Check for updates

Wiley
Dermatologic Therapy
Volume 2025, Article ID 5548750, 10 pages
https://doi.org/10.1155/dth/5548750

WILEY

Research Article

Effectiveness and Safety of JAK Inhibitors in Patients With Atopic Dermatitis Unresponsive Versus Naïve to Dupilumab: A Multicentric Real-World Retrospective Study

Filip Rob,[1] **Jan Hugo**,[2] **Jiří Horaždovský**,[3] **Yvetta Vantuchová**,[4] **Jarmila Čelakovská**,[5] **Lucie Jarešová**,[6] **Marie Policarová**,[7] **Jan Šternberský**,[8,9] **Martina Kojanová**,[10] **Petra Cetkovská**,[11] **Terézia Thomová**,[12] **Kristýna Sokolová**,[1] **Jan Finsterle**,[2] **Hana Janatová**,[3] **Lenka Tomaško**,[4,11] **Lenka Čáková**,[5] **Martin Tichý**,[8,9] **Martin Cetkovský**,[10] **and Michaela Nováková**[1]

[1]*Department of Dermatovenerology, Second Faculty of Medicine, Bulovka University Hospital, Charles University, Prague, Czech Republic*
[2]*Department of Dermatovenereology, Third Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic*
[3]*Department of Dermatology, Hospital Ceske Budejovice, Ceske Budejovice, Czech Republic*
[4]*Department of Dermatology, University Hospital Ostrava and Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic*
[5]*Department of Dermatology and Venereology, Faculty Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic*
[6]*DermaMedEst Pro, Prague, Czech Republic*
[7]*Dermatology Department, Hospital Jihlava, Jihlava, Czech Republic*
[8]*Department of Dermatology and Venereology, Faculty of Medicine and Dentistry, Palacký University Olomouc, Olomouc, Czech Republic*
[9]*Department of Dermatology and Venereology, University Hospital Olomouc, Olomouc, Czech Republic*
[10]*Department of Dermatovenereology, First Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic*
[11]*Department of Dermatovenereology, Faculty of Medicine and University Hospital in Pilsen, Charles University, Pilsen, Czech Republic*
[12]*1st Department of Dermatovenereology, St. Anne's University Hospital Brno, Brno, Czech Republic*

Correspondence should be addressed to Filip Rob; filip.rob@bulovka.cz

Received 27 February 2025; Revised 21 August 2025; Accepted 2 September 2025

Academic Editor: Suraiya Saleem

Copyright © 2025 Filip Rob et al. Dermatologic Therapy published by John Wiley & Sons Ltd. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Introduction: Janus kinase (JAK) inhibitors are novel therapies for atopic dermatitis (AD); however, only limited data exist on their effectiveness in patients with previous failures in biological treatment.
Methods: Patients with moderate-to-severe AD and having completed a minimum of 16 weeks of JAK inhibitor therapy were divided into subgroups based on prior dupilumab exposure: those without prior exposure and those whose treatment was discontinued due to lack of efficacy (dupilumab nonresponders [DNR]). Eczema Area and Severity Index (EASI), DLQI, and Itch Numeric Rating Scale (Itch NRS) changes from baseline were assessed in Weeks 16 and 24 (when available). Adverse events during the follow-up were recorded.
Results: In total, 241 patients were included; 148 received upadacitinib (99 dupilumab-naïve, 49 post-dupilumab failure), 47 were with baricitinib (32 dupilumab-naïve, 15 post-dupilumab failure), and 46 received abrocitinib (35 dupilumab-naïve, 11 post-dupilumab failure). At Week 16, an EASI-75 response in the upadacitinib group was achieved in 86% naïve versus 82% DNR

patients, 91% naïve versus 73% DNR patients in the abrocitinib group, and 81% naïve versus 67% DNR in the baricitinib group. Itch NRS ≥ 4-point reduction was achieved in 82% naïve versus 76% DNR patients on upadacitinib, 83% naïve versus 91% DNR patients on abrocitinib, and 72% naïve versus 40% DNR patients on baricitinib.
Conclusion: In conclusion, our retrospective analysis suggests that previous dupilumab failure did not significantly affect the short-term effectiveness of JAK inhibitor therapy for AD.

Keywords: abrocitinib; atopic dermatitis; baricitinib; dupilumab; upadacitinib

1. Introduction

Atopic dermatitis (AD) is a chronic skin disease common in young children but can occur at any age [1]. Historically, therapeutic options for severe disease manifestations were limited to phototherapy and conventional systemic treatments. A significant change occurred with dupilumab, the first targeted treatment, which blocks interleukin (IL)-4 and IL-13. However, despite dupilumab treatment, a subset of patients shows limited improvement in AD [2, 3]. The arrival of Janus kinase (JAK) inhibitors meant new hope for effective treatment for these patients. In clinical studies, JAK inhibitors, including abrocitinib, baricitinib, and upadacitinib, have shown effectiveness in patients previously treated with dupilumab [4–6]. However, these studies did not differentiate between patients who discontinued dupilumab due to treatment failure and those who terminated treatment for other reasons.

Recent real-world studies have evaluated the effectiveness of JAK inhibitors (e.g., upadacitinib and abrocitinib) following dupilumab treatment [7–9]. This study compared the effectiveness of all available JAK inhibitors for AD therapy between patients who discontinued dupilumab therapy due to lack of effectiveness versus patients who were never exposed to dupilumab (or other biological treatments).

