REVIEW

Recent advances in understanding and managing cutaneous T-cell lymphomas [version 1; peer review: 2 approved]

Patrick M. Brunner , Constanze Jonak, Robert Knobler

Department of Dermatology, Medical University of Vienna, Währinger Gürtel 18-20, Vienna, 1090, Austria

V1 First published: 05 May 2020, 9(F1000 Faculty Rev):331
<https://doi.org/10.12688/f1000research.21922.1>

Latest published: 05 May 2020, 9(F1000 Faculty Rev):331
<https://doi.org/10.12688/f1000research.21922.1>

Abstract

Cutaneous T-cell lymphomas (CTCLs) comprise a heterogeneous group of extranodal non-Hodgkin lymphomas involving primarily the skin and mycosis fungoides is its most frequent entity. Whereas most patients show an indolent course in early disease (clinical stages IA to IIA), some patients progress to advanced disease (stage IIB or higher), and the 5-year survival rate is unfavorable: only 47% (stage IIB) to 18% (stage IVB). Except for allogeneic stem cell transplantation, there is currently no cure for CTCL and thus treatment approaches are palliative, focusing on patients' health-related quality of life. Our aims were to review the current understanding of the pathogenesis of CTCL, such as the shift in overall immune skewing with progressive disease and the challenges of making a timely diagnosis in early-stage disease because of the lack of reliable positive markers for routine diagnostics, and to discuss established and potential treatment modalities such as immunotherapy and novel targeted therapeutics.

Keywords

Cutaneous T cell lymphoma, Mycosis fungoides, Sézary Syndrome, health-related quality of life, tissue resident memory T cells

Open Peer Review

Approval Status

	1	2
version 1		
05 May 2020		

Faculty Reviews are review articles written by the prestigious Members of **Faculty Opinions**. The articles are commissioned and peer reviewed before publication to ensure that the final, published version is comprehensive and accessible. The reviewers who approved the final version are listed with their names and affiliations.

1. **Vincent Liu**, University of Iowa Hospitals & Clinics, Iowa City, USA
2. **Sam Hwang**, University of California Davis, School of Medicine, Sacramento, USA

Any comments on the article can be found at the end of the article.

Corresponding author: Robert Knobler (robert.knobler@meduniwien.ac.at)

Author roles: **Brunner PM:** Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing; **Jonak C:** Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing; **Knobler R:** Conceptualization, Writing – Review & Editing

Competing interests: PMB is an employee of the Medical University of Vienna; has received personal fees from LEO Pharma, Pfizer, Sanofi, Eli Lilly and Company, Novartis, Celgene, UCB Pharma, Biotest, Boehringer Ingelheim, AbbVie, Amgen, and Arena Pharmaceuticals; is an investigator for Novartis (grant paid to his institution); and has received a grant from Celgene (paid to his institution). CJ is an employee of the Medical University of Vienna; has received personal fees from LEO Pharma, Pfizer, Eli Lilly and Company, Novartis, Takeda, Mallinckrodt/Therakos, AbbVie, Janssen, and Almirall; and is an investigator for Eli Lilly and Company, Novartis, and 4SC (grant paid to her institution). RK is an employee of the Medical University of Vienna and has received personal fees from Mallinckrodt/Therakos.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2020 Brunner PM *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Brunner PM, Jonak C and Knobler R. **Recent advances in understanding and managing cutaneous T-cell lymphomas [version 1; peer review: 2 approved]** F1000Research 2020, 9(F1000 Faculty Rev):331 <https://doi.org/10.12688/f1000research.21922.1>

First published: 05 May 2020, 9(F1000 Faculty Rev):331 <https://doi.org/10.12688/f1000research.21922.1>

Introduction

Cutaneous T-cell lymphomas (CTCLs) are primary lymphomas of the skin, and the estimated incidence is about 5.6 per million^{1,2}. The term CTCL comprises a group of malignancies that develop from skin-homing T cells, which are of the CD4⁺ T helper cell type in more than 90% of cases^{1,2}. The most frequent clinical entity of CTCL is mycosis fungoides (MF), accounting for about 60% of all cases, followed by primary cutaneous CD30⁺ lymphoproliferative disorders and much rarer entities such as Sézary syndrome (SS). The 2018 update of the World Health Organization–European Organization for Research and Treatment of Cancer (WHO-EORTC) classification for cutaneous lymphomas describes new provisional entities—namely chronic active Epstein–Barr virus infection, CD8⁺ aggressive epidermotropic CTCL, primary cutaneous CD4⁺ small/medium T-cell lymphoproliferative disorder, and primary acral CD8⁺ T-cell lymphoma—which are now included³. In early disease stages, MF presents clinically with erythematous patches or plaques and this stage can last for many years without clinical progression and without affecting the life expectancy of the patient⁴. Nevertheless, CTCLs may be disfiguring and thus have an impact on patients' health-related quality of life (HRQoL)^{5,6}. In about 30% of patients presenting with early-stage CTCL, the disease progresses to advanced-stage disease within 10 years⁷ by gradually developing into tumors and may disseminate to lymph nodes, blood, and internal organs, resulting in an unfavorable prognosis^{8,9}; 5-year overall survival rates decrease from 94% in stage IA to as low as 18% in stage IVB¹⁰. However, in rare cases, MF can also initially present with tumors representing the disease variant “tumeur d'emblée”. It is still unclear why about 30% of patients with CTCL⁷ progress to advanced disease; currently, prediction of prognosis is based predominantly on clinical staging by using the TNMB (tumor, node, metastasis, blood) classification for MF/SS¹¹ and there are additional roles for gender, age, blood lactate dehydrogenase concentration, folliculotropism, large-cell transformation, and the detection of clonality¹⁰. Of note, no validated biomarkers, favorable or unfavorable, are available for the prediction of the disease course¹².

