Pegem Journal of Education and Instruction, Vol. 14, No. 3, 2024 (pp. 1001-1007)

RESEARCH ARTICLE WWW.PEGEGOG.NET

Therapeutic Strategies and Emerging Treatments in Mycosis Fungoides: A Translational Perspective on Disease and Symptom Control

Manal Mohamed El-Sayed [1], Rania Abdelaziz Alakad [1], Hayam Elsayed Hassan Rashed [2], Amina Ahmed Mohamed Abdelhadi [3], Afnan Samy Ali Hussein Aziza [1]

1 Dermatology, Venereology and Andrology, Department, Faculty of Medicine, Zagazig University
2 Pathology Department, Faculty of Medicine, Zagazig University
3 Medical Microbiology and Immunology Department, Faculty of Medicine, Zagazig University
Corresponding author: Afnan Samy Ali Hussein Aziza

ABSTRACT

***Background*:** Mycosis Fungoides is a clinically heterogeneous cutaneous lymphoma that presents significant challenges in long-term management due to its relapsing course, variable progression, and substantial impact on patient quality of life. Therapeutic decision-making is often complex, requiring a balance between effective disease control, minimization of treatment-related toxicity, and alleviation of distressing symptoms such as chronic pruritus.

Current management strategies are largely stage-driven, with early disease typically managed using skin-directed therapies, while advanced stages necessitate systemic and combination approaches. However, conventional treatment paradigms are frequently limited by incomplete responses, disease relapse, and inadequate control of symptoms. This has prompted a shift toward more integrated therapeutic models that combine clinical staging with individualized treatment planning and longitudinal monitoring.

Recent developments have expanded the therapeutic armamentarium to include a range of targeted and immunomodulatory agents that offer improved specificity and potential for sustained disease control. These therapies not only address malignant cell proliferation but also influence the broader tumor microenvironment and symptom burden. In parallel, increasing recognition of pruritus as a major determinant of patient well-being has led to the exploration of novel symptom-directed interventions that extend beyond traditional antipruritic therapies.

This review provides a comprehensive and clinically oriented overview of therapeutic strategies in mycosis fungoides, emphasizing practical treatment approaches, emerging therapies, and the integration of symptom management into routine care. By highlighting the evolving landscape of treatment and the importance of personalized care, this work underscores the need for multidisciplinary strategies that optimize both clinical outcomes and quality of life in affected patients.

Keywords: Therapeutic Strategies, Mycosis Fungoides, Symptom Control

INTRODUCTION

Mycosis Fungoides represents the most common form of cutaneous T-cell lymphoma and is characterized by a chronic, often relapsing clinical course that poses significant challenges in long-term management. While early-stage disease is typically confined to the skin and follows an indolent course, progression to advanced stages may involve tumor formation, erythroderma, and systemic dissemination. This clinical heterogeneity necessitates a dynamic and individualized therapeutic approach that evolves according to disease stage and patient-specific factors [1,2].

From a dermatological perspective, the management of mycosis fungoides extends beyond lesion clearance to include preservation of skin barrier function, prevention of disease progression, and effective control of symptoms such as pruritus. Skin-directed therapies remain the cornerstone of treatment in early stages; however, their effectiveness may be limited by incomplete responses and frequent relapses. In advanced disease, systemic therapies become necessary, yet these are often associated with cumulative toxicity and variable clinical outcomes, emphasizing the need for optimized therapeutic strategies [2,3].

A major limitation in current clinical practice is the absence of a definitive curative therapy, with most available interventions aiming to achieve disease control rather than eradication. Consequently, treatment is often delivered in a sequential or combination manner, integrating multiple modalities to enhance efficacy while minimizing adverse effects. This approach reflects the complexity of the disease and highlights the importance of individualized treatment planning and continuous reassessment of therapeutic response [3,4].

Recent advances in translational research have significantly expanded the therapeutic landscape of mycosis fungoides. The development of targeted therapies and immunomodulatory agents has introduced more specific treatment options that act on defined cellular and molecular pathways. These therapies not only improve disease control in advanced or refractory cases but also offer the potential to modify the tumor microenvironment, thereby influencing long-term disease behavior [4,5].

