Beneficial effects of upadacitinib on alopecia areata associated with atopic dermatitis: A multicenter retrospective study

To the Editor: A clinical association of alopecia areata (AA) with other immune-mediated disorders including atopic dermatitis (AD) has been reported, with a 26-fold higher risk of developing AA in AD patients compared with healthy controls.[1]

In this study we retrospectively assessed therapeutic effects of upadacitinib on concomitant AA in AD patients, collecting data from the registry dedicated to the national compassionate use program on upadacitinib, a JAK-1 inhibitor, for the treatment of moderate-to-severe AD adult patients.[2] Of 118 charts of AD patients treated with upadacitinib, 19 (16.1%) also suffered from concomitant AA (Table I). All patients were initially treated with 30 mg upadacitinib daily and the dosage was maintained, except for 2 patients that reduced the daily dose to 15 mg because of nonsevere adverse events, namely increased alanine transaminase and homocysteine blood levels, and leukocyte count in both cases. No patients used upadacitinib in combination with topical or intralesional corticosteroids and none interrupted upadacitinib treatment throughout the observation period.

A significant reduction of mean baseline severity of alopecia tool (SALT) score (95.1 ± 9.6) was detected as early as after 4 weeks of treatment (77.6 ± 28.2, $P = .0087$), with incremental decreases over time that reflected an increasing percentage of patients achieving $SALT_{50}$, $SALT_{75}$, $SALT_{90}$, and $SALT_{100}$ responses (Table II). Eight out of 17 (47.1%) patients were nonresponder (response < $SALT_{50}$)[3] after 16 weeks of therapy, and no meaningful amelioration was detected thereafter. A progressively larger percentage of patients obtained alopecia areata − investigator global assessment 0-1 through the observation period (Table II).

Neither baseline SALT score ($P = .447$) nor duration of AA ($P = .378$) significantly correlated with SALT score variation during the observation period, whereas a slight positive correlation (Pearson r = 0.48, $P = .0446$) between changes in SALT score throughout upadacitinib treatment and the age of AA onset was found. This was confirmed by a multivariable regression analysis, revealing a prediction of 2.1-point SALT reduction for each 1-unit increase in the age of onset ($P = .025$), independently from baseline

Table I. Baseline demographic and clinical characteristics of patients with AD and concomitant AA

Items	*N* = 19
Sex, *n* pts (%)	
Male	6 (31.6)
Female	13 (68.4)
Age [median (IQR)]	38 (26-51)
BMI [median (IQR)]	23.9 (21.0-25.6)
Total serum IgE level (patients)	
>100 IU/ml, [*n* (%)]	7 (36.8)
≤100 IU/ml, [*n* (%)]	12 (63.2)
Alcohol consumption, *n* pts (%)	
Yes	3 (15.8)
No	16 (84.2)
AD family history, *n* pts (%)	
Yes	6 (50.0)
No	6 (50.0)
AA localization, *n* pts (%)	
Scalp (fronto-parietal)	19 (100)
Scalp (ophiasis)	15 (78.9)
Eyebrows	17 (89.5)
Beard	7 (38.8)
Trunk and limbs	12 (63.2)
Universalis	12 (63.2)
Nail involvement, *n* pts (%)	1 (5.3)
Mean AA duration, months ± SD	131.9 ± 95.9
Median age of AA onset [median (IQR)]	25 [20-40]
Concomitant autoimmune disease, *n* pts (%)	
No	13 (68.4)
Graves' disease	1 (5.56)
Hashimoto thyroiditis	4 (32.2)
Autoimmune gastritis type A	1 (11.1)
Atopic Comorbidity (asthma, rhinitis, food allergy, conjunctivitis), *n* pts (%)	
Yes	9 (47.4)
No	10 (52.6)
Asthma	6 (66.7)
Rhinitis	5 (55.6)
Food allergy	1 (11.1)
Conjunctivitis	2 (22.2)
*Anxiety, *n* pts (%)	
Yes	8 (47.0)
No	9 (52.9)
†Previous systemic therapies for AD, *n* pts (%)‡	
Cyclosporine	12 (63.2)
Oral corticosteroids	4 (21.0)
Azathioprine	1 (5.2)
Dupilumab	8 (42.1)

AA, Alopecia areata; *AD*, atopic dermatitis; *BMI*, body mass index; *IQR*, interquartile range; *n pts*, number of patients; *SD*, standard deviation.
*The sum does not match the total number of patients due to missing data.
†The sum does not match the total due to concomitant multiple drug administration.
‡Prior to upadacitinib therapy, a washout period of at least 4 weeks was recommended in patients using systemic immunosuppressive agents, and a washout period of 5 half-lives or within 12 weeks (whichever is longer) was considered in case of targeted biologic treatments.

