

Effectiveness and Safety of Upadacitinib in Patients with Moderate-to-Severe Atopic Dermatitis and Previous Failures of Th2 Biologics: A Propensity Score-Matched Study

Francesca Barei,¹ Alessandra Chiei-Gallo,² Alessandra Narcisi,³ Ruggero Cascio Ingurgio,³ Piergiorgio Malagoli,⁴ Giampiero Girolomoni,⁵ Martina Maurelli,⁵ Elena Pezzolo,⁶ Claudio Sciarrone,⁷ Massimo Gola,⁸ Manfredi Magliulo,⁸ Paola Savoia,⁹ Elia Esposto,¹⁰ Anna G Burroni,¹¹ Fabrizio Amoruso,¹² Vittoria Giulia Bianchi,¹³ Santo R Mercuri,¹³ Francesca Satolli,¹⁴ Maria Beatrice De Felici Del Giudice,¹⁴ Paolo Pella,¹⁵ Roberto Pinto,² Gianluca Avallone,^{1,2} Carlotta Gurioli,^{16,17} Bianca Maria Piraccini,^{16,17} Anna Balato,¹⁸ Eugenia V Di Brizzi,¹⁷ Rosa Giuseppa Angileri,¹⁹ Flavia Manzo Margiotta,²⁰ Marco Romanelli,²⁰ Mariateresa Rossi,²¹ Mario Bruno Guanti,²² Giuseppe Lauretta,²³ Stefano Dastoli,²⁴ Cataldo Patruno,²⁴ Maddalena Napolitano,²³ Michela Ortoncelli,²⁵ Simone Ribero,²⁵ Angelo V Marzano^{1,2} and Silvia Ferrucci¹

¹ Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

² Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy

³ Dermatology Unit, IRCCS Humanitas Research Hospital, Milan, Italy

⁴ Department of Dermatology, Dermatology Unit Azienda Ospedaliera San Donato Milanese, Milan, Italy

⁵ Section of Dermatology, Department of Medicine, University of Verona, Verona, Italy

⁶ Dermatology Unit, Ospedale San Bortolo, Vicenza, Italy

⁷ Department of Dermatology, Papardo Hospital, Messina, Italy

⁸ Allergological and Pediatric Dermatology Unit, Department of Health Sciences, University of Florence, Florence, Italy

⁹ Department of Health Science, University of Eastern Piedmont, Novara, Italy

¹⁰ SCDU Dermatologia, AOU Maggiore della Carità, Novara, Italy

¹¹ Section of Dermatology, Department of Health Sciences (Di.S.Sal), University of Genoa, IRCCS-San Martino Polyclinic Hospital, Genoa, Italy

¹² Dermatology Unit, Azienda Ospedaliera di Cosenza, Cosenza, Italy

¹³ Dermatology and Cosmetology Unit, IRCCS San Raffaele Hospital, Milan, Italy

- 14 Unit of Dermatology, University of Parma, Parma, Italy
- 15 Oncology Department, Section of Dermatology, Degli Infermi Hospital, ASL BI, Biella, Italy
- 16 Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy
- 17 Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Italy
- 18 Dermatology Unit, University of Campania Luigi Vanvitelli, Naples, Italy
- 19 UOC Dermatologia, ARNAS Civico Di Palermo, Palermo, Italy
- 20 Department of Dermatology, University of Pisa, Pisa, Italy
- 21 Dermatology Unit Spedali Civili Hospital, Brescia, Italy
- 22 Azienda Ospedaliera Universitaria Policlinico di Modena, Struttura Complessa di Dermatologia, Modena, Italy
- 23 Section of Dermatology-Department of Clinical Medicine and Surgery, University of Naples Federico II, Napoli, Italy
- 24 Department of Medicine and Health Sciences "Vincenzo Tiberio", University of Molise, Campobasso, Italy
- 25 Dermatology Clinic, University of Turin, Turin, Italy

Corresponding author: Francesca Barei

Email: francesca.barei@policlinico.mi.it

Funding sources: This work was supported by Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan and by the Italian Ministry of Health.

Conflicts of interest: S.F. is principal investigator in clinical trial to Amgen, Sanofi, Novartis, Lilly, Leo Pharma, Abbvie and she is advisory board or speaker to Novartis, Menarini, Sanofi, Abbvie and Leo Pharma. F. Barei received honoraria from LeoPharma. M.B.G. received honoraria from Leopharma, Abbvie, Sanofi, Menarini, Novartis, Cantabria, Lilly, Pfizer. A.V. Marzano reports consultancy/advisory boards disease-relevant honoraria from AbbVie, Boehringer-Ingelheim, Novartis, Pfizer, Sanofi and UCB. M.B. Guanti received honoraria from Leopharma, Abbvie, Sanofi, Menarini, Novartis, Cantabria, Lilly, Pfizer. M. Rossi served as speaker and consultant for Abbvie, Sanofi, Leo Pharma, Pfizer, L'Oreal, Almirall. E. Pezzolo has been

consultant and speaker for Sanofi, Leo Pharma, Abbvie, Pfizer. Novartis, Galderma, Janssen, Almirall, Boehringer Ingelheim. **G. Girolomoni** has received personal fees from AbbVie, Almirall, Amgen, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli-Lilly, Leo Pharma, Merck Serono, Novartis, Pfizer, Pierre Fabre, Samsung bioepis and Sanofi. **S. Ribero** received honoraria from Sanofi, Abbvie, Almirall, Ucb, Novartis, Leo Pharma, Eli Lilly. **M. Gola** has been consultant and/or speaker, has participated to advisory boards and has received personal fees from AbbVie, Almirall, Leo Pharma, Pfizer and Sanofi. **Maria B. De Felici Del Giudice** has conflict of interest with Sanofi, Leopharma and AbbVie. **C. Patruno** has conflict of interest with AbbVie, Almirall, Amgen, Galderma, Leo Pharma, Lilly, Novartis, Pfizer, Pierre Fabre, Sanofi. **M.B. Piraccini** has conflict of interest with Pierre fabre-Ducray , Difa Cooper, Dercos-L'Oreal, ISDIN, Legacy Healthcare , Pfeizer, Eli- Lilly. **A. Burrioni** has conflict of interest with Sanofi, Abbvie, Lilly and Almirall. The other authors have no conflict of interest.

Data availability: Not available due to privacy restriction

Ethics statement: Institutional review board approval was exempted as the study protocol did not deviate from standard clinical practice. All patients received upadacitinib as in good clinical practice, in accordance with European guidelines. All included patients had provided written consent for retrospective study of data collected during routine clinical practice. The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy.

Patient consent: Written patient consent for publication was obtained.

What is already known about this topic?

- Real-world data on AD patients primarily treated with upadacitinib, compared to those who received other biological therapies and experienced treatment failure due to lack of efficacy or adverse effects, are limited. The available studies mainly focus on prior treatment with dupilumab, are based on small populations, or involve comparisons between populations with differing baseline characteristics.

What does this study add?