Equally important is the growing recognition of symptom burden, particularly chronic pruritus, as a key determinant of patient quality of life. Pruritus in mycosis fungoides is often severe, persistent, and inadequately controlled by conventional therapies, necessitating a more integrated approach that combines disease-directed and symptom-directed treatments. Addressing pruritus as a primary therapeutic target reflects a shift toward patient-centered care in CTCL management [6].

Despite these therapeutic advancements, several challenges remain, including variability in treatment response, lack of predictive biomarkers, and difficulty in achieving durable remission. These limitations underscore the need for continued integration of translational insights into clinical practice, with the goal of developing personalized therapeutic strategies that address both disease progression and symptom burden.

Skin-Directed Therapies in Mycosis Fungoides

Skin-directed therapies (SDTs) represent the cornerstone of management in early-stage Mycosis Fungoides and remain essential components of treatment across all stages when integrated with systemic approaches. These therapies are particularly effective in patients with disease confined to the skin, where malignant T lymphocytes predominantly localize within the epidermis and superficial dermis. Beyond their role in reducing tumor burden, SDTs contribute significantly to restoring skin barrier integrity and alleviating symptoms such as pruritus, which is a major determinant of patient morbidity and quality of life [6,7].

Management typically begins with supportive and topical therapies that aim to improve the cutaneous microenvironment and reduce inflammatory activity. Regular use of emollients is fundamental in maintaining epidermal barrier function, decreasing transepidermal water loss, and minimizing xerosis-associated itching. This is particularly important in mycosis fungoides, where barrier disruption may exacerbate inflammation and facilitate disease persistence. Building on this foundation, topical corticosteroids are widely utilized due to their potent anti-inflammatory, immunosuppressive, and anti-proliferative effects. By inhibiting cytokine production and T-cell activation, they lead to both clinical regression of lesions and reduction in pruritus intensity [7].

For patients requiring more targeted anti-neoplastic effects, topical chemotherapeutic agents are introduced as a logical escalation. Mechlorethamine (nitrogen mustard) acts as an alkylating agent that interferes with DNA replication, resulting in apoptosis of malignant T cells and demonstrating efficacy in both induction and maintenance phases of treatment. Carmustine similarly induces DNA cross-linking but is less frequently used due to the risk of systemic absorption and hematologic toxicity,

particularly when applied over larger surface areas. These therapies reflect a shift toward direct cytotoxic targeting of malignant cells within the skin while maintaining localized delivery [7].

Advancing further in the therapeutic spectrum, topical retinoids such as bexarotene and tazarotene provide a mechanism-based approach by modulating gene transcription involved in cellular differentiation and apoptosis. These agents not only suppress malignant cell proliferation but also exert anti-inflammatory effects within the skin. In parallel, immune response modifiers such as imiquimod stimulate toll-like receptor pathways, enhancing local production of interferons and other cytokines that promote anti-tumor immunity. This transition toward immunomodulatory therapy highlights the evolving understanding of CTCL as both a neoplastic and immune-mediated disease [7].

When topical therapies alone are insufficient or when disease involvement becomes more extensive, phototherapy represents a critical next step that combines dermatologic intervention with immunologic modulation. Narrowband ultraviolet B (NB-UVB) is particularly effective in early-stage disease, where its action is largely confined to the epidermis. It induces apoptosis of malignant T cells and reduces pro-inflammatory cytokine production while enhancing anti-inflammatory mediators, contributing to both lesion improvement and pruritus reduction. Its favorable safety profile and ease of administration make it a preferred first-line phototherapeutic option in patch-stage disease [8].

