FDA approval of Deuruxolitinib: A New Treatment Option for Severe Alopecia Areata

*Tooba Javed**

Fourth Year Medical Student, Ziauddin Medical College, Karachi, Pakistan

Corresponding author:

Tooba Javed

Fourth Year Medical Student, Ziauddin Medical College, Karachi, Pakistan, Phone: 03331270058,
E-mail: tooba.javed@nixorcollege.edu.pk

Received : August 03, 2024
Published : October 22, 2024

ABSTRACT

Alopecia areata (AA) is an autoimmune condition leading to non-scarring hair loss, affecting 1-2% of the population. It results from T-cell infiltration in hair follicles, driven by cytokines such as interferon-gamma (IFN-γ) and common gamma chain cytokines, which activate JAK signaling pathways. Traditional therapies have included corticosteroids and immunosuppressants; however, JAK inhibitors have shown greater efficacy. In June 2022, the FDA approved baricitinib for AA, followed by ritlecitinib, and in July 2023, deuruxolitinib (Leqselvi) was approved for severe AA in adults. This approval stemmed from two phase 3 trials (THRIVE-AA1 and THRIVE-AA2) involving 1,220 patients, which demonstrated that deuruxolitinib significantly improved hair regrowth compared to placebo, with 29.6% and 41.5% of participants achieving a SALT score of ≤20 at 24 weeks for the 8 mg and 12 mg doses, respectively. The treatment was associated with manageable side effects, including headaches and acne, and did not present significant cardiovascular risks. Overall, deuruxolitinib offers a promising and effective treatment option for severe alopecia areata, warranting further investigation into long-term safety and effects post-treatment.

Keywords: Alopecia Areata, Cytokines, Cardiovascular Risks, Adults

INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder driven by T-cells that primarily affects hair follicles in the anagen phase and nails. Clinically, AA is characterized by localized, patchy, non-scarring hair loss [1]. Multiple studies have shown that AA affects 1-2% of the general population with an estimated lifetime risk of 1.7% [2]. Histologically, AA is marked by the infiltration of cytotoxic CD8+NKG2D+ T cells into the hair follicles, a phenomenon driven by heightened levels of interferon-gamma (IFN-γ) and common gamma chain (γc) cytokines such as IL-2, IL-7, and IL-15. These cytokines stimulate Janus kinase (JAK) signaling pathways, leading to the phosphorylation of STAT proteins. Specifically, the activation of

JAK 1/2 and JAK 1/3 intensifies the cellular immune response, resulting in increased production of IFN-γ and IL-15 within the hair follicles [3].

Traditional therapies for alopecia areata consist of topical, intralesional, and oral glucocorticosteroids, as well as cyclosporine and methotrexate. However, JAK inhibitors have now proven to be the most effective treatment strategy for addressing the condition [4]. In June 2022, first-ever Food and Drug Administration (FDA) approval of a treatment for AA, baricitinib, was made, followed a year later by the second one, ritlecitinib [5]. Subsequently, on July 26th, the US FDA approved deuruxolitinib (Leqselvi; Sun Pharma), an oral JAK inhibitor, for treating severe alopecia areata in adults.

The approval of this drug was based on the results of two phase 3 clinical trials, THRIVE-AA1 and THRIVE-AA2 which were conducted to measure the efficacy and safety of this drug. Both the studies all together included 1220 patients with at least 50% scalp hair loss as measured by the Severity of Alopecia Tool (SALT). The phase 3 trial THRIVE-AA1 trial was a randomized, double-blind, placebo-controlled study to assess deuruxolitinib for alopecia areata. The trial featured a 28-day screening phase, a 24-week treatment phase. Participants were assigned to receive either deuruxolitinib 12 mg twice daily (BID), 8 mg BID, or a placebo. The efficacy was measured using the SALT score every 4 weeks and Results showed that both doses of deuruxolitinib significantly improved the percentage of patients achieving a SALT score of ≤20 at 24 weeks compared to placebo, with 29.6% of the 8 mg BID group and 41.5% of the 12 mg BID group achieving this outcome. The results indicated that both 8 mg and 12 mg doses of deuruxolitinib significantly outperformed placebo, with the 8 mg dose showing a risk difference of 0.28 and the 12 mg dose a risk difference of 0.39, both statistically significant which resulted in the swift approval of this drug by FDA. However, the use of this drug is not bereft of side effects which mostly included headaches and acne. There were no myocardial, stroke, malignancies or any other thromboembolic events noted as compared to the other approved oral JAK inhibitors for AA [6].

CONCLUSION

In conclusion, the approval of deuruxolitinib represents a valuable addition to the treatment regimen for severe alopecia areata, showing significant efficacy in hair regrowth compared to placebo in Phase 3 trials. Notably, deuruxolitinib has a minimal side effect profile, particularly benefiting those with other pre-existing health conditions and offers a safer alternative to other oral JAK inhibitors. Although side effects after treatment cessation should be fully assessed in the future, deuruxolitinib's current safety and efficacy makes it a promising option for improving outcomes and quality of life for patients suffering from this challenging disorder.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST

Author declare that there is no conflict of interest.

REFERENCES

1. Uzuncakmak TK, Engin B, Serdaroglu S, Tuzun Y. (2021). Demographic and Clinical Features of 1,641 Patients with Alopecia Areata, Alopecia Totalis, and Alopecia Universalis: A Single-Center Retrospective Study. Skin Appendage Disord. 7(1):8-12.

2. Juárez-Rendón KJ, Rivera Sánchez G, Reyes-López MÁ, García-Ortiz JE, Bocanegra-García V, Guardiola-Avila I, et al. (2017). Alopecia Areata. Current situation and perspectives. Arch Argent Pediatr. 115(6):e404-e411.

3. Xing L, Dai Z, Jabbari A, Cerise JE, Higgins CA, Gong W, et al. (2014). Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. Nat Med. 20(9):1043-1049.

4. Papierzewska M, Waśkiel-Burnat A, Rudnicka L. (2023). Safety of Janus Kinase inhibitors in Patients with Alopecia Areata: A Systematic Review. Clin Drug Investig. 43(5):325-334.

5. Haughton RD, Herbert SM, Ji-Xu A, Downing L, Raychaudhuri SP, Maverakis E. (2023). Janus kinase inhibitors for alopecia areata: A narrative review. Indian J Dermatol Venereol Leprol. 89(6):799-806.

6. King B, Senna MM, Mesinkovska NA, Lynde C, Zirwas M, Maari C, et al. (2024). Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: Results from the Phase 3 randomized, controlled trial (THRIVE-AA1). J Am Acad Dermatol. S0190-9622(24)02550-7.

7. 1- King B, Senna MM, Mesinkovska NA, Lynde C, Zirwas M, Maari C, et,al. Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: Results from the Phase 3 randomized, controlled trial (THRIVE-AA1). Journal of the American Academy of Dermatology. 2024 Jul 23.

Citation: Javed T. (2024). FDA approval of Deuruxolitinib: A New Treatment Option for Severe Alopecia Areata. Clin Res. 5(1):23.

DOI: https://doi.org/10.35702/clinres.10023