Disease etiology and pathogenesis

The etiology of most variants of CTCL remains only poorly understood. Potential etiologic factors include infectious agents, ultraviolet (UV) light, or occupational exposures^{13,14}. Large-scale mutational genome profiling analyses identified genomic alterations in several putative oncogenes and tumor suppressor genes, including *CARD11*, *CCR4*, *TP53*, *NF-κB*, and Janus kinase signaling members^{15–19}, but heterogeneity between individual patients can be considerable^{15–19}. It is assumed that, besides a dysfunctional regulation of cytokines and other signaling molecules that most likely play a decisive role for malignant transformation, epigenetic modifications such as pathologic gene methylation and histone deacetylation play a role in malignant transformation of CTCL cells²⁰.

In MF, the malignant T cells have been identified as typically CD4⁺ skin-resident effector memory T cells of clonal origin²¹. Their skin-resident nature explains why MF lesions tend to be primarily present in the skin in most patients^{21,22}. By contrast, SS cells are classified as of the central memory phenotype

(expressing the lymph node homing molecules CCR7 and L-selectin), enabling these cells to freely move from the periphery to lymphoid organs^{21,22}. Consistently, the phenotype of SS typically shows erythroderma as well as blood and lymph node involvement.

CTCL cells have been described to express cytokines of various helper cell subtypes, including T helper 2 (Th2), Th17, and regulatory T cells^{23–25}. In addition, many other chemokines and cytokines are being produced within lesions, adding to the overall complexity of the disease²⁶. Histologically, malignant T cells are characterized by epidermotropism—that is, they are preferentially present in the upper parts of the skin (epidermis)—whereas non-malignant T cells are detected primarily in the dermis, especially in early MF. This early immune infiltrate consists primarily of non-malignant Th1 cells, regulatory T cells, and cytotoxic CD8⁺ T cells (tumor-infiltrating lymphocytes, or TILs), which are hypothesized to (initially) keep the malignant T cells under control^{27,28}, but the precise mechanisms remain unclear. During progression of the disease, a switch from the benign “bystander” infiltrate of Th1 cells and CD8⁺ TILs to a more Th2-biased phenotype, including the appearance of blood eosinophilia and markedly elevated IgE blood levels²⁶, has been documented²⁹. Conversely, therapeutic success in MF during skin-directed psoralen plus UVA (PUVA) therapy was linked to a shift from Th2 toward a Th1 phenotype with clearance of the skin lesions irrespective of tumor cell burden, implicating an increased turnover of benign T cells³⁰. Thus, Th1 immune skewing in early-stage disease is traditionally considered protective (produced by the accompanying “anti-tumor” infiltrate), whereas a gradual loss of this Th1 signature, with an increase in Th2 mediators, is regarded as a sign of disease progression³¹. It is assumed that, mechanistically, tumor-derived Th2 cytokines suppress proliferation of benign T cells and inhibit dendritic cell (DC) maturation³². Such a Th2-dominant skin immune skewing is also found in atopic dermatitis; intriguingly, both patients with MF and those with atopic dermatitis have *Staphylococcus aureus* colonization and increased rates of infectious complications^{33,34}. Recent data even suggest that staphylococcal alpha toxin itself may promote disease progression through positive selection of CD4⁺ tumor cells³⁵. In line with its opposing effect toward Th2-associated inflammation, the major Th1 cytokine interferon-gamma (IFN-γ) shows some efficacy in CTCL treatment³⁶. However, other cells, including fibroblasts, keratinocytes, and endothelial cells, are thought to promote and augment a Th2 microenvironment in advanced-stage MF, thereby further attenuating Th1 immune responses³⁷.

DCs have the unique capacity to induce primary immune responses by activating naïve T cells and thus are the central gatekeepers for the initiation of adaptive immune responses³⁸. As recently shown, c-Kit⁺OX40L⁺CD40L⁺ DCs can foster the visible skin inflammation within skin lesions by recruiting and activating benign T cells and this mechanism likely provides key tumorigenic signals within the CTCL immune microenvironment³⁰. In advanced-stage CTCL, the maturation of DCs is thought to be suppressed by Th2 cytokines³². Importantly, immature DCs can induce tolerance by presenting antigens to T cells without appropriate co-stimulation, thus fostering a

tumor-tolerating (micro)environment rather than an anti-tumor immune defense³⁹. Consistently, increased levels of immature DCs are found in MF lesions, which might be an important mechanism for tolerance against malignant T cells⁴⁰.

Keratinocytes produce multiple chemokines, including CCL17, CCL26, CCL27, CXCL9, and CXCL10, which are potent chemo-attractants for several immune cell populations. They also produce nerve growth factor, which is suggested to be involved in itch development, a typical symptom for CTCL²⁶. Mast cells might also be involved in CTCL pathogenesis, as their number correlates with disease progression⁴¹. Similarly, myeloid-derived suppressor cells increase with advanced disease stage⁴², and immunosuppressive M2 macrophages are known to promote tumor growth in various cancers⁴³ and could also play a role in CTCL^{44–46}. Overall, there is a complex interplay between tumor cells and the tissue microenvironment, which is not yet fully elucidated.

