-like T cell Lymphoma (SPTCL)</td>
<td></td>
</tr>
</tbody>
</table>
Mycosis Fungoides

• Typically the neoplastic T cell in CTCL express **mature memory** T-cell markers
  - TCRαβ (Beta-F1+)
  - CD3+**CD4+**CD8-CD5+CD45RA-**CD45RO**+

• Clonal

• **Loss of CD7 or CD26**
  - CD7 = glycoprotein normally expressed in 80-90% of CD4+ T cells and all CD8+ T cells and most NK cells
  - CD26 = glycosylated transmembrane protein that possesses proteolytic enzyme activity and is expressed on majority of circulating T cells
MF/SS: CD4+ Th2 phenotype

Loss of CD7, CD26, CD3

Malignant T-Cell

T\(_\text{H}2\) Cytokines:
- IL-4
- IL-5
- IL-10

↓

IgE

Th1 effects

Eosinophilia

↓

Th1 effects

Cell-mediated immunity

↓

Dendritic cells

Inherent immunosuppression

Courtesy of Dr. Alain Rook
Clinical Presentation
• Patches
• Plaques
• Tumors
• Erythroderma
Sezary Syndrome

- Keratoderma
- Erythroderma
- Ectropion

Courtesy of Dr. E Kim
Variants of Mycosis Fungoides

- Hypopigmented/Vitiligenous
- Pagetoid Reticulosis
- Follicular (+/- follicular mucinosis)
- Syringotropic
- Granulomatous MF and Granulomatous Slack Skin
- Bullous/Vesicular
- Palmoplantar
- Pigmented Purpuric Dermatosis-like
- Interstitial MF

- Hyperkeratosis/Verrucous
- Vegetating/Papillomatous
- Icthyosiform
- Acanthosis nigricans-like
- Perioral dermatitis-like
- PLEVA-like
- Poikilodermatous
- Pustular
- Parapsoriasis
- Zosteriform
- Invisible
MF/SS Diagnosis

• Challenging
  • Average time from appearance lesions to diagnosis is 3-6 years
• Routine histology
  • >1 punch biopsy, off topical therapy
• Immunophenotyping
  • Immunohistochemistry, flow cytometry
• Molecular methods
  • TCR gene rearrangements (clonality)
• Gene sequencing
• Clinical correlation
## TNMB Classification Staging for MF/SS

### T (Skin)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Limited patch/plaques (&lt;10% of total skin surface)</td>
</tr>
<tr>
<td>T2</td>
<td>Generalized patch/plaques (≥ 10% of total skin surface)</td>
</tr>
<tr>
<td>T3</td>
<td>Tumors</td>
</tr>
<tr>
<td>T4</td>
<td>Generalized erythema</td>
</tr>
</tbody>
</table>

### N (Nodes)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No clinically abnormal LN2</td>
</tr>
<tr>
<td>N1</td>
<td>Clinically abnormal LN2; histopath Dutch Gr 1 or NCI LN0-2 (clone+/-)</td>
</tr>
<tr>
<td>N2</td>
<td>Clinically abnormal LN2; histopath Dutch Gr 2 or NCI LN3 (clone+/-)</td>
</tr>
<tr>
<td>N3</td>
<td>Clinically abnormal LN2; histopath Dutch Gr 3 or NCI LN4 (clone+/-)</td>
</tr>
<tr>
<td>Nx</td>
<td>Clinically abnormal LNs; no histo info</td>
</tr>
</tbody>
</table>

### M (Viscera)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No visceral involvement</td>
</tr>
<tr>
<td>M1</td>
<td>Visceral involvement</td>
</tr>
</tbody>
</table>

### B (Blood)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B0</td>
<td>No significant blood involvement</td>
</tr>
<tr>
<td>B1</td>
<td>Low blood tumor burden</td>
</tr>
<tr>
<td>B2</td>
<td>High blood tumor burden</td>
</tr>
</tbody>
</table>
# Lymph Node Grading MF/SS