2. Materials and Methods

2.1. Study Population. This real-world retrospective study extracted effectiveness and safety data from 11 dermatologic centers in the Czech Republic between January 2022 and September 2024. The study included patients with moderate-to-severe AD who had at least one follow-up visit after starting treatment with JAK inhibitors. For the effectiveness analysis, only patients who completed at least 16 weeks of JAK inhibitor therapy in on-label dosing (abrocitinib 100 mg/daily or 200 mg/daily, baricitinib 2 mg/daily or 4 mg/daily, and upadacitinib 15 mg/daily or 30 mg/daily) were included. These patients were divided into two subgroups based on their current therapy: those who were naïve to dupilumab and those who discontinued dupilumab treatment due to lack of efficacy (both primary and secondary dupilumab nonresponders [DNR]) before starting JAK inhibitors. The study did not include patients who had dupilumab discontinued for another reason (e.g., an adverse effect or intolerance).

2.2. Data Collection and Outcomes. Baseline personal and demographic data (including body mass index, BMI), AD duration, AD phenotype, presence of atopic comorbidities, and previous AD treatment (phototherapy, conventional systemic, or biologic therapy) were gathered for each patient. The Eczema Area and Severity Index (EASI), Itch Numeric Rating Scale (Itch NRS), and Dermatology Life Quality Index (DLQI) were collected at Weeks 0, 16, and 24 (if available) of therapy. In addition, clinical effectiveness was evaluated using EASI-50, -75, and -90 at each time point. In our analysis patients could stop treatment for ineffectiveness after 16 weeks, the earliest point allowed by national reimbursement criteria. A review of each patient's medical records throughout the observation period was conducted to evaluate treatment safety, with a focus on the incidence of adverse events. All adverse events were studied to check if they could be classified as serious according to the International Council for Harmonisation (ICH) E6 (R2) Good Clinical Practice Guidelines [10].

2.3. Statistical Analysis. Descriptive statistics were used to present baseline patient and treatment characteristics. Continuous variables were compared between patient groups using one-way analysis of variance (ANOVA) for parametric and Mann–Whitney U tests for nonparametric distributions. We used chi-square tests (Pearson's or Fisher's test when there were < 5 observations) for binomial outcome measures and Student's t-test for continuous outcome measures, as appropriate. A two-tailed p-value < 0.05 was considered significant (MedCalc software Version 22, MedCalc Software Ltd, Belgium).

3. Results

3.1. Study Population. In total, 241 patients were included: 148 were treated with upadacitinib (99 dupilumab naïve—DNI, 49 DNR), 47 were treated with baricitinib (32 DNI, 15 DNR), and 46 were treated with abrocitinib (35 DNI, 11 DNR). Across all groups, the distribution of men and women was approximately equal. However, a significantly higher proportion of men (73%) was found in the groups of patients on abrocitinib and baricitinib who were nonresponders to dupilumab. In patients treated with upadacitinib and baricitinib, the average patient age was approximately 36 years; patients treated with abrocitinib were, on average, slightly older (40 years). The mean BMI was very similar in all groups, ranging from 25 to 27. The average duration of AD was approximately 30 years, suggesting that most patients had AD since their childhood. Across all study groups, more than half of the patients had a generalized form of AD, followed by an erythrodermic

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

form; flexural and nummular forms of AD were observed less frequently. Atopic comorbidities were frequent in all study groups, including food allergies, rhinitis, and bronchial asthma. Fewer patients had a history of eye comorbidities. Almost all patients had a history of systemic cyclosporine therapy; roughly half had undergone previous phototherapy, and a minority had a history of methotrexate treatment. Overall, for all types of treatment, patient subgroups had very similar demographic and disease characteristics (Table 1).

3.2. Effectiveness. At Week 16, the mean EASI score for DNI patients in the upadacitinib group was 3.4 (range 0–25.0), and 3.1 (range 0–25.0) for DNR patients. Similarly, at Week 24, the mean EASI was 3.5 (range 0–22.5) for DNI patients and 3.4 (range 0–18.4) for DNR patients. The mean Itch NRS was 2 (range 0–8) in both DNI and DNR groups at Weeks 16 and 24. At Week 16, the mean DLQI for DNI patients was 4 (range 0–23) and 3 (range 0–17) for DNR patients; both groups exhibited a mean score of 4 at Week 24.

In patients using abrocitinib, the mean EASI was 2.9 (range 0–11.2) for DNI patients versus 3.1 (range 0–7.8) for DNR patients at Week 16. At Week 24, the mean EASI for DNI patients was 2.3 (range 0–6.4) versus 2.5 (range 0–5.8) for DNR patients. The mean Itch NRS score was 2 (range 0–7) for DNI patients and 1 (range 0–4) for DNR patients at Week 16, and 2 in both groups at Week 24. The mean DLQI scores at 16 weeks were 3 (range 0–14) for DNI patients and 5 (range 0–11) for DNR patients; at 24 weeks, these scores were 2 (range 0–11) and 4 (range 0–11), respectively.

Among participants treated with baricitinib, mean EASI scores at Week 16 were 6.6 (range 0–42.9) and 6.9 (range 0–26.0) for DNI and DNR patients, respectively; at Week 24, these values were 4.8 (range 0–28.0) and 8.9 (range 0–30.5), respectively. At Week 16, the mean itch score was 3 (range 0–10) for DNI patients and 4 (range 0–9) for DNR; at Week 24, these values were 2 (range 0–7) and 4 (range 0–10), respectively. The mean DLQI score was 6 (range 0–26) in DNI patients and 5 (range 0–12) in DNR patients after 16 weeks, and 5 (range 0–20) and 4 (range 0–16), respectively, after 24 weeks (Table 2).

