Cutaneous T-Cell Lymphoma: From Genetics to Clinical Practice

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This challenging supplement to ONCOLOGY is based on the proceedings of a closed expert symposium, and provides an overview of our current knowledge on primary cutaneous T-cell lymphomas (CTCL). The complete spectrum from genetics to clinical practice is covered.

This group of lymphoproliferative disorders is characterized by the accumulation of malignant T-cell clones that home to the skin. Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common manifestations, with the former accounting for about 60% of new cases and the latter for only 5%.[1-4] Sézary syndrome, the leukemic form of CTCL, has a poor prognosis, with a median survival of less than 3 years.[5] By contrast, MF typically follows an indolent course, although progression may occur, and prognosis depends on tumor stage (IA-IIVB) at presentation. Among those with early-stage disease (IA), median survival is similar to an age-matched control population, whereas those with disease stages IVA and IVB have a median overall survival of only 1.5 to 2.5 years from the time of diagnosis.[6-9]

An accurate diagnosis of CTCL is of paramount importance, first to distinguish between neoplastic and inflammatory processes, but also to determine the precise type of lymphoma; this is based on the proper clinicopathologic correlation. The first paper in this supplement reviews the histopathology and differential diagnosis of MF and its variants, and discusses several skin conditions that are similar in appearance to MF at the early stages. These range from the benign and transient to malignant and chronic; therefore, accurate diagnosis has important implications for patients’ treatment. Successful diagnosis of CTCL requires not only accurate histopathology, including immunocytochemistry, but also good clinical appraisal and is supported by molecular biologic analysis for T-cell clonality.

Other tools that may help in the diagnosis and clinical management of CTCL are on the horizon,[10] based on our increasing knowledge of the molecular and cytogenetic changes found in these disorders, and these provide the topic of our second paper. Chromosomal aberrations have long been recognized in patients with CTCL. More recently, specific sites on chromosomes that are affected by the disease, with resulting gene deletions, have been identified. In addition, genes known to be down- or up-regulated in CTCL have also been identified, and the possible pathogenic and diagnostic significance of these genetic changes proposed. It is hoped that these findings will both increase our understanding of CTCL and provide some disease-specific treatment options. The final four papers in the supplement provide comprehensive reviews of the treatment options available for patients with CTCL, which is responsive to current treatments but resistant to cure. Therapeutic strategies in this chronic disease therefore concentrate on inducing remission, reducing symptoms and tumor burden, and preventing disease progression, while minimizing treatment-related toxicity. Skin-directed therapies, such as bexarotene gel (Targretin) and psoralen plus ultraviolet A are effective in the early disease stages (stages IA-IIB). Those with resistant or advanced disease require systemic therapies such as oral bexarotene and interferon α, which, both alone and in combination with other therapies, are highly effective in producing and maintaining remission in many patients. Other promising therapies include targeted treatments, such as denileukin diftitox (Ontak), which is proving highly effective in tumor-stage disease, and the histone deacetylase inhibitors. Finally, some conventional chemotherapies are effective in CTCL, although their efficacy must be offset against their side effects. In patients who are responsive to chemotherapy, allogeneic stem-cell transplantation provides a potentially curative treatment. However, again, the toxicity of this therapy must be balanced by its possible benefits for patients. There are many therapeutic options available for the management of CTCL, and therefore a large number of possible combinations available to clinicians, making choices in CTCL treatment complex.
The results of testing some combinations are reviewed here. Other combinations should be systematically investigated as new treatments enter the therapeutic armamentarium to try to identify which treatments and combinations are optimal, and at which disease stage. These treatments and studies provide hope for improvement in the long-term management of patients with these chronic disorders, with the goal being to provide lasting complete remission and, hopefully, cure. Moreover, improved knowledge of CTCL biology, as well as better treatments for this condition, may result in enhanced understanding and management of noncutaneous peripheral T-cell lymphomas, for which information, in general, is still lacking. These T-cell lymphomas often have a poor prognosis, and represent the next largely unexplored frontier in lymphoma treatment.[11]

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**Disclosures:** Dr. Dummer has worked on advisory boards for Ligand Pharmaceuticals and Cephalon Europe, and was chairman at sponsored symposia. Dr. Zucca was chairman for the Cephalon Europe-sponsored symposium that provided the basis for this supplement.

**References:**


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