Diagnosis of disease

In CTCL, genetic markers are currently under intense investigation as potential diagnostic tools, but single diagnostic biomarkers are still lacking. Thus, the integration of clinical morphology, histology, immune-phenotype, and molecular biological data remains essential for an accurate diagnosis³. Accordingly, the diagnosis of CTCL is based on the combination and correlation of the three following assessments: (a) clinical observations, (b) (immuno)histological examination of skin biopsies, and (c) additional laboratory tests such as flow cytometry of peripheral blood and the analysis of T-cell receptor (TCR) clonality by polymerase chain reaction (PCR)⁴⁷. The parameter of large-cell transformation of MF cells, based on histological criteria, is found in 56 to 67% of patients with advanced-stage MF⁹ and linked to an aggressive disease course with shortened survival. Besides malignant T cells, an abundant number of reactive immune cells, including high numbers of non-malignant T cells, accompany the malignant clone. Molecular and immunohistochemistry markers that are currently used to diagnose MF are usually negative markers, such as loss of expression of, for example, CD7 or CD26, but this kind of aberrant surface expression shows considerable variability from case to case⁴⁸. Useful positive diagnostic markers are still lacking for routine diagnostics. Importantly, the actual lymphoma cells are present in only small numbers during early stages of the disease. Thus, analyses of clonality (TCR rearrangement) are often falsely negative in early MF⁴⁹. Rea *et al.* showed that, for CTCL diagnosis, high-throughput sequencing was more specific than *TCR gamma chain* gene PCR (100% versus 88%) but that sensitivity (68% versus 72%) and accuracy (84% versus 80%) were similar⁵⁰. Thus, high-throughput sequencing, assessing both clonality and T-cell fractions in skin biopsies, is a promising tool to increase diagnostic accuracy in CTCL⁵⁰.

TOX (thymocyte selection-associated high-mobility group box) has been found to be strongly upregulated in early MF compared with lower levels in benign inflammatory dermatitis⁵¹. Although TOX has insufficient sensitivity and specificity to serve as a single diagnostic marker, it might have an adjunctive diagnostic role together with other clinical and histological data⁵². For SS, CD27 might serve as a diagnostic tool to

distinguish this disease from benign inflammatory erythroderma⁵³. Nevertheless, the overall lack of validated and specific diagnostic markers adds to the fact that, in MF, for instance, it takes a median of about 3 years⁷ from the initial appearance of skin lesions until a definitive diagnosis can be made, demonstrating the difficulty of making a timely diagnosis, which mandates further research.

Current lack of prognostic biomarkers that can predict disease progression

The prediction of disease progression and overall survival in patients with MF has turned out to be a challenging endeavor⁵⁴. A Cutaneous Lymphoma International Prognostic Index (CLIPi), which includes age, gender, folliculotropism, and TNMB staging, has been developed but has limited utility in early-stage patients^{55,56}. The CXCR4–CXCL12 axis has been described as a potential player in MF progression⁵⁷, but other authors did not consistently find differences between early and late disease stages⁵⁸. Recently, however, De Masson *et al.* used high-throughput sequencing of the *TCR beta* gene and found that an increased frequency of the malignant T-cell clone in MF skin lesions is strongly correlated with reduced overall survival in patients with early-stage disease⁵⁵.

Several authors showed associations of poor disease outcome with *TOX*^{59,60} as well as *miR-155*, *miR-21*, and *let-7i* microRNA expression^{17,47}. Lefrançois *et al.*⁵⁴ described *TOX*, *FYB*, *CCR4*, and *CD52* as markers for disease progression and decreased survival in MF, and the authors confirmed these markers in an independent cohort of patients with SS. KIR3DL2, a recently discovered marker of the malignant clonal cell population in SS, was suggested as an independent prognostic factor for SS-specific death⁶¹. Nevertheless, none of these potential biomarkers has been fully validated so far^{55,62} and thus they are not yet available for clinical use.

One major factor limiting our insight into MF/SS pathogenesis is likely rooted in the considerable disease heterogeneity seen between individual patients⁶³. Importantly, significant heterogeneity of gene expression was present not only between different patients but also within the same individual over time^{12,64,65}. Importantly, all of these studies used bulk tissue investigations or conventional immunohistochemistry studies or both. However, bulk tissue investigations do not distinguish between individual cell types (for example, the actual tumor cell and the tumor microenvironment), and conventional measurements of cell heterogeneity such as immunohistochemistry can suffer from artifacts and are impractical when several markers are investigated at the same time⁶⁶. Single-cell RNA sequencing has been shown to be a powerful tool to characterize complex as well as rare immune cell populations and to reveal unexpected or undescribed cell subpopulations, allowing the acquisition of large amounts of transcriptional information for the accurate and unbiased molecular characterization of these rare cells⁶⁷. Gaydosik *et al.*⁶³ performed a first investigation in advanced-stage CTCL and healthy control samples using single-cell RNA sequencing and found large inter- and intra-tumor gene expression heterogeneity in the T lymphocyte subset. Borchering *et al.*⁶⁸ investigated CTCL heterogeneity in circulating SS cells, giving insight into the heterogeneity

of SS cells within a single patient and putting transcriptomic differences into context with published MF data. Though still at the beginning in CTCL, the evolution of single-cell transcriptomics might offer exciting new opportunities to better understand tumor cell heterogeneity and to facilitate the development of stratified diagnostic and prognostic approaches for patients with CTCL.

Novel treatment approaches

There is currently no cure for CTCL, except for allogeneic stem cell transplantation, which carries a significant risk of relapse as well as treatment-related toxicity and death⁶⁹. Immunotherapy including checkpoint inhibitors for CTCL is only at the beginning and might be a promising tool to achieve long-term disease control⁷⁰, but the results of ongoing clinical trials must be awaited before making firm conclusions. Currently, CTCL treatment is based on a stage-related therapeutic approach. Thus, early-stage disease is first treated with skin-directed therapies^{2,71}. These include topical application of glucocorticosteroids, topical mechlorethamine⁷², topical bexarotene, and the use of phototherapy (UVB and PUVA)⁷³ or localized radiation therapy (photon or electron beam). In addition, early-phase clinical trials or case series (or both) suggest a potential role for topical Toll-like receptor (TLR) agonists such as imiquimod⁷⁴ or resiquimod⁷⁵, photodynamic therapy⁷⁶, and excimer laser therapy⁷⁷, but data are limited and need corroboration in larger clinical trials. Interestingly, resiquimod showed regression not only of treated but also of untreated lesions in a phase 1 study⁷⁵ and is being further investigated as a skin-directed compound.