Table II. Evaluation of AA severity, clinical improvement, and treatment response during upadacitinib administration

Items	Baseline	Week 4	Week 16	Week 28	Week 40
Number of observed patients	19	19	17	14	9
SALT score, mean ± SD[†]	95.1 ± 9.6	77.6 ± 28.2*	43.4 ± 39.2**	31.0 ± 40.4***	34.9 ± 42.8****
ΔSALT, mean ± SD[†]	_____	−17.5 ± 26.0	−51.2 ± 37.9	−65.1 ± 38.5	−62.5 ± 40.9
AA-IGA, *n* pts (%)					
0		___	4/17 (23.5)	8/14 (57.1)	5/9 (55.6)
1		2/19 (10.5)	4/17 (23.5)	___	___
2		3/19 (15.8)	2/17 (11.8)	1/14 (7.1)	___
3	4/19 (21.0)	6/19 (31.6)	6/17 (35.3)	4/14 (28.6)	3/9 (33.3)
4	15/19 (78.9)	8/19 (42.1)	1/17 (5.9)	1/14 (7.1)	1/9 (11.1)
Patients achieving a 50%-74% improvement in the baseline SALT score; *n* (%)	_____	1/19 (5.3)	1/17 (5.9)	1/14 (7.1)	0/9 (0.0)
Patients achieving a 75%-89% improvement in the baseline SALT score; *n* (%)	_____	2/19 (10.5)	2/17 (11.8)	0/14 (0.0)	0/9 (0.0)
Patients achieving a 90%-99% improvement in the baseline SALT score; *n* (%)	_____	0 (0.0)	2/17 (11.8)	0/14 (0.0)	0/9 (0.0)
Patients achieving 100% improvement in the baseline SALT score (complete hair regrowth); *n* (%)	_____	0 (0.0)	4/17 (23.5)	8/14 (57.1)	5/9 (55.6)

AA-IGA, Alopecia areata − investigator global assessment; *n pts*, number of patients; *SALT*, severity of alopecia tool; *SD*, standard deviation.
**P* value = .0087 for comparison between week 4 and baseline.
***P* value < .0001 for comparison between week 16 and baseline.
****P* value < .0001 for comparison between week 28 and baseline.
*****P* value = .0018 for comparison between week 40 and baseline.
[†]Presumably the decrease in the delta SALT and the increase in the mean SALT score between weeks 28 and 40 were due to the low number of patients achieving 40 weeks of observation and the great variability of SALT values in this small patient cohort. Clinically they might be explained by the fact that a proportionally higher number of patients showed poor response at week 40 (relatively higher percentage of patients with 3-4 IGA scores and lower percentage of patients with an at least 50%-improvement in SALT score) compared with week 28.

SALT scoring and sex (Prob > F = 0.04; Adj R-squared = 0.34).

A rapid and diffuse hair regrowth, with a greater improvement in SALT score, was detected in patients with high serum IgE levels (>100 kU/L) and/or with personal history of noncutaneous atopic comorbid conditions, who represented 7 out of 9 cases (77.8%) obtaining an at least $SALT_{50}$ response through the 40-week treatment period.

In this subcohort of patients an immune pathogenic mechanism skewed toward the type 2 inflammation, might be responsible for AA and, thereby, the inhibition of JAK-1 by upadacitinib or baricitinib, a JAK 1/2 inhibitor recently approved for the treatment of both conditions, may be advantageous in obtaining a marked suppression of type 2 inflammation together with the signal mediated by IFN-γ.[4] This study owns some limitations that include the relatively small number of patients, the short period of observation, gender skew, limited generalizability to broader AA population, and the retrospective and ad-interim analysis which did not allow obtaining the same treatment duration for all patients, causing great variability in terms of number of patients observed at each time point.

This study and the eCRF platform were promoted and supported by the Italian Society of Dermatology, SIDeMaST (Società Italiana di Dermatologia e Malattie Sessualmente Trasmesse).

The authors received no external funding to perform this study. Study drug (upadacitinib) was provided by the manufacturer (AbbVie) through an expanded preapproval access program. AbbVie was provided courtesy presubmission proof reading with final content that was determined by the authors.

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Funding sources: None.

IRB approval status: Reviewed and approved by Ethical Committee - Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore, Prot N.: 4434.

Patient consent: Obtained by all patients according to IRB requirements.

Key words: alopecia areata; atopic dermatitis; eczema; JAK inhibitors; SALT score; upadacitinib.

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Conflicts of interest

None declared for the authors with the exception of Ketty Peris who has served on advisory board, received honoraria for lectures and/or research grants for AbbVie, Almirall, Lilly, Galderma, Leo Pharma, Pierre Fabre, Novartis, Sanofi, Sun Pharma, Janssen; Andrea Chiricozzi who served as advisory board member and consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Almirall, Leo Pharma, Lilly, Janssen, Novartis, Pfizer, and Sanofi Genzyme; Maria Concetta Fargnoli has served on advisory boards, received honoraria for lectures and research grants from AMGEN, Almirall, Abbvie, BMS, Galderma, Kyowa Kyrin, Leo Pharma, Pierre Fabre, UCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi-Regeneron, Sunpharma; Maria Esposito who served as advisory board member, speaker and consultant and has participated in clinical trials for AbbVie, Almirall, Leo Pharma, Eli Lilly, Janssen, Novartis, and Sanofi Genzyme, UCB; Cataldo Patruno who served as advisory board member and consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Amgen, Eli Lilly, Leo Pharma Novartis, Pfizer, Pierre Fabre, Sanofi.

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https://doi.org/10.1016/j.jaad.2023.05.001

Alopecia areata clinical trial enrollment and retention outcome factors among underrepresented ethnic and racial groups: A cross-sectional study

To the Editor: Although Hispanic and Black patients have greater lifetime incidence of alopecia areata (AA) compared with White patients in the United States, the etiology and pathology of this disparity are not well characterized, likely due to lack of inclusion in clinical trials.[1,2] Furthermore, data on enrollment and retention rates across underserved groups are limited.[1] Therefore, we sought to examine enrollment