Summary

The symposium discussed the pathobiology, classification, and treatment of cutaneous lymphomas. Drs. Burg and Kadin commented on the pathophysiology of mycosis fungoides/Sezary syndrome and cutaneous CD30+ lymphoproliferative disorders, respectively. A proposed classification of primary cutaneous lymphomas from the EORTC was presented by Drs. Kerl and Sterry. Dr. Jaffe presented a classification of cutaneous lymphomas based on the REAL classification. All speakers agreed that primary cutaneous lymphomas are usually distinctive in their clinical behavior and biology, and differ from their nodal counterparts. The symposium concluded with remarks from Drs. Vonderheid and Hoppe on the therapeutic approach to primary cutaneous lymphoid malignancies.

Key words: cutaneous lymphoma, T cell, B cell, lymphocyte biology, skin

A symposium chaired by Prof. Gunter Burg and Dr. Elaine S. Jaffe focused on the pathophysiology, classification, and treatment of cutaneous lymphomas. Primary lymphomas of the skin differ in many ways from their nodal counterparts, and these malignancies require special consideration from the specialist. The program began with a review of the pathogenesis of cutaneous T-cell lymphoma (CTCL) or mycosis fungoides/Sezary syndrome (MF/SS) by Gunter Burg. He noted that the pathologic and clinical manifestations of CTCL follow from complex interactions between the neoplastic T cells and the cells of the cutaneous microenvironment, mainly keratinocytes and dendritic cells. An important factor may be a switch from TH (T helper) 1 cells to TH 2 cells during tumor development. The cytokines elaborated by the neoplastic cells and bystander cells play a role both in tumor development and the ensuing clinical manifestations. CTCL, like most other malignancies, goes through stages of tumor evolution. Tumor progression may be explained by stepwise accumulation of mutations involving DNA repair- and tumor-suppressor genes. The risk for the accumulation of gene mutations increases with the number of cell divisions, which normally is limited by cell death owing to apoptosis or senescence of the cell. These events depend on bcl-2 expression and telomerase activity, both of which are increased in CTCL and, therefore, may be important factors in promoting unlimited cell proliferation, driven by persistent antigenic stimulation.

CD30+ lymphoproliferative disorders (LPDs) of the skin include lymphomatoid papulosis (LyP) and primary cutaneous anaplastic large-cell lymphoma (ALCL). These disorders, which were reviewed by Marshall Kadin, exhibit a spectrum in both their pathologic features and clinical behavior. Multiple cytokines (TNF-α and TGF-β) produced by the T-cell clone appear to influence the histologic features and clinical regression of the cutaneous lesions. CD30+ cutaneous LPDs appear distinct from classical ALCL, and lack the t(2;5)(p23;q35) of the latter malignancy. The most common cytogenetic abnormalities involve chromosomal breakpoints at 1p36 and 10q24-26. Although the disease typically remains confined to the skin for many years, extracutaneous disease is seen in 25% of patients and is associated with a more aggressive clinical course.

The symposium proceeded to a discussion of the classification of primary cutaneous lymphomas. The EORTC, noting that cutaneous lymphomas differ from nodal lymphomas in clinical behavior and functional markers, has proposed a classification for these diseases (Table 1). Helmut Kerl presented an overview of cutaneous B-cell lymphomas and Wolfram Sterry presented the EORTC perspective on T-cell malignancies. The tumors are classified according to their usual clinical behavior, indolent or aggressive. In addition, some entities have been identified as provisional, and still others are undergoing continued discussion regarding their inclusion. The EORTC group identifies a primary cutaneous lymphoma as one presenting solely with cutaneous disease, without detected extracutaneous spread for at least six months.

Elaine Jaffe presented a classification of cutaneous lymphomas based on the principles of the revised European–American lymphoma (REAL) classification proposed by the International Lymphoma Study Group (ILSG). She noted that the premise of the REAL classification is the identification of disease entities, based on pathologic, immunophenotypic, genetic and clinical features. Therefore, if cutaneous involvement is a unique aspect of a disease entity, this clinical fact is considered integral to disease recognition. Indeed, there are a num-

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patients. Such approaches are also useful in palliating
and/or radiotherapy may be curative in 30%-50% of
with limited cutaneous disease, skin-directed chemother-
stage MF representing the opposite extreme. In patients
considered part of this continuum, with plaque- and tumor-
parapsoriasis en plaques and patch-stage MF are con-
ting features common to diseases involving multiple
required. Indeed, such schemes may impede the recogni-
classification are applicable to cutaneous lymphomas,
intrinsic different biology.