<table>
<thead>
<tr>
<th>Updated ISCL/EORTC classification</th>
<th>Dutch system&lt;sup&gt;58&lt;/sup&gt;</th>
<th>NCI-VA classification&lt;sup&gt;13,57,59&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>N&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Grade 1: dermatopathic lymphadenopathy (DL)</td>
<td>LN&lt;sub&gt;0&lt;/sub&gt;: no atypical lymphocytes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LN&lt;sub&gt;1&lt;/sub&gt;: occasional and isolated atypical lymphocytes (not arranged in clusters)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LN&lt;sub&gt;2&lt;/sub&gt;: many atypical lymphocytes or in 3-6 cell clusters</td>
</tr>
<tr>
<td>N&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Grade 2: DL; early involvement by MF (presence of cerebriform nuclei &gt; 7.5 ( \mu )m)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LN&lt;sub&gt;3&lt;/sub&gt;: aggregates of atypical lymphocytes; nodal architecture preserved</td>
</tr>
<tr>
<td>N&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Grade 3: partial effacement of LN architecture; many atypical cerebriform mononuclear cells (CMCs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 4: complete effacement</td>
<td>LN&lt;sub&gt;4&lt;/sub&gt;: partial/complete effacement of nodal architecture by atypical lymphocytes or frankly neoplastic cells</td>
</tr>
</tbody>
</table>
Blood Compartment Grading in MF/SS

• B0 No significant blood involvement
  • ≤5% of peripheral lymphocytes are atypical (by morphology of Sezary cells) or <15% CD4+/CD26- or CD4+/CD7- cells (by flow cytometry)

• B1 Low blood tumor burden
  • >5% peripheral lymphocytes are atypical (by morphology of Sezary cells) or ≥15% CD4+/CD26- or CD4+/CD7- cells (by flow cytometry)

• B2 High blood tumor burden
  • ≥1000 peripheral lymphocytes are atypical (by morphology of Sezary cells) or ≥30% CD4+/CD26- or ≥40% CD4+/CD7- cells (by flow cytometry), or CD4/CD8 ≥10

New EORTC Proposal

• B0 <250/µL absolute cells
• B1 Low blood tumor burden
  • 250-<1000 /µL absolute cells
• B2 High blood tumor burden
  • ≥1000/µL absolute cells

• T-cell blood clone

Eur J Cancer 2018 93:47-56
Flow Cytometry Report

**Specimen Type:** Blood

**Interpretation:** ABERRANT T CELL POPULATION IDENTIFIED: INCREASED CD3+CD4+CD26- CELLS.

**Comment:** 98% of the CD3+CD4+CD26- T-cells were positive for V-Beta 13.1.

Please refer to the HP FC MF SS Followup for quantitation of lymphocyte subsets.

Aberrant cells are % of total analyzed events.
Aberrant cells are 84% of lymphocytes.

**Aberrant Population:** T cells

### Aberrant Cell Phenotype:

<table>
<thead>
<tr>
<th>Marker</th>
<th>Result</th>
<th>Intensity</th>
<th>CD3+CD8+ Absolute</th>
<th>82 - 831 cells/mcL</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3</td>
<td>Positive</td>
<td></td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>CD4</td>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD7</td>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD8</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD26</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Intensity levels are described relative to normal mature T cells)

**Markers Assessed:** CD3, CD4, CD7, CD8, CD26, CD45, VB13.1, VB13.6, VB8

### Percentage of lymphocytes:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Result</th>
<th>Reference Range</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3+</td>
<td>95.5</td>
<td>64.6 - 88.6</td>
<td>%</td>
</tr>
<tr>
<td>CD3+CD4+</td>
<td>92.6</td>
<td>37.7 - 64.2</td>
<td>%</td>
</tr>
<tr>
<td>CD3+CD4+ Absolute</td>
<td>3511</td>
<td>188 - 1883</td>
<td>cells/mcL</td>
</tr>
<tr>
<td>CD3+CD8+</td>
<td>2.8</td>
<td>10.9 - 35.3</td>
<td>%</td>
</tr>
</tbody>
</table>
# Staging

<table>
<thead>
<tr>
<th>Clinical Staging/Classification for MF/SS</th>
</tr>
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<tbody>
<tr>
<td>T</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>IA</td>
</tr>
<tr>
<td>IB</td>
</tr>
<tr>
<td>IB</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IIIA</td>
</tr>
<tr>
<td>IIIB</td>
</tr>
<tr>
<td>IVA</td>
</tr>
<tr>
<td>IVAr</td>
</tr>
</tbody>
</table>

