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LETTER TO THE EDITOR

Upadacitinib improves symptoms of concomitant allergic rhinitis or allergic asthma in patients with severe atopic dermatitis: A 16-week multicentre retrospective study

Dear Editor,

Atopic dermatitis (AD) is the most common inflammatory skin disease often associated with comorbidities, including allergic rhinitis (AR; 40.3% of patients) and allergic asthma (AA; 51.3%).[1] Among systemic treatments approved for severe AD, dupilumab is also indicated for the treatment of chronic rhinosinusitis with nasal polyps, AA and eosinophilic esophagitis.[2,3] Upadacitinib, a selective JAK1-inhibitor approved for severe AD, lacks approval for AA and AR.[4–6]

We retrospectively analysed data from 11 Italian dermatology units to determine whether upadacitinib could improve symptoms related to AA or AR in patients with severe AD.

All enrolled patients had previously received a diagnosis of mild-to-moderate AA or AR from the pulmonologist. The patient's eligibility for upadacitinib was assessed in accordance with European Guidelines.[4] AA and AR severity were evaluated using the Asthma Control Questionnaire-5 (ACQ-5; range 0–6) and Rhinitis Control Assessment Test (RCAT; range 6–30), respectively.[7,8] Moreover, patients assessed their symptoms using the visual analogue scale (VAS, range 0–10). Patients completed the questionnaires at Week 16, referring to their previous and current clinical picture. The effectiveness of upadacitinib was evaluated at Week 16 in terms of EASI75 and EASI90 (reduction of at least 75% and 90%, compared with baseline Eczema Area and Severity Index).

A total of 116 patients, all treated with upadacitinib for severe AD and concomitantly affected by AA and/or AR, were included. A diagnosis of asthma was reported by 79 patients (68.10%), while 106 (91.38%) had AR. 66 patients (56.90%) had previously failed dupilumab. At baseline, the mean (standard deviation, SD) EASI, ACQ-5 and RCAT scores were 25.42 (12.10), 1.95 (1.63) and 17.2 (5.74), respectively. An RCAT ≤21 (uncontrolled AR) was reported by 85 patients (90.19%) at baseline. The mean VAS for AR was 5.42 (2.78). Regarding asthma, 44 patients (55.70%) had an ACQ-5 ≥1 (uncontrolled asthma), and 14 (17.72%) reported a partial control ($0.5 \leq$ ACQ-5 < 1), with a mean VAS of 3.64 (2.86). Additional characteristics of our population are summarized in Table 1.

After 16 weeks, 95 (81.90%) and 65 (56.03%) of patients achieved EASI75 and EASI90, respectively. Upadacitinib demonstrated a slight improvement in AA and AR (Figure 1a,b), as after 16 weeks, the mean ACQ-5 score was 1.12 (1.62; $p < 0.0001$), and the mean RCAT score was 23.55 (7.16; $p < 0.0001$). An RCAT >21 (controlled rhinitis) was reported by 78 patients (73.58%). An ACQ-5 <0.5 (controlled asthma) was achieved by 44 patients (55.70%), while partial control was reported by 7 (8.86%). Mean VAS scores for AR and AA decreased significantly to 2.08 ($p < 0.0001$) and 1.37 ($p < 0.0001$), respectively (Figure 1c,d).

TABLE 1 Demographic and clinical characteristics of our cohort at baseline.

	Mean (SD)
Patients	116
Age, years	35.88 (14.43)
BMI	23.57 (3.53)
Disease duration, years	25.97 (13.14)
EASI at baseline	25.42 (12.10)
IGA at baseline	3.29 (0.67)
pp-NRS at baseline	7.86 (1.85)
s-NRS at baseline	6.84 (2.34)
	***N* (%)**
Male	65 (56.03)
Involvement of face/neck	104 (89.66)
Allergic conjunctivitis	58 (50)
Allergic rhinitis	106 (91.38)
Allergic asthma	79 (68.10)
Cardiometabolic comorbidities	24 (20.69)
Previous treatment with dupilumab	66 (56.90)

Note: Data are presented as absolute numbers and percentages or mean and standard deviation, as appropriate.

Abbreviations: BMI, body mass index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; pp-NRS, Peak Pruritus-Numerical Rating Scale; SD, standard deviation; s-NRS, Sleep-Numerical Rating Scale.

