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LETTER TO THE EDITOR

Preliminary experience with abrocitinib in severe atopic dermatitis

Dear Editor,

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by intense itching and eczematous lesions.[1,2] Abrocitinib is an oral small-molecule inhibitor of Janus kinase (JAK) 1, that was approved in October 2021 for the treatment of moderate-to-severe AD in adults.[3] Multiple phase three studies have shown positive results in adults, with a good tolerance and safety profile[4-6], In particular, the proportion of patients who had achieved a 75% reduction from baseline in the Eczema Area and Severity Index (EASI-75) was 40% in the abrocitinib 100 mg group and 63% in the abrocitinib 200 mg group at Week 12, respectively[4] while EASI-90 was reached in the 37.7% and in the 23.9% of patients respectively in the 200 and 100 mg group.[5] At Week 16 an ≥4-point improvement from baseline to Week 16 in Nighttime Itch Scale severity was 64.3% and 52.4% for 200 and 100 mg, respectively,[6] Moreover, the proportion of patients achieving ≥4-point improvement from baseline in Dermatological Life Quality Index (DLQI) was 85.0% and 74.4% for 200 and 100 mg.[6]

We herein describe eight cases of severe AD treated with abrocitinib at 100 mg daily. The population was composed of seven males and one female with a median age of 34.5 (Q1–Q3: 26.3–41.5). Most of them have an early onset persistent pattern (7/8) and a classic exudative AD phenotype (6/8). One patient has a generalized lichenoid pattern, and one has a classical type associated with chronic hand eczema. The greater part of patients has at least one atopic comorbidity, only two of them did not have any. Most patients (7/8) received cyclosporin as a previous traditional systemic treatment, one patient received methotrexate. They were previously treated with either dupilumab (5/8), tralokinumab (3/8), upadacitinib (2/8) or baricitinib (1/8). Regarding JAK inhibitors, the patient treated with upadacitinib discontinued the treatment due to side effects, while the patient treated with baricitinib discontinued it because the drug was unavailable in Italy (he had moved from Holland).

EASI, DLQI, pruritus and sleep Numerical Rating Scale (P-NRS and S-NRS) were used for clinical monitoring in all the patients at baseline and after 4 (T4) and 8 weeks (T8) of therapy (Table 1). Considering EASI, all the patients (7/7) reached EASI-50 at T4, while 7/8 and 5/8 achieved EASI-75 and EASI-90 at T8, respectively. Figure 1 represents the clinical improvement of one of our cases. A ≥4-point improvement in P-NRS was achieved by 5/7 patients at T4 and by 6/8 patients at T8. A ≥4-point improvement in DLQI was achieved by 5/7 patients at T4 and by 7/8 patient at T8. About AEs, three patients had CPK elevation, without the necessity for drug discontinuation. No severe AEs were recorded. In addition, the patient with cholinergic urticaria reported a subjective improvement in symptoms, allowing him to play sports without symptoms after many years.

In our experience, abrocitinib 100 mg was shown to be effective with excellent rapidity of action in our small group of patients. The fastest and the best improvement was seen for S-NRS. The results of EASI were better than those of the trial, since EASI-90 was reached in five patients (more than 50%) after only 8 weeks of therapy,[5] The improvement in P-NRS and DLQI is better than the results of JADE-COMPARE.[6] Also, the good clinical response is consistent with an important improvement of the quality-of-life score (QoL): baseline DLQI score denoted that AD had a 'very large effect on the QoL', while the DLQI score at T8 indicated that AD had a 'no effect' or 'small effect'. Moreover, 4/8 of our patients reached a minimal disease activity (optimal target of response): EASI-90, P-NRS ≤ 1 and S-NRS ≤ 1,[7] The fact that these patients had been unresponsive to a variety of traditional and biologic therapies underscores the severity and intractability of their AD. Our findings align with a systematic literature review that focused on phase II and III randomized clinical trials involving biologics and oral small molecules in AD.[8] Notably, oral small molecules demonstrated greater efficacy when compared to biologics in the treatment of AD. In particular, the higher doses of upadacitinib and abrocitinib exhibited similar levels of effectiveness to lebrikizumab. These three medications displayed the most substantial

TABLE 1 Clinical outcomes and improvement (expressed in percentage) at baseline and after, 4 and 8 weeks of treatment.