- The study compares patients treated with upadacitinib who previously failed Th2 biologics with those who discontinued these treatments for reasons other than inefficacy or who were naïve to biologics on an adequate sample size.
- We used Propensity Score matching, a statistical method that allows for the comparison of two populations by matching them based on sample size and epidemiological/clinical characteristics, thereby reducing potential confounding factors.
- Upadacitinib proved to be effective in the long term not only as a first-line therapy but also in patients with a history of biologic treatment failure. However, bio-naïve patients and those who did not discontinued these treatments due to inefficacy consistently demonstrated better clinical responses at later follow-ups (week 36 and 52), suggesting that biologic-naïve individuals and those who discontinued Th2 biologics for reasons other than inefficacy may respond more favorably to upadacitinib

1 ABSTRACT

2 Introduction: Real-world data comparing patients with atopic dermatitis (AD) initially treated with
3 upadacitinib versus those previously treated with biologics or other JAK inhibitors are limited.

4 Methods: We conducted a retrospective multicenter study of 524 patients with moderate-to-severe
5 AD treated with upadacitinib to assess clinical outcomes over 52 weeks. A sub-analysis of 316
6 patients compared outcomes between those who had previously failed Th2 biologics (group A) and
7 those who discontinued these treatments for reasons other than inefficacy or were bio-naïve (group
8 B), using a Propensity Score matching method.

9 Results: A significant clinical improvement starting from week 4 and continuing throughout the
10 study period was observed in the overall population and both in group A and B. Group B showed
11 greater improvements at later follow-up times, with a higher median EASI (Eczema Area and
12 Severity Index) percentage improvement at week 52 ($p=0.030$), a significantly higher proportion of
13 patients achieving EASI-90 and EASI-100 at week 36 ($p=0.023$, $\chi^2=9.497$). As for the P-NRS
14 (Pruritus Numerical Rating Scale) and SD-NRS (Sleep Disturbances Numerical Rating Scale),
15 group B had a significantly greater percentage of patients reporting a score of 0 or 1 at week 52 (P-
16 NRS: $p=0.017$, $\chi^2=5.665$; SD-NRS: $p=0.049$, $\chi^2=3.870$). Group B also had a significantly higher
17 percentage of patients reaching minimal disease activity at week 52 ($p=0.014$, $\chi^2=5.980$).

18 Conclusion: Upadacitinib proved to be effective in the long term not only as a first-line therapy but
19 also in patients with a history of biologic treatment failure. However, patients in Group B
20 consistently demonstrated better clinical responses at later follow-ups, suggesting that bio-naïve
21 individuals and those who discontinued Th2 biologics for reasons other than inefficacy may respond
22 more favorably to upadacitinib.

1 INTRODUCTION

2 Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense itching and
 3 significant impairment of patients' quality of life (QoL) ¹. The prevalence of AD in adults is
 4 increasing, with an estimated 8.1% in Italy ². The therapeutic management of AD relies on topical
 5 and/or systemic immunosuppressive/immunomodulatory therapies, which can be particularly
 6 challenging to maintain over the long term, especially in cases of severe AD. Selecting an effective
 7 and safe long-term treatment is very important due to the chronic nature of AD. In addition to
 8 conventional systemic agents like cyclosporine, targeted therapies have been approved for AD
 9 treatment ³⁻⁵. Upadacitinib is an oral selective inhibitor of Janus associated kinase (JAK)-1, whose
 10 efficacy and safety in AD have been shown in both short- and long-term clinical trials ⁶⁻¹⁰. The
 11 effectiveness of upadacitinib has been confirmed in real-world studies as well ^{2, 11-14}. Additionally,
 12 a direct comparison between upadacitinib and dupilumab (Heads-up trial) revealed that upadacitinib
 13 was superior, with a significantly higher percentage of patients achieving both primary and
 14 secondary treatment endpoints at 16 and 24 weeks ¹⁵⁻¹⁶. Moreover, a meta-analysis proved that
 15 upadacitinib 30 mg is the most effective therapy among systemic targeted therapies at week 12 or
 16 16 ¹⁷⁻¹⁸. It must although admitted that both these studies focused on the short-term. Real-world
 17 data on AD patients treated primarily with upadacitinib versus those who received other biological
 18 therapies and failed due to lack of efficacy or adverse effects are limited, with the few available
 19 studies specifically focusing on previous treatment with dupilumab ¹⁹⁻²¹. We herein report a
 20 retrospective multicenter study aimed at comparing the clinical outcomes in 524 patients treated
 21 with upadacitinib up to 52 weeks. This study compares patients treated with upadacitinib who
 22 previously failed Th2 biologics (dupilumab and tralokinumab) with those who were bio-naïve or
 23 had discontinued these treatments for reasons other than inefficacy, using a Propensity Score
 24 matching method ²².

26 METHODS

27 *Patients and Data Collection*

28 This retrospective study enrolled 524 patients with moderate-to-severe AD receiving upadacitinib
 29 15 mg or 30 mg across 22 tertiary centers in Italy. Baseline data included sex, age, atopic
 30 comorbidities, predominant clinical AD phenotype, involvement of specific sites (head and neck
 31 and hands), AD onset age, and previous treatments. Clinical scores such as Eczema Assessment

Severity Index (EASI), Pruritus Numerical Rating Scale (P-NRS), Sleep Disorder NRS (SD-NRS) and Dermatology Life Quality Index (DLQI) were recorded at baseline, then after 4, 16, 36 and 52 weeks (W) of treatment. Given the retrospective nature of the study and variable follow-up intervals, data were collected at as many follow-up points as possible. The progressive reduction in sample size across time points was due to some patients not having yet reached the corresponding follow-up visits at the time of data collection. Minimal disease activity was defined as EASI-90, P-NRS 0/1 and SD-NRS 0/1)²³. A sub analysis compares patients treated with upadacitinib who previously discontinued Th2 biologics due to primary or secondary inefficacy (here on group A) with those who were bio-naïve or discontinued these treatments for reasons other than inefficacy, e.g. adverse events or non-drug related reasons (here on group B). The authors decided to include in Group B both bio-naïve patients and those who had discontinued prior treatment for reasons other than inefficacy, to avoid bias related to misclassifying as 'difficult-to-treat' patients who may not truly meet that definition as previously described in the literature (Napolitano et al.¹¹).

Statistical analyses

Descriptive statistics are reported as mean and standard deviation (SD) or median and quartiles (Q1-Q3) for quantitative variables based on the distribution of the population. Absolute numbers (n) and frequencies (%) are used for categorical variables. The analysis between two groups was performed using the Mann-Whitney U test for unpaired data, while comparisons involving more than two groups were conducted using the Friedman test with Bonferroni post-hoc correction. Categorical variables were analyzed using a chi-square test or Fisher's exact test as appropriate. Drug survival was analyzed using unadjusted Kaplan-Meier survival curves to estimate the risk and time to discontinuation. Patients were censored if, at the July 2024 data lock, they were still under treatment with upadacitinib, lost to follow-up or discontinued due to causes not related to upadacitinib.