In contrast, psoralen plus ultraviolet A (PUVA) therapy offers deeper dermal penetration and is therefore more effective in plaque-stage and folliculotropic variants of mycosis fungoides. Psoralens intercalate into DNA and, upon activation by UVA radiation, form cross-links that inhibit DNA replication and induce apoptosis. PUVA also exerts significant immunomodulatory effects by altering cytokine production and suppressing pathogenic T-cell activity. However, its use is associated with cumulative phototoxicity and an increased long-term risk of skin malignancies, necessitating careful patient selection and monitoring [8].

Additional phototherapeutic modalities provide further refinement in selected cases. UVA1 therapy allows deeper dermal penetration without the need for photosensitizers, reducing phototoxicity, while photodynamic therapy utilizes reactive oxygen species to induce targeted cytotoxicity in malignant cells. Excimer laser therapy enables precise treatment of localized lesions, minimizing exposure of unaffected skin and reducing cumulative ultraviolet dose. These modalities underscore the importance of individualized treatment selection based on lesion characteristics and disease distribution [8].

For patients with localized refractory lesions or more extensive disease, radiotherapy provides a highly effective treatment option due to the intrinsic radiosensitivity of mycosis fungoides. Localized radiotherapy achieves excellent control of individual lesions and may be curative in limited disease. In contrast, total skin electron beam therapy (TSEB) delivers uniform radiation across the entire skin surface and is particularly valuable in patients with widespread involvement. While TSEB demonstrates high response rates, its use is associated with adverse effects such as erythema, alopecia, and potential reproductive implications, including reduced sperm counts, which are particularly relevant in long-term management and younger patients [9].

Overall, skin-directed therapies represent a continuum of escalating interventions, beginning with supportive care and progressing through anti-inflammatory, cytotoxic, immunomodulatory, phototherapeutic, and radiotherapeutic modalities. Their integration into a structured and individualized treatment approach allows effective disease control while minimizing systemic toxicity, forming the foundation upon which more advanced systemic and targeted therapies are subsequently introduced.

Systemic Therapies in Mycosis Fungoides

As disease burden increases beyond the capacity of skin-directed therapies, systemic treatments become a critical component in the management of Mycosis Fungoides, particularly in patients with tumor-stage disease, erythroderma, blood involvement, or refractory early-stage disease. Unlike localized therapies, systemic agents target both cutaneous and circulating malignant T cells, addressing the broader immunological and neoplastic processes underlying disease progression. In clinical practice, systemic therapies are frequently combined with skin-directed modalities to enhance therapeutic efficacy and achieve more durable responses while maintaining symptom control [10,11].

Retinoids represent one of the foundational systemic treatment classes due to their dual anti-proliferative and immunomodulatory properties. Bexarotene, a selective retinoid X receptor agonist, modulates transcriptional pathways involved in cellular differentiation, apoptosis, and immune regulation. It also reduces malignant T-cell trafficking to the skin, thereby limiting disease progression. Clinically, it is used across multiple stages and often combined with phototherapy or interferons. However, its use requires careful monitoring due to predictable metabolic adverse effects, including hyperlipidemia and central hypothyroidism,

which frequently necessitate adjunctive therapy [10].

Interferons, particularly interferon-α, play a central role in restoring immune balance in CTCL. Their mechanism involves activation of cytotoxic CD8+ T cells and natural killer cells while suppressing Th2 cytokine production, which is typically elevated in advanced disease. This shift toward a Th1 immune profile contributes to tumor control and symptom improvement. Interferons are frequently used in combination regimens, enhancing therapeutic outcomes, although their use may be limited by flu-like symptoms, fatigue, and hematologic adverse effects [10,11].

Methotrexate remains a key systemic agent due to its effectiveness and versatility. As an antifolate, it inhibits dihydrofolate reductase, thereby impairing DNA synthesis and reducing malignant T-cell proliferation. It can be used as monotherapy in early disease or in combination regimens for advanced stages. Despite its long-standing use, methotrexate requires strict monitoring due to potential toxicities, including hepatotoxicity, bone marrow suppression, and pulmonary complications, necessitating careful patient selection and follow-up [11].