NCCN.org and Olsen et al, Blood 2007
Goals of Therapy for CTCL

**IDEAL**
- Cure
- Extend Life
- Alleviate Symptoms
- Durable Response
- High Response Rate

**ACTUAL**
- Alleviate Symptoms
- Variable Response Duration
- Extend Life
- Cure
Treatment Approach in MF and SS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Limited Dz, T1</td>
<td>Topical steroids, Topical retinoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Topical nitrogen mustard</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NB-UVB/PUVA ± Bexarotene or IFN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSEBT, Bexarotene or IFN</td>
</tr>
<tr>
<td>IB/IIA</td>
<td>Generalized, T2</td>
<td>Clinical Trial (TLR agonist, miRNA inhibitors, new MoAb eg. CD47, BET inhibitor, IL-2 fusion protein (CD25))</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single-agent Monoclonal Antibodies/HDAC (Brentuximab, Mogamulizumab, Romidepsin)</td>
</tr>
<tr>
<td>IIB</td>
<td>Tumors, T3</td>
<td>Single Agent Chemotherapy (Pralatrexate, Gemcitabine, Doxorubicin)</td>
</tr>
<tr>
<td></td>
<td>Erythroderma, T4</td>
<td>Combination Chemo</td>
</tr>
<tr>
<td>IV</td>
<td>Extracutaneous Dz</td>
<td>ECP± Bexarotene, IFN</td>
</tr>
</tbody>
</table>
# Topical Treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Response</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>At least PR: 94% in T1 and 82% in T2 (high potency class I-III)</td>
<td>Variable</td>
</tr>
<tr>
<td>Nitrogen Mustard</td>
<td>CR: 70-80% in T1 or 50-60% in T2 (aqueous); ORR 58% in T1 and 47% in T2 (by CAILS) in gel form</td>
<td>AWP $4026 for 60g tube (Valchlor Commercial Gel Formulation)</td>
</tr>
</tbody>
</table>
| Bexarotene or Tazotene Gel | ORR 63% (CR21%) (B) At least PR in 58% of patients (T)                  | AWP Bexarotene Gel $34,990 per 60g tube  
AWP Tazarotene Gel 0.1% $790 per 60g tube |
| Imiquimod cream         | PR 50% in T1-T3 disease                                                  | AWP Zyclara 3.75% $1296 per 7.5gram pump        |
Phototherapy

- Narrow Band UVB: 311-312 nm-1 emission
  - CR 54-90% in patients with stage IA to IIA

- Psoralen Plus UVA (PUVA):
  - CR 85% (Stage IA), 65% (Stage IB)

- Risk for skin cancer
Radiation Therapy

• Localized treatment
  • Use: Doses range from 10-30 Gy for each treatment field
  • Newer studies showing efficacy with $2\text{Gy} \times 2$
  • CR rates 95-100%

• Total skin electron beam (TSEB)
  • Use: 30 Gy; lower doses used 12 Gy (Stanford)
  • CR rates >75% in traditional dosing: ORR 88% in 12 Gy

• Side effects: burn, dermatitis, radiation recall
Oral Retinoids

• Bexarotene
  • Indication: Patients with advanced stage MF and SS, or refractory early stage
  • Pharmacologic category: Retinoid RXR receptor agonist
  • ORR 45% (CR 2%)
  • Use: The manufacturer's recommended dosing is 300mg/m²/day.
  • Side effects: severe central hypothyroidism, hyperlipidemia
  • AWP: Bexarotene 300mg daily: $25,760 per month

• Isotretinoin and acitretin
  • Pharmacologic category: Retinoid RAR receptor agonist
  • AWP: Isotretinoin 30mg daily: $370 per month
  • AWP: Acitretin 25mg daily: $1153 per month
Interferons

• Indication: As a second line therapy in patients with stage IA and IB disease and a first line for those with more advanced stages

• Pharmacologic category: Biologic response modifier/Immune potentiator

• Interferon alfa and Interferon gamma

• Response: PR 20-40% CR 4-14% in varying doses

• Typically used in combination treatment with phototherapy or multimodality approach

• AWP: Interferon alfa 2b 1.5MU TIW- $667 per month
Folate Antagonists

- Methotrexate and Pralatrexate
- Dihydrofolate reductase inhibitors
- AWP: MTX 25mg weekly: $150 per month
- AWP: PDX 15mg/m2 weekly 3 of 4 weeks: $16,875
Histone Deacetylase Inhibitors