Widespread, advanced disease or refractory early-disease requires systemic therapy. Established treatment modalities include low-dose methotrexate, systemic bexarotene, IFN, the histone deacetylase inhibitors romidepsin and vorinostat, the anti-CD52 antibody alemtuzumab⁷⁸, extracorporeal photopheresis, and single-agent or combination chemotherapy.

Mogamulizumab is a monoclonal antibody directed against the chemokine receptor CCR4 and has been investigated in a phase 3 trial in comparison with vorinostat in patients with previously treated CTCL⁷⁹. The investigators showed that mogamulizumab resulted in a median progression-free survival of 7.7 months, compared with only 3.1 with the active comparator, and an objective response rate of 28% versus 5%. Surprisingly, vorinostat response rates were actually lower than in initial studies^{80,81}. Response rates to mogamulizumab were independent of previous therapies⁸²; long-term treatment seems to be safe and well tolerated⁸². Thus, mogamulizumab might also be an option for heavily pre-treated patients, and besides MF, this agent seems to be particularly promising for patients with SS⁷⁹.

Brentuximab vedotin is an antibody–drug conjugate designed to target CD30 in CD30⁺ CTCL⁸³. Although efficacy was reported to be better in CD30-expressing CTCL, clinical responses were still observed in patients with lower CD30 expression⁸². Thus, this treatment might also be an option for a wider range of CTCLs beyond those highly expressing CD30.

Owing to the chronic-relapsing nature of CTCLs, there are also investigations into maintenance therapy using lower treatment doses or frequencies or both. There are some promising data on maintenance PUVA therapy extending median disease-free remission from 4 to 15 months⁷³. Resminostat is being investigated in a phase 2 clinical trial for maintenance therapy in patients with advanced-stage MF or SS (ClinicalTrials.gov Identifier: NCT02953301). Another promising treatment modality includes low-dose total skin electron beam treatment followed by mechlorethamine⁸⁴, which is being investigated in a phase 2 trial (ClinicalTrials.gov Identifier: NCT02881749). A phase 3 trial on lenalidomide maintenance in advanced CTCL was terminated early following withdrawal of funding support and thus was underpowered for analysis⁸⁵.

Immune checkpoint inhibitors have revolutionized treatment of many cancer types, and there have been durable responses in some patients even after cessation of therapy⁸⁶. As briefly mentioned above, these new agents might also be an option for CTCL⁸⁷. In a phase II trial of patients with advanced, heavily pre-treated MF and SS, the PD-1 inhibitor pembrolizumab demonstrated significant anti-tumor activity and had overall response rates of 38% and a favorable safety profile⁸⁸. Ongoing treatment responses at last follow-up were observed in one third of patients⁸⁸. Besides pembrolizumab, the PD-1 blocker nivolumab and the PD-L1 inhibitors durvalumab and atezolizumab are being investigated in clinical trials. Despite promising initial results, caution needs to be exerted as PD-1 blockade might also accelerate growth of T-cell malignancies, as seen in adult T-cell leukemia/lymphoma that showed explosive progression of disease in the first three patients⁸⁹.

Other treatment approaches being evaluated in early clinical trials include the SYK/JAK inhibitor cerdulatinib, an anti-KIR antibody (IPH4102), the microRNA Mir-155 inhibitor cobomarsen, and the CD70 blocker cusatuzumab⁸².

Outlook

Our understanding of the pathogenesis of CTCL has steadily increased within the last few years, but many aspects are still only insufficiently understood, necessitating further basic and translational research approaches. Whereas many patients show an indolent and self-limiting course, some patients progress. For those patients, treatment options are often limited and can harbor significant toxicity. In line with this, early-stage disease should preferentially be treated with skin-directed therapies and, in case of relapse and after initial therapeutic success, should be used in a repetitive manner. Systemic treatment should preferably be kept for advanced-stage disease or patients with refractory cutaneous involvement (for example, after secondary loss of efficacy with skin-directed therapies). Generally, the management of patients with CTCL should be reserved for specialized centers, which also offer the advantage of access to multicenter clinical trials. It is noteworthy that HRQoL is of significant importance in CTCL, profoundly influencing patients' quality of life in terms of a visible stigma and its potential lethality⁹⁰. Accordingly, HRQoL and its maintenance in MF/SS are of utmost importance in the face of current palliative treatment approaches in the majority of cases.

