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SHORT REPORT

Observational 24-week study to assess clinical response to upadacitinib posttrial in patients with moderate-to-severe atopic dermatitis

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Abstract

Background: The oral anti-janus kinase 1 inhibitor upadacitinib has shown a good efficacy–safety profile in the treatment of moderate-to-severe atopic dermatitis (AD) in clinical trials; however, few data from real clinical practice have been published so far.

Objectives: To evaluate the efficacy and safety of upadactinib in clinical practice.

Methods: An observational and multicentric study was conducted. Inclusion criteria consisted of patients who had previously received upadacitinib in the clinical trial M19-850 and continued treatment with upadacitinib (15 mg or 30 mg) under daily clinical practice conditions for 12 months. Demographic data, characteristics of AD, treatment response and adverse events were recorded. Preliminary results at 24-week follow-up are herein presented.

Results: A total of 26 patients (61.54% males, mean age: 35.58 years) were included in the study; of these, 92.31% received upadacitinib 30 mg at baseline. At 24 weeks, mean values of Eczema Area and Severity Index and body surface area were 2.26 and 2.37%, respectively, 82.35% of the patients reached the Investigator's Global Assessment 0/1 and the mean value of peak pruritus numerical rating scale was 1.74. Adverse events were present in 19.23% of the cases, causing one definitive treatment interruption (due to herpes zoster) and two temporary treatment discontinuations (due to temporary elevation of creatine kinase).

Conclusions: These data support the maintenance of the efficacy of upadacitinib at 24-week posttrial follow-up, with no unexpected safety concerns. More real-world data are needed to confirm these results.

KEYWORDS
atopic dermatitis, treatment, upadacitinib

INTRODUCTION

Upadacitinib is an oral anti-janus kinase 1 (JAK1) inhibitor that has shown a good efficacy–safety profile in the treatment of moderate-to-severe atopic dermatitis (AD) in clinical trials.[1,2] However, data regarding upadacitinib in daily practice have been scarcely reported so far.[3,4] The main objective of this study was to assess the efficacy and safety of upadacitinib under clinical practice conditions in patients who had previously participated in two clinical trials of upadacitinib.

METHODS

This is an observational, ambispective and multicentric study including a population that had previously participated in the clinical trial M19-850 (52-week open-label extension study of upadacitinib in adult participants with moderate-to-severe AD)[5] and continued receiving upadacitinib posttrial during a period of 12 months. Patients of the M19-850 clinical trial had successfully completed a previous M16-046 study (a study to compare the safety and efficacy of upadacitinib to dupilumab in adult participants with moderate-to-severe AD), with inclusion criteria to have values of Eczema Area and Severity Index (EASI) ≥ 16, Investigator's Global Assessment (IGA) ≥ 3, body surface area (BSA) ≥ 10%, a weekly average of daily peak pruritus numerical rating scale (NRS) ≥ 4, and being a candidate for systemic therapy or recently require systemic therapy for AD.[6]

Throughout 2021 patients finished their participation in the M19-850 study and they all had the opportunity to continue treatment, provided by the promoter, under off-label conditions. There was no interruption in the drug administration between the end of the clinical trial and the beginning of this observational study. The use of topical corticosteroids on demand was permitted during this posttrial observational study.

Demographic data, characteristics of AD, treatment dosage, response to treatment (physician-evaluated scores: EASI, BSA, IGA; and patient-reported outcome measures: peak pruritus NRS, Head and Neck-Patient Global Impression of Severity questionnaire [HN-PGIS]), adverse events and blood tests (complete blood cell count, biochemical parameters and IgE) were collected from patient's medical record at baseline and at 6 and 12 months. We present the preliminary results at a 24-week follow-up.

The study was approved by the Research Ethics Committee and all patients signed an informed consent before participation.