Cytotoxic chemotherapy is generally reserved for advanced or refractory disease due to its systemic toxicity and limited durability of response. Agents such as gemcitabine and liposomal doxorubicin disrupt DNA synthesis and induce apoptosis, while combination regimens such as CHOP may achieve high initial response rates. However, relapse is common, and toxicity profiles limit long-term use, making chemotherapy a later-line option in most treatment algorithms [11].

Epigenetic therapies, particularly histone deacetylase inhibitors such as vorinostat and romidepsin, represent an important advancement in CTCL management. These agents alter chromatin structure and gene expression, promoting apoptosis and inhibiting malignant cell proliferation. Their introduction reflects a shift toward targeted molecular therapy, offering an alternative for patients with refractory disease and providing a more favorable toxicity profile compared to conventional chemotherapy [12].

Targeted immunotherapies further expand systemic treatment options by selectively targeting malignant T cells. Monoclonal antibodies such as brentuximab vedotin (anti-CD30) and mogamulizumab (anti-CCR4) induce tumor cell death through immune-mediated mechanisms, offering improved specificity and efficacy. These therapies exemplify the transition toward precision medicine in CTCL, allowing treatment to be tailored according to tumor phenotype and molecular characteristics [13].

Extracorporeal photopheresis represents a unique immunomodulatory therapy, particularly effective in erythrodermic disease. By inducing apoptosis of circulating malignant T cells and promoting immune tolerance, this modality provides disease control with a favorable safety profile. It is frequently used in combination with other systemic therapies to enhance response and maintain long-term remission [10].

Combination therapy remains a cornerstone of modern CTCL management, integrating systemic agents with skin-directed therapies or combining multiple systemic modalities to improve outcomes. These strategies enhance therapeutic efficacy, prolong remission, and reduce resistance, but require careful balancing of toxicity and patient tolerance. Individualized treatment planning is therefore essential to optimize results and maintain quality of life.

Targeted and Immunomodulatory Therapies

Building upon conventional systemic therapies, the management of Mycosis Fungoides has increasingly shifted toward targeted and immunomodulatory approaches that offer improved specificity and enhanced therapeutic outcomes. These therapies are designed to selectively interfere with molecular pathways and cellular interactions that sustain malignant T-cell survival, while minimizing damage to normal tissues. This transition reflects a broader movement toward precision medicine, where treatment strategies are tailored according to disease biology and patient characteristics [14].

A key component of targeted therapy in CTCL involves monoclonal antibodies directed against surface markers expressed on malignant T cells. Brentuximab vedotin, an antibody-drug conjugate targeting CD30, delivers a cytotoxic payload directly into tumor cells following receptor binding, resulting in microtubule disruption and apoptosis. This targeted delivery enhances efficacy while reducing systemic toxicity compared to conventional chemotherapy. Similarly, mogamulizumab targets CCR4, a chemokine receptor involved in T-cell trafficking, leading to antibody-dependent cellular cytotoxicity and depletion of malignant cells. These agents have demonstrated significant clinical benefit, particularly in patients with advanced or refractory disease [13,14].

In parallel, therapies targeting immune regulation have emerged as critical tools in modulating the tumor microenvironment. Extracorporeal photopheresis (ECP) represents a unique immunomodulatory modality that induces apoptosis of circulating malignant T cells and promotes the development of immune tolerance. Its mechanism involves reinfusion of photoactivated leukocytes, which subsequently alter antigen presentation and cytokine signaling, leading to long-term immune modulation. ECP is particularly effective in erythrodermic disease and Sézary syndrome and is often combined with other systemic therapies to enhance response [14].

Histone deacetylase (HDAC) inhibitors further exemplify the evolution of targeted therapy by acting at the epigenetic level. By inhibiting histone deacetylase enzymes, agents such as vorinostat and romidepsin induce accumulation of acetylated histones, leading to altered gene expression, cell cycle arrest, and apoptosis of malignant T cells. These therapies provide an important option for patients with refractory disease and highlight the relevance of epigenetic dysregulation in CTCL pathogenesis [12].