References

1. Trautinger F, Knobler R, Willemze R, *et al.*: **EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome.** *Eur J Cancer.* 2006; 42(8): 1014–30.
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Trautinger F, Eder J, Assaf C, *et al.*: **European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome - Update 2017.** *Eur J Cancer.* 2017; 77: 57–74.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Willemze R, Cerroni L, Kempf W, *et al.*: **The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas.** *Blood.* 2019; 133(16): 1703–14.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Kim YH, Jensen RA, Watanabe GL, *et al.*: **Clinical stage IA (limited patch and plaque) mycosis fungoides. A long-term outcome analysis.** *Arch Dermatol.* 1996; 132(11): 1309.
[PubMed Abstract](#) | [Publisher Full Text](#)
5. Porkert S, Lehner-Baumgartner E, Valencak J, *et al.*: **Patients' Illness Perception as a Tool to Improve Individual Disease Management in Primary Cutaneous Lymphomas.** *Acta Derm Venereol.* 2018; 98(2): 240–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
6. Molloy K, Jonak C, Woei-A-Jin FJSH, *et al.*: **Characteristics associated with significantly worse quality of life in mycosis fungoides/Sézary syndrome from the Prospective Cutaneous Lymphoma International Prognostic Index (PROCLIP) study.** *Br J Dermatol.* 2019; 182(3): 770–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
7. Scarisbrick JJ, Quaglino P, Prince HM, *et al.*: **The PROCLIP international registry of early-stage mycosis fungoides identifies substantial diagnostic delay in most patients.** *Br J Dermatol.* 2019; 181(2): 350–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Willemze R, Jaffe ES, Burg G, *et al.*: **WHO-EORTC classification for cutaneous lymphomas.** *Blood.* 2005; 105(10): 3768–85.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
9. Arulogun SO, Prince HM, Ng J, *et al.*: **Long-term outcomes of patients with advanced-stage cutaneous T-cell lymphoma and large cell transformation.** *Blood.* 2008; 112(8): 3082–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
10. Agar NS, Wedgeworth E, Crichton S, *et al.*: **Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: Validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal.** *J Clin Oncol.* 2010; 28(31): 4730–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
11. Wilcox RA: **Cutaneous T-cell lymphoma: 2017 update on diagnosis, risk-stratification, and management.** *Am J Hematol.* 2017; 92(10): 1085–102.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Litvinov IV, Tetzlaff MT, Thibault P, *et al.*: **Gene expression analysis in Cutaneous T-Cell Lymphomas (CTCL) highlights disease heterogeneity and potential diagnostic and prognostic indicators.** *Oncoimmunology.* 2017; 6(5): e1306618.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
13. Damsky WE, Choi J: **Genetics of Cutaneous T Cell Lymphoma: From Bench to Bedside.** *Curr Treat Options Oncol.* 2016; 17(7): 33.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Dereure O, Levi E, Kadin ME, *et al.*: **Infrequent Fas Mutations but No Bax or p53 Mutations in Early Mycosis Fungoides: A Possible Mechanism for the Accumulation of Malignant T Lymphocytes in the Skin.** *J Invest Dermatol.* 2002; 118(6): 949–56.
[PubMed Abstract](#) | [Publisher Full Text](#)
15. Wang L, Ni X, Covington KR, *et al.*: **Genomic profiling of Sézary syndrome identifies alterations of key T cell signaling and differentiation genes.** *Nat Genet.* 2015; 47(12): 1426–34.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
16. Ungewickell A, Bhaduri A, Rios E, *et al.*: **Genomic analysis of mycosis fungoides and Sézary syndrome identifies recurrent alterations in TNFR2.** *Nat Genet.* 2015; 47(9): 1056–60.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
17. Sandoval J, Díaz-Lagares A, Salgado R, *et al.*: **MicroRNA Expression Profiling and DNA Methylation Signature for Deregulated MicroRNA in Cutaneous T-Cell Lymphoma.** *J Invest Dermatol.* 2015; 135(4): 1128–37.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. McGirt LY, Jia P, Baerenwald DA, *et al.*: **Whole-genome sequencing reveals oncogenic mutations in mycosis fungoides.** *Blood.* 2015; 126(4): 508–19.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. da Silva Almeida AC, Abate F, Khiabani H, *et al.*: **The mutational landscape of cutaneous T cell lymphoma and Sézary syndrome.** *Nat Genet.* 2015; 47(12): 1465–70.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
20. Mervis JS, McGee JS: **Epigenetic therapy and dermatologic disease: Moving beyond CTCL.** *J Dermatolog Treat.* 2018; 30(1): 68–73.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
21. Campbell JJ, Clark RA, Watanabe R, *et al.*: **Sézary syndrome and mycosis fungoides arise from distinct T-cell subsets: A biologic rationale for their distinct clinical behaviors.** *Blood.* 2010; 116(5): 767–71.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Clark RA, Watanabe R, Teague JE, *et al.*: **Skin Effector Memory T Cells Do Not Recirculate and Provide Immune Protection in Alemtuzumab-Treated CTCL Patients.** *Sci Transl Med.* 2012; 4(117): 117ra7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Krejsgaard T, Ralfkiaer U, Clasen-Linde E, *et al.*: **Malignant cutaneous T-cell lymphoma cells express IL-17 utilizing the Jak3/Stat3 signaling pathway.** *J Invest Dermatol.* 2011; 131(6): 1331–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
24. Berger CL, Tigelaar R, Cohen J, *et al.*: **Cutaneous T-cell lymphoma: Malignant proliferation of T-regulatory cells.** *Blood.* 2005; 105(4): 1640–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Geskin LJ, Viragova S, Stolz DB, *et al.*: **Interleukin-13 is overexpressed in cutaneous T-cell lymphoma cells and regulates their proliferation.** *Blood.* 2015; 125(18): 2798–805.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
26. Fujii K: **New Therapies and Immunological Findings in Cutaneous T-Cell Lymphoma.** *Front Oncol.* 2018; 8: 198.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
27. Gjerdrum LM, Woetmann A, Odum N, *et al.*: **FOXP3+ regulatory T cells in cutaneous T-cell lymphomas: Association with disease stage and survival.** *Leukemia.* 2007; 21(12): 2512–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
28. Wherry EJ, Kurachi M: **Molecular and cellular insights into T cell exhaustion.** *Nat Rev Immunol.* 2015; 15(8): 486–99.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
29. Vowels BR, Lessin SR, Cassin M, *et al.*: **Th2 cytokine mRNA expression in skin in cutaneous T-cell lymphoma.** *J Invest Dermatol.* 1994; 103(5): 669–73.
[PubMed Abstract](#) | [Publisher Full Text](#)
30. Vieyra-Garcia P, Crouch JD, O'Malley JT, *et al.*: **Benign T cells drive clinical skin inflammation in cutaneous T cell lymphoma.** *JCI Insight.* 2019; 4(1): pii: 124233.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
31. Guenova E, Watanabe R, Teague JE, *et al.*: **TH2 cytokines from malignant cells suppress TH1 responses and enforce a global TH2 bias in leukemic cutaneous T-cell lymphoma.** *Clin Cancer Res.* 2013; 19(14): 3755–63.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
32. Thumann P, Lüftl M, Moc I, *et al.*: **Interaction of cutaneous lymphoma cells with reactive T cells and dendritic cells: Implications for dendritic cell-based immunotherapy.** *Br J Dermatol.* 2003; 149(6): 1128–42.
[PubMed Abstract](#) | [Publisher Full Text](#)
33. Talpur R, Singh L, Daulat S, *et al.*: **Long-term Outcomes of 1,263 Patients with Mycosis Fungoides and Sezary Syndrome from 1982 to 2009.** *Clin Cancer Res.* 2012; 18(18): 5051–60.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
34. Talpur R, Bassett R, Duvic M: **Prevalence and treatment of Staphylococcus aureus colonization in patients with mycosis fungoides and Sézary syndrome.** *Br J Dermatol.* 2008; 159(1): 105–12.
[PubMed Abstract](#) | [Publisher Full Text](#)
35. Blümel E, Willerslev-Olsen A, Gliud M, *et al.*: **Staphylococcal alpha-toxin tilts the balance between malignant and non-malignant CD4+ T cells in cutaneous T-cell lymphoma.** *Oncoimmunology.* 2019; 8(11): e1641387.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
36. Dummer R, Eichmüller S, Gellrich S, *et al.*: **Phase II Clinical Trial of Intratumoral Application of TG1042 (Adenovirus-interferon-γ) in Patients With Advanced Cutaneous T-cell Lymphomas and Multilesional Cutaneous B-cell Lymphomas.** *Mol Ther.* 2010; 18(6): 1244–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
37. Miyagaki T, Sugaya M, Fujita H, *et al.*: **Eotaxins and CCR3 interaction regulates the Th2 environment of cutaneous T-cell lymphoma.** *J Invest Dermatol.* 2010; 130(9): 2304–11.
[PubMed Abstract](#) | [Publisher Full Text](#)
38. Banachereau J, Steinman RM: **Dendritic cells and the control of immunity.** *Nature.* 1998; 392(6673): 245–52.
[PubMed Abstract](#) | [Publisher Full Text](#)
39. Lüftl M, Feng A, Licha E, *et al.*: **Dendritic cells and apoptosis in mycosis fungoides.** *Br J Dermatol.* 2002; 147(6): 1171–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
40. Schlaupbach C, Ochsenbein A, Kaelin U, *et al.*: **High numbers of DC-SIGN+ dendritic cells in lesional skin of cutaneous T-cell lymphoma.** *J Am Acad Dermatol.* 2010; 62(6): 995–1004.
[PubMed Abstract](#) | [Publisher Full Text](#)
41. Rabenhorst A, Schlaak M, Heukamp LC, *et al.*: **Mast cells play a protumorigenic role in primary cutaneous lymphoma.** *Blood.* 2012; 120(10): 2042–54.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)