RESULTS

The study included 26 patients from 6 hospitals in Spain (61.54% males, mean age: 35.58 years) (Table 1). Most of the patients (19/26, 73.08%) were diagnosed with AD at paediatric ages and 18 out of 26 (69.23%) suffered from atopic comorbidities. Twenty-one patients (80.77%) had previously received systemic treatments, with cyclosporin the most frequently used drug (18/26, 69.23%). The dosage of upadacitinib at baseline was 30 mg/day in 24 out of 26 patients (92.31%), while the remaining 2 received 15 mg daily. At 24 weeks, 3 out of 19 patients (15.79%) received a lower dosage (reduction from 30 to 15 mg/day), while the dosage was increased in 2 patients (10.53%) (from 15 to 30 mg). After 24 weeks with upadacitinib posttrial, mean values of EASI and BSA were 2.26 and 2.37%, respectively, and 14 out of 17 patients (82.35%) reached the IGA 0/1. In addition, the mean value of peak pruritus NRS was 1.74 (16/19, 84.21% of the cases, with a score < 4), and 12 out of 16 patients (75%) reached an HN-PGIS value of 0/1. Seven adverse effects were found in 5 out of 26 patients (19.23%), 4 of them possibly related to upadacitinib, causing 2 temporary and 1 definitive treatment interruption (temporary elevation of creatine kinase and herpes zoster). No other significant abnormalities were detected in blood tests.

DISCUSSION

Upadacitinib 15 mg and upadacitinib 30 mg, either in monotherapy or in combination with topical corticosteroids, have shown to be safe and effective in adolescent and adult patients with moderate-to-severe AD under clinical trial conditions.[7–9]

Despite the good results reported in clinical trials, data in daily clinical practice are scarce. To our knowledge, Pereyra-Rodríguez et al.[3] and Chiricozzi et al.[4] have published the largest series to date, both including 43 patients with moderate-to-severe AD and an endpoint assessment at 16 weeks. In the first one, 60.4% of the patients received upadacitinib 30 mg daily, while in the second one, all cases were treated with 30 mg of upadacitinib. Data from these studies showed that the

TABLE 1 Patients' baseline characteristics and response to upadacitinib at 24-week follow-up.

Patients' baseline characteristics and response to upadacitinib at 24-week follow-up	
Patients' characteristics at baseline ($n = 26$)	
Gender (M:F)	16 (61.54%): 10 (38.46%)
Age (mean ± SD, years)	35.58 ± 12.12
Date of AD diagnosis	Paediatric ages: 19/26 (73.08%) Adolescence: 1/26 (3.85%) Adulthood: 6/26 (23.08%)
Atopic comorbidities	18/26 (69.23%) – Respiratory allergy: 8/26 (30.77%) – Food allergy: 5/26 (19.23%) – Rhinoconjunctivitis: 8/26 (30.77%) – Asthma: 7/26 (26.92%)
Previous systemic treatments	21/26 (80.77%): – CsA: 18/26 (69.23%) – MTX: 6/26 (23.08%) – Biologics: 3/26 (11.54%)
Upadacitinib dosage	30 mg/day: 24/26 (92.31%) 15 mg/day: 2/26 (7.69%)
Mean values of scores at 24-week follow-up ($n = 19$)[a]	
EASI (mean ± SD)	2.26 ± 4.62
BSA (mean ± SD)	2.37 ± 7.14%
IGA 0/1	14/17 (82.35%)
Peak pruritus NRS (mean ± SD)	1.74 ± 2.40 (16/19, 84.21% NRS < 4)
HN-PGIS 0/1	12/16 (75%)
Possibly related to upadacitinib adverse events	
Four adverse events (three patients) • *Molluscum contagiousum*: No drug interruption • Temporary CK elevation: Temporary interruption (two patients) • Herpes zoster: Definitive interruption	

Abbreviations: AD, atopic dermatitis; BSA, body surface area; CK, creatine kinase; CsA, cyclosporin; EASI, Eczema Area and Severity Index; F, female; HN-PGIS, Head and Neck-Patient Global Impression of Severity questionnaire; IGA, Investigator's Global Assessment; M, male; MTX, methotrexate; NRS, numerical rating scale; SD, standard deviation.