Clinical score	Baseline ($n = 8$)	4 weeks ($n = 7$)	Improvement (%) at Week 4 ($n = 7$)	8 weeks ($n = 8$)	Improvement (%) at Week 8 ($n = 8$)
EASI, median (Q1–Q3)	24 (23.5–27.6)	6.2 (5.9–7.5)	75.0 (67.9–78.7)	1.6 (0.9–4.5)	93.6 (81.3–93.6)
Pruritus NRS, median (Q1–Q3)	7.0 (7.0–8.0)	2.0 (1.5–4.5)	66.7 (42.1–80.4)	1.5 (0.8–3.5)	80.6 (50.0–90.6)
Sleep NRS, median (Q1–Q3)	7.0 (6.8–8.0)	2.0 (0.0–4.5)	75.0 (35.7–100.0)	0.0 (0.0–3.5)	100.0 (52.2–100.0)
DLQI, median (Q1–Q3)	18.0 (14.0–18.0)	7.0 (5.0–8.5)	60.0 (40.0–69.0)	2 (0–9.3)	87.3 (27.0–100.0)

Note: Of the eight patients, 7/8 were assessed at T4, and 8/8 at T8.

Abbreviations: DLQI, dermatological life quality index; EASI, Eczema Area and Severity Index; NRS, numerical rating scale; Q1, first interquartile; Q3, third interquartile.