42. Pileri A, Agostinelli C, Sessa M, *et al.*: Langerhans, plasmacytoid dendritic and myeloid-derived suppressor cell levels in mycosis fungoides vary according to the stage of the disease. *Virchows Arch.* 2017; **470**(5): 575–82.
[PubMed Abstract](#) | [Publisher Full Text](#)
43. **F** Pham LV, Pogue E, Ford RJ: The Role of Macrophage/B-Cell Interactions in the Pathophysiology of B-Cell Lymphomas. *Front Oncol.* 2018; **8**: 147.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
44. Furudate S, Fujimura T, Kakizaki A, *et al.*: The possible interaction between periostin expressed by cancer stroma and tumor-associated macrophages in developing mycosis fungoides. *Exp Dermatol.* 2016; **25**(2): 107–12.
[PubMed Abstract](#) | [Publisher Full Text](#)
45. Wu X, Schulte BC, Zhou Y, *et al.*: Depletion of M2-like tumor-associated macrophages delays cutaneous T-cell lymphoma development *in vivo*. *J Invest Dermatol.* 2014; **134**(11): 2814–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
46. Sugaya M, Miyagaki T, Ohmatsu H, *et al.*: Association of the numbers of CD163⁺ cells in lesional skin and serum levels of soluble CD163 with disease progression of cutaneous T cell lymphoma. *J Dermatol Sci.* 2012; **68**(1): 45–51.
[PubMed Abstract](#) | [Publisher Full Text](#)
47. Ralfkiaer U, Hagedorn PH, Bangsgaard N, *et al.*: Diagnostic microRNA profiling in cutaneous T-cell lymphoma (CTCL). *Blood.* 2011; **118**(22): 5891–900.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
48. **F** Jokinen CH, Fromm JR, Argenyi ZB, *et al.*: Flow cytometric evaluation of skin biopsies for mycosis fungoides. *Am J Dermatopathol.* 2011; **33**(5): 483–91.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
49. Ponti R, Quaglino P, Novelli M, *et al.*: T-cell receptor gamma gene rearrangement by multiplex polymerase chain reaction/heteroduplex analysis in patients with cutaneous T-cell lymphoma (mycosis fungoides/Sézary syndrome) and benign inflammatory disease: Correlation with clinical, histological and immunophenotypical findings. *Br J Dermatol.* 2005; **153**(3): 565–73.
[PubMed Abstract](#) | [Publisher Full Text](#)
50. **F** Rea B, Haun P, Emerson R, *et al.*: Role of high-throughput sequencing in the diagnosis of cutaneous T-cell lymphoma. *J Clin Pathol.* 2018; **71**(9): 814–20.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
51. Zhang Y, Wang Y, Yu R, *et al.*: Molecular markers of early-stage mycosis fungoides. *J Invest Dermatol.* 2012; **132**(6): 1698–706.
[PubMed Abstract](#) | [Publisher Full Text](#)
52. Schrader AM, Jansen PM, Willemze R: TOX expression in cutaneous T-cell lymphomas: an adjunctive diagnostic marker that is not tumour specific and not restricted to the CD4⁺ CD8⁻ phenotype. *Br J Dermatol.* 2016; **175**(2): 382–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
53. Fierro MT, Novelli M, Quaglino P, *et al.*: Heterogeneity of circulating CD4⁺ memory T-cell subsets in erythrodermic patients: CD27 analysis can help to distinguish cutaneous T-cell lymphomas from inflammatory erythroderma. *Dermatology.* 2008; **216**(3): 213–21.
[PubMed Abstract](#) | [Publisher Full Text](#)
54. Lefrançois P, Xie P, Wang L, *et al.*: Gene expression profiling and immune cell-type deconvolution highlight robust disease progression and survival markers in multiple cohorts of CTCL patients. *Oncoimmunology.* 2018; **7**(8): e1467856.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
55. **F** de Masson A, O'Malley JT, Elco CP, *et al.*: High-throughput sequencing of the T cell receptor β gene identifies aggressive early-stage mycosis fungoides. *Sci Transl Med.* 2018; **10**(440): eaar5894.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
56. Sanz-Bueno J, Lora D, Monsálvez V, *et al.*: The new Cutaneous Lymphoma International Prognostic index (CLIPi) for early mycosis fungoides failed to identify prognostic groups in a cohort of Spanish patients. *Br J Dermatol.* 2016; **175**(4): 794–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
57. Daggett RN, Kurata M, Abe S, *et al.*: Expression dynamics of CXCL 12 and CXCR 4 during the progression of mycosis fungoides. *Br J Dermatol.* 2014; **171**(4): 722–31.
[PubMed Abstract](#) | [Publisher Full Text](#)
58. Maj J, Jankowska-Konsur AM, Haloń A, *et al.*: Expression of CXCR4 and CXCL12 and their correlations to the cell proliferation and angiogenesis in mycosis fungoides. *Postepy Dermatol Alergol.* 2015; **32**(6): 437–42.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
59. Huang Y, Litvinov IV, Wang Y, *et al.*: Thymocyte selection-associated high mobility group box gene (TOX) is aberrantly over-expressed in mycosis fungoides and correlates with poor prognosis. *Oncotarget.* 2014; **5**(12): 4418–25.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
60. Dulmage BO, Geskin LJ, *et al.*: Lessons learned from gene expression profiling of cutaneous T-cell lymphoma. *Br J Dermatol.* 2013; **169**(6): 1188–97.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
61. Hurabielle C, Thonnart N, Ram-Wolff C, *et al.*: Usefulness of KIR3DL2 to Diagnose, Follow-Up, and Manage the Treatment of Patients with Sézary Syndrome. *Clin Cancer Res.* 2017; **23**(14): 3619–27.