After 16 weeks of therapy, EASI-75 responses were slightly higher (but not statistically significant) for dupilumab-naïve patients treated with upadacitinib (86% vs. 82%), abrocitinib (91% vs. 73%), and baricitinib (81% vs. 67%). Similarly, EASI-90 was achieved in 60% of DNI patients and 55% of DNR patients treated with upadacitinib, compared to 57% vs. 64% of patients treated with abrocitinib and 50% and 33% treated with baricitinib, respectively (Figure 1).

Improvement in quality of life (QoL), defined as ≥ 4-point reduction in DLQI, was observed in 89% of DNI patients and 98% of DNR patients receiving upadacitinib after 16 weeks. Similar improvements were seen in 97% of DNI and 100% of DNR patients treated with abrocitinib and 88% and 93% of patients treated with baricitinib, respectively (Figure 1).

At 16 weeks, a significant reduction in itch (Itch NRS ≥ 4 points) was observed in 82% of the DNI group and 76% of the DNR group treated with upadacitinib; 83% of the DNI group and 91% of the DNR group treated with abrocitinib; and 72% of the DNI group and 40% of the DNR group treated with baricitinib (Figure 1).

3.3. Safety. During the first 16 weeks of treatment, 31.8% of patients treated with updacitinib, 41.3% of patients treated with abrocitinib, and 17.0% of patients treated with baricitinib experienced at least one adverse event. The most common adverse events in the upadacitinib group were acne (9.5%), hyperlipidemia (6.1%), and herpes simplex infection (4.8%). In the abrocitinib group, hyperlipidemia (15.2%), herpes simplex infection (8.7%), headache (4.3%), and bacterial skin infections (4.3%) were the most common adverse events. The most common adverse events in patients treated with baricitinib were hyperlipidemia (10.6%), upper respiratory tract infections (6.4%), and herpes simplex infection (4.3%). Only two serious adverse events occurred in participants receiving upadacitinib: one case of facial herpes zoster necessitating hospitalization and one instance of jaw inflammation requiring both hospitalization and surgical intervention (Table 3). All patients completed at least 16 weeks of treatment. After a 16-week treatment period, 3 of 32 (9.4%) baricitinib-treated patients naïve to dupilumab and 1 of 15 (6.7%) patients treated with baricitinib who had previously failed dupilumab therapy discontinued treatment owing to a lack of efficacy. None of the patients on abrocitinib or upadacitinib discontinued treatment within the first 24 weeks of therapy.

4. Discussion

In this real-world study, we aimed to investigate whether prior dupilumab failure affects the effectiveness of subsequent JAK inhibitor therapy. Dupilumab is generally well-tolerated in the long term with a very good safety profile; however, a subset of patients exhibits inadequate response, necessitating alternative therapeutic strategies. In a recent real-world study, which included 1286 patients with AD who were treated with dupilumab for up to 5 years, 24% discontinued therapy after a median of 54 weeks. A similar proportion of patients discontinued treatment due to adverse effects (7.6%) or ineffectiveness (6.6%) [3]. A retrospective study of 709 patients with severe AD treated with dupilumab yielded similar outcomes. In this study, 13.6% of patients discontinued treatment exclusively due to primary or secondary ineffectiveness within 5 years of treatment [11]. However, it is important to note that many of these studies were conducted at a time when dupilumab was the only targeted therapy for AD. Therefore, some patients may have remained on treatment despite suboptimal effects because of a lack of alternative therapies.

Several considerations influence the choice of therapy in AD, including drug characteristics (short- and long-term effectiveness, onset of action, safety), patient characteristics (age, comorbidities, family planning in women), and disease

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline demographic and clinical characteristics of the study participants.

Characteristics	Upadacitinib (dupi-naïve, $n = 99$)	Upadacitinib (dupi-nonresponders, $n = 49$)	Baricitinib (dupi-naïve, $n = 32$)	Baricitinib (dupi-nonresponders, $n = 15$)	Abrocitinib (dupi-naïve, $n = 35$)	Abrocitinib (dupi-nonresponders, $n = 11$)
Female, *n* (%)	51 (51.5)	21 (42.9)	17 (53.1)	4 (26.7)	16 (45.7)	3 (27.3)
Age, mean (range), years	37 (17–67)	36 (16–66)	36 (20–62)	36 (19–76)	41 (20–68)	40 (25–64)
BMI, mean (range)	26.7 (16.7–43.8)	26.2 (17.0–35.2)	24.6 (17.6–40.1)	25.3 (19.6–30.8)	26.4 (19.5–36.0)	27.2 (20.0–40.9)
AD duration, mean (range), years	34 (13–55)	31 (5–58)	29 (5–51)	28 (5–49)	35 (9–60)	29 (4–60)
Clinical phenotype of AD, *n* (%)						
Generalized	57 (57.8)	25 (51.0)	17 (53.1)	8 (53.3)	22 (62.9)	9 (81.8)
Nummular	10 (10.1)	7 (14.3)	2 (6.3)	2 (13.3)	3 (8.6)	0 (0.0)
Erythroderma	27 (27.3)	13 (26.5)	8 (25.0)	5 (33.3)	6 (17.1)	2 (18.2)
Flexural	5 (5.1)	4 (8.2)	5 (15.6)	0 (0.0)	4 (11.4)	0 (0.0)
Atopic comorbidities, *n* (%)						
Food allergy	35 (35.4)	23 (46.9)	13 (40.6)	10 (66.7)	18 (51.4)	3 (27.3)
Asthma	31 (31.1)	23 (46.9)	12 (37.5)	10 (66.7)	18 (51.4)	5 (45.5)
Rhinitis	43 (43.4)	19 (38.8)	17 (53.1)	11 (73.3)	17 (48.6)	3 (27.3)
Allergic conjunctivitis	16 (16.2)	13 (26.5)	6 (18.8)	4 (26.7)	5 (14.3)	1 (9.1)
Prior systemic therapy, *n* (%)						
UVB phototherapy	51 (51.5)	22 (44.9)	12 (37.5)	11 (73.3)	15 (42.9)	6 (54.5)
Cyclosporine	97 (98.0)	49 (100.0)	30 (93.8)	15 (100.0)	34 (97.1)	11 (100.0)
Methotrexate	5 (5.1)	5 (10.2)	2 (6.3)	2 (13.3)	1 (2.9)	3 (27.3)
Dupilumab	0 (0.0)	49 (100.0)	0 0 (0.0)	15 (100.0)	0 (0.0)	11 (100.0)