- Indication: Patients with more advanced disease as a second line agent, or as a first line in those with Stage IV or Sezary Syndrome
- Mechanism of action: small molecules that interact with histone acetyltransferases and histone deactylases that modify histone acetylation in proteins
- Vorinostat and Romidepsin only agents approved for cutaneous lymphoma
- Vorinostat (oral): ORR 29% (phase II)
- Romidepsin (IV): ORR 34% and CR 6% (global response)
- Side effects: GI, QT prolongation (electrolytes)
- AWP: Vorinostat 400mg daily: $14,911 per month
- AWP: Romidepsin 14mg/m2/week 3 of 4 weeks: $31,608 per month
Photopheresis
What’s New?
Brentuximab Vedotin (BV)

• Anti-CD30 antibody drug conjugate to cytotoxin monomethyl auristatin E (MMAE)

• Two Phase II open label studies with high response rates in CTCL

• Phase III randomized trial reported improved response compared to physician choice (Methotrexate/Bexarotene)

• BV was added into NCCN guidelines

• FDA approval for CD30 expressing MF and pcALCL
<table>
<thead>
<tr>
<th>Clinical Trials</th>
<th>Phase/Trial Design</th>
<th>Number of evaluable patients</th>
<th>CD30 Eligibility</th>
<th>ORR</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duvic et al J. Clin. Oncol. 33(32), 3759–3765 (2015)</td>
<td>Phase II Open label, single center</td>
<td>28</td>
<td>CD30+ (no lower limit but expression graded)</td>
<td>15 (54%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Kim et al J. Clin. Oncol. 33(32), 3750–3758 (2015)</td>
<td>Phase II Open label, investigator initiated, multicenter trial</td>
<td>30</td>
<td>negligible to 100% CD30 expression levels</td>
<td>21 (70%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Prince et al Lancet 390 (10094), 555–566 (2017)</td>
<td>Phase III Randomized open label, multicenter, international study</td>
<td>48</td>
<td>CD30-positive (10% tumor cells expressing CD30)</td>
<td>31 (65%)</td>
<td>5 (10%)</td>
</tr>
</tbody>
</table>
CD30 expression varies in same patient
Mogamulizumab in CTCL

- Anti-CC chemokine 4 (CCR4) monoclonal antibody

- CCR4 is involved in skin trafficking of lymphocytes
  - Expressed in CTCL including MF and SS, ATLL, PTCL

- FDA approval 2018 for relapsed refractory mycosis fungoides or Sezary syndrome after at least one prior systemic therapy
Response to Mogamulizumab in phase I/II trial

<table>
<thead>
<tr>
<th>Patients</th>
<th>Blood% (n)</th>
<th>Skin% (n)</th>
<th>Nodes% (n)</th>
<th>Global% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>95 (18)</td>
<td>42 (16)</td>
<td>25 (7)</td>
<td>37 (14)</td>
</tr>
<tr>
<td>Sezary</td>
<td>94 (16)</td>
<td>53 (9)</td>
<td>33 (5)</td>
<td>47 (8)</td>
</tr>
<tr>
<td>MF</td>
<td>100 (2)</td>
<td>33 (7)</td>
<td>15 (2)</td>
<td>28 (6)</td>
</tr>
</tbody>
</table>
## Adverse Events

<table>
<thead>
<tr>
<th>AE</th>
<th>All Grades (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>31</td>
</tr>
<tr>
<td>Chills</td>
<td>24</td>
</tr>
<tr>
<td>Infusion Reaction</td>
<td>21</td>
</tr>
<tr>
<td>Headache</td>
<td>21</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>19</td>
</tr>
<tr>
<td>Fatigue</td>
<td>17</td>
</tr>
<tr>
<td>Rash</td>
<td>17</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14</td>
</tr>
</tbody>
</table>

*Blood 2015; 125 (12) 1883-1889*
Active Clinical Trials

• Early stage
  • SGX 301 (Hypericin)
  • TLR agonists (TLR7 and 8)
    • topical resiquimod

• Advanced stage
  • RP 6530 (PI3K inhibitor)
  • E7777 (Denileukin difftitox)
  • MRG-106 microRNA antagonist
  • BET inhibitor
Early Stage Disease- NEW

- SGX 301 (Synthetic Hypericin)
  - Natural compound found in stems and petals of plants in family of *hypericum*
  - Photosensitizing agent to visible light
  - Cell death through O2 radicals, activity in malignant T cells in vitro
  - Stage IA, IB, IIA
  - Application to isolated lesions day before and come for light treatment (non UV) the next day twice weekly
Early Stage Disease-NEW