[PubMed Abstract](#) | [Publisher Full Text](#)
62. Dulmage B, Geskin L, Guitart J, *et al.*: The biomarker landscape in mycosis fungoides and Sézary syndrome. *Exp Dermatol.* 2017; **26**(8): 668–76.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
63. **F** Gaydosik AM, Tabib T, Geskin LJ, *et al.*: Single-Cell Lymphocyte Heterogeneity in Advanced Cutaneous T-cell Lymphoma Skin Tumors. *Clin Cancer Res.* 2019; **25**(14): 4443–54.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
64. Litvinov IV, Jones DA, Sasseville D, *et al.*: Transcriptional profiles predict disease outcome in patients with cutaneous T-cell lymphoma. *Clin Cancer Res.* 2010; **16**(7): 2106–14.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
65. Shin J, Monti S, Aires DJ, *et al.*: Lesional gene expression profiling in cutaneous T-cell lymphoma reveals natural clusters associated with disease outcome. *Blood.* 2007; **110**(8): 3015–27.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
66. Shen-Orr SS, Gaujoux R: Computational deconvolution: extracting cell type-specific information from heterogeneous samples. *Curr Opin Immunol.* 2013; **25**(5): 571–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
67. **F** Nguyen A, Khoo WH, Moran I, *et al.*: Single Cell RNA Sequencing of Rare Immune Cell Populations. *Front Immunol.* 2018; **9**: 1553.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
68. **F** Borcherdig N, Voigt AP, Liu V, *et al.*: Single-Cell Profiling of Cutaneous T-Cell Lymphoma Reveals Underlying Heterogeneity Associated with Disease Progression. *Clin Cancer Res.* 2019; **25**(10): 2996–3005.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
69. **F** Iqbal M, Reljic T, Klocksieben F, *et al.*: Efficacy of Allogeneic Hematopoietic Cell Transplantation in Human T Cell Lymphotropic Virus Type 1-Associated Adult T Cell Leukemia/Lymphoma: Results of a Systematic Review/Meta-Analysis. *Biol Blood Marrow Transplant.* 2019; **25**(8): 1695–700.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
70. **F** Sivanand A, Surmanowicz P, Alhusayen R, *et al.*: Immunotherapy for Cutaneous T-Cell Lymphoma: Current Landscape and Future Developments. *J Cutan Med Surg.* 2019; **23**(5): 537–44.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
71. **F** Ramelyte E, Dummer R, Guenova E: Investigative drugs for the treatment of cutaneous T-cell lymphomas (CTCL): an update. *Expert Opin Investig Drugs.* 2019; **28**(9): 799–809.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
72. **F** Lessin SR, Duvic M, Guitart J, *et al.*: Topical chemotherapy in cutaneous T-cell lymphoma: positive results of a randomized, controlled, multicenter trial testing the efficacy and safety of a novel mechlorethamine, 0.02%, gel in mycosis fungoides. *JAMA Dermatol.* 2013; **149**(1): 25.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
73. **F** Vieyra-Garcia P, Fink-Puches R, Porkert S, *et al.*: Evaluation of Low-Dose, Low-Frequency Oral Psoralen-UV-A Treatment With or Without Maintenance on Early-Stage Mycosis Fungoides: A Randomized Clinical Trial. *JAMA Dermatol.* 2019; **155**(5): 538–47.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
74. Shipman AR, Scarisbrick J: New Treatment Options for Mycosis Fungoides. *Indian J Dermatol.* 2016; **61**(1): 119.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
75. **F** Rook AH, Gelfand JM, Wysocka M, *et al.*: Topical resiquimod can induce disease regression and enhance T-cell effector functions in cutaneous T-cell lymphoma. *Blood.* 2015; **126**(12): 1452–61.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
76. **F** Quéreux G, Brocard A, Saint-Jean M, *et al.*: Photodynamic therapy with methyl-aminolevulinic acid for paucilesional mycosis fungoides: a prospective open study and review of the literature. *J Am Acad Dermatol.* 2013; **69**(6): 890–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
77. Deaver D, Cauthen A, Cohen G, *et al.*: Excimer laser in the treatment of mycosis fungoides. *J Am Acad Dermatol.* 2014; **70**(6): 1058–60.
[PubMed Abstract](#) | [Publisher Full Text](#)
78. Lundin J, Hagberg H, Repp R, *et al.*: Phase 2 study of alemtuzumab (anti-CD52 monoclonal antibody) in patients with advanced mycosis fungoides/Sézary syndrome. *Blood.* 2003; **101**(11): 4267–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
79. **F** Kim YH, Bagot M, Pinter-Brown L, *et al.*: Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. *Lancet Oncol.* 2018; **19**(9): 1192–204.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
80. **F** Olsen EA, Kim YH, Kuzel TM, *et al.*: Phase IIb multicenter trial of vorinostat in patients with persistent, progressive, or treatment refractory cutaneous T-cell lymphoma. *J Clin Oncol.* 2007; **25**(21): 3109–15.
[PubMed Abstract](#) | [Publisher Full Text](#) | **F1000 Recommendation**
81. Duvic M, Talpur R, Ni X, *et al.*: Phase 2 trial of oral vorinostat (suberoylanilide hydroxamic acid, SAHA) for refractory cutaneous T-cell lymphoma (CTCL). *Blood.* 2006; **109**(1): 31–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
82. Geskin LJ: Highlights in cutaneous T-cell lymphoma from the 60th American