Another emerging therapeutic strategy involves targeting cytokine-driven pathways and immune signaling networks that contribute to both disease progression and symptom burden. Although not always directly tumoricidal, these therapies can significantly modulate the tumor microenvironment and reduce inflammatory signaling, thereby improving both disease control and associated symptoms such as pruritus. This dual impact underscores the importance of integrating immune-targeted therapies into comprehensive treatment strategies [14,15].

In addition to tumor-directed therapies, increasing attention has been given to agents targeting neuro-immune interactions, particularly in the context of refractory pruritus. Neurokinin-1 receptor antagonists and biologic agents targeting specific cytokine pathways have demonstrated promising results in reducing itch severity. These therapies represent an important advancement in symptom-directed treatment, addressing a major unmet need in CTCL management and further emphasizing the link between immune signaling and neural activation [15].

Management of Pruritus and Symptom Control

Pruritus represents one of the most distressing and challenging symptoms in patients with Mycosis Fungoides, often persisting despite adequate control of skin lesions. Its severity frequently correlates with disease stage, being more pronounced in advanced disease and erythrodermic forms, where it significantly impairs sleep, psychological well-being, and overall quality of life. Effective management of pruritus is therefore a critical component of comprehensive care and requires a multimodal, patient-centered approach [16].

Initial management typically involves optimization of skin-directed therapies and supportive care measures. Restoration of the skin barrier through regular use of emollients plays a fundamental role in reducing xerosis-associated itch and preventing further irritation. Topical corticosteroids and other anti-inflammatory agents may provide symptomatic relief by reducing local inflammation and cytokine-mediated irritation. Additionally, antihistamines are frequently used in clinical practice; however, their efficacy in CTCL-associated pruritus is often limited, reflecting the complex, non-histaminergic mechanisms underlying itch in this condition [16].

As pruritus becomes more severe or refractory, systemic approaches are often required. Optimization of disease-directed therapies, including retinoids, interferons, and phototherapy, can lead to indirect improvement in pruritus by reducing tumor burden and modulating the inflammatory microenvironment. In many cases, effective control of the underlying disease correlates with partial or complete resolution of itch, highlighting the close relationship between disease activity and symptom severity [17].

For patients with persistent pruritus despite standard therapies, targeted antipruritic treatments have emerged as important therapeutic options. Neurokinin-1 receptor antagonists, such as aprepitant, have demonstrated efficacy in reducing severe, refractory itch by inhibiting substance P–mediated signaling pathways. These agents provide rapid symptomatic relief in selected patients and represent a significant advancement in the management of CTCL-associated pruritus [15].

In addition, biologic therapies targeting immune pathways have shown promise in alleviating pruritus, particularly in cases where conventional treatments fail. Agents that modulate cytokine signaling can reduce neural sensitization and inflammatory activation, thereby improving itch severity. Although primarily developed for inflammatory dermatoses, these therapies have demonstrated potential utility in CTCL, especially in patients with overlapping immune-mediated features [18].

Combination Therapies and Treatment Algorithms

The management of Mycosis Fungoides increasingly relies on combination therapeutic strategies, reflecting the complex and multifactorial nature of the disease. Monotherapy is often insufficient to achieve durable responses, particularly in patients with advanced or refractory disease. Consequently, combining different treatment modalities allows for simultaneous targeting of multiple pathogenic mechanisms, including malignant cell proliferation, immune dysregulation, and symptom generation. This integrative approach has become a cornerstone of modern CTCL management [19,20].

Combination strategies frequently involve the integration of skin-directed therapies with systemic agents. For example, phototherapy combined with retinoids or interferons has demonstrated enhanced efficacy compared to monotherapy, as these treatments act synergistically to reduce tumor burden while modulating the immune microenvironment. Similarly, the addition of systemic agents to ongoing skin-directed therapy may improve response rates and prolong remission, particularly in patients with partial or suboptimal responses to initial treatment [20,21].