A sub-analysis using Propensity score (PScore) matching was conducted on 316 patients to compare the effectiveness of upadacitinib between group A and group B. The variables considered as regressors included sex, age of AD onset (dichotomized into onset during childhood/adolescence and adult-onset), involvement of the head and neck or hands, phenotype (dichotomized into classical and non-classical), the presence of at least one atopic comorbidity and the dose of upadacitinib, EASI at baseline and upadacitinib dose. Considering that patients were treated with the dose of either 15 mg or 30 mg, that the dosage could change and that the month distance between follow-

ups was not the same, the weighted dose was considered. Patients that did not reach W4 and patients whose reason of previous biological discontinuation was missing were excluded from the PScore analysis.

In our study, to calculate the sample size, the power*G software (version 3.1) was used. Considering a Mann-Whitney test with a significance level of 0.05 and 80% power, and assuming an effect size of 0.5 we determined that a minimum total sample size of 134 patients was necessary. All statistical analyses were two-tailed with an alpha error set at 0.05, considering a p-value < 0.05 as significant. Statistical analyses were carried out using SPSS-IBM software (version 29.0).

RESULTS

Effectiveness and safety in the overall population

Table 1 presents the clinical and epidemiological characteristics of the overall study population. Most patients (276/524, 52.7%) had not been previously treated with biologics or other systemic JAK-inhibitors. We observed a significant improvement in the clinical signs and symptoms of AD starting from week 4 and continuing throughout the study period. The overview of clinimetric outcomes, drug retention, and discontinuation reasons are represented in Table 2, and in the Supplementary Material. At week 52, drug survival (DS) was 91.5%, 9/524 (1.7%) patients were lost at follow-ups and a total of 32/524 (6.1%) discontinuations were recorded [Table 2]. Regardless of discontinuation, the following AEs were recorded: herpes simplex reactivation (12/524 [2.3%]), herpes zoster reactivation (7/524 [1.3%]), hypercholesterolemia or hypertriglyceridemia (40/524 [7.7%]), blood count alterations (10/524 [2%]), creatine-phosphokinase elevation (24/524 [4.6%]), hypertransaminemia (5/524 [1%]), respiratory-tract infections (8/524 [1.5%]), urinary-tract infections (1/524, [0.2%]), and acne (16/524 [3.1%]).

Propensity score matching sub-analysis

A sub-analysis using PScore matching method was conducted to compare group A and group B. The PScore populations comprised 158 patients each group at baseline, and Table 2 presents the clinical and epidemiological characteristics. The overview of clinimetric outcomes, drug retention, and discontinuation reasons, divided by group A and B are represented in Table 4, Table 5 and in the Supplementary Material. Regarding the EASI percentage improvement trend, group A initially showed a higher score at week 4 (p = 0.045); however, group B showed greater improvements at

later follow-up times, with a significantly higher proportion of patients achieving EASI-90 and EASI-100 at week 36 ($p = 0.023$, $\chi^2 = 9.497$), and a higher median EASI percentage improvement at week 52 ($p = 0.030$). As for the P-NRS ($p = 0.017$, $\chi^2 = 5.665$) and SD-NRS ($p = 0.049$, $\chi^2 = 3.870$), a significant difference between groups was found at week 52, with group B having a greater percentage of patients reporting a score of 0 or 1. Furthermore, group B demonstrated a greater percentage improvement in DLQI scores at weeks 36 ($p = 0.032$) and 52 ($p = 0.040$). Group B also had a significantly higher percentage of patients reaching MDA at week 52 ($p = 0.014$, $\chi^2 = 5.980$). A significant difference in DLQI was observed at weeks 36 and 52, with Group B showing a higher median percentage improvement from baseline.

DISCUSSION

Effectiveness and safety in the overall population

Our results at week 16 show that 81.3% of patients achieved EASI-75 and 63.2% achieved EASI-90. These values are comparable to those reported in the literature^{11,12}. At week 52, the EASI endpoint (EASI-75/90/100) are comparable to those achieved by Gargiulo et al.¹³ but inferior when compared to the overall population of Napolitano et al.¹¹ In our study, 16.98% of patients experienced at least one AE during the treatment period, with most events not leading to treatment discontinuation. This aligns with the findings of Chiricozzi et al.¹², who reported an AE rate of 17.8%. Finally, real-world data on long-term drug survival of upadacitinib are limited. To date, only the study by Pezzolo et al.² has assessed this outcome up to 52 weeks. Our drug survival rate at week 52 was 91.2%, closely matching the 91.5% reported in their analysis.

Propensity Score Matching Sub-Analysis

Both Group A (patients who discontinued Th2 biologics due to primary or secondary inefficacy) and Group B (bio-naïve patients or those who discontinued biologics for reasons other than inefficacy) showed significant improvements in the evaluated scores from baseline through 52 weeks of treatment. The comparative analysis of the two groups revealed some differences in treatment responses over time. At week 4, Group A showed a significantly higher percentage improvement in EASI; however, this difference was not clinically important, was not consistent with improvements in other scores, and was not maintained in subsequent follow-ups. On the other hand, group B consistently demonstrated better clinical responses in the later follow-ups, including

greater EASI percentage improvement at week 52, superior EASI-90 and EASI-100 achievement at week 36, P-NRS and SD-NRS percentage improvement at week 52, and superior MDA achievement at week 52. These findings suggest that patients who have not experienced treatment failure with prior biologics, or who discontinued these due to reasons rather than inefficacy, may respond more favorably to upadacitinib. In our study, potential confounding factors were minimized by applying propensity score matching to ensure comparable baseline characteristics, including EASI and P-NRS scores between the two groups. According to the sample size calculation (see Methods), the total sample size was adequate at each time point, except for the DLQI analysis at week 52. Despite the differences observed, it is worth noting that over three-quarters of patients in group A achieved EASI-75 or an SD-NRS score of 0/1 at week 52, and more than half reported a P-NRS score of 0 or 1. These results indicate that upadacitinib is effective in the long term, not only as a first-line therapy but also in patients with a history of biologic treatment failure.

Napolitano et al.¹¹ evaluated the effectiveness of upadacitinib in dupilumab-exposed and dupilumab-naïve patients. At week 52, EASI and P-NRS percentage improvements were generally comparable to those observed in our study, except for the P-NRS score, which was nearly 10 points higher in our cohort. Unlike our findings, they did not observe significant differences at week 52. However, consistent with our results, they reported greater improvement in the biologic-experienced group at week 4, although this difference was not sustained in the subsequent follow-ups. They speculated that the difference might be attributed to including in the dupilumab-exposed group patients who discontinued treatment due to ineffectiveness or AEs and to the latter subgroup having lower baseline EASI scores. In our study, these confounding factors were eliminated by excluding from group A patients who discontinued innovative therapies for reasons other than inefficacy and by using PScore matching to ensure comparable EASI and P-NRS scores at baseline. Differently from our results, Boesjes et al.²⁰ found no differences in the upadacitinib effectiveness in dupilumab responder or bio-naïve versus dupilumab non-responder at week 4, albeit their study was based on a small population (n=57) and multiple imputation was used for missing data (overall 33.4%).