Abbreviations: AD, atopic dermatitis; BMI, body mass index.

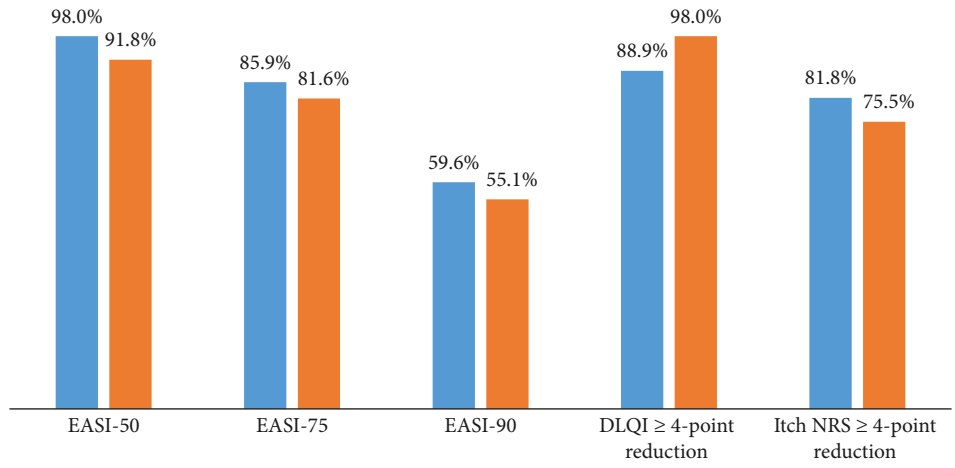
dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Fiilp - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Treatment baseline and efficacy outcomes.

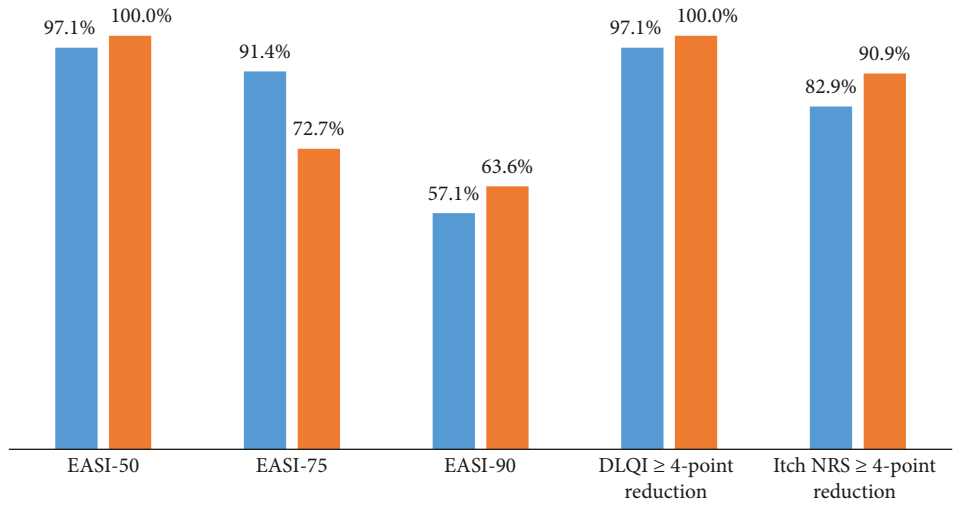
Characteristics	Upadacitinib (dupi-naïve)	Upadacitinib (dupi-nonresponders)	Baricitinib (dupi-naïve)	Baricitinib (dupi-nonresponders)	Abrocitinib (dupi-naïve)	Abrocitinib (dupi-nonresponders)
Baseline						
Mean EASI (range)	28.2 (16.0–51.5)	23.6 (10.0–46.0)	28.5 (18.6–51.0)	26.1 (20.4–33.5)	28.5 (21.0–56.6)	26.5 (18.2–41.2)
Mean DLQI (range)	18 (5–28)	15 (3–29)	18 (8–30)	13 (0–25)	19 (10–30)	18 (13–29)
Mean Itch NRS (range)	8 (0–10)	7 (0–10)	8 (2–10)	7 (4–10)	8 (0–10)	7 (0–10)
Week 16						
Mean EASI (range)	3.4 (0–25.0)	3.1 (0–25.0)	6.6 (0–42.9)	6.9 (0–26.0)	2.9 (0–11.2)	3.1 (0–7.8)
Mean DLQI (range)	4 (0–23)	3 (0–17)	6 (0–26)	5 (0–12)	3 (0–14)	5 (0–11)
Mean Itch NRS (range)	2 (0–8)	2 (0–8)	3 (0–10)	4 (0–9)	2 (0–7)	1 (0–4)
Week 24						
Mean EASI (range)	3.5 (0–22.5)	3.4 (0–18.4)	4.8 (0–28.0)	8.9 (0–30.5)	2.3 (0–6.4)	2.5 (0–5.8)
Mean DLQI (range)	4 (0–21)	4 (0–24)	5 (0–20)	4 (0–16)	2 (0–11)	4 (0–11)
Mean Itch NRS (range)	2 (0–8)	2 (0–6)	2 (0–7)	4 (0–10)	2 (0–4)	2 (0–7)