• Resiquimod (TLR 7 and 8 agonist)
  • Phase II
  • Topical Gel
  • Directly activates innate immune cells expressing TLR7 and/or 8, resulting in innate and adaptive immune modulation
  • Stage IA, IB, IIA
Advanced Stage-NEW

- RP6530- Phosphoinositide-3-kinase (PI3K) inhibitor (dual gamma and delta)
  - PI3K involved in cell function, proliferation, trafficking, immunity
  - Oral medication for relapsed/refractory patients
  - Phase I/Ib, dose escalation study
  - Collaboration with lymphoma department (PTCL)
  - Adverse effects include rash, LFT changes
Advanced Stage-NEW

• E7777 (purified Denileukin diftitox)
  • Phase III
  • IL-2 receptor fusion protein to Diphtheria toxin
  • IL-2 receptor with 3 domains (CD25, CD122, CD132)
  • Toxicity associated with previous version of DD includes capillary leak syndrome, hypersensitivity reaction
  • This is an improved formulation of DD
  • Multi-center open-label single-arm study in Stage IA-IVA
Advanced Stage-NEW

• MRG-106
  • Oligonucleotide antagonist of microRNA miR-155-5p
  • MicroRNAs are small non-coding RNAs acting as negative gene regulators
  • MiR-155-5p is linked to treatment resistance and poor prognosis, upregulated in lymphoma
  • Phase II randomized study vs vorinostat in relapsed/refractory patients Stage I, II, III
Advanced Stage-NEW

- Bromodomain (BET) proteins inhibitor
- Epigenetic protein upregulated in expression in lymphomas and associated in MF and SS
- Oral capsule
- Adverse effects include GI (nausea, weight loss), QTC prolongation, myelosuppression
Other Options

• Stem cell transplantation

• New monoclonal antibody targets
  • KIR (anti-killer cell immunoglobulin-like receptor 3DL2)
  • Anti-CD47 (“eat me”) signaling antibody
  • PD-1 inhibitor immune checkpoint inhibitors
Other Updates
High-Throughput Sequencing

• Genetic sequencing potential applications
  • Improvement in diagnosis
  • Gene profile and study of disease
  • Determination of remission and prognosis
Supportive Care
Association of Cutaneous Lymphoma and Staphylococcus Infection

RAPID COMMUNICATION

Association of Erythrodermic Cutaneous T-Cell Lymphoma, Superantigen-Positive Staphylococcus aureus, and Oligoclonal T-Cell Receptor Vβ Gene Expansion

By Clotilde M. Jackow, Jennifer C. Cather, Vicki Hearne, Arisa T. Asano, James M. Musser, and Madeleine Duvic

Prevalence and treatment of *Staphylococcus aureus* colonization in patients with mycosis fungoides and Sézary syndrome

R. Talpur, R. Bassett* and M. Duvic

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Wound Care

- High bacteria and/or biofilm can be obstacles to healing
- MF patients typically with thick hyperkeratotic plaques preventing penetration of topical agents
- Physical therapy consult
Pruritus in Cutaneous Lymphoma

Report

Prevalence and severity of pruritus in cutaneous T cell lymphoma

Alok Vij¹, MD, and Madeleine Duvic², MD

Gabapentin for the Treatment of Cutaneous Lymphoma Associated Pruritus

Results

- 290 patients with cutaneous lymphoma were treated with gabapentin and/or pregabalin from 2005 to 2015
- 82 patients met criteria with adequate follow-up information
- Majority of patients were treated with gabapentin (N=81) vs pregabalin (N=1)

Chin et al. Presented at Medical Dermatology Society 2017
Gabapentin for the Treatment of Cutaneous Lymphoma Associated Pruritus

Results

PERCENTAGE REPORTING IMPROVEMENT

- First Follow-up Visit: 52%
- 6-month Visit: 71%
- 12-month Visit: 63%

N=82  N=52  N=38

Chin et al. Presented at Medical Dermatology Society 2017
Conclusion

• Mycosis fungoides has indolent course but some patients progress with poor prognosis
• Standard treatments are available but limited by cost and eventual lost of response
• Exciting new treatment options for patients in horizon
• Skin infections and pruritus are a significant cause of morbidity and mortality in these patients
Cutaneous Lymphoma Research Team

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Thank you