Our study has some limitations including its retrospective nature, the numerous misses for SD-NRS and DLQI values that did not allow them to be included as regressors in the PScore matching analysis, and the progressive reduction in sample sizes for Groups A and B over time, although they

remained above the threshold established by the sample size calculation—except for the DLQI analysis at week 52.

Additionally, most patients were treated with dupilumab rather than tralokinumab, which limits the conclusions that can be drawn specifically for tralokinumab. However, these findings may still provide valuable insights and serve as a basis for future studies with larger cohorts.

Also, we do not have information on the timeframe between upadacitinib initiation and the previous treatment. On the other hand, the study included a large number of patients, with most outcome measures fully recorded.

To summarize, upadacitinib proved to be effective in the long term not only as a first-line therapy but also in patients with a history of biologic treatment failure. However, patients in Group B consistently demonstrated better clinical responses at later follow-ups, suggesting that bio-naïve individuals and those who discontinued Th2 biologics for reasons other than inefficacy may respond more favorably to upadacitinib.

REFERENCES

1. Weidinger S, Beck LA, Bieber T, et al. Atopic dermatitis. *Nat Rev Dis Primers*. 2018 Jun 21;4(1):1. doi: 10.1038/s41572-018-0001-z. PMID: 29930242.
2. Pezzolo E, Ortoncelli M, Ferrucci SM, et al. Drug survival of upadacitinib and predicting factors of discontinuation in adult patients affected by moderate-to-severe atopic dermatitis: an Italian multicenter analysis. *J Clin Med*. 2024 Jan 18;13(2):553. doi: 10.3390/jcm13020553. PMID: 38256686; PMCID: PMC10816142.
3. Siegels D, Heratizadeh A, Abraham S, et al. Systemic treatments in the management of atopic dermatitis: a systematic review and meta-analysis. *Allergy*. 2021 Apr;76(4):1053-1076. doi: 10.1111/all.14631. PMID: 33074565.
4. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol*. 2018 May;32(5):657-682. doi: 10.1111/jdv.14891. PMID: 29676534.

5. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. *J Eur Acad Dermatol Venereol*. 2018 Jun;32(6):850-878. doi: 10.1111/jdv.14888. PMID: 29878606.
6. Guttman-Yassky E, Thaçi D, Pangan AL, et al. Upadacitinib in adults with moderate to severe atopic dermatitis: 16-week results from a randomized, placebo-controlled trial. *J Allergy Clin Immunol*. 2020 Mar;145(3):877-884. doi: 10.1016/j.jaci.2019.11.025. PMID: 31786154.
7. Reich K, Teixeira HD, de Bruin-Weller M, et al. Safety and efficacy of upadacitinib in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis (AD Up): results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2021 Jun 5;397(10290):2169-2181. doi: 10.1016/S0140-6736(21)00589-4. PMID: 34023009.
8. Simpson EL, Prajapati VH, Leshem YA, et al. Upadacitinib rapidly improves patient-reported outcomes in atopic dermatitis: 16-week results from phase 3 clinical trials (Measure Up 1 and 2). *Dermatol Ther (Heidelb)*. 2024 May;14(5):1127-1144. doi: 10.1007/s13555-024-01157-5. PMID: 38696027; PMCID: PMC11116320.
9. Silverberg JI, de Bruin-Weller M, Bieber T, et al. Upadacitinib plus topical corticosteroids in atopic dermatitis: Week 52 AD Up study results. *J Allergy Clin Immunol*. 2022 Mar;149(3):977-987.e14. doi: 10.1016/j.jaci.2021.07.036. PMID: 34403658.
10. Simpson EL, Papp KA, Blauvelt A, et al. Efficacy and safety of upadacitinib in patients with moderate to severe atopic dermatitis: analysis of follow-up data from the Measure Up 1 and Measure Up 2 randomized clinical trials. *JAMA Dermatol*. 2022 Apr 1;158(4):404-413. doi: 10.1001/jamadermatol.2022.0029. PMID: 35262646; PMCID: PMC8908226.
11. Napolitano M, Ferrucci SM, Foggia L, et al. Comparison of long-term effectiveness and safety of upadacitinib for atopic dermatitis between dupilumab-exposed and dupilumab-naïve patients. *Clin Drug Investig*. 2024 Jan;44(1):71-77. doi: 10.1007/s40261-023-01336-w. PMID: 38105393.
12. Chiricozzi A, Ortoncelli M, Schena D, et al. Long-term effectiveness and safety of upadacitinib for atopic dermatitis in a real-world setting: an interim analysis through 48 weeks of observation. *Am J Clin Dermatol*. 2023 Nov;24(6):953-961. doi: 10.1007/s40257-023-00798-0. PMID: 37322324; PMCID: PMC10570196.

13. Gargiulo L, Ibba L, Piscazzi F, et al. Effectiveness and safety of upadacitinib for moderate-to-severe atopic dermatitis in a real-world setting: a 52-week retrospective study. *J Eur Acad Dermatol Venereol*. 2024 Feb;38(2):e152-e154. doi: 10.1111/jdv.19507. PMID: 37714196.
14. Hagino T, Yoshida M, Hamada R, et al. Predictive factors for responders to upadacitinib treatment in patients with atopic dermatitis. *J Dermatolog Treat*. 2024 Dec;35(1):2310643. doi: 10.1080/09546634.2024.2310643. PMID: 38297496.
15. Blauvelt A, Teixeira HD, Simpson EL, et al. Efficacy and safety of upadacitinib vs dupilumab in adults with moderate-to-severe atopic dermatitis: a randomized clinical trial. *JAMA Dermatol*. 2021 Sep 1;157(9):1047-1055. doi: 10.1001/jamadermatol.2021.3023. PMID: 34347860; PMCID: PMC8340015.
16. Blauvelt A, Ladizinski B, Prajapati VH, et al. Efficacy and safety of switching from dupilumab to upadacitinib versus continuous upadacitinib in moderate-to-severe atopic dermatitis: results from an open-label extension of the phase 3, randomized, controlled trial (Heads Up). *J Am Acad Dermatol*. 2023 Sep;89(3):478-485. doi: 10.1016/j.jaad.2023.05.033. PMID: 37230366.
17. Silverberg JI, Thyssen JP, Fahrbach K, et al. Comparative efficacy and safety of systemic therapies used in moderate-to-severe atopic dermatitis: a systematic literature review and network meta-analysis. *J Eur Acad Dermatol Venereol*. 2021 Sep;35(9):1797-1810. doi: 10.1111/jdv.17351. PMID: 33991374; PMCID: PMC8453983.
18. Silverberg JI, Hong HC, Calimlim BM, et al. Comparative efficacy of targeted systemic therapies for moderate-to-severe atopic dermatitis without topical corticosteroids: an updated network meta-analysis. *Dermatol Ther (Heidelb)*. 2023 Oct;13(10):2247-2264. doi: 10.1007/s13555-023-01000-3. PMID: 37658223; PMCID: PMC10539231.
19. Georgakopoulos JR, Sheka D, Rankin B, et al. Real-world effectiveness and safety of upadacitinib for the treatment of atopic dermatitis in adult patients switched from dupilumab: a multicenter retrospective study. *J Am Acad Dermatol*. 2023 Dec;89(6):1308-1311. doi: 10.1016/j.jaad.2023.08.059. PMID: 37648068.
20. Sood S, Bagit A, Heung M, et al. Outcomes of systemic Janus kinase inhibitors following prior dupilumab use for atopic dermatitis: an evidence-based review. *JAAD Int*. 2024 Apr 6;16:31-33. doi: 10.1016/j.jdin.2024.03.023. PMID: 38774339; PMCID: PMC11107228.