Abbreviations: DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; NRS, Numeric Rating Scale.

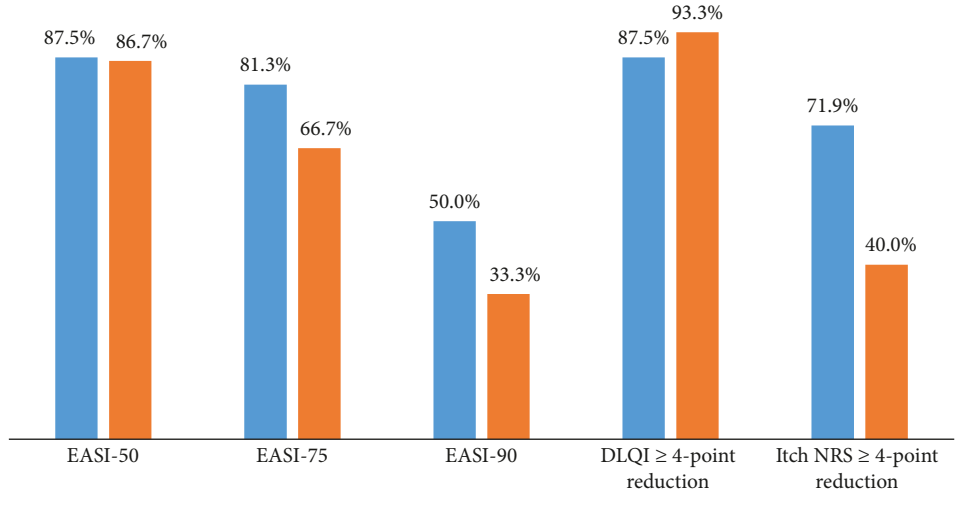
dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Fiilp - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(a)



(b)



(c)

Figure 1: Treatment response after 16 weeks on JAK inhibitor therapy by subgroups based on prior dupilumab exposure. $^{*}p < 0.05$, EASI (Eczema Area and Severity Index), DLQI (Dermatology Life Quality Index), NRS (Numeric Rating Scale).

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Safety profile—adverse events during first 16 weeks of treatment.

Variable	Upadacitinib	Abrocitinib	Baricitinib
At least one adverse event	47/148 (31.8%)	19/46 (41.3%)	8/47 (17.0%)
Serious adverse event*	2 (1.4%)	0 (0.0%)	0 (0.0%)
Adverse event type			
Acne	14 (9.5%)	0 (0.0%)	0 (0.0%)
Upper respiratory tract infection	4 (2.7%)	1 (2.2%)	3 (6.4%)
COVID-19	1 (0.7%)	0 (0.0%)	0 (0.0%)
Bacterial skin infection	1 (0.7%)	2 (4.3%)	1 (2.1%)
Herpes simplex infection	7 (4.8%)	4 (8.7%)	2 (4.3%)
Shingles	2 (1.4%)	0 (0.0%)	0 (0.0%)
Mucocutaneous fungal infections	1 (0.7%)	0 (0.0%)	0 (0.0%)
Headache	2 (1.4%)	2 (4.3%)	0 (0.0%)
Muscle pain	4 (2.7%)	0 (0.0%)	1 (2.1%)
Urticaria	1 (0.7%)	0 (0.0%)	0 (0.0%)
Conjunctivitis	1 (0.7%)	1 (2.2%)	0 (0.0%)
NMSC	1 (0.7%)	0 (0.0%)	0 (0.0%)
Facial erythema	0 (0.0%)	1 (2.2%)	0 (0.0%)
Rosacea	0 (0.0%)	1 (2.2%)	0 (0.0%)
Alopecia areata	0 (0.0%)	1 (2.2%)	0 (0.0%)
Nausea	0 (0.0%)	1 (2.2%)	0 (0.0%)
Jaw bacterial infection	1 (0.7%)	0 (0.0%)	0 (0.0%)
Anemia	1 (0.7%)	0 (0.0%)	0 (0.0%)
Hyperlipidemia	9 (6.1%)	7 (15.2%)	5 (10.6%)
Creatine kinase elevation	4 (2.7%)	0 (0.0%)	0 (0.0%)

Abbreviation: NMSC, nonmelanoma skin cancer.
*Serious adverse events on upadacitinib (1x herpes zoster of face, 1x bacterial infection of jaw).

characteristics (AD phenotype, extent of skin diseases, severity of itch). Moreover, patient preference for oral over injectable treatments, coupled with cost and insurance coverage limitations, may influence treatment selection. Given the multitude of factors affecting systemic treatment selection, collaborative decision-making between patient and physician is important [12]. However, in the event of treatment failure, the primary goal for these difficult-to-treat patients is to offer an alternative therapeutic approach that maximizes the likelihood of disease control. In our practice, we lack evidence on whether it is more appropriate for patients who fail biological therapy to switch to another biological agent or to change treatment to JAK inhibitors and vice versa.