In advanced disease, combinations of systemic therapies are often required to achieve adequate disease control. Regimens incorporating interferons, retinoids, extracorporeal photopheresis, or targeted therapies can be tailored according to disease characteristics and patient tolerance. These combinations allow clinicians to exploit complementary mechanisms of action, such as enhancing immune-mediated tumor clearance while simultaneously inhibiting malignant cell proliferation. However, careful consideration must be given to cumulative toxicity and potential drug interactions, necessitating close monitoring throughout treatment [21,22].

Targeted therapies are increasingly incorporated into combination regimens to improve specificity and reduce systemic toxicity. For instance, monoclonal antibodies may be combined with immunomodulatory agents or phototherapy to enhance therapeutic response. Similarly, histone deacetylase inhibitors may be used alongside other systemic treatments to overcome resistance and improve clinical outcomes. These approaches reflect the evolving role of precision medicine in CTCL, where treatment is tailored to the biological characteristics of the disease [22,23].

An important aspect of combination therapy is the ability to reduce the cumulative dose of individual treatments, thereby minimizing long-term adverse effects. For example, combining phototherapy with systemic agents may allow for lower ultraviolet exposure, reducing the risk of photodamage and secondary malignancies. This dose-sparing effect is particularly relevant in patients requiring prolonged treatment or those with increased susceptibility to treatment-related complications [20].

Treatment algorithms in mycosis fungoides are typically stage-based but must remain flexible to accommodate individual patient factors. In early-stage disease, a stepwise approach beginning with skin-directed therapies and progressing to combination strategies is generally recommended. In contrast, advanced-stage disease often requires early introduction of systemic and combination therapies to achieve disease control. Continuous reassessment of treatment response is essential, allowing timely modification of therapeutic strategies in cases of progression or inadequate response [19,21].

Another critical consideration is the sequencing of therapies, which plays a significant role in long-term disease management. Sequential use of different therapeutic classes can help delay resistance and maintain disease control over time. For example, patients may transition from skin-directed therapies to systemic treatments and subsequently to targeted therapies as the disease evolves. This dynamic approach reflects the chronic nature of CTCL and the need for long-term therapeutic planning [22,23].

CONCLUSION

Mycosis Fungoides remains a therapeutically challenging condition due to its chronic, relapsing course and marked clinical heterogeneity. Effective management requires a dynamic, stage-adapted approach that integrates skin-directed therapies, systemic treatments, and emerging targeted modalities. While significant progress has been made in expanding the therapeutic armamentarium, achieving sustained disease control and minimizing treatment-related toxicity continue to represent major clinical challenges. The increasing incorporation of combination strategies and individualized treatment algorithms reflects a shift toward more comprehensive and adaptive care models.

Advances in targeted and immunomodulatory therapies have transformed the treatment landscape, offering improved specificity and the potential for better long-term outcomes. Equally important is the growing emphasis on symptom control, particularly pruritus, as a key determinant of patient quality of life. Future directions should focus on refining precision medicine approaches, integrating biomarkers into therapeutic decision-making, and optimizing treatment sequencing to enhance efficacy while reducing adverse effects. A multidisciplinary, patient-centered approach remains essential to achieving optimal outcomes and

improving the overall quality of life for affected individuals.

How to cite this article: Manal Mohamed El-Sayed 1, Rania Abdelaziz Alakad, Hayam Elsayed Hassan Rashed, Amina Ahmed Mohamed Abdelhadi, Afnan Samy Ali Hussein Aziza (2024). Therapeutic Strategies and Emerging Treatments in Mycosis Fungoides: A Translational Perspective on Disease and Symptom Control, Vol. 14, No. 3, 2024,999-1005.

Source of support: None.

Conflict of interest: Nil.