21. Boesjes CM, Van derGang LF, Zuithoff NPA, 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 Derm Venereol.* 2023 Feb 16;103:adv00872. doi: 10.2340/actadv.v103.5243. PMID: 36794894; PMCID: PMC9949218.
22. Kane LT, Fang T, Galetta MS, et al. Propensity score matching: a statistical method. *Clin Spine Surg.* 2020 Apr;33(3):120-122. doi: 10.1097/BSD.0000000000000932. PMID: 31913173.
23. Silverberg JI, et al. Optimizing the management of atopic dermatitis with a new minimal disease activity concept and criteria and consensus-based recommendations for systemic therapy. *Br J Dermatol.* 2023 Feb;188(Suppl 2):ljac140.022.

Figure legends

Figure 1. Distribution of group A and group B population (expressed in percentage) in the different EASI percentage improvement class from baseline at week 4, week 16, week 36 and week 52. Group A, patients who failed Th2 biologics; Group B, bio-naïve patients or patients that discontinued these treatments not due to inefficacy. EASI, Eczema Area and Severity Index.

Figure 2. Percentage of patients, in group A and B, with P-NRS 0/1 at week 4, 16, 36 and 52. Group A, patients who failed Th2 biologics; Group B, bio-naïve patients or patients that discontinued these treatments not due to inefficacy. P-NRS, Pruritus Numerical Rating Scale.

1 **Table 1. Clinical and epidemiological characteristics of the overall population.**

Characteristics	Overall population (n=524)
Sex, n (%)	
- Female	228 (43.5)
- Male	296 (56.5)
Baseline age, median (Q1-Q3)	33.0 (24.0-51.0)
AD onset age, median (Q1-Q3)	5.0 (1.0-33.0)
AD onset age, n (%)	
- Childhood or adolescence	339 (64.7)
- Late onset	185 (35.3)
AD phenotype, n (%)	
- Classical	444 (84.7)
- Generalized inflammatory	36 (6.9)
- PN-like	17 (3.2)
- EN-like	16 (3.1)
- Erythrodermic	10 (1.9)
- missing	1 (0.2)
Atopic comorbidities, n (%)	
- Conjunctivitis	124 (23.7)
- Rhinitis	174 (33.2)
- Polypsis	2 (0.4)
- Asthma	112 (21.4)
- Food allergy	51 (9.7)
- Drug allergy	13 (2.5)
- Patients without atopic comorbidity	291 (55.5)
- Patients with at least one atopic comorbidity	233 (44.5)
Involvement of specific sites, n (%)	
- Head and neck	356 (67.9)
- Hands	271 (51.7)
Previous traditional systemic treatment, n (%)	
- Methotrexate	19 (3.6)
- Cyclosporin	207 (39.5)
Previous treatment with biologics or JAK-inhibitors and reason of discontinuation	
- Dupilumab	228 (43.5)
- Inefficacy	185/228 (81.1)
- AEs	29/228 (12.7)
- Other	6/228 (2.6)
- missing	8/228 (3.5)
- Tralokinumab	26 (5.0)
- Inefficacy	23/26 (88.5)
- missing	3/26 (11.5)
- Baricitinib	10 (1.9)
- Inefficacy	8/10 (80.0)
- missing	2/10 (2.0)
- Abrocitinib	2 (0.4)
- Inefficacy	2/2 (100.0)
Baseline dose	
- 15 mg, n (%)	381 (72.7)
- 30 mg, n (%)	143 (27.3)
Clinimetric score at baseline	
- EASI, mean (SD)	23.3 (11.9) [n=524/524]
- P-NRS, median (Q1-Q3)	8.0 (6.5-9.0) [n=521/524]
- SD-NRS, median (Q1-Q3)	7.0 (4.0-8.0) [n=521/524]
- DLQI, median (Q1-Q3)	20.0 (13.0-24.0) [n=287/524]

1 AD, atopic dermatitis; JAK, Janus Kinase; PN, prurigo-nodularis; EN, nummular eczema; EASI,
2 Eczema Area and Severity Index; P-NRS, Pruritus Numerical Rating Scale; SD-NRS, Sleep NRS;
3 DLQI, Dermatology Life Quality Index; *n*, proportion of valid data.
4
5

ACCEPTED MANUSCRIPT

Table 2. Overview of clinimetric outcomes, drug retention, and discontinuation reasons at weeks 4, 16, 36, and 52

Score	Week 4 (n=434)	Week 16 (n=357)	Week 36 (n=278)	Week 52 (n=214)
EASI percentage improvement, median (Q1-Q3)	81.8 (60.0-93.8) <i>n</i> =430/434	94.1 (80.0-100.0) <i>n</i> =353/357	96.2 (83.3-100.0) <i>n</i> =274/278	100.0 (87.5-100.0) <i>n</i> =210/214
EASI-75, <i>n</i> (%)	271 (63.0)	287 (81.3)	239 (87.2)	178 (84.8)
EASI-90, <i>n</i> (%)	134 (31.2)	223 (63.2)	182 (66.4)	150 (71.4)
EASI-100, <i>n</i> (%)	88 (20.5) <i>n</i> =430/434	152 (43.1) <i>n</i> =353/357	126 (46.6) <i>n</i> =274/278	119 (56.7) <i>n</i> =210/214
P-NRS percentage improvement, median (Q1-Q3)	77.8 (50.0-100.0) <i>n</i> =420/434	100.0 (60.0-100.0) <i>n</i> =347/357	100.0 (60.0-100.0) <i>n</i> =268/278	100.0 (70.0-100.0) <i>n</i> =207/214
P-NRS 0/1, <i>n</i> (%)	202 (47.2) <i>n</i> =428/434	225 (63.6) <i>n</i> =354/357	177 (64.6) <i>n</i> =274/278	146 (68.5) <i>n</i> =213/214
Delta P-NRS ≥ 4 , <i>n</i> (%)	316 (73.8) <i>n</i> =428/434	274 (77.6) <i>n</i> =354/357	213 (77.0) <i>n</i> =274/278	169 (79.3) <i>n</i> =213/214
SD-NRS percentage improvement, median (Q1-Q3)	100.0 (60.0-100.0) <i>n</i> =383/434	100.0 (83.3-100.0) <i>n</i> =315/357	100.0 (100.0-100.0) <i>n</i> =244/278	100.0 (100.0-100.0) <i>n</i> =184/214
SD-NRS 0/1, <i>n</i> (%)	267 (62.8) <i>n</i> =425/434	277 (78.5) <i>n</i> =353/357	223 (82.0) <i>n</i> =272/278	184 (86.4) <i>n</i> =213/214
DLQI percentage improvement, median (Q1-Q3)	83.3 (62.5-96.6) <i>n</i> =207/434	90.0 (68.2-100.0) <i>n</i> =183/357	91.3 (66.7-100.0) <i>n</i> =150/278	95.7 (73.6-100.0) <i>n</i> =117/214
Delta DLQI ≥ 4 , <i>n</i> (%)	186 (89.0) <i>n</i> =228/434	160 (86.0) <i>n</i> =203/357	132 (86.3) <i>n</i> =167/278	99 (82.5) <i>n</i> =129/214
MDA, <i>n</i> (%)	106 (25.0%)	179 (51.1%)	152 (56.5%)	125 (59.8%)
Discontinuations and lost at follow-up, <i>n</i>				
- Inefficacy	1	1	4	7
- AEs	2	2	2	4
- Other (non-drug-related)	0	1	2	5
- Inefficacy and AEs	0	0	0	1
- Lost at FU	2	2	2	3
Drug survival, %	99.4	98.6	96.6	91.5

