Correspondence (European Journal of Dermatology)

Prolonged real-life experience with baricitinib in patients with moderate-to-severe atopic dermatitis.

Axel De Greef, M.D., Pierre-Dominique Ghislain, M.D., Marie Baeck, M.D., Ph.D

Dermatology Department, Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium

Correspondence:

Dr. Axel De Greef, M.D.

Department of Dermatology

Cliniques universitaires Saint-Luc (UCLouvain)

Avenue Hippocrate 10, B-1200 Brussels, Belgium

Tel: +32 (0)2 764 80 83 / Fax: +32 (0)764 89 58

Email: axel.degreef@saintluc.uclouvain.be

ORCIDs: 0000-0003-0713-8283

Running title: Baricitinib in real-life for moderate-to-severe atopic dermatitis

Text word count: 698

Table count: 1

Figure count: 0

References: 10

Ethics Statement section: The patients in this manuscript have given written informed consent to publication of their case details.

Funding sources: None

Conflicts of interest: Pierre-Dominique Ghislain discloses his past participation as an investigator and as a scientific advisor for Lilly Eli. Pierre-Dominique Ghislain and Marie Baeck have previously participated as speakers in events sponsored by Lilly Eli.

None of the authors has scientific or financial conflicts of interests to declare in the current reported study.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Dear Editor,

Baricitinib is an oral selective Janus-kinase (JAK) 1 and 2 inhibitor, for the treatment of moderate-to-severe atopic dermatitis (AD). Its efficacy and safety have already been demonstrated clinical trials [1,2], but only in short-termed real-life studies [3-5].

We retrospectively collected real-life data from a monocentric adult patient cohort treated with bariticinib for moderate-to-severe AD in Belgium from January 2021 to May 2023. Patients received baricitinib (4 milligrams (mg) daily, orally) after ineffectiveness or contra-indication of a previous systemic agent. The outcome for effectiveness was evaluated by the percentage of patients who achieved a validated Investigator's Global Assessment for AD (vIGA-AD) of 0 (clear) or 1 (almost clear) at the end of the follow-up. As the prescription was in a real-life setting, patients were allowed to use topical steroids and/or calcineurin inhibitors.

Of the 19 patients included, 14 were male, median age ± interquartile range (IQR) was 39.0 ± 29.0 years and the median ± IQR follow-up duration was 54.4 ± 64.2 weeks. Baseline demographic and clinical characteristics are summarized in Table Ia. All patients were previously treated with cyclosporine, which was discontinued due to ineffectiveness or adverse event. One patient had received dupilumab, stopped because of severe conjunctivitis. For all patients, baricitinib was the first JAK inhibitor prescribed.

At baseline, median vIGA-AD ± IQR was 3.0 ± 1.0. The proportion of patients reaching a vIGA-AD of 0 (clear) or 1 (almost clear) was 47.4% (9/19 patients) at the end of the follow-up (May 2023). Improvement of vIGA-AD was significant (*P* value <.001, using a pairwise Wilcoxon signed-rank test) when comparing baseline values with last follow-up visit scores. Patients with less than 2-points improvement were those with severe disease at baseline (vIGA-AD score of 4). Only 1 of the 7 patients (14.3%) with severe disease at baseline reached a vIGA-AD score of 0, compared to 6 of the 10 patients (60%) with moderate disease.

No serious adverse events (AEs) were reported. One patient presented with mild facial acne and another one with nausea. Two patients presented with a transient increase of creatinine phosphokinase (10.5% - range, 186-301 units/L; normal value <170 units/L). Increased total cholesterol (>200 mg/dL) and triglycerides (>150 mg/dL) were observed in six patients (31.6%). The rate of any AEs (including biological changes) was 52.6%.

Seven patients (36.8%; 6 men; mean age 43.4 years; with child-onset AD; severe vIGA-AD score in 4 and moderate in 3) discontinued treatment due to lack of effectiveness, with a mean duration of treatment ± standard deviation before stopping of 19.6 ± 13.3 weeks. Six of them then rapidly improved with upadacitinib 30mg daily and one with dupilumab.