A few small retrospective studies are looking at the effectiveness of tralokinumab (anti-IL-13 monoclonal antibody) in patients who had adverse effects or were unresponsive to dupilumab. George and Yu reported a series of 27 patients in whom partial (IGA 1 or 2) or complete remission was achieved in 59% after 6 months, and 41% showed no improvement with tralokinumab treatment [13]. In a comparable cohort of 25 dupilumab-discontinued patients, Fossati et al. documented that 52% of patients who subsequently received tralokinumab remained on treatment, with a median treatment duration of 47 weeks. Six patients (24%) discontinued tralokinumab therapy due to ineffective initial treatment; three (12%) additional patients discontinued due to loss of treatment effectiveness [14]. In the third case series, 50% of the 17 patients exhibiting treatment resistance to dupilumab or upadacitinib achieved an EASI-75 response at 16 weeks following tralokinumab administration [15]. Based on these limited data, it appears that approximately 50% of patients an exhibiting inadequate response to dupilumab have a satisfactory therapeutic response upon transitioning to tralokinumab. No real-world studies have investigated the transition from dupilumab to lebrikizumab.

Similarly, we have limited data on patients with insufficient dupilumab effectiveness who switched to JAK inhibitors. A study by Boesjes et al. analyzed the results of upadacitinib in patients who were either naive to dupilumab or had been good responders to it (24 patients) versus those who were DNR (23 patients). No significant differences in disease severity (EASI), itch, or QoL (DLQI) were observed between groups over the study period. The mean EASI after 16 weeks was 6.5 (range 4.0–8.9) for DNR and 4.8 (range 3.3–6.3) for dupilumab-naïve patients. However, the results showed that after 16 weeks of upadacitinib treatment, 22% of nonresponders to dupilumab and 38% of patients naive (or with a good response in the past) to dupilumab did not continue treatment with upadacitinib [7]. An Italian study compared a cohort of 73 dupilumab-exposed patients (various reasons for discontinuation) to 40 dupilumab-naïve patients who received upadacitinib. The authors reported no significant differences between the two groups up to Week 52 in either EASI, Itch, or QoL (DLQI). After 16 weeks, EASI-75 achieved 85% and EASI-90 76% of the patients [8].

Tong et al. reported an EASI-75 response in 29% (5 of 16) of patients who had previously inadequate responses to dupilumab after 12 weeks of treatment with abrocitinib [9]. Another study on 25 patients who previously failed therapy with dupilumab or tralokinumab showed much better

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

results, with 76% achieving EASI-75 after 16 weeks of abrocitinib therapy. This study's findings align with ours, demonstrating that 73% of DNR achieved EASI-75 [16].

In our study, only baricitinib showed some differences between dupilumab-naive patients and those who failed dupilumab. Baricitinib was less effective after 16 weeks in DNR, particularly for higher therapeutic targets such as EASI-90. The mean baseline EASI was comparable among patients receiving different JAK inhibitors. At 16 weeks, the mean EASI for patients on baricitinib was approximately twice that of patients on abrocitinib and upadacitinib in both subgroups. After 24 weeks of baricitinib, only dupilumab-naive patients showed further EASI improvement compared to those who had failed dupilumab. These findings align with a recent meta-analysis examining the efficiency of JAK inhibitors in real-world settings, which reported that baricitinib had the lowest average reduction in EASI [17].

Itch is the most bothersome symptom for most AD patients. Itchy skin impairs QoL and quality of sleep and, thus, patient productivity. Rapid relief of itching is very important for most patients. Our findings indicate substantial relief from itching in all patient groups treated with JAK inhibitors after 16 and 24 weeks, irrespective of prior failure with dupilumab treatment. These data are consistent with other studies demonstrating no discernible difference in JAK inhibitor effectiveness against itch in patients who failed on dupilumab [7–9, 16]. A single study investigated the effectiveness of switching from dupilumab to tralokinumab for itch; however, only 40% of participants experienced a significant improvement [15]. In our analysis, the reduction in itch was observed across all groups, with only baricitinib showing a significant difference between patients who had failed and those who were naïve to dupilumab. After 16 weeks of baricitinib, a ≥ 4-point reduction in Itch NRS was achieved in significantly fewer patients following dupilumab failure (40.0% vs. 71.9%, $p = 0.04$).

JAK inhibitor treatment is associated with typical adverse events. In our cohort, no statistically significant difference in adverse events was observed between dupilumab-naive and dupilumab-experienced patients. Patients experienced common adverse events, including acne, herpes simplex infections, upper respiratory tract infections, and hyperlipidemia. Findings from this retrospective work suggest a favorable short-term safety profile of JAK inhibitors for patients with AD, a conclusion supported by other real-world studies [18–20].