EASI, Eczema Area and Severity Index; P-NRS, Pruritus Numerical Rating Scale; SD-NRS, Sleep NRS; DLQI, Dermatology Life Quality Index; EASI-75, improvement of at least 75.0; EASI-90, improvement between 90.0% and 99.9%; *n*, proportion of valid data; AEs, adverse events; FU, follow-up. MDA, minimal disease activity (defined as EASI-90, P-NRS 0/1 and SD-NRS 0/1). At baseline, 9 (1.7%) patients had an EASI of 0, 61 patients (11.6%) had an SD-NRS of 0, 16 patients (3.1%) had a P-NRS of 0, and 3 patients (0.6%) had a DLQI of 0. These patients could not be included in the percentage improvement calculations for subsequent follow-ups.

1 **Table 3. Clinical and epidemiological characteristics of group A and group B.**

Characteristics	Group A (n=158)	Group B (n=158)
Sex, n (%)		
- Female	63 (39.9)	64 (40.5)
- Male	95 (60.1)	94 (59.5)
Baseline age, mean (SD)	36.5 (15.7)	37.5 (15.3)
AD onset age, median (Q1-Q3)	5.0 (1.0-27.5)	5.0 (1.0-33.5)
AD onset age, n (%)		
- Onset during childhood or adolescence	105 (66.5)	101 (63.9)
- Late onset	53 (33.5)	57 (36.1)
AD phenotype, n (%)		
- Classical	130 (82.3)	135 (85.4)
- Generalized inflammatory	14 (8.9)	9 (5.7)
- PN-like	4 (2.5)	4 (2.5)
- EN-like	5 (3.2)	5 (5.1)
- Erythrodermic	5 (3.2)	2 (1.3)
Atopic comorbidities, n (%)		
- Conjunctivitis	39 (24.7)	42 (26.6)
- Rhinitis	55 (34.8)	57 (36.1)
- Polyposis	1 (0.6)	1 (0.6)
- Asthma	45 (28.5)	36 (22.8)
- Food allergy	18 (11.4)	19 (12.0)
- Drug allergy	4 (2.5)	5 (3.2)
- Patients without atopic comorbidity	81 (51.3)	80 (50.6)
- Patients with at least one atopic comorbidity	77 (48.7)	78 (49.4)
Involvement of specific sites, n (%)		
- Head and neck	122 (77.2)	113 (71.5)
- Hands	90 (57.0)	90 (57.0)
Previous traditional systemic treatment, n (%)		
- Methotrexate	13 (8.2)	4 (2.5)
- Cyclosporin	62 (39.2)	64 (40.5)
Previous treatment with biologics or JAK-inhibitors and reason of discontinuation, n (%)		
- Dupilumab	151 (95.6)	30 (19.0)
- Inefficacy	150/151 (99.3)	0/30 (0.0)
- AEs	1/151 (0.7)	24/30 (80.0)
- Other	0/0 (0.0)	6/30 (20.0)
- Tralokinumab	14 (8.9)	0 (0.0)
- Inefficacy	14/14 (100.0)	0 (0.0)
Baseline dose, n (%)		
- 15 mg	105 (66.5)	109 (69.0)
- 30 mg	53 (33.5)	49 (31.0)

Characteristics	Group A (n=158)	Group B (n=158)
Clinimetric score at baseline		
- EASI, median (Q1-Q3)	20.0 (14.8-25.0) [n=158/158]	20.0 (14.0-26.0) [n=158/158]
- P-NRS, median (Q1-Q3)	8.0 (6.0-10.0) [n=158/158]	8.0 (6.8-9.0) [n=158/158]
- SD-NRS, median (Q1-Q3)	7.0 (4.0-8.0) [n=157/158]	7.0 (5.0-8.0) [n=158/158]
- DLQI, median (Q1-Q3)	16.5 (8.0-22.0) [n=90/158]	19.0 (12.0-24.0) [n=90/158]

Group A, patients who failed biologics; Group B, bio-naïve patients or patients that discontinued these treatments not due to inefficacy. AD, atopic dermatitis; JAK, Janus Kinase; PN, prurigo-nodularis; EN, nummular eczema; EASI, Eczema Area and Severity Index; P-NRS, Pruritus Numerical Rating Scale; SD-NRS, Sleep NRS; DLQI, Dermatology Life Quality Index; *n*, proportion of valid data.

Table 4. Improvement of the clinical score evaluated from baseline at week 4, 16, 36 and 52 between group A and group B.