The symposium concluded with an overview of the
Aggressive
Large-cell CTCL, CD30+, including
inflammatory, pleomorphic

For discussion: angiocentricity, gamma/delta CTCL, marginal-zone
B-cell lymphoma, and subcutaneous lymphoma.
Abbreviations: CTCL – cutaneous T-cell lymphoma; CBL – cutaneous
B-cell.

patients with more advanced disease. Biological response
modifiers and cytotoxics or immunotoxins targeted
against T cells hold promise for the future.

Dr. Hoppe confirmed the effectiveness of topical
therapies in control of disease. Because systemic disease
at presentation is rare, only limited staging is required
(chest radiographs, hematological evaluation with Sézary
cell counts, and routine chemistries). If significant
lymphadenopathy is present, lymph node biopsy may be
indicated. Electron beam and topical nitrogen mustards
are both effective. Visceral disease requires systemic che-
motherapy, but chemotherapy generally has not been
effective. Interferon has shown some promise, and other
investigational approaches are indicated in patients with
advanced disease. Primary localized cutaneous B-cell
lymphoma is often treated successfully with localized
radiation therapy.

In conclusion, all speakers agreed that primary cuta-
aneous lymphomas differ significantly from nodal and most
extranodal lymphomas, and that these malignancies re-
quire specialized diagnostic and therapeutic approaches.
The site of presentation must be taken into consideration
by both the pathologist and the clinician.

**Table 1. EORTC classification of primary cutaneous lymphomas**

<table>
<thead>
<tr>
<th>Primary cutaneous T-cell lymphomas</th>
<th>Primary cutaneous B-cell lymphomas</th>
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<tbody>
<tr>
<td>Indolent</td>
<td>Indolent</td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>Follicle center cell lymphoma of</td>
</tr>
<tr>
<td>Sézary syndrome</td>
<td>head and trunk</td>
</tr>
<tr>
<td>Pagetoid reticulosis</td>
<td>Immunoctoma</td>
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<tr>
<td>Lymphomatoid papulosis</td>
<td></td>
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<tr>
<td>Large-cell CTCL, CD30+, including</td>
<td></td>
</tr>
<tr>
<td>anaplastic, immunoblastic,</td>
<td></td>
</tr>
<tr>
<td>pleomorphic</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td></td>
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<tr>
<td>Large B-cell lymphoma of the leg</td>
<td></td>
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</tbody>
</table>

**Table 2. Classification of cutaneous lymphomas based on the REAL classification.**

<table>
<thead>
<tr>
<th>Cutaneous T-cell lymphomas</th>
<th>Mycosis fungoides/ Sézary syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pagetoid reticulosis (x;10 and y;8)</td>
</tr>
<tr>
<td></td>
<td>Granulomatous slack skin disease</td>
</tr>
<tr>
<td></td>
<td>Follicular mucinosis</td>
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<tr>
<td></td>
<td>CD30+ cutaneous lymphoproliferative</td>
</tr>
<tr>
<td></td>
<td>disease</td>
</tr>
<tr>
<td></td>
<td>Lymphomatoid papulosis</td>
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<tr>
<td></td>
<td>Cutaneous anaplastic large cell lymphoma</td>
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<td></td>
<td>Subcutaneous panniculitis-like T-cell lymphoma</td>
</tr>
</tbody>
</table>

**Other T-cell lymphomas with cutaneous involvement (nearly all)**

T-PLL/T-CLL

Aggressive NK-cell leukemias
NK/T-cell 'angiocentric' lymphomas
Angioimmunoblastic T-cell lymphoma
Peripheral T-cell lymphoma, NOS
Adult T-cell leukemia/lymphoma
Classical anaplastic large-cell lymphoma

**Cutaneous B-cell lymphomas**

Cutaneous follicle-center lymphoma
(Usually bcl-2 rearrangement/expression–negative)
Cutaneous marginal-zone B-cell lymphoma (cutaneous MALT-type lymphoma)
So-called 'cutaneous immunocytoma'
Large B-cell lymphoma
Intravascular large B-cell lymphoma
Precursor B-lymphoblastic lymphoma

Abbreviations: T-PLL/T-CLL = T-cell prolymphocytic leukemia/T-cell chronic lymphocytic leukemia; NK = natural killer; NOS = not otherwise specified; MALT = mucosal-associated lymphoid tissue.