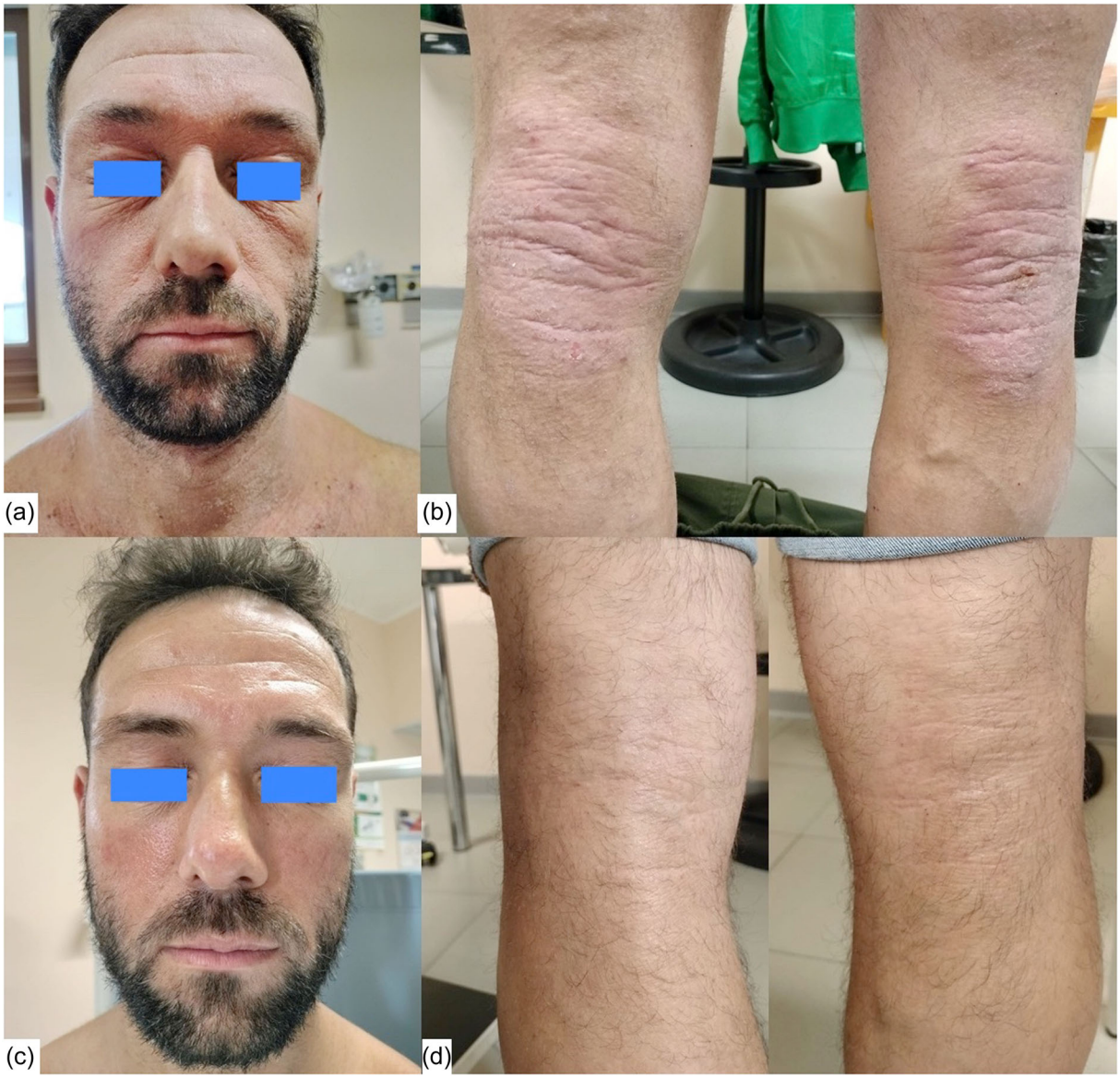

FIGURE 1 Clinical pictures of one of our cases at baseline (a, b) and after 8 weeks of treatment with abrocitinib 100 mg daily (c, d). This is a case of a 41-year-old male patient with a history of atopic dermatitis (AD) and allergic rhinitis from childhood. At baseline the patient had a severe AD a widespread presentation of eczema with bilateral patches and plaques predominantly in the flexural regions, the facial and cervical regions showed prominent eczema signs, with thickening and pruritic lesions, additionally, many ulcers and scabs were discovered; Eczema Area and Severity Index (EASI) was 28.8. At 8 weeks of treatment, there was a considerable improvement in the condition of the eczema (EASI 1.2). The lichenification and the excoriation signs were greatly improved and also the erythema was less intense.

improvements in the clinical signs and symptoms of AD, surpassing the outcomes achieved by dupilumab. Moreover, abrocitinib emerged as a standout by significantly enhancing the quality of life in comparison to other targeted therapies. Obviously, this is only preliminary data on a small group of patients, which needs to be confirmed by larger real-life studies with longer follow-ups.

KEYWORDS
abrocitinib, atopic dermatitis

AUTHOR CONTRIBUTIONS
Silvia Ferrucci, Anna Campanati, Maddalena Napolitano and Francesca Barei have contributed to the conception, realization and writing the paper. Luca Valtellini, Emanuela Martina and Cataldo Patruno helped in collecting the clinical data of the patients. Angelo V. Marzano has revised the manuscript.

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CONFLICTS OF INTEREST STATEMENT
Silvia Ferrucci is principal investigator in clinical trial to Amgen, Sanofi, Novartis, Lilly, Leo Pharma, Galderma and Abbvie and she is an advisory board or speaker to Novartis, Menarini, Sanofi, Pfizer, Abbvie and Leo Pharma. Maddalena Napolitano acted as speaker, consultant and advisory board member for Sanofi, Abbvie, Leo Pharma and Novartis, Lilly C. Patruno acted as investigator, speaker, consultant and advisory board member for AbbVie, Amgen, Eli Lilly Leo Pharma, Novartis, Pfizer, Pierre Fabre and Sanofi. Anna Campanati has been involved as principal or subinvestigator in clinical trial for Sanofi, Novartis, Leo pharma, Abbvie, Amgen, Almirall and Eli-Lilly; she has been involved in advisory board or speaker for Novartis, Eli-Lilly, Sanofi, Abbvie, Leo Pharma, Almirall, Novartis, Pfizer and Amgen. Emanuela Martina is subinvestigator in clinical trial to Sanofi and Novartis. Francesca Barei and Luca Valtellini have no conflict of interest. Angelo V. Marzano has no conflict of interest for this publication.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no data sets were generated or analysed during the current study.

ETHICS STATEMENT
This is a retrospective study, so no ethics committee approval was needed. All patients in this manuscript have given written informed consent for participation in the study and the use of their identified, anonymized, aggregated data and their case details (including photographs) for publication.

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