# USE OF JAK INHIBITORS IN T-CELL LYMPHOMAS ON THE OCCASION OF A CASE

**Esra PIRINCCI** [1], **Vehbi DEMIRCAN**[1], **Abdullah KARAKUS**[1], **Orhan AYYILDIZ**[1]

1. Dicle University Faculty of Medicine, Hematology Department, DİYARBAKIR, TÜRKİYE

## Introduction

Cutaneous T-cell lymphomas represent a diverse group of non-Hodgkin lymphomas that primarily affect the skin, accounting for approximately %65 to %75 of all cutaneous lymphomas (1). Primary cutaneous lymphomas are characterized by skin involvement without any extracutaneous disease at the time of diagnosis, and they typically remain localized to the skin for extended periods. Extracutaneous spread usually occurs only in advanced stages of the disease (2).

The goals of treatment for cutaneous T-cell lymphomas are to control symptoms, maintain quality of life, and improve survival rates. Treatment strategies vary and may include watchful waiting, skin-directed therapies such as topical steroids, nitrogen mustard, phototherapy, and radiotherapy. Systemic therapies can involve immunomodulators, antimetabolites, retinoids, epigenetic modulators, monoclonal antibodies, chemotherapy, and in some cases, allogeneic hematopoietic stem cell transplantation. Janus kinases (JAKs) are a group of four tyrosine kinases activated by various ligands including intracellular, non-receptor, cytokine, and growth factors (3). The JAK/STAT pathway is frequently activated in many T-cell lymphomas, with multiple cytokines and factors in the T-cell lymphoma microenvironment, such as IL-2, IL-6, and IL-15, driving JAK/STAT signaling.

## Aim /Objectives

Our aim is to share the malignancy process of a patient who was followed up with JAK inhibitor treatment with a pathological diagnosis of atopic dermatitis.

The objective of this poster is to present a perspective on the potential for targeted therapies—used with increasing frequency in recent years—to produce unanticipated outcomes

## Case

A 55-year-old Caucasian female patient was referred to us due to pancytopenia while hospitalized in the dermatology department of our hospital. She had been under follow-up for 3 years with a diagnosis of atypical dermatitis. The patient reported that over the past 20 days, she developed widespread lesions on her skin, accompanied by fever, night sweats, and joint pain that had persisted for the last 3 months. During the physical examination, we observed extensive dark brown-black hyperpigmentation throughout her body. Additionally, there were multiple hard nodular lesions fixed to the underlying tissue on the presternal area, with the largest measuring approximately 3 x 3 cm. The examination also revealed hyperkeratosis and dystrophic changes in her fingernails and toe nails.

The patient, who received Upadasatinib and Abrocitinib treatments for approximately 15 months due to atopic dermatitis, was admitted to our hospital when he noticed that his lesions were worsening. A new skin biopsy was conducted. Upon her arrival, laboratory results showed hemoglobin at 8.8 g/dl, platelets at 116,000/uL, white blood cell count at 8.27 x $10^3$/uL, and neutrophils at 5.68 x $10^3$/uL. Peripheral blood smear revealed normochromic, normocytic erythrocytes, a platelet count consistent with whole blood, and the presence of atypical lymphoid cells (monocytoid and cerebriform). Radiological imaging revealed hepatomegaly (175 mm), splenomegaly (133 mm), and pathological lymphadenopathy in the neck and axillary region. However, the patient died before a bone marrow aspiration biopsy could not be performed. The patient's last skin biopsy diagnosed her with 'CD30 Positive Cutaneous Anaplastic Large Cell Lymphoma'.



## Discussion

Primary cutaneous anaplastic large cell lymphoma (ALCL) is the second most common type of cutaneous T-cell lymphoma, following mycosis fungoides. For peripheral T-cell lymphomas, which have relatively low cure rates with initial treatments and limited treatment options for relapsed /refractory disease, there is an urgent need for additional biomarker-based treatments other than romidepsin, belinostat, pralatrexate, brentixumab vedotin and the anti-CCR4 antibody mogamulizumab.

The JAK/STAT pathway is used in the treatment of autoimmune diseases with intense inflammation such as Atopic Dermatitis; it has also been evaluated as a potential therapeutic target for various malignancies where this pathway is overactive. This pathway, which has attracted much attention especially with the discovery of JAK2 mutation in myeloproliferative diseases, is noted to be active in the pathogenesis of many T-cell lymphomas. JAK inhibitors have been investigated as potential therapies for peripheral T-cell lymphomas. A study investigating ruxolitinib, a JAK/STAT pathway inhibitor, in peripheral T-cell lymphoma including ALCL reported favorable outcomes. However, some reports suggest JAK inhibitors may contribute to the onset or progression of cutaneous T-cell lymphomas. For instance, cases of lymphomatoid papulosis have been reported following Upadacitinib treatment for rheumatoid arthritis and Tofacitinib treatment for refractory erythema elevatum diutinum. Additionally, cases of aggressive cutaneous T-cell lymphoma relapse have been reported in patients treated with ruxolitinib for chronic GvHD and Sézary syndrome in a patient receiving baricitinib for seronegative rheumatoid arthritis (4,5).

When our case is considered from this perspective, and the accelerated disease process after the use of JAK inhibitors is taken into account, it suggests that the disease may have developed or accelerated due to the drug. However, due to the patient's very late presentation to hematology, sufficient clinical, laboratory and molecular evaluations could not be performed

## References

1. **Ortiz-Hidalgo C et al**. Primary Cutaneous Anaplastic Large Cell Lymphoma-A Review of Clinical, Morphological, Immunohistochemical, and Molecular Features. Cancers (Basel). 2023 Aug 14;15(16):4098. doi: 10.3390/cancers15164098.
2. **Morgenroth S. et al.** What Is New in Cutaneous T Cell Lymphoma? Curr Oncol Rep. 2023 Nov;25(11):1397-1408. doi: 10.1007/s11912-023-01464-8. Epub 2023 Oct 24.
3. **Chovatiya R. et al**. JAK inhibitors in the treatment of atopic dermatitis. J Allergy Clin Immunol. 2021 Oct;148(4):927-940.
4. **Vahabi SM et al**. JAK Inhibitors in Cutaneous T-Cell Lymphoma: Friend or Foe? A Systematic Review of the Published Literature. Cancers (Basel). 2024 Feb 21;16(5):861.
5. **Cohen E et al.** (2024), Severe relapses of cutaneous T-cell lymphoma after treatment of chronic graft-versus-host disease with ruxolitinib. J Eur Acad Dermatol Venereol, 38: e32-e34.

## Contact Information

Esra PİRİNÇÇİ

Dicle University Faculty of Medicine, Hematology Department, DİYARBAKIR, TÜRKİYE

E-mail: chemiyee@gmail.com