Our study has a few limitations. The number of patients on abrocitinib and baricitinib therapy is low. Furthermore, patients on all three therapies could use in-label doses or adjust dosages as needed during the study period. Patients who were lost to follow-up after starting JAK inhibitor treatment were excluded from the analysis, which could also have been due to ineffectiveness or adverse events. In our analysis, patients could stop treatment for ineffectiveness after 16 weeks, the earliest point allowed by national reimbursement criteria. The strength of our study is that it compares several drugs in the same population and monitors not only the clinical extent and severity of the disease (EASI) but also the effect on QoL and reduction of itch.

In conclusion, our retrospective analysis suggests that previous dupilumab failure did not significantly affect the short-term effectiveness of JAK inhibitor therapy for AD. Long-term data are needed to guide physicians in adjusting AD-targeted therapies.

Data Availability Statement

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Ethics Statement

This study was reviewed and approved by the University Hospital Ethics Committee, approval number 3.12.2024/11213/EK-Z. Since we used anonymized routine data, participants did not need informed consent.

Conflicts of Interest

Filip Rob has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, Amgen, BMS, Eli Lilly, Janssen, Leo Pharma, MSD, Novartis, Pfizer, Sanofi Genzyme, and UCB.

Jan Hugo has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB.

Jiří Horaždovský has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Janssen, Leo Pharma, MSD, Novartis, Pfizer, Sanofi Genzyme, and UCB.

Yvetta Vantuchová declares no conflicts of interest.

Jarmila Čelakovská declares no conflicts of interest.

Lucie Jarešová received honoraria as a speaker, investigator, and/or consultant for AbbVie, Amgen, Leo Pharma, Sanofi, Novartis, Pfizer, and Johnson & Johnson.

Marie Policarová received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Leo Pharma, Novartis, Sanofi Genzyme, UCB, and Janssen.

Jan Šternberský has received honoraria as a speaker, investigator, and/or consultant for AbbVie, BMS, Eli Lilly, Janssen, Leo Pharma, Novartis, Sanofi Genzyme, and UCB.

Martina Kojanová has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB.

Petra Cetkovská has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Janssen, Leo Pharma, MSD, Novartis, Pfizer, Sanofi Genzyme, and UCB.

Terézia Thomová has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Pfizer, and Sanofi Genzyme.

Kristýna Sokolová has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, Pfizer, and Sanofi Genzyme.

Jan Finsterle has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Belupo, Leo

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Pharma, NextForce, Novartis, PearsHealthCyber, Sanofi, and UCB.

Hana Janatová has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Amgen, Eli Lilly, Janssen, and UCB.

Lenka Tomaško declares no conflicts of interest.

Lenka Čáková declares no conflicts of interest.

Martin Tichý has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Almirall, BMS, Eli Lilly, Janssen, Leo Pharma, Novartis, Sanofi Genzyme, and UCB.

Michaela Nováková has received honoraria as a speaker, investigator, and/or consultant for AbbVie, Celgene, Johnson & Johnson, Kenvue, LEO Pharma, Lilly, L'Oréal, Novartis, Pfizer, Sanofi, UCB, and Wörwag Pharma.

Author Contributions

Filip Rob contributed to the conception and design of the work, acquisition, analysis, and interpretation of data for the work, and drafting and revising of the submitted work. Jan Hugo, Jiří Horaždovský, Yvetta Vantuchová, Jarmila Čelakovská, Lucie Jarešová, Marie Policarová, Jan Šternberský, Martina Kojanová, Petra Cetkovská, Terézia Thomová, Kristýna Sokolová, Jan Finsterle, Hana Janatová, Lenka Tomaško, Lenka Čáková, Martin Tichý, and Michaela Nováková participated in the acquisition, interpretation of the data, preparation, and critical review of the manuscript and approved the final version of the manuscript.

Funding

The authors received no specific funding for this work.

Acknowledgments

The authors sincerely thank all participating dermatologists for their valuable contributions and collaboration in this study, including Jorga Fialová, Natálie Kunešová, and others.

References

[1] H. A. Hadi, A. I. Tarmizi, K. A. Khalid, M. Gajdács, A. Aslam, and S. Jamshed, "The Epidemiology and Global Burden of Atopic Dermatitis: A Narrative Review," *Life* 11, no. 9 (2021): 936, https://doi.org/10.3390/life11090936.

[2] C. Linder, J. Shourick, A. T. Touhouche, et al., "Analysis of Non-Responders to Dupilumab in Clinical Practice: A Cohort Study," *Journal of the European Academy of Dermatology and Venereology: JEADV* 35, no. 3 (2021): 192–194, https://doi.org/10.1111/jdv.16900.

[3] C. M. Boesjes, E. Kamphuis, M. de Graaf, et al., "Long-Term Effectiveness and Reasons for Discontinuation of Dupilumab in Patients With Atopic Dermatitis," *JAMA Dermatology* 160, no. 10 (2024): 1044–1055, https://doi.org/10.1001/jamadermatol.2024.2517.

[4] E. L. Simpson, J. Lacour, L. Spelman, 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," *British Journal of Dermatology* 183, no. 2 (2020): 242–255, https://doi.org/10.1111/bjd.18898.

[5] J. P. Thyssen, D. Thaçi, T. Bieber, et al., "Upadacitinib for Moderate-To-Severe Atopic Dermatitis: Stratified Analysis From Three Randomized Phase 3 Trials by Key Baseline Characteristics," *Journal of the European Academy of Dermatology and Venereology: JEADV* 37, no. 9 (2023): 1871–1880, https://doi.org/10.1111/jdv.19232.