Five patients with concomitant alopecia areata (AA) showed signs of hair regrowth. At the end of the follow-up, three achieved a Severity of Alopecia Tool (SALT) score of 0 (complete regrowth), and two showed encouraging signs of regrowth but SALT score remained > 20. Table Ib summarizes the demographic and clinical characteristics of patients with concomitant AD and AA.

The results of this extended real-life study are consistent with those of BREEZE AD7 (31% of patients with vIGA-AD score of 0/1 at week 16), and BREEZE AD3 long-term study (47.1% at week 68) [6]. Data about safety are consistent with the pooled safety analysis [7]. Lipid level changes was the most frequent AE encountered but did not lead to treatment discontinuation or MACE. However, the proportion of patients discontinuing treatment due to lack of efficacy was 36.8%, compared to the 1-2% drop-out in clinical trials.

The efficient shift of patients with history of difficult-to-treat AD to another systemic immunomodulatory agent (upadactitinib or dupilumab) is consistent with a recent systematic review and network meta-analysis [8], and with real-life data [9], assessing the superiority of these treatments, compared to baricitinib.

To conclude, baricitinib in real-life seems to be more effective in treating patients with moderate rather than severe and long-lasting AD. Safety data are reassuring, in particular no thromboembolic or cardiovascular AEs were observed, within the limits of the follow-up period. Lipid changes are the most frequent AE. Effectiveness of baricitinib in hair regrowth among patients with concomitant AD and alopecia areata [10] may guide the choice towards barititinib for this specific patient phenotype.

References

1. Simpson EL, Lacour JP, Spelman L, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: results from two randomized monotherapy phase III trials. *Br J Dermatol*. 2020;183(2):242-255.

2. Reich K, Kabashima K, Peris K, et al. Efficacy and safety of baricitinib combined with topical corticosteroids for treatment of moderate to severe atopic dermatitis: a randomized clinical trial. *JAMA Dermatol.* 2020;156(12):1333-1343.

3. Rogner D, Biedermann T, Lauffer F. Treatment of atopic dermatitis with baricitinib: first real-life experience. *Acta Derm Venereol.* 2022;102:adv00677. Published 2022 Mar 22.

4. Uchiyama A, Fujiwara C, Inoue Y, Motegi SI. Real-world effectiveness and safety of baricitinib in Japanese patients with atopic dermatitis: A single-center retrospective study. *J Dermatol.* 2022;49(4):469-471.

5. Vittrup I, Elberling J, Skov L, et al. Short-term real-world experience with baricitinib treatment in Danish adults with moderate-severe atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2023;37(4):e543-e546.

6. Silverberg JI, Simpson EL, Wollenberg A, et al. Long-term efficacy of baricitinib in adults with moderate to severe atopic dermatitis who were treatment responders or partial responders: an extension study of 2 randomized clinical trials. *JAMA Dermatol*. 2021;157(6):691-699.

7. Bieber T, Thyssen JP, Reich K, et al. Pooled safety analysis of baricitinib in adult patients with atopic dermatitis from 8 randomized clinical trials. *J Eur Acad Dermatol Venereol.* 2021;35(2):476-485.

8. Drucker AM, Morra DE, Prieto-Merino D, et al. Systemic immunomodulatory treatments for atopic dermatitis: update of a living systematic review and network meta-analysis. *JAMA Dermatol*. 2022;158(5):523-532.

9. De Greef A, Ghislain PD, de Montjoye L, Baeck M. Real-life effectiveness and tolerance of upadacitinib for severe atopic dermatitis in adolescents and adults. *Adv Ther*. 2023;40(5):2509-2514.

10. King B, Ohyama M, Kwon O, et al. Two phase 3 trials of baricitinib for alopecia areata. *N Engl J Med.* 2022;386(18):1687-1699.