[a]One patient was lost to follow-up and one stopped treatment after 1 month. One patient discontinued therapy at Month 5.5 due to herpes zoster. Scores of one patient were not assessed at 24 weeks due to temporal treatment interruption. Three patients were excluded from the analysis at Week 24 due to missing data.

efficacy and safety of upadacitinib were at least similar to those reported in clinical trials, even under difficult-to-treat conditions, as more than 90% of the patients had previously received cyclosporin, and 74.4%[3] and 97.7%[4] of the cases, respectively, had previously failed to dupilumab.[3,4]

In our study, we evaluated the efficacy and safety of upadacitinib in daily clinical practice in patients who had previously participated in the clinical trial M19-850.[5] These patients had successfully completed treatment in study M16-046, without developing any permanent discontinuation criteria and without EASI score worsening of 25% or more compared with their baseline (mean baseline EASI score and mean peak pruritus NRS in the upadacitinib arm 30.8 and 7.4, respectively).[10] We would like to highlight that the vast majority of our patients received upadacitinib 30 mg and maintained a very good 24-week posttrial response, both in physician-evaluated scores and in patient-reported outcomes, with no notable adverse events except for one drug interruption due to herpes zoster.

Our study has some limitations: observational design, small sample size and patients previously treated in the M19-850 and M16-046 studies. It should be mentioned that although the good responders without serious adverse events in the previous trials are probably the most representative population of this observational study, we have observed the persistence of a good

response and a low percentage of remarkable adverse events. Thus, we consider that these findings provide relevant and original clinical data in terms of maintained efficacy through the 24-week treatment period added to the 52-week M19-850 study, with no new safety signals.

Additional studies performed in daily clinical practice are needed to confirm these results.

AUTHOR CONTRIBUTIONS

Ana Batalla and Hae Jin Suh-Oh collected and analysed the data and drafted the manuscript. Gregorio Carretero Hernández, Javier Miquel-Miquel, Rafael Botella-Estrada, Antonio Martorell-Calatayud, Virginia Sanz-Motilva, Ignasi Figueras-Nart collected and analysed the data and critically reviewed the final manuscript. Angeles Flórez contributed to the study design and conception, drafting and critical revision of the manuscript.

CONFLICTS OF INTEREST STATEMENT

Ana Batalla has received honoraria, support for training activities or has participated in clinical trials from: Abbvie, Celgene, Faes Pharma, Isdin, Janssen, Leo-Pharma, Leti Pharma, Lilly, Mylan, Novartis, Pfizer, Pierre Fabre and Sanofi-Genzyme. Hae Jin Suh-Oh has received honoraria, support for training activities or has participated in clinical trials from: Abbvie, Leo-Pharma, Leti Pharma, Lilly, Novartis, Pfizer, Pierre Fabre, Sanofi-Genzyme, Kyowa Kirin, Takeda, Sun Pharma and Roche Farma. Javier Miquel-Miquel has served as a consultant and received speaking fees at educational events for Sanofi-Genzyme, Abbvie, Leo Pharma, Amgen, Almirall and Novartis; and has served as the principal investigator in clinical trials sponsored by AbbVie, Amgen and Novartis. Rafael Botella-Estrada has served as a consultant, and/or paid speaker for, and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including Pfizer, Abbvie, Almirall, Novartis, Janssen, Leo Pharma, Lilly, Celgene, Sanofi, Roche and Sun Pharma. Antonio Martorell-Calatayud has received honoraries from sponsored symposiums, advisory board meetings and has participated as principal investigator of phases II, III and IV from the following companies: AbbVie, Celgene, Janssen, Novartis, Merck Sharp & Dohme, UCB, Pfizer, Gebro Pharma, Leo Pharma, Lilly, Sandoz and Galderma. Ignasi Figueras-Nart has been an investigator, speaker and/or advisor for: AbbVie, Amgen, Lilly, Galderma, Pierre Fabre, LEO Pharma, Novartis, Regeneron and Sanofi Genzyme. Ángeles Flórez has performed clinical trials and acted as consultant and lecturer for Abbvie, Almirall, Amgen, Celgene, Janssen, Kyowa Kirin, Leo-Pharma, Lilly, Novartis, Pfizer, Roche Farma, Sanofi, Sun Pharma, Takeda and UCB Pharma. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Study data are available from the authors and are present in this manuscript in an anonymized way.

ETHICS STATEMENT

The study was approved by the pertinent Research Ethics Committee (Comité de ética de la investigación con medicamentos de Galicia) and all patients in this manuscript have given written informed consent for participation in the study and the use of their deidentified, anonymized, aggregated data and their case details (including photographs) for publication.

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