Follow-up	Score		Group A	Group B	p-value
Week 4	EASI	percentage	83.3 (66.7-95.0)	81.2 (50.0-93.3)	0.045
	improvement, median		<i>n=147/148</i>	<i>n=151/152</i>	
	(Q1-Q3)				
	EASI-75, <i>n</i> (%)		96 (65.3)	92 (60.9)	
	EASI-90, <i>n</i> (%)		53 (36.1)	44 (29.1)	0.643
	EASI-100, <i>n</i> (%)		34 (23.1)	29 (19.2)	
			<i>n=147/148</i>	<i>n=151/152</i>	
	P-NRS	percentage	80.0 (50.0-100.0)	77.8 (50.0-100.0)	0.231
	improvement, median		<i>n=140/148</i>	<i>n=151/152</i>	
	(Q1-Q3)				
	P-NRS 0/1, <i>n</i> (%)		75 (52.1)	72 (47.4)	
			<i>n=144/148</i>	<i>n=152/152</i>	0.417
	Delta P-NRS ≥ 4 , <i>n</i> (%)		109 (75.7)	111 (73.0)	
			<i>n=144/148</i>	<i>n=152/152</i>	
Week 16	SD-NRS	percentage	100.0 (66.7-100.0)	88.9 (60.0-100.0)	0.128
	improvement, median		<i>n=123/148</i>	<i>n=138/152</i>	
	(Q1-Q3)				
	SD-NRS 0/1, <i>n</i> (%)		98 (69.0)	97 (63.8)	
			<i>n=142/148</i>	<i>n=151/152</i>	0.346
	DLQI	percentage	86.7 (55.2-100.0)	85.7 (75.0-100.0)	
	improvement, median		<i>n=72/148</i>	<i>n=70/152</i>	
	(Q1-Q3)				
	Delta DLQI ≥ 4 , <i>n</i> (%)		62 (84.9)	64 (90.1)	0.354
			<i>n=73/148</i>	<i>n=71/152</i>	
	MDA, <i>n</i> (%)		45 (31.9)	35 (23.2)	
			<i>n=141/148</i>	<i>n=151/152</i>	
	EASI	percentage	93.2 (76.7-100.0)	95.8 (83.3-100.0)	0.248
	improvement, median		<i>n=126/127</i>	<i>n=120/121</i>	
	(Q1-Q3)				
	EASI-75, <i>n</i> (%)		101 (80.2)	97 (80.8)	0.636
	EASI-90, <i>n</i> (%)		73 (57.9)	77 (64.2)	
	EASI-100, <i>n</i> (%)		49 (38.9)	55 (45.8)	
			<i>n=126/127</i>	<i>n=120/121</i>	
Week 16	P-NRS	percentage	100.0 (50.0-100.0)	95.0 (60.6-100.0)	0.965
	improvement, median		<i>n=122/127</i>	<i>n=120/121</i>	
	(Q1-Q3)				
	P-NRS 0/1, <i>n</i> (%)		75 (60.0)	75 (62.0)	
			<i>n=125/127</i>	<i>n=121/121</i>	0.750
	Delta P-NRS ≥ 4 , <i>n</i> (%)		93 (75.0)	92 (76.0)	
			<i>n=125/127</i>	<i>n=121/121</i>	
	SD-NRS	percentage	100.0 (74.1-100.0)	100.0 (86.1-100.0)	0.708
	improvement, median		<i>n=106/127</i>	<i>n=108/121</i>	
	(Q1-Q3)				
	SD-NRS 0/1, <i>n</i> (%)		96 (76.8)	97 (80.8)	
					0.440

Follow-up	Score		Group A	Group B	p-value
			<i>n</i> =125/127	<i>n</i> =120/121	
	DLQI	percentage improvement, median (Q1-Q3)	83.3 (56.6-100.0) <i>n</i> =62/127	88.5 (79.1-100.0) <i>n</i> =62/121	0.409
	Delta DLQI ≥ 4 , <i>n</i> (%)		49 (77.8) <i>n</i> =63/127	54 (84.4) <i>n</i> =64/121	0.342
	MDA, <i>n</i> (%)		58 (47.2) <i>n</i> =123/127	62 (52.1) <i>n</i> =119/121	0.442
Week 36	EASI	percentage improvement, median (Q1-Q3)	93.8 (81.5-100.0) <i>n</i> =101/102	96.2 (84.2-100.0) <i>n</i> =89/90	0.163
	EASI-75, <i>n</i> (%)		90 (89.1)	75 (84.3)	0.023 ($\chi^2=9.497$)
	EASI-90, <i>n</i> (%)		56 (55.4)	62 (69.7)	
	EASI-100, <i>n</i> (%)		35 (34.7) <i>n</i> =101/102	41 (46.1) <i>n</i> =89/90	
	P-NRS	percentage improvement, median (Q1-Q3)	87.5 (45.0-100.0) <i>n</i> =97/102	100.0 (71.4-100.0) <i>n</i> =89/90	0.063
	P-NRS 0/1, <i>n</i> (%)		54 (54.5) <i>n</i> =99/102	61 (67.8) <i>n</i> =90/90	0.063
	Delta P-NRS ≥ 4 , <i>n</i> (%)		73 (73.7) <i>n</i> =99/102	70 (77.8) <i>n</i> =90/90	0.518
	SD-NRS	percentage improvement, median (Q1-Q3)	100.0 (87.5-100.0) <i>n</i> =84/102	100.0 (100.0-100.0) <i>n</i> =90/90	0.225
	SD-NRS 0/1, <i>n</i> (%)		78 (79.6) <i>n</i> =98/102	76 (85.4) <i>n</i> =90/90	0.299
	DLQI	percentage improvement, median (Q1-Q3)	80.0 (58.6-100.0) <i>n</i> =53/102	92.3 (69.0-100.0) <i>n</i> =49/90	0.032
	Delta DLQI ≥ 4 , <i>n</i> (%)		40 (74.1) <i>n</i> =54/102	46 (90.2) <i>n</i> =51/90	0.032 ($\chi^2=4.600$)
	MDA, <i>n</i> (%)		45 (46.4) <i>n</i> =97/102	52 (59.8) <i>n</i> =87/90	0.070
Week 52	EASI	percentage improvement, median (Q1-Q3)	93.3 (79.2-100.0) <i>n</i> =77/78	100.0 (88.6-100.0) <i>n</i> =76/77	0.030
	EASI-75, <i>n</i> (%)		60 (77.9)	66 (86.8)	0.210
	EASI-90, <i>n</i> (%)		46 (59.7)	56 (73.7)	
	EASI-100, <i>n</i> (%)		32 (41.6) <i>n</i> =77/78	44 (57.9) <i>n</i> =76/77	
	P-NRS	percentage improvement, median (Q1-Q3)	88.8 (40.7-100.0) <i>n</i> =76/78	100.0 (77.8-100.0) <i>n</i> =75/77	0.023
	P-NRS 0/1, <i>n</i> (%)		42 (53.8) <i>n</i> =78/78	55 (72.4) <i>n</i> =76/77	0.017 ($\chi^2=5.665$)
	Delta P-NRS ≥ 4 , <i>n</i> (%)		55 (70.5)	63 (82.9)	0.070

Follow-up	Score	Group A	Group B	p-value
		<i>n</i> =78/78	<i>n</i> =76/77	
	SD-NRS percentage improvement, median (Q1-Q3)	100.0 (83.3-100.0) <i>n</i> =63/78	100.0 (100.0-100.0) <i>n</i> =67/77	0.078
	SD-NRS 0/1, <i>n</i> (%)	62 (79.5) <i>n</i> =77/78	69 (90.8) <i>n</i> =76/77	0.049 ($\chi^2=3.870$)
	DLQI percentage improvement, median (Q1-Q3)	83.3 (48.9-100.0) <i>n</i> =41/78	94.7 (82.1-100.0) <i>n</i> =41/77	0.040
	Delta DLQI ≥ 4 , <i>n</i> (%)	31 (73.8) <i>n</i> =42/78	34 (79.1) <i>n</i> =43/77	0.568
	MDA, <i>n</i> (%)	33 (42.9) <i>n</i> =77/78	47 (62.7) <i>n</i> =75/77	0.014 ($\chi^2=5.980$)