[6] E. L. Simpson, R. Sinclair, S. Forman, et al., "Efficacy and Safety of Abrocitinib in Adults and Adolescents With Moderate-to-Severe Atopic Dermatitis (JADE MONO-1): A Multicentre, Double-Blind, Randomised, Placebo-Controlled, Phase 3 Trial," *Lancet* 396, no. 10246 (2020): 255–266, https://doi.org/10.1016/s0140-6736(20)30732-7.

[7] C. M. Boesjes, L. F. Van der Gang, N. P. Zuithoff, et al., "Effectiveness of Upadacitinib in Patients With Atopic Dermatitis Including Those With Inadequate Response to Dupilumab and/or Baricitinib: Results from the BioDay Registry," *Acta Dermato-Venereologica* 103 (2023): adv00872, https://doi.org/10.2340/actadv.v103.5243.

[8] M. Napolitano, S. M. Ferrucci, L. Foggia, et al., "Comparison of Long-Term Effectiveness and Safety of Upadacitinib for Atopic Dermatitis Between Dupilumab-Exposed and Dupilumab-Naïve Patients," *Clinical Drug Investigation* 44, no. 1 (2024): 71–77, https://doi.org/10.1007/s40261-023-01336-w.

[9] Z. Tong, Y. Zhang, K. Zhou, et al., "An Observational Study of Abrocitinib in Adults With Moderate-to-Severe Atopic Dermatitis After Switching From Dupilumab," *Journal of the American Academy of Dermatology* 89, no. 4 (2023): 826–828, https://doi.org/10.1016/j.jaad.2023.05.077.

[10] European Medicines Agency, *ICH E6 (R2) Good Clinical Practice* (European Medicines Agency, 2016).

[11] F. Barei, P. Calzari, L. Valtellini, et al., "Five-Year Real-World Drug Survival of Dupilumab in Severe Atopic Dermatitis and Associate Predictors," *Journal of Dermatological Treatment* 35, no. 1 (2024): 2404718, https://doi.org/10.1080/09546634.2024.2404718.

[12] R. W. Kim, M. Lam, K. Abuabara, E. L. Simpson, and A. M. Drucker, "Targeted Systemic Therapies for Adults With Atopic Dermatitis: Selecting From Biologics and JAK Inhibitors," *American Journal of Clinical Dermatology* 25, no. 2 (2024): 179–193, https://doi.org/10.1007/s40257-023-00837-w.

[13] S. E. George and J. Yu, "Tralokinumab as an Effective Alternative After Dupilumab Treatment Failure in Moderate-to-Severe Atopic Dermatitis: A Real-World Study," *Journal of the American Academy of Dermatology* 91, no. 6 (2024): 1228–1230, https://doi.org/10.1016/j.jaad.2024.08.019.

[14] C. Fossati, E. Guenova, C. Conrad, M. Gilliet, and T. Seremet, "Single-Centre Experience With Tralokinumab in Dupilumab-Experienced and Naïve Patients With Atopic Dermatitis," *Journal of the European Academy of Dermatology and Venereology: JEADV* 39, no. 2 (2025): e184–e186, https://doi.org/10.1111/jdv.20348.

[15] N. Gori, E. Ippoliti, S. M. Ferrucci, et al., "Successful Response to Tralokinumab in Patients Unresponsive, Intolerant or With Contraindications to Dupilumab and JAK Inhibitors: A Case Series," *Journal of the European Academy of Dermatology and Venereology: JEADV* 38, no. 10 (2024): 852–854, https://doi.org/10.1111/jdv.19929.

[16] S. Keow and M. Abu-Hilal, "Effectiveness of Abrocitinib for the Treatment of Moderate-to-Severe Atopic Dermatitis in Patients Switched from Dupilumab and/or Tralokinumab: A

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Real-World Retrospective Study," *Journal of the American Academy of Dermatology* 91, no. 4 (2024): 734–735, https://doi.org/10.1016/j.jaad.2024.05.081.

[17] Y. Kim, G. Seo, J. J. Koopman, and J. Yee, "Real-World Effectiveness and Safety of JAK Inhibitors in Atopic Dermatitis: A Systematic Review and Meta-Analysis," *Clinical and Experimental Allergy: Journal of the British Society for Allergy and Clinical Immunology* (2025): cea.70125, https://doi.org/10.1111/cea.70125.

[18] L. Gargiulo, L. Ibba, F. Piscazzi, et al., "Effectiveness and Safety of Upadacitinib for Moderate-To-Severe Atopic Dermatitis in a Real-World Setting: A 52-Week Retrospective Study," *Journal of the European Academy of Dermatology and Venereology: JEADV* 38, no. 2 (2024): e152–e154, https://doi.org/10.1111/jdv.19507.

[19] I. Vittrup, J. Elberling, L. Skov, et al., "Short-Term Real-World Experience With Baricitinib Treatment in Danish Adults With Moderate-Severe Atopic Dermatitis," *Journal of the European Academy of Dermatology and Venereology: JEADV* 37, no. 4 (2023): e543–e546, https://doi.org/10.1111/jdv.18804.

[20] E. Kamphuis, C. M. Boesjes, L. Loman, et al., "Real-World Experience of Abrocitinib Treatment in Patients With Atopic Dermatitis and Hand Eczema: Up to 28-Week Results From the BioDay Registry," *Acta Dermato-Venereologica* 104 (2024): adv19454, https://doi.org/10.2340/actadv.v104.19454.

dth, 2025, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1155/dth/5548750 by Rob Filip - <Shibboleth>-member@cuni.cz , Wiley Online Library on [22/09/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License