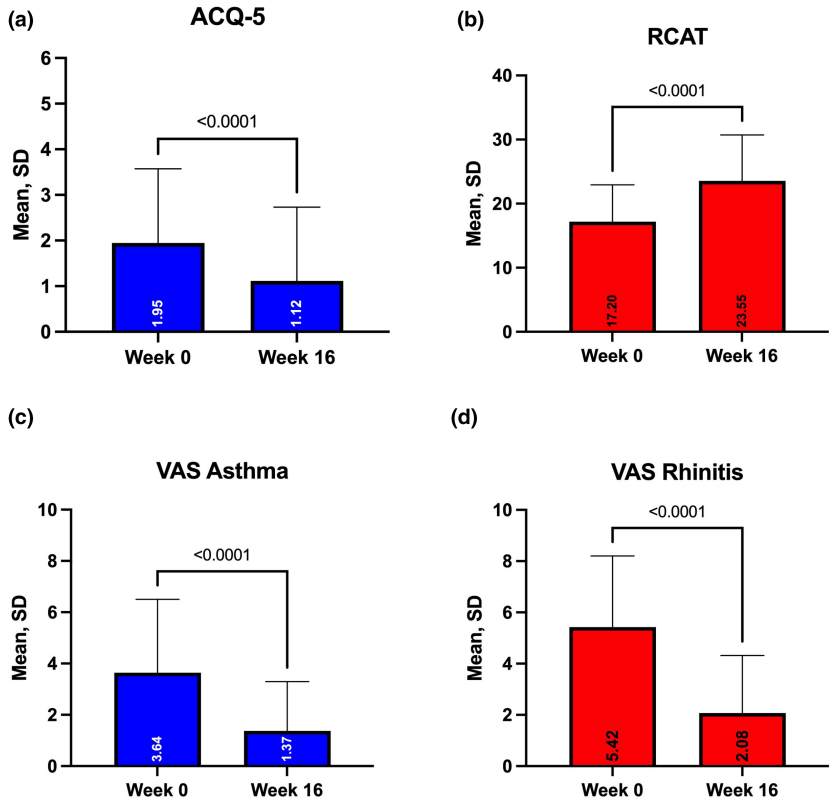

FIGURE 1 Mean decrease in ACQ-5 (a), RCAT (b), VAS Asthma (c) and VAS Rhinitis (d) after 16 weeks of treatment with upadacitinib. The within-group comparison of continuous variables between baseline and Week 16 was performed by the paired Student *t*-test. A *p*-value <0.05 was considered significant. ACQ-5, Asthma Control Questionnaire-5; RCAT, Rhinitis Control Assessment Test; VAS, visual analogue scale.

Our experience confirmed the effectiveness of upadacitinib in AD, with stability or slight improvement in ACQ-5 or RCAT. Different from the trials evaluating dupilumab for severe asthma,[9] in routine clinical practice patients with AD referred to dermatologists often exhibit mild-to-moderate concomitant AA or AR. This could partially explain the low ACQ-5 and RCAT scores at baseline, which are consistent with a recent real-world experience evaluating dupilumab in patients with AD and asthma.[7]

AA and AR involve airway inflammation induced by Th2 cells-dependent cytokines, like interleukins (ILs) 4, 5 and 13.[10] Since upadacitinib targets JAK1, it inhibits the signalling of these ILs, likely improving asthma and rhinitis symptoms. Betancor et al.[10] described a case of severe AD, AR and AA who experienced remission of all diseases with upadacitinib.

Our experience, despite a few limitations, including its retrospective nature, short follow-up, limited sample size and a possible selection bias, showed a beneficial impact of upadacitinib on AA and AR symptoms in patients with severe AD, providing initial data for further research on the possible role of JAK-inhibitors in treating other atopic conditions.

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CONFLICT OF INTEREST STATEMENT
L. Gargiulo has been a consultant for Almirall. A. Balato has received honoraria for participation in advisory boards, meetings, or as speaker for AbbVie, Celgene, Janssen-Cilag, Eli Lilly, Novartis Pharma, Pfizer, Sanofi-Genzyme and UCB Pharma. S. Ferrucci has been principal investigator in clinical trials for ABBVIE, Almirall, Galderma, Leo Pharma, Sanofi, Amgen, Novartis, Bayer and received honoraria for lectures for Novartis and Menarini C. Foti has been consultant or speaker for Abbvie, Pfizer, Sanofi, Novartis, Lilly, LeoPharma. F. M. Gaiani acted as a speaker or consultant for Novartis, Abbvie, Eli Lilly, Celgene, LeoPharma and Almirall. G. Girolomoni has received personal fees from AbbVie, Abiogen, Almirall, Amgen, Biogen, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli-Lilly, Leo Pharma, Merck Serono, Novartis, Pfizer, Pierre Fabre, Samsung bioepis and Sanofi. P. Malagoli has been a speaker for AbbVie, Lilly, Novartis, Janssen-Cilag, Celgene, Leopharma and Almirall. M. Napolitano acted as speaker, consultant and advisory board member for Sanofi, AbbVie, LEO Pharma, Amgen, PFIZER, Bionike, Pierre Fabre and Eli Lilly. M. Ortoncelli has served as advisory board member and/or consultant and has received fees and speaker's honoraria or has participated for clinical studies for AbbVie, Leo Pharma

and Sanofi Genzyme. C. Patruno acted as investigator, speaker, consultant and advisory board member for AbbVie, Amgen, Eli Lilly, LEO Pharma, Novartis, Pfizer, Pierre Fabre and Sanofi. S. Ribero has served as advisory board member and/or consultant and has received fees and speaker's honoraria or has participated for clinical studies for AbbVie, Almirall, Leo Pharma, Elli Lilly, Novartis, Pfizer and Sanofi Genzyme. P. Romita has been consultant or speaker for Sanofi, Novartis, Abbvie, Leopharma. A. Costanzo has served as an advisory board member, consultant and has received fees and speaker's honoraria or has participated in clinical trials for Abbvie, Almirall, Biogen, LEO Pharma, Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme and UCB-Pharma. A. Narcisi has served on advisory boards, received honoraria for lectures and research grants from Almirall, Abbvie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Genzyme, Amgen and Boehringer Ingelheim. The other Authors have nothing to declare.

DATA AVAILABILITY STATEMENT

Additional data supporting the findings of this manuscript are available on reasonable request to the corresponding author.

ETHICS STATEMENT

Institutional review board approval was exempted, as the study procedures did not deviate from standard clinical practice. For some of the patients, AbbVie provided the drug upadacitinib through a Compassionate Use Program activated according to the DM 7/9/2017. All included patients had provided written informed consent for the retrospective analysis of their clinical data. The study was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments.

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[Correction added on 15 June 2024, after first online publication: M. B. Guanti has been added to the author list.]

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