- Society of Hematology Annual Meeting: A dermatologist's perspective.** *Clin Adv Hematol Oncol.* 2019; 17(Suppl 3(2)): 21–3.
[PubMed Abstract](#)
83. Prince HM, Kim YH, Horwitz SM, *et al.*: **Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial.** *Lancet.* 2017; 390(10094): 555–66.
[PubMed Abstract](#) | [Publisher Full Text](#)
84. Jennings T, Duffy R, Gochoco A, *et al.*: **Valchlor maintenance therapy for patients with mycosis fungoides who received low dose total skin electron beam treatment.** *Chin Clin Oncol.* 2019; 8(1): 13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
85. Bagot M, Hasan B, Whittaker S, *et al.*: **A phase III study of lenalidomide maintenance after debulking therapy in patients with advanced cutaneous T-cell lymphoma - EORTC 21081 (NCT01098656): results and lessons learned for future trial designs.** *Eur J Dermatol.* 2017; 27(3): 286–94.
[PubMed Abstract](#) | [Publisher Full Text](#)
86. Robert C, Ribas A, Hamid O, *et al.*: **Durable Complete Response After Discontinuation of Pembrolizumab in Patients With Metastatic Melanoma.** *J Clin Oncol.* 2018; 36(17): 1668–74.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
87. Wu X, Singh R, Hsu DK, *et al.*: **A Small Molecule CCR2 Antagonist Depletes Tumor Macrophages and Synergizes with Anti-PD-1 in a Murine Model of Cutaneous T-Cell Lymphoma (CTCL).** *J Invest Dermatol.* 2020. S0022-202X(19)33562-6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
88. Khodadoust MS, Rook AH, Porcu P, *et al.*: **Pembrolizumab in Relapsed and Refractory Mycosis Fungoides and Sézary Syndrome: A Multicenter Phase II Study.** *J Clin Oncol.* 2020; 38(1): 20–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
89. Ratner L, Waldmann TA, Janakiram M, *et al.*: **Rapid Progression of Adult T-Cell Leukemia-Lymphoma after PD-1 Inhibitor Therapy.** *N Engl J Med.* 2018; 378(20): 1947–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
90. Jonak C, Porkert S, Oerlemans S, *et al.*: **Health-related Quality of Life in Cutaneous Lymphomas: Past, Present and Future.** *Acta Derm Venereol.* 2019; 99(7): 640–6.
[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

Current Peer Review Status:

Editorial Note on the Review Process

Faculty Reviews are review articles written by the prestigious Members of **Faculty Opinions**. The articles are commissioned and peer reviewed before publication to ensure that the final, published version is comprehensive and accessible. The reviewers who approved the final version are listed with their names and affiliations.

The reviewers who approved this article are:

Version 1

1. **Sam Hwang**

Department of Dermatology, University of California Davis, School of Medicine, Sacramento, CA, USA

Competing Interests: No competing interests were disclosed.

2. **Vincent Liu**

Department of Dermatology, University of Iowa Hospitals & Clinics, Iowa City, IA, USA

Competing Interests: No competing interests were disclosed.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research