Group A, patients who failed biologics; Group B, bio-naïve patients or patients that discontinued these treatments not due to inefficacy. The p-values refers to the differences between group A and group B. Continuous non-normal distributions were tested using the Mann-Whitney U test. Categorical variables were analyzed using a chi-square test or Fisher's exact test as appropriate. EASI, Eczema Area and Severity Index; P-NRS, Pruritus Numerical Rating Scale; SD-NRS, Sleep NRS; DLQI, Dermatology Life Quality Index; *n*, proportion of valid data. At baseline, in the group A, 21 patients had an SD-NRS of 0, 4 had a P-NRS of 0, and 1 had a DLQI of 0. In the group B, 14 patients had an SD-NRS of 0, 1 had a P-NRS of 0, and 2 had a DLQI of 0. These patients could not be included in the percentage improvement calculations for subsequent follow-ups.

Table 5. Overview of Drug Retention and Discontinuation Reasons at Weeks 4, 16, 36, and 52 between group A and B

	Week 4	Week 16	Week 36	Week 52
Group A	Discontinuations and lost at follow-up, <i>n</i>			
- Inefficacy	0	0	1	4
- AEs	0	0	2	1
- Other (non-drug-related)	0	1	1	3
- Inefficacy and AEs	0	0	0	1
- Lost at FU	0	0	2	2
Drug survival, %	100.0	100.0	97.2	90.5
Group B	Discontinuations and lost at follow-up, <i>n</i>			
- Inefficacy	0	1	1	2
- AEs	0	1	0	3
- Other (non-drug-related)	0	0	1	1
- Inefficacy and AEs	0	0	0	1
- Lost at FU	0	0	0	0
Drug survival, %	100.0	98.4	97.4	91.2

Group A, patients who failed Th2 biologics; Group B, bio-naïve patients or patients that discontinued these treatments not due to inefficacy. DS, drug survival; FU, follow-up.

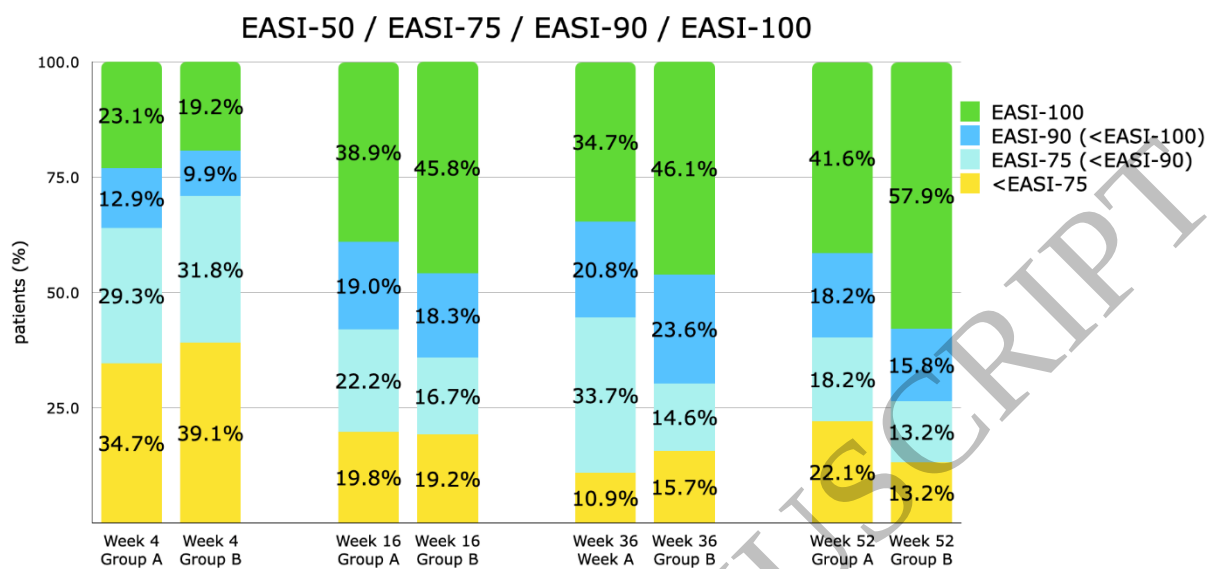


Figure 1
160x90 mm (x DPI)

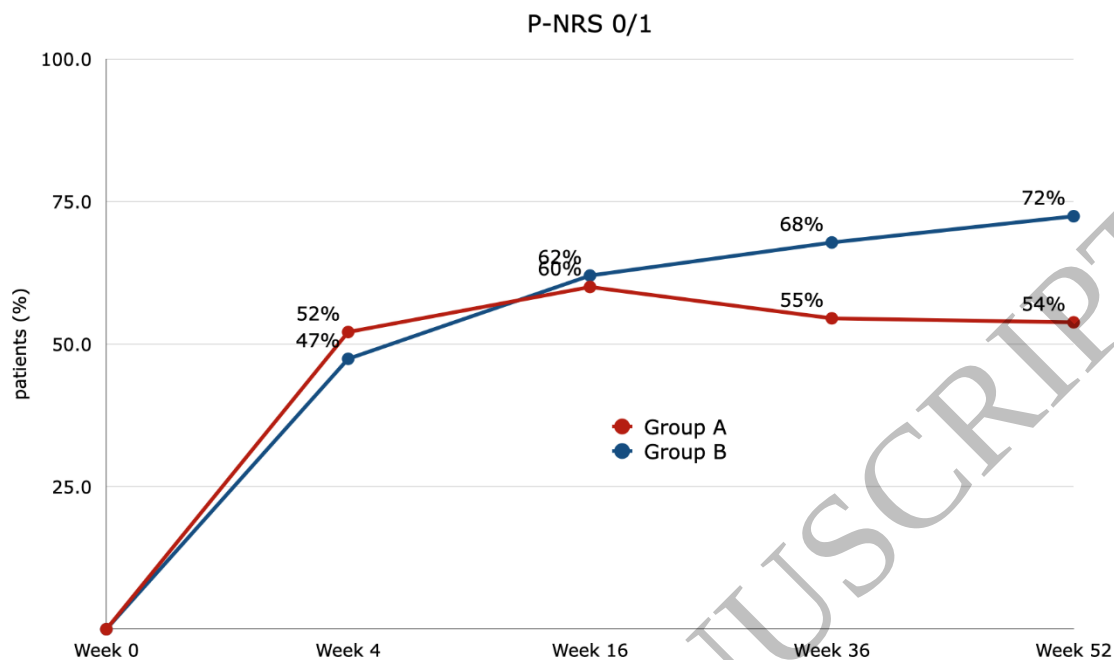


Figure 2
160x90 mm (x DPI)