Accepted: 26.06.2024 **Received** 03.06.2024

REFERENCES

1. Willemze R, Cerroni L, Kempf W, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. *Blood*. 2019;133(16):1703-1714.
2. Ibrahim MA, Eltayeb N, Ibrahim MM, et al. Suggested guidelines for the treatment of mycosis fungoides in countries with limited resources. *Dermatol Res Pract*. 2023;2023:1360740.
3. Tarabadkar ES, Shinohara MM. Skin-directed therapy in cutaneous T-cell lymphoma. *Front Oncol*. 2019;9:260.
4. Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C. Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): Part II. Prognosis, management, and future directions. *J Am Acad Dermatol*. 2014;70(2):223.e1-17.
5. Alpdogan O, Kartan S, Johnson W, et al. Systemic therapy of cutaneous T-cell lymphoma. *Chin Clin Oncol*. 2019;8(1):10.
6. Ibrahim MA, Eltayeb N, Ibrahim MM, et al. Suggested guidelines for the treatment of mycosis fungoides in countries with limited resources. *Dermatol Res Pract*. 2023;2023:1360740.
7. Tarabadkar ES, Shinohara MM. Skin-directed therapy in cutaneous T-cell lymphoma. *Front Oncol*. 2019;9:260.
8. Olsen EA, Hodak E, Anderson T, et al. Guidelines for phototherapy of mycosis fungoides and Sézary syndrome: A consensus statement. *J Am Acad Dermatol*. 2016;74(1):27-58.
9. Amitay-Laish I, Prag-Naveh H, Dalal A, et al. Treatment of folliculotropic mycosis fungoides: A retrospective study. *Acta Derm Venereol*. 2018;98(10):951-955.
10. Jawed SI, Myskowski PL, Horwitz S, et al. Primary cutaneous T-cell lymphoma: Prognosis and management. *J Am Acad Dermatol*. 2014;70(2):223.e1-17.
11. Alpdogan O, Kartan S, Johnson W, et al. Systemic therapy of cutaneous T-cell lymphoma. *Chin Clin Oncol*. 2019;8(1):10.
12. Whittaker SJ, Demierre MF, Kim EJ, et al. Final results from a multicenter, international, pivotal study of romidepsin in refractory cutaneous T-cell lymphoma. *J Clin Oncol*. 2010;28(29):4485-4491.
13. Kim YH, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): An international, open-label, randomized, controlled phase 3 trial. *Lancet Oncol*. 2018;19(9):1192-1204.
14. Bobrowicz M, Fassnacht C, Ignatova D, et al. Pathogenesis and therapy of cutaneous T-cell lymphoma. *Int Arch Allergy Immunol*. 2020;181(10):733-745.
15. Maroñas-Jiménez L, Estrach T, Gallardo F, et al. Aprepitant for refractory pruritus in cutaneous T-cell lymphoma. *Br J Dermatol*. 2018;178(4):e273-e274.
16. Serrano L, Martinez-Escala ME, Zhou XA, et al. Pruritus in cutaneous T-cell lymphoma and its management. *Dermatol Clin*. 2018;36(3):245-258.
17. Lewis DJ, Huang S, Duvic M. Inflammatory cytokines and peripheral mediators of pruritus in cutaneous T-cell lymphoma. *J Eur Acad Dermatol Venereol*. 2018;32(10):1652-1656.
18. Silverberg JI, Yosipovitch G, Simpson EL, et al. Dupilumab treatment results in early and sustained improvements in pruritus in atopic dermatitis. *J Am Acad Dermatol*. 2020;82(6):1328-1336.
19. Willemze R, Cerroni L, Kempf W, et al. WHO-EORTC classification update for primary cutaneous lymphomas. *Blood*. 2019;133(16):1703-1714.
20. Tarabadkar ES, Shinohara MM. Skin-directed therapy in cutaneous T-cell lymphoma. *Front Oncol*. 2019;9:260.
21. Jawed SI, Myskowski PL, Horwitz S, et al. Management of CTCL: Current and future perspectives. *J Am Acad Dermatol*. 2014;70(2):223.e1-17.
22. Alpdogan O, Kartan S, Johnson W, et al. Advances in systemic therapy of CTCL. *Chin Clin Oncol*. 2019;8(1):10.
23. Whittaker SJ, Foss FM, et al. Combination and emerging therapies in CTCL. *Hematol Oncol Clin North Am*. 